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PERSPECTIVE

COVID-19: A Call for Physical Scientists and Engineers

Haiyue Huang, Chunhai Fan, Min Li, Hua-Li Nie, Fu-Bing Wang, Hui Wang, Ruilan Wang, Jianbo Xia, Xin Zheng, Xiaolei Zuo, and Jiaxing Huang*

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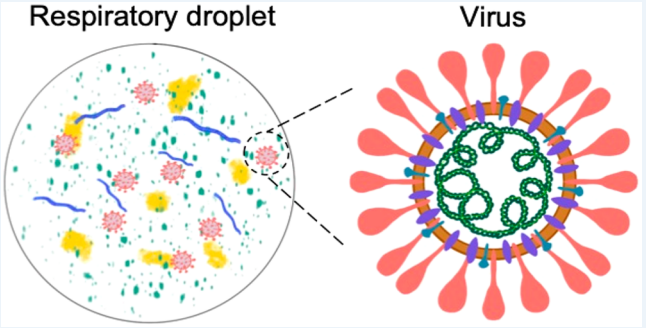
ABSTRACT: **The COVID-19 pandemic is one of those global challenges that transcends territorial, political, ideological, religious, cultural, and certainly academic boundaries. Public health and healthcare workers are at the frontline, working to contain and to mitigate the spread of this disease. Although intervening biological and immunological responses against viral infection may seem far from the physical sciences and engineering that typically work with inanimate objects, there actually is much that can—and should—be done to help in this global crisis. In this Perspective, we convert the basics of infectious respiratory diseases and viruses into physical sciences and engineering intuitions, and through this exercise, we present examples of questions, hypotheses, and research needs identified based on clinicians' experiences. We hope researchers in the physical sciences and engineering will proactively study these challenges, develop new hypotheses, define new research areas, and work with biological researchers, healthcare, and public health professionals to create user-centered solutions and to inform the general public, so that we can better address the many challenges associated with the transmission and spread of infectious respiratory diseases.**



COVID-19, an infectious respiratory disease caused by a novel coronavirus SARS-CoV-2, has quickly evolved into a global pandemic in just over two months.[1] Public health and healthcare professionals are at the frontline, working to contain and to mitigate the spread of this disease. Remarkably rapid progress has been made in biological and biomedical research, including identifying the virus, sequencing its genes, and resolving cogent protein structures.[2−4] The manufacture of testing and diagnosis kits and development and trials of vaccines, antiviral drugs, and other medical and psychological interventions are also being accelerated. Although these activities may seem a bit far from the fields of physical sciences and engineering that typically work with inanimate objects, there actually is much that can—and should—be done to help in such a global crisis. To start, one would need to establish basic understanding of the infection pathways of respiratory diseases and the virion (*i.e.*, viable virus) structure.

GENERAL INFECTION PATHWAYS

The general infectious pathways for respiratory diseases such as influenza, SARS, MERS, and COVID-19 are illustrated in Figure 1, all of which start from virion-laden respiratory fluid droplets (from <1 to 2000 μm in diameter) released by an infected person through coughing, sneezing, and potentially even talking.[5] These droplets immediately start to evaporate and to shrink. Most of the droplets and dried nuclei deposit on various objects (*e.g.*, door knobs, tabletops, buttons, handrails, and touchscreens), turning them into potentially infectious "fomites", but some may even become airborne for a period of time. Direct infection could thus occur through inhalation by other people within close proximity (*e.g.*, 1−2 m), especially for a crowd in a relatively closed space. Infection could also occur when virions released by an infected person are spread on their hands and clothing and then transferred to others through close contact, such as handshaking. Fomites infection[6] is indirect and rather stealthy; it occurs only if a person first picks up the virions from contaminated objects and surfaces (*e.g.*, by their hands) and then transfers them to his or her

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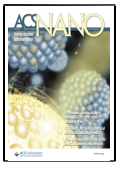

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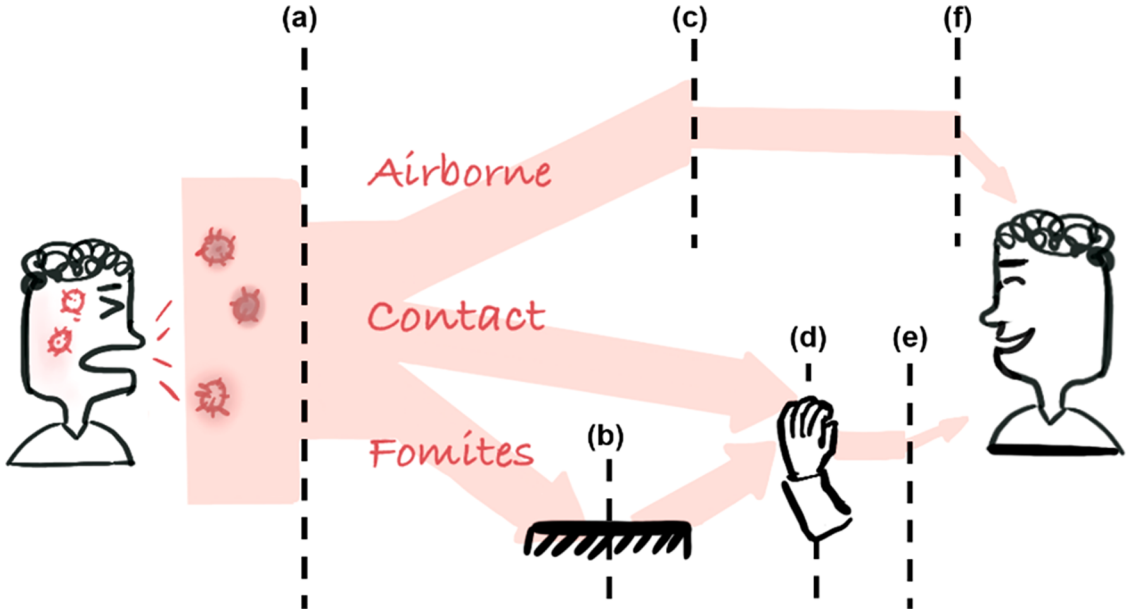

Figure 1. Graphic illustrating common transmission pathways of respiratory diseases, which start with an infected person releasing virion-laden respiratory fluid droplets (left). Within close proximity, other people could be infected by directly inhaling airborne droplets or dried nuclei or by receiving virions through contact transfer. Indirect fomite infection occurs when virion-laden nuclei are picked up from contaminated surfaces (*e.g.*, by hands) and then delivered to the mouth, nose, or eyes. There are many opportunities to set up several layers of defense barriers (dashed lines a–f) along the infection pathways to remove or to deactivate virions before they reach the next person.

mouth, nose, or eyes. Throughout these processes, the virions need to endure a complex and dynamic set of environmental conditions outside the human body. Therefore, there are many opportunities to set up barriers using physical sciences and engineering (dashed lines in Figure 1) to block and to deactivate the overwhelming majority of released virions before they reach hosts and breach the final biological and immunological defenses. Some examples include (a) isolating infectious patients and/or reducing the spread of their respiratory fluid droplets, (b) cleaning and sanitizing objects and surfaces, (c) filtering potentially contaminated air, (d) washing hands frequently, (e) establishing better personal hygiene habits, and (f) wearing personal protection equipment (PPE). Understanding the basic structure of virions and their surroundings is required for designing inactivation and removal strategies and maximizing the effectiveness of these barriers (Figure 1a–f). All of these defense barriers contribute to blocking the source of virions, breaking the spread pathways, and protecting the susceptible hosts. Compared to other known infectious diseases caused by coronaviruses, COVID-19 can spread through an additional stealth mode of asymptomatic transmission,[7−9] which dramatically increases the difficulty of detecting, monitoring, and preventing its spread.

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BASIC VIRION STRUCTURE

Generally speaking, viruses are essentially metastable, core–shell nanoparticles that are biologically produced in cells with a quite remarkable self-assembly process.[10] The core is made of a coiled genomic polymer and tightly packaged in a protective protein shell called a capsid, which is tiled up by presynthesized subunits. For coronaviruses (Figure 2), such as those that cause SARS, MERS, and COVID-19, the RNA is directly complexed with and protected by a helical protein shell to form a coiled nucleocapsid. It is then enveloped by a lipid bilayer membrane decorated with various other proteins, such as the protruding "corona" spikes, which interact with the host cell. The biological function of viruses to preserve and, eventually, to deliver their nucleic acids to host cells depends on the virus' structural integrity. For example, for enveloped viruses, their lipid bilayer must stay intact throughout the pathways to keep them infectious. The protein capsid must be sufficiently strong to confine the elastically strained genomic coil and sufficiently tough to sustain osmotic pressure fluctuation in changing surroundings, yet they must be able to disassemble readily inside the host cells to release the genomic core. These constraints demand rather intricate protein building blocks that also must maintain desirable configurations to avoid malfunction. The envelope and capsid, however, can be compromised by an array of physical treatments, such as UV irradiation, heating, and desiccation, as well as by chemical sanitization using acids, oxidants, alcohols, or some specialized surfactants.[10−12] Approaches like these may seem relatively primitive; however, they can be extremely effective in slowing down or even preventing virus spread and transmission.

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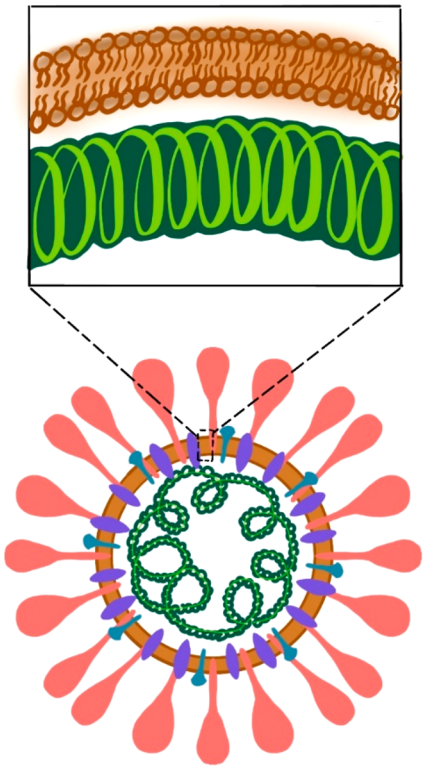

Figure 2. Structural model of a coronavirus particle, showing the nucleocapsid coil (green) inside an envelope (brown) with protruding spike proteins (red). The inset shows the bilayer structure of the envelope and a segment of the nucleocapsid.

QUESTIONS, HYPOTHESES, AND RESEARCH NEEDS IN PHYSICAL SCIENCES AND ENGINEERING

Although intervening biological and immunological responses against viral infection seem to be out of the realm of physical sciences and engineering, surfactant bilayers, core−shell nanoparticles, self-assembly, surface functionalization, and mechanical stability of hollow shells are familiar subjects. There are many ways to contribute, so that more effective and user-centered strategies can be developed to battle virus transmission. To begin, one should examine the very beginning of the chain of events.

Virions Are Usually a Minority Component in Respiratory Droplets. The first barrier to infection should be put up at the starting point (Figure 1, dashed line a) to reduce the number and viability of virions released by an infected person. To this end, infected patients are required to wear medical masks, which can block and absorb large coughed droplets and reroute the smaller ones to reduce their forward traveling distance.[13,14] Masks are an important component in PPE (Figure 1, dashed line f) for frontline healthcare workers. In the current COVID-19 pandemic, there has been much discussion about whether masks are capable of blocking virus nanoparticles, which are typically around 100 nm in diameter.[15] However, this implies that virions released by an infected person stay airborne as individual uncoated nanoparticles, which is rather misleading. As shown in Figure 3, respiratory fluid droplets contain a variety of other components, typically of a few weight percent,[16,17] including insoluble particulates such as proteins, enzymes, commensal microflora (*i.e.*, bacteria) colonized in the upper respiratory tract, and cell debris from the respiratory tract lining; amphiphilic liposomal matter such as lung surfactants and cholesterol; and soluble molecular species such as salt and lactate. Therefore, in the flying droplets or the final dried nuclei, virions are always surrounded by these materials and are usually a minority component, the loading of which varies by the conditions of the patients.

> When designing physical and chemical approaches to deactivate virions, their surrounding respiratory mass must be factored in.

The pictorial representation in Figure 3 reminds us that when designing physical and chemical approaches to deactivate virions, their surrounding respiratory mass must be factored in. These noninfectious components may act as a protective matrix for the virions, rendering sanitization treatments ineffective, or they can be manipulated for accelerated inactivation. For example, it has been reported that both

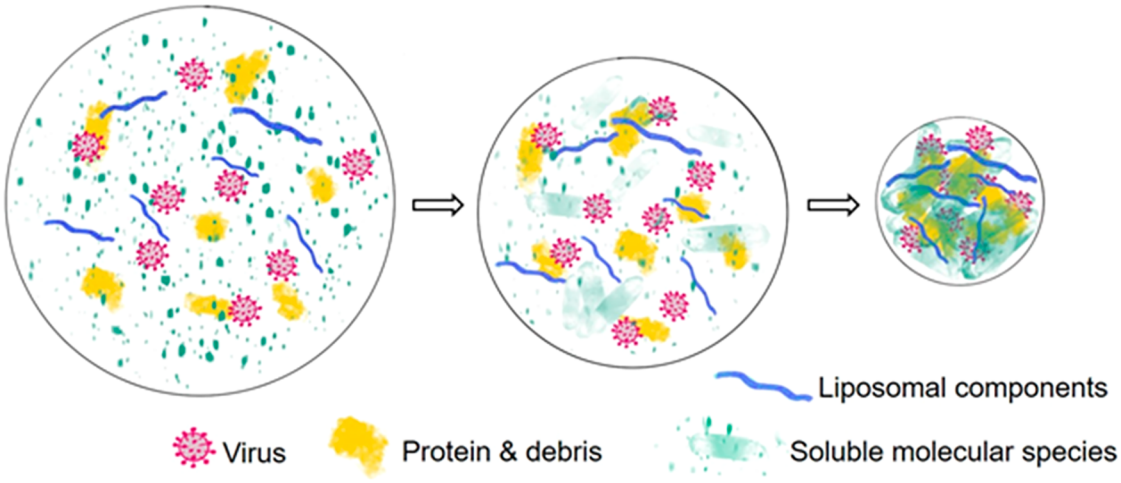

Figure 3. Typical components of a virus-laden respiratory fluid droplet. As it shrinks during evaporation, all components are concentrated. Finally, the virus particles are embedded in a semidried mass called "nuclei".

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SARS-CoV-1 and SARS-CoV-2 virions can remain infectious for days on smooth surfaces such as glass, plastics, and stainless steel, whereas they remain infectious for just hours on porous surfaces such as textile and paper materials.[18,19] This observation is somewhat surprising and worrisome, especially because stainless steel is ubiquitous for making medical supplies and equipment, as well as most engineering structures and appliances. However, to the best of our knowledge, the effect of surface porosity is not well-understood. One hypothesis is that nuclei particles are more likely to pick up moisture from the air through capillary condensation on smooth surfaces than on porous ones.[20,21] The water-soluble, hygroscopic components in the nuclei can hold condensed water to protect embedded virions from desiccation. On porous surfaces, condensed water can be drained away from the nuclei to equilibrate with the rest of the surface, leading to faster water loss around the virions. Desiccation is effective for deactivating enveloped virions because the assembly of the membrane bilayer relies on water.[22,23] Moreover, capillary compression[24] can also mechanically squeeze the mixture in the drying droplets and potentially deform and damage the virion particles inside.

Chemical Modulation of Respiratory Fluid Droplets. In addition to blocking the droplets, it would also be effective to deactivate virions at the origin of the chain events leading up to infection. Here, one might employ ways to "pollute" virion-laden droplets with antiviral or sanitizing molecules[25] when they pass through a mask. For example, a useful strategy may involve on-mask chemical modulation in which such molecules are loaded on the mask to presanitize the exhaled droplets. These molecules should be released in the warm and moisturized air during exhalation but stay fixed on the mask during the inhalation of colder and drier air. It would be most useful to use the chemical modifier as a drop-in accessory, such as in the form of a sticky and permeable film that can adhere to the outer surface of a mask as needed. This may facilitate widespread use and does not need to disrupt the manufacturing and supply chain management of masks, which is already highly stressed by the explosive surge in demand.[26]

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It is also well-known that metabolism and food can dramatically affect the composition of exhaled air (*e.g.*, bad breath). Therefore, with the help of medical researchers and doctors, perhaps one could think of some *in situ* methods for altering the chemical composition of respiratory fluids by taking "saliva modifiers" (*e.g.*, ingredients that help to inactivate virions) in the form of pills, lozenges, cough drops, or even chewing gums. One may even customize a diet or use food supplements such that antiviral molecules can be self-generated in the respiratory fluids by metabolism. Both on-mask and *in situ* chemical modulation approaches would benefit from the third power scaling law of droplet volume and diameter, which can greatly concentrate the antiviral molecules during droplet evaporation. Both strategies can be enhanced by deeper and more relevant scientific understandings in the molecular mechanisms of virion inactivation.

Self-Sanitizing Surfaces. Fomite transmission is hard to trace but common for many respiratory diseases.[6] This transmission is often mitigatable with physical and chemical sanitization, such as through spraying or wiping. However, sanitization is labor- and materials-intensive, impractical for covering all exposed areas, and needs to be reapplied periodically. Water- or alcohol-based sanitizers may not be able to act fully and uniformly across entire surfaces during practical operation due to issues related to dewetting and volatility. Therefore, it will be useful to engineer self-sanitizing surfaces that can slowly release disinfecting chemicals to mitigate fomite transmission. Such coatings should be durable against rubbing and washing, long-lasting, and nontoxic and should be grown easily on the surfaces of already-installed objects that people frequently touch. This direction can leverage knowledge gained through numerous material studies about control-release processes and may even define new research needs.

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For metal objects, copper metal or cations have broad spectrum antiviral effects and low toxicity to humans.[27,28] Therefore, surface copperization could provide stainless steel objects self-sanitizing properties, which could significantly cut down fomite infection rates due to stainless steel's widespread use in hospitals and public spaces. In addition, properly patterned surfaces can avoid local capillary condensation of water,[21] which can bring additional self-desiccation property to deactivate virions. One may even design active or stimuli-responsive antiviral coatings based on photocatalytic, photothermal, or electrothermal treatments, either continuously or in pulsed mode, all of which are quite well-studied in materials science.

Personal Protection Equipment. The PPE used by healthcare professionals tending COVID-19 patients includes facial masks or respirators, protective suits, spill gowns, gloves, boot covers, and goggles or face shields for eye protection (Figure 4), and they are critical for protecting healthcare workers. It typically takes 30 min just to suit up to ensure proper protection, and frontline workers usually need to wear it continuously for extended hours.[29] During usage, the entire outer surface of their PPE must be treated as fomites, which requires extra caution when undressing.[30] User experiences under high stress speak for much needed improvement over current PPE. For example, goggle fogging turns out to be quite problematic because one cannot risk contamination to clear them by usual means. Therefore, antifogging functionality must be added.[31] For facial masks such as N95 aspirators, they usually need to be tightly fit to one's face (*e.g.*, with strong rubber bands) and can cause a great deal of discomfort or allergic reactions.[32] In practice, the one-size-fits-all aspirators sometimes do not match the diverse facial profiles of different users, leading to potential safety issues due to leakage or skin damage. Therefore, more adaptive, skin-friendly materials and interface design are needed to ensure good seal over extended periods of time and changing skin conditions due to perspiration.

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Figure 4. (a) Photo showing a typical set of personal protection equipment used by clinicians tending COVID-19 patients in Wuhan, China, including N95 respirator, protective suit (with marker-written information for identification purposes), gloves, goggles, and boot covers (shown in b). (b) Additional medical mask, spill gown, and face shield are used before entering the isolation ward. (c) Additional helmet with pressured air (on the right) is needed before tracheal intubation procedures for COVID-19 patients. Image credit: Zhengyu Liu.

The development of smart, multifunctional PPE with wireless communication and capabilities for detecting virus, controlling humidity and temperature, and monitoring clinicians' physiological conditions without compromising protective function and flexibility, will be extremely helpful.

Hazmat suits are usually made of broad-spectrum protective synthetic fabrics with vapor-blocking functions. Although such fabrics serve as an effective barrier to virions and virion-laden droplets and nuclei, due to poor ventilation and heat dissipation, they become uncomfortable to wear for frontline healthcare workers, who often need to wear them for extended periods of time when there is a shortage in PPE supply or manpower. This discomfort adds to healthcare workers' already high physical and psychological stress. Therefore, smart fabrics that can effectively block virions but enable better heat transfer and moisture control would be an ideal suit material. In addition, for the clinicians in emergency departments, the tedious and time-consuming processes of dressing up and undressing the entire set of PPE takes valuable time away from treating critically ill patients. Therefore, a multifunctional helmet-like unit with integrated mask compartment, goggles, and face shield, yet still maintain lightweight and durability, would be desirable. The development of smart, multifunctional PPE suits equipped with wireless communication capabilities and microsensors or even actuators for detecting virus, controlling humidity and temperature, and monitoring clinicians' physiological conditions without compromising protective function and flexibility, will be extremely helpful. This need suggests many new research directions for researchers in materials chemistry, flexible electronics, and wearable devices, which have rapidly progressed in the past decade.

The shortage of PPE has been reported globally, especially at the early stages of outbreak in various areas,[33] which prevents frontline healthcare workers from replacing their PPE as needed and, under extreme conditions, may even need to reuse them. Therefore, durable antiviral surface coatings on PPE,[34] especially at the junctions of different parts, would be useful to prevent users from being infected and from infecting others.

On the other hand, when the supply of PPE is stabilized, another point of concern is their safe disposal and sustainable waste processing. Disposable PPE, such as facial masks, protective suits, facial shields, gowns, gloves, and boot covers, are mostly made of plastic materials, and they are used in massive quantities in a global pandemic. It will be worthwhile to develop biodegradable PPE for the future, enabling alternative ways to process this waste safely in addition to incineration.

Disposable PPE generates massive quantities of plastic waste, and it will be worthwhile to develop biodegradable PPE for the future, enabling alternative ways to process this waste safely in addition to incineration.

High-Throughput and Reconfigurable Manufacturing. Any innovation in diagnosis, prevention, or treatment of infectious respiratory diseases must be compatible with high-throughput manufacturing to be relevant because the explosive surge in demand puts great stress on the healthcare infrastructure and supply chains. Over the long-term, flexible manufacturing design should be implemented so that the production lines can be readily reconfigured and repurposed to meet the surging demands during a pandemic. Learning from and collaborating with manufacturing engineers would help to accelerate the impact of new discoveries. Innovations that can retrofit existing products (*e.g.*, PPE) or already-installed appliances and surfaces to endow them with antiviral functions would also be desirable.

Testing is crucial for monitoring and containing the spread of all infectious disease. Current virus tests are typically accomplished by first collecting samples and then sending them to centralized analytical facilities for genome extraction, amplification, and analysis. If portable systems with sample-in-result-out rapid turnaround become available and widely deployed, it will enable much faster data acquisition, enabling public health workers and policy makers to respond to an outbreak more rapidly and precisely. To acquire such

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capability, close collaboration among scientists, engineers, and biomedical researchers will be needed.

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Model Systems for Virions. One of the major roadblocks preventing physical scientists and engineers from making more contributions is the lack of access to virions, such as those causing infectious diseases, because access is limited to only a small number of specialized laboratories. Many physical sciences and engineering approaches for virion deactivation are based on rather broad-spectrum mechanisms, and model systems for such studies, at least in the initial stages, do not need to be genome specific nor to contain any genomic material at all. For example, model systems that enable the study of how the lipid envelope bilayer is stabilized and destabilized, how the capsid or nucleocapsid is assembled and disintegrated, or how the virion particles interact with their surroundings in the flying droplets and surfaces after they land, with or without the respiratory mass, would be extremely useful and would help accelerate engineering solutions to slow and to prevent virus transmission and spread and to enhance our overall readiness to respond to any future virus outbreaks.

OUTLOOK

The COVID-19 pandemic is the type of global challenge that transcends territorial, political, ideological, religious, cultural, and academic boundaries. Researchers in physical sciences and engineering should rally to study such challenges, to develop new hypotheses, to define new research problems, to create user-centered solutions, and to educate ourselves and the general public, so that we can better work with biological and medical researchers to address the many aspects of challenges associated with the transmission and spread of infectious respiratory diseases.[35]

AUTHOR INFORMATION

Corresponding Author

Jiaxing Huang − *Department of Materials Science and Engineering, Northwestern University, Evanston, Illinois 60208, United States;* orcid.org/0000-0001-9176-8901; Email: jiaxing-huang@northwestern.edu

Authors

Haiyue Huang − *Department of Materials Science and Engineering, Northwestern University, Evanston, Illinois 60208, United States*

Chunhai Fan − *School of Chemistry and Chemical Engineering, Frontiers Science Center for Transformative Molecules and Institute of Molecular Medicine, Shanghai Key Laboratory for Nucleic Acid Chemistry and Nanomedicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200240, China;* orcid.org/0000-0002-7171-7338

Min Li − *Department of Laboratory Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200127, China*

Hua-Li Nie − *College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, Shanghai 201620, China*

Fu-Bing Wang − *Department of Laboratory Medicine, Zhongnan Hospital of Wuhan University, Wuhan 430071, China*

Hui Wang − *Center for Single-Cell Omics, School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai 200025, China*

Ruilan Wang − *Department of Critical Care Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 201600, China*

Jianbo Xia − *Department of Laboratory Medicine, Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430070, China*

Xin Zheng − *Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China*

Xiaolei Zuo − *School of Chemistry and Chemical Engineering, Frontiers Science Center for Transformative Molecules and Institute of Molecular Medicine, Shanghai Key Laboratory for Nucleic Acid Chemistry and Nanomedicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai 200240, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsnano.0c02618

Author Contributions

H.H. and J.H. drafted the first version of the manuscript. Other authors placed in the middle are alphabetically ordered. All authors made substantial contributions through discussions of ideas, as well as commenting and polishing of the manuscript.

Notes

The authors declare no competing financial interest.

Biographies

Haiyue Huang (haiyuehuang2022@u.northwestern.edu) is a graduate student in the Department of Materials Science and Engineering at Northwestern University, Evanston, IL, United States. She believes all problems have solutions, some are just waiting to be created or discovered. She is developing material solutions to enhance personal protection equipment (PPE) for better protecting clinicians.

Chunhai Fan (fanchunhai@sjtu.edu.cn) is a K.C. Wong Chair Professor at Shanghai Jiao Tong University. He is a member of the Chinese Academy of Sciences, an Associate Editor of *ACS Applied Materials & Interfaces*, and on the editorial advisory board of *ACS Nano*. He is conducting research in nucleic acid chemistry and biophotonics.

Min Li (rjlimin@shsmu.edu.cn) is the Director of Department of Laboratory Medicine, Renji Hospital, School of Medicine, Shanghai Jiao Tong University. Her work focuses on the pathogenic mechanism and rapid laboratory diagnosis of infectious pathogens. She supervises the laboratory tests in Renji Hospital to assist clinicians in screening for suspected COVID-19 patients.

Hua-Li Nie (niehuali@dhu.edu.cn) is an Associate Professor in the College of Chemistry, Chemical Engineering and Biotechnology at Donghua University in Shanghai, China. She is conducting research about responsive materials enhanced PPE for healthcare workers.

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Fu-Bing Wang (wfb20042002@sina.com) is a professor in the Department of Laboratory Medicine, Zhongnan Hospital of Wuhan University. He is interested in circulating biomarker and tumor biopsy. He oversees the nucleic acid and antibody tests to help clinicians screen for suspected COVID-19 cases and leads a team to investigate environmental contamination of SARS-CoV-2 in hospitals and methods of mitigation.

Hui Wang (huiwang@shsmu.edu.cn) is the Dean of the School of Public Health, Shanghai Jiao Tong University School of Medicine. Her research areas include drug discovery and molecular pharmacology and toxicology. She is leading a major public health campaign to inform the general public and combat misinformation about COVID-19.

Ruilan Wang (wangyusun@hotmail.com) is a Professor and the Director of Emergency and Critical Care Medicine, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine. She conducts basic and clinical research on severe pneumonia, including viral pneumonia. At the early stage of COVID-19 outbreak in Wuhan, she led a team of ICU clinicians from Shanghai to work in the Wuhan Third Hospital with their counterparts to treat COVID-19 patients for 55 days.

Jianbo Xia (xiajianbo@hbfy.com) is the director of the Department of Laboratory Medicine, Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China. His work focuses on laboratory diagnosis of viral infections. He oversees the laboratory tests in the Maternal and Child Health Hospital of Hubei Province to screen and to evaluate COVID-19 cases.

Xin Zheng (xin11@hotmail.com) is a Professor and Director of the Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology in Wuhan, China. She is the head of the COVID-19 expert team in her hospital and supervises the isolation wards of COVID-19 patients.

Xiaolei Zuo (zuoxiaolei@sjtu.edu.cn) is a Professor in the Institute of Molecular Medicine at Renji Hospital, School of Medicine, Shanghai Jiao Tong University. His research focuses on the biosensor development and biomedical applications. He is developing RNA standard reference material of SARS-CoV-2.

Jiaxing Huang (jiaxing-huang@northwestern.edu) is a Professor of Materials Science and Engineering at Northwestern University in Evanston, IL, United States. He is interested in materials innovations for better living. He is developing physical science hypotheses and solutions to mitigate the spread of infectious respiratory diseases.

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