

# A Critical Review on Ultraviolet Disinfection Systems against COVID-19 Outbreak: Applicability, Validation, and Safety Considerations

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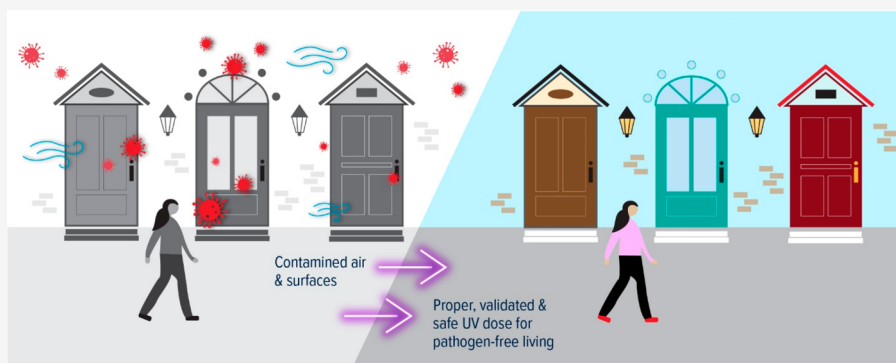


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**ABSTRACT:** The global health-threatening crisis from the COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), highlights the scientific and engineering potentials of applying ultraviolet (UV) disinfection technologies for biocontaminated air and surfaces as the major media for disease transmission. Nowadays, various environmental public settings worldwide, from hospitals and health care facilities to shopping malls and airports, are considering implementation of UV disinfection devices for disinfection of frequently touched surfaces and circulating air streams. Moreover, the general public utilizes UV sterilization devices for various surfaces, from doorknobs and keypads to personal protective equipment, or air purification devices with an integrated UV disinfection technology. However, limited understanding of critical UV disinfection aspects can lead to improper use of this promising technology. In this work, fundamentals of UV disinfection phenomena are addressed; furthermore, the essential parameters and protocols to guarantee the efficacy of the UV sterilization process in a human-safe manner are systematically elaborated. In addition, the latest updates from the open literature on UV dose requirements for incremental log removal of SARS-CoV-2 are reviewed remarking the advancements and existing knowledge gaps. This study, along with the provided illustrations, will play an essential role in the design and fabrication of effective, reliable, and safe UV disinfection systems applicable to preventing viral contagion in the current COVID-19 pandemic, as well as potential future epidemics.

**KEYWORDS:** COVID-19, SARS-CoV-2, transmission prevention, UV disinfection, performance validation, UV safety

## INTRODUCTION

Coronaviruses (CoVs) are a large family of viruses that can cause illness, ranging from the common cold to more severe disease like the Middle East Respiratory Syndrome (MERS-CoV) or the Severe Acute Respiratory Syndrome (SARS-CoV).<sup>1,2</sup> First reported in Asia in February 2003, SARS spread over the next few months to more than two dozen countries on various continents, including North America, South America, Europe, and Asia, before the SARS global outbreak of 2003 was contained.<sup>3</sup> According to the World Health Organization (WHO), a total of 8096 people worldwide became sick with SARS during the 2003 outbreak and 774 of them died.<sup>4,5</sup> In a similar case of a fatal outbreak, in September 2012, health officials first reported a disease in Saudi Arabia. Through investigations, it was identified that the first known cases of MERS occurred in Jordan in April 2012.<sup>6</sup> At the end of January

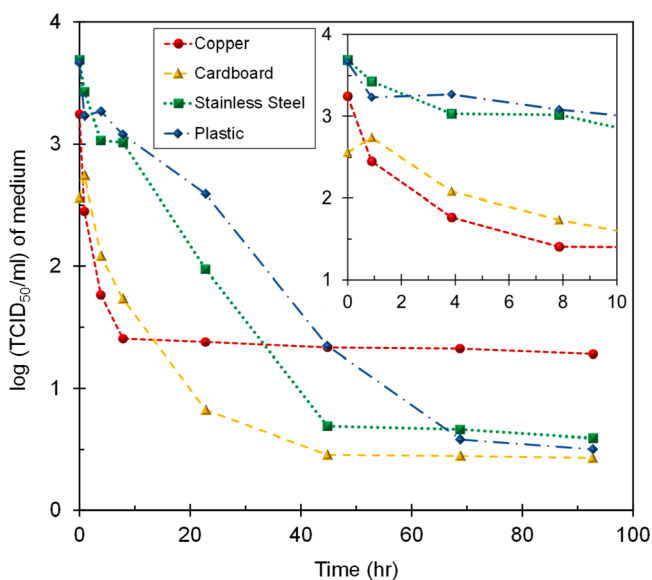
2020, a total of 2519 laboratory-confirmed cases of MERS, including 866 associated deaths (case-fatality rate 34.3%), were reported globally. The majority of these cases were reported from Saudi Arabia (2121 cases), including 788 related deaths with a case-fatality rate of 37.1%.<sup>7</sup>

The novel coronavirus (SARS-CoV-2) is a new strain from the CoV family that has not been previously identified in humans. The emergence of COVID-19, the disease caused by

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SARS-CoV-2 in late 2019 in Wuhan, China, created a pandemic that resulted in large-scale scientific, economic, and public efforts to contain viral transmission.<sup>2,8–10</sup> As of August 1, 2020, a situation report from the World Health Organization (WHO) states that more than 17 million confirmed cases and more than 675 thousand deaths have been identified in 213 countries or regions.<sup>11</sup> Thus far, the novel CoV is being transmitted directly person to person, among other routes. The best way of dealing with the CoV pandemic is first simply to reduce the risk of being infected by the virus through blocking the transmission routes.<sup>12</sup> Pathogens, including viruses, are able to spread and be transmitted by environmental routes, including air and inert surfaces or indirectly through touching a contaminated surface.<sup>13,14</sup> In this regard, avoiding close contact with anyone showing COVID-19 symptoms, such as coughing, sneezing, fever, and difficulty breathing, is strongly recommended by various infection control agencies.<sup>15</sup> WHO urges everyone, particularly those in high-risk areas, to prevent infection spread through regular hand washing and wearing facial masks or any other physical transmission barriers. However, the efficacy of these preventative actions is limited, particularly in indoor environments where biocontaminated circulating air or frequently touched surfaces can mediate transmission.

Coughing by a COVID-19 infected individual can produce about 3000 droplets in a wide size range ( $10^{-1}$  to  $10^2 \mu\text{m}$ ).<sup>16</sup> Droplets larger than  $100 \mu\text{m}$  deposit rapidly on surfaces.<sup>16,17</sup> According to a study published in the New England Journal of Medicine, SARS-CoV-2 can live on surfaces for several hours to days, depending on the surface material (Figure 1), similar



**Figure 1.** Viability of SARS-CoV-2 on various surfaces based on the data reported by van Doremalen et al. (with permission).<sup>18</sup>

to durations previously reported for SARS-CoV-1.<sup>18</sup> Tiny droplets ( $0.1\text{--}5 \mu\text{m}$ ) are capable of dissolving with the aerosol, remaining airborne, and traveling hundreds of meters.<sup>17,19</sup> Intermediate size range ( $5\text{--}100 \mu\text{m}$ ) droplets also shrink to tiny sizes due to evaporation,<sup>17</sup> and the peak concentration of droplets in bioaerosols are in two diameter ranges:  $0.25\text{--}1.0 \mu\text{m}$  and  $2.5\text{--}10 \mu\text{m}$ .<sup>20</sup> Factors such as air current, temperature, and humidity can also affect bioaerosol transmission rates. Traces of the SARS-CoV-2 virus were first detected in aqueous

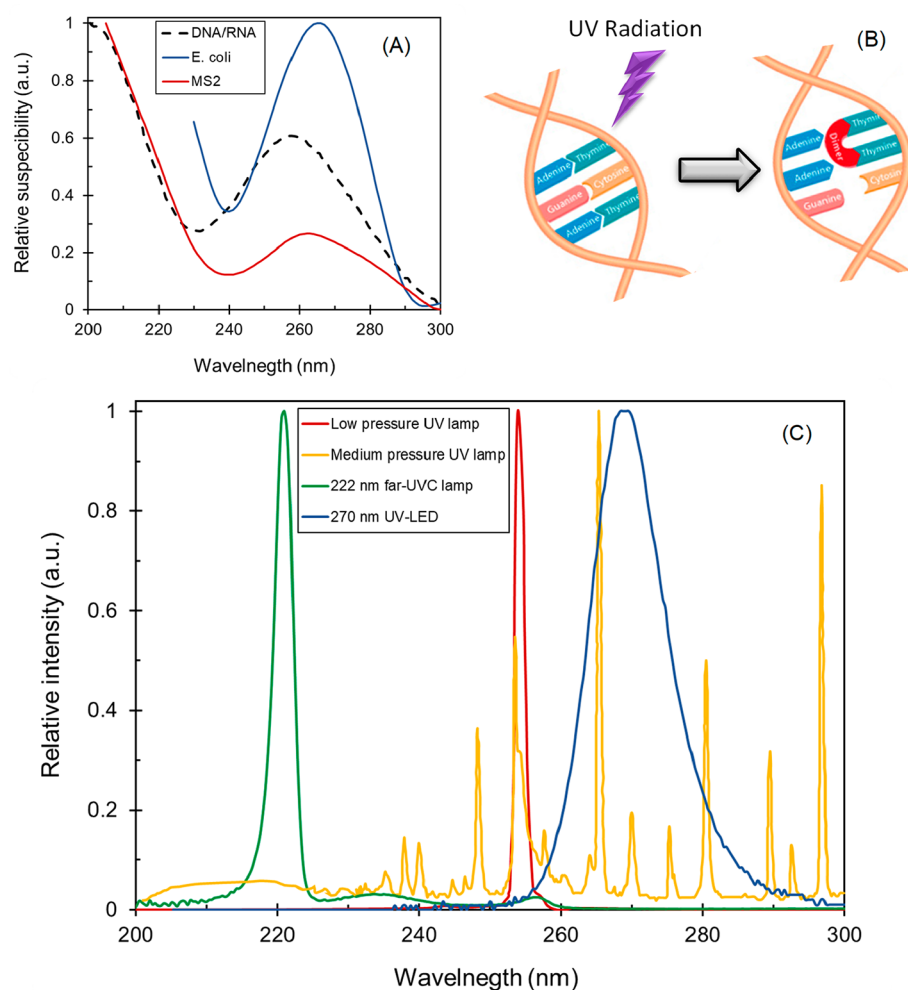
media in Paris' nonpotable water, which is used for cleaning streets and watering parks.<sup>21</sup> More recently, various studies identified SARS-CoV-2 RNA, and not the infectious particle, in municipal wastewater for different countries;<sup>22–25</sup> however, there is no evidence of COVID-19 transmission through contaminated water so far.<sup>26</sup>

The risk of viral infection could be reduced through many control techniques, including heat sterilization, chemical disinfectants, filtration, and ultraviolet (UV) irradiation. The possible material damage caused by heat sterilization, in addition to the shortages of consumer chemical disinfectants and filters on the market, poses a critical challenge throughout pandemics leading to demand for more sustainable disinfection systems. Disinfection using UV radiation has been a fast-growing chemical-free technology over the past decades. UV radiation is highly efficient at controlling microbial growth in any medium, such as water and air, as well as on any type of surface.

In the latest COVID-19 pandemic, UV air and surface disinfection has attracted tremendous attention, and many products became available on the market.<sup>27</sup> Various public places with different levels of contaminated air and surface probabilities, from hospitals and health care facilities to restaurants and cafeterias, started using UV surface disinfection systems. Widespread use of UVC disinfectors is also advised to limit virus spread after reopening of public places.<sup>17</sup> However, limited understanding of the critical aspects of UV disinfection, not only among the majority of general public but also with some of the UV surface disinfection manufacturers, has led to inappropriate use of this promising technology. Dubious and nonscientific performance claims by some of the UV system designers and manufacturers are unfortunately widespread. This review elaborates on the application of UV radiation for disinfecting biocontaminated media with an emphasis on the SARS-CoV-2 case. The authors' objective is presenting a technical-rich critical review and discussing the scientific fundamentals of UV dose requirements for disinfection, protocols for performance validation of UV systems, and safety considerations regarding the use of UV radiation.

## FUNDAMENTALS OF UV DISINFECTION

UV disinfection has been a validated technology for the disinfection of pathogens on surfaces, as well as in air and water, for several decades.<sup>28,29</sup> A particular spectrum of UV radiation between 200 and 280 nm, the so-called UVC spectrum, has been employed extensively as the germicidal range of UV radiation. Over the UVC range, a more detrimental effect on microbial cells occurs because the intercellular components of microbes (e.g., RNA, DNA, and proteins) can sensitively absorb UVC photons,<sup>30</sup> as displayed in Figure 2A. Absorbed UVC photons cause critical damage to the genomic system of microorganisms (nucleic acid and microorganismal proteins), preventing them from replicating and surviving, as illustrated schematically in Figure 2B, where the adenine–thymine bond is collapsed and a covalent linkage, pyrimidine dimer, is generated between two adenines leading to inability of the cell to replicate. Therefore, the effect of UV irradiation on microorganisms is called “inactivation” and not “killing”. Although the effectiveness of UV irradiation on the infectivity of viruses and the nucleic acid of the virion is well documented, an increased environmental UV dose is likely to lead to an increased rate of viral mutation.<sup>31</sup> The virus can replicate even in the presence of induced mutations, but the



**Figure 2.** (A) Relative UV susceptibility of a general RNA or DNA, as well as *E. coli* bacteria and MS2 virus, over the germicidal region extracted from published values.<sup>39</sup> (B) Schematic of thymine dimerization for a UV exposed double-stranded DNA. (C) Sample spectral power distribution (SPD) for different germicidal UV sources.

effect on the viral genes could be different.<sup>32</sup> The lethal effect of the UV-induced nucleic acid (DNA or RNA) damage depends on the location of changes within the viral genome.<sup>33</sup> In addition, many mutations will not have any discernible effect on the virus, as they are repaired by the host nucleic acid repair mechanism. The majority of the mutations diminish the infectivity of the viruses since most viral genes have a specific role to perform. However, some mutations may lead to the evolution of more pathogenic viruses. For instance, a novel receptor-binding protein can be synthesized within the virus structure that enables the virus to infect a different cell type in host. It is also likely that some UV-resistant strains of viruses will emerge, perhaps as a result of evolving a thicker capsid structure to protect the nucleic acid from UVC damage.<sup>33</sup>

Different UVC sources have been utilized in academic research, as well as industry, such as low and medium pressure mercury UV lamps,<sup>34</sup> UV light-emitting diodes (UV-LEDs),<sup>35</sup> and far-UVC (200–240 nm) radiating excimer and microplasma lamps.<sup>36</sup> Figure 2C demonstrates the spectral power distribution (SPD) of the different UVC sources. Note that UV-LEDs can generate different peak wavelengths in the UVC region,<sup>37,38</sup> ranging from 255 to 285 nm, and the SPD of a 270 nm UV-LED is depicted in Figure 2C as an example.

UV disinfection is an energy-based process, where the inactivation ratio is determined by the applied UV dose via the disinfecting unit. The UV dose ( $\text{mJ cm}^{-2}$ ) is calculated by the delivered irradiance or fluence rate to microbial cells ( $\text{mW cm}^{-2}$ ) multiplied by the exposure time (s).<sup>30</sup> Thus, for UV-induced reactions, the most accurate fashion to report the kinetic data is as a function of UV dose rather than time.<sup>40</sup> The disinfection of biocontaminated air and surfaces could be assumed as more straightforward and predictable applications of UV radiation, as compared to water treatment.<sup>41</sup> However, to achieve a valid inactivation value, e.g., 99.99%, by a UV air or surface disinfectant, several factors are involved, which can be grouped into two categories: inherent microbial characteristics and target medium characteristics.

### ■ INHERENT MICROBIAL CHARACTERISTICS

The UV disinfection mechanism is absorption-based ruled by the susceptibility of microbe genetic material to UV wavelength. This susceptibility varies widely among species of microbes. Viruses, as an example, are composed of a nucleic acid identified as either double-stranded DNA (dsDNA), single-stranded DNA (ssDNA), double-stranded RNA (dsRNA), or single-stranded RNA (ssRNA).<sup>28</sup> In general, single-stranded viruses are more sensitive to UV irradiation

because of lacking the redundancy of genetic information in a second strand that allows double-stranded viruses to repair the damage.<sup>42</sup> The viral nucleic acid, independent of its type, is encased in a protein capsid,<sup>43</sup> and in some viruses, such as the influenza virus<sup>44</sup> and SARS-CoV-2,<sup>45</sup> the protein capsid is itself encased in a lipid envelope. Nonenveloped viruses are typically more UV resistant than enveloped viruses, since proteins and lipids of the envelope may be disrupted more easily than other viral parts.<sup>46</sup>

The UV susceptibility governing specifications are not limited to the RNA or DNA structure. The virus also contains proteins, for example, spike proteins in the CoV family, which are necessary for binding of the virus to receptors on the host cell and infecting the cell.<sup>44</sup> Physical size, molecular weight, surface hydrophilicity, and presence of repair mechanism are the other effective species-dependent microorganismal properties. All mentioned intrinsic characteristics of viruses determine the kinetics of UV induced inactivation of a virus. Considering the inherent characteristics and genomic structure of microorganisms, Kowalski presented a genomic model to predict the sensitivity of different viruses to 254 nm UV exposure and reported kinetic data that is fairly in agreement with experimental analysis.<sup>47</sup>

The inherent sensitivity of microbial DNA/RNA and proteins also depends on the wavelength of incident UV photons. As illustrated in Figure 2B, the DNA/RNA maximum UV absorption is around 265 nm. In other words, a UV disinfection system with a 265 nm emitting UV source needs a lower UV dose to achieve the same amount of damage to DNA/RNA compared to the one with 254 nm emitting UV source. However, as mentioned above, the genomic material, that is, DNA or RNA, is not the only ruling specification. Understanding of a convolution of utilized UV source SPD (Figure 2C) and microorganism UV susceptibility over the UVC spectrum is crucial in identifying the germicidal power of a UV disinfection system.<sup>48</sup> As an example, the actual UV susceptibility of *Escherichia coli* (*E. coli*) bacteria and MS2 virus is compared to the one for DNA and RNA in Figure 2A. For example, the germicidal power of a UV-LED with 265 nm peak wavelength for inactivating MS2 virus is reported to be roughly 1.15 times higher than that of a conventional 254 nm mercury UV lamp.<sup>48,49</sup>

## TARGET MEDIUM CHARACTERISTICS

The kinetics of UV virus inactivation can be significantly different between a controlled system in the laboratory and a practical system. The inactivation rates for microbes depend on material and structure of the surface and turbidity of the air stream as well as the ambient conditions, for example, relative humidity (RH) and temperature.

Certain metallic surfaces such as copper or silver naturally provide biocidal effects that may be additive with UV exposure.<sup>50</sup> In addition, the materials vary in affinity for microbe–surface attachment; for example, surfaces with organic paints may encourage surface colonization and microbial aggregation,<sup>51</sup> which changes the required UV dose for a certain inactivation ratio. It has been shown that the required UV dose for 90% viral reduction is increased by a factor of 1.5–2 for a surface compared with air due to aggregation on surfaces.<sup>42</sup> Moreover, some surfaces have irregularities, crevices, and roughness at the microscopic level, which create dark spots on the surface and offer shadowing or protection against UV exposure. A similar shadowing effect in

the case of air treatment can be caused by the presence of larger particles and dust in the air stream. In addition, the microbial cells may be attached and agglomerated on dust, which leads to generation of tiny biofilms requiring higher UV dose to be inactivated. Biofilms are a collective of one or more types of microorganisms that can grow on many different surfaces, and it is commonly accepted that biofilm-forming microorganisms include bacteria, fungi, and protists.<sup>41</sup> However, formation of complex biofilm-like assemblies, similar to bacterial biofilms, is reported in literature for certain viruses.<sup>52</sup> Extracellular “viral biofilms” would appear to be a major mechanism of propagation for certain viruses with structure, composition, and function resembling those of bacterial biofilms. These extracellular infectious structures may protect viruses from UV radiation and enable them to spread efficiently. Hence, the emitted UV dose from the disinfectant would not necessarily be the same as the actual dose that the treated virus receives. Although the applied UV dosage is easy to measure experimentally, the received dose is not. A well-known example of the effect of surface structure is the UV disinfection of N95 masks, owing to the mask’s porous and multilayer structure, that requires roughly 2 orders of magnitude higher applied UVC dose for sufficient inactivation of studied viruses (as compared to a smooth surface material).<sup>53–56</sup> It should be noted that UV radiation has only a superficial effect that does not penetrate materials. Hence, the disinfection obtained can be limited to only surfaces and not the internal structures of the mask.

RH plays a part in determining the nucleic acid conformation and subsequently affects the survival of microbial cells. The major part of literature supports that increasing RH leads to lower UV susceptibility because when RH increases, water sorption onto the microbe surface may provide protection against UV-induced DNA or RNA damage.<sup>28,42,57,58</sup> If microbe-containing aerosols evaporate water vapor and approach the size of the actual microbe, the resistance to UV becomes lower, due to lack of water scattering. The effect of RH is reported to be more pronounced for UV susceptibility of bacteria than viruses.<sup>13,26</sup> However, some research, such as the work conducted by Tseng and Li, suggests that the UV susceptibility for the viruses is higher at low RH (<55%) than at high RH (>80%).<sup>42</sup> The RH effects on UV inactivation effectiveness also depends on the type of virus nucleic acid, since the alteration in UV inactivation of ssRNA and ssDNA viruses is greater than that of dsDNA and dsRNA.<sup>42</sup> Therefore, as a conservative technique, the UV surface disinfection systems should be designed based on a high RH situation.

## KINETICS OF SARS-COV-2 UV INACTIVATION

A significant amount of information remains unknown about the novel SARS-CoV-2 because of difficulties of the laboratory-scale isolation, identification, and characterization of various strains. However, the current understanding could help us to explore the kinetic data for the UVC inactivation process of the virus. SARS-CoV-2 is an RNA virus,<sup>59</sup> similar to other notable viruses causing human diseases, such as SARS-CoV-1, Ebola virus, rabies virus, rhinoviruses, influenza viruses, hepatitis A virus, West Nile virus, polioviruses, and rubeola virus.<sup>60</sup> Identified as a ssRNA, the novel CoV is similar to other benchmark surrogate microorganisms such as bacteriophages MS2 and Q $\beta$ ,<sup>28</sup> as well as the influenza virus and earlier strains of the CoV family, such as SARS-CoV-1.<sup>61</sup> This is an essential piece of information because the genomic structure and

Table 1. Overview of Recently Published CoV Inactivation Studies

virus	wavelength (nm)	medium	log reduction	UV dose (mJ cm <sup>-2</sup> )	remarks	source
SARS-CoV-2	254	250 μL liquid	2.1 3.9 6	10 20 40	viral samples were tested in a 24-well plate; linear dose response in the 0–6 log reduction range (no tailing) due to sufficient initial concentration (10 <sup>7</sup> )	72
SARS-CoV-2	280 ± 5	150 μL liquid	0.9 3.1 3.3	3.75 37.5 75	viral samples were tested in a 60 mm Petri dish; tailing region after 3.3 log, due to the low initial concentration (10 <sup>4</sup> )	73
SARS-CoV-2	254	976 μL liquid	3 6 6	3.7 16.9 84.4	three virus concentrations were tested (low, closed hospital rooms; medium, sputum of a patient; high, terminally diseased patient); 3.7 mJ cm <sup>-2</sup> was enough for low concentration but for high concentration a minimum of 16.9 mJ cm <sup>-2</sup> is required to avoid long-term replication	77
SARS-CoV-2	broad (200–320)	hard surface	3.56 4.54 4.12	1 min 2 min 5 min	air-dried droplets on surface were tested; time-based kinetic data; no UV dose data is presented	78
HCoV-229E	222	air	3	1.7	as studied HCoVs are airborne; they were tested aerosolized; required dose for same reduction on surface could be higher	79
HCoV-OC43			3	1.2		
SARS-CoV-2	254	surface	1	2.14	no experimental data; all reported kinetic data are based on genomic model; authors suggested murine hepatitis CoV as the suitable surrogate for SARS-CoV-2	80
SARS-CoV-1 murine hepatitis CoV				1.8 2.1		
MERS-CoV				2.81		

chemistry of a virus are critical factors in determining how the pathogen responds to UV radiation. Therefore, the UV disinfection kinetics of a novel virus, such as SARS-CoV-2, can be extracted from data available for a similarly structured pathogen. Several databases have summarized the UV inactivation rate constant for bacteria, viruses, fungi, and protozoa. The *Ultraviolet Germicidal Irradiation Handbook*<sup>28</sup> tabulates a comprehensive list of photokinetic data for over 600 microorganisms studied under various UV radiation sources in different media (water, air, and surfaces).

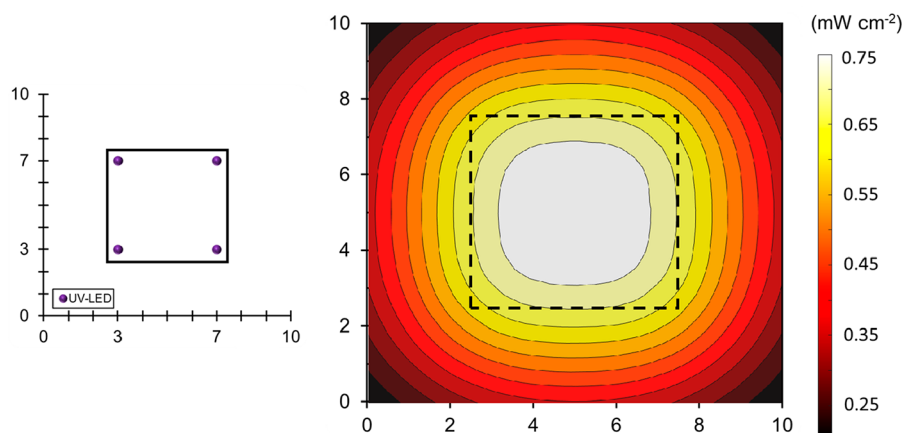
In addition, the CoV family has been extensively studied and their response to UVC radiation is well-established. In the absence of accurate UV inactivation kinetics for SARS-CoV-2, the previously established data could be utilized to estimate the required UV dose to inactivate the novel strain of coronavirus. SARS-CoV-2 is very similar to previous SARS-CoV-1 in terms of genomic characteristics important for UV-induced damage. Both are enveloped viruses with a positive-sense ssRNA of animal origin belonging to the β-CoV group. The amino acid sequence of spike protein in SARS-CoV-2 is 76.47% identical to that of SARS-CoV, with the same structural conformation and electrostatic properties.<sup>62,63</sup>

The CoV family shows slightly more resistance to UV compared to commonly studied bacteria such as *E. coli*.<sup>28</sup> According to the *Ultraviolet Germicidal Irradiation Handbook*, the CoV family response to UVC radiation is comparable to known benchmark viruses such as bacteriophage-MS2,<sup>28</sup> showing more UV sensitive characteristics in most cases. The UV inactivation rate constant for CoV is reported as 1.49 cm<sup>2</sup> mJ<sup>-1</sup>, an order of magnitude greater than those reported for MS2 (0.13 cm<sup>2</sup> mJ<sup>-1</sup>).<sup>42,58</sup> Experimental studies on various strains of CoV have also outlined a similar conclusion. For example, Walker and Ko suggested 0.7 mJ cm<sup>-2</sup> for 90% inactivation of CoV aerosols<sup>58</sup> in agreement with the result of earlier studies by Wiess and Horzinek<sup>64</sup> and Hirano et al.,<sup>65</sup> as well as those reported by Saknimit et al.<sup>66</sup> Duan and co-workers have proposed a 4.0 mJ cm<sup>-2</sup> UV dose for 90% inactivation of SARS strain CoV-P9.<sup>67</sup> A recent genomic model proposed by Kowalski indicates the UV rate constant for

SARS-CoV-1 to be 3.289 cm<sup>2</sup> mJ<sup>-1</sup>, suggesting 0.7 mJ cm<sup>2</sup> for 90% reduction, in agreement with earlier experimental data.<sup>68</sup> This data suggests that the CoV family is likely more sensitive to UV inactivation than the MS2 virus.

On the other hand, a few studies observed more resistant behavior for SARS-CoV-1, suggesting higher UV dosage requirement.<sup>69</sup> The survey by Tsend and Li confirmed that the inactivation of airborne viruses, regardless of their nucleic acid type, can be achieved under mild UV radiation in a laboratory test chamber.<sup>42</sup> Kariwa and co-workers have evaluated different means for the inactivation of SARS-CoV-1, including UV. Their study suggested nearly 120 mJ cm<sup>-2</sup> of UV dose is needed to reduce the infectivity from 3.8 × 10<sup>7</sup> to 180 TCID<sub>50</sub>/mL, which is more than 99.999% reduction.<sup>61</sup> From this perspective, SARS-CoV-1 is similar to influenza virus and hepatitis A virus, which can be readily eliminated using UV radiation. Reports indicate 16–35 mJ cm<sup>-2</sup> UV dose has reduced 99.99% of hepatitis A virus<sup>55</sup> and 99% of influenza virus.<sup>70</sup>

Experimental studies on ssRNA viruses, even the early strains of the CoV family, strongly support the opinion that the SARS-CoV-2 can be inactivated by UV radiation.<sup>71</sup> However, the required UV dose and the corresponding level of inactivation is yet to be determined by the regulatory health organizations for the novel CoV. Testing of an ongoing pathogenic microbe, such as the SARS-CoV-2, could be challenging due to the required biosafety level (BSL) precautions. Therefore, it is a standard technique to deploy surrogate viral species as a reference to high BSL species. The surrogate species should have a similar response to UV treatment. In general, bacteriophages are more resistant to UV radiation than other pathogenic viruses; therefore, they are widely considered as conservative indicators. Based on the available data in the open literature, the authors of this article hold the opinion that the SARS-CoV-2 can likely be categorized with SARS-CoV-1 as a mildly resistant virus to UV radiation, similar to the hepatitis A virus, influenza virus, and bacteriophage MS2. It would then be safe to assume a



**Figure 3.** Incident irradiance pattern of an array of 4 UV-LEDs with the shown layout on a parallel 10 cm  $\times$  10 cm surface at 5 cm distance. The dashed square illustrates a virtual 5 cm  $\times$  5 cm surface in the center of the target (10  $\times$  10 cm) surface.

required UV dose higher than 20 mJ cm<sup>-2</sup> for likely 99.9% reduction.

Over the last few months, a significant number of technical reports, news, and whitepapers have been released, claiming the eligibility of various UV disinfection systems and commercial products against SARS-CoV-2. However, a majority of above-mentioned reports do not refer to any validated kinetic data for UV dose requirements for incremental log removal and rather present time-based data. Nevertheless, several recently published research articles suggested experimental photokinetic data for the UVC-induced SARS-CoV-2 inactivation. Patterson and co-workers reported that 20 mJ cm<sup>-2</sup> and 40 mJ cm<sup>-2</sup> doses of 254 nm UVC could be sufficient to achieve 4-log and 6-log inactivation of SARS-CoV-2, respectively.<sup>72</sup> Inagaki and her team reported the performance for a 280 nm UV-LED to be 3.1-log at 37.5 mJ cm<sup>-2</sup>, with a lagging response to reach to higher log inactivation values due to the insufficient initial concentration of virus.<sup>73</sup> A comprehensive list of recently published articles on SARS-CoV-2 inactivation is tabulated in Table 1 with important remarks for each work. Readers are advised to note that the available materials in literature are not necessarily peer-reviewed, due to urgency of publishing the experimental data that may become helpful to research community in combating the COVID-19 pandemic.

Here, it should be noted that the essential point in conducting any photokinetic study experiments is deploying standardized protocols to design appropriate apparatus to accurately calculate the UV dose delivered by the UV source to microbial cells. Otherwise, the reported kinetic data will be hardly reliable and irreproducible.<sup>74</sup> For mercury UVC lamps, the design approach for standard apparatus, referred to as “collimated beams”, has been proposed and accepted by the International Ultraviolet Association (IUVA) and US Environmental Protection Agency (USEPA).<sup>74</sup> More recently, new methods have been developed for UVC-LEDs<sup>75,76</sup> and microplasma far-UVC lamps<sup>36</sup> by systematically revising the UV lamp protocol considering the unique characteristics of mentioned sources.

## ■ PERFORMANCE VALIDATION

Throughout the current outbreak, the fight against COVID-19 has been mostly (and understandably) focused on the disinfection of commonly touched surfaces<sup>17</sup> and personal

protective equipment.<sup>53</sup> UV radiation, along with chemical disinfectants, have been utilized extensively as a no-touch automated disinfection technique to disinfect surfaces in public transport systems such as airplanes, as well as patient rooms and operating theaters in hospitals.<sup>81</sup> Pictures of UV robots marching through airplanes or hospital corridors made their way into the news and created awareness regarding the effectiveness of UV radiation in the elimination of SARS-CoV-2. In parallel, there has been a surge in online purchases of various UV disinfection personal merchandise, such as UV sterilization boxes for personal items and cellphones or handheld UV surface disinfection tools. For the case of air treatment, UV disinfection systems are either integrated into the central air conditioning system for a building or used as an individual air purifying device for home or personal usage. More recently, several concepts of UV-LED integrated facial masks have appeared online. A significant number of start-up companies have also been established worldwide in this period to develop UV disinfection systems.

The final goal of designing a UV disinfection system is to provide a robust product with reliable and reproducible performance. In this regard, the performance of any product must be validated prior to the introduction to market. While obtaining the reported UV doses for SARS-CoV-2 inactivation (see Table 1) is not challenging (by extending the exposure time), the development of UV disinfection devices to deliver the required dose consistently and uniformly urges design considerations and extensive validation through well-established protocols. This section aims to discuss the gaps in the information provided as claimed performances seen in the current market products of which users must be aware. In other words, when a UV disinfection product advertisement claims a certain percentage of disinfection, for example, 99.99% of germs, what does it mean?

As discussed in the Fundamentals of UV Disinfection section, microbial sensitivity to UV radiation varies widely. For instance, a 254 nm UV dose of 10 mJ cm<sup>-2</sup> can lead to more than 99.99% (4-log) elimination of *E. coli* bacteria yet less than 70% reduction of MS2 virus (0.5log).<sup>82</sup> Hence, scientifically speaking, the performance of a UV disinfectant, either for air or surface, should be claimed based on benchmark microbes, and a general claim such as “99.99% of all germs” is meaningless.

For UV air treatment, to avoid UV shadowing and biofilm generation by incoming dust, a filtration system, for example,

HEPA or carbon filters, has to be implemented prior to the UV inactivation area to clarify the validation of UV inactivation performance in various air stream situations. In addition, particularly for UV surface disinfection devices, the performance is a strong function of the distance between disinfectant and the target surface, as well as the size of the target surface. Therefore, the performance must be declared by indicating the specified distance and size of the surface at which the performance has been validated. To simplify this, an example case is studied in Figure 3. The given array of 4 UV-LEDs, with certain specifications, provides the illustrated radiation pattern on a parallel 10 cm  $\times$  10 cm surface at 5 cm distance. As can be seen in the figure, the minimum irradiance on the 10 cm  $\times$  10 cm surface is about 0.2 mW cm<sup>-2</sup>. However, if a 5  $\times$  5 cm surface within that larger surface is considered, the minimum irradiance would be around 0.6 mW cm<sup>-2</sup> (3 times more). In other words, the irradiation time required for a certain disinfection ratio for the 10 cm  $\times$  10 cm surface is 3 times more than that of 5 cm  $\times$  5 cm. Therefore, for claiming the performance of this UV-LED array, the specific covered surface must be indicated. Given the minimum UV irradiance of 0.6 mW cm<sup>-2</sup> in this area, one can claim this arrangement of UV-LEDs can maintain at least 24 mJ cm<sup>-2</sup> UV dose after 40 s of irradiation (0.6 mW cm<sup>-2</sup>  $\times$  40 s), only if the LEDs are secured 5 cm above the surface (not more or less) during this time. On the other hand, the indication of delivered irradiance by the UV emitting system in a certain configuration on a specific area is a more appropriate parameter than any disinfection rate claims. Last but certainly not least, the surface type and material, in addition to the ambient conditions (temperature and humidity level) must be indicated in the claimed performance.

Additionally, even if the UV disinfection device is validated to be 99.9% effective against the microorganism, if the initial concentration of the microbe is very high, the remaining 0.1% might be sufficient to cause illness. Highly contaminated surfaces could be frequently touched surfaces in public places, such as elevator pads, ATM keypads, money bills, door handles, and toilets, or personal protective equipment, such as masks or gloves. Hence, the performance of a UV disinfection product should be appropriately indicated for different log removal of microorganisms as initial concentrations would be higher or lower. That is providing sufficient information on the required exposure time by the user for providing different incremental log removals (for example, 1–4-logs). During pandemics such as COVID-19, it is essential to note that even a 4-log reduction of the virus should not be taken to mean that sterilized surfaces no longer pose an infectivity threat. Pan et al.<sup>83</sup> reported SARS-CoV-2 viral loads from COVID-19 patient samples ranging from 641 to  $1.34 \times 10^{11}$  with a reported median of  $7.52 \times 10^5$ ; all expressed in copies per milliliters. Imagining that a surface is infected with the median value, a theoretical 4-log reduction in virus concentration would keep the viral load in the 0–100 copies per milliliter range. Hence, a 6-log reduction is required to be translated to complete sterilization of the surface.

The performance of a UV disinfection system can be validated in two stages: (i) by the manufacturer of UV disinfection product through using standard experimental protocols and (ii) by certified third-party laboratory testing via laboratories certified by health agencies such as US Food and Drug Administration (FDA). USEPA<sup>41,84</sup> and the *Ultraviolet Germicidal Irradiation Handbook*<sup>28</sup> have provided

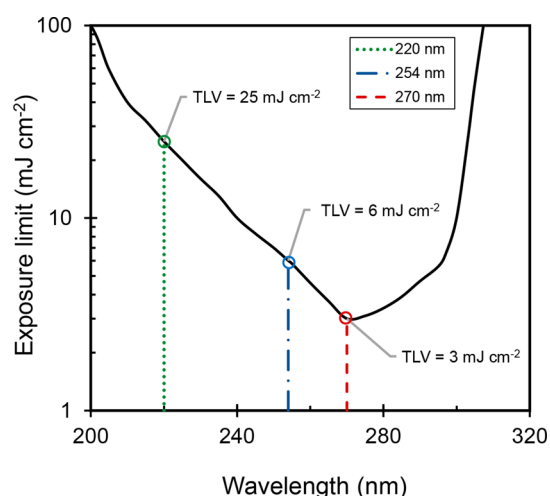
detailed protocols for validation of UV surface disinfection devices. For air purifiers, the Generic Verification Protocol recommended by USEPA<sup>85</sup> to design appropriate testing apparatus for evaluating the performance of bioaerosol treatment systems should be utilized. A copy of the scientific validation document should be provided by the manufacturer to ensure the claimed performance. Consumers should take care in selecting devices and look for third-party testing evidence, as well as the certification of device materials and electrical components by regulatory organizations worldwide such as the National Sanitation Foundation (NSF), Underwriter Laboratories (UL), Canadian Standards Association (CSA), and Deutscher Verein des Gas- und Wasserfaches (DVGW), as applicable.

## ■ SAFETY CONSIDERATIONS

UV has many effects on skin physiology, with some consequences occurring acutely and others in a delayed manner. One of the most apparent acute effects of UV on the skin is the induction of a cascade of mediators in the skin that together causes “sunburn”. UV radiation is also classified as a “complete carcinogen” because it is both a mutagen and a nonspecific damaging agent and has properties of both a tumor initiator and a tumor promoter. The risk of skin cancer is heavily influenced by UV exposure and skin pigmentation.<sup>86</sup> Moreover, if the eye is exposed to excessive UV radiation, several severe consequences are likely to take place, including photokeratitis, erythema of the eyelid, cataracts, solar retinopathy, and retinal damage.<sup>87</sup>

Dangerous UV exposure to human skin or eye includes direct irradiation, in addition to secondary exposure due to the UV reflection from surfaces. The secondary exposure from materials with high reflectance in the UV region must be a crucial consideration in designing UV surface disinfection devices. For instance, PTFE, aluminum, and stainless-steel surfaces can reflect up to 95%, 90%, and 50% of UVC radiation, respectively. The threshold limit value (TLV) for human UV exposure is an “effective” UV dose (irradiance  $\times$  exposure time) of 3 mJ cm<sup>-2</sup> in an 8 h time frame based on regulation provided by different associations such as the American Cancer Society, American Conference of Governmental Industrial Hygienists, and European Agency for Safety and Health at Work. The word “effective” in this regulation is crucial and defined based on the maximum sensitivity of the human eye, which was found to be at approximately 270 nm.<sup>88</sup> This wavelength is used as a reference for the effectiveness of other UV wavelengths to elicit a biological response. For example, the spectral effectiveness of 254 nm UVC rays is 0.5, which means that 6 mJ cm<sup>-2</sup> of 254 nm UVC can cause the same effect as 3 mJ cm<sup>-2</sup> of 270 nm (TLV for human exposure). The TLV values over the UVC region are extracted from the Ultraviolet Radiation Guide provided by the US Navy Environmental Health Center<sup>88</sup> and described in Figure 4. If the dose of UV exceeds the TLV, severe sunburn-like reactions could be initiated, leading to “sunburn cells” on the skin. In addition to use of appropriate PPE, such as UV protective goggles and gloves, providing some safety features such as a child lock and motion sensors, as well as designing a shield for the UV exposure area could significantly diminish the chance of human exposure.

Even when the manufacturer provides the most effective system, the degree of diligence on the user side will ultimately determine the success of the UV disinfection with the same



**Figure 4.** Threshold limit values (TLVs) for human UV exposure over the UVC spectrum extracted from literature.<sup>88</sup>

situation for the safety of the operation. For example, hand-held UV disinfection equipment should not be used for any kind of hand or wound sterilization. General public users may also not be aware of how long one must irradiate any specific surface type at what distance and with what safety considerations. Hence, providing a comprehensive operation manual with the product is necessary for UV surface disinfection units. Additional exposure is also required for the folds and crevices of surfaces. Thus, for hand-held UV surface disinfectors, the minimum necessary exposure time must be presented in product guidelines similar to existing hygiene protocols that provide a recommendation for the use of chemical wipes for defined periods, ranging from 1 to 10 min to treat frequently touched surfaces adequately.

Ozone generation is identified among the risks associated with UV disinfection, particularly for air disinfection application. The competing processes of ozone generation and dissociation from and to molecular oxygen catalyzed by deep UV irradiation is described in the literature extensively.<sup>89</sup> It is known that radiation in the far-UVC region is capable of generating ozone via photolysis of environmental oxygen molecules. Therefore, systems designed to apply far-UVC radiation for air disinfection could generate ozone during their operation; however, the risk posed by this generation is a function of the UV source power output and its emission spectrum, as well as air flow or stagnation and operation duty cycle. For example, the generated ozone in air by 222 nm far-UVC exposure is measured to be <0.005 ppm in the work by Welch et al.<sup>90</sup> They studied the inactivation of aerosolized microorganisms and stated that the ozone concentration is not a significant level to provide an antimicrobial effect. Accordingly, risk of ozone exposure should be included in an overall evaluation of safety for far UV-C irradiation in the presence of humans. The safe limit of ozone generation is reported by various regulatory organizations and is tabulated in Table 2.

Last but not least, UV irradiation is known to cause degradation of materials that are irradiated (i.e., polymers). Such degradation can dissociate the material structure and reduce the lifetime of the irradiated material by creating radicals on the surface that could interact with the virus and cause in situ mutation. Therefore, the applied dose of UVC energy should be balanced to achieve acceptable levels of

**Table 2.** Overview of Available Regulations for Ozone Generation

organization	regulation	ref
US Food and Drug Administration (FDA)	limits ozone generation from indoor medical devices to be no more than 0.05 ppm	91
Occupational Safety and Health Administration (OSHA)	requires exposure to a concentration of not more than 0.10 ppm for 8 h	92
National Institute of Occupational Safety and Health (NIOSH)	regulates an upper limit of 0.10 ppm, not to be exceeded at any time	93
US Environmental Protection Agency (USEPA)	publishes National Ambient Air Quality Standard for ozone as maximum 8 h outdoor concentration of 0.08 ppm	94

biocidal efficacy and avoid excessive energy that would damage the surfaces throughout the anticipated lifetime.<sup>95</sup> This is not possible unless microscale damage on polymeric surfaces of target surfaces, such as those in health care facility, are carefully characterized. A group of characterization methods has been recommended in the literature to detect early onset damage to plastic surfaces.<sup>96</sup> Using these characterization methodologies, a very recent work by Teska et al. studied the induced damage to various polymers.<sup>97</sup>

## CONCLUDING INSIGHT

The recent COVID-19 outbreak has been deemed a global health emergency. Internationally, the number of confirmed reports has continued to rise. Time alone will tell how human intervention has affected the course of the COVID-19 pandemic. It is perhaps clear now that stay-at-home alone may not be sufficient to prevent the spread of COVID-19; thus, in addition to conventional preventive measures, innovative disinfection technologies, including UV radiation, grabbed tremendous attention. The surge in the use of UVC sterilization devices for air and surface disinfection testifies to the fact that the general public craves effective and convenient disinfection methods. In the absence of an established protocol and guidelines to validate commercial UV disinfection products, numerous UV-based sterilization devices with unknown efficacies against SARS-CoV-2 and lack of safety measured caused a major concern whether such products are yet at a stage to be used by amateur users. Here, we provided an authoritative review on the applicability, validation, operation, and safety of UV disinfection devices from the perspective of the COVID-19 pandemic. We believe this review will open the discussion on the necessity of careful validation processes for UV disinfection devices before they become available to untrained users. This, in turn, is anticipated to generate a great deal of interest among researchers and industry on developing and manufacturing new viable UV air and surface treatment devices for current and future epidemics.

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## Notes

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## REFERENCES

- (1) Macnaughton, M. R.; Davies, H. A. Coronaviridae. *Perspect. Med. Virol.* **1987**, *3*, 173.
- (2) Wu, F.; Zhao, S.; Yu, B.; Chen, Y. M.; Wang, W.; Song, Z. G.; Hu, Y.; Tao, Z. W.; Tian, J. H.; Pei, Y. Y.; Yuan, M. L.; Zhang, Y. L.; Dai, F. H.; Liu, Y.; Wang, Q. M.; Zheng, J. J.; Xu, L.; Holmes, E. C.; Zhang, Y. Z. A New Coronavirus Associated with Human Respiratory Disease in China. *Nature* **2020**, *579*, 265.
- (3) Berger, A.; Drosten, C.; Doerr, H. W.; Stürmer, M.; Preiser, W. Severe Acute Respiratory Syndrome (SARS) - Paradigm of an Emerging Viral Infection. *J. Clin. Virol.* **2004**, *29*, 13.
- (4) Enwemeka, C. S.; Bumah, V. V.; Masson-Meyers, D. S. Light as a Potential Treatment for Pandemic Coronavirus Infections: A Perspective. *J. Photochem. Photobiol., B* **2020**, *207*, 111891.
- (5) World Health Organization (WHO). Summary of probable SARS cases with onset of illness from 1 November 2002 to 31 July 2003 [https://www.who.int/csr/sars/country/table2004\\_04\\_21/en/](https://www.who.int/csr/sars/country/table2004_04_21/en/) (accessed Jun 1, 2020).
- (6) Aguanno, R.; Elidrissi, A.; Elkholly, A. A.; Ben Embarek, P.; Gardner, E.; Grant, R.; Mahrous, H.; Malik, M. R.; Pavade, G.; VonDobschuetz, S.; Wiersma, L.; Van Kerkhove, M. D. MERS: Progress on the Global Response, Remaining Challenges and the Way Forward. *Antiviral Res.* **2018**, *159*, 35.
- (7) World Health Organization Eastern Mediterranean Region (WHO EMRO). *MERS Situation Update*; 2020.
- (8) Ahidjo, B. A.; Loe, M. W. C.; Ng, Y. L.; Mok, C. K.; Chu, J. J. H. Current Perspective of Antiviral Strategies against COVID-19. *ACS Infect. Dis.* **2020**, *6*, 1624.
- (9) Osman, E. E. A.; Toogood, P. L.; Neamati, N. COVID-19: Living through Another Pandemic. *ACS Infect. Dis.* **2020**, *6*, 1548.
- (10) Sahin, A. R. 2019 Novel Coronavirus (COVID-19) Outbreak: A Review of the Current Literature. *Eurasian J. Med. Oncol.* **2020**, DOI: [10.14744/ejmo.2020.12220](https://doi.org/10.14744/ejmo.2020.12220).
- (11) World Health Organization (WHO). Situation Reports; 2020.
- (12) Wu, D.; Wu, T.; Liu, Q.; Yang, Z. The SARS-CoV-2 Outbreak: What We Know. *Int. J. Infect. Dis.* **2020**, *94*, 44.
- (13) Tan, L.; Ma, B.; Lai, X.; Han, L.; Cao, P.; Zhang, J.; Fu, J.; Zhou, Q.; Wei, S.; Wang, Z.; Peng, W.; Yang, L.; Zhang, X. Air and Surface Contamination by SARS-CoV-2 Virus in a Tertiary Hospital in Wuhan, China. *Int. J. Infect. Dis.* **2020**, *99*, 3.
- (14) Pinon, A.; Viallette, M. Survival of Viruses in Water. *Intervirology* **2019**, *61* (5), 214–222.
- (15) Mandavkar, P. Coronavirus: Basic Information and Precautionary Measures. *SSRN Electron. J.* **2020**, DOI: [10.2139/ssrn.3573881](https://doi.org/10.2139/ssrn.3573881).
- (16) Wang, J.; Du, G. COVID-19 May Transmit through Aerosol. *Ir. J. Med. Sci.* **2020**, DOI: [10.1007/s11845-020-02218-2](https://doi.org/10.1007/s11845-020-02218-2).
- (17) García de Abajo, F. J.; Hernández, R. J.; Kaminer, I.; Meyerhans, A.; Rosell-Llompart, J.; Sanchez-Elsner, T. Back to Normal: An Old Physics Route to Reduce SARS-CoV-2 Transmission in Indoor Spaces. *ACS Nano* **2020**, *14*, 7704.
- (18) van Doremalen, N.; Bushmaker, T.; Morris, D. H.; Holbrook, M. G.; Gamble, A.; Williamson, B. N.; Tamin, A.; Harcourt, J. L.; Thornburg, N. J.; Gerber, S. I.; Lloyd-Smith, J. O.; de Wit, E.; Munster, V. J. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. *N. Engl. J. Med.* **2020**, *382*, 1564.
- (19) Morawska, L.; Cao, J. Airborne Transmission of SARS-CoV-2: The World Should Face the Reality. *Environ. Int.* **2020**, *139*, 105730.
- (20) Liu, Y.; Ning, Z.; Chen, Y.; Guo, M.; Liu, Y.; Gali, N. K.; Sun, L.; Duan, Y.; Cai, J.; Westerdahl, D.; Liu, X.; Xu, K.; Ho, K.-f.; Kan, H.; Fu, Q.; Lan, K. Aerodynamic Analysis of SARS-CoV-2 in Two Wuhan Hospitals. *Nature* **2020**, *582*, 557.
- (21) Wurtzer, S.; Marechal, V.; Mouchel, J.-M.; Maday, Y.; Teysou, R.; Richard, E.; Almayrac, J. L.; Moulin, L. Evaluation of Lockdown Impact on SARS-CoV-2 Dynamics through Viral Genome Quantification in Paris Wastewaters. *medRxiv* **2020**, [10.1101/2020.04.12.20062679](https://doi.org/10.1101/2020.04.12.20062679).
- (22) Ahmed, W.; Angel, N.; Edson, J.; Bibby, K.; Bivins, A.; O'Brien, J. W.; Choi, P. M.; Kitajima, M.; Simpson, S. L.; Li, J.; Tschärke, B.; Verhagen, R.; Smith, W. J. M.; Zaugg, J.; Dierens, L.; Hugenholtz, P.; Thomas, K. V.; Mueller, J. F. First Confirmed Detection of SARS-CoV-2 in Untreated Wastewater in Australia: A Proof of Concept for the Wastewater Surveillance of COVID-19 in the Community. *Sci. Total Environ.* **2020**, *728*, 138764.
- (23) Rimoldi, S. G.; Stefani, F.; Gigantiello, A.; Polesello, S.; Comandatore, F.; Mileto, D.; Maresca, M.; Longobardi, C.; Mancon, A.; Romeri, F.; Pagani, C.; Moja, L.; Gismondo, M. R.; Salerno, F. Presence and Vitality of SARS-CoV-2 Virus in Wastewaters and Rivers. *medRxiv* **2020**, [10.1101/2020.05.01.20086009](https://doi.org/10.1101/2020.05.01.20086009).
- (24) Randazzo, W.; Truchado, P.; Cuevas-Ferrando, E.; Simón, P.; Allende, A.; Sánchez, G. SARS-CoV-2 RNA in Wastewater Anticipated COVID-19 Occurrence in a Low Prevalence Area. *Water Res.* **2020**, *181*, 115942.
- (25) La Rosa, G.; Iaconelli, M.; Mancini, P.; Bonanno Ferraro, G.; Veneri, C.; Bonadonna, L.; Lucentini, L.; Suffredini, E. First Detection of SARS-CoV-2 in Untreated Wastewaters in Italy. *Sci. Total Environ.* **2020**, *736*, 139652.
- (26) La Rosa, G.; Bonadonna, L.; Lucentini, L.; Kenmoe, S.; Suffredini, E. Coronavirus in Water Environments: Occurrence, Persistence and Concentration Methods - A Scoping Review. *Water Res.* **2020**, *179*, 115899.
- (27) Shining a Light on COVID-19. *Nat. Photonics.* **2020**, *14*, 337.
- (28) Kowalski, W. *Ultraviolet Germicidal Irradiation Handbook: UVGI for Air and Surface Disinfection*; Springer: Berlin Heidelberg, 2009. DOI: [10.1007/978-3-642-01999-9](https://doi.org/10.1007/978-3-642-01999-9).
- (29) Adeli, B. Not If, But When: UV LED Beverage Disinfection. *IUVA News* **2020**, 10–11.
- (30) Bolton, J. R.; Cotton, C. A. *The Ultraviolet Disinfection Handbook*; American Water Works Association, 2008.
- (31) Norval, M. The Effect of Ultraviolet Radiation on Human Viral Infections. *Photochem. Photobiol.* **2006**, *82*, 1495.
- (32) Cornelis, J. J.; Su, Z. Z.; Rommelaere, J. Direct and Indirect Effects of Ultraviolet Light on the Mutagenesis of Parvovirus H-1 in Human Cells. *EMBO J.* **1982**, *1*, 693.
- (33) NORVAL, M.; EL-GHORR, A.; GARSSSEN, J.; VAN LOVEREN, H. The Effects of Ultraviolet Light Irradiation on Viral Infections. *Br. J. Dermatol.* **1994**, *130*, 693.
- (34) Craik, S. A.; Weldon, D.; Finch, G. R.; Bolton, J. R.; Belosevic, M. Inactivation of *Cryptosporidium Parvum* Oocysts Using Medium- and Low-Pressure Ultraviolet Radiation. *Water Res.* **2001**, *35* (6), 1387–1398.
- (35) Song, K.; Taghipour, F.; Mohseni, M. Microorganisms Inactivation by Wavelength Combinations of Ultraviolet Light-Emitting Diodes (UV-LEDs). *Sci. Total Environ.* **2019**, *665*, 1103–1110.
- (36) Raeeszadeh, M.; Taghipour, F. Microplasma UV Lamp as a New Source for UV-Induced Water Treatment: Protocols for Characterization and Kinetic Study. *Water Res.* **2019**, *164*, 114959.

- (37) Saifaddin, B. K.; Almogbel, A. S.; Zollner, C. J.; Wu, F.; Bonef, B.; Iza, M.; Nakamura, S.; Denbaars, S. P.; Speck, J. S. AlGaIn Deep-Ultraviolet Light-Emitting Diodes Grown on SiC Substrates. *ACS Photonics* **2020**, *7*, 554.
- (38) Song, K.; Mohseni, M.; Taghipour, F. Application of Ultraviolet Light-Emitting Diodes (UV-LEDs) for Water Disinfection: A Review. *Water Res.* **2016**, *94*, 341–349.
- (39) Chen, R. Z.; Craik, S. A.; Bolton, J. R. Comparison of the Action Spectra and Relative DNA Absorbance Spectra of Microorganisms: Information Important for the Determination of Germicidal Fluence (UV Dose) in an Ultraviolet Disinfection of Water. *Water Res.* **2009**, *43*, 5087.
- (40) Bolton, J. R.; Mayor-Smith, I.; Linden, K. G. Rethinking the Concepts of Fluence (UV Dose) and Fluence Rate: The Importance of Photon-Based Units - A Systemic Review. *Photochem. Photobiol.* **2015**, *91*, 1252.
- (41) Gora, S. L.; Rauch, K. D.; Ontiveros, C. C.; Stoddart, A. K.; Gagnon, G. A. Inactivation of Biofilm-Bound *Pseudomonas Aeruginosa* Bacteria Using UVC Light Emitting Diodes (UVC LEDs). *Water Res.* **2019**, *151*, 193.
- (42) Tseng, C.-C.; Li, C.-S. Inactivation of Virus-Containing Aerosols by Ultraviolet Germicidal Irradiation. *Aerosol Sci. Technol.* **2005**, *39* (12), 1136–1142.
- (43) Perlmutter, J. D.; Hagan, M. F. Mechanisms of Virus Assembly. *Annu. Rev. Phys. Chem.* **2015**, *66*, 217.
- (44) Li, F. Structure, Function, and Evolution of Coronavirus Spike Proteins. *Annu. Rev. Virol.* **2016**, *3* (1), 237–261.
- (45) Meo, S. A.; Alhowikan, A. M.; Khelaiwi, T. A. L.; Meo, I. M.; Halepoto, D. M.; Iqbal, M.; Usmani, A. M.; Hajjar, W.; Ahmed, N. Novel Coronavirus 2019-NCoV: Prevalence, Biological and Clinical Characteristics Comparison with SARS-CoV and MERS-CoV. *European Review for Medical and Pharmacological Sciences* **2020**, 2012.
- (46) Pinon, A.; Vialette, M. Survival of Viruses in Water. *Intervirology* **2019**, *61*, 214.
- (47) Kowalski, W. A Genomic Model for the Prediction of Ultraviolet Inactivation Rate Constants for RNA and DNA Viruses. *IUVA News*, 2009.
- (48) Keshavarzfathy, M.; Taghipour, F. Computational Modeling of Ultraviolet Light-Emitting Diode (UV-LED) Reactor for Water Treatment. *Water Res.* **2019**, *166*, 115022.
- (49) Hull, N. M.; Linden, K. G. Synergy of MS2 Disinfection by Sequential Exposure to Tailored UV Wavelengths. *Water Res.* **2018**, *143*, 292.
- (50) Thurman, R. B.; Gerba, C. P.; Bitton, G. The Molecular Mechanisms of Copper and Silver Ion Disinfection of Bacteria and Viruses. *Crit. Rev. Environ. Control* **1989**, *18*, 295.
- (51) Ahearn, D. G.; Simmons, R. B.; Switzer, K. F.; Ajello, L.; Pierson, D. L. Colonization by *Cladosporium* Spp. of Painted Metal Surfaces Associated with Heating and Air Conditioning Systems. *J. Ind. Microbiol.* **1991**, *8*, 277.
- (52) Pais-Correia, A. M.; Sachse, M.; Guadagnini, S.; Robbiati, V.; Lasserre, R.; Gessain, A.; Gout, O.; Alcover, A.; Thoulouze, M. I. Biofilm-like Extracellular Viral Assemblies Mediate HTLV-1 Cell-to-Cell Transmission at Virological Synapses. *Nat. Med.* **2010**, *16*, 83.
- (53) Zhao, Z.; Zhang, Z.; Lanzarini-Lopes, M.; Sinha, S.; Rho, H.; Herckes, P.; Westerhoff, P. Germicidal Ultraviolet Light Does Not Damage or Impede Performance of N95 Masks Upon Multiple Uses. *Environ. Sci. Technol. Lett.* **2020**, *7*, 600.
- (54) Mills, D.; Harnish, D. A.; Lawrence, C.; Sandoval-Powers, M.; Heimbuch, B. K. Ultraviolet Germicidal Irradiation of Influenza-Contaminated N95 Filtering Facepiece Respirators. *Am. J. Infect. Control* **2018**, *46*, e49.
- (55) McDevitt, J. J.; Rudnick, S. N.; Radonovich, L. J. Aerosol Susceptibility of Influenza Virus to UV-C Light. *Appl. Environ. Microbiol.* **2012**, *78* (6), 1666–1669.
- (56) Cadnum, J. L.; Li, D.; Redmond, S. N.; John, A. R.; Pearlmutt, B.; Donskey, C. Effectiveness of Ultraviolet-C Light and a High-Level Disinfection Cabinet for Decontamination of N95 Respirators. *Pathog. Immun.* **2020**, *5*, 52.
- (57) Peccia, J.; Werth, H. M.; Miller, S.; Hernandez, M. Effects of Relative Humidity on the Ultraviolet Induced Inactivation of Airborne Bacteria. *Aerosol Sci. Technol.* **2001**, *35*, 728.
- (58) Walker, C. M.; Ko, G. Effect of Ultraviolet Germicidal Irradiation on Viral Aerosols. *Environ. Sci. Technol.* **2007**, *41* (15), 5460–5465.
- (59) Lai, C. C.; Shih, T. P.; Ko, W. C.; Tang, H. J.; Hsueh, P. R. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and Coronavirus Disease-2019 (COVID-19): The Epidemic and the Challenges. *Int. J. Antimicrob. Agents* **2020**, *55*, 105924.
- (60) Poltronieri, P.; Sun, B.; Mallardo, M. RNA Viruses: RNA Roles in Pathogenesis, Coreplication and Viral Load. *Curr. Genomics* **2015**, *16* (5), 327–335.
- (61) Kariwa, H.; Fujii, N.; Takashima, I. Inactivation of SARS Coronavirus by Means of Povidone-Iodine, Physical Conditions and Chemical Reagents. *Dermatology* **2006**, *212* (1), 119–123.
- (62) Scheller, C.; Krebs, F.; Minkner, R.; Astner, I.; Gil-Moles, M.; Wätzig, H. Physicochemical Properties of SARS-CoV-2 for Drug Targeting, Virus Inactivation and Attenuation, Vaccine Formulation and Quality Control. *Electrophoresis* **2020**, *41*, 1137.
- (63) Xie, M.; Chen, Q. Insight into 2019 Novel Coronavirus — An Updated Interim Review and Lessons from SARS-CoV and MERS-CoV. *Int. J. Infect. Dis.* **2020**, *94*, 119.
- (64) Weiss, M.; Horzinek, M. C. Resistance of Berne Virus to Physical and Chemical Treatment. *Vet. Microbiol.* **1986**, *11* (1–2), 41–49.
- (65) Hirano, N.; Hino, S.; Fujiwara, K. Physico-Chemical Properties of Mouse Hepatitis Virus (MHV-2) Grown on DBT Cell Culture. *Microbiol. Immunol.* **1978**, *22* (7), 377–390.
- (66) Saknimit, M.; Inatsuki, I.; Sugiyama, Y.; Yagami, K. Virucidal Efficacy of Physico-Chemical Treatments against Coronaviruses and Parvoviruses of Laboratory Animals. *Jikken Dobutsu.* **1988**, *37* (3), 341–345.
- (67) Duan, S. M.; Zhao, X. S.; Wen, R. F.; Huang, J. J.; Pi, G. H.; Zhang, S. X.; Han, J.; Bi, S. L.; Ruan, L.; Dong, X. P. Stability of SARS Coronavirus in Human Specimens and Environment and Its Sensitivity to Heating and UV Irradiation. *Biomed. Environ. Sci.* **2003**, *16* (3), 246–255.
- (68) Kowalski, W. J. SARS Coronavirus UV Susceptibility. 2015, DOI: 10.13140/RG.2.1.4332.1680.
- (69) Darnell, M. E. R.; Subbarao, K.; Feinstone, S. M.; Taylor, D. R. Inactivation of the Coronavirus That Induces Severe Acute Respiratory Syndrome, SARS-CoV. *J. Virol. Methods* **2004**, *121* (1), 85–91.
- (70) Guillot, E.; Loret, J.-F. Global Water Research Coalition. *Waterborne Pathogens: Review for the Drinking-Water Industry*; IWA Pub, 2010.
- (71) Heßling, M.; Hönes, K.; Vatter, P.; Lingensfelder, C. Ultraviolet Irradiation Doses for Coronavirus Inactivation - Review and Analysis of Coronavirus Photoinactivation Studies. *GMS Hyg. Infect. Control* **2020**, DOI: 10.3205/dgkh000343.
- (72) Patterson, E. I.; Prince, T.; Anderson, E. R.; Casas-Sanchez, A.; Smith, S. L.; Cansado-Utrilla, C.; Turtle, L.; Hughes, G. L. Methods of Inactivation of SARS-CoV-2 for Downstream Biological Assays. *bioRxiv* 2020, 10.1101/2020.05.21.108035.
- (73) Inagaki, H.; Saito, A.; Sugiyama, H.; Okabayashi, T.; Fujimoto, S. Rapid Inactivation of SARS-CoV-2 with Deep-UV LED Irradiation. *Emerging Microbes Infect.* **2020**, *9*, 1744.
- (74) Bolton, J. R.; Linden, K. G. Standardization of Methods for Fluence (UV Dose) Determination in Bench-Scale UV Experiments. *J. Environ. Eng.* **2003**, *129*, 209.
- (75) Sholtes, K.; Keliher, R.; Linden, K. G. Standardization of a UV LED Peak Wavelength, Emission Spectrum, and Irradiance Measurement and Comparison Protocol. *Environ. Sci. Technol.* **2019**, *53*, 9755.
- (76) Kheyrandish, A.; Mohseni, M.; Taghipour, F. Protocol for Determining Ultraviolet Light Emitting Diode (UV-LED) Fluence for Microbial Inactivation Studies. *Environ. Sci. Technol.* **2018**, *52*, 7390.
- (77) Bianco, A.; Biasin, M.; Pareschi, G.; Cavalleri, A.; Cavatorta, C.; Fenizia, C.; Galli, P.; Lessio, L.; Lualdi, M.; Redaelli, E.; Saule, I;

Trabattoni, D.; Zanutta, A.; Clerici, M. UV-C Irradiation Is Highly Effective in Inactivating and Inhibiting SARS-CoV-2 Replication. *medRxiv* 2020, [10.1101/2020.06.05.20123463](https://doi.org/10.1101/2020.06.05.20123463).

(78) Simmons, S.; Carrion, R.; Alfson, K.; Staples, H.; Jinadatha, C.; Jarvis, W.; Sampathkumar, P.; Chemaly, R.; Khawaja, F.; Povroznik, M.; Jackson, S.; Kaye, K.; Rodriguez, R.; Stibich, M. Disinfection Effect of Pulsed Xenon Ultraviolet Irradiation on SARS-CoV-2 and Implications for Environmental Risk of COVID-19 Transmission. *medRxiv* 2020, [10.1101/2020.05.06.20093658](https://doi.org/10.1101/2020.05.06.20093658).

(79) Buonanno, M.; Welch, D.; Shuryak, I.; Brenner, D. J. Far-UVC Light (222 Nm) Efficiently and Safely Inactivates Airborne Human Coronaviruses. *Sci. Rep.* **2020**, DOI: [10.1038/s41598-020-67211-2](https://doi.org/10.1038/s41598-020-67211-2).

(80) Pendyala, B.; Patras, A.; D'Souza, D. Genomic Modeling as an Approach to Identify Surrogates for Use in Experimental Validation of SARS-CoV-2 and HuNoVs Inactivation by UV-C Treatment. *bioRxiv* 2020, [10.1101/2020.06.14.151290](https://doi.org/10.1101/2020.06.14.151290).

(81) Tarka, P.; Nitsch-Osuch, A. No-Touch Automated Disinfection System for Decontamination of Surfaces in Hospitals. *Int. J. Environ. Res. Public Health* **2020**, *17* (14), 5131.

(82) Haji Malayeri, A.; Mohseni, M.; Cairns, B.; Bolton, J. R. Fluence (UV Dose) Required to Achieve Incremental Log Inactivation of Bacteria, Protozoa, Viruses and Algae. *IUVA News* 2016.

(83) Pan, Y.; Zhang, D.; Yang, P.; Poon, L. L. M.; Wang, Q. Viral Load of SARS-CoV-2 in Clinical Samples. *Lancet Infect. Dis.* **2020**, *20*, 411.

(84) US Environmental Protection Agency Standard Operating Procedure for Growing a *Pseudomonas Aeruginosa* Biofilm Using the CDC Biofilm Reactor, Office of Pesticide Programs, 2013/

(85) US Environmental Protection Agency Generic Verification Protocol for Biological and Aerosol Testing of General Ventilation Air Cleaners. Environmental Technology Verification, 2006.

(86) D'Orazio, J.; Jarrett, S.; Amaro-Ortiz, A.; Scott, T. UV Radiation and the Skin. *Int. J. Mol. Sci.* **2013**, *14*, 12222.

(87) Van Kuijk, F. J. G. M. Effects of Ultraviolet Light on the Eye: Role of Protective Glasses. *Environ. Health Perspect.* **1991**, *96*, 177.

(88) Ultraviolet Radiation Guide, Technical Manual NEHC-TM92-5, Bureau of Medicine and Surgery, Navy Environmental Health Center, 1992.

(89) Chapman, S. XXXV. On Ozone and Atomic Oxygen in the Upper Atmosphere. *London, Edinburgh, Dublin Philos. Mag. J. Sci.* **1930**, *10*, 369.

(90) Welch, D.; Buonanno, M.; Grilj, V.; Shuryak, I.; Crickmore, C.; Bigelow, A. W.; Randers-Pehrson, G.; Johnson, G. W.; Brenner, D. J. Far-UVC Light: A New Tool to Control the Spread of Airborne-Mediated Microbial Diseases. *Sci. Rep.* **2018**, DOI: [10.1038/s41598-018-21058-w](https://doi.org/10.1038/s41598-018-21058-w).

(91) U.S. Food & Drug Administration (FDA) Overview of Medical Device Regulation. U.S. Department of Health and Human Services, 2018, DOI: [10.1109/ICHIInfS.2012.6304792](https://doi.org/10.1109/ICHIInfS.2012.6304792).

(92) Occupational Safety & Health Administration. Toxic and Hazardous Substances. Occupational Safety and Health Standards, 1910.1000, 2006.

(93) National Institute for Occupational Safety and Health *Pocket Guide to Chemical Hazards*, 2007, DOI: [10.1109/icnn.1993.298588](https://doi.org/10.1109/icnn.1993.298588).

(94) Environmental Protection Agency. Ozone Generators That Are Sold as Air Cleaners. <https://www.epa.gov/indoor-air-quality-iaq/ozone-generators-are-sold-air-cleaners>, 2014.

(95) Jo, H.; West, A. M.; Teska, P. J.; Oliver, H. F.; Howarter, J. A. Assessment of Early Onset Surface Damage from Accelerated Disinfection Protocol. *Antimicrob. Resist. Infect. Control* **2019**, DOI: [10.1186/s13756-019-0467-9](https://doi.org/10.1186/s13756-019-0467-9).

(96) Strader, P.; Lee, Y.; Teska, P.; Li, X.; Jones, J. L. Approaches for Characterizing Surfaces Damaged by Disinfection in Healthcare. *Nano LIFE* **2019**, *9*, 1950002.

(97) Teska, P.; Dayton, R.; Li, X.; Lamb, J.; Strader, P. Damage to Common Healthcare Polymer Surfaces from UV Exposure. *Nano LIFE* **2020**, *10*, 2050001.