As part of the “Materials Science and Coronavirus Series,” Advanced Materials & Processes readers were introduced to the way copper can assist in the fight against COVID-19 (Can Copper Help Fight COVID-19?, May/June 2020), and a discussion was presented surrounding the renewed interest Cu has enjoyed as of late because of its antimicrobial behavior (Copper’s Conductivity and Antimicrobial Properties Inspire Renewed Interest, July/August 2020). Most recently, Barber et al. pivoted toward the role stainless-steel can play when the commonly found alloyed material in hospitals and medical settings contains an adequate amount of Cu and Cu phases via compositional optimization and proper processing as well (Antimicrobial Copper-Containing Stainless Steels Show Promise, September 2020). The present article shall turn to the enhanced antimicrobial and antiviral performance associated with antipathogenic Cu material consolidations obtained using cold gas-dynamic spray (cold spray) processing.

**Fomite Transmission of SARS-CoV-2**

Before one spends time on the matter of antimicrobial copper coatings, contact-mediated (or fomite) transmission of SARS-CoV-2 must be established as a non-negligible transmission pathway. Fomite transmission from contaminated high-touch surfaces is considered a mode for COVID-19 transmission. Since fomite transmission of SARS-CoV-2 acts as an indirect disease vector and has been demonstrated numerous times as being non-negligible, surfaces that have been developed to inactivate SARS-CoV-2 will be discussed first; followed by copper as an antiviral surface; contemporary antimicrobial materials, generally; antipathogenic copper cold spray coatings; and then the matter of understanding copper cold spray’s antimicrobial behavior, hereafter. To substantiate the fact that contact-mediated fomite transmission of SARS-CoV-2 plays a non-negligible role in the transference of COVID-19, readers are encouraged to consider the following reference[1].

Since the emergence of SARS-CoV-2 as a lethal infectious agent, which can remain active on common material surfaces for significant periods of time, researchers and global members of the materials science and engineering community began to develop coating technologies as viral transmission mitigators. Specifically, Mantlo et al. studied Luminore CopperTouch surfaces to evaluate the inactivation of SARS-CoV-2 and several filoviruses[2]. Mantlo et al. demonstrated the fact that their Luminore CopperTouch surfaces were found to be able to inactivate 99% of SARS-CoV-2 virions before two hours of exposure. Behzadinasab et al. reported another copper-based surface that was able to inactivate 99.9% of the SARS-CoV-2 virus after just one hour of exposure, relative to the uncoated surfaces, thus possibly outperforming the Luminore CopperTouch coating/surface[3]. Behzadinasab et al.’s coating was achieved by way of unifying cuprous oxide particles with polyurethane as a binding agent. Lastly, Hutasoit et al. demonstrated the fact that 96% of the SARS-CoV-2 virions were inactivated upon two hours of incubation time and exposure to an as-deposited Cu cold spray coating[4]. This is consistent with the observation reported in April 2020, by van Doremalen et al.[5], which noted that viable SARS-CoV-2 was no longer measurable upon four hours of exposure to a wrought Cu material.

**Copper as an Antipathogenic Material**

Numerable elemental metals, including Cu, Ag, and Sn, among others, have been classified as oligodynamic[6]; that is to say they’ve been shown to inhibit or kill microorganisms. However, copper has been isolated as the most actionable oligodynamic elemental metal studied by the biological community to date. Even though Cu maintains an appreciable oligodynamic capacity, many microbial agents shown to be susceptible to copper-based contact killing, in the case of bacteria, or contact inactivation, in the case of viruses, still require trace amounts of Cu to ensure that physiological coherency and homeostasis are both maintained[7]. More specifically, Cu acts as a critical trace metal for all aerobic organisms, for example, wherein Cu commonly serves as an enzymatic cofactor for the catalyzation of various redox reactions[8]. Indeed, this is because of Cu’s ability to cycle between

---

*Member of ASM International

Bryer C. Sousa* and Danielle L. Cote*

Worcester Polytechnic Institute, Massachusetts
Cu$^{1+}$ and Cu$^{2+}$. An extreme example of a class of aerobic microorganisms (under ideal conditions) follows from the aerobic methane-oxidizing bacterium known as methanotrophs. More specifically, methanotrophs are a gram-negative and methane oxidative form of bacteria with more than thirty Cu-containing proteins$^{[9]}$. As such, researchers have attempted to invoke methanotrophs as a potential surrogate for understanding how microbes generally uptake or remove Cu in a regulated fashion$^{[9]}$.

However, in doing so, researchers appeared to be unaware of the fact that the critical Cu-methanobactin responsible for the uptake and removal of Cu ions in methanotrophs have been shown to be unable to be internalized by non-methanotrophs, such as E. coli, in contrast with the internalization of Cu-methanobactin from one methanotroph to another$^{[9]}$. As such, one cannot consider methanotrophs as suitable surrogate microbes for garnering wide-ranging Cu regulation mechanisms across various pathogens, as has previously been suggested elsewhere$^{[9]}$. Accordingly, attention will be refocused back toward the vast span of Cu-sensitive pathogens, which are also non-methanotrophs, to potentially identify prospective commonalities underpinning Cu-regulation in microbial agents of interest. Therefore, one may consider the fact that gram-negative bacterial cells have been shown to commit metabolic self-destruction$^{[10]}$, wherein “the outer membrane is the initial target and Fenton reactions between respiration generated oxygen radicals and copper ions results in the generation of reactive oxygen species,” thus leading to “metabolic suicide” as expressed by Warnes et al.$^{[11]}$.

In contrast with gram-negative bacteria, Warnes et al. found that viral copper contact inactivation efficacy (via viral RNA destruction) was proportional to the Cu-content associated with the dry Cu-surfaces that were inoculated with noroviruses. Warnes et al. also observed a reduction in the total copy number of viral-protein-genome-linked proteins, which are required for infectivity, with increasing copper content relative to a stainless-steel control$^{[10]}$.

The work by Warnes et al. that was just discussed is concerned with the viral inactivation mechanism associated with a non-enveloped viral pathogen that was directly exposed to and inoculated upon copper surfaces. However, SARS-CoV-1, MERS, and SARS-CoV-2 are examples of enveloped viruses, rather than non-enveloped viruses, and therefore react with Cu ions in a manner that is uniquely distinguishable from non-enveloped pathogens – precisely because of the presence of said envelope. Therefore, one currently hypothesized mechanism for copper contact inactivation of enveloped coronaviruses was achieved via the use of human coronavirus 229E$^{[12]}$. In this case, Warnes et al. found that “Exposure to copper destroyed the viral genomes and irreversibly affected virus morphology, including disintegration of envelope and dispersal of surface spikes... the inactivation... was enhanced by reactive oxygen species generation” on the copper surface.

While it is appreciable to note that the microbiologists who penned the references cited above also observed the fact that the contact killing or inactivation rates vary as a function of Cu content, less intuitive material-level characteristics are also known to affect the antipathogenic performance of Cu surfaces too. Such characteristics include surface roughness$^{[13]}$, microstructure$^{[14–16]}$, and the like. For example, Champagne et al. hypothesized that the distinctive microstructures affiliated with pure copper arc sprayed, plasma sprayed, and cold sprayed, surfaces would yield dissimilar antipathogenic activity as a direct consequence of the microstructures associated with each material processing condition. Examination of microstructures associated with each of the three thermally sprayed coatings led to the following observation made by Champagne et al.$^{[17]}$: “[differences] in microstructure are evident, suggesting that differences in biological activity may also occur.” Such an observation is consistent with Champagne et al.’s hypothesis that antipathogenic performance depends upon not only copper content but also the microstructure associated with the deposited copper. Figure 1 presents the cross-sectional renderings of the resultant microstructures just discussed via optical microscopy.

**Fig. 1** — (a) Cross-sectional optical micrograph of the Cu wire arc sprayed coating; (b) cross-sectional optical micrograph of the Cu plasma sprayed coating; and (c) cross-sectional optical micrograph of the conventional Cu cold spray consolidation. Adapted from Champagne et al.$^{[17]}$.
The conventional Cu cold spray coating process was redeployed two additional times using two additionally gas-atomized and pure copper powders from different powder suppliers. This was reportedly pursued by Champagne et al. in 2015 to ensure that the MRSA-based contact killing capacity of the consolidated surfaces could be reproduced for verification and validation of the observations first reported upon in 2013. Each additional version of the Cu cold spray coatings produced using conventional feedstock powder was found to be consistent with the original findings, wherein each of the surfaces reached a bacterial reduction rate greater than 99.9% of the inoculated MRSA following two hours of direct contact.

Nearly six years after Champagne et al.’s proof-of-concept study was published, da Silva et al. reported upon the antimicrobial properties of another conventionally deposited copper cold spray coating. They found that their Cu cold spray coating was able to effectively achieve nearly complete inhibition of Staphylococcus aureus’s growth after ten minutes of continuous contact with the Cu surface. One month after da Silva et al.’s work was published, Sousa et al. reinvigorated the interest in the antipathogenic nanostructured Cu cold spray coatings by way of exploring the nanomechanical behavior of the consolidated surfaces through spherical nanoindentation stress-strain curve analysis. Sousa et al. explored the mechanical properties of the novel nanostructured as well as conventional Cu cold spray coatings to assess their mechanical suitability and durability for common touch surfaces in hospital rooms that require resistance to plastic deformation and to also probe a hypothesis presented by Champagne et al., which concerned the use of hardness and/or strength to assess the amount of defect-mediated Cu ion diffusion pathways present in the coatings (Fig. 2).

With the aforementioned in mind, Champagne et al. continued to critically examine their own research by way of synthesizing work reported between 2013 and 2019 through the lens of a hypothesis that identified the dislocation densities brought about by the cold spray deposition process as the microstructural feature most responsible for the antibacterial and antiviral functionality of the coatings. As has been discussed elsewhere, the claim by Champagne et al. that dislocation density generation serves as cold spray’s “application-dependent mechanism for antimicrobial effectiveness” has been refined and has refocused upon the degree of dynamic recrystallization grain refinement experienced by copper during cold spray processing. In other words, Champagne et al., in 2019, reported dislocation density as the microstructural constituent responsible for enhanced antiviral contact inactivation or antibacterial contact killing, whereas Sousa et al. combined dislocation density with grain-boundary mediated atomic Cu diffusion. Regardless, Fig. 3 attests to the viral inactivation...
rate of cold sprayed Cu vs. structural Cu, irrespective of the scientifically reducible microstructural feature most able to enhance atomic Cu ion diffusivity from the consolidated coatings for the purpose of contact killing/inactivation applications.

Moreover, the virus-length-scale and bacterial-length-scale surface roughness of the conventional Cu and nanostructured Cu cold spray surfaces have also been reported\[13\]. Performed using atomic force microscopy (AFM) and 3D-confocal microscopy, the research by Sundberg et al. aimed to procure a more holistic understanding of the mechanisms underpinning the nanostructured Cu cold spray surface’s enhanced antiviral performance when compared with the conventional Cu cold spray coatings’ efficacy. Coupled AFM-confocal microscopy-based characterization of the nanostructured Cu and conventional Cu cold spray consolidations enabled prospective surface-phenomena and surface-mediated mechanisms underlying the antiviral efficacies to be investigated. Soon thereafter, Sundberg et al. continued their alternative analysis via the incorporation of corrosion studies and surface effects to thoroughly probe the ionic copper chemical reactivities associated with the conventional Cu and nanostructured Cu cold spray surfaces\[21\].

Turning to the research published to date and concerned with functionalized antimicrobial copper cold spray coatings since the global COVID-19 pandemic took effect, four additional research articles of immediate relevance are considered next. In large part, two studies\[16,22\] aimed to initialize the formulation of a properties-processing-structure-performance framework for antimicrobial copper cold spray. Also, additional microscopy-based, mechanically based, and chemically/physically based characterization of the nanostructured and conventional copper coatings, single-particle deposits, and feedstock materials was performed and reported upon\[15\]. In terms of microstructural inspection, Fig. 4 presents the cross-sectional renderings of the polycrystallinity associated with the conventional copper cold sprayed coatings.

As for Cu cold spray research that was published and specifically concerned with SARS-CoV-2 as the viral pathogen being explicitly studied, Hutasoit et al.’s testing resulted in 96% inactivation of the novel coronavirus within two hours of exposure to a conventional Cu cold spray surface via direct contact of the pathogen with their coatings. Hutasoit et al. also demonstrated that 99.2% inactivation was achieved at a five-hour exposure period. At the same time, Hutasoit et al. found that annealing the as-deposited conventional Cu cold spray coating resulted in a decrease in the anti-pathogenic efficacy, which is consistent with the framework presented by Sousa et al.\[16\]. In any case, the speed at which the coatings were applied, as well as the 45-degree angle relative to the stainless-steel push plate substrate, likely prevented the feedstock powder from being maximally deformed and therefore incapable of reaching optimal atomic Cu ion diffusivity. Thus, inactivation rates with more idealized processing parameters would likely achieve greater than 96% reduction of SARS-CoV-2 at the two-hour mark\[4\]. Lastly, Hutasoit et al.’s recorded reduction percentage at two hours is also consistent with the as-deposited conventional copper cold spray coating procured for Influenza A inactivation, wherein a 97.3% reduction was achieved for another viral agent\[18\].

Around the same time, Lucas et al. reported a greater than seven log decrease in microbes exposed to a conventional copper cold spray coating; wherein noteworthy decreases in
microbial concentration were recorded within minutes when numerous pathogens were inoculated. This is in comparison with their finding that only a one log decrease of infectious microbial agents on wrought copper sheets, after three hours of direct contact. Moreover, Lucas et al. found that copper-coated 3D printed ABS realized complete contact killing of the inoculated microbes within 15 minutes of exposure; copper-on-copper reached microbial inhibition after 10 minutes, and a five-minute elimination period was identified for the copper cold spray coatings that included a 5 wt. % addition of silver, i.e., the second most oligodynamic elemental agent next to copper, into the feedstock. This included gram-positive Staphylococcus aureus, gram-negative Pseudomonas aeruginosa, Candida albicans, gentamicin-methicillin–resistant S. aureus, azlocillin-carbenicillin–resistant P. aeruginosa, and fluconazole-resistant C. albicans[23].

CONCLUSION

This article invoked the non-negligible nature of contact-mediated fomite transmission of SARS-CoV-2 from contaminated high-touch surfaces; discussed Cu’s oligodynamic activity; and analyzed the performance and application of copper cold spray processing for the purpose of procuring antimicrobial and antiviral coatings with enhanced functionality. By introducing the preventive role supersonically deposited antiviral copper coatings can play as a pandemic countermeasure, materials scientists and engineers can more readily engage in prospective optimization and deployment of antipathogenic Cu cold spray surfaces. For example, the discussion surrounding the link between microstructure, atomic Cu ion diffusivity, and antiviral/antibacterial performance, provides materials researchers with a target microstructure that may be tunable via advanced processing parameter development. Installing antimicrobial Cu cold spray coatings as a technology well-suited for rapid inactivation of SARS-CoV-2 can enhance the resiliency of populations in the short-term. In the long-term, prolonged public health benefits will also be achieved since the supersonically deposited Cu coatings remain antiviral and antibacterial for prolonged periods of time, thus remaining functional when future pandemics (which could center upon a pathogen with a greater tendency of disease transmission via fomite pathways) follow COVID-19.

~AM&P

Lead image: 2019-nCoV spike protein, courtesy of Jason McLellan/University of Texas at Austin.

For more information: Bryer C. Sousa, doctoral candidate, materials science and engineering, Worcester Polytechnic Institute (WPI), 100 Institute Road, Worcester, MA 01609, bcsousa@wpi.edu, wpi.edu or Danielle L. Cote, assistant professor, materials science and engineering, WPI, dlcote2@wpi.edu, wpi.edu.

References


