PANDEMIC
Supermind Activation
DIAGNOSTICS & MONITORING

The MIT Center for Collective Intelligence, MIT Media Lab's Community Biotechnology Initiative, and MilliporeSigma—the life science business of Merck KGaA, Darmstadt, Germany—convened more than 180 experts and global leaders in science, healthcare, public policy, and other sectors for a three-week exercise to address the following challenge:

How can we develop pandemic resilience—the ability for society to recover quickly from global disease outbreaks—both in resolving the current COVID-19 pandemic and in building the public health and other infrastructure to prepare for future pandemics?

This chapter covers insights generated from the Supermind related to diagnostics and monitoring for controlling the pandemic.

The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.

INTRODUCTION

Methodologies for widespread and rapid testing and disease surveillance, such as digital contact tracing, can play a crucial role in suppressing the pandemic. The Supermind proposed novel modalities for how to detect COVID-19, including identifying novel biomarkers; where to look for signs of the disease, including in the air, in the sewers, and in our "digital health breadcrumbs," and also how to quickly build new testing labs and infrastructure. The Supermind also focused on aspects of smart phone technologies for contact tracing, known as digital contact tracing: how to ensure equitable access and increase efficacy and interoperability, while critically protecting privacy.

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Detecting COVID-19: Novel biomarkers in our voices and in digital health breadcrumbs

The bedrock of public health response for mitigating and suppressing the spread of infectious disease involves widespread and rapid testing. The most common method for detecting active cases of COVID-19 has involved analyzing patient samples for the presence of viral RNA, usually through variants of polymerase chain reaction (PCR). There are, however, other types of biomarkers that could indicate the presence of an infection.

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For example, an ongoing clinical study of digital biomarkers involving data from over 45,000 volunteers across the United States and India indicates that voice acoustics could be used to detect and monitor various health conditions affecting brain, respiratory, and motor functions required for healthy speech. In response to the COVID-19 pandemic, respiratory-responsive vocal biomarkers (RRVB) have shown promise to detect and measure COVID-19 associated respiratory impairments that also could be tracked over time to understand disease status and symptom severity. Furthermore, because the methods used to collect and analyze speech samples could be gathered from smart phones, such detection could reduce infection risks by eliminating the need for close contact with healthcare workers. Detecting vocal biomarkers using smart phones could provide cost-effective and near universal access to diagnostics and monitoring, making the allocation and use of these resources more timely and efficient and providing valuable assessment and risk stratification capability when gold standard tools, like viral RNA detection, may not be available or are too slow.

Digital health breadcrumbs: digital signals that can provide health surveillance data for tracking infectious disease

Biomarkers for COVID-19 can also be found in our "digital health breadcrumbs," or digital signals that can provide health surveillance data for tracking infectious disease. Some of these include search history keywords for symptoms; networked digital thermometers tracking fever trends; device usage changes correlating to cognitive, behavioral, and mental health changes that occur with infectious disease; and acoustic biomarkers as described above. Such bio-surveillance techniques have been successfully used to track the flu, including FluNearYou and Healthmap. It is possible that an integrated and systemic approach, fusing complementary digital signals with advanced machine learning and artificial intelligence techniques, could provide a robust monitoring system that could detect community spread of COVID-19 days or weeks earlier than current timelines for testing and patient notification. Current approaches can take longer than a week, rendering diagnostic tests largely useless for containing outbreaks.

Making diagnostic tests and labs accessible and scalable

The lack of sufficient COVID-19 diagnostic testing is still a significant problem in the United States and globally. The Supermind emphasized the critical importance of massive-scale testing to enable the isolation of asymptomatic individuals and proposed several approaches to make viral testing more accessible and scalable.

With tens of thousands of COVID-19 cases confirmed per day in the United States alone, and the significant rate of transmission by asymptomatic individuals that one study estimates to be between 6% to 41% of cases (Bradshaw et al., 2020), universal testing is desired. Large-scale detection of infected individuals without symptoms (either pre- or asymptomatic) is incredibly challenging without ubiquitous testing. An additional benefit of universal testing is the ability to relax social distancing measures, enabling the return of socioeconomic activities while limiting future outbreaks (Bradshaw et al., 2020).

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One approach to scale the number of tests conducted is to pool samples from multiple patients in a single test. In such a scenario, a negative test result indicates that no viral RNA was detected in any of the patient samples, thus returning valuable data on multiple patients with only a single test, thus enabling large-scale screening. If, however, a positive result was returned, subsequent rounds of pool testing or testing of individuals from within the pool would be required to determine whom was infected. Pooling samples is particularly effective when rates of community transmission are low.

The Supermind proposed generating the necessary data standards and guidelines for how best to pool samples based on the type of diagnostic test and their prevalence to facilitate regular population-level screening. Such approaches have been successfully conducted in parts of the world, including in China, for example.

Other approaches the Supermind highlighted to make testing more accessible include developing rapid tests that could be conducted at home using saliva samples, which can be easier to collect than, for example, nasopharyngeal swab tests, which require specialized training. The Supermind also pointed to the recent FDA emergency use authorization (EUA) approval to Rutgers Clinical Genomics Laboratory to permit testing of samples self-collected by patients using saliva (Giordano et al., 2020). University of Colorado, Boulder has also recently developed a saliva test with a 45-minute sample-to-results turnaround (Meyerson et al., 2020).

Finally, the Supermind also acknowledged that collecting more samples alone is insufficient; infrastructure to conduct the tests also must be scaled. In the United States, for example, numerous outbreaks across the country during the summer of 2020 have overwhelmed centralized testing facilities, causing a processing backlog. To address this challenge, the Supermind proposed designing highly automated units, like 20-ft. shipping containers, that could be self-sufficient, containing a small number of staff with automated testing solutions capable of handling different diagnostic tests. For example, Open Cell, an organization in London, has designed a bio lab in a shipping container. These mobile labs could be deployed quickly to hot spot areas in close proximity to locations where samples could be collected (e.g., subway stations, hospitals, large factories) to augment existing testing infrastructure.

Similarly, more modular, reagent-agnostic testing systems could provide flexibility and remove points-of-failure in supply chains that potentially rely on single, large manufacturers. The Supermind pointed to entities like OpenTrons, who make open source pipetting robots, along with the Global Biofoundry Alliance and the London Biofoundry, which are also working on developing systems to automate lab protocols and diagnostic testing. Such modular and automated systems would be ideally suited to operate in mobile testing labs that could also be deployed to offer testing for underserved populations like the homeless, or in rural areas that are experiencing outbreaks and require additional infrastructure.

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COVID-19 surveillance for the air, sewage, and our genomes

AIR MONITORING

One area the Supermind identified that requires significant research and study is the analysis of viral prevalence in air, both indoor and outdoor. A recent article from The Atlantic (Tufekci, 2020) similarly highlighted this need. The Supermind proposed rigorous analysis of outdoor transmission in settings like golf courses, outdoor markets, restaurants, and learning environments for schools, for example. A deep understanding of these dynamics could play a critical role in designing public policies for many socio-economic activities that potentially could be conduced safely outdoors.

Similarly, for indoor transmission, rigorous analysis of air filters or air monitoring devices in schools, workplaces, or transportation systems could also provide critical data, which could influence public health policies. Such monitors could be placed strategically with either sample collection or molecular diagnostics tools in situ. Understanding airflow dynamics inside buildings and ventilation systems is critical for designing circulation systems that refresh air and dilute the presence of any viral particles. Finally, the Supermind highlighted the need to understand the particle sizes and concentration in exhaled breath of COVID-19 infected individuals to elucidate the infection dynamics of aerosol transmission.

SEWAGE SURVEILLANCE

Sewage can be an early indicator of epidemics. The Supermind proposed developing a monitoring program based on metagenomic sequencing of all nucleic acids found in sewage that could establish a baseline against which novel pandemic zoonosis (the process of a virus infecting humans from animals) could be detected. Moreover, particularly dangerous engineered viruses are likely to have telltale signatures of alteration by humans, and those changes could be detected by automated algorithms. This type of sewage monitoring could be done not only in municipal sewer systems but also in transportations systems like airplanes, ships, or trains, which, when coupled with pool testing, could trigger targeted testing and contact tracing.

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Such systems could provide a vital early warning, with studies showing that sewage screening could provide communities as much as a week's early notice of a COVID-19 outbreak (Peccia et al., 2020). When coupled with exposure notification and contact tracing technologies, local outbreaks could be controlled before they became pandemics. Furthermore, the existence of such an early warning system may provide the additional benefit of deterring malevolent actors from making engineered bioweapons.

Digital contact tracing is sensitive to uptake, but powerful if universal

One of the most promising technology solutions for suppressing the pandemic is digital contact tracing (DCT). Such technologies rely upon individuals having contact tracing applications installed on their smart phones that through, for example, blue-tooth technology, enable the logging of close proximity contacts. In the event of a positive test, all potentially exposed individuals could be instantly contacted so they can then be tested and potentially isolated. Models predict that, if such digital technologies were universal, the pandemic could be controlled without requiring lockdowns or face coverings (U.S. Food & Drug Administration, 2020). However, strong privacy protections would be required for adoption to succeed, particularly in liberal democracies where installing such applications would be largely voluntary.

To help adoption, the Supermind proposed, for example, buying every adult in the United States an inexpensive smartphone with a basic data plan that is DCT-enabled. This could cost approximately $4.2b. Such an approach could also help provide low income communities and frontline workers access to low cost technologies to help keep their families safe while bridging the "digital divide" that has exposed profound inequities in society, including access to life-saving digital tools. DCT applications could also be enabled with "bidirectional" contact tracing, which is predicted to reduce the effective reproductive number (Reff) of SARS-CoV-2 by roughly 0.3 (U.S. Food & Drug Administration, 2020). Finally, to manage the complexities of multiple DCT applications (potentially a unique app for each state in the United States or each country in Europe), particularly when individuals cross state or country borders, the Supermind proposed using interoperable data standards to prevent data silos and to enable connected systems updated in real time.

References:

Bradshaw, W. J., Alley, E. C., Huggins, J. H., Lloyd, A. L., & Esvelt, K. M. (2020). Bidirectional contact tracing dramatically improves COVID-19 control. *medRxiv*. doi: 10.1101/2020.05.06.20093369

Byambasuren, O., Cardona, M., Bell, K., Clark, J., McLaws, M. L., & Glasziou, P. (2020). Estimating the extent of true asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. *medRxiv*. doi: 10.1101/2020.05.10.20097543

Giordano, G., Blanchini, F., Bruno, R., Colaneri, P., Di Filippo, A., Di Matteo, A., & Colaneri, M. (2020). Modelling the COVID-19 epidemic and implementation of population-wide interventions in Italy. *Nature Medicine*, 1-6.

Meyerson, N. R., Yang, Q., Clark, S. K., Paige, C. L., Fattor, W. T., Gilchrist, A. R., ... & Sawyer, S. L. (2020). A community-deployable SARS-CoV-2 screening test using raw saliva with 45 minutes sample-to-results turnaround. *medRxiv*. doi: 10.1101/2020.07.16.20150250

Peccia, J., Zulli, A., Brackney, D. E., Grubaugh, N. D., Kaplan, E. H., Casanovas-Massana, A., ... & Weinberger, D. M. (2020). SARS-CoV-2 RNA concentrations in primary municipal sewage sludge as a leading indicator of COVID-19 outbreak dynamics. *medRxiv*. doi: 10.1101/2020.05.19.20105999

Tufekci, Z. (2020, July 30). We Need to Talk About Ventilation. The Atlantic. https://www.theatlantic.com/health/archive/2020/07/why-arent-we-talking-more-about-airborne-transmission/614737/

U.S. Food & Drug Administration. (2020, May 08). Coronavirus (COVID-19) Update: *FDA Authorizes First Diagnostic Test Using At-Home Collection of Saliva Specimens.* https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-diagnostic-test-using-home-collection-saliva

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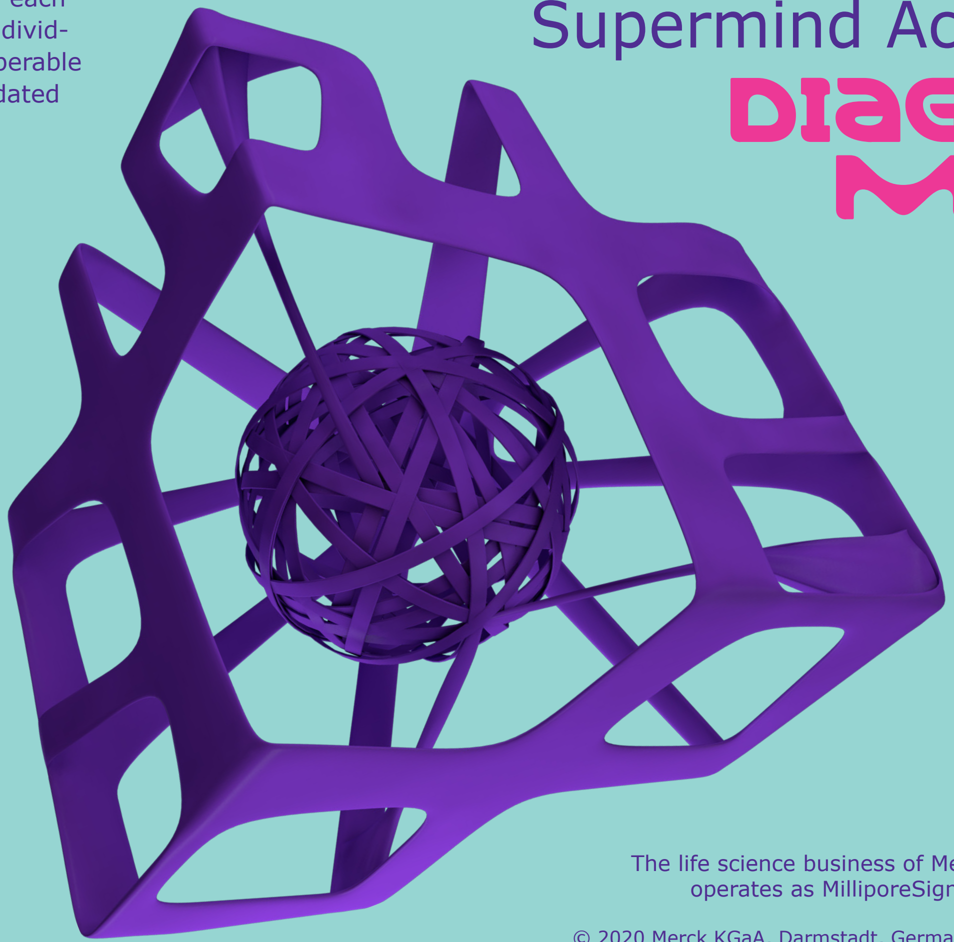

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