

Mathematicians Quickly Respond to the COVID-19 Pandemic

By Juan C. Meza, Zhilan Feng, Tie Luo, and Junping Wang

The Division of Mathematical Sciences (DMS) at the National Science Foundation (NSF) recently participated in an NSF-wide Dear Colleague Letter,¹ which was published on April 3 and requested proposals that address the COVID-19 pandemic. The mathematical sciences community was quick to respond! Ideas ranged from developing tools to help decision-makers better understand the possible outcomes of proposed nonpharmaceutical intervention policies to combining mathematicians' expertise with other disciplines—like biology and chemistry, for example—to study new approaches and accelerate the identification of potential therapeutic treatments.

Overall, the DMS issued a set of 15 Rapid Response Research (RAPID) awards over the span of several weeks that could have a significant impact in mitigating the spread of COVID-19. These awards highlight the critically important need for swift and reliable prediction of epidemics' spatial and temporal risks. Furthermore, many of them use mathematical, statistical, and computational models to evaluate various therapeutic and non-therapeutic mitigation policies, thus allowing policymakers to quickly identify intervention strategies that effectively slow the inevitable. Such strategies can buy additional time to put pandemic plans into effect, reducing peak demand for hospital-based care and ultimately saving lives.

The collection of RAPID awards spans a range of diverse ideas, including novel variations of well-known SIR (susceptible-infected-recovered) models, statistical inference approaches for rapidly changing situations where only partial data is available, and techniques that employ a combination of deep learning and mechanistic methods to quickly improve mathematical models that capture the specific characteristics of COVID-19. Other awards dive deeper into our understanding of how the novel coronavirus infects host cells, targeting the identification of critical areas in the viral genome that could be attacked during drug design. Yet another common theme is the use of data and corresponding mathematical procedures to improve existing models, particularly in situations where the data is incomplete and changes rapidly.

In general, the awards fell into one of two major areas: (i) mathematical models for predicting the spread of COVID-19 and the effects of different mitigation strategies, and (ii) study of the novel coronavirus, the

¹ <https://www.nsf.gov/pubs/2020/nsf20052/nsf20052.jsp>

viral evolution, and subsequent plans for detecting target areas in the viral genome for drug compounds. We can subdivide the awards in the first major area into three general categories: (i) SIR/SEIR (susceptible-exposed-infected-recovered) types of compartmental models with various levels of extensions and complexities; (ii) stochastic, statistical, or probabilistic models; and (iii) network or graph theory-based models.

The DMS made five awards in the first subgroup that will investigate various aspects of the well-known SIR/SEIR model. **Andrea Bertozzi** and **Mason Porter** (DMS – 2027438) plan to integrate a basic SIR framework with high-resolution societal mixing patterns in epidemics and models with self-exciting point processes that are fitted to real-world data. These actions will allow them to study the stochasticity of infection and latency, analyze the uncertainty in disease transmission rates, and evaluate intervention policies. The pair will also examine the outcomes of social distancing using data from a Princess Cruise ship and lecture halls at the University of California, Los Angeles.

Jeffrey Shaman (DMS – 2027369) will utilize SIR-type models with spatial movements and statistical/computational tools to estimate critical epidemiological characteristics that are associated with the transmission of SARS-CoV-2. He will then forecast future COVID-19 incidence, estimate the effectiveness of public health policies (such as school closures and travel restrictions), and project the geographic spread of COVID-19 for given scenarios with various levels of intervention.

Yulia Gel and **Georgiy Bobashev** (DMS – 2027793/2027802) plan to use a predictive approach based on multiple data sources and dynamical SEIR models to train deep learning networks. If one then views simulation SEIR models as surrogate pre-trainers for deep learning models, Gel and Bobashev's work could minimize the amount of real data needed to retrain the predictive model and reflect real-world COVID-19 progression. In contrast, **Grzegorz Rempala** (DMS – 2027001) will employ dynamical survival analysis—which exploits aggregated mean field equations for the underlying large stochastic network approach—to estimate parameters that are similar to those in SIR models. The survival dynamical system may yield new understanding of the pandemic, as it does not require knowledge of the susceptible population's size or overall disease prevalence.

Folashade Augusto (DMS – 2028297) and her collaborators intend to develop disease transmission models that incorporate various factors, including public perception of

risk, age structure within a hospitalized population, population demographics, socioeconomic conditions, and spatial structure. They will then use the models to inform coordination of disease control policies with different scales, ranging from local communities to entire countries. Finally, **Cameron Browne** (DMS – 2028728) and his team will create a modeling framework at the interface of mathematics, epidemiology, and genetics. Their approach may help derive the outbreak size's dependence on contact tracing and broad quarantine intervention parameters, thus quantifying region-specific control characteristics for COVID-19.

Deterministic models are not the only possible tactic. To study systems with high stochasticity, **Jason Xu** and **Allison Aiello** (DMS – 2030355/2030242) will generate new stochastic compartmental models that extend classical mechanisms to explicitly account for changes to the social contact network that underlies disease spread. They will combine these developments with likelihood-based methods to infer key epidemic parameters that offer mechanistic interpretations with uncertainty quantification.

Two other interesting techniques involve modeling the COVID-19 pandemic via network and graph theory. In this group, **Nicole Eikmeier** and **Matthew Junge** (DMS – 2028880/2028892) plan to study quarantine's effect on the network connectivity of graphs to better model societal connections. Individual quarantine is akin to removing a vertex from a graph; the systematic removal of vertices is called site percolation. Eikmeier and Junge will explore biased site percolation's effect on graph structure, particularly the way in which different percolation rules influence the size of a given graph's largest component. The second part of the project will then focus on how an epidemic's critical threshold and size change after percolation for an SIR model.

Faryad Darabi Sahneh's (DMS-2028401) research will take a similar approach but emphasize a data-driven mathematical modeling framework for the forecast of temporal and spatial COVID-19 trends. His team's modeling framework can handle a constantly evolving environment, including individuals' behavioral changes in response to mitigation efforts. Interestingly, Darabi Sahneh borrows this idea from economics.

The second major area of network and graph theory addresses the infectivity and virulence of the novel coronavirus itself, such as the viral evolution, virus structure, and effect on host cells. Here the general line of attack involves studying the RNA viral genome for clues on the way in which it infects the host cells, and determining treatments that might disrupt the infective process.

Gregory Forest's (DMS – 2028758) group has teamed up with two experimental biology laboratories to develop a mathematical modeling platform that will explore the delicate interplay among inhaled loads of SARS-CoV-2 and their diffusion within—and potentially through—the mucus-coated respiratory tract. This will allow the researchers to determine infectivity onset as the virus reaches and invades epithelial cells and propagates the infection. Their ultimate goal is to optimize design of monoclonal antibodies (mAb), characterize efficiency of given mAb affinities to COVID-19 and mucus, and quantify the inhaled mAb dose required to arrest COVID-19 infection at various stages of progression.

Two other awards seek to understand the specific protein that is key to the coronavirus' invasion of host cells: the so-called spike or S-protein in the RNA viral genome. **Tamar Schlick's** (DMS – 2030377) project involves comprehending the COVID-19 RNA viral genome through structural analysis and molecular dynamics studies. The coronavirus is known to mutate over time, but few specifics are currently established. **Javier Arsuaga**, **Raymond Rodriguez**, and **Mariel Vasquez** (DMS – 2030491) intend to employ a combination of Markov processes, graph theory, and topological data analysis to better understand this mutation process and estimate evolutionary parameters and the S-protein's fitness function.

The DMS is thankful to the mathematical sciences community for its incredible response to our call for proposals regarding the worldwide COVID-19 pandemic.

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Electric Semi-trucks

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the best estimate of the number of inoperable semi-trucks that would be replaced by electric ones in five, 10, and 20 years," Pragna Govindu of Pine View said. "With these values, we ultimately predicted the percentage of semis that will be electric." The team's model forecasts that electric semi-trucks will comprise 27.39, 69.49, and 97.77 percent of operational semi-trucks in the next five, 10, and 20 years respectively.

The Pine View students then generated another model to discern the mandatory quantity of charging infrastructure for sustainable, large-scale electronic trucking. This task demanded consideration of electric vehicles' varying ranges and charging times. "Electric vehicle batteries are tricky because they charge quickly in the beginning but slowly at the end," team member Michael Gutierrez said. "We didn't want the trucks to use their full charge capacity, as it would waste a lot of time. So we developed a model to find the optimal stopping interval and based our charging station locations around that."

To test their model, the group simulated the resource needs of a large fleet of trucks on the following five major trucking routes: to/from (i) San Antonio, Texas, and New Orleans, La.; (ii) Minneapolis, Minn., and Chicago, Ill.; (iii) Boston, Mass., and Harrisburg, Pa.; (iv) Jacksonville, Fla., and Washington, D.C.; and (v) Los Angeles, Calif., and San Francisco, Calif. "Initially, we created a formula for the number of stations needed along a given route," Nicholas Butakow said. "With this formula, we used the Monte Carlo method to determine the number of stations with randomly generated values, which reflect projected distributions of commercial electric semi-trucks."

Interestingly, Butakow and his teammates found that all five truck routes required charging points roughly every 90 minutes, given the nature of electric batteries. They used a second Monte Carlo simulation—based on the average number of trucks present at each stop at any given time—to determine the necessary number of charging stations per stop, which ranged from 14 to 29.

Finally, the team created an importance score based on three different factors—economic growth, environmental consid-

eration, and total cost of installation—to rank the five corridors. A higher importance score indicated a higher priority for projected development, and the students determined that developers should target the Minneapolis-Chicago corridor first.

The Pine View team—which included Kristoffer Selberg and Christiana Guan, in addition to Govindu, Gutierrez, and Butakow—will split \$20,000 in scholarship funds for their winning solution. The group also nabbed an Outstanding Communication of Results Award, which recognized the excellence and clarity of their video demonstration (submitted in lieu of a physical presentation) and delivered an additional \$1,000.

"It was really different because we had to work over Zoom instead of communicating and presenting in person, which was difficult," Guan said. "But being able to use visuals—which likely wouldn't have been as possible during an in-person presentation—was helpful."

Working together under stringent time and resource constraints provides participating students with unique collaborative modeling experience — much like the type

of projects that computational scientists and professional mathematicians tackle in the real world. In addition to showcasing the vast potential of a career in applied mathematics, M3 Challenge illustrates the practical applicability of mathematical modeling as an acute problem-solving tool, something that most students do not experience in the traditional classroom setting.

"Typically, the math education that I get in school rigorously teaches the fundamentals of mathematics," Selberg, who is interested in pursuing a career in applied mathematics, said. "M3 Challenge takes what students have learned in school and provides a platform for the expression of mathematics in unique ways that are rarely exhibited in classrooms today."

Pine View School's winning paper is available online,⁵ as is their final presentation.⁶

Lina Sorg is the managing editor of SIAM News.

⁵ https://m3challenge.siam.org/sites/default/files/uploads/M3%20CHAMPION_13343.pdf

⁶ <https://youtu.be/uS4JKTfgYVU>