Pandemic Informatics: Variants of Concern (VOC)

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A year ago, few experts correctly predicted the toll the pandemic has now taken, nor the extraordinarily rapid development and administration of effective vaccines. A handful of wealthy countries have begun to curb COVID-19 infections and deaths through vaccination. The vaccine rollout has ramped up to cover half of all adults in the US with mRNA vaccines that are over 90% effective at preventing particularly severe disease, and also appear to greatly diminish transmission. Scientists have dramatically increased understanding of the SARS-CoV-2 virus, treatment, and vaccines. Yet, where the pandemic will be a year from now remains very difficult to predict, due in large part to rapidly spreading *variants of concern* (VOC).

Thus far, the three VOC spreading globally, and the two additional VOC recognized by the CDC in the US, have some combination of increased transmissibility, higher mortality, and/or ability to overcome immunity from prior infection or vaccination to varying degrees. These VOC present three challenges that computer science research can help address.

First, computing researchers, working in close collaborations with geneticists, immunologists, virologists, epidemiologists, and data scientists, can improve monitoring and tracking of VOC by developing methods to infer meaningful changes in epidemic dynamics from sparse and unevenly sampled data. The sequencing resources required to identify a small number of genetic changes in a 30,000 base pair genome are time-consuming, expensive, and often concentrated in high-resource places: not necessarily the locations where new variants will emerge. Additionally, sequencing is often concentrated on particular populations—i.e., health care workers and travelers—further complicating efforts to track how variants are spreading through the general population. Computer scientists can help develop optimization techniques for where, when, and how to selectively and effectively sample the effects of the evolving pandemic. This problem is complicated by the available technologies and associated costs but can be studied using ideas of robust optimization and location and estimation theory. Computational methods are needed to quickly identify globally when new variants are (a) spreading more rapidly than expected by chance or in relation to other variants, or (b) when the prevalence of a VOC is associated with increased mortality or hospitalization. These computational methods could help scientists to infer how much a particular increase in the viral spread is likely driven by a VOC versus social changes such as the loosing of restrictions or holiday gatherings.

Second, through collaboration with geneticists, immunologists, virologists, epidemiologists, and data scientists, computer scientists can help develop models of viral evolution and vaccine design to understand and, ideally, counter that evolution. Game-theoretic frameworks can aid in the understanding of the interplay between viral evolution and immunity by analyzing vaccination and prior infection. Anticipating which variants are likely to become dominant in the short and long term, based on estimates of current VOC prevalence and trends in viral evolution, can help in the design of boosters or wholly new vaccines that reduce infection, transmission, and severe disease. Modeling how the virus has, and may in the future, evolve—for example, in populations with uncontrolled transmission or in immunocompromised patients—may provide particularly useful insights into future VOC. Simple aggregated models or more detailed agent-based models can be developed by computing researchers to capture the interplay of immunity, viral evolution, and vaccine development.

Third, computing researchers, again working in close collaborations with scientists in other domains, can model treatments, the likely effect of vaccinations on transmission, and personal risk models for both vaccinated and unvaccinated people as new variants emerge. At a larger scale, computing research can contribute to risk models of different global vaccination programs. Currently, there is reason to hope that the US vaccination program will soon protect the majority of people who are most vulnerable to severe COVID-19 disease and death. However, that success could be short-lived if VOC evolved to evade the protection offered by those vaccinations. Modeling efforts are needed to understand how much risk is reduced, both globally and in the US, if worldwide vaccination were accelerated.

The past year should have taught us that apparent control of the virus can be temporary. Resurgences have been seen in wave after wave in place after place across the globe. We hope that the apparently successful efforts seen in the UK and Israel are harbingers of successful worldwide suppression of the virus, particularly in view of the nature of the more dangerous and more transmissible variant that is now dominant in the UK. However, when other variants (like those originating in Brazil, South Africa, and now possibly India) may evade prior immunity, the game may be changed. Models are essential to help us to understand where VOC emerge, how fast they spread, and how much they limit protection from vaccination or prior infection. Computer science can help with the rapid analysis given that uncertainty and the urgency of controlling VOC when they appear.

Much of the recent focus is on current VOC, which involves a handful of mutations that appear to increase viral transmission, infection, and/or immune escape. It is unknown whether this is a likely endpoint for the virus—i.e., whether continued evolution will lead to foreseeable changes—or whether this is simply the first generation of new variants that will open the door to further evolutionary possibilities. Computing research can help to address this uncertainty by developing models of how the virus may traverse the evolutionary landscape[1] and tools to quantify how evolutionary change may be driven by or affect the immune response [2].

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[1] https://www.jstor.org/stable/j.ctt4cgcnc
[2] https://pubmed.ncbi.nlm.nih.gov/15218094/

These computational models and associated lab studies highlight that it is even harder to predict evolutionary trajectories than one might think.

Working closely with geneticists, immunologists, virologists, epidemiologists and data scientists computer scientists can (1) help to reduce the uncertainty about whether and how variants diminish the effectiveness of vaccination campaigns, (2) guide actions to limit VOCs that diminish effective vaccination, and (3) advance scientific understanding about the nature of the uncertainty of viral evolution.

See the initial November 2020 Paper [here](https://cra.org/ccc/wp-content/uploads/sites/2/2020/11/Pandemic-Informatics_-Preparation-Robustness-and-Resilience.pdf).