

LAY ABSTRACT

Our project aligns with the FY23 PRMRP Portfolio Category: Infectious Diseases, FY23 PRMRP Topic: proteomics, and FY23 PRMRP Strategic Goal: Epidemiology: Identify strategies for surveillance or develop modeling tools and/or biomarkers to predict outbreaks or epidemics.

Influenza A viruses have the potential to cause devastating pandemics, and ongoing surveillance efforts are insufficient to reliably identify and rank strains with high pandemic potential. The current solution to this problem, the Influenza Risk Assessment Tool (IRAT) by the CDC, is subjective and slow requiring multiple experimental assays, and thus cannot keep up with the scale of current global biosurveillance efforts.

To address this challenge, we propose to develop the BioNORAD platform to proactively identify the risks posed by emerging Influenza A strains with high pandemic potential. The platform will use novel pattern discovery algorithms to automatically parse evolutionary constraints operating on Influenza A viruses in the wild, and provide an experimentally validated scalable solution to emergence prediction.

The Emergenet algorithm, at the core of the BioNORAD platform, is the first of its kind to learn an adaptive biologically meaningful comparison metric from data, enabling an actionable pandemic early warning system. By reliably estimating the numerical probability of a strain giving rise to another strain in the wild, the platform can preempt strains expected to be in future circulation, and approximate IRAT scores of non-human strains without experimental assays or subject matter expert scoring.

We will validate this core algorithm by demonstrating that Emergenet predicted variations of genes from strains observed in the wild express correctly on host cell surfaces, are functional, and do not lose replicative fitness, and hence present potential future variants.

Ultimately the inferred models will be used to power the BioNORAD platform that can track global threats from potential near-time emergence events as new strains are uploaded to the platform, along with estimates of the threat severity and estimated time to emergence.

This represents a transformative capability, addressing the problem of unknown unknowns in the field of emergence modeling: state of the art tools are severely limited in their ability to predict or track emergence of novel strains. This knowledge gap renders the current substantial bio-surveillance efforts largely ineffective for precise actionable prediction of emergence events. These surveillance paradigms, while crucial for mapping disease ecosystems, fail to address the challenge of higher edit-similarity between strains not implying a high likelihood of a jump. Ongoing efforts at tracking and modeling ecological factors driving up the odds of zoonotic spill-over, while expensive, have not improved our ability to quantify future risk of emergence of a specific strain from a specific host. Recent reported advances in predicting seasonal epidemic strain distributions do not generalize to predicting emergence events as well, especially for novel subtypes that do not yet circulate in humans.

By automating the analysis of influenza strains, the BioNORAD platform has the potential to revolutionize our ability to prevent pandemics before they emerge. It is a transformative technology that is urgently needed in a world where pandemics are a growing concern. By providing early warning of emerging strains, the platform can help prevent widespread outbreaks and save lives.

Furthermore, the BioNORAD platform has the potential to enable more proactive vaccination efforts. By identifying animal reservoirs of emerging strains before they jump to humans, public health officials could vaccinate these animals and prevent the emergence of pandemic strains, saving countless lives.

The BioNORAD platform can play a crucial role in protecting DoD assets and personnel deployed in potentially high-risk centers of emergence, and may make prophylactic inoculation possible against future strains. Thus, the investment in the BioNORAD platform is a strategic step towards ensuring the health and safety of military personnel and the success of the DoD's mission in a world where pandemic threats are a growing concern.

Our project is a collaborative effort between experts in computer science, biology, and epidemiology, and all tools, software and data generated will be shared in accordance with DoD mandates. This interdisciplinary approach is essential for developing a platform that can effectively address the complex problem of predicting pandemic risk. By bringing together experts from different fields, the platform can take advantage of cutting-edge advances in machine learning, bioinformatics, and epidemiology.