Characterizing evolution pressures in Sars-CoV-2 on a broader scale

Peter C. Jentsch[1,4], Finlay Maguire[3,5], and Samira Mubareka[1,2]

[1] *Sunnybrook Research Institute, Toronto, Canada*
[2] *University of Toronto, Toronto, Canada*
[3] *Dalhousie University, Halifax, Canada*
[4] *Simon Fraser University, Burnaby, Canada*
[5] *Shared Hospital Laboratory, Toronto, Canada*

October 12, 2022

1 Background

Previous work on these models do not use data to estimate parameters, focusing on broad characterization of dynamics with numerical or analytical approaches. However, genomic data does include a huge amount of admittedly very noisy information. There is some recent work on parameter estimation by comparing simulated phylogeny with observed phylogeny using a suite of summary statistics for tree structures [2, 4, 6], but these models do not explicitly include genomic structure, which might provide additional inferential power.

Placing individual samples into the collapsed strain space could be done by using neutralizing antibody studies. The neutralizing response has been characterized for most variants of concern with respect to monoclonal antibodies, convalescent plasma, and plasma from vaccinated persons [9]. To an even higher level of detail. Starr et al. characterized polyclonal antibody binding over all mutations of the Receptor Binding Domain (RBD) [8]. If the neutralizing response is known, we assign strains positions such that the distance between any two strains is equal to that neutralizing response. If the response is not known, we just assume that the position is close to the most recent ancestor for which the response is known (likely a VoC). This approach is especially appropriate for recurrent mutations, since it is unlikely that a mutation that has occurred many times in the viral history but has not evolved further confers a significant advantage. The immune-space position of vaccinate-induced immunity can also be computed this way, although we will still need to make significant assumptions on their geometry. It might be best to assume a simple symmetric shape with a centre given by neutralization results.

Mirroring the work on mapping the strain space for influenza [1,3,7] computing this embedding is a metric multidimensional scaling problem. This method

has been applied to the antigenic space of the Sars-CoV-2 as well [5, 10, 11].

2 Methods

References

[1] Zhipeng Cai, Tong Zhang, and Xiu-Feng Wan. A computational framework for influenza antigenic cartography. *PLoS computational biology*, 6(10):e1000949, 2010.

[2] Gonché Danesh, Victor Virlogeux, Christophe Ramière, Caroline Charre, Laurent Cotte, and Samuel Alizon. Quantifying transmission dynamics of acute hepatitis c virus infections in a heterogeneous population using sequence data. *PLoS pathogens*, 17(9):e1009916, 2021.

[3] Alan Lapedes and Robert Farber. The Geometry of Shape Space: Application to Influenza. *Journal of Theoretical Biology*, 212(1):57–69, September 2001.

[4] Gabriel E Leventhal, Roger Kouyos, Tanja Stadler, Viktor Von Wyl, Sabine Yerly, Jürg Böni, Cristina Cellerai, Thomas Klimkait, Huldrych F Günthard, and Sebastian Bonhoeffer. Inferring epidemic contact structure from phylogenetic trees. *PLoS computational biology*, 8(3):e1002413, 2012.

[5] Nathaniel L. Miller, Thomas Clark, Rahul Raman, and Ram Sasisekharan. An Antigenic Space Framework for Understanding Antibody Escape of SARS-CoV-2 Variants. *Viruses*, 13(10):2009, October 2021.

[6] Emma Saulnier, Olivier Gascuel, and Samuel Alizon. Inferring epidemiological parameters from phylogenies using regression-abc: A comparative study. *PLoS computational biology*, 13(3):e1005416, 2017.

[7] Derek J. Smith, Alan S. Lapedes, Jan C. de Jong, Theo M. Bestebroer, Guus F. Rimmelzwaan, Albert D. M. E. Osterhaus, and Ron A. M. Fouchier. Mapping the Antigenic and Genetic Evolution of Influenza Virus. *Science*, 305(5682):371–376, July 2004.

[8] Tyler N Starr, Allison J Greaney, Sarah K Hilton, Daniel Ellis, Katharine HD Crawford, Adam S Dingens, Mary Jane Navarro, John E Bowen, M Alejandra Tortorici, Alexandra C Walls, et al. Deep mutational scanning of sars-cov-2 receptor binding domain reveals constraints on folding and ace2 binding. *Cell*, 182(5):1295–1310, 2020.

[9] Philip Tzou, Kaiming Tao, Janin Nouhin, Soo-Yon Rhee, Benjamin Hu, Shruti Pai, Neil Parkin, and Robert Shafer. Coronavirus antiviral research database (cov-rdb): An online database designed to facilitate comparisons between candidate anti-coronavirus compounds. *Viruses*, 12(9):1006, Sep 2020.

[10] Karlijn van der Straten, Denise Guerra, Marit van Gils, Ilja Bontjer, Tom G Caniels, Hugo D van Willigen, Elke Wynberg, Meliawati Poniman, Judith A Burger, Joey H Bouhuijs, et al. Mapping the antigenic diversification of sars-cov-2. *medRxiv*, 2022.

[11] Samuel H. Wilks, Barbara Mühlemann, Xiaoying Shen, Sina Türeli, Eric B. LeGresley, Antonia Netzl, Miguela A. Caniza, Jesus N. Chacaltana-Huarcaya, Xiaoju Daniell, Michael B. Datto, Thomas N. Denny, Christian Drosten, Ron A. M. Fouchier, Patricia J. Garcia, Peter J. Halfmann, Agatha Jassem, Terry C. Jones, Yoshihiro Kawaoka, Florian Krammer, Charlene McDanal, Rolando Pajon, Viviana Simon, Melissa Stockwell, Haili Tang, Harm van Bakel, Richard Webby, David C. Montefiori, and Derek J. Smith. Mapping SARS-CoV-2 antigenic relationships and serological responses. Preprint, Immunology, January 2022.