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Game-Theoretic Approach Explains – on the Qualitative Level – the Antigenic Map of Covid-19 Variants

Olga Kosheleva, Vladik Kreinovich, and Nguyen Hoang Phuong

Abstract To effectively defend the population against future variants of Covid-19, it is important to be able to predict how it will evolve. For this purpose, it is necessary to understand the logic behind its evolution so far. At first glance, this evolution looks random and thus, difficult to predict. However, we show that already a simple game-theoretic model can actually explain – on the qualitative level – how this virus mutated so far.

1 Formulation of the Problem

An important problem. Like many viruses, the virus that causes Covid-19 rapidly evolves, so that vaccines which are very efficient for the original variants are not as efficient for the new variants. To be better prepared for the future variants, it is desirable to predict how the virus will evolve in the future. To be able to do it, we need to understand how (and why) it evolved the way it did.

The problem looks complicated. A recent map [1, 2] provides a visual 2-D description of the evolution of the main Covid-19 variants, from the original Alpha to Beta, Gamma, Delta, and Omicron. At first glance, the changes look somewhat random

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and chaotic, leaving us with an impression that probably no reasonable predictions are possible.

What we do in this paper. In this paper, we show that, at least on the qualitative level, natural game-theoretic ideas explain the current evolution – and thus, hopefully enable us to predict the direction of future changes.

2 A Simplified Game-Theoretic Model and the Resulting Explanation

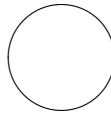
Main idea. As the virus starts affecting the population, people’s bodies start developing antibodies to the virus’s original version. So, to stay effective, the virus has to mutate. The mutated version also causes the bodies to develop protection, so further mutations are needed.

The larger the distance between the two variants A and B , the less effective A -caused antibodies against the variant B . Thus, from the virus’s viewpoint, after variants A_1, \dots, A_n , it makes sense to select, as the next variant, the variant A for which the smallest of the distances $\min(d(A, A_1), \dots, d(A, A_n))$ is the largest possible – this will guarantee that the new variant will be the most effective against all A_i -produced antibodies.

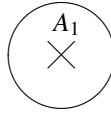
If there are several variants A with this largest value, then, for the virus, it is reasonable to select the variant for which the second smallest of the distances $d(A, A_i)$ is the largest, etc.

Comment. Of course, the virus is not an intelligent being, it does not directly select its next mutation: mutations happen randomly, some lead to more effective variants, some to less effective ones, and the most effective one becomes dominant. In this sense, after the variants A_1, \dots, A_n , the next effective one – the next dominant variant – is the one for which the value $\min(d(A, A_1), \dots, d(A, A_n))$ describing the variant’s effectiveness is the largest.

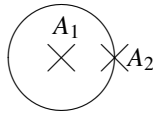
Let us trace this idea on a simple geometric example. In the 2-D description, all possible variants belong to some reasonable planar area. Let us consider the simplest case, when this area is a disk:



The first variant A_1 appears somewhere inside this disk-shaped area. For simplicity, let us assume that it is located in the center of the disk:

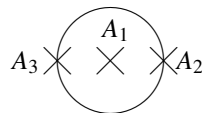


Following the above description, as the next variant A_2 , we select the point in the disk for which the distance to the center is the largest possible. One can easily see that the largest possible distance is equal to the radius r of the disk, and this distance is attained at any point on the corresponding circle. So, the next variant is located on the circle that borders the disk:

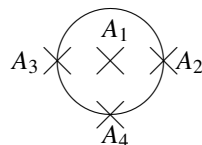


What happens next? The distance from any point A inside the disk to its center A_1 cannot exceed r . So the smallest distance from A to points A_1 and A_2 cannot be larger than r . So, ideally, as the next point A_3 , we should select a point A for which this smallest distance $\min(d(A, A_1), d(A, A_2))$ is equal to the largest possible value r . This means, in particular, that the distance $d(A, A_1)$ is at least r – and since this distance cannot exceed r , this means that it must be exactly equal to r , i.e., that the point A_3 should also be located on the circle.

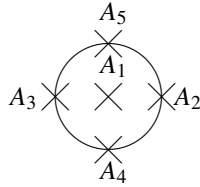
All the points A on the circle has the exact same distance $d(A, A_1)$. So, in line with the above description, of all points A from the circle, we should select the point for which the distance $d(A, A_2)$ is the largest possible. One can see that this largest distance – equal to $2r$ – is attained when the point A_3 is on the same line as A_1 and A_2 but on the opposite side of A_1 :



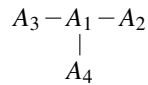
What now? Similarly to the previous case, we can conclude that the next point A_4 should also be located on the circle, and it should be selected in such a way that the smallest of the two distances $\min(d(A, A_2), d(A, A_3))$ should be the largest possible. One can check that this point should be located on the circle exactly in the middle between A_2 and A_3 :



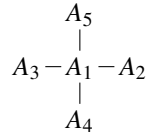
Similarly, the next point A_5 should be located on the same circle, also exactly in the middle between A_2 and A_3 :



Let us map the consequent locations of different variants. If we map the locations of variants A_1 through A_4 , then we get the following picture:



If we add A_5 , then we get the following:



On the qualitative level, the A_1 - A_4 map is almost exactly the Covid-19 antigen map. Indeed, we start with the first variant Alpha (A_1 in our notations). Then, the variant Beta (A_2) is one side of A_1 , while the variant Delta (A_3) is approximately on the same line on the other side of A_1 . (We skipped Gamma, which is exactly in between Beta and Delta on the antigen map, so it must simply be a transitional state.)

Then comes Omicron (A_4) which is obtained by moving in a different direction than before.

So what next? Our model's prediction is the next variant A_5 will be along the line A_1A_4 , but on the other side of A_1 than Omicron (A_4).

Of course, this is a very crude model. The above model is very approximate. For example, in this model the distance from all three consequent variants to the original variant A_1 is the same, while in reality, the distance from Alpha (A_1) to Omicron (A_4) is much larger than the distances from Alpha to Beta and Delta.

However, the fact that this simple model explains the seemingly random changes gives us hope that a further development of this model can lead to quantitative explanations – and thus, more reliable predictions.

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