Modeling Antibody Levels Post SARS-CoV-2 Infection

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Introduction and Goals

Using SARS-CoV-2 antibody data from convalescent patients obtained from a longitudinal study by Yang et al:

- Model SARS-CoV-2 antibody data with higher dimensionality and capture time dependence of antibody response.
- Select variables for better data separation and biological significance.
- visualize patterns in the variability in immune response within a population of patients infected with SARS-CoV-2 over time.

Definition (Antibodies)

- Proteins that bind to viral antigens.
- Mark antigens for destruction or block cell entry.
- Quantitatively measure immune response.
- IgG and IgA: immunoglobulin G and A, respectively; types of antibodies.
- Anti-RBD and N: Indicates the antibody targets the receptor binding domain 'spikes' or the nucleocapsid surface on the virus, respectively

Definition (Maximum Likelihood Estimation)

- Optimizes the parameters of a probabilistic distribution function to maximize the likelihood of observing a given set of data, assuming an underlying distribution.
- Numerically, the parameters are identified by minimizing the negative logarithm of the likelihood function (the product of the pdf evaluated at each point in the dataset).
- As opposed to a deterministic model, probabilistic models are better suited to capturing variability in natural phenomena.

Let $\vec{x}$ = a list of data points $(x_1 \ldots x_n)$

Let $P(\vec{x}, \vec{p})$ = model with data $\vec{x}$ and list of parameters $\vec{p}$

Optimize the negative log likelihood over the parameters $\vec{p}$:

$$\min\left(-\ln L(\vec{p})\right) = \min\left(-\sum_{i=1}^{n} \ln P(x_i, \vec{p})\right)$$

Selecting the Gamma Distribution

- Following Bedekar et. al. (1), we select a gamma distribution to model immune response.
- Frank, 2009 (2) indicates that many biological phenomena follow this distribution.
- This distribution has two parameters: shape and scale.

$$f(r, a, b) = \frac{r^{a-1} e^{-r/b}}{\Gamma(a) b^a} \tag{1}$$

Model Details

- Figure 1 depicts a convalescent population antibody levels over time.
- the gamma distribution equation is modified to reflect the time dependence

Time-dependent gamma distribution:

$$a(t) = \frac{\theta_1 t}{1 + (\theta_2 t^2)} + a \tag{2}$$

$$f(r, a(t), b) = \frac{r^{a(t)-1} e^{-r/b}}{\Gamma(a(t)) b^{a(t)}} \tag{3}$$

- The modifications seen above are done to naturally show that at time t = 0 the equation will simplify to:

$$a(0) = a$$

which simplifies to the negative distribution

- Similarly another biological phenomenon that is accounted for is

$$\lim_{t \to \infty} a(t) = a$$

which demonstrates that as time approaches infinity the positive results will decay to similar levels as the negative distribution

- Figure 2 plots the distribution of nucleocapsid antibodies against receptor binding domain antibodies
- We use the assumption that these antibodies are independent of one another to be able to multiply their respective probability density functions and obtain the equation:

$$f(x, y, a_x, b_x, a_y, b_y) = \gamma(x, a_x, b_x) * \gamma(y, a_y, b_y) \tag{4}$$

- When the two antibodies are plotted we see a linear correlation in the data which is also represented by the gamma distribution in Figure 2 naturally
- Though we assume independence, the correlation of the data does not require any additional change of variables to uncorrelated variables to account for it.
- Figure 3 plots three antibodies: anti-RBD IgG, anti-N IgG, and anti-RBD IgA
- This represents the first step in generating 3 dimensional models similar to what was done for the 2 dimensional model in Figure 2

Graphics

Figure 1: Time Dependent Probability Model of Anti-RBD IgG

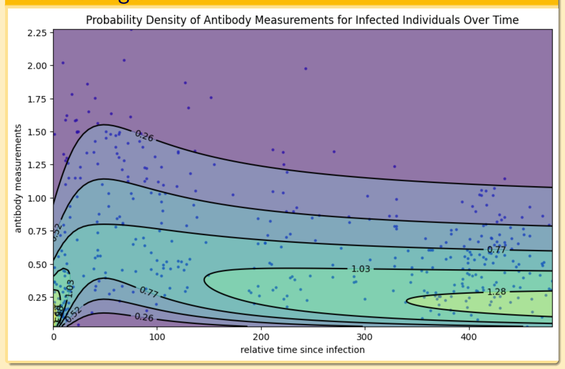


Figure 2: 2D Probability Model of Anti-RBD IgG and Anti-N IgG

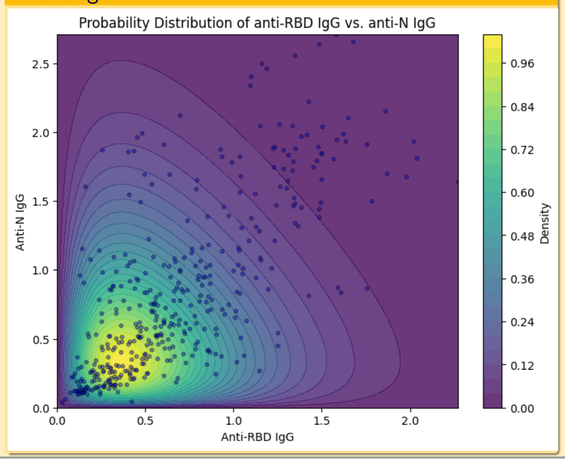
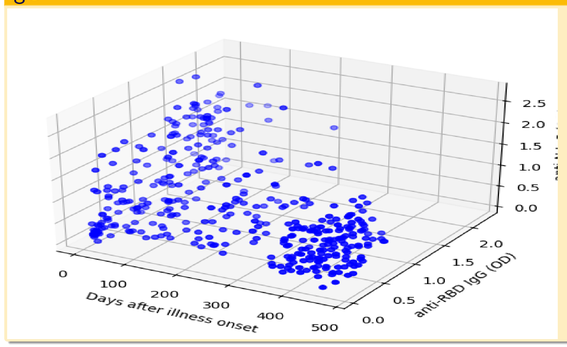


Figure 3: 3D Scatterplot of Anti-RBD IgG and IgA and Anti-N IgG



Conclusions/Future Work

- Expand dimensionality to 3 dimensions, and later 4 dimensions, for better data separation and understanding the structure of the data by identifying biologically significant variables.
- Prevalence Estimation to determine the percentage of the population that has certain characteristics of interest.
- Predict positive versus negative cases.

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References

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