

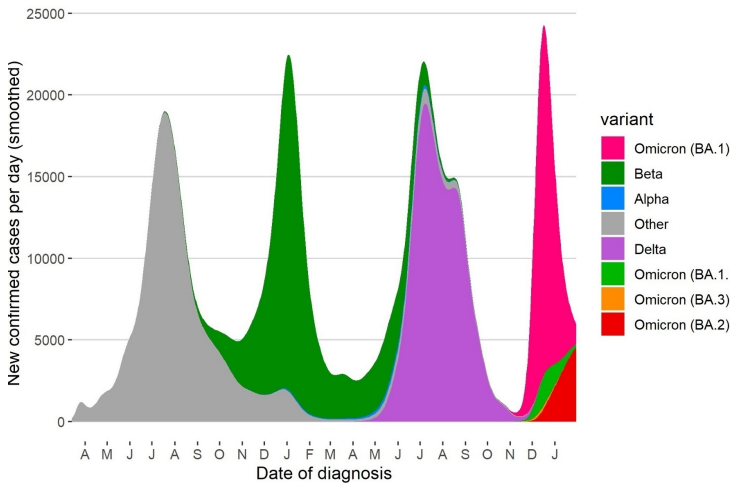
The Calculus of Covid Variant Competition

DOmath 2022, Team 3

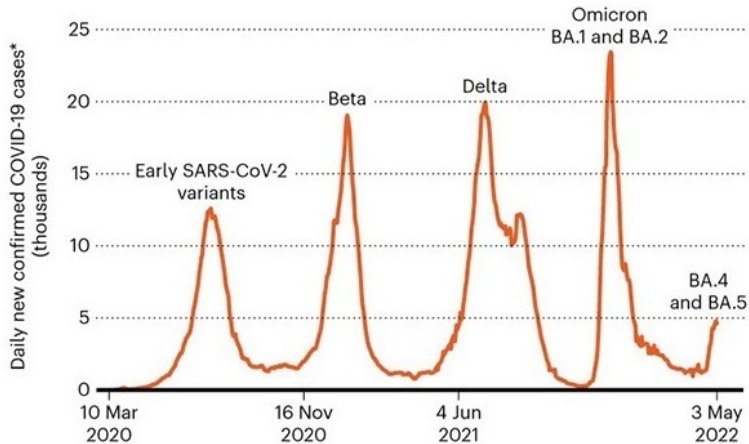
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June 15, 2022

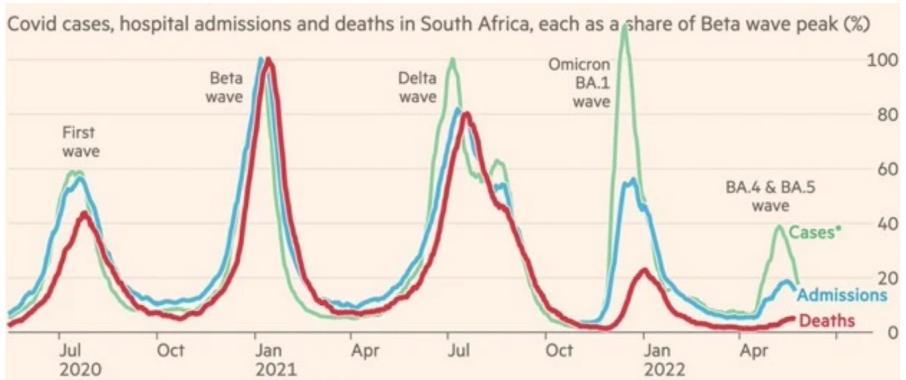
How the dominant covid strain has progressed in South Africa



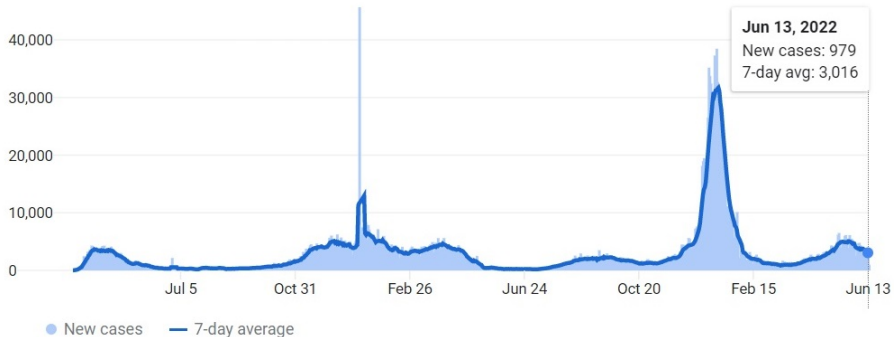
and in the United States



South Africa data suggests the fifth wave will not be severe.



New Jersey data shows that the fifth wave has peaked, while Beta and Delta were small compared to Omicron.



Take home messages for the talk

Math. Change of variables in the ODE for the competition of covid variants shows that $x(t) = I_2/(I_1 + I_2)$ satisfies the logistic differential equation

$$x'(t) = \lambda(t)x(t)(1 - x(t))$$

which models selective sweeps. Data shows that this correctly predicts the rapid turnover from one dominant variant to another.

Biology. Evolution has worked in our favor. The virus has evolved to be more transmissible, which means adapting to replicate faster in the nasal passages rather than in the lungs. Our analysis (and expert opinion) suggests that new variants that are successful will be the ones that can evade immunity from infection by previous strains.

Delta variant (B.1.617.2)

Notation comes from the phylogeny of samples.

First identified in India in late 2020, Delta had additional mutations that increase the ability of the spike protein to infect cells.

Delta was believed to be more than twice as contagious as previous variants, and studies have shown it to be more likely than the original virus to put infected people in the hospital.

It swept rapidly through that country and Great Britain before reaching the U.S., where it quickly surged and became the predominant SARS-CoV-2 variant.

Beta to Delta transition (cross immunity)

If we take a two strain SIR model and write it in terms of the scaled variables $s = S/N$, $i_j = I_j/N$, and $r = R/N$ we have

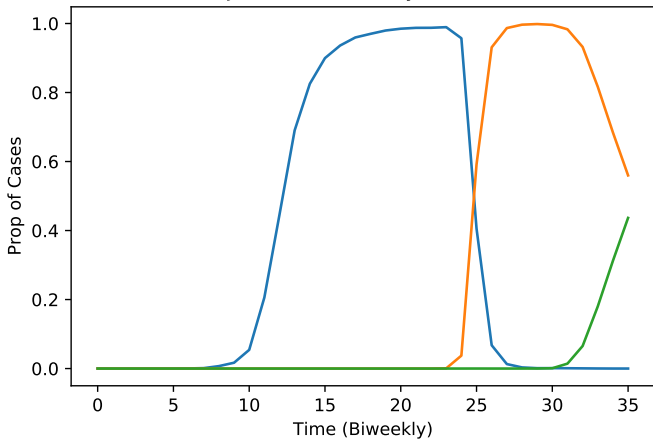
$$\begin{aligned}\frac{ds}{dt} &= -s(\beta_1 i_1 + \beta_2 i_2) \\ \frac{di_1}{dt} &= s\beta_1 i_1 - \gamma_1 i_1 \\ \frac{di_2}{dt} &= s\beta_2 i_2 - \gamma_2 i_2\end{aligned}$$

Let $x(t) = i_2(t)/(i_1(t) + i_2(t))$ and assume $\gamma_1 = \gamma_2$:

$$x'(t) = \lambda x(t)(1 - x(t)) \quad \lambda = (\beta_2 - \beta_1)s(t) \quad (1)$$

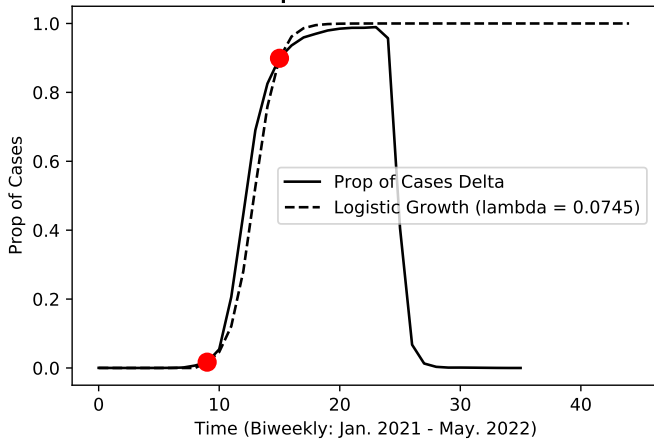
which is a Logistic differential equation (selective sweep).

Proportion of Cases By Strain (U.S.)
Jan 11 2021 - May 2 2022

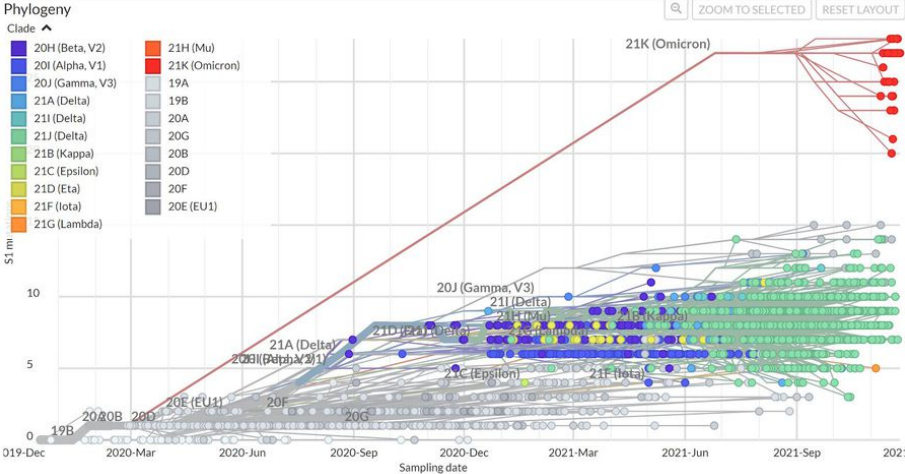


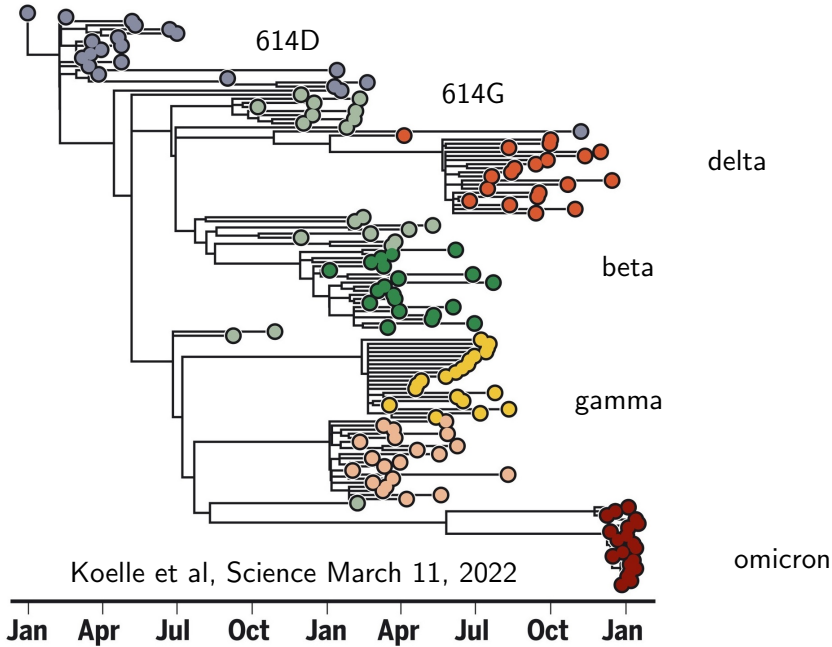
blue Delta, orange Omicron BA1's and 2's, green BA.4/5

Proportion Delta



Emergence of Omicron Dec 3, 2021, Science





Delta to Omicron (breakthrough infections)

r_1 immune to Delta due to previous infection or vaccination

$$\frac{ds}{dt} = -s(\beta_1 i_1 + \beta_2 i_2)$$

$$\frac{di_1}{dt} = s\beta_1 i_1 - \gamma i_1$$

$$\frac{di_2}{dt} = s\beta_2 i_2 + r_1\beta_2\theta i_2 - \gamma i_2$$

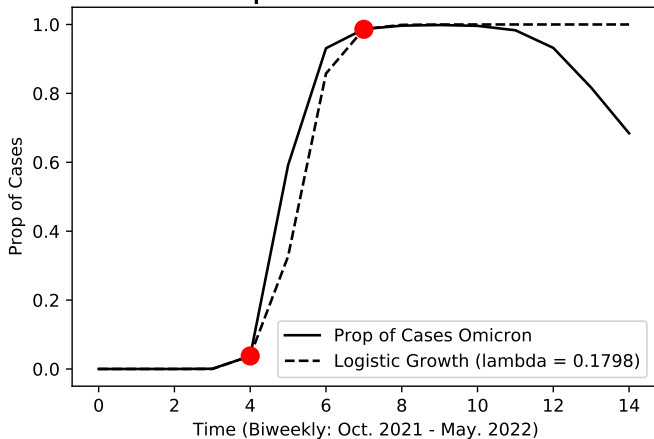
$$\frac{dr_1}{dt} = \gamma i_1 - r_1\beta_2\theta i_2$$

Letting $x = i_2/(i_1 + i_2)$ we have

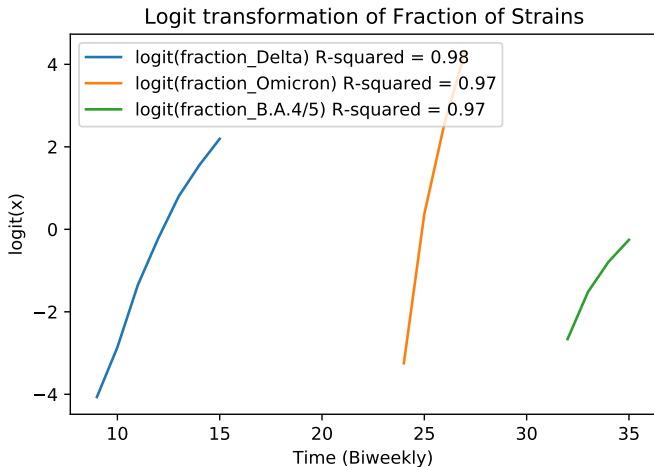
$$x'(t) = \lambda x(t)(1 - x(t)) \quad \lambda = (\beta_2 - \beta_1)s(t) + \theta\beta_2 r_1(t) \quad (2)$$

$\lambda = 0.1758$ here versus 0.0745 for Beta to Delta

Proportion Omicron



If $x(t)$ satisfies the logistic equation then $\log[x(t)/(1 - x(t))]$ is linear.
Curvature indicates reduction in $s(t)$? or spatial stucture?.



Omicron variants - early

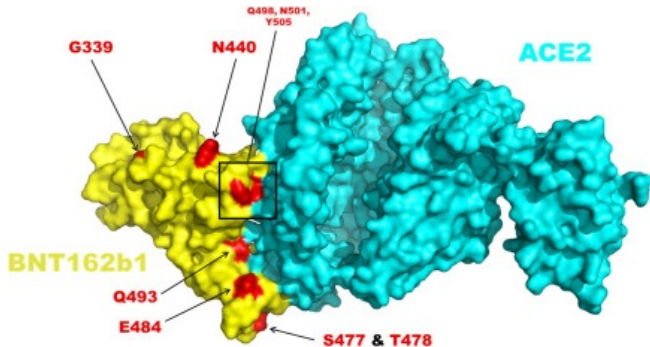
BA.1, BA.2 diverged in Feb 2021 before emerging in South Africa in Oct 2021. The BA.2 variant spreads more quickly than BA.1. Antibodies against BA.1 can protect against BA.2

BA.1.1 is BA.1 with a R346K mutation in the spike protein.]

B.1.1.529 identified in Botswana November 11, 2021 was labeled as a variant of concern due to its 30 mutations in the spike protein including 15 mutations in the receptor binding domain (RBD).

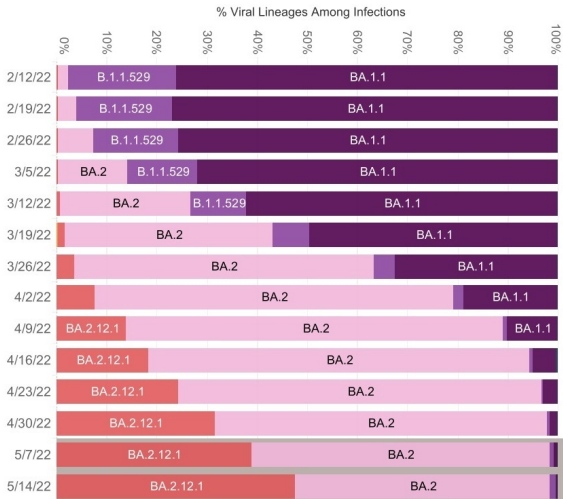
BA.2.12.1 carries BA.2 a mutation in a section of its spike protein called L452Q which has helped other COVID-19 variants, including Delta and Lambda, to become more transmissible.

The new omicron variants improve the binding of the spike protein to the cell surface protein ACE2 which it uses to enter cells



BNT162b2 is a lipid nanoparticle–formulated, nucleoside-modified RNA vaccine that encodes a prefusion stabilized, membrane-anchored SARS-CoV-2 full-length spike protein used in vaccines.

Omicron Variants: US National Data, Fractions



Multivariate competition

$$\frac{di_1}{dt} = s\beta_1 i_1 - \gamma i_1$$

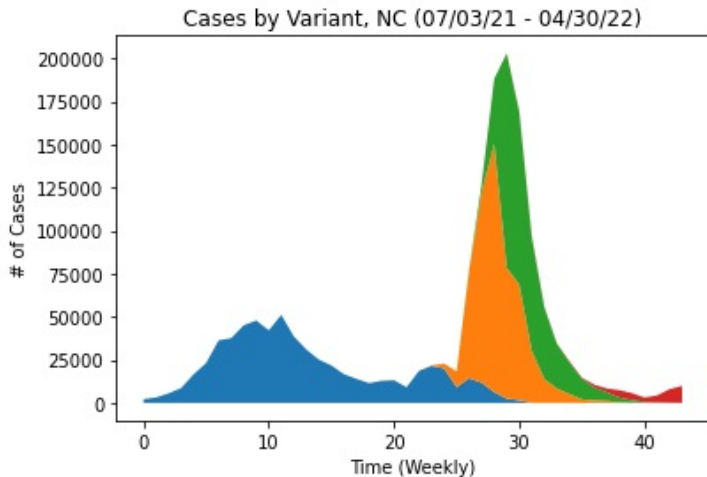
$$\frac{di_2}{dt} = s\beta_2 i_2 - \gamma i_2$$

$$\frac{di_3}{dt} = s\beta_3 i_3 - \gamma i_3$$

letting $x_k = i_k / (i_1 + i_2 + i_3)$ and $\ell < m$ be the other two indices

$$\frac{dx_k}{dt} = x_k x_\ell (\beta_k - \beta_\ell) s(t) + x_k x_m (\beta_k - \beta_m) s(t)$$

Omicron Variants: North Carolina Cases



Blue: Delta, Orange: B.1.1.529, **before** Green: BA.1.1, Red: BA.2

BA.4 and BA.5

The earliest samples of these variants were collected at the end of March 2022. Generally they cause mild disease but spread in large numbers potentially because unlike the Wuhan strain, which settles in the lungs, these new variants seem to attach to the more benign upper nasal passage. The incubation time of these new variants seems to be slightly shorter (2 to 3 days).

The two sub-variants are often discussed together because the mutations in the spike protein are the same.

They have shown a remarkable ability to evade immunity from vaccines, previous infection or both. (Science 13 May 2022, 679–680)

Future covid variants

Immune escape will be important for success

$$x'(t) = \lambda x(t)(1 - x(t)) [(\beta_2 - \beta_1)s(t) + \theta\beta_2 r_1(t)]$$

(Nature 9 December 2021, p. 204-207) Studies suggest that Delta made significant improvement in its ability to infect human cells. Yet researchers expect such gains to become even smaller.

Sarah Cobey, an evolutionary biologist at U. of Chicago. As gains in infectivity start to slow, the virus will have to maintain its fitness by overcoming immunity.

Kristian Andersen of Scripps Research: Variants such as Omicron that gain much of their transmission advantage from evading immune response may become the norm, as is the case for seasonal influenza.

References

Callaway, E. (9 Dec 2021) Beyond Omicron: What's next for SARS-CoV2 Evolution? *Nature*. 600, 204–208 **excellent article by a Nature staff member**

Katelyn Jetelina's blog **great series by an asst. prof.**
<https://yourlocalepidemiologist.substack.com>

Koelle, K., et al (11 March 2022) The changing epidemiology of SARS-CoV2. *Science*. 375, 1116–1121 **good survey of “early evolution”**

Jackson, Cody B. (2022) Mechanisms of SARS-CoV-2 entry into cells. *Nature Reviews Molecular Cell Biology*. 23, 3-20
an 18 page summary of 300 papers. good luck reading this.