

Phylogenetics for Predicting Virus Evolution

Can we anticipate next seasons dominant influenza strain from sequence alignment?

Paul Wiesemeyer

Problem

- Influenza evading immunity
- Pandemics as with SARS-CoV-2
- "Houston, we have aah—CHOO!"
- 3 – 11% of the population catch symptomatic influenza each season. CITATION
- Influenza mutates quickly at \sim 2 mutations / kilobases / year
- No one can tell next seasons circulating influenza strains.
- Antigenic shift can cause sudden epidemics and even pandemics.
- How can we take informed counter measures on a global level?

Outline for Section 1

1. Influenza and Vaccines
 - 1.1 Basics
 - 1.2 The Hemagglutination Inhibition Assay
2. Phylogenetics
 - 2.1 The Molecular Clock
 - 2.2 Sequence Alignment
 - 2.3 Building A Phylogenetic Tree
3. *Nextstrain*
 - 3.1 How to use the Framework
 - 3.2 The Powerful Metadata
 - 3.3 Confidence Levels and Limitations

Influenza and Vaccines

Influenza—an artful disguise master

Basics

Where does influenza come from?

- *Zoonotic events*, the jumping from one species to another.
- *Antigenic shift* events, when different virus types infect the same host cell and recombine their 8 RNA parts.
- *Antigenic drift*, driven by point mutations and *indels*

Basics

Antigenic shifts and zoonoses can cause pandemics

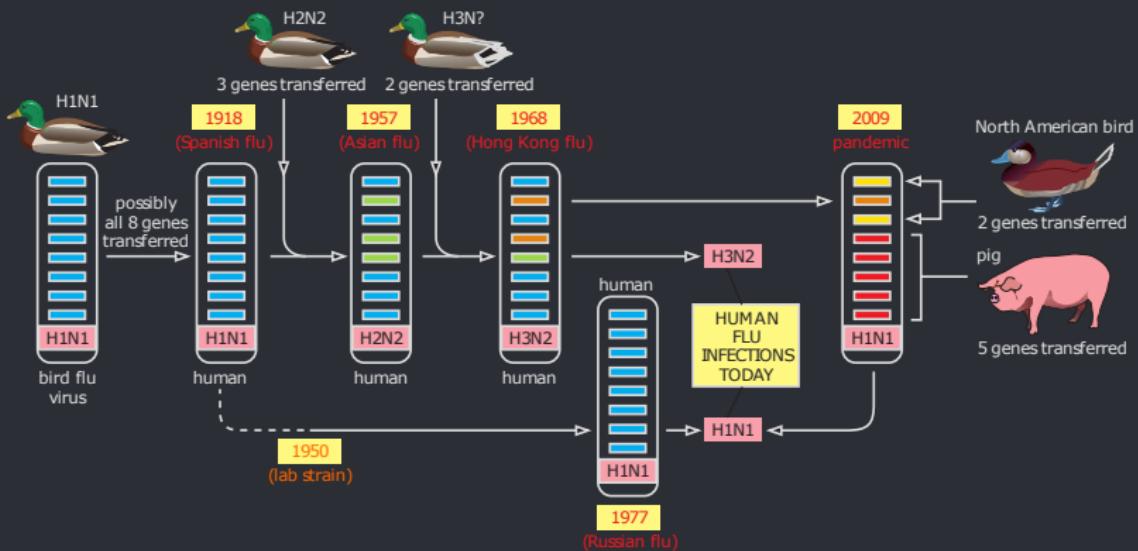


Figure: taken from [Alberts, 2015]

Basics

Antigenic drift—a race

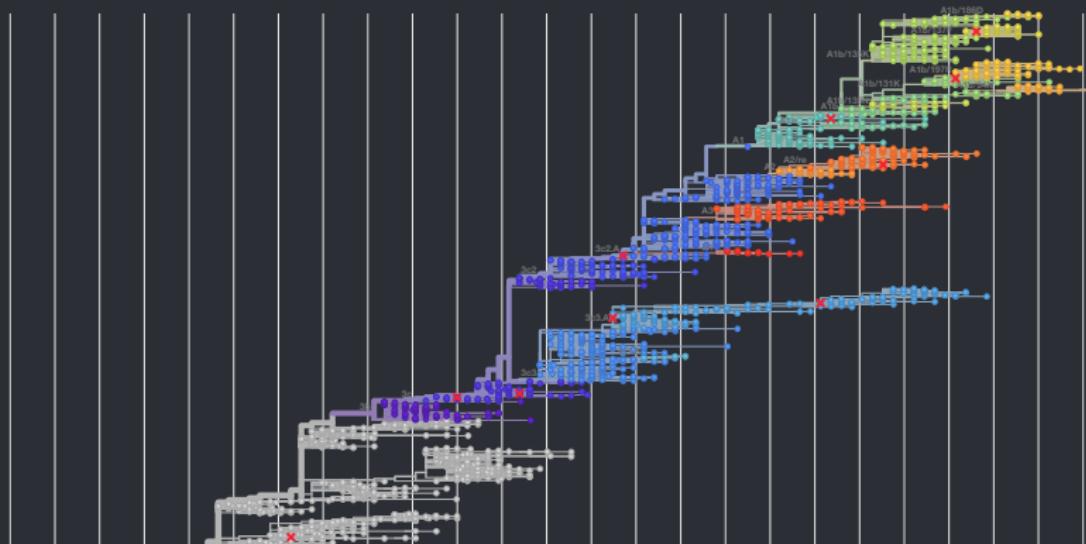


Figure: Here, one antiserum is tested in 12 different dilutions against 8 different virus strains. The highest dilution that prevents agglutination is called the titer.

Basics

Antigenic drift—a race



Figure: Here, one antiserum is tested in 12 different dilutions against 8 different

The Hemagglutination Inhibition Assay

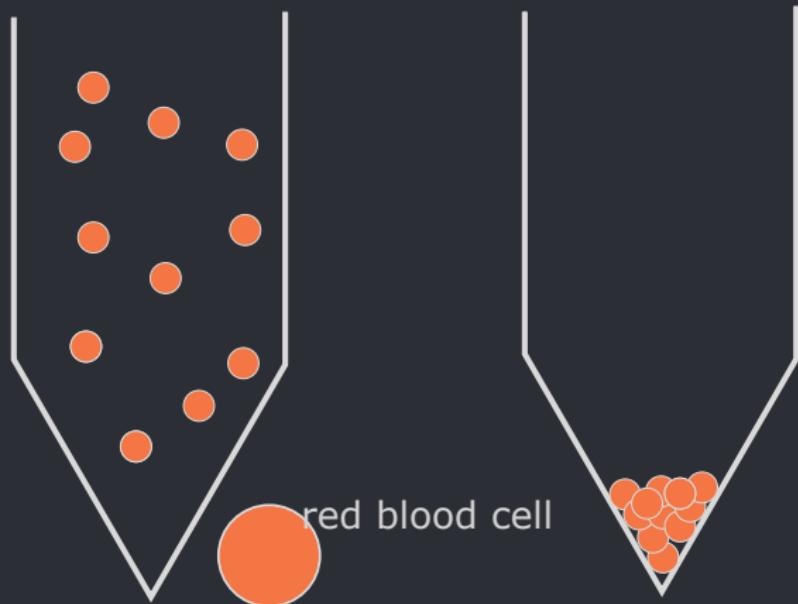


Figure: Red blood cells (RBC) precipitate.

The Hemagglutination Inhibition Assay

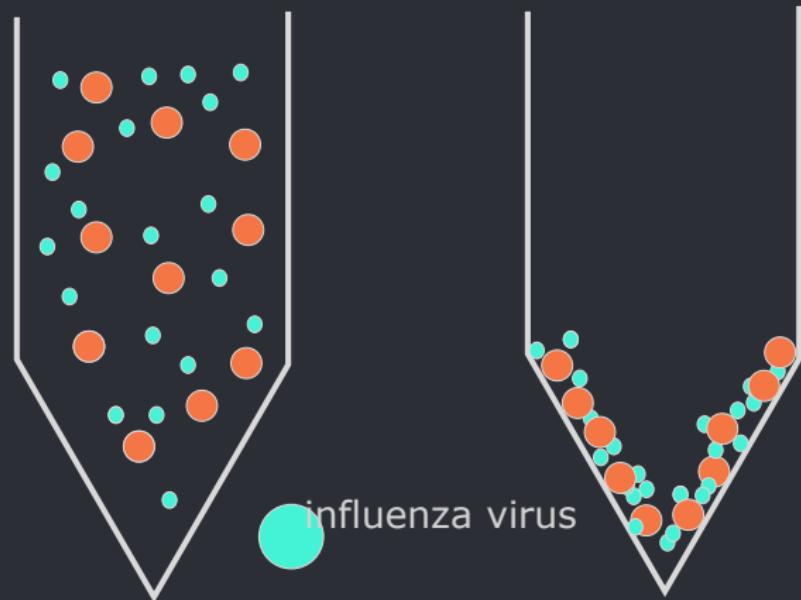


Figure: Influenza Hemagglutinin (HA) coagulates the RBC, forming a mat.

The Hemagglutination Inhibition Assay

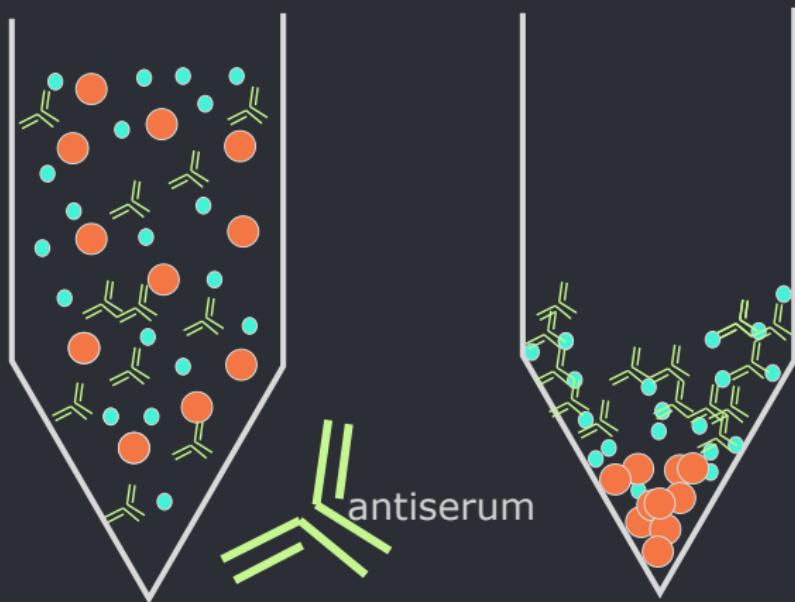


Figure: Antisera of the same serotype clump the HA, letting the RBC sink to the bottom. This is an (antiserum) concentration dependent process.

The Hemagglutination Inhibition Assay

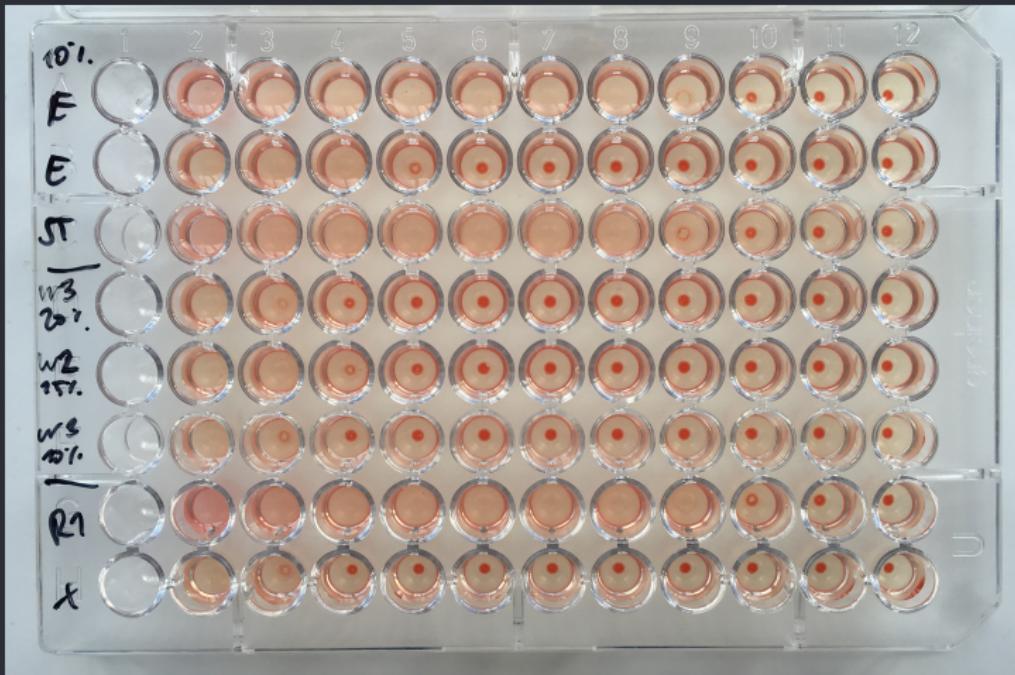


Figure: Here, one antiserum is tested in 12 different dilutions against 8 different virus strains. The highest dilution that prevents agglutination is called the titer.

Outline for Section 2

1. Influenza and Vaccines
 - 1.1 Basics
 - 1.2 The Hemagglutination Inhibition Assay
2. Phylogenetics
 - 2.1 The Molecular Clock
 - 2.2 Sequence Alignment
 - 2.3 Building A Phylogenetic Tree
3. *Nextstrain*
 - 3.1 How to use the Framework
 - 3.2 The Powerful Metadata
 - 3.3 Confidence Levels and Limitations

Phylogenetics

An old idea

Phylogenetics: The Molecular Clock

Phylogenetics: Sequence Alignment

Phylogenetics: Building A Phylogenetic Tree

—from sequenced data

Outline for Section 3

1. Influenza and Vaccines

1.1 Basics

1.2 The Hemagglutination Inhibition Assay

2. Phylogenetics

2.1 The Molecular Clock

2.2 Sequence Alignment

2.3 Building A Phylogenetic Tree

3. *Nextstrain*

3.1 How to use the Framework

3.2 The Powerful Metadata

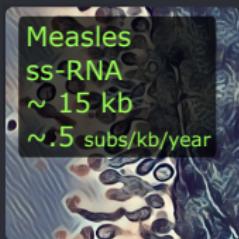
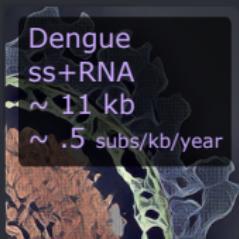
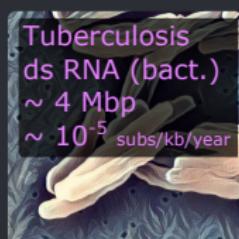
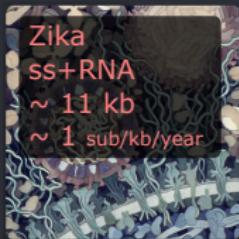
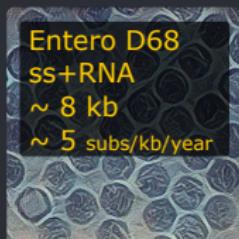
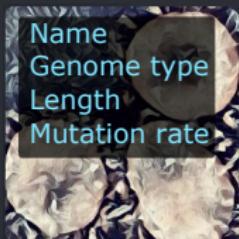
3.3 Confidence Levels and Limitations

Nextstrain

Mending pieces together

Please visit nextstrain.org/narratives/

Nextstrain: How to use the Framework (this is mirrored in the narrative)



Nextstrain: The Powerful Metadata

(this is mirrored in the narrative)

Nextstrain: Confidence Levels and Limitations

(this is mirrored in the narrative)

Conclusion

...and why Nextstrain is awesome

References

[Alberts, 2015] Alberts, B. (2015).
Molecular biology of the cell.