Multi-host Modelling of Influenza A

Edward Hill, Thomas House, Mike Tildesley
Centre for Complexity Science, University of Warwick

EPSRC Engineering and Physical Sciences Research Council

1. Background

Influenza has been described as the `last great plague' of mankind.

- Influenza A has **many strains** and inhabits **many hosts.**
- Between-species transmission of influenza A is possible (see Figure 1).
- For each host species, the biology and epidemiology of an influenza A strain can be **radically different**.
- Occasionally, a strain enters the human population that is capable of causing a **pandemic**.

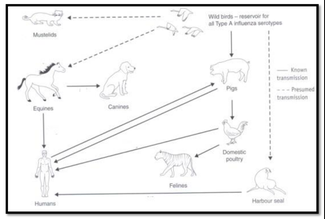

Figure 1: Influenza Type A transmitted between different animal species and humans. Adapted from [1].

Case Study: H1N1 Pandemic, 2009-2010

- This influenza pandemic was caused by the **H1N1 virus**, thought to have originated in **swine**.
- It caused **over 18,449 deaths** worldwide, with confirmed cases in over 214 countries and overseas territories [2].

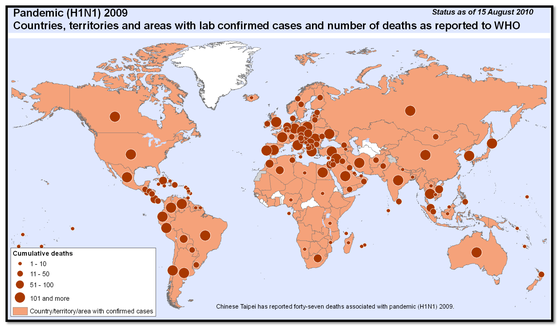

Figure 2: Countries with lab confirmed cases and cumulative number of deaths at the end of the H1N1 pandemic, August 2010. Reproduced from [3].

- The recent H7N9 outbreak is feared to be dangerous to humans, like H5N1.
- A current question of interest is does exposure to the past H1N1 pandemic provide protection against H7N9?

2. Objectives

- It is critically important to understand how likely it is that more **lethal strains** will cause a **pandemic** in the human population.

We aim to model the **complex strain diversity** and **between-species epidemiology** of influenza A.

3. Methods

A multi-strain, multi-host **stochastic susceptible-infected-recovered (SIR) model** was used, which incorporated the Gillespie algorithm.

To model each strain, each host population was split into susceptible, infected, and recovered classes.

For host species j, the number of individuals in each of the classes, with respect to strain k, is denoted by S_k^j, I_k^j and R_k^j respectively.

The **transition rates** which define the stochastic model for a given strain k, are:

(1) Host j susceptible individual infected by host j infectious individual:

$$T(S_k^j - 1, I_k^j + 1, R_k^j \mid S_k^j, I_k^j, R_k^j) = \frac{\beta_k^{j,j} S_k^j I_k^j}{N^j}$$

(2) Host i susceptible individual infected by host j infectious individual:

$$T(S_k^i - 1, I_k^i + 1, R_k^i \mid S_k^i, I_k^i, R_k^i) = \beta_k^{i,j} S_k^i I_k^i$$

(3) Recovery of infected host j individual:

$$T(S_k^j, I_k^j - 1, R_k^j + 1 \mid S_k^j, I_k^j, R_k^j) = g_k^j I_k^j$$

(4) Spontaneous infection of a host j individual:

$$T(S_k^j - 1, I_k^j + 1, R_k^j \mid S_k^j, I_k^j, R_k^j) = \alpha_k^j$$

A **demographic process** is included, with the following rates:

(5) Birth of a host j individual: $B^j N^j$

(6) Death of a host j individual: $d^j N^j$

where:

- N^j is the **size of the population** of host j.
- B^j and d^j are the **birth and death rates** for host j.
- $\beta_k^{i,j}$ is the **rate of transmission** of strain k infection to host i from host j.
- g_k^j is the **rate of recovery** from strain k infection for host j.
- α_k^j is the **import rate** of strain k infection for host j.

The model includes the following main **assumptions**:

- An individual can be infected by at most one strain at any one time; **"super infection" is not possible**.

4. Results

Analysis of a multi-strain, one host stochastic model

Figure 3 gives an example of the expected dynamics for four strains with varying transmission and recovery rates.
The reproductive ratio for all strains is equal.

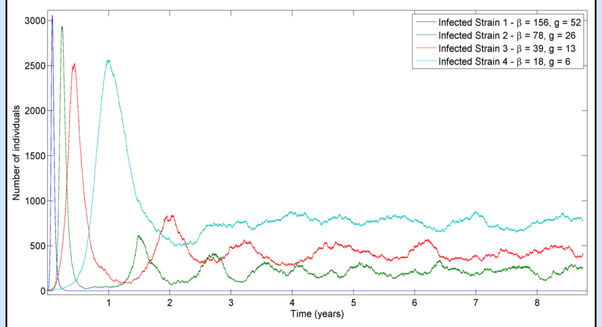

Figure 3: Plot of one host, four strain dynamics. Each strain has a reproductive ratio of 3. Initially, five distinct individuals are infected with each strain.

- In general, the strain with the lowest recovery rate, thus the longest infectious period, infects the most individuals.

Analysis of a one strain, multi-host stochastic model

We consider a two host model, with chickens (host 1) and ducks (host 2). Ducks are infected for longer, but the transmission rate is lower, compared to chickens infected by the same strain.
Figure 4 shows the expected dynamics.

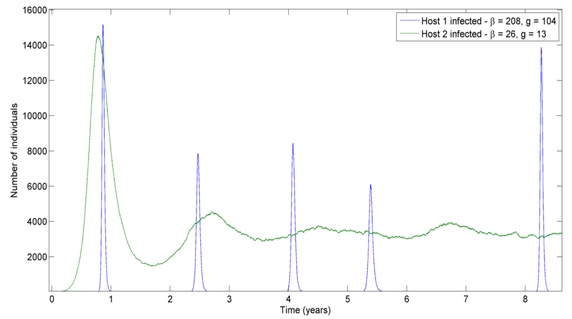

Figure 4: Plot of two host, one strain dynamics. For both hosts, the initial population was 100,000, and the strain had a reproductive ratio of 2. Cross transmission was only from host 2 to host 1, with rate of transmission 1×10^{-8}. Initially, five host 2 individuals and zero host 1 individuals were infected.

- After an initial epidemic, the number of infected ducks settles to a much reduced total.
- The strain intermittently enters the chicken population. It causes a large outbreak of infection, though it fails to establish itself over a long time period.

5. Discussion

For the multi-strain, one host model, after all strains have caused their initial epidemic, the strain with the longest infectious period **dominates**.

- The dominant strain has a **larger susceptible pool of individuals**, $\overline{S}$, to infect.
- This results in an **effective reproductive ratio** $R_{eff} = R_0 \overline{S}$ for the dominant strain that is greater than all other strains.
- Consequently, the dominant strain has the **highest number of infected individuals**.

For the two-host one strain model, in the **duck population** the strain has a long enough infectious period for it to **persist**. In the **chicken population**, the number of individuals infected **grows rapidly** when the strain is introduced. As a result, the susceptible population **depletes quickly**. The lack of susceptible hosts causes the infection to die out.

6. Future Work

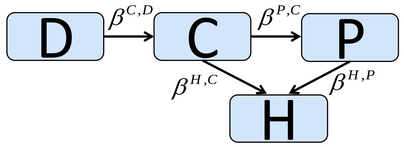

Figure 5: Diagram of the possible cross-transmission between different host species (ducks(D), chickens(C), pigs(P), humans(H)) in our four host model.

The model displayed considers strains emerging in the duck population, then transferring between different hosts as shown. It will be used to investigate the likelihood of transmission of strains, with differing characteristics, into the human population. This includes:

- **Strain specific transmission**, where some strains are more likely to cross into humans than others.
- **Cross-strain immunity**, where infection by past strains may help protect against infection from new strains.

References

[1] Jennings, R. & Read, R. *C. Influenza: Human and Avian.* Royal Society of Medicine Press (2006).
[2] World Health Organisation. *Pandemic (H1N1) 2009 – update 112*. Available at: http://www.who.int/csr/don/2010_08_06/en/index.html (2010) [Accessed: 18 April 2013].
[3] World Health Organisation. *Pandemic (H1N1) 2009 – update 115*. Available at: http://www.who.int/csr/don/2010_08_27/en/index.html (2010) [Accessed: 18 April 2013].

Contact: Edward.Hill@warwick.ac.uk