



POPULATION STRUCTURE AND THE RECURRENCE OF INFLUENZA A

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BACKGROUND

- Influenza:**
- Known as 'the flu', seasonal influenza is a highly infectious acute viral infection. Globally, an estimated 3-5 million people are infected annually
 - Influenza A** strains undergo a complex evolutionary pattern
 - Antigenic shift** results in a sharp change in antigenic coding and may result in a pandemic
 - After pandemic, strain evolves with **gradual** antigenic evolution called **antigenic drift**
 - Drifted strain may cause new outbreaks (i.e., establish itself as a seasonal strain)

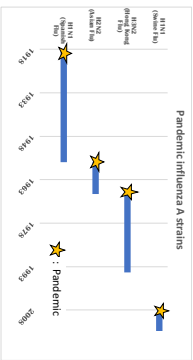


Figure 1: The evolutionary pattern of influenza A viruses.

The basic reproduction number \mathcal{R}_0 :

- The expected number of secondary infections caused by an infected individual in a wholly susceptible population
- If $\mathcal{R}_0 > 1$ an epidemic is possible

PROBLEM

Two natural questions arise:

- How much antigenic drift is required for the recurrence of a pandemic strain?
- Do assumptions on the population structure affect the prediction?

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FRAMEWORK AND DEFINITIONS

Three types of population structures:

- Well mixed (full homogeneity):** Every individual is identical and interactions occur at random with any other individual at a constant rate of daily contacts
- Well mixed with varying number of contacts (multigroup model):** Every individual interacts at random with any other individual with varying rates of daily contacts
- Network structure with fixed contacts:** Every individual has a fixed set of contacts and the number of contacts varies with individuals.

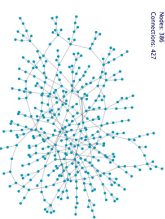


Figure 2: Fixed networks offer a more realistic population model

Susceptibility factor $\sigma \in [0, 1]$:

Susceptibility of previously infected individuals to drifted strain

$\sigma = 1$: full susceptibility or no immunity
 $\sigma = 0$ no susceptibility or full immunity

Degree probability generating function:

$\Psi(x) = \sum_k p_k x^k$ where p_k represents the probability that an individual has k contacts

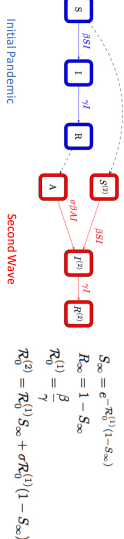
MODELLING OVERVIEW

For each population structure we:

- Model the initial pandemic
- Analytically extract the final state after the pandemic
- Develop model for the second wave with initial conditions being the final state of the pandemic
- Plot the curve of \mathcal{R}_0 vs. σ

DERIVING $\mathcal{R}_0^{(2)}$ FOR EACH MODEL

Fully homogeneous model:



$$S_{\infty} = e^{-\mathcal{R}_0^{(1)}(1-S_{\infty})}$$

$$R_{\infty} = 1 - S_{\infty}$$

$$\mathcal{R}_0^{(1)} = \beta$$

$$\mathcal{R}_0^{(2)} = \mathcal{R}_0^{(1)} S_{\infty} + \sigma \mathcal{R}_0^{(1)} (1 - S_{\infty})$$

Multi-group model:

$$\mathcal{R}_0^{(1)} = \frac{\beta \sum_k k^2 p_k}{\gamma \Psi'(1)}$$

$$\mathcal{R}_0^{(2)} = \frac{\beta \sum_k k^2 p_k (e^{-(1-\theta_{\infty})} - \theta_{\infty})}{\gamma \Psi'(1)}$$

Where $\theta_{\infty} \in (0, 1)$ is the solution to the equation:

$$\theta_{\infty} = \exp\left(\frac{\beta}{\gamma} \left(1 - \theta_{\infty} \Psi'(\theta_{\infty})\right)\right)$$

Contact network model with max. degree n:

$\mathcal{R}_0^{(1)} = \frac{\beta}{\gamma} \Psi'(0)$, $\mathcal{R}_0^{(2)} = \rho(FV^{-1})$ where ρ is the spectral radius and FV^{-1} is the next generation matrix:

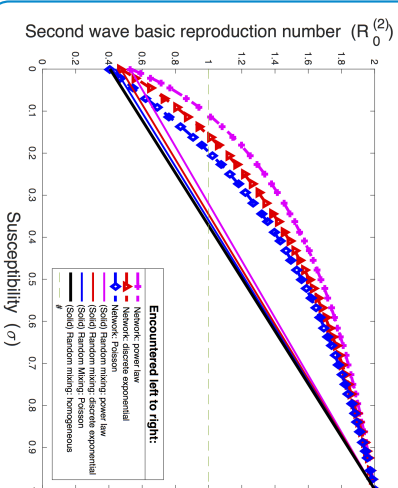
$$\begin{pmatrix} 0 & \frac{\sigma \beta}{\sigma \beta + \gamma} P_{A,1A}(0) & \dots & (n-1) \frac{\sigma \beta}{\sigma \beta + \gamma} P_{A,nA}(0) & \dots & \sum_j \frac{\beta}{\sigma \beta + \gamma} (j-1) P_{S,jA}(0) \\ \frac{\beta}{\sigma \beta + \gamma} P_{A,1A}(0) & 0 & \dots & (n-1) \frac{\beta}{\sigma \beta + \gamma} P_{A,nA}(0) & \dots & \sum_j \frac{\beta}{\sigma \beta + \gamma} (j-1) P_{S,jA}(0) \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ \frac{\sigma \beta}{\sigma \beta + \gamma} P_{A,1A}(0) & \dots & (n-1) \frac{\sigma \beta}{\sigma \beta + \gamma} P_{A,nA}(0) & \dots & \sum_j \frac{\beta}{\sigma \beta + \gamma} (j-1) P_{S,jA}(0) \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \frac{\sigma \beta}{\sigma \beta + \gamma} P_{A,nA}(0) & \dots & (n-1) \frac{\sigma \beta}{\sigma \beta + \gamma} P_{A,nA}(0) & \dots & \sum_j \frac{\beta}{\sigma \beta + \gamma} (j-1) P_{S,jA}(0) \end{pmatrix}$$

Correlations	How to compute
$P_{S,1A}(0)$	$\frac{\beta k_1 p_{k_1}}{\beta k_1 + \gamma} (1 - \theta_{\infty}^{-2})$
$P_{A,1S}(0)$	$\frac{\beta k_1 p_{k_1}}{\beta k_1 + \gamma} (1 - \theta_{\infty}^{-2})$
$P_{A,1A}(0)$	$\frac{\beta k_1 p_{k_1}}{\beta k_1 + \gamma} (1 - \theta_{\infty}^{-2})$
$P_{S,1S}(0)$	$\frac{\beta k_1 p_{k_1}}{\beta k_1 + \gamma} (1 - \theta_{\infty}^{-2})$

Here, θ_{∞} is the solution to the equation:
$$\theta_{\infty} = \frac{\gamma}{\beta + \gamma} + \frac{\beta}{\beta + \gamma} \Psi'(\theta_{\infty})$$

RESULTS AND CONCLUSION

For the numerics shown, the parameters were set so that $\mathcal{R}_0^{(1)} = 2$, $\Psi'(1) = 3$, $\gamma = 1$. Adding heterogeneity to the model leads to recurrence possible at approximately 50% of antigenic drift. This suggests that **stable contacts** like classmates, coworkers and family members are a crucial path for the spread of influenza in human population



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