Viral evolution within heterogeneous human contact patterns

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Abstract

Understanding the interplay between network structure and viral evolution is essential for predicting disease spread, particularly for rapidly mutating pathogens. Small-world networks, characterized by clusters of local connections with occasional long-range links, closely resemble real-world interaction and transport patterns, which are pivotal in determining the likelihood of a localized outbreak escalating into a global pandemic. Our research focuses on the impact of heterogeneity in human contact patterns on evolving virus strains during epidemic spread. We model three viral strains, examining their competition and coexistence, with mutations driving increases in transmissibility. Key epidemiological measures (such as the basic reproductive number, peak infection, and epidemic size) are used to systematically compare parameter space across different levels of transmissibility and network topologies. Additionally, we analyze how network heterogeneity influences the fixation of new strains and the evolution of disease transmissibility. The evolving virus further alters network heterogeneity through mortality, dynamically influencing the network's structure. By examining the percolation threshold, we assess how network resilience and connectivity contribute to the spread and containment of viral strains. Our findings provide insights into how viral mutations interact with network structures to either promote or hinder outbreaks, informing public health policies aimed at containment and optimizing responses to emerging infectious diseases.

Introduction

Infectious disease modeling is essential for understanding disease spread, especially as we face new and evolving pathogens. Rapid mutation adds another layer of complexity to modeling, particularly when multiple strains coexist or compete within a population. Epidemiological models that integrate mutation, strain competition and network effects are vital for predicting and controlling disease outbreaks effectively. Our work incorporates these three factors into a single model, simulating disease spread with mutation-driven strain evolution resulting in varying infection rates and observing the impact of varying contact network heterogeneity on the simulation. In doing so, we provide a more comprehensive and realistic framework for understanding and predicting the spread of mutating pathogens.

Modeling Viral Evolution on Human Contact Networks

Viral evolution

Infection dynamics considered using 3 strains of a virus (V_1, V_2, and V_3). Mutations alter transmission probability. This model assumes sequential evolution where V_{i+1} evolves from V_i through genetic mutations.

$$V1 \xrightarrow{\mu} V2 \xrightarrow{\mu} V3$$

Disease spread dynamics with $SI_1I_2I_3SD$

- Transmission probabilities **[$\beta_1 < \beta_2 < \beta_3$],** Recovery rate **[γ],** Mortality rate **[δ]**
- **Cross-infection** between individuals carrying different strains
- Mutation rate **[μ]** is **constant** and applies to **sequential genetic mutations**

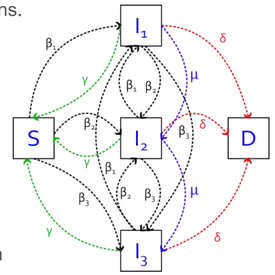


Fig 1: $SI_1I_2I_3SD$ model

Human Contact Networks

- **ODE model** - expectation for disease dynamics in the given parameter space
- **Fully connected network** - expectation for stochasticity within well-mixed population
- **Regular lattice network** - expectation for homogeneous interactions with fewer long-range connections
- **Degree distribution heterogeneous networks** - effect of hub nodes (superspreaders) on disease spread
- **Clustering coefficient heterogeneous networks** - effect of clustered interactions on disease spread
- **Real world networks** - model calibration to reflect realistic disease spread parameters

$$P_c = \frac{\beta}{R_0} \qquad R_{0,\text{eff}} = \beta \frac{\langle k^2 \rangle - \langle k \rangle}{\langle k \rangle (\gamma + \delta)} \qquad E = 1 - \frac{S_\infty}{N}$$

Metrics

1. $R_{0,eff}$ depicts heterogeneity in terms of degree distribution
2. **E** Epidemic size depicts the toll of the disease in the population
3. P_t, P_I Peak infection time and proportion (obtained from simulations)
4. p_c Percolation threshold

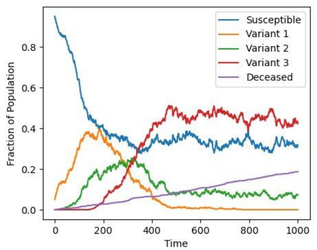
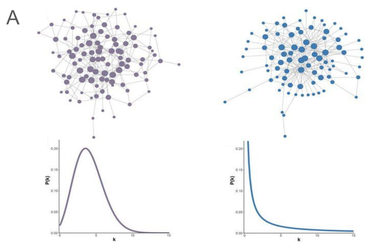


Fig 2: SID proportions over time using regular lattice

Heterogeneity in human interactions

Varying Degree Distributions



Varying Clustering Coefficients

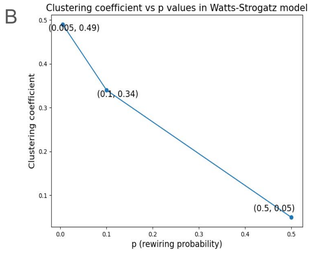


Fig 3: A) Higher variance in degree distributions form highly heterogeneous networks B) Higher clustering causes more cliques and increases heterogeneity in the network

SISD calibration through influenza spread in U.S. high school

- **About:** Contact patterns between students, staff and teachers in US high school (name masked for confidentiality) - to track spread of influenza through close proximity contacts
- **Network information:**
  - **Number of nodes:** 788 **Number of edges:** 118291
  - **Mean degree:** 300.231 **Variance of degree:** 10667.066
  - **Clustering coefficient:** 0.5
- Parameters inferred were used for the simulation of theoretical networks

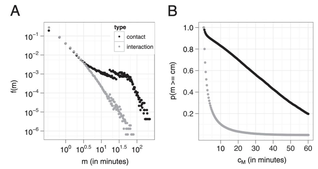
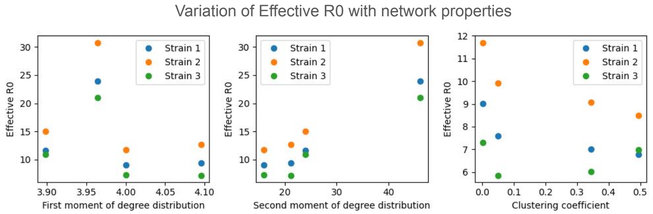


Fig 3: Normalized frequency, f, of interactions and contacts of duration m (in minutes) (B) Percentage, p, of total time of all CPIs by interactions and contacts with a minimum duration, cm (in minutes).

Metrics compared across networks



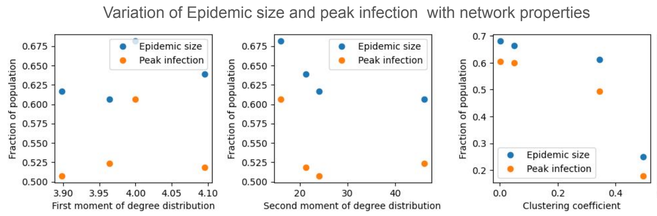
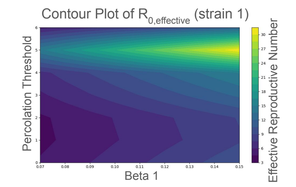


Fig 5: Response across metrics to changes in network structure—average degree, second moment of degrees and clustering coefficient

Sensitivity analyses



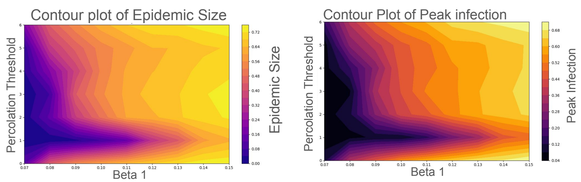
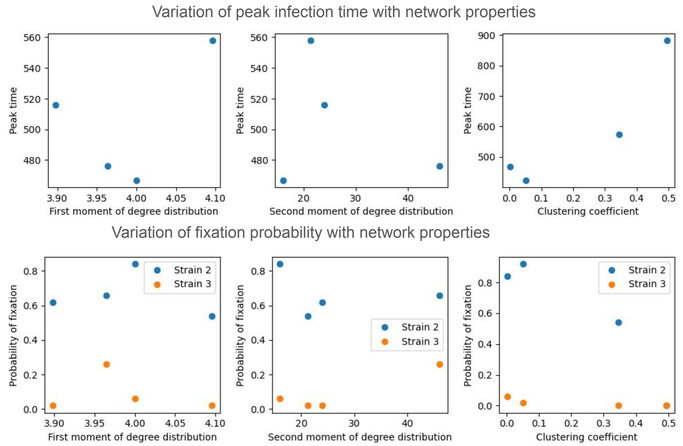


Fig 6: Sensitivity analysis for *beta1* parameter



Viral evolution increases heterogeneity through mortality

$$P_{c,effective} = \frac{\beta}{R_{0,effective}}$$

Highly heterogeneous networks (with higher $\langle k^2 \rangle$) have lower percolation thresholds, making them more prone to epidemics.

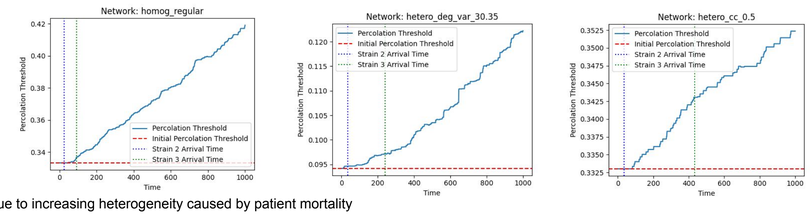


Fig 8: Percolation Threshold evolves over time due to increasing heterogeneity caused by patient mortality

Conclusions and Future Directions

1. Heterogeneity in human contact patterns slows down viral evolution and disease spread across populations
2. Network topologies with higher variance in their degree distributions tend to have lower potential for disease spread and an earlier peak in the number of infections compared to networks with high clustering which have higher epidemic sizes on average and delayed peaks in infections
3. Consistent with theory, lower percolation thresholds yield higher epidemic sizes and bigger infection peaks over a large range of viral transmissibilities
4. Viral evolution amplifies heterogeneity through patient mortality, highlighting the dynamic interplay between the two factors driving disease spread

References and Acknowledgements

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