Modeling Spillovers of Emerging Infectious Diseases with Intermediate Hosts

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Abstract

According to the World Health Organization, zoonotic diseases–which spread from animals to humans—are a top-10 pandemic threat, and modeling the behavior of such diseases is a key component of their control. Many emerging zoonoses, such as SARS, Nipah, and avian influenza, mutate from their wild type while circulating in an intermediate host population, usually a domestic species, to become more transmissible among humans, and this transmission route will only become more likely as agriculture intensifies around the world. Passage through an intermediate host enables many otherwise rare diseases to become better adapted to humans, and so understanding this process with accurate mathematical models is necessary to prevent epidemics of emerging zoonoses, guide policy interventions in public health, and predict the behavior of a pathogen.

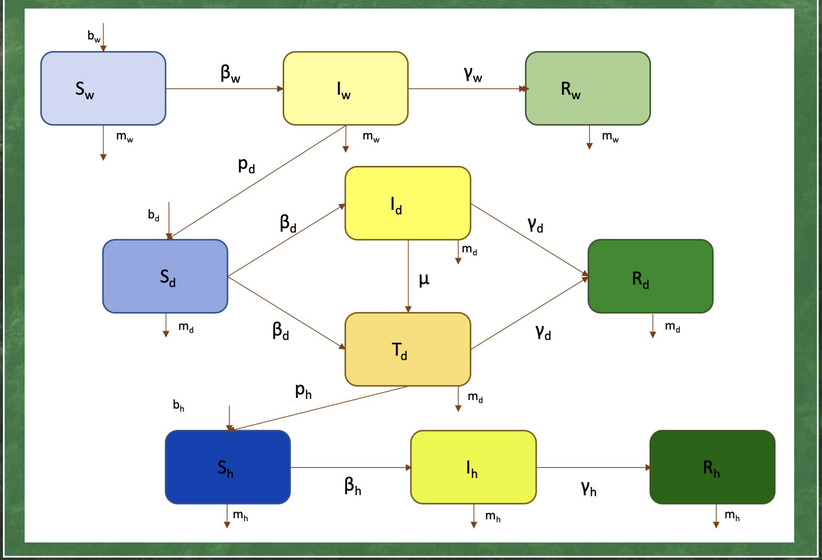
Here, we account for a zoonosis mutating in an intermediate host by introducing a new mathematical model for disease transmission. We present a model of zoonotic disease dynamics, including the equilibria of the three-species system and the basic reproductive number of the pathogen, and find that in the presence of an initial force of infection from wildlife and nonzero spillover and mutation rates, a zoonosis will reach an endemic equilibria in humans even if it fails in any one species. This model and result can be used to predict the behavior of any zoonosis with an intermediate host and guide public health interventions in emerging diseases.

Background

- Zoonoses are a major pandemic threat: 75% of emerging infectious diseases originate in wild reservoir host populations
- These pathogens emerge in a convoluted way: 60% of emerging zoonoses infect a domestic intermediate host species before infecting humans
- These intermediate hosts are exposed to diseases from both wild animals and humans and can serve as 'mixing vessels', where pathogens can mutate to become more adapted to humans
- Despite the importance of mathematical modeling in epidemiology, there is no current mathematical model for this type of behavior

A New Model

- Based on traditional SIR framework: here, SIR-SITR-SIR
- Deterministic, with vital dynamics
- Intentionally broad parameters to permit future modification



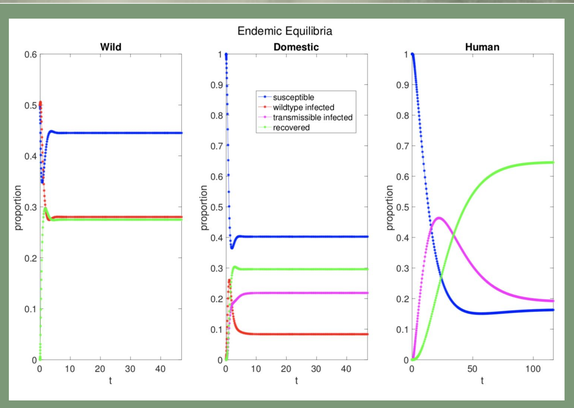
The Math!

Wild	$dS_w/dt = b_w - \beta_w S_w I_w - m_w S_w$ $dI_w/dt = \beta_w S_w I_w - \gamma_w I_w - m_w I_w$ $dR_w/dt = \gamma_w I_w - m_w R_w$
Domestic	$dS_d/dt = b_d - \beta_d S_d I_d - p_d S_d I_w - \beta_d S_d T_d - m_d S_d$ $dI_d/dt = \beta_d S_d I_d + p_d S_d I_w - \mu I_d - \gamma_d I_d - m_d I_d$ $dT_d/dt = \mu I_d + \beta_d S_d T_d - \gamma_d T_d - m_d T_d$ $dR_d/dt = \gamma_d I_d + \gamma_d T_d - m_d R_d$
Humans	$dS_h/dt = b_h - \beta_h S_h I_h - p_h S_h T_d - m_h S_h$ $dI_h/dt = \beta_h S_h I_h + p_h S_h T_d - \gamma_h I_h - m_h I_h$ $dR_h/dt = \gamma_h I_h - m_h R_h$

10 equations in three compartments with two viable equilibria for each species (one endemic, one disease-free)

Stability depends on basic reproduction number of the system and thus disease dynamics in all three species

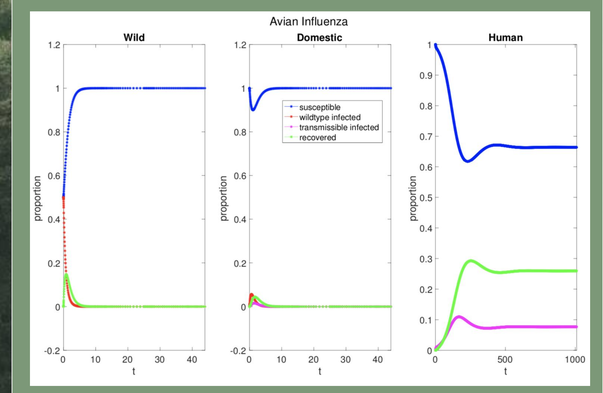
$$R_0 = \max\left\{\frac{\beta_w b_w}{m_h(\gamma_w + m_w)}, \frac{\beta_d b_d}{m_d(\mu + \gamma_d + m_d)}, \frac{\beta_d b_d}{m_d(\gamma_d + m_d)}, \frac{\beta_h b_h}{m_h(\gamma_h + m_h)}\right\}$$



Model behaves normally with a viable infection in all three species…

…but also permits an endemic equilibria in humans even if the disease dies out in both animal hosts.

This graph uses actual avian influenza data: bad news for public health officials



Disease Amplification

Setting each transmission parameter to 0 in an otherwise endemic equilibrium reveals that the disease can establish itself in humans even if it fails in an individual species compartment, refuting current transmissibility framework for zoonoses

Parameter	Maximum I_h	Equilibrium I_h
–	46.33	19.04
p_d	0	0
μ	0	0
p_h	0	0
β_w	49.77	19.62
β_d	18.81	11.16
β_h	36.13	18.06

Results

- Mathematically modeling all stages of an emerging zoonosis shows that transition parameters (spillover and mutation rates) alone determine human infections in the presence of an epidemic in wildlife or domestic animals
- Threshold conditions for an epidemic's spread to humans are more detailed than the traditional R_0: (βi , γi) matter for isolated species, but not the global system
- With nonzero contact and mutation rates and a seed infection in wild animals, it's impossible to avoid an endemic equilibrium in humans, the downstream hosts—even if the epidemic fails in upstream ones

Discussion

- We have shown that with the capacity to mutate in an intermediate host, emerging zoonoses can be a threat to humans even while evading traditional markers for epidemic success (R_0 in humans < 1)
- Our results call the current framework for classifying emerging zoonoses into question, on both a theoretical and practical level
- This work offers priorities for public health intervention: lowering transition parameters can delay and lessen an epidemic, but focus should be on early identification in animals rather than health interventions in humans

Conclusions

- We have met the need for a mathematical framework for an emerging zoonosis
- Practical: public health officials and policymakers should be more concerned about wildlife diseases with the capacity to mutate in an intermediate host, because these diseases will spread to humans under realistic conditions (spillover/mutation rates > 0) even if they evade detection under traditional threat classifications
- Philosophical: we have quantified and confirmed a key assumption in global health, that human health is inextricably and inexorably linked to that of other species

Future Research

With the capacity to model the entire course of an emerging zoonosis introduced through this project, future researchers can:

- Gather accurate data, especially for wildlife compartment/transmission parameters
- Examine effect of varying β, γ in domestic animal strains
- Model more realistic dynamics such as seasonal variation or migration in wildlife
- Model different types of mutations: reassortment, adaptation
- Include backward transmission to model stuttering chains

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Acknowledgements
Thank you to the Dartmouth math department for their support;
Feng Fu and Dana Williams for their encouragement;
Noam Ross and Cale Basaraba of EcoHealth Alliance for an introduction to mathematical modeling;
April Johnson and Rachel Matsumoto for graphic design;
the Dartmouth College Fencing Club and Cabin and Trail for stress relief;
and KAF coffee for motivation

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