The Undead

A Plague on Humanity...
Or a powerful new tool for epidemiological modelling?

Rise of the Undead

- *Undead*, n. pl. a being who is technically dead, but still animate
  - eg zombies
  - vampires
  - former vice president Dick Cheney

- In recent years, the undead have advanced considerably
- Both in numbers and their abilities
  - flesh-eating
  - blood-sucking
  - writing autobiographies.

Urban infestation

- Cities overrun with zombies include
  - London
  - New York
  - Milwaukee suburbs
- Cities infested with vampires include
  - Los Angeles
  - Beaumont, Louisiana
  - Forks Washington
- Hideouts where Dick Cheney was last seen:
  - A bunker, somewhere in Wyoming.

A potential advantage

- Zombies may want to eat our brains
- Vampires may want to suck our blood
- ...but these actions, while unfortunate, may also be the last best hope for understanding key epidemiological concepts
- Specifically:
  - – Bubonic plague
  - – Spanish flu
  - – HIV/AIDS

- Conversely, Dick Cheney has no known redeeming features.

A short history of zombies

Zombies were not always recognised as an international threat because they were:

- Limited in number
  - likely due to the small number of Voodoo sorcerers available for their creation
- Principally confined to remote regions
  - Central Africa, Haiti
- Without the desire to consume human flesh
  - no flesh-eating observed before 1964
- Apparently uninfectious
  - no zombie-to-human transmission until 1968.

A short history of bubonic plague

Y. pestis was not recognised as a threat because it was:

- Limited in number
  - – no large-scale infestation until the “Justinian” plague of 550 AD
- Principally confined to remote regions
  - – Northern Africa, Middle East trade routes
- Without the desire to consume human flesh
  - – not virulent in humans before Justinian plague
- Apparently uninfectious
  - – despite a 20,000 year-long genetic history.

A short history of Dick Cheney

Dick Cheney was not recognised as a threat because he was:

- Limited in number
  - thankfully
- Principally confined to remote regions
  - hunting grounds, underground bunkers
- Without the desire to consume human flesh
  - as far as we know, anyway
- Apparently uninfectious
  - until it was too late.

Zombies and the plague

- A related commonality is the necessity for some kind of mutation
- In 1968, the shambling undead were suddenly able to transmit their condition to living beings by eating their brains
- *Y. pestis* underwent a significant evolutionary change just prior to the 550 AD plague outbreak.

Mortality

- However, zombies and the plague diverge in terms of mortality
- Annually, there are only 1000-3000 cases of bubonic plague
  - minor epidemics occur in sub-Sarahan Africa
- Zombies, of course, are much more deadly
- Plague has a 50-90% mortality rate for those it infects (in the absence of treatment)
- Zombies have a 100% mortality rate
  - (“mortality” may be the wrong word, here).

Treatment

- Bubonic plague can be treated with antibiotics
- Mortality falls to 1-15%

Zombie treatment involves:

- small-arms fire
  - but you run out of bullets
- cricket bats
  - so North America is in big trouble then.

Modelling epidemics

- It is possible to build a model to predict (say) how many people in Alaska will die from an outbreak of bubonic plague
- However, to do this, we need to know the exact population of Alaska
- This may be unstable and unmeasurable
- Instead, it is usually better to think of proportions of a population
- Thus, it is not necessary to focus on only one group of survivors.

Modelling proportions

- We would like to say something like
  - "At the peak of the epidemic, which will occur 37 days after the outbreak first starts, 50% of the population will have been infected and 30% will have died"
- Relative predictions may not be as satisfying as hard numbers and may be less useful for small populations
- However, thinking in relative terms frees us from knowing initial conditions
  - total population size, initial number infected etc.

Composition of populations

- However, it would be helpful to know something about the composition of this population
  - gender ratio, age distribution, general health etc
- Also their living conditions
  - how spread out they are, level of sanitation etc
- Are any of them likely to be our previously deceased friends and relatives, returned from the dead to wreak an unholy vengeance upon us all?
  - it would be good to know this, regardless.

Demographics of survival

- In the case of a zombie outbreak, survivors will barricade themselves inside shopping malls or the local pub
  - this gives us an indication of population density
- Groups of survivors tend to encounter at least one other, nearly identical group
  - this gives us an idea of population mixing
- Survivors always consist of at least one representative of a racial minority, a woman and a child who may hold the key to human survival.

Parameters

- To keep things simple, we will instead “roll” this information into the most important parameters
- These are the rates at which disease-related events occur
  - eg transmission
  - death
  - birth/immigration
  - recovery (if applicable).

The basics of model design

Our population of living humans can thus be separated into three classes:

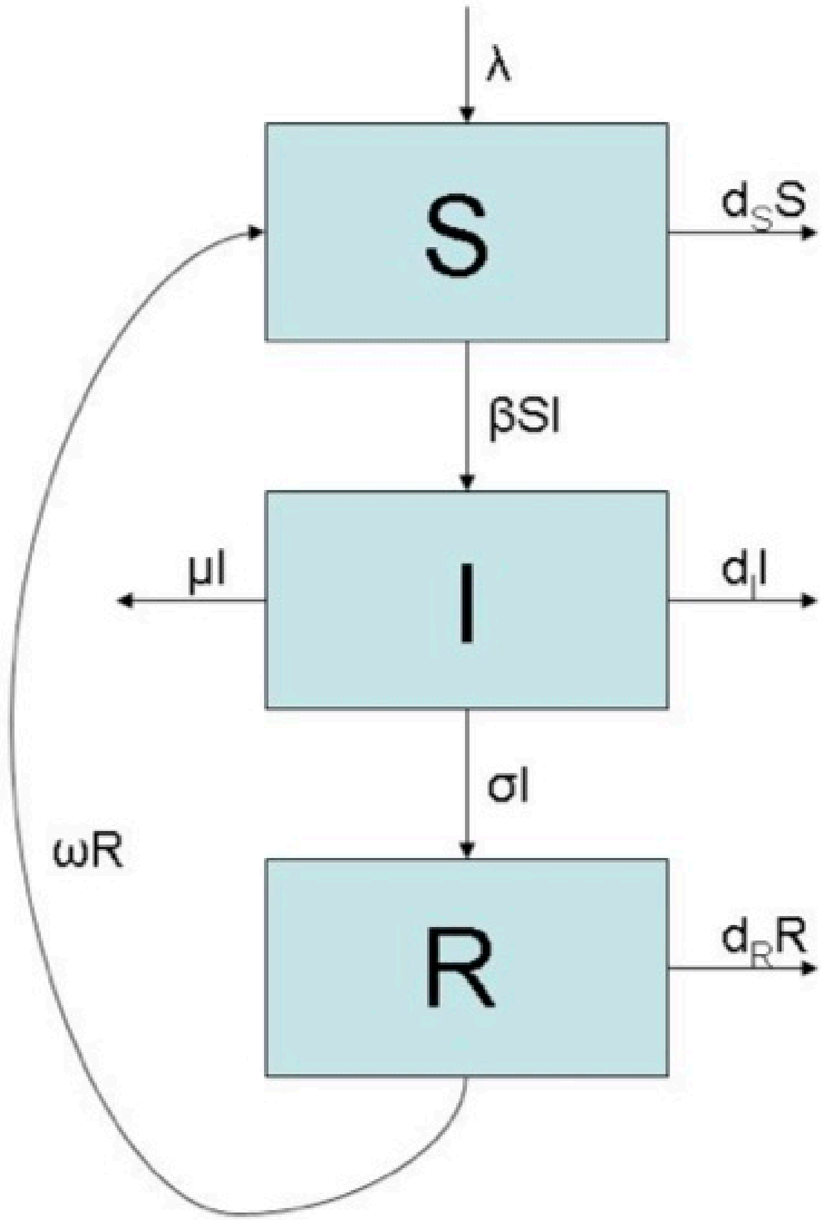
- Susceptible (S)
  - healthy, living humans who can get the disease
- Infected (I)
  - those who have contracted the disease and can spread it to susceptibles
  - (the key point here is the ability to spread the disease)
- Removed, aka recovered (R)
  - individuals who have survived and are immune.

Movement between classes

- *Infection* moves individuals between S and I
  - transmission occurs when an S and I meet, with rate β
- *Recovery* moves individuals from I to R
  - this occurs at rate σ
- *Loss of Immunity* moves individuals from R to S
  - this occurs with rate ω
- *Birth/Death*
  - Each class has its own birth and death rates.

S: susceptible I: infected
R: removed

The model diagram



S: susceptible I: infected
R: removed λ: birth
β: transmissibility
d_j: background death
μ: disease death
σ: recovery
ω: loss of immunity

The ODEs

- The differential equations are thus

$$\frac{dS}{dt} = \lambda - \beta SI - d_S S + \omega R$$
$$\frac{dI}{dt} = \beta SI - d_I I - \mu I - \sigma I$$
$$\frac{dR}{dt} = \sigma I - d_R R - \omega R$$

- These depict the change in the S, I and R populations over time, with respect to birth, death, infection, recovery and waning immunity.

S: susceptible I: infected
R: removed λ: birth
β: transmissibility
d_j: background death
μ: disease death
σ: recovery
ω: loss of immunity

Using zombies to understand plague

- Zombies are a special case of the plague where the parameters are such that S ultimately approaches zero
- From this, we can predict boundaries for these parameters which mark the “tipping points” between ultimate survival of humanity and utter destruction
- If a pathogen appears whose rate parameters lie on the destruction side, we may be able to take action soon enough to avoid this fate.

How to determine parameters?

- The most common epidemic studies is that of plague in a town called Eyam, which lost 76% of its population
- The rate of infection was 0.1507 per infected per day
- Infected individuals recovered at a rate of 0.063 per day
- Death rate was 0.027 per day
- Thus, the mortality rate is approximately 30%

  $= 0.027/(0.027+0.063)$.

Loss of immunity

- This parameter is more challenging to determine experimentally
- These is consequently less literature to work with
- Some individuals were infected by plague more than once
- Others seemed immune for life
- Thus, we will assume immunity may be lost in a few years

  = 0.0005 per day (approximately).

Estimating zombie parameters

- Recent records from London provide estimates for the zombie-generating “rage” virus
- Infected individuals are compelled to consume the flesh of the uninfected
- This is an efficient route for saliva-to-blood transmission
- Depopulation of London took 28 days
- Thus, the infection rate of the rage virus is approximately 0.5048 per infected per day.

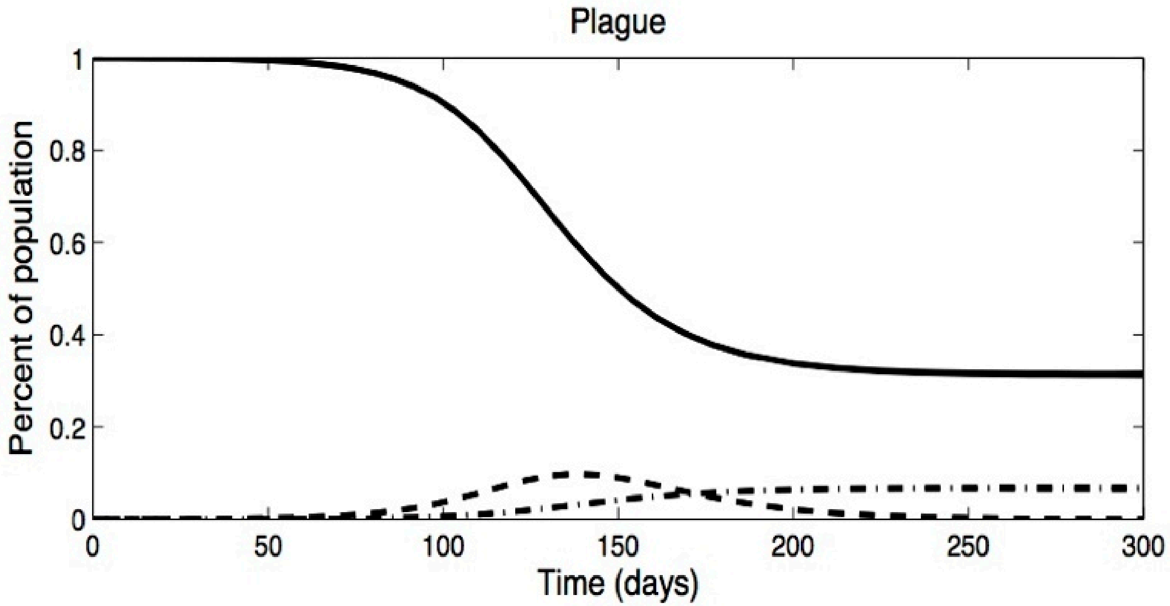
Recovery from the rage virus

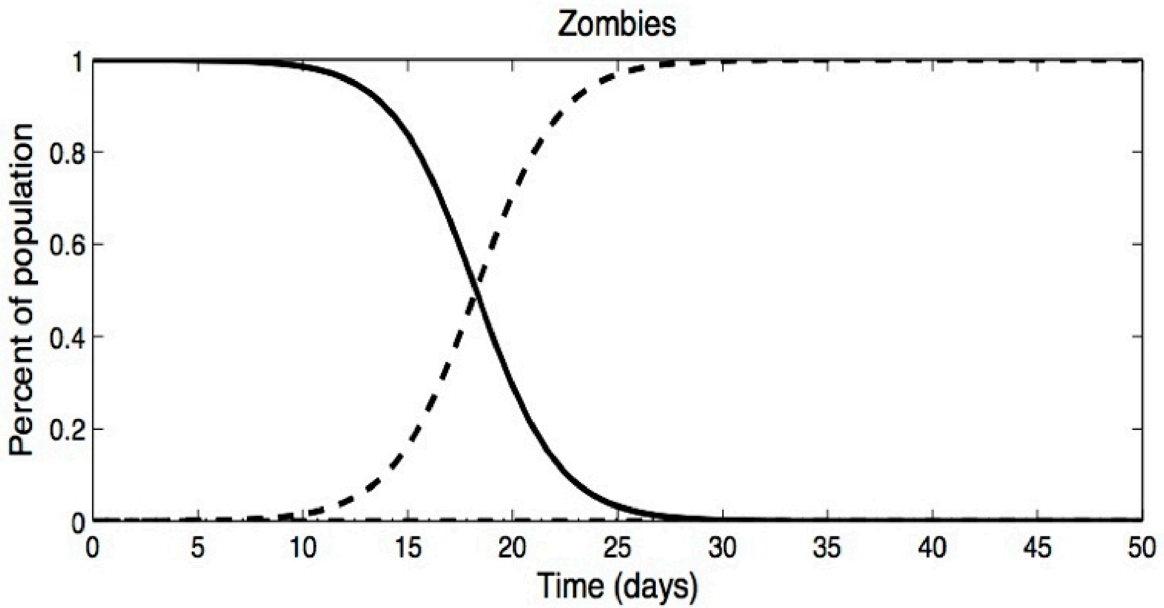
- During the 28 day period, there was at least one case of “recovery”
- The subject was bitten, but not subsequently consumed with the desire to eat flesh
- Thus, a reasonable recovery rate is
- $1/(7,000,000\times 28)=5\times 10^{-9}$ per day
- Zombies seem to be permanently functional after infection
- Thus, we can assume the disease-“death” rate is negligible compared to humans.

Birth and background death

- During a fast-moving epidemic, birth and background death rates are very small
- Thus, we will ignore these parameters
- We now have a model for both the plague and for zombies
- Running each model with specific data, we can see the long-term outcome.

Results of the two models





Why the different outcomes?

- The difference depends on the values of the disease death rate (μ) and the recovery rate (σ)
- When these are small, infected individuals spend an infinite amount of time in the infected class
- ie zombies take over because they don't "recover" and they don't "die".

Implications

- Thus, humanity survived the plague because it was too lethal
  - the infected died faster than they could transmit
- For Spanish flu, the opposite was true: it wasn't lethal enough
  - the recovery rate moved people rapidly into the immune class
- Thus, we see how understanding zombie outbreaks gives us insight into understanding other diseases.

Basic reproductive ratio

- Sometimes, an infectious disease will not cause an epidemic
- If infected individuals do not successfully transmit the infection, the disease will die out
- This is related to the basic reproductive ratio

$$R_0 = \frac{\beta}{\mu + \sigma}$$

(in our case)

- In general, if $R_0<1$, the disease will die out
- If $R_0>1$, the disease will cause secondary infections and thus trigger an epidemic.

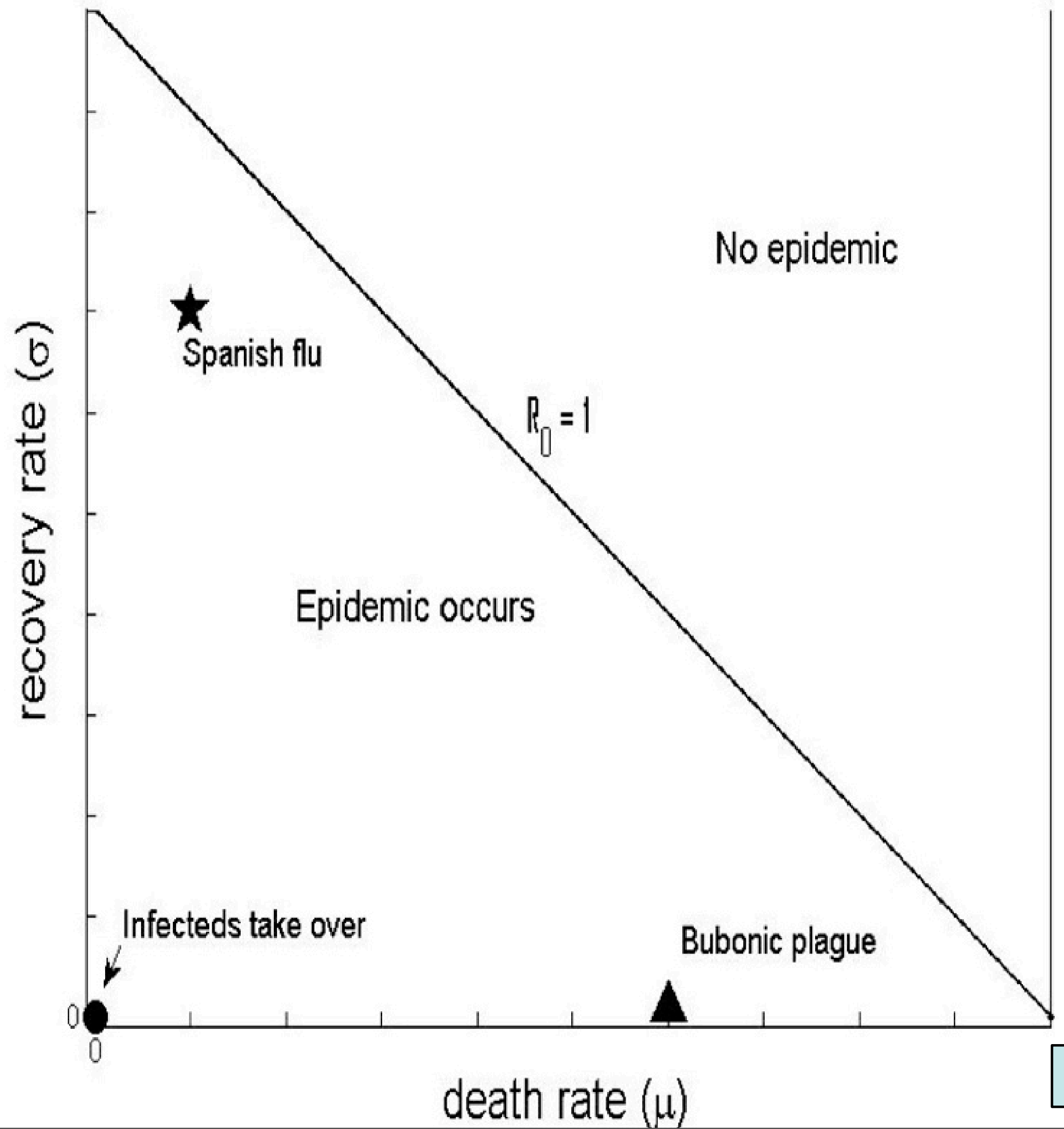
β: transmissibility
μ: disease death
σ: recovery

Making predictions

- We can now examine the properties of a classical versus apocalyptic plague
- We plot the death rate versus the recovery rate
- We identify regions where the disease will
  – die out ($R_0<1$)
  – cause an epidemic ($R_0>1$ and moderate)
  – take over the population (R_0 very big, $\mu,\sigma\approx 0$).

R_0: basic reproductive ratio
μ: disease death
σ: recovery

Predicting epidemics



R_0: basic reproductive ratio

The final size

- The final size relation measures the number of susceptibles who never get infected

$$\log(S_0) - \log(S_\infty) = R_0 \left[1 - \frac{S_\infty}{K}\right]$$

  - S_0 is the number of susceptibles at the beginning of the epidemic
  - S_∞ is the number after the epidemic clears
  - K is the original uninfected population
- It only applies when susceptibles are uniformly decreasing.

R_0: basic reproductive ratio
S: susceptibles

The final zombie size

- When R_0 is large, S_∞ is small
- In the case of zombies, R_0 is very large, so S_∞ is almost zero
- Thus, when the zombie apocalypse comes, you shouldn't feel bad about not surviving it
- See, mathematics can be very reassuring.

$$\log(S_0) - \log(S_\infty) = R_0 \left[1 - \frac{S_\infty}{K}\right]$$

R_0: basic reproductive ratio
S_0: initial susceptibles
S_∞: final susceptibles
K: total population

Living with vampires

- While zombies have appeared globally since the mid-1940s, vampires have been feeding on humans for all of recorded history
- This includes
  - bloodsucking demons of Mesopotamia
  - charismatic, romantic vampires of the gothic era
  - New World Order businessmen
  - teen heart-throbs.

A long-lasting equilibrium

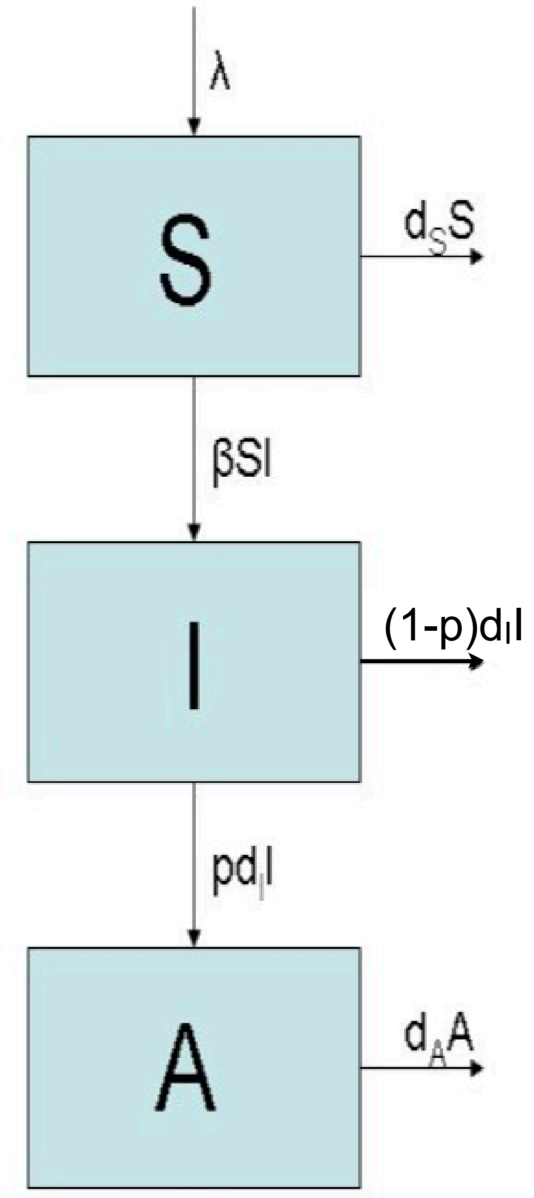
- The one thing they have in common:
- Establishing a long-lasting equilibrium with humans
- Vampires tend to persist among humans without sudden, large population fluctuations
- This is an excellent model for endemic diseases such as HIV.

A model without recovery

The model consists of:

- Susceptibles
  - who have not been infected
- Infected
  - vampires or HIV-infected
- Note that there is no recovered class in either case
- There is also an A class
  - infected individuals who abstain from infecting, either because they are too sick or because they are in love with a mortal human.

The SIA model diagram



S: susceptible I: infected
A: abstinent λ: birth
β: transmissibility
d_j: background death
p: abstinence progression

The SIA model equations

- This model is given by

$$\frac{dS}{dt} = \lambda - \beta SI - d_S S$$
$$\frac{dI}{dt} = \beta SI - d_I I$$
$$\frac{dA}{dt} = p d_I I - d_A A$$

- The basic reproductive ratio is

$$R_0 = \frac{\beta S_0}{d_I}$$

with S_0 the initial number of susceptibles

- As before, the disease will spread if $R_0>1$.

S: susceptible I: infected
A: abstinent λ: birth
β: transmissibility
d_j: background death
p: abstinence progression

Endemic, rather than epidemic, dynamics

- Endemic dynamics are a result of infection occurring over long timescales
- This allows for the replenishment of susceptibles
- Vampirism is deliberately transmitted in only a very small fraction of biting events
- Thus, the infection rate of vampires is much lower than that of zombies
- HIV transmission only occurs in a fraction of sexual encounters.

Birth/death

- With relatively slow transmission, birth and background death rates are now relevant
- Thus, the S class may grow at a rate that meets or exceeds the depletion rate
- Ultimately, this will lead to stable relative populations of susceptibles and infecteds
- Vampires also have a significant death rate
  - sunlight, garlic, vampire hunters
- HIV infected individuals also have significant death rates
  - AIDS-related infections.

Invisible symptoms

- Furthermore, both zombies and plague sufferers have easily identifiable symptoms
  - shambling gait, red eyes, open sores
- However, it is not possible to identify vampires or HIV-infected individuals by visual inspection
- This makes responsive strategies like quarantine or selective vaccination much less effective.

Low infection rates

- Thus, a low rate of infection can be sustained
- HIV infection occurs in 1 per 1000 to 1 per 100 sexual contacts
- Simple means of prevention are also available
  - condoms, abstinence, not inviting a vampire into your home
- Nevertheless, these epidemics can be much more long-lasting than apocalyptic outbreaks.

Parameters

- Average human lifespan = 60 years
  - ∴ $1/d_S=60$
- We can assume the healthy population is constant so $\lambda=d_S S_0$
- We assume the vampire infection rate is 1 in 500,000 contacts between humans and a vampire per year
- For HIV, we assume 1 in 250,000 contacts between susceptibles and an infected individual per year
  - – contact can also occur during the day.

S: susceptibles
λ: birth rate
d_S: background death

Weapons and death

- Modern weaponry has little effect on vampires
- Older technology is more effective
  - eg wooden stakes, fire, religious symbols
- Death is heightened in AIDS patients due to compromised immune systems
- We assume 86% of individuals leaving the I class are abstinent
  - due to AIDS symptoms or choice
- For vampires, this is closer to 10%
  - mainly among vampires with a soul.

Parameter estimation

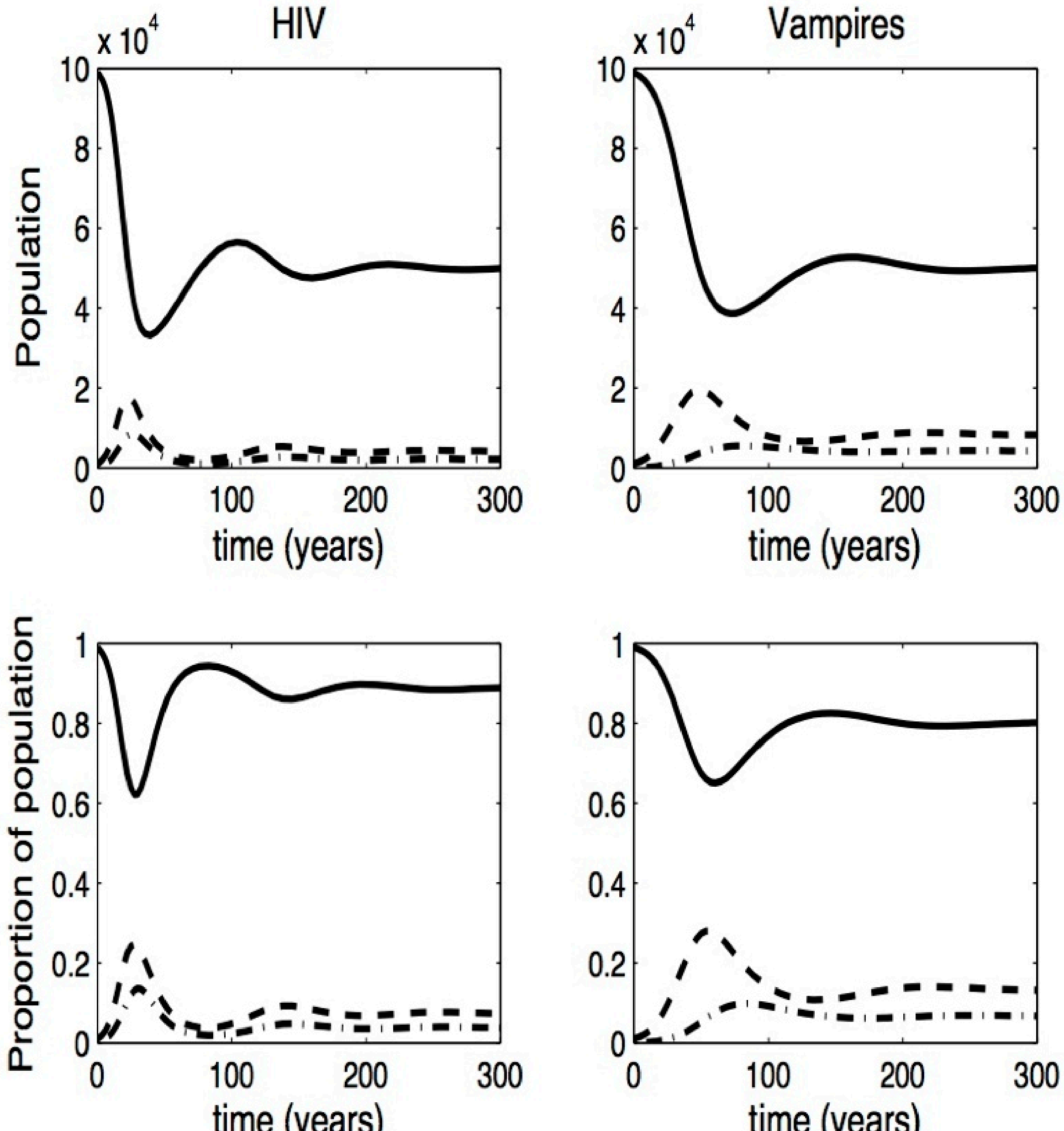
- We estimate a vampire-infected removal rate of 0.1 per year
- For HIV, we increase this to 0.2 per year
  - reflects the higher death rate but also increased success at abstinence
- Abstinent vampires live longer than those in the I class, say 0.02 per year
  - due to less contact with humans
- (Remember that the death rate is 1/lifespan).

Death rates

- For HIV, we assume 30% of the A class are AIDS patients, with a lifespan of 1 year
- 70% are abstinent HIV infected with lifespans of 20 years
  - this includes treatment
- Thus, d_A=0.335 per year
- With these rates, we can plot the dynamics of each disease.

d_A: abstinence death rate

Dynamics of HIV and vampires



Conclusions

- Although they are harbingers of human destruction, the undead are also good models for both epidemic and endemic disease
- Zombies, with their ravenous appetite, are an excellent model for highly virulent, epidemic diseases such as bubonic plague
- Vampires, with their subtle infestation and low transmission rates, provide valuable insights into endemic diseases such as HIV.

Future directions

- These models are just a starting point
- They could easily be extended to address specific questions
  - eg given the available countermeasures, what is the most cost-effective way to fight the undead?
- Other correlations could be examined
  - eg periodic outbreaks in both werewolves and herpes
  - This might be a useful project.

Finally...

- What about Dick Cheney?
- The threat seems to have finally passed, but we can never be too cautious
- Mathematical modelling can provide an early warning system against such horrors
- But it's probably best to arm yourself with a wooden stake anyway
- Just in case.

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J.M. Heffernan, D.J. Wilson. The Undead: A Plague on Humanity of a Powerful new Tool for Epidemiological Research. (In: R. Smith? (ed) Mathematical Modelling of Zombies, University of Ottawa Press, *in press*.)