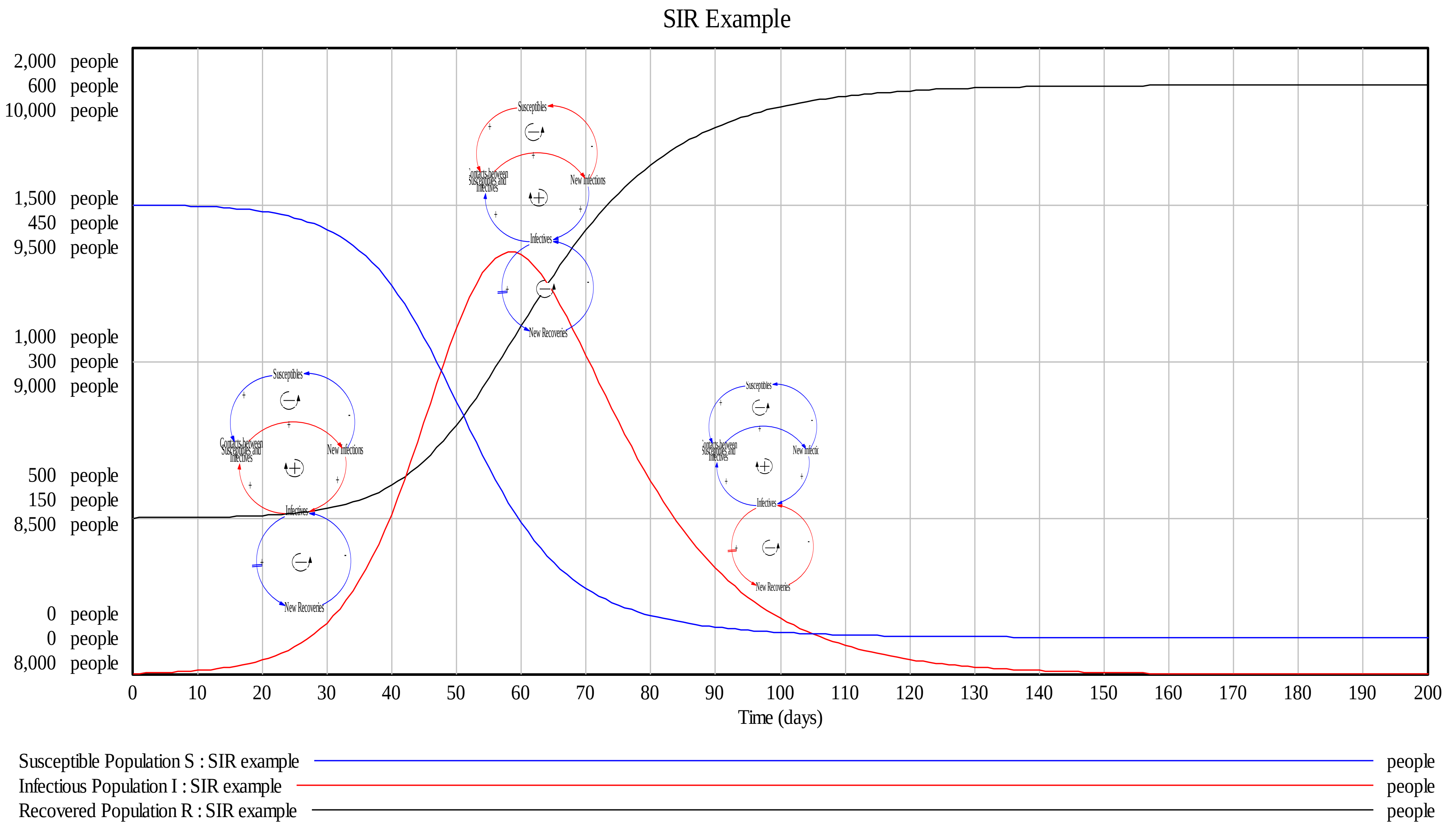
Infectious Disease Model Wrapup

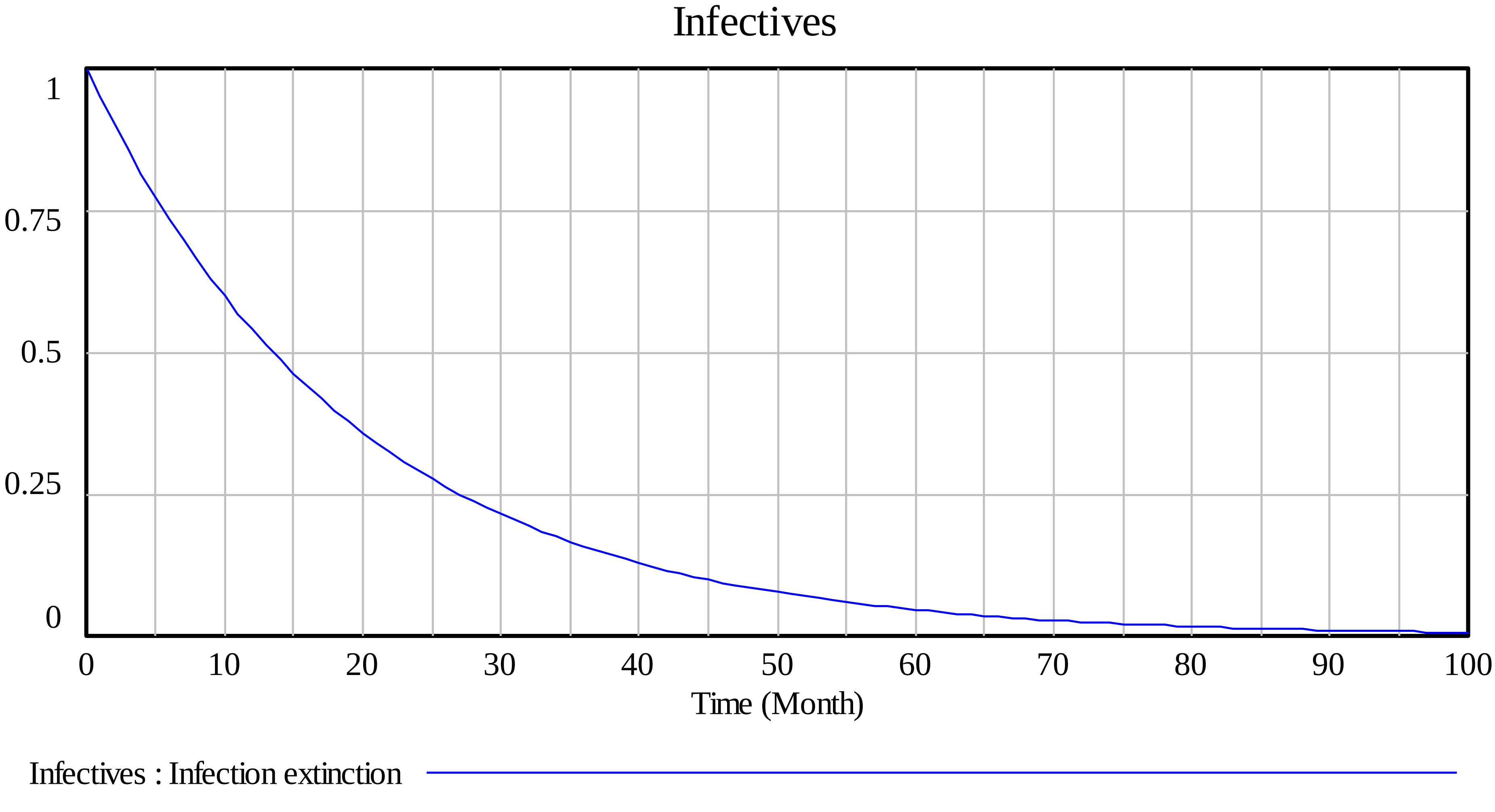
CMPT 858

February 8, 2011

Case 1: Outbreak



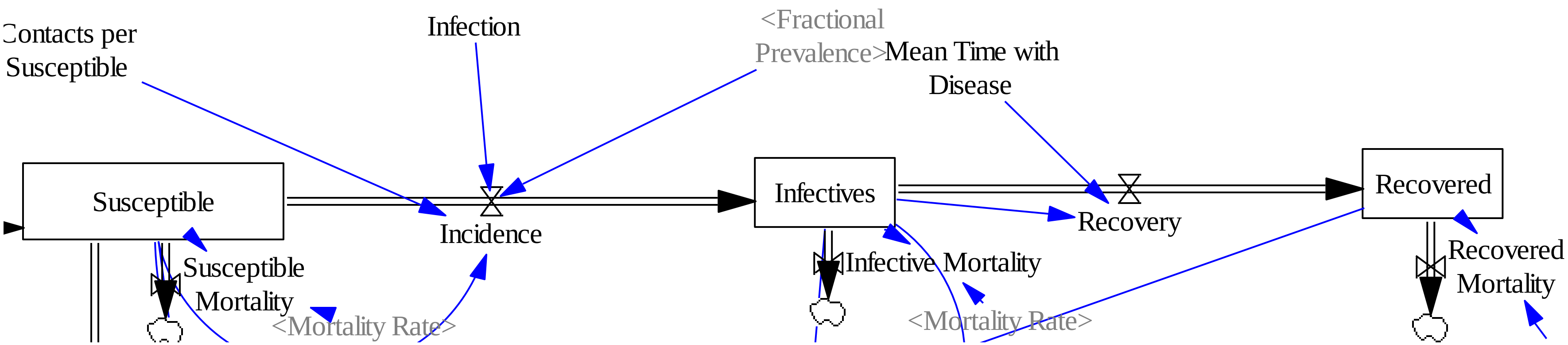
Case 2: Infection declines immediately



Recall: Closed Population (No Birth & Death)

- Infection always dies out in the population
- Some infections will take longer to die out
- There is a "tipping point" between two cases
  - # of people infected declines out immediately
  - Infection causes an outbreak before the infection dies down (# of people infected rises and then falls)

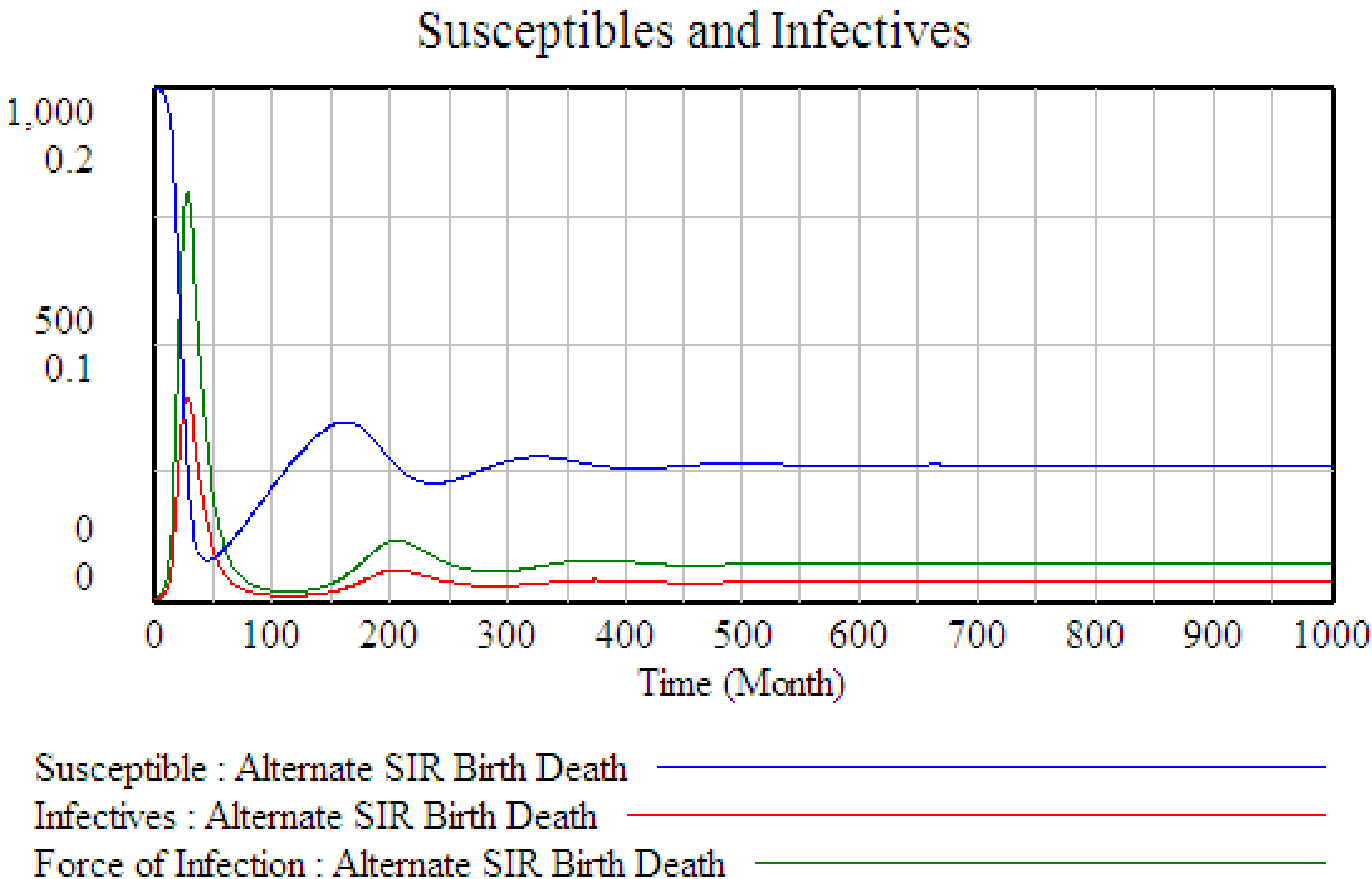
Recall: Simple Model Incorporating Population Turnover



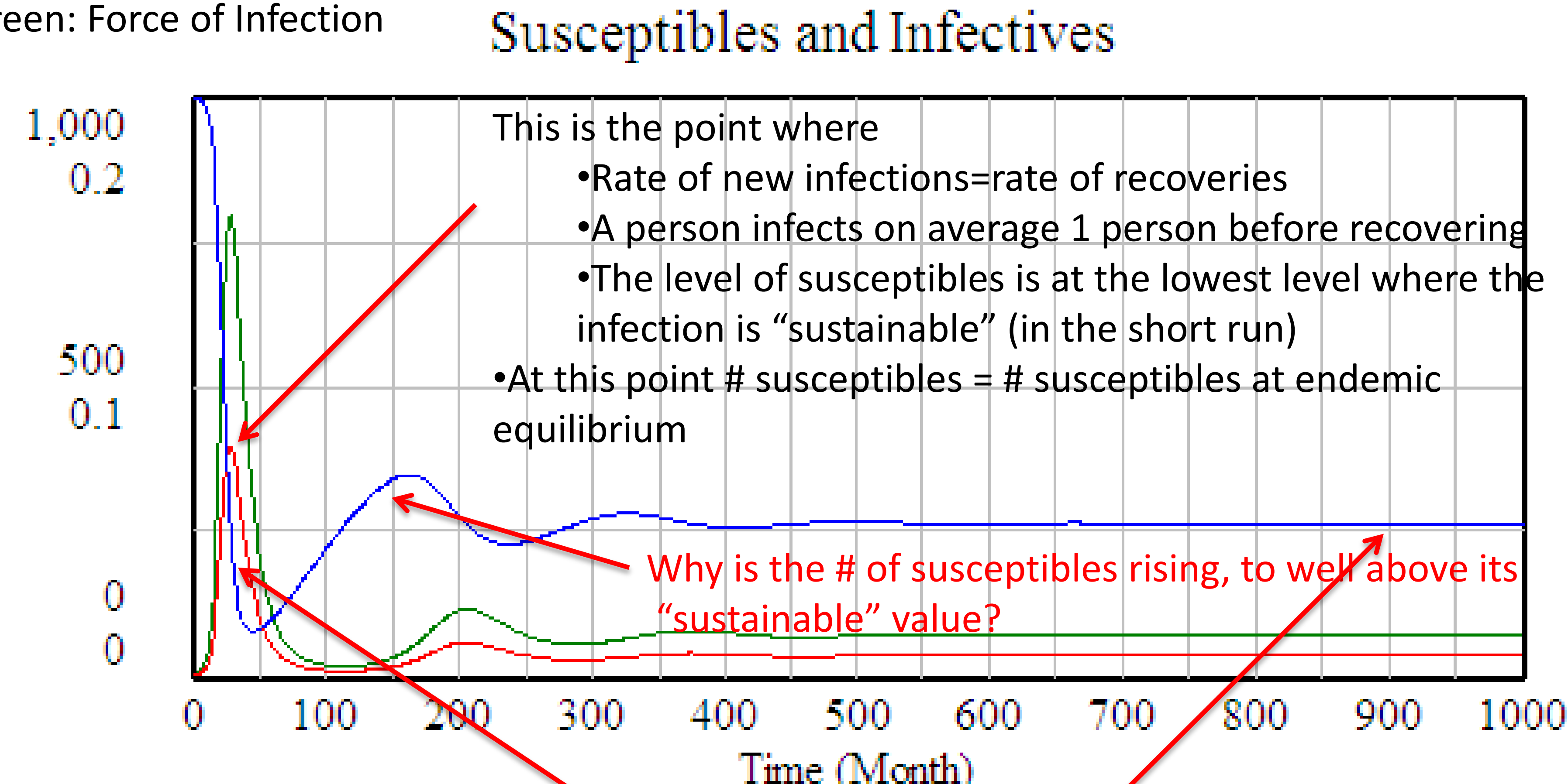
Recall: Our model

- Set
  - c=10 (people/month)
  - β=0.04 (4% chance of transmission per S-I contact)
  - μ=10
  - Birth and death rate=0.02
  - Initial infectives=1, other 1000 susceptible

Here, the Infection Can Remain (Endemic)



Blue: # Susceptible
Red: # infective
Green: Force of Infection



This is the point where

- Rate of new infections=rate of recoveries
- A person infects on average 1 person before recovering
- The level of susceptibles is at the lowest level where the infection is “sustainable” (in the short run)

- At this point # susceptibles = # susceptibles at endemic equilibrium

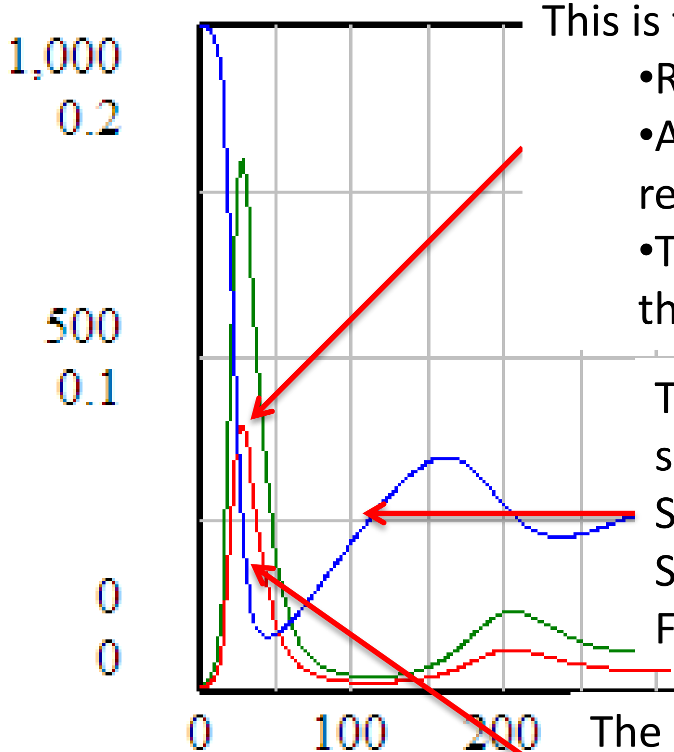
Why is the # of susceptibles rising, to well above its “sustainable” value?

Why is the # of susceptibles still declining?

This fraction of susceptibles at endemic equilibrium is the minimum “sustainable” value of susceptible – i.e. the value where the properties above hold.

- Above this fraction of susceptibles, the # infected will rise
- Below this fraction of susceptibles, the # infected will fall

Susceptibles and Infectives



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- Rate of new infections=rate of recoveries
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The rise is occurring because infectives are so low that so few infections occur that births >infections+deaths. S rises above the sustainable value because infectives are Still in decline until that point – so infectives remain low For a while!

The susceptibles are still declining here because the large # of infectives still causes enough infections that
rate of immigration < rate of infections + deaths

Susceptible : Alternate SIR Birth Death
Infectives : Alternate SIR Birth Death
Force of Infection : Alternate SIR Birth Death

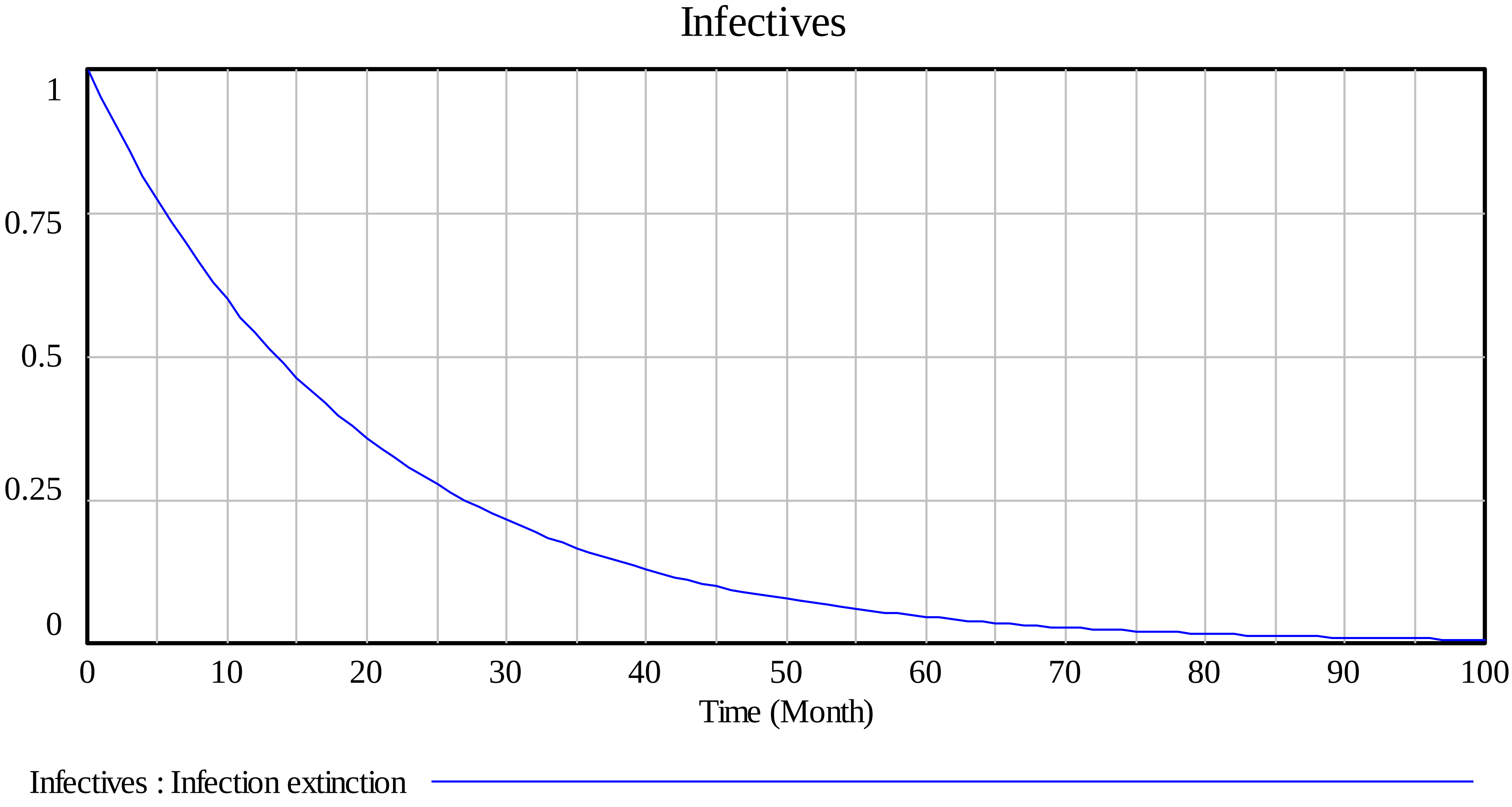
Equilibrium Behaviour

- With Births & Deaths, the system can approach an “endemic equilibrium” where the infection stays circulating in the population – but in balance
- The balance is such that (simultaneously)
  - The rate of new infections = The rate of immigration
    - Otherwise # of susceptibles would be changing!
  - The rate of new infections = the rate of recovery
    - Otherwise # of infectives would be changing!

Tipping Point

- Now try setting transmission rate β to 0.005

Case 2: Infection declines immediately



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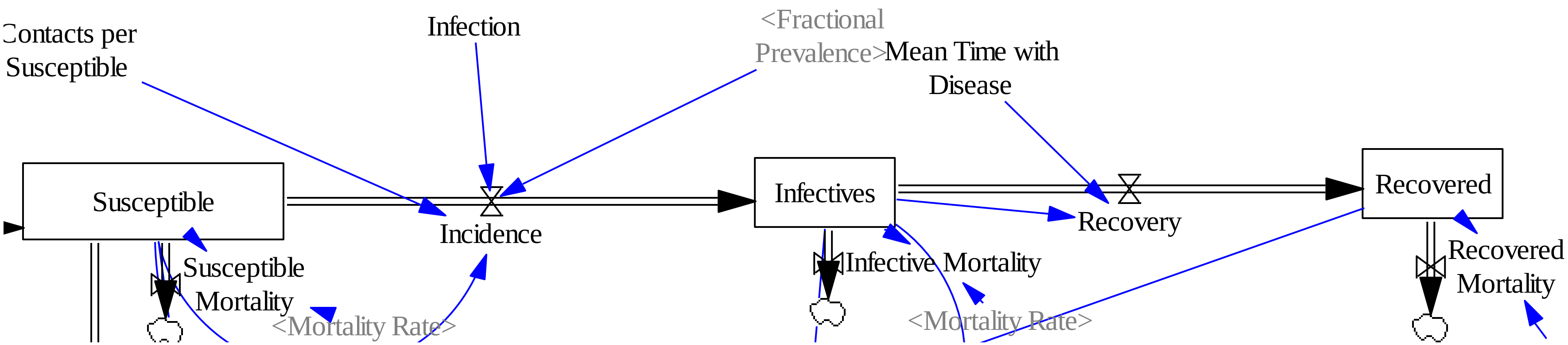

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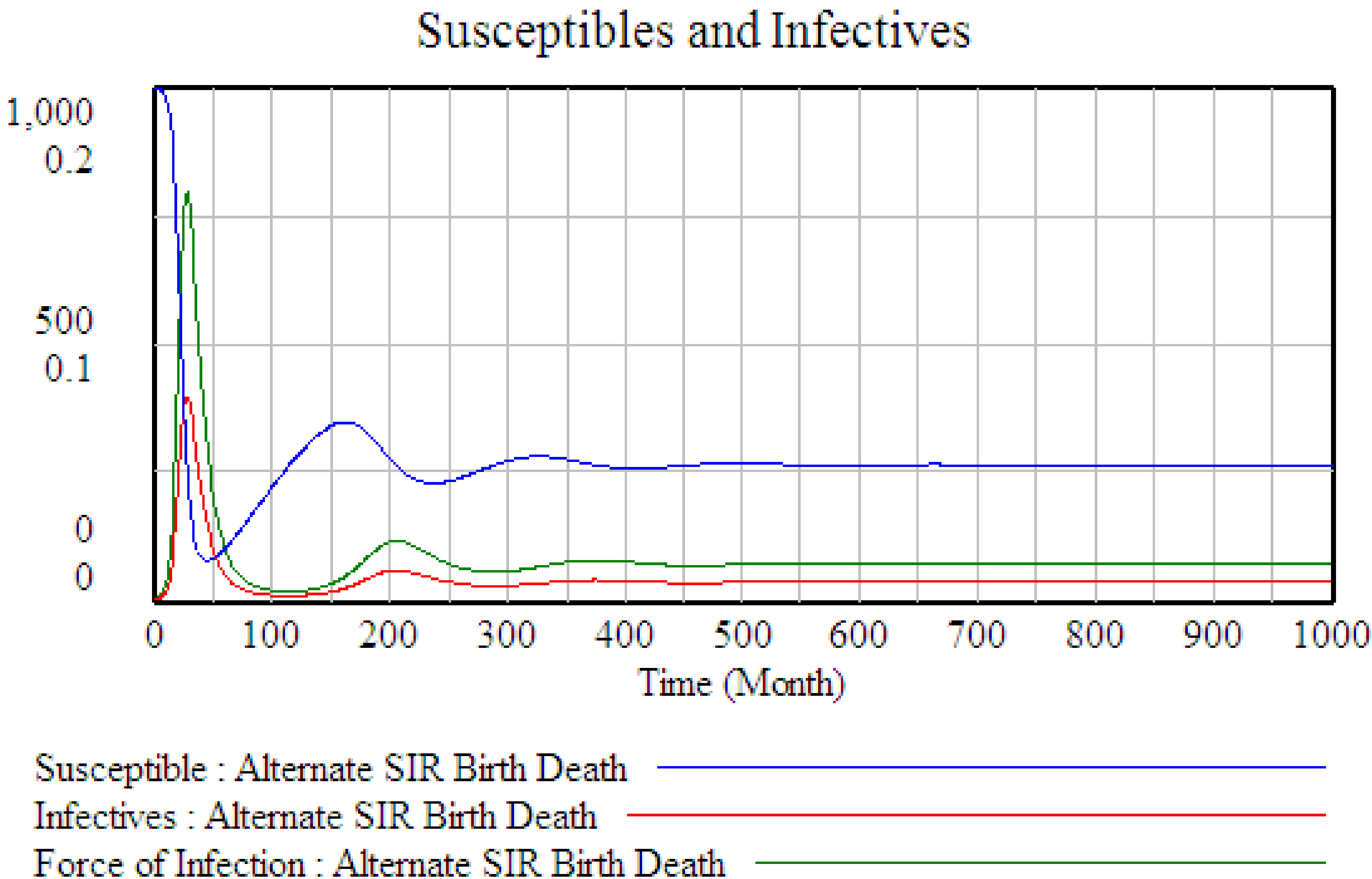


Damped Oscillatory Behavior

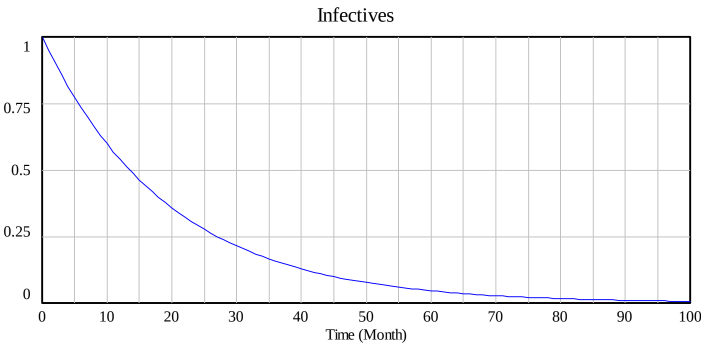
- Modify model to have births and deaths, with an annual birth-and-death rate
- Set Model/Settings/Final Time to 1000 (long time frame)
- In “Synthesim” (“Running man”) mode, set Birth/death rates
  - 0.02
  - 0.05
  - 0.07
  - 0.01
  - 0.001

Exploring the Tipping Point

- Now try setting transmission rate β to 0.005

Infection Extinction

- As for the case with a closed population, an open population has two cases
  – Infection dies out immediately



  – Outbreak: Infection takes off
    - Here – in contrast to the case for a closed population – the infection will typically go to an endemic equilibrium

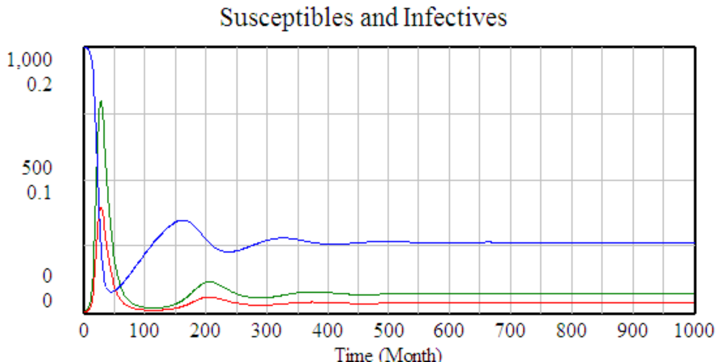
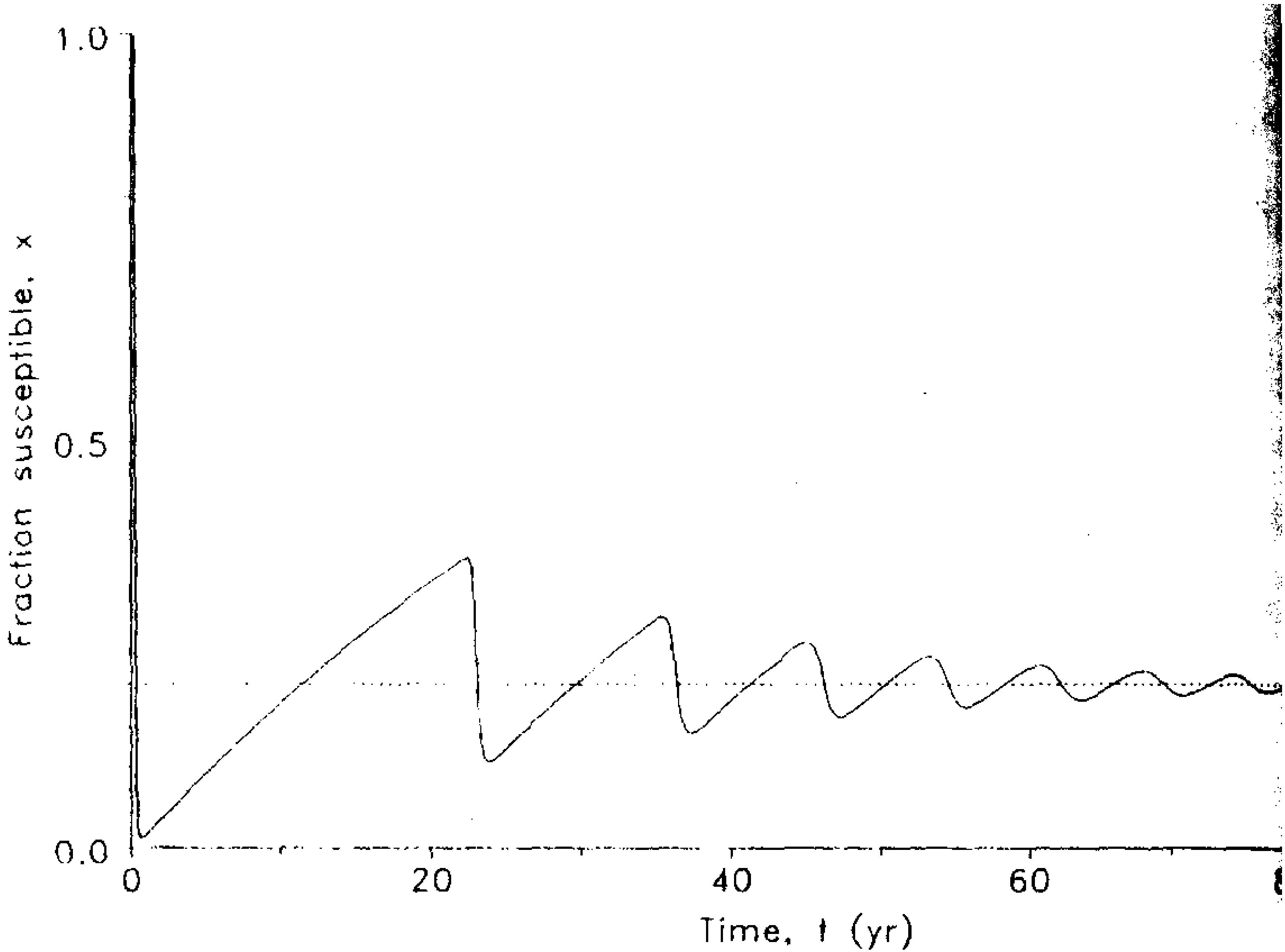


Table 6.1 Inter-epidemic period, T, of some common infections (from Anderson and May 1985c) and theoretical predictions of the period (eqn (6.15))

Infection	Inter-epidemic period, T, (years) (observed)	Geographical location and time period	Average age at infection, A	Latent plus infectious period, $D + D'$, (days)	Inter-epidemic period, T, (years) (calculated)
Measles	2	England and Wales, 1948–68	4–5	12	2
	2	Aberdeen, Scotland, 1883–1902	4–5		2
	2	Baltimore, USA, 1900–27	4–5		2
	2	Paris, France, 1880–1910	4–5		2
	1	Yaounde, Cameroun, 1968–75	2		1–2
	1	Ilesha, Nigeria, 1958–61	2		1–2
Rubella	3.5	Manchester, UK, 1916–83	11	18	4–5
	3.5	Glasgow, Scotland, 1929–64	11		4–5
Parvovirus (HPV)	3–5	England and Wales, 1960–80	?	?	
Mumps	3	England and Wales, 1948–82	6–7	16–26	3
	2–4	Baltimore, USA, 1928–73	8–9		3–4
Poliomyelitis	3–5	England and Wales, 1948–65	11–12	15–23	4–5
Echovirus (type II)	5	England and Wales, 1965–82	?	?	–
Smallpox	5	India, 1868–1948	12	10–14	4–5
Chickenpox	2–4	New York City, USA, 1928–72	6–8	18–23	3–4
	2–4	Glasgow, Scotland, 1929–72	6–8		3–4
Coxsackie virus (type B2)	2–3	England and Wales, 1967–82	?	?	
Scarlet fever	3–6	England and Wales, 1897–1978	10–14	15–20	4–5
Diphtheria	4–6	England and Wales, 1897–1979	11	16–20	4–5
Pertussis	3–4	England and Wales, 1948–85	4–5	27	3–4
Mycoplasma pneumoniae	4	England and Wales, 1970–82	?	?	


1.0
0.5
0.0
Fraction susceptible, x
0
20
40
60
Time, t (yr)

Typically, in Endemic Equilibrium, the Uninfected Fraction of the Population (S/N) is the Young

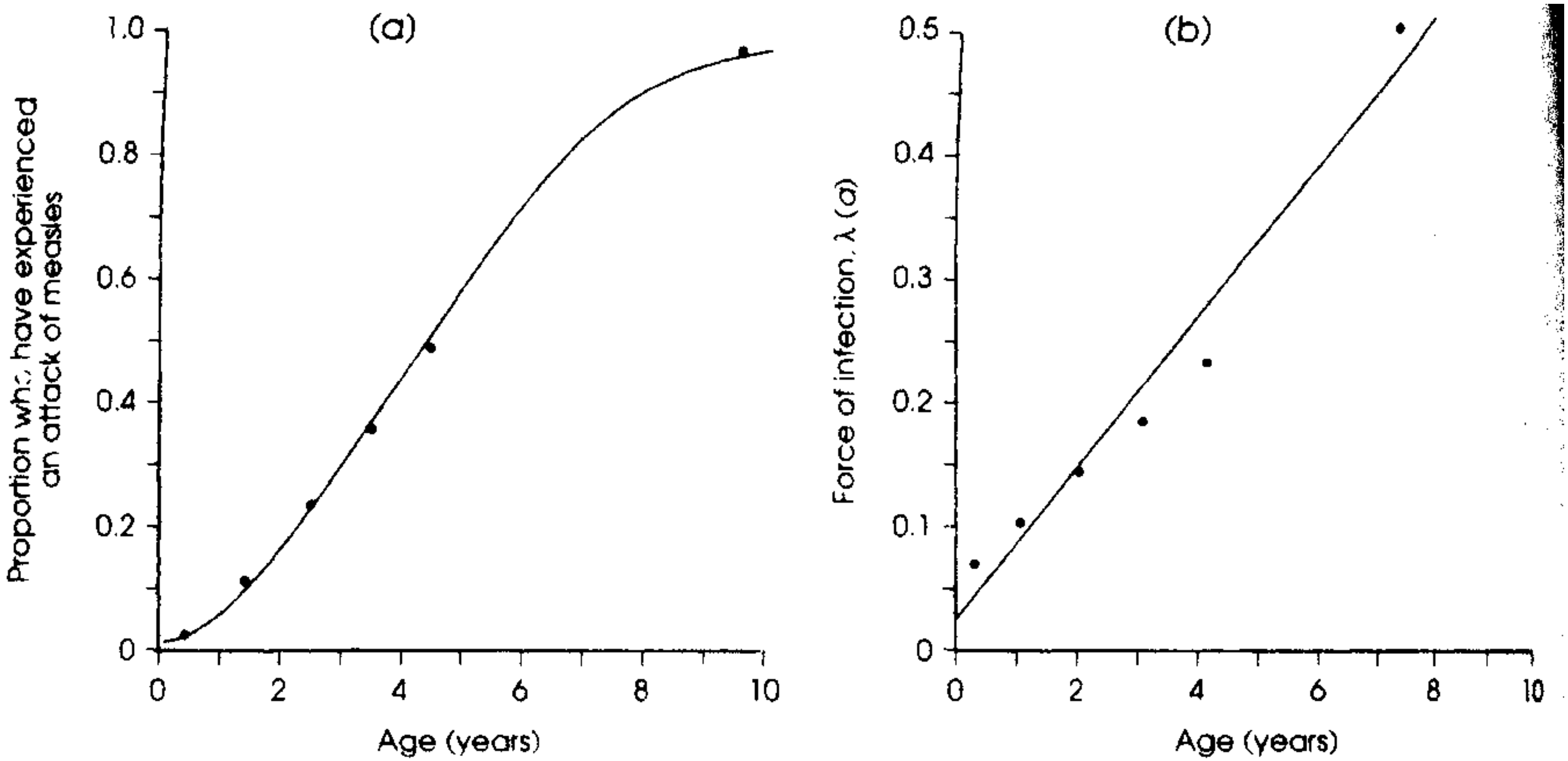


Fig. 5.14. Measles. (a) Proportion of children who had experienced an attack of measles at various ages in England and Wales in 1958 (based on case notification records). Dots, observed values; full curve, predictions of a simple catalytic model with age-dependent rates of infection (see text). (b) The age dependency in the rate or force of infection $\lambda(a)$. Dots, calculated values; full curve, best-fit linear model of the form $\lambda(a) = m + va$, where $m = 0.0178$ and $v = 0.063$ ($r^2 = 0.96$).

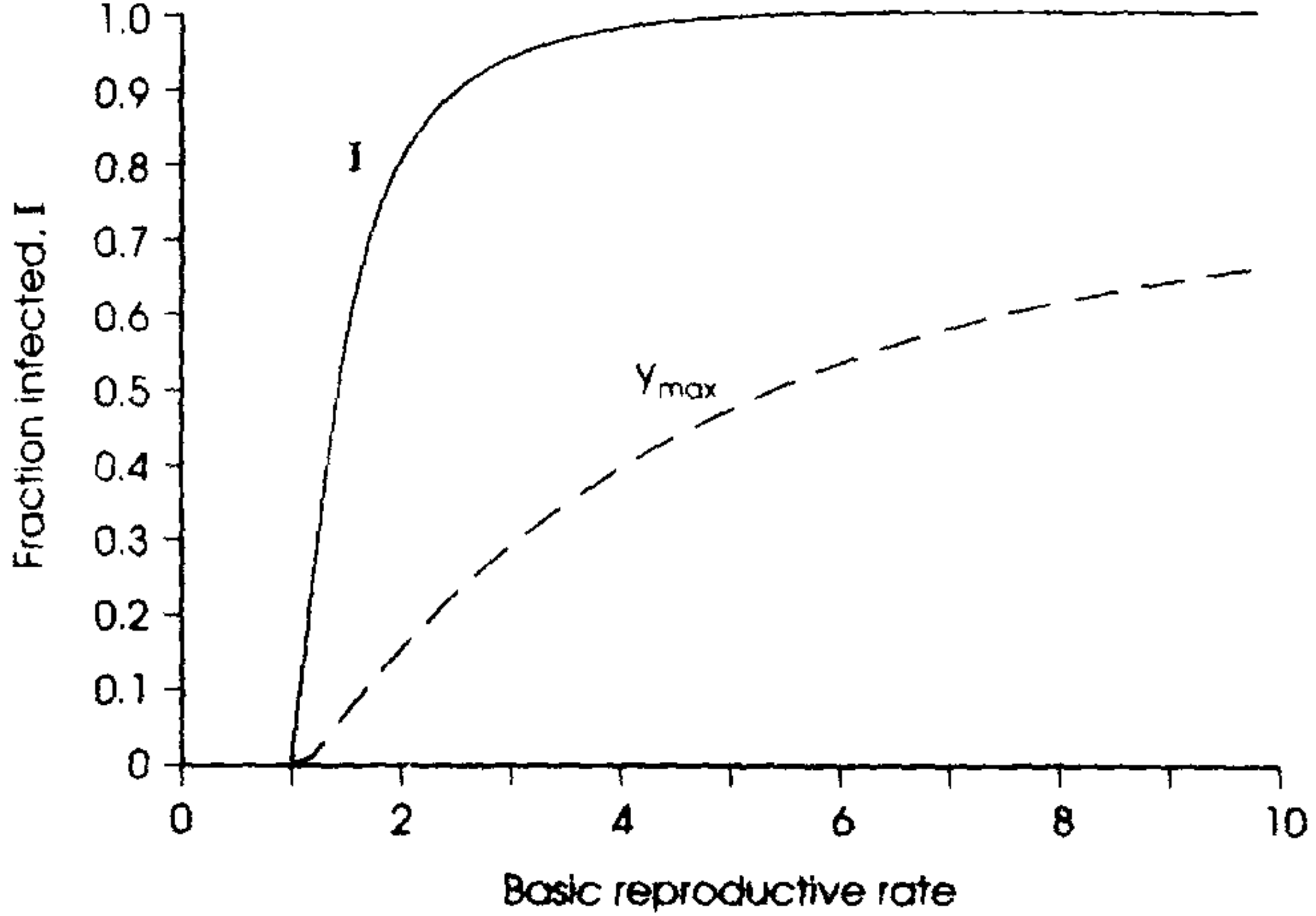


Fig. 6.2. The peak fraction infected, y_{max}, and the fraction ever infected, I, plotted as functions of R_0 (see text and eqns (6.20) and (6.21)).

Table 4.1 Estimated values of the basic reproductive rate, R_0, for various infections (data from Anderson (1982*b*), Anderson and May (1982*d*, 1985*c*, 1988), Anderson *et al.* (1988), Nokes and Anderson (1988)).

Infection	Geographical location	Time period	R_0
Measles	Cirencester, England	1947–50	13–14
	England and Wales	1950–68	16–18
	Kansas, USA	1918–21	5–6
	Ontario, Canada	1912–13	11–12
	Willesden, England	1912–13	11–12
	Ghana	1960–8	14–15
	Eastern Nigeria	1960–8	16–17
Pertussis	England and Wales	1944–78	16–18
	Maryland, USA	1943	16–17
	Ontario, Canada	1912–13	10–11
Chicken pox	Maryland, USA	1913–17	7–8
	New Jersey, USA	1912–21	7–8
	Baltimore, USA	1943	10–11
	England and Wales	1944–68	10–12
Diphtheria	New York, USA	1918–19	4–5
	Maryland, USA	1908–17	4–5
Scarlet fever	Maryland, USA	1908–17	7–8
	New York, USA	1918–19	5–6
	Pennsylvania, USA	1910–16	6–7
Mumps	Baltimore, USA	1943	7–8
	England and Wales	1960–80	11–14
	Netherlands	1970–80	11–14
Rubella	England and Wales	1960–70	6–7
	West Germany	1970–7	6–7
	Czechoslovakia	1970–7	8–9
	Poland	1970–7	11–12
	Gambia	1976	15–16
Poliomyelitis	USA	1955	5–6
	Netherlands	1960	6–7
Human Immunodeficiency Virus (Type I)	England and Wales (male homosexuals)	1981–5	2–5
	Nairobi, Kenya (female prostitutes)	1981–5	11–12
	Kampala, Uganda (heterosexuals)	1985–7	10–11

Delays

- For a while after infectives start declining (i.e. susceptibles are below sustainable endemic value), they still deplete susceptibles sufficiently for susceptibles to decline
- For a while after susceptibles are rising (until susceptibles=endemic value), infectives will still decline
- For a while after infectives start rising, births > # of infections =>susceptibles will rise to a peak well above endemic level

Infection

- Recall: For this model, a given infective infects $c(S/N)\beta$ others per time unit
  - This goes up as the number of susceptibles rises
- Questions
  - If the mean time a person is infective is μ, how many people does that infective infect before recovering?
  - With the same assumption, how many people would that infective infect if everyone else is susceptible?
  - Under what conditions would there be more infections after their recovery than before?

Fundamental Quantities

- We have just discovered the values of 2 famous epidemiological quantities for our model
  - Effective Reproductive Number: R_*
  - Basic Reproductive Number: R_0

Effective Reproductive Number: R_*

- Number of individuals infected by an ‘index’ infective in the current epidemological context
- Depends on
  - Contact rates/frequency
  - Transmission probability
  - Length of time infectives
  - (Fraction) of Susceptibles
- Affects
  - Whether infection spreads
    - If $R_*> 1$, # of cases will rise, If $R_*<1$, # of cases will fall
      - Alternative formulation: Largest real eigenvalue <> 0
  - Endemic Rate

Basic Reproduction Number: R_0

- Number of individuals infected by an 'index' infective *in an otherwise disease-free equilibrium*
  - This is just R_* at disease-free equilibrium all (other) people in the population are susceptible other than the index infective
- Depends on
  - Contact number
  - Transmission probability
  - Length of time infected
- Affects
  - Whether infection spreads
    - If $R_0 > 1$, Epidemic Takes off, If $R_0 < 1$, Epidemic dies out
      - Alternative formulation: Largest real eigenvalue <> 0
    - Initial infection rise $\propto$ exp(t*(R0-1)/D)
  - Endemic Rate

Basic Reproductive Number R_0

- If contact patterns & infection duration remain unchanged and if fraction f of the population is **susceptible**, then mean # of individuals infected by an infective over the course of their infection is f^*R_0
- In endemic equilibrium: Inflow=Outflow $\Rightarrow (S/N)\cdot R_0=1$
  - Every infective infects a "replacement" infective to keep equilibrium
  - Just enough of the population is susceptible to allow this replacement
  - The higher the R_0, the lower the fraction of susceptibles in equilibrium!
    - *Generally some* susceptibles remain: At some point in epidemic, susceptibles will get so low that can't spread

Open/Closed Population

	Case	Does Epidemic Occur?	Steady-state (Endemic)	
			Fraction infective	**Fraction susceptible**
Open Population	$R_0>1$	Yes	Such that Infection rate=Recovery rate	$1/R_0$
	$R_0<1$	No	0	1
Closed Population	$R_0>1$	Yes	0	<1 (often <<1) but >0
	$R_0<1$	No	0	≈ 1

Our model

- Set
  - c=10 (people/month)
  - β=0.04 (4% chance of transmission per S-I contact)
  - μ=10
  - Birth and death rate= 0
  - Initial infectives=1, other 1000 susceptible
- What is R_0?
- What should we expect to see ?

Thresholds

- R_*
  - Too low # susceptibles => R* < 1: # of infectives declining
  - Too high # susceptibles => R* > 1: # of infectives rising
- R_0
  - $R_0>1$: Infection is introduced from outside will cause outbreak
  - $R_0<1$: "Herd immunity": infection is introduced from outside will die out (may spread to small number before disappearing, but in unsustainable way)
    - **This is what we try to achieve by control programs, vaccination, etc.**
- Outflow from susceptibles (infections) is determined by the # of Infectives

Equilibrium Behaviour

- With Births & Deaths, the system can approach an "endemic equilibrium" where the infection stays circulating in the population – but in balance
- The balance is such that (simultaneously)
  - The rate of new infections = The rate of immigration
    - Otherwise # of susceptibles would be changing!
  - The rate of new infections = the rate of recovery
    - Otherwise # of infectives would be changing!

Equilibria

- Disease free
  - No infectives in population
  - Entire population is susceptible
- Endemic
  - Steady-state equilibrium produced by spread of illness
  - Assumption is often that children get exposed when young
- The stability of the these equilibria (whether the system departs from them when perturbed) depends on the parameter values
  - For the disease-free equilibrium on R_0