Mathematical Modelling of Infectious Diseases

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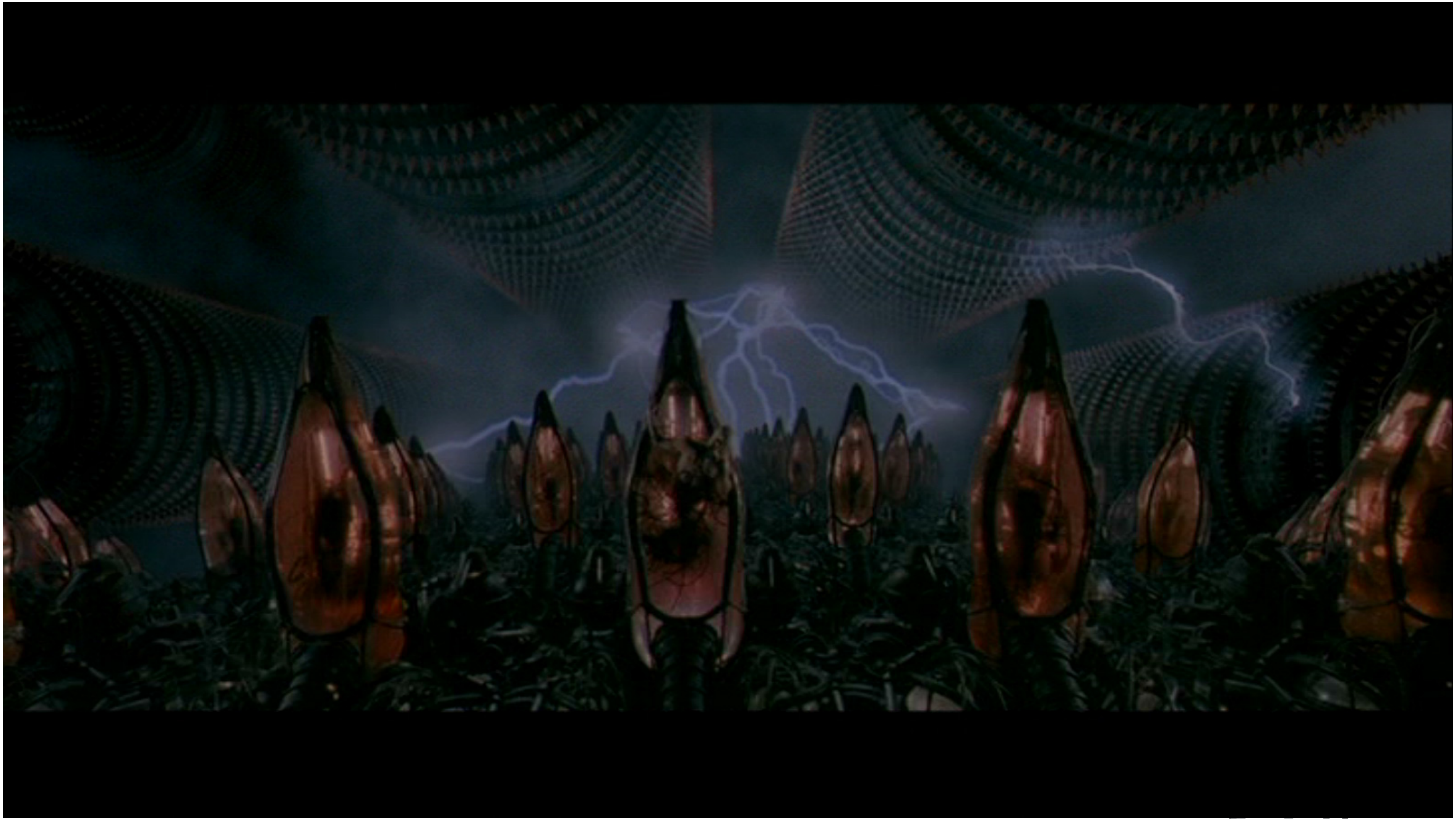

If We Had That Much Computing Power We Could...

- Run infection experiments
- Infect "people"
- Change behaviour
- Change the environment
- Observe the impact on the disease process
- But we don't have that much computing power. Yet.

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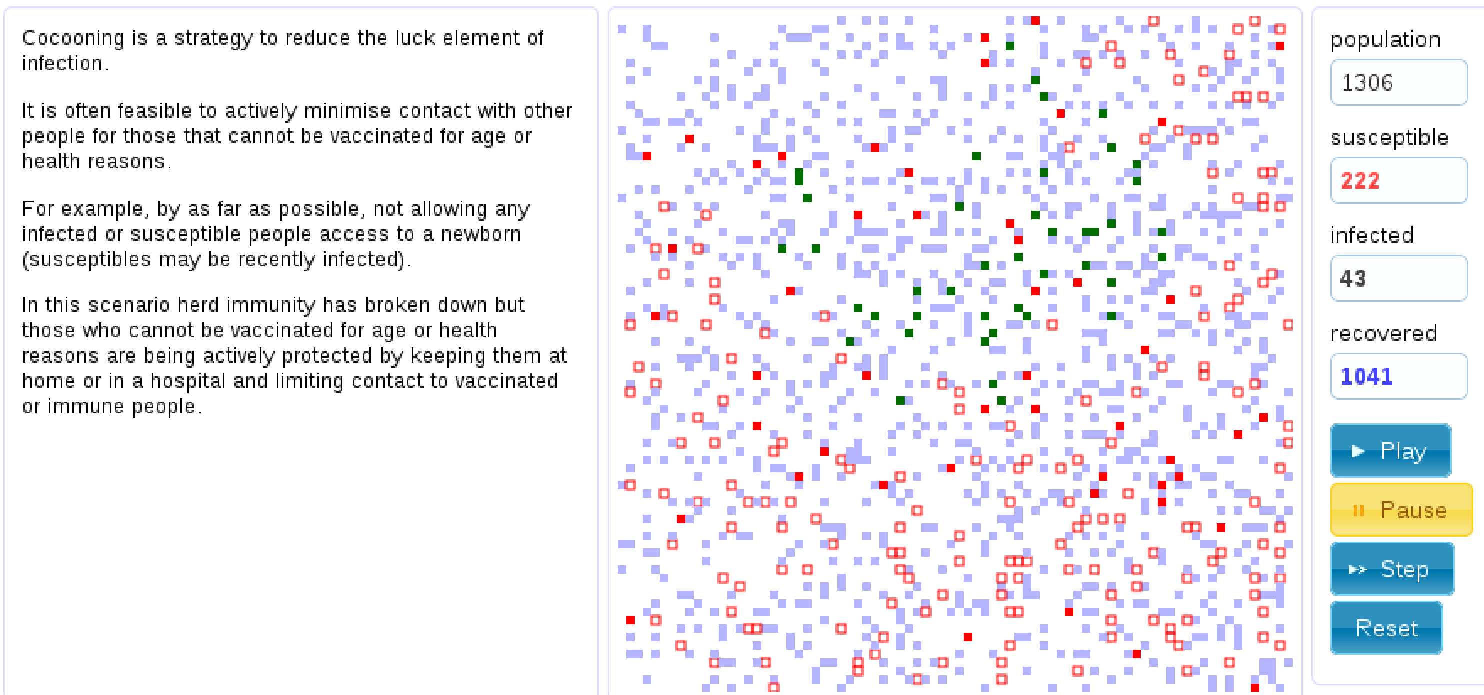
How Simple Can We Make This?

- http://op12no2.me/toys/herd/



- People are squares on a grid
- Illustrates transmission and immunity

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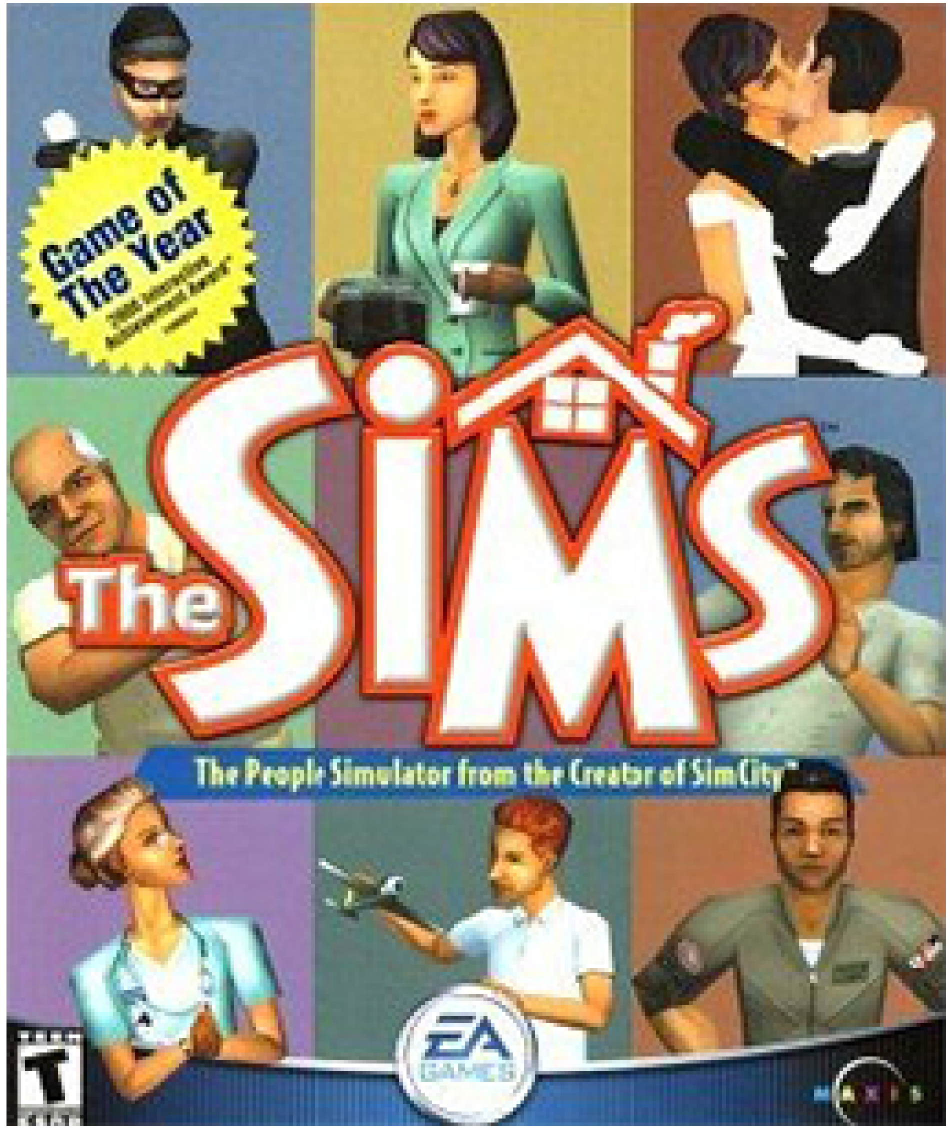
Game of
The Year
The Sims
The People Simulator from the Creator of SimCity
EA
GAMES
MAXIS
T

“Guinea Pig Disease”

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“Guinea Pig Disease”

- Example of a “Zoonosis”

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Dysentery

...can be passed on to other sims

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Agent-based Modelling

- Smallest modelled unit is an individual
- Mathematical model of agent behaviour
- Multiple simulations to get probabilistic answers to “if” questions.
- Found in other disciplines, eg traffic modelling, finance

But what if we have too many agents to model?

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Numerical Models

- Start with one infectious person
- Each day, every infectious person infects two more people
- People are infectious for two days
- What happens?

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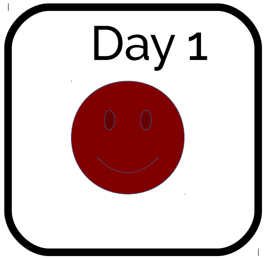
Infectious Model



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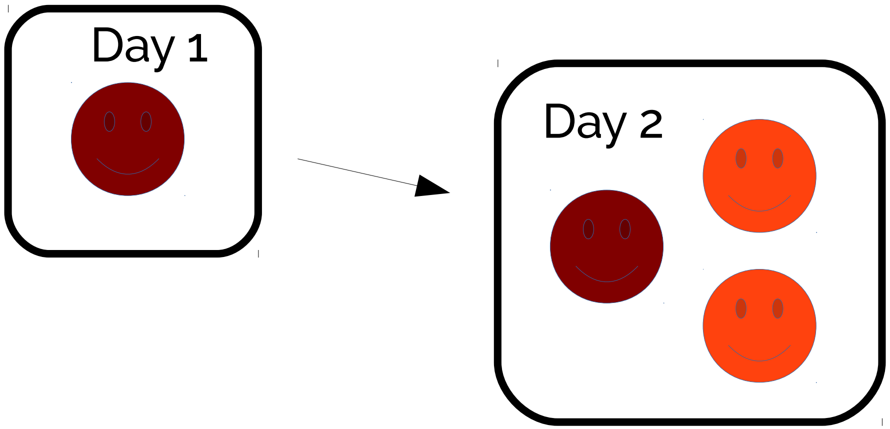
Infectious Model



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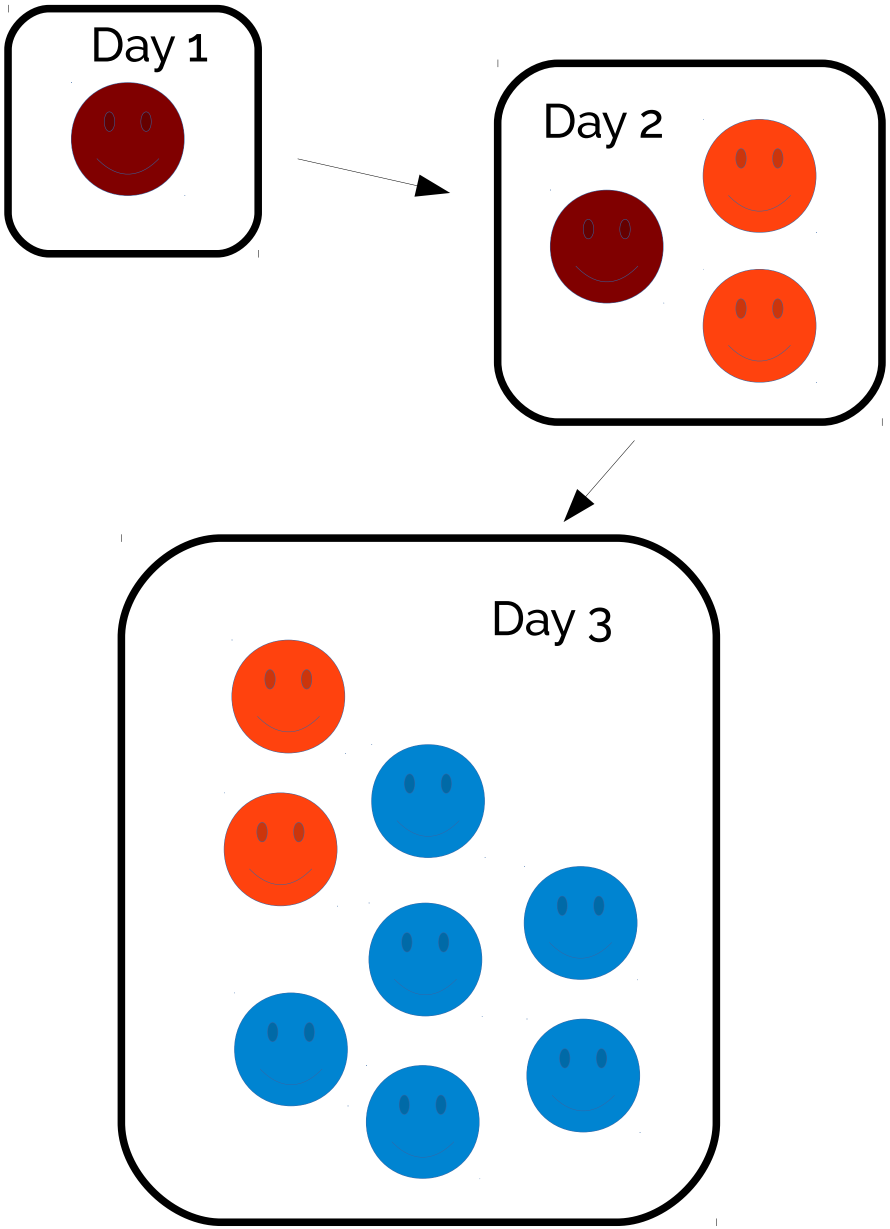
Infectious Model



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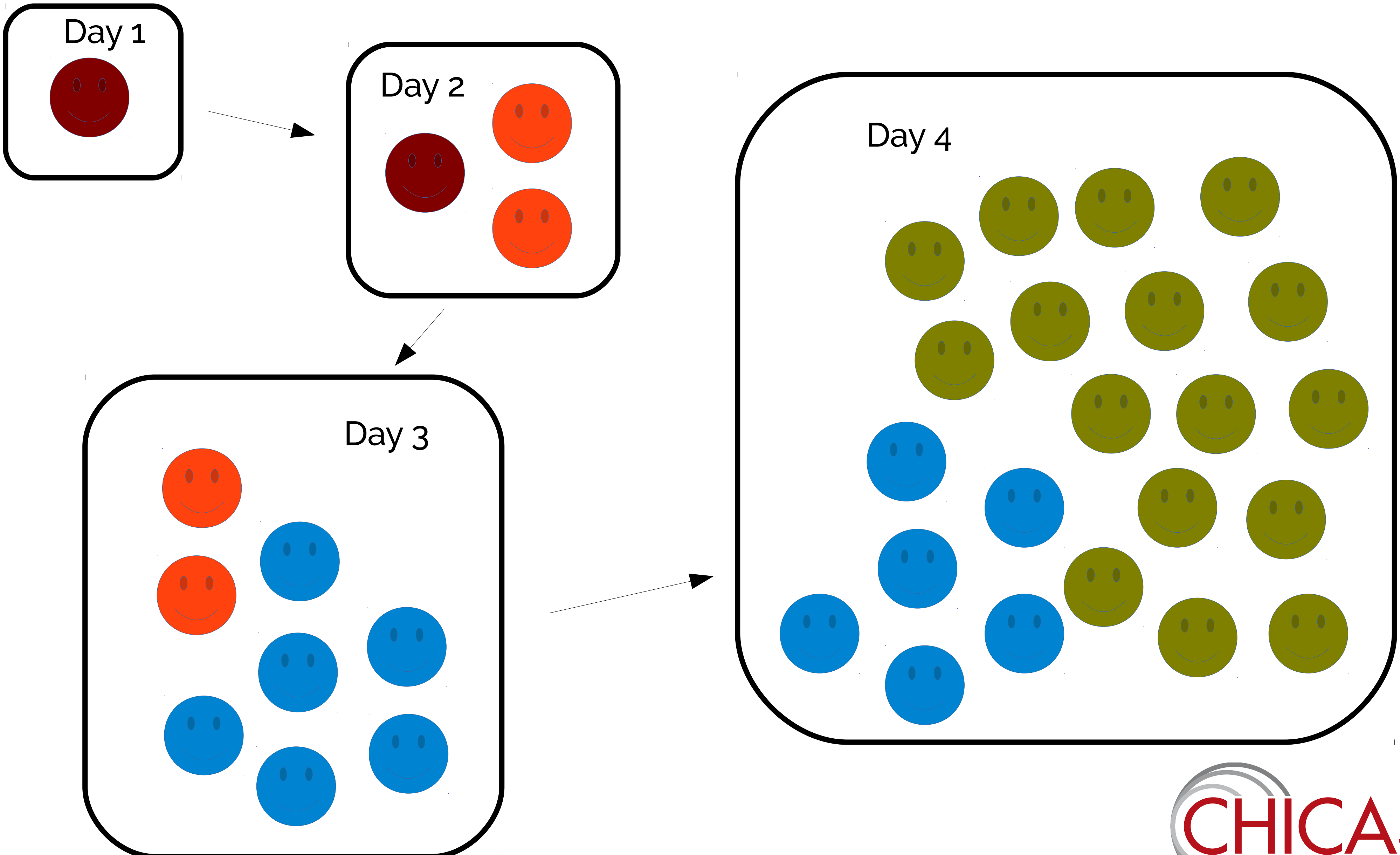
Infectious Model



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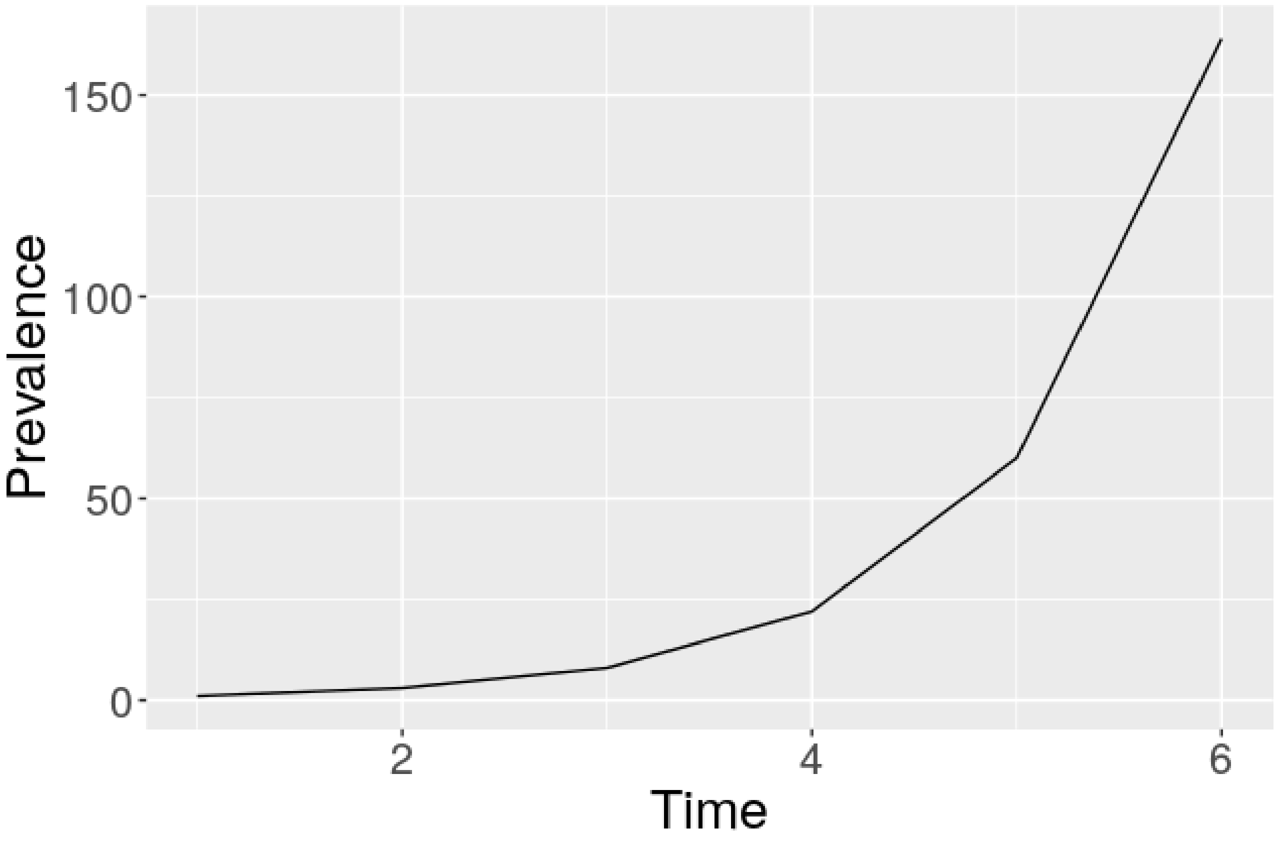
Rapid Growth

Time	Prevalence
1	1
2	3
3	8
4	22
5	60
6	164



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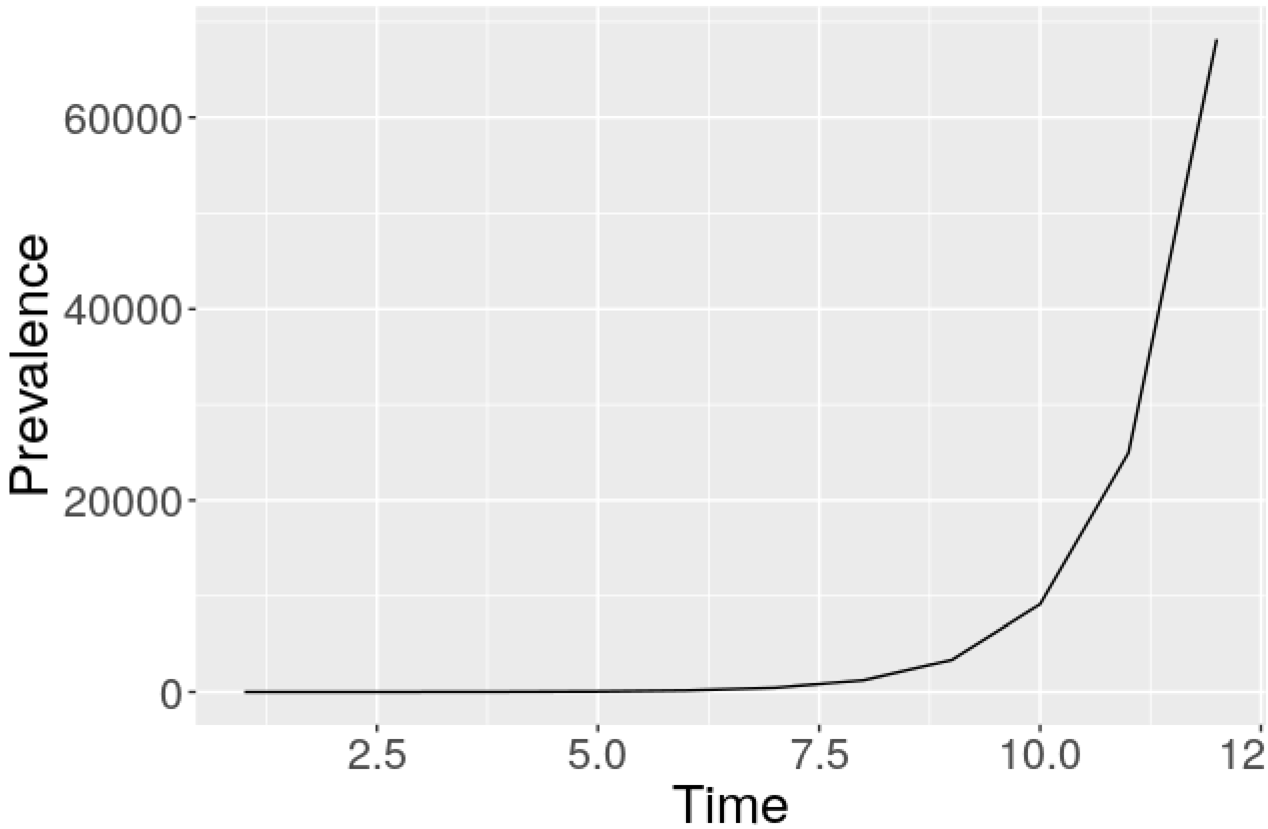
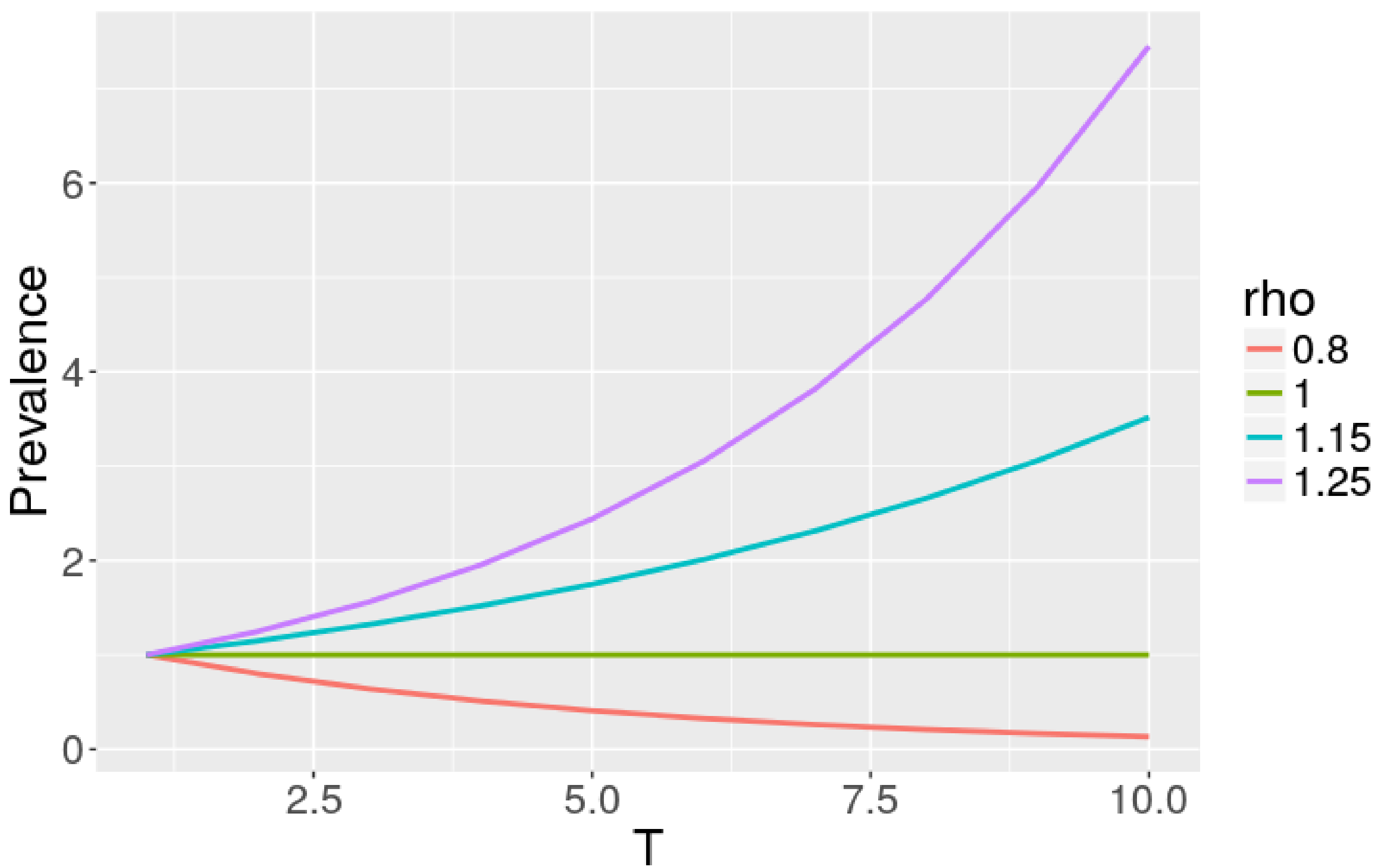
Rapid Growth.....

Time	Prevalence
1	1
2	3
3	8
4	22
5	60
6	164
...	...
12	68192
...	...
24	11 billion



Reproduction number



Is Exponential Growth Valid?

- Yes, when:
  - Initial Stages of an Infection
  - Large Susceptible Population
  - Thorough Mixing of Infectious Cases
- No, when:
  - Finite Population
  - Few Susceptible Population
  - Poor Mixing of Infectious Cases and Population

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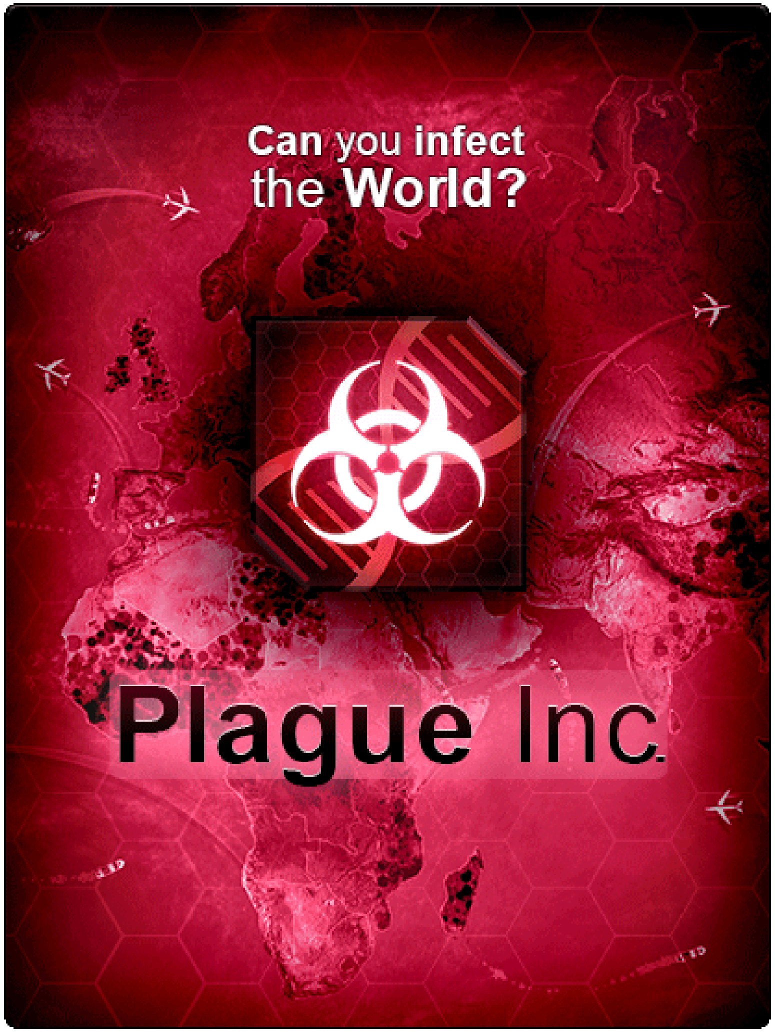
Finite Population



http://www.ndemiccreations.com/en/

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Aggregate Infection Tables

Country	Uninfected	Infectious	Dead
China	903,452,543	1,063,345	8,365
USA	325,753,342	0	1,20546
Brazil	180,537,623	20,663,634	7,653,634
Nigeria	191,836,451	0	0
…			
Pitcairn Islands	0	0	57

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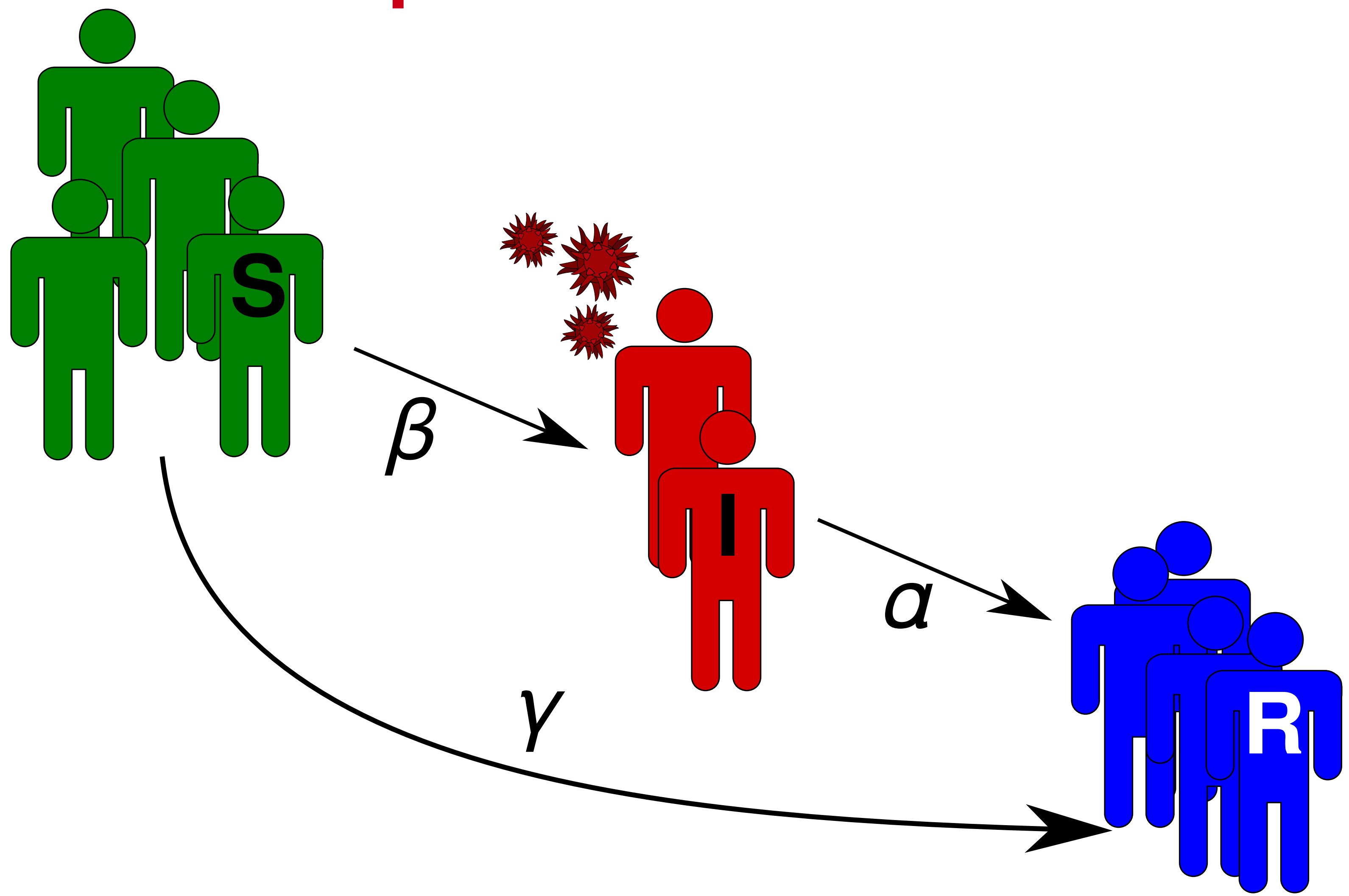
Compartment Model



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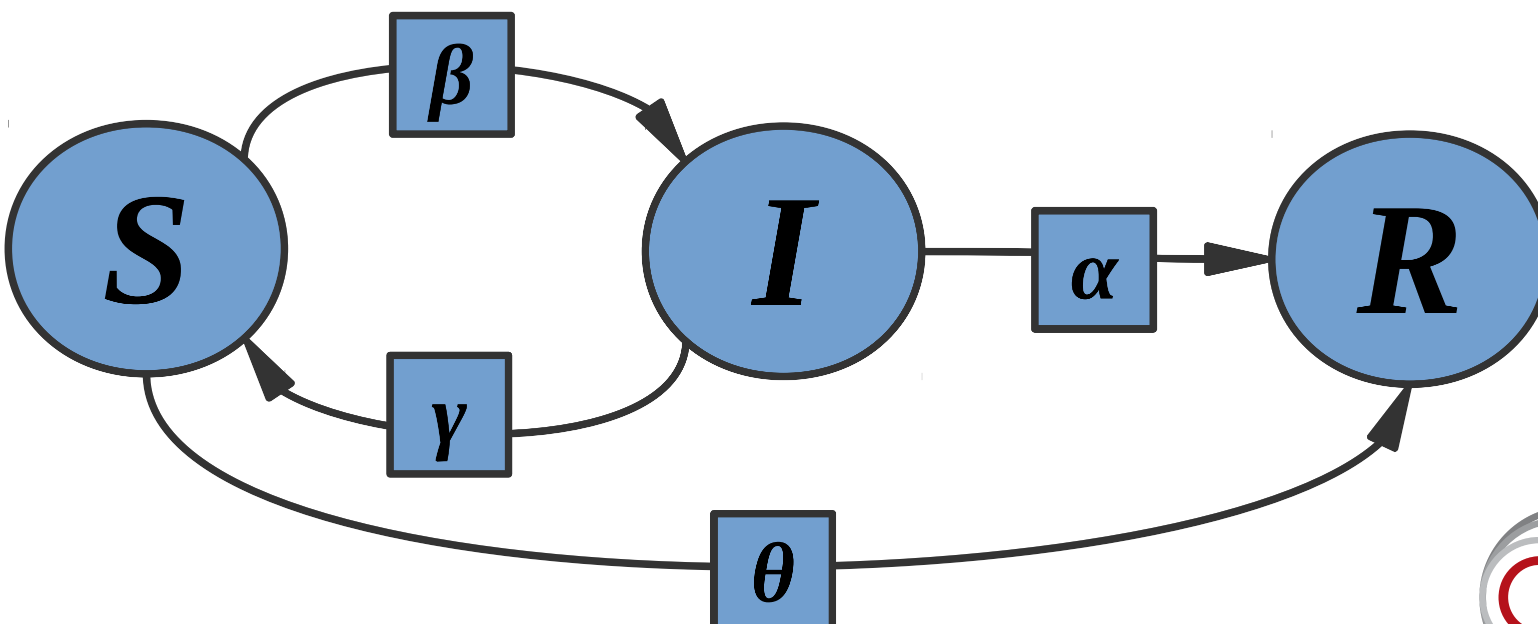
Compartment Model Diagram

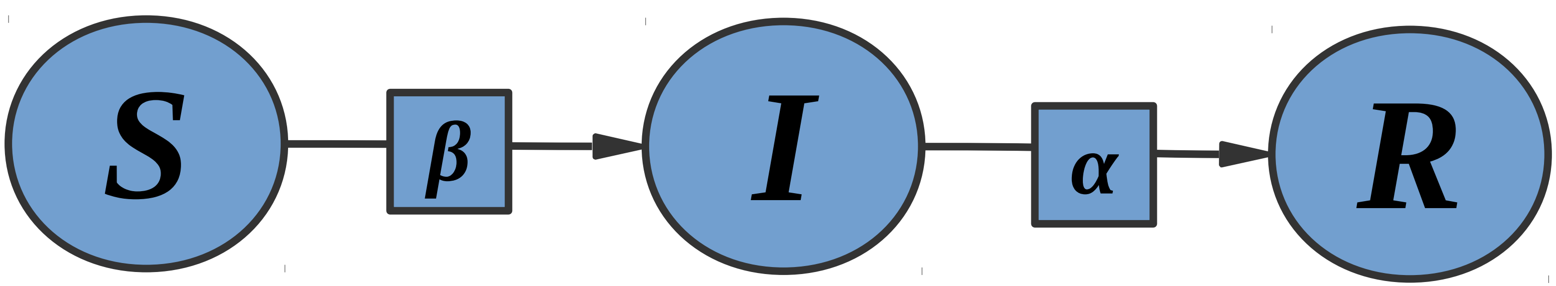
- S = #Susceptible
- I = #Infectious
- R = #Removed or Recovered

- Greek letters are parameters
- Control rates of change



SIR Compartment Model

- Three states
- Two parameters
- No re-infection (no arrows back to $\boldsymbol{S}$)
- Ignore other causes of death (no $\boldsymbol{S} \rightarrow \boldsymbol{R}$)



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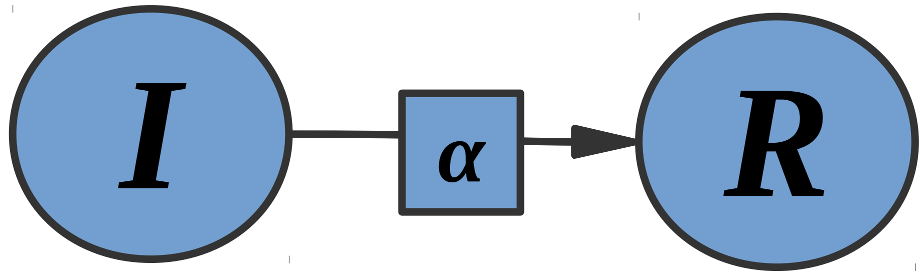
Removal/Death Rate



- Suppose today:
  - I = <u>1000</u>, R = <u>0</u>
  - α = 0.01
- Then tomorrow
  - I changes to 1000 – 1000 × α = <u>990</u>
  - R changes to 0 + 1000 × α = <u>10</u>

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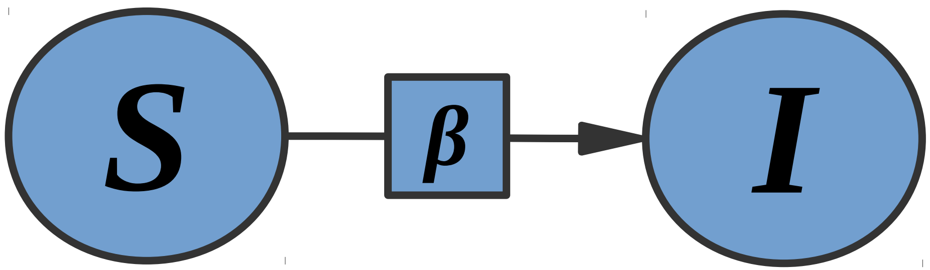
Infection Rate



- **Depends on number of infectious**, I
- Suppose today:
  - S = <u>1000</u>, I = <u>10</u>
  - β = 0.002
- Then tomorrow:
  - S becomes 1000 – 10 × 0.002 × 1000 = <u>980</u>
  - I becomes 10 + 10 × 0.002 × 1000 = <u>30</u>

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Time Notation

- S_1 is the number of susceptibles on day 1
  - Could be week 1, month 1, year 1...
- S_2 is the number of susceptibles on day 2
- S_t is the number on some day t
- S_{t+1} is number on the day after t
- Time can start at $t=0$

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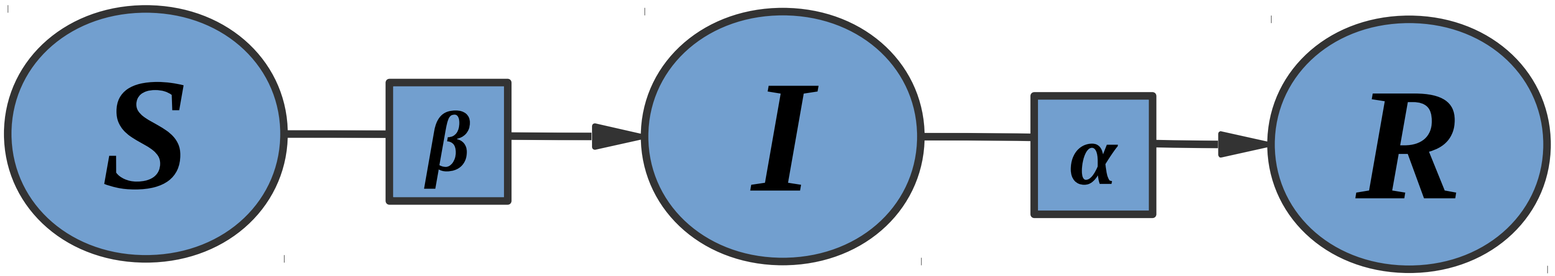
Updating Steps



- $S_t - (\beta \times I_t \times S_t) \rightarrow S_{t+1}$
- $R_t + (\alpha \times I_t) \rightarrow R_{t+1}$
- $I_t - (\alpha \times I_t) + (\beta \times I_t \times S_t) \rightarrow I_{t+1}$
  - *Increase t, and repeat...*

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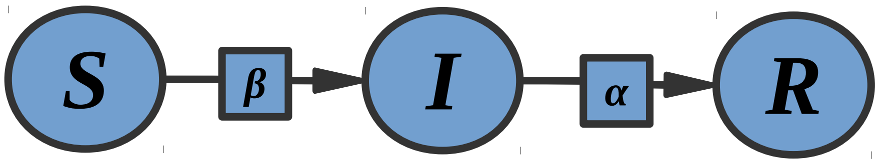
Example 1

- 100 people in total
- Start with one infection
- 99 susceptibles
- Set α=0
  - Nobody recovers
  - Effectively an SI model
- Set β=0.001



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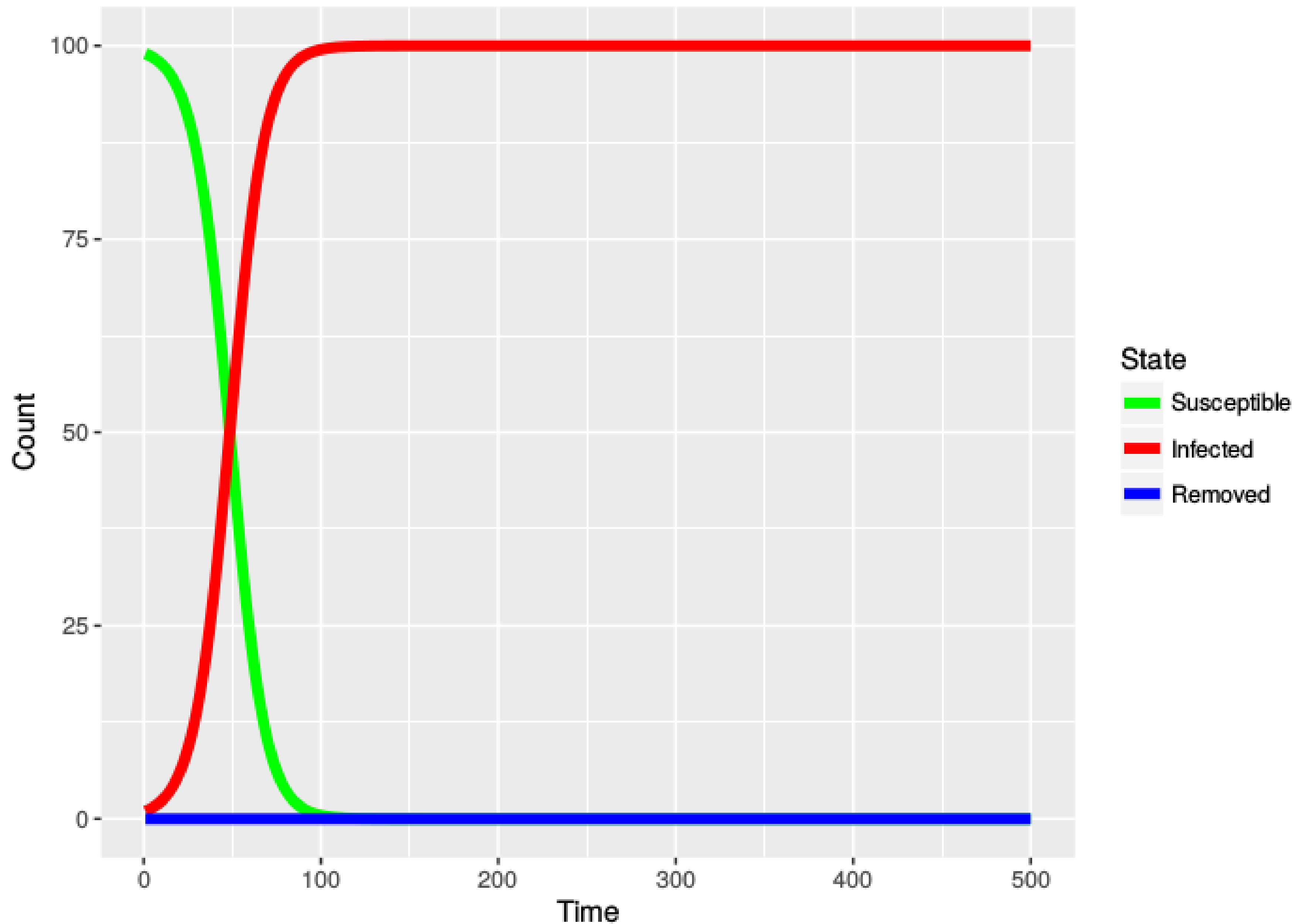
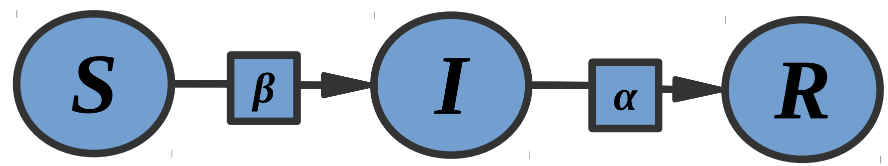
Epidemic Chart



Example 2 - recovery

- 100 people in total
- Start with one infection
- 99 susceptibles
- Set α=0.025
  - Some recovery
- Set β=0.001



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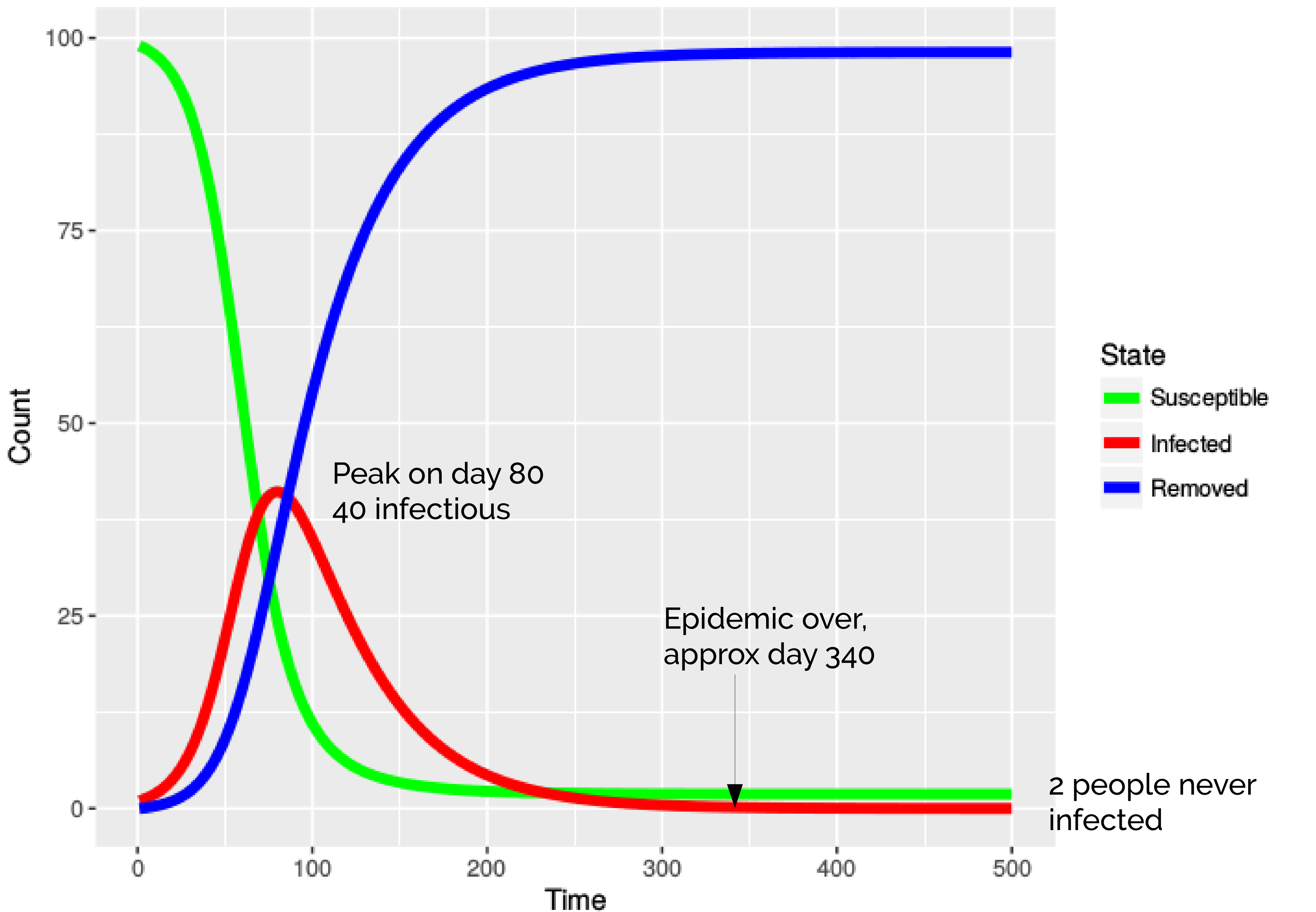
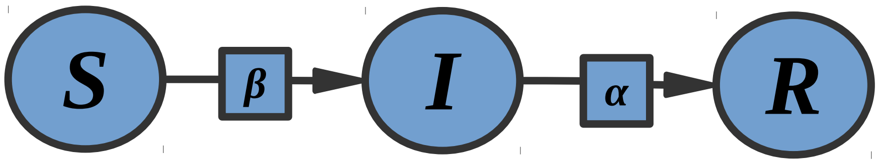
Epidemic Chart



Example 3 – faster recovery

- 100 people in total
- Start with one infection
- 99 susceptibles
- Set α=0.050
  - Double previous value
- Set β=0.001



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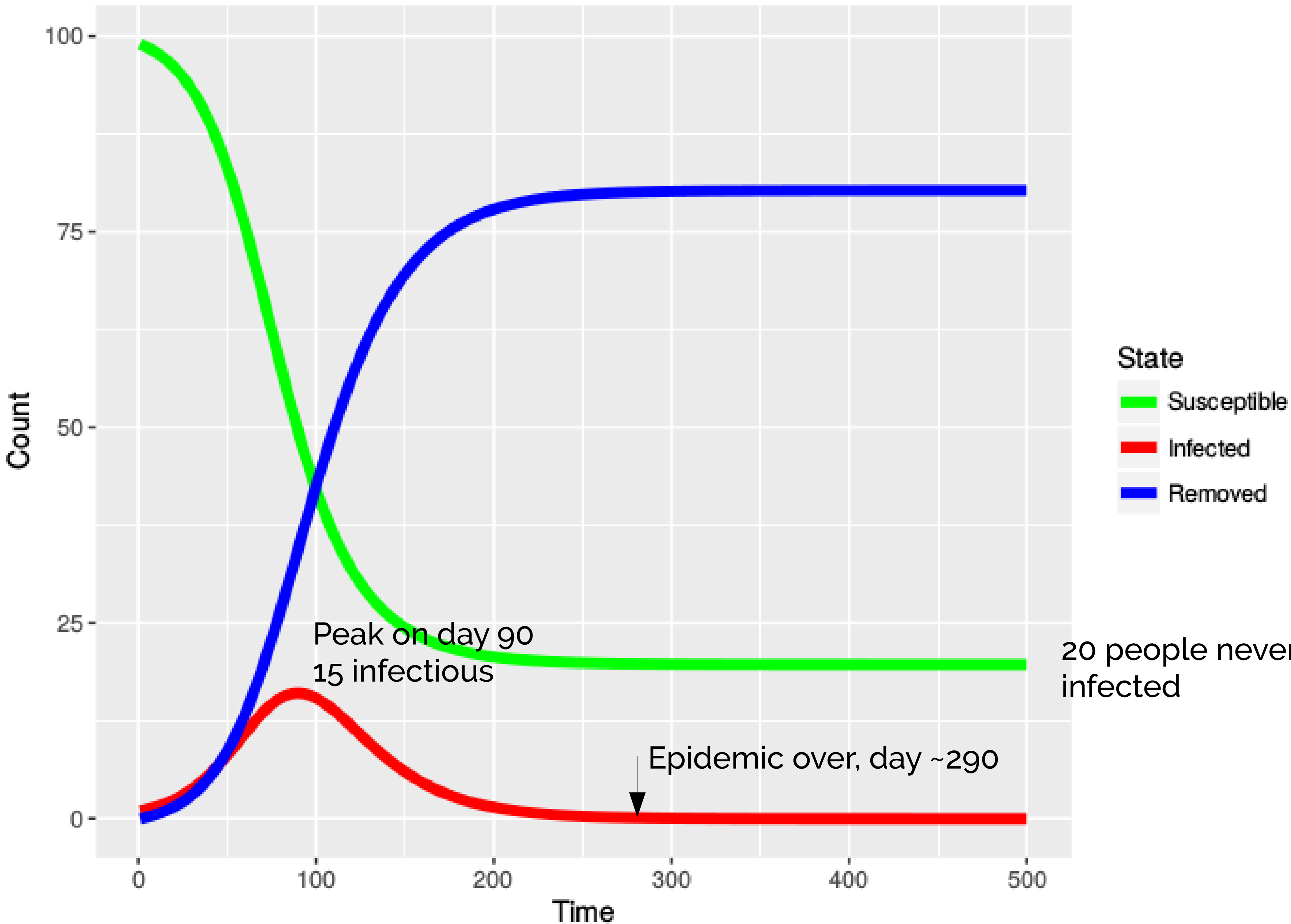
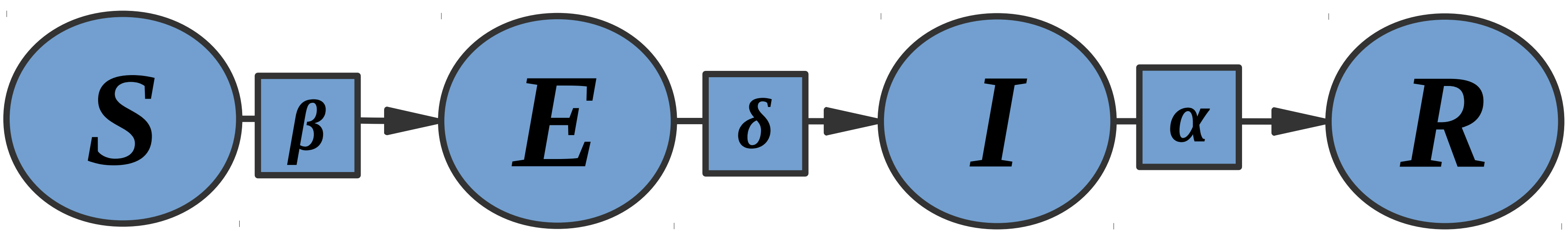
Epidemic Chart



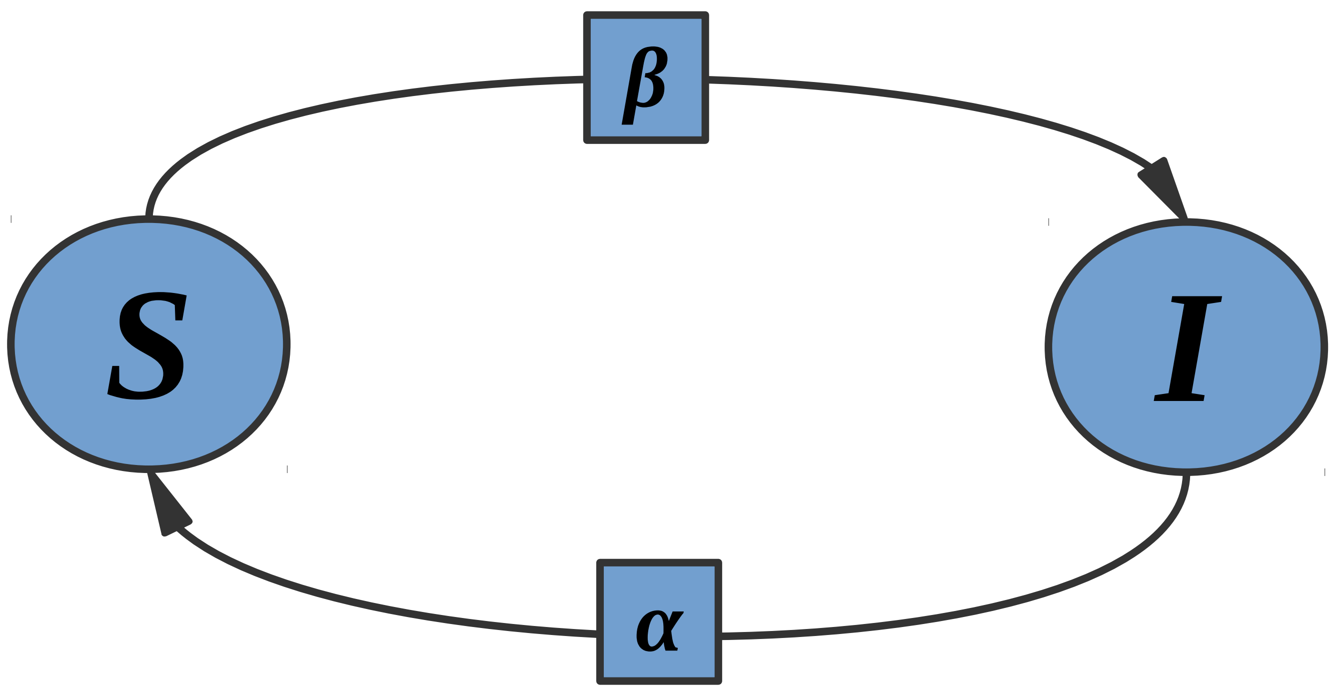
More Complex Models

- Add a "Latent" infected state
- Infected, and will progress to infectious at some rate δ
- Usually "E"

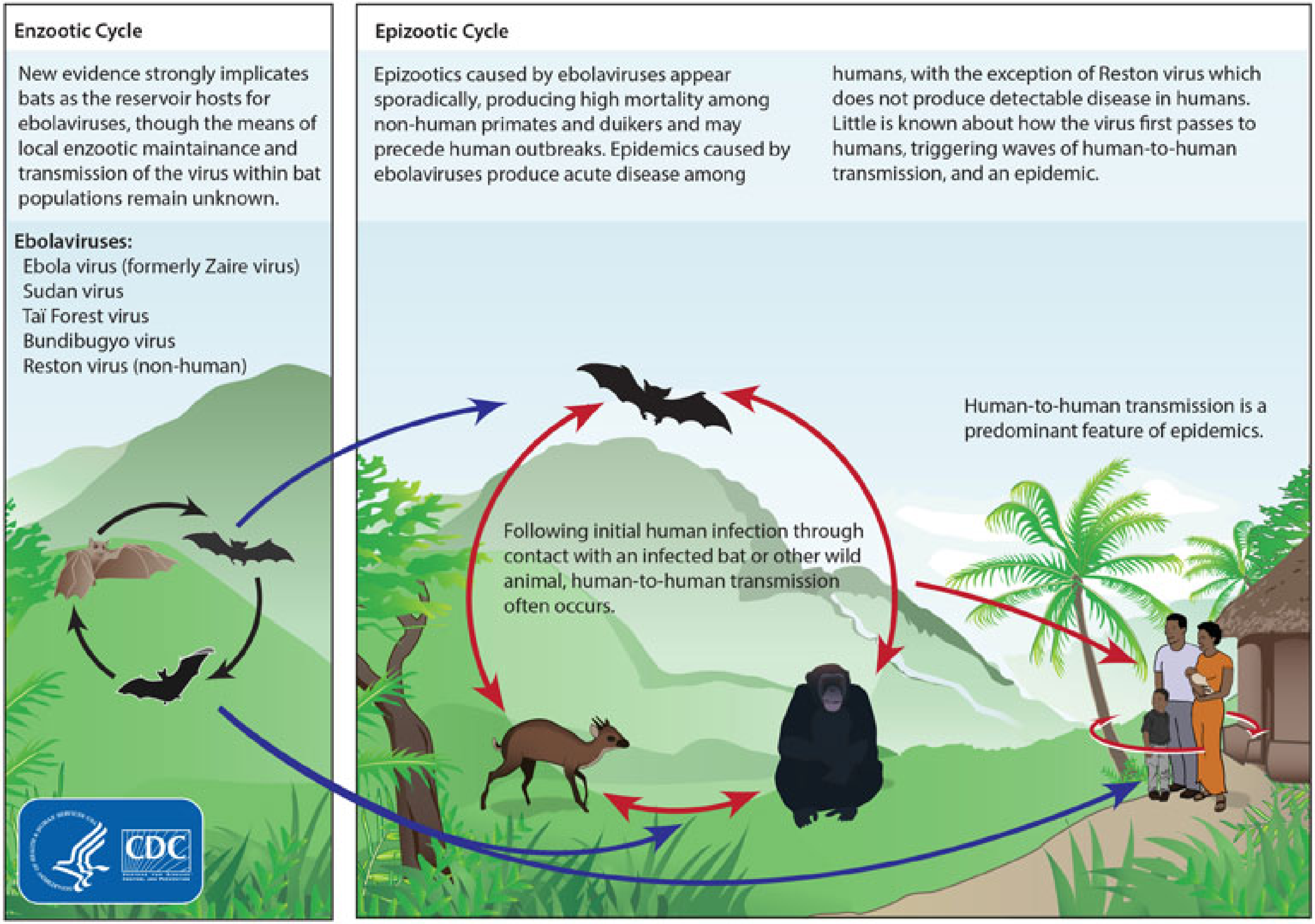


SIS Model

- Susceptible people become infectious
- Infected people recover
- How does the system end up?



More Species



Human Ectoparasites

Human ectoparasites and the spread of plague in Europe during the Second Pandemic

Katharine R. Dean, Fabienne Krauer, Lars Walløe, Ole Christian Lingjærde, Barbara Bramanti, Nils Chr. Stenseth, and Boris V. Schmid

PNAS 2018; published ahead of print January 16, 2018, https://doi.org/10.1073/pnas.1715640115

Contributed by Nils Chr. Stenseth, December 4, 2017 (sent for review September 4, 2017; reviewed by Xavier Didelot and Kenneth L. Gage)

- Can we blame the rats?

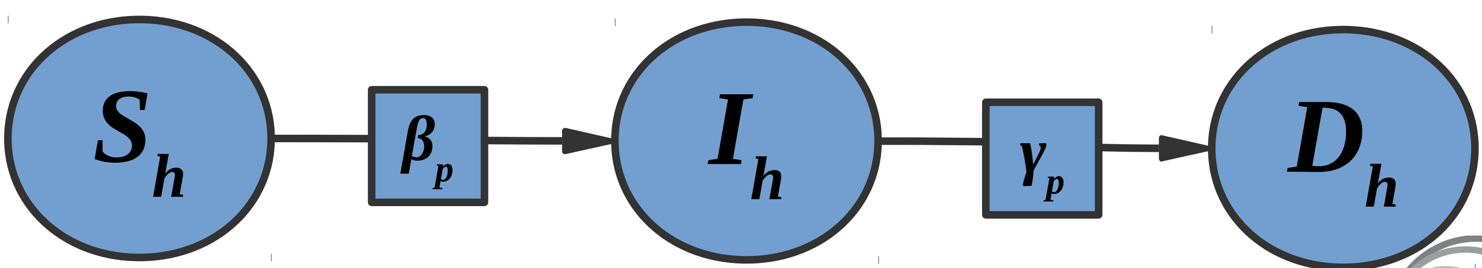
Pneumonic Model

- Human-Human Transmission

$$\frac{dS_h}{dt} = -\beta_p \frac{S_h I_h}{N_h},$$

$$\frac{dI_h}{dt} = \beta_p \frac{S_h I_h}{N_h} - \gamma_p I_h,$$

$$\frac{dD_h}{dt} = \gamma_p I_h.$$



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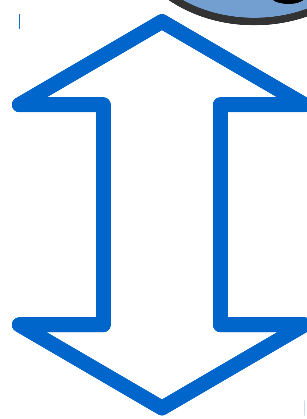
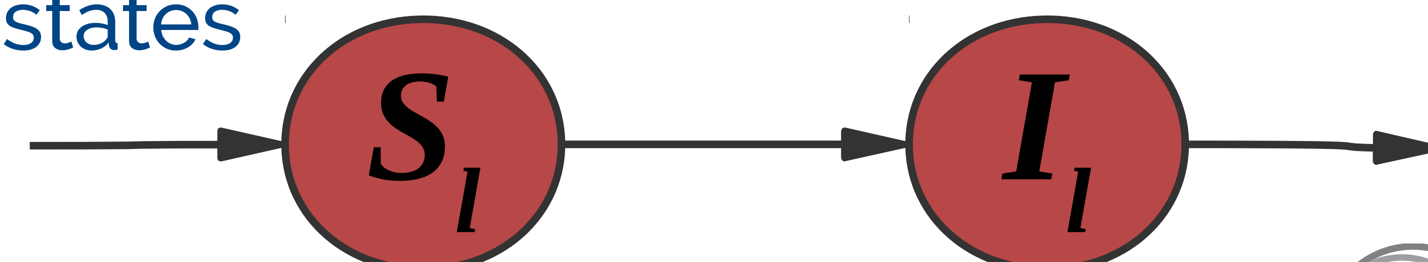
Human Ectoparasites

- Human infection states



Coupled systems

- Flea states



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Human Ectoparasites

$$\frac{dS_h}{dt} = -\beta_l \frac{S_h I_l}{N_h},$$

$$\frac{dI_{\text{low}}}{dt} = \beta_l \frac{S_h I_l}{N_h} - \sigma_b I_{\text{low}},$$

$$\frac{dI_{\text{high}}}{dt} = (1 - g_h)\,\sigma_b I_{\text{low}} - \gamma_b I_{\text{high}},$$

$$\frac{dR_h}{dt} = g_h \sigma_b I_{\text{low}},$$

$$\frac{dD_h}{dt} = \gamma_b I_{\text{high}},$$

$$\frac{dS_l}{dt} = r_l S_l \left(1 - \frac{N_l}{K_l}\right) - \left[\left(\beta_{\text{low}} I_{\text{low}} + \beta_{\text{high}} I_{\text{high}}\right) \frac{S_l}{N_h}\right],$$

$$\frac{dI_l}{dt} = \left[\left(\beta_{\text{low}} I_{\text{low}} + \beta_{\text{high}} I_{\text{high}}\right) \frac{S_l}{N_h}\right] - \gamma_l I_l.$$

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Human/Rat/Flea Model

$$\frac{dS_r}{dt} = -\beta_r \frac{S_r F}{N_r}\left[1 - e^{-aN_r}\right],$$

$$\frac{dI_r}{dt} = \beta_r \frac{S_r F}{N_r}\left[1 - e^{-aN_r}\right] - \gamma_r I_r,$$

$$\frac{dR_r}{dt} = g_r \gamma_r I_r,$$

$$\frac{dD_r}{dt} = (1 - g_r)\,\gamma_r I_r,$$

$$\frac{dH}{dt} = r_f H\left(1 - \frac{H}{K_f}\right),$$

$$\frac{dF}{dt} = (1 - g_r)\,\gamma_r I_r H - d_f F,$$

$$\frac{dS_h}{dt} = -\beta_h \frac{S_h F}{N_h}\left[e^{-aN_r}\right],$$

$$\frac{dI_h}{dt} = \beta_h \frac{S_h F}{N_h}\left[e^{-aN_r}\right] - \gamma_h I_h,$$

$$\frac{dR_h}{dt} = g_h \gamma_h I_h,$$

$$\frac{dD_h}{dt} = (1 - g_h)\,\gamma_h I_h.$$

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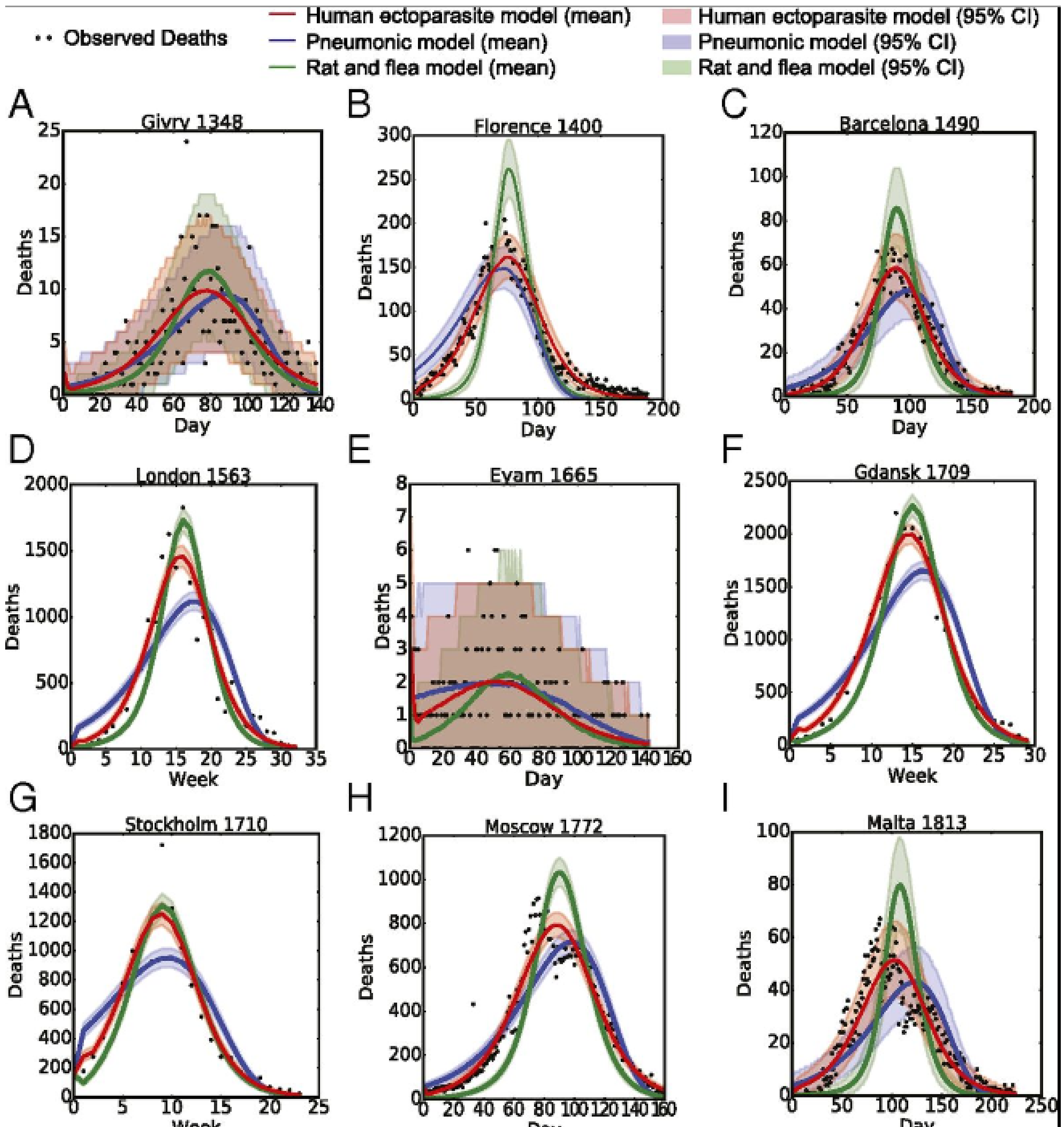

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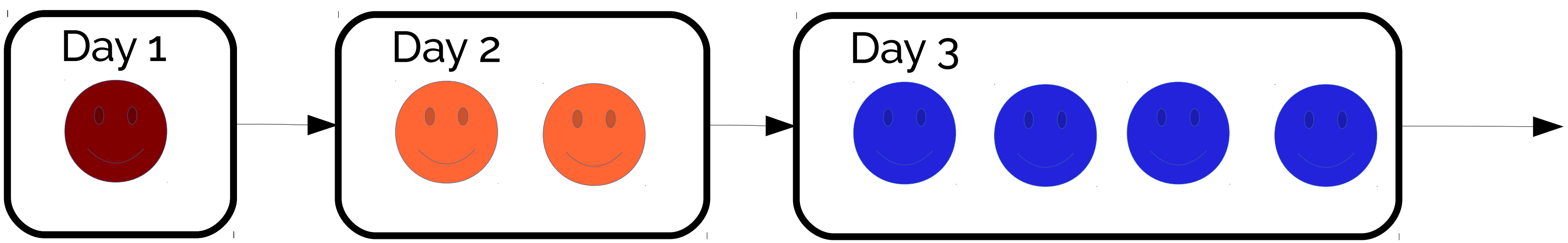
Deterministic

- Each infectious person infects 2 new people
- Infectious period is one day



Time	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Count	1	2	4	8	16	32	64	128

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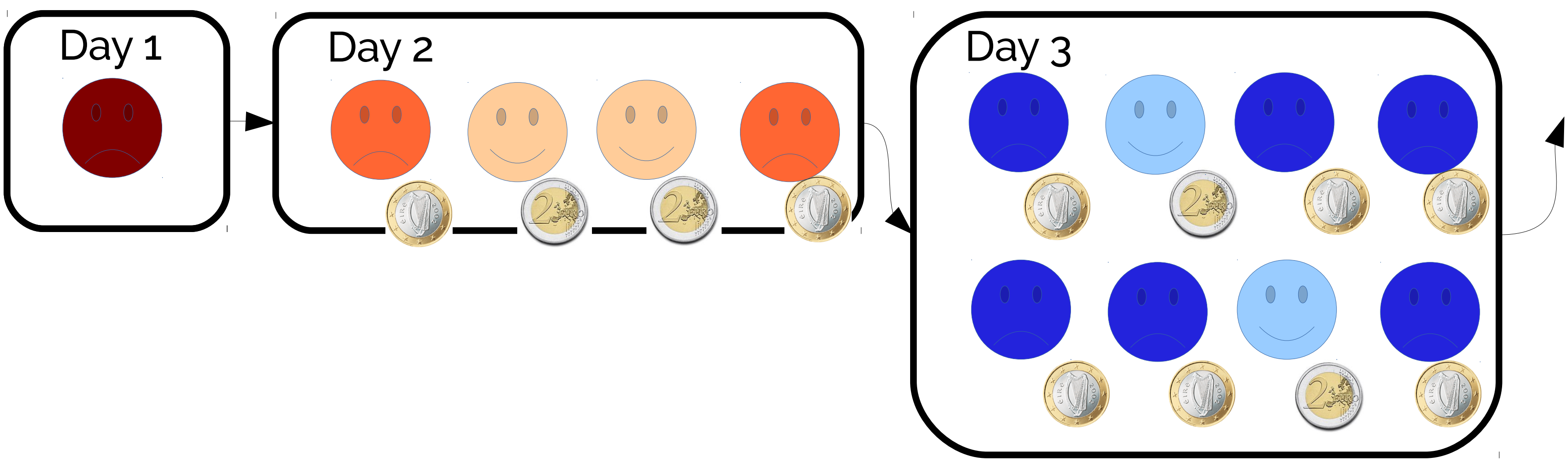
Stochastic

- Each infectious person → 4 new contacts
- Chance of new infection is ½



Time	1	2	3	4	5	6	7	8
Count	1	2	6	15	27	54	111	207

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Repeated Randomness

Time	1	2	3	4	5	6	7	8
	1	2	6	15	27	54	111	207
	1	3	9	16	31	68	120	250
	1	2	4	6	17	23	50	115
	1	1	2	1	0	0	0	0
	1	1	3	7	17	32	69	118
	1	3	6	12	26	43	83	156

- Deterministic:

Time	1	2	3	4	5	6	7	8
Count	1	2	4	8	16	32	64	128

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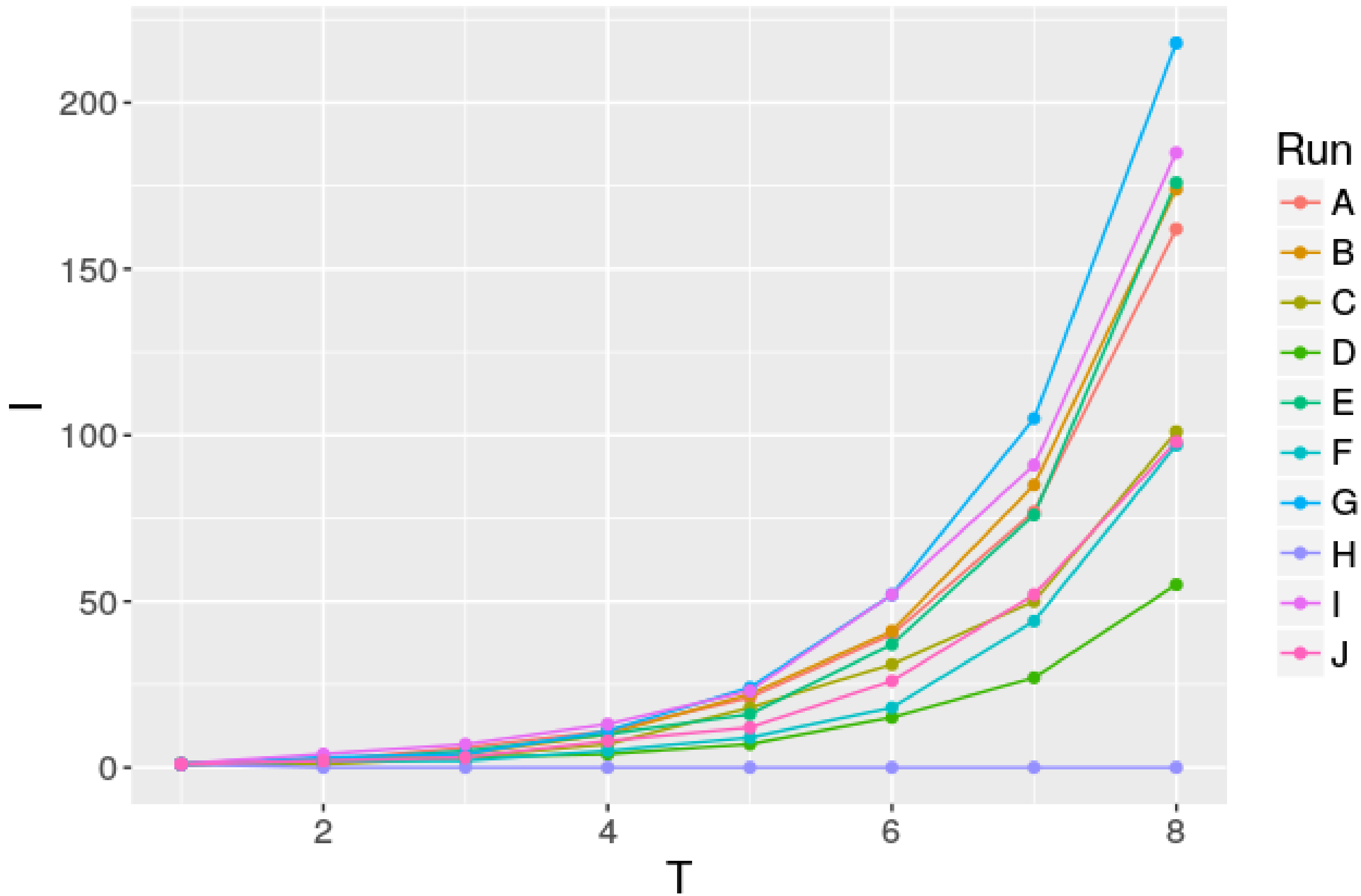
Results



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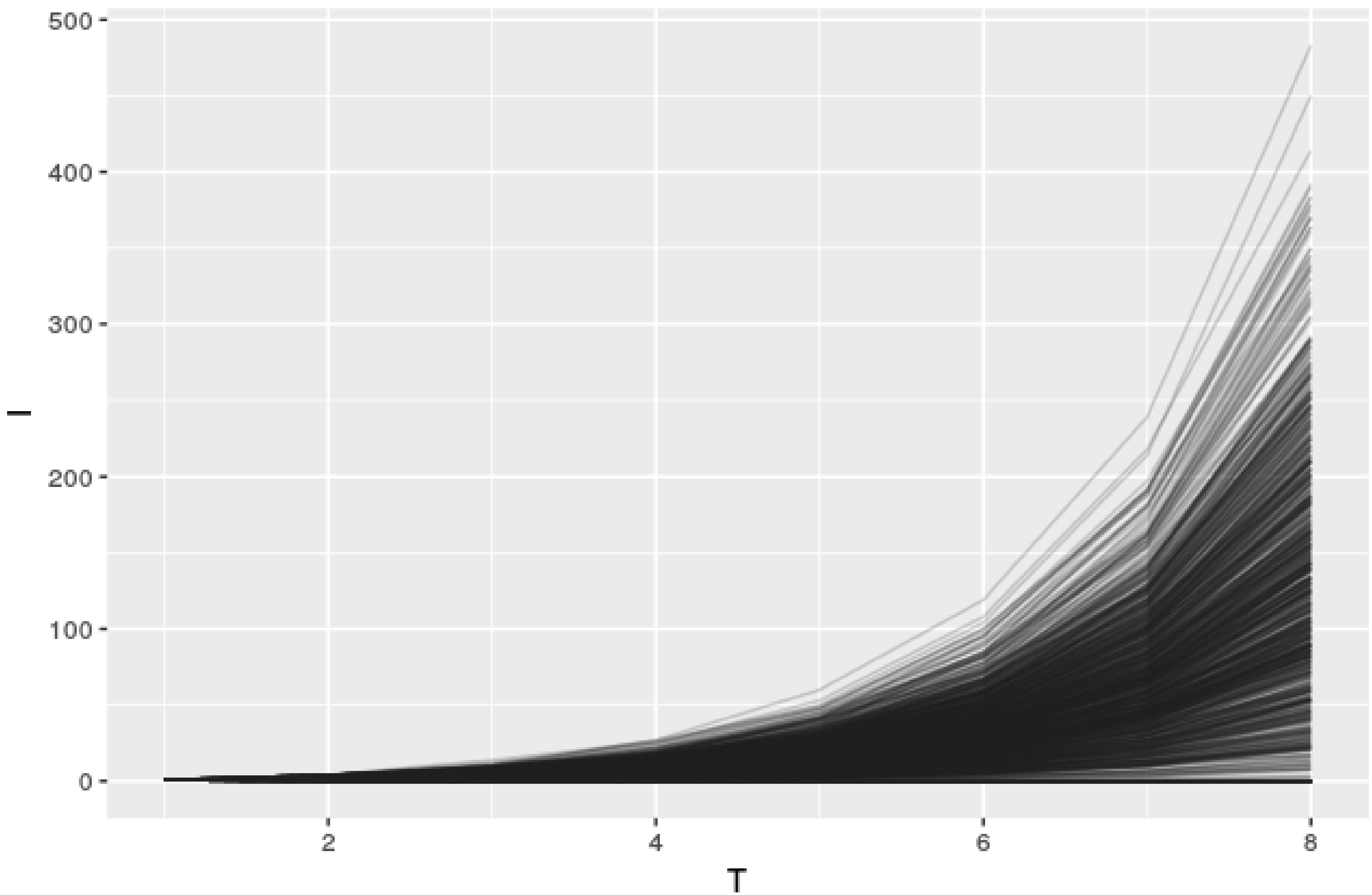
More Results



Randomness

- Previously...
  - Each infectious person → 4 new contacts
- Who meets the same number of people every day?
- The number of people you meet is the result of a *probability distribution*

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Probability Distributions

- Uniform

P = 1/2

P = 1/6

P = 1/10

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Non-Uniform

Non-Uniform

2	3	4	5	6	7
3	4	5	6	7	8
4	5	6	7	8	9
5	6	7	8	9	10
6	7	8	9	10	11
7	8	9	10	11	12

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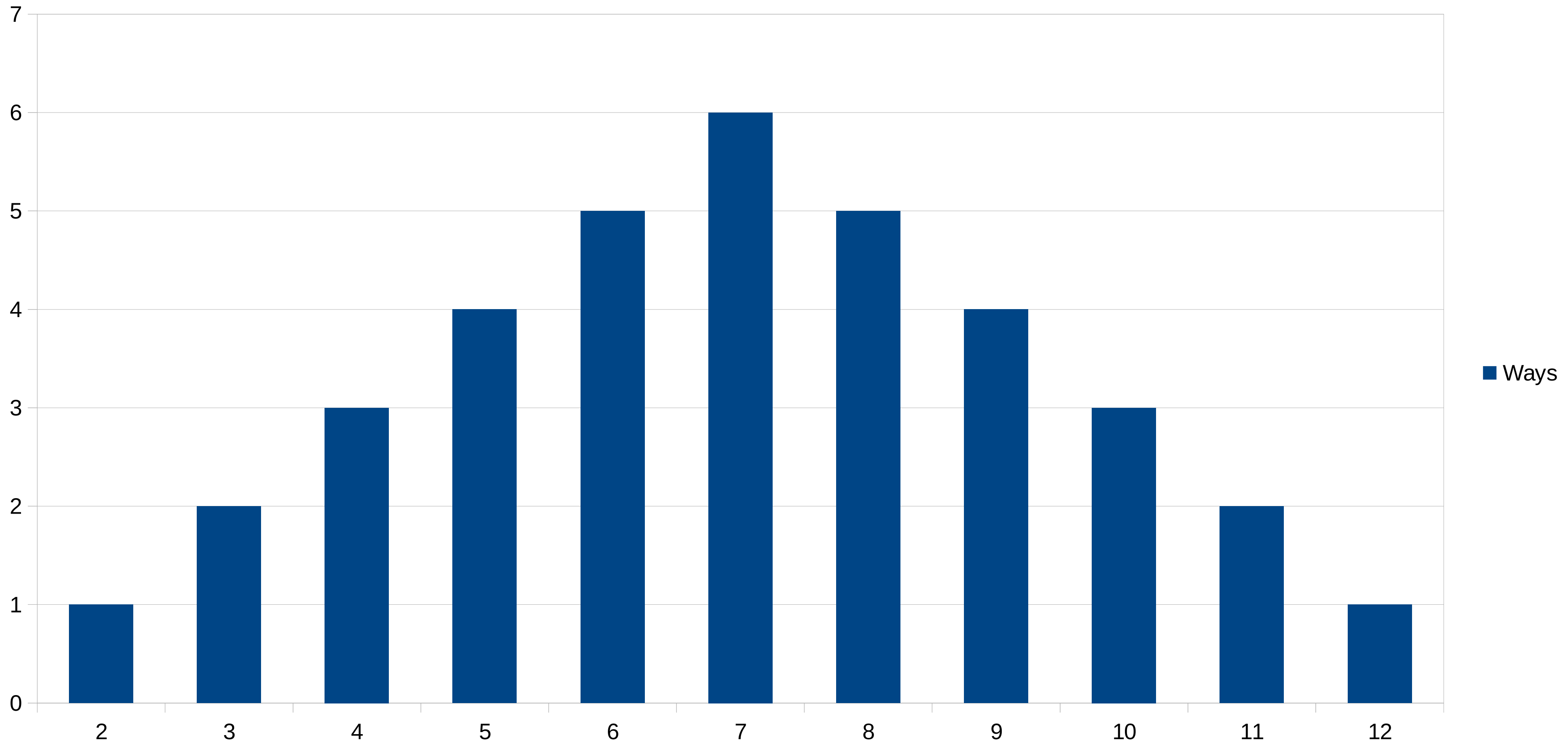
Rolling Two Dice

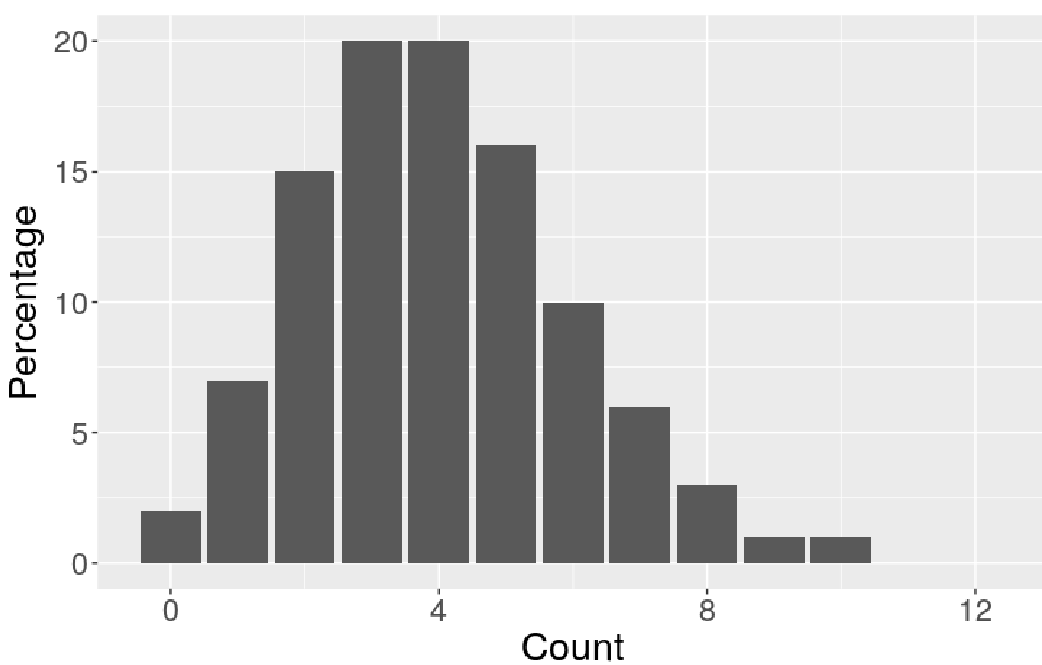


Simple Count Distribution

- Need a distribution that:
  - Is always greater than or equal to zero
  - Has no upper bound
  - As few parameters as possible

Poisson Distribution, mean=4

$$\frac{\lambda^k e^{-\lambda}}{k!}$$



Count	Percentage
0	2
1	7
2	15
3	20
4	20
5	16
6	10
7	6
8	3
9	1
10	1
11	0
12	0
...	0

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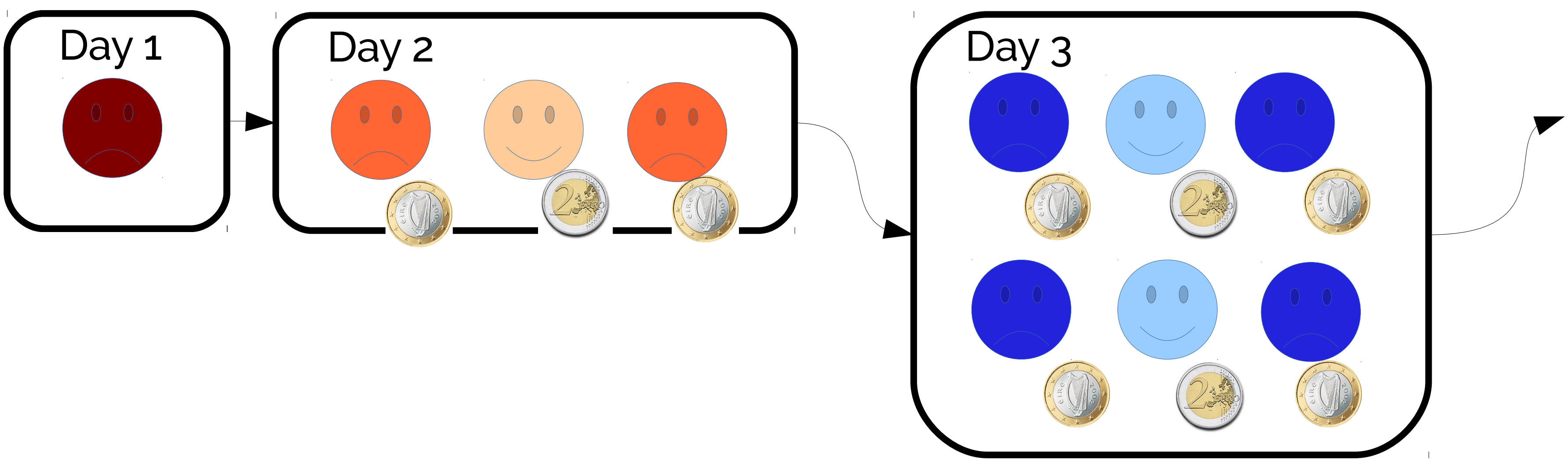
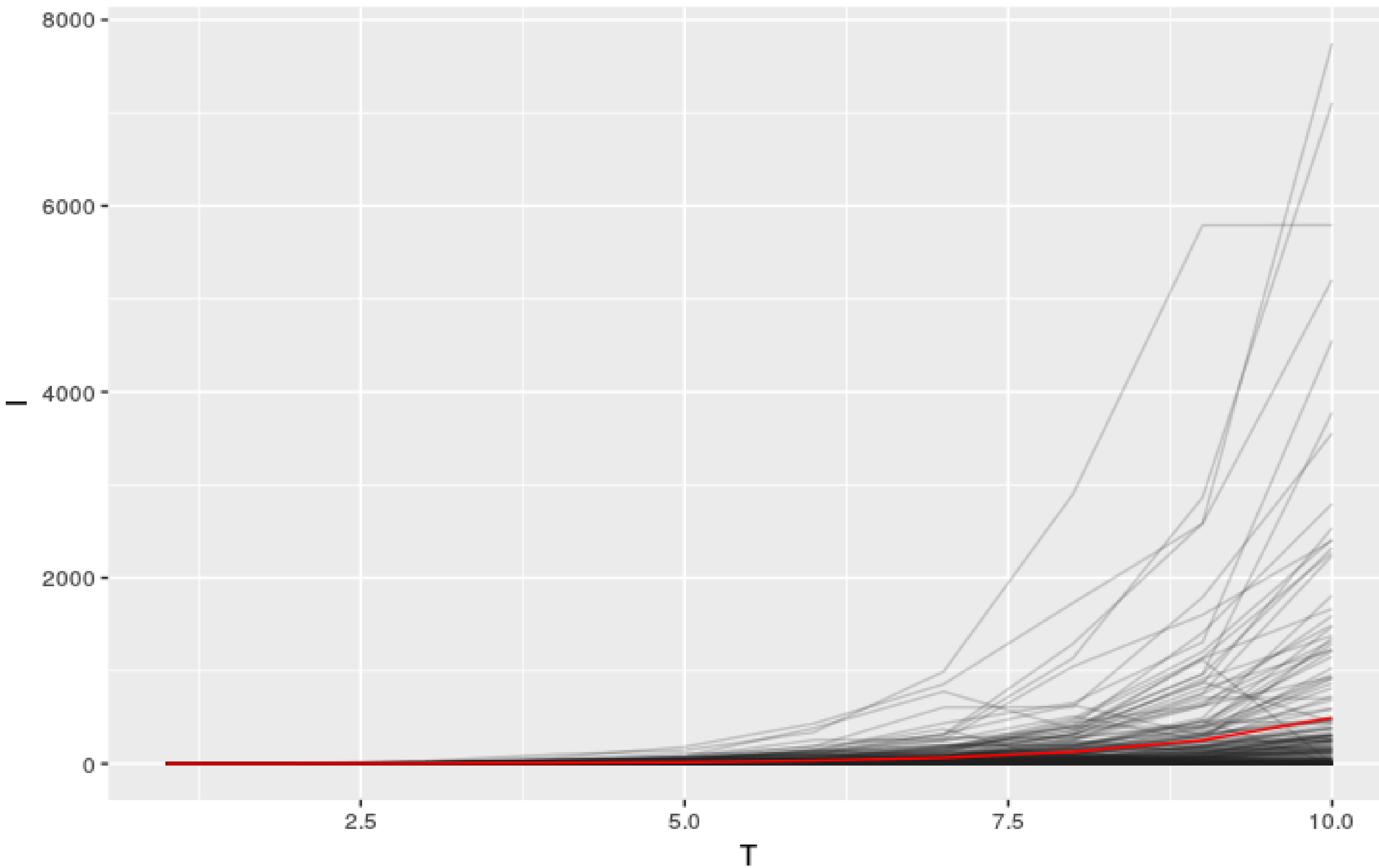
Poisson Contacts

- Each infectious person → P(4) new contacts
- Chance of new infection is ½



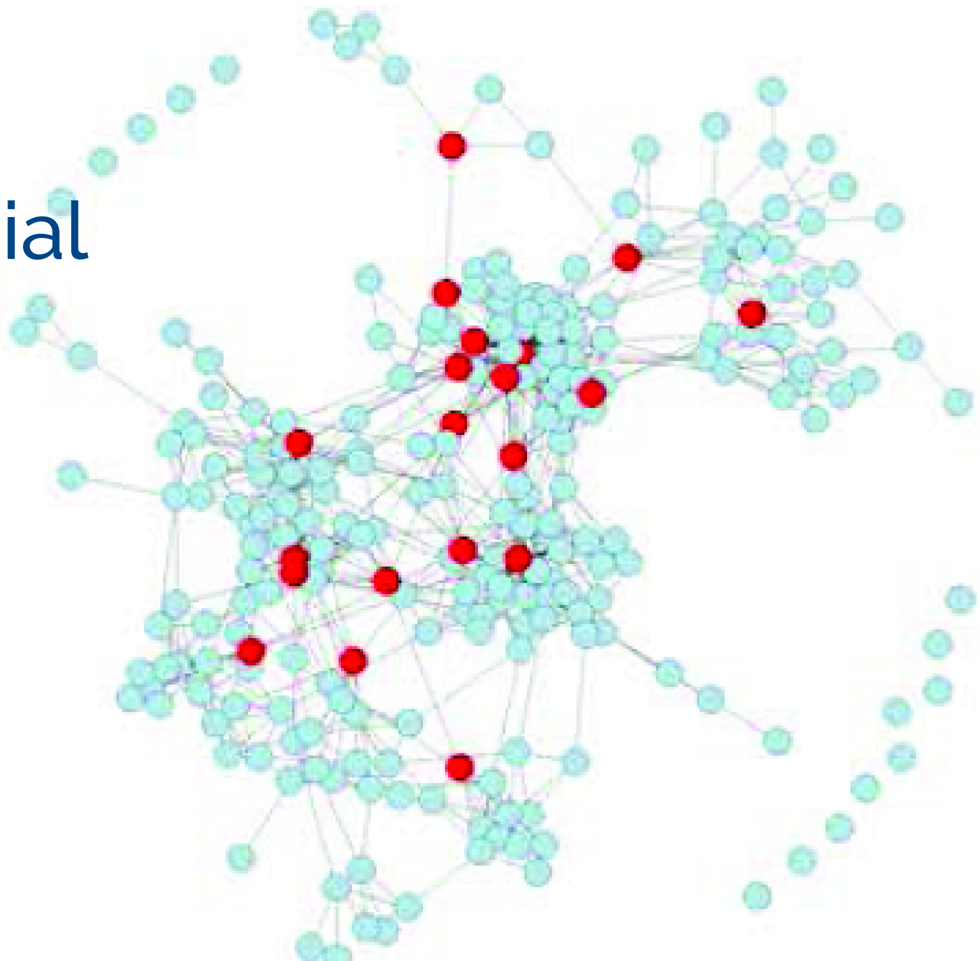
Time	1	2	3	...
Count	1	2	4	...

t up to 10



Network Model Analysis

- People interact with neighbours
- People group in cliques
- Some people highly social



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Popular medical students 'should get flu jab first'

COMMENTS (168)

The government wants three-quarters of healthcare workers to be vaccinated

Prioritising medical students with lots of friends for flu jabs could help increase the number of healthcare workers protected against the virus, say Lancaster University researchers.

In a study in The Lancet, they calculated that vaccination rates would rise if people with large social networks influenced their peers.

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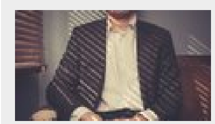

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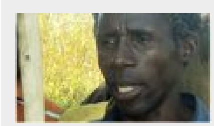

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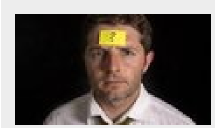

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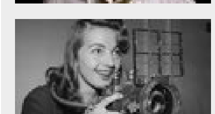

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Conclusions

- Disease modelling helps understand the epidemic process
- Simple models can be useful
- Complex models give more insight, but take longer to compute

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