A mathematical model for the eradication of Guinea worm disease

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Outline

- Biology/epidemiology of Guinea worm disease

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- Mathematical model

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- Implications.

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- Europeans first saw the disease on the Guinea coast of West Africa in the 17th century.

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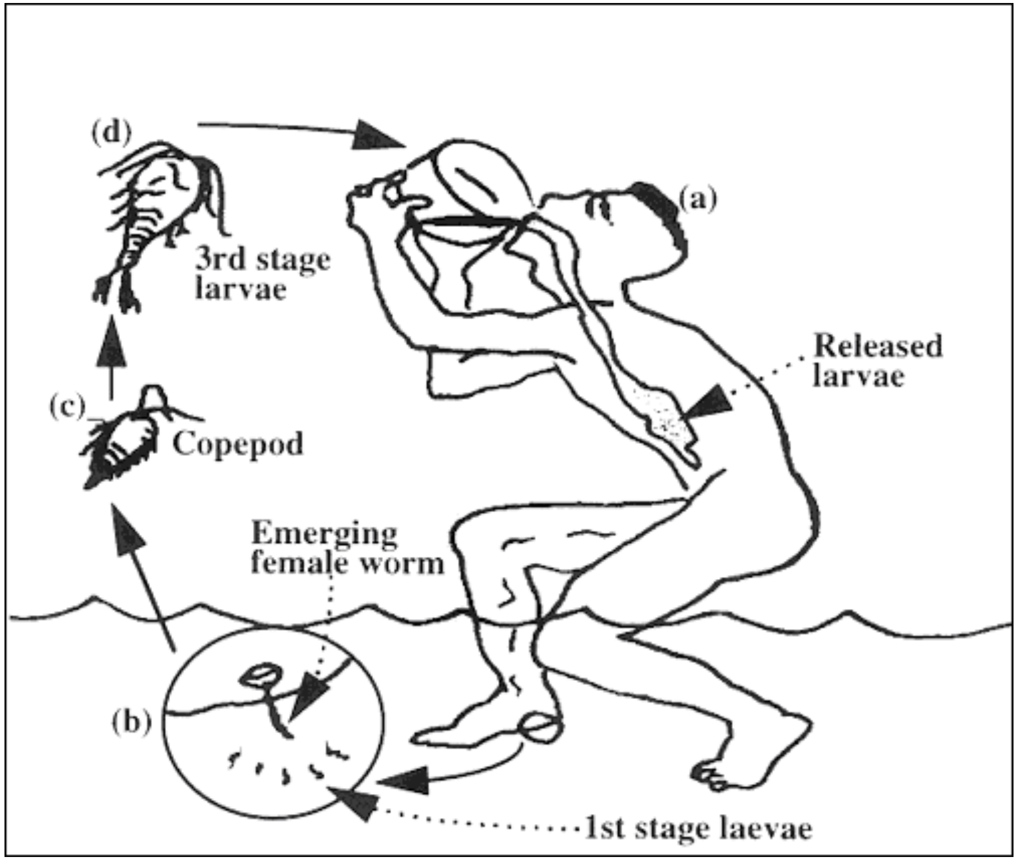
- It resides here for about a year.

The Guinea Worm

Transmission

- When ready to burst, the worm causes a burning and itching sensation



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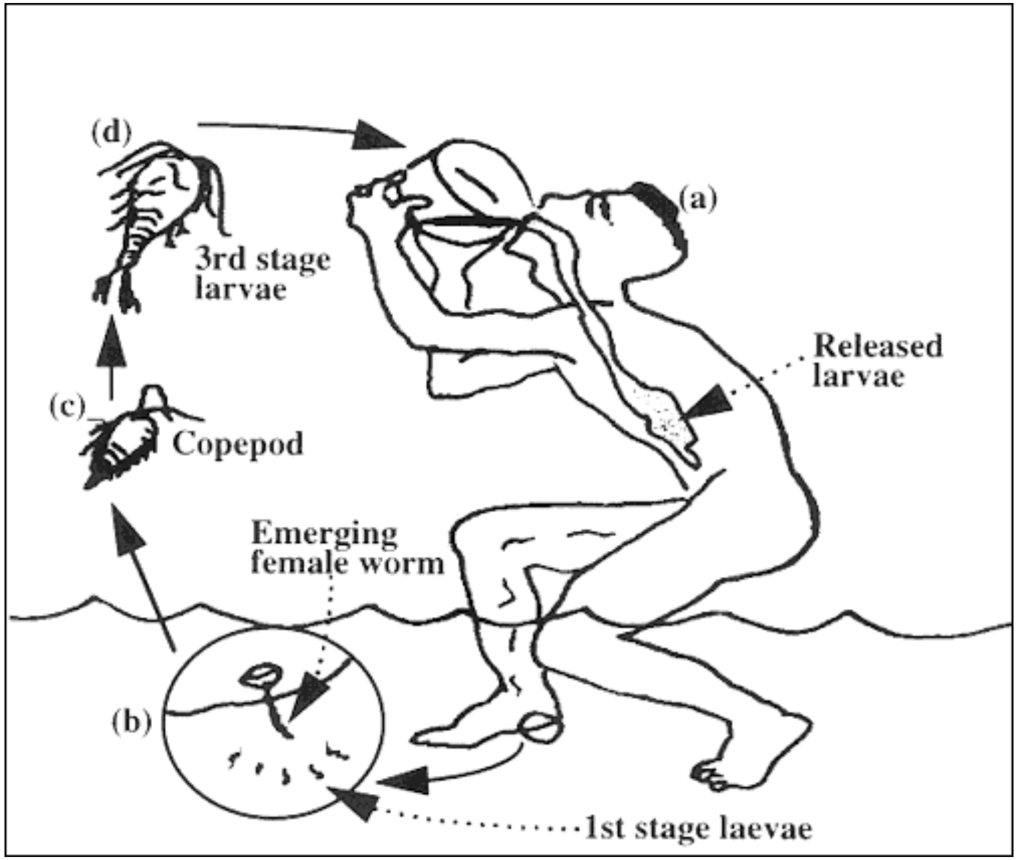
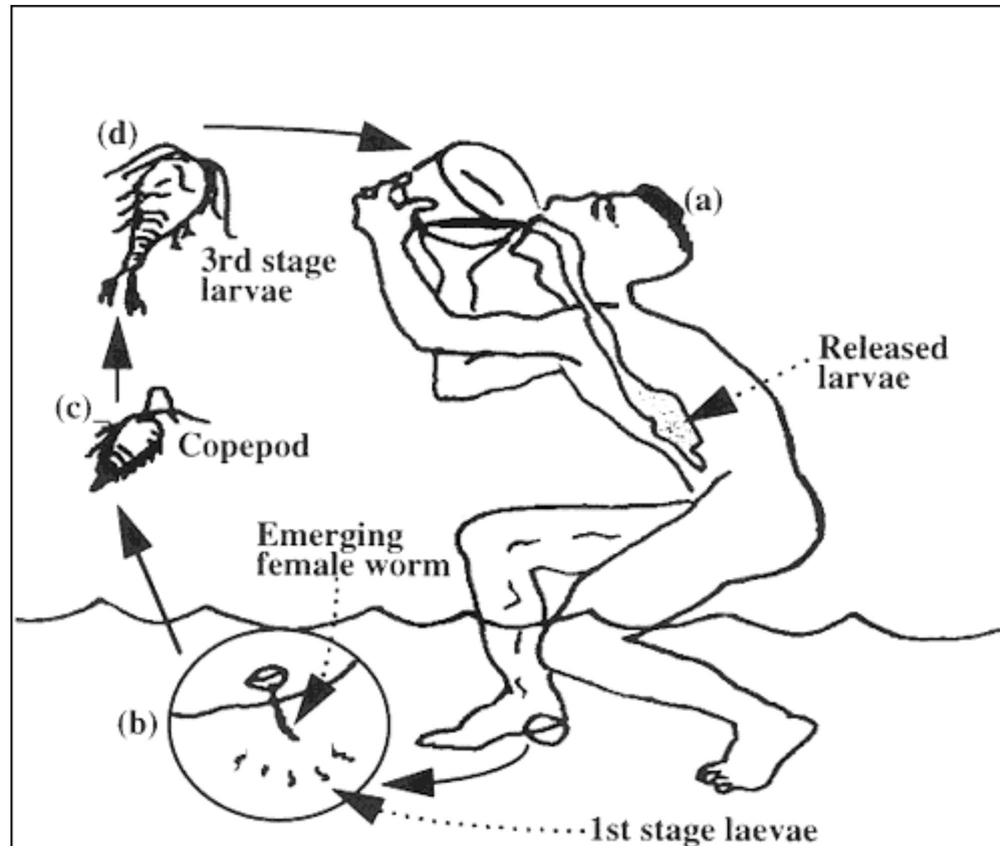


Transmission

- When ready to burst, the worm causes a burning and itching sensation
- The host places the infected limb in water
- At this point, the worm ejects hundreds of thousands of larvae, restarting the cycle.



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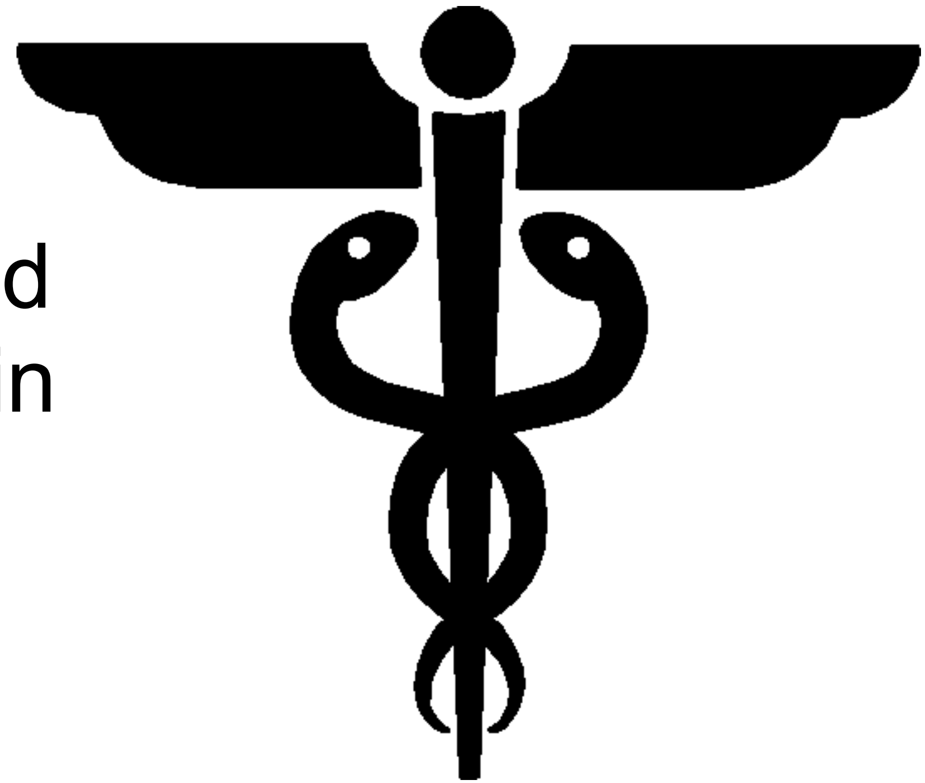
- This takes up to two months.

Burden of infection

- The medical symbol of the Staff of Asclepius is based upon the stick used to extract guinea worms in ancient times



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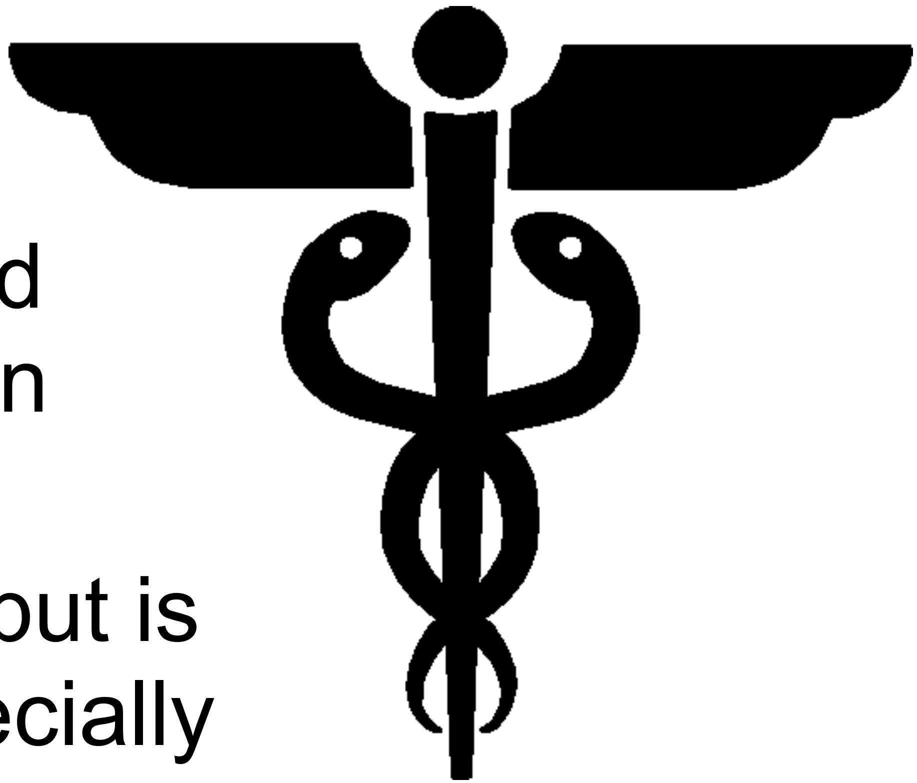

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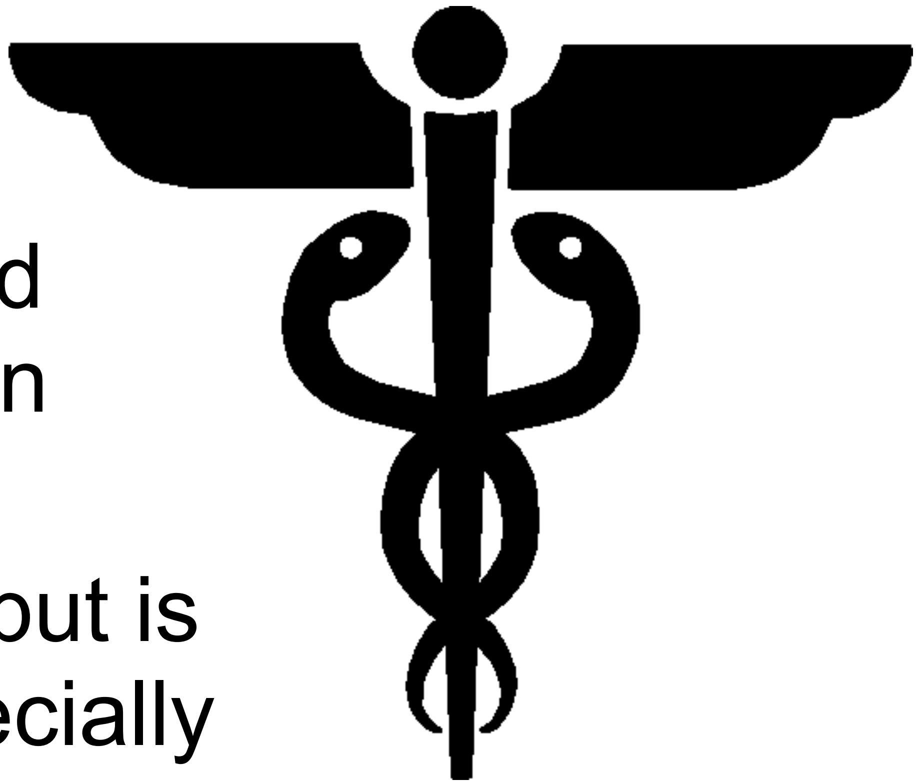

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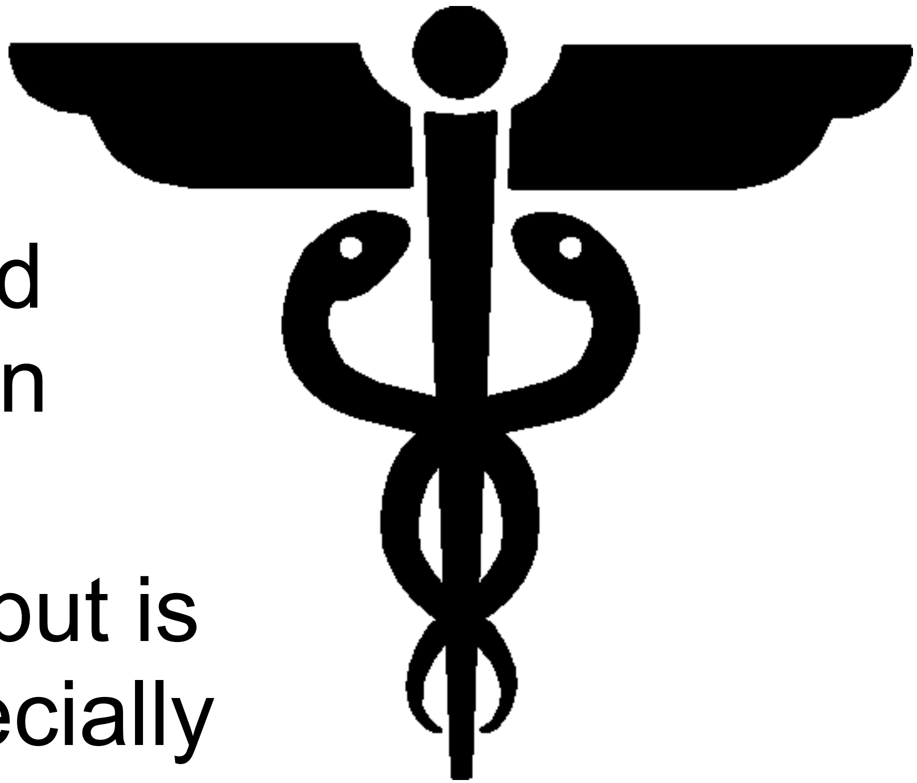
- Individuals do not develop immunity.



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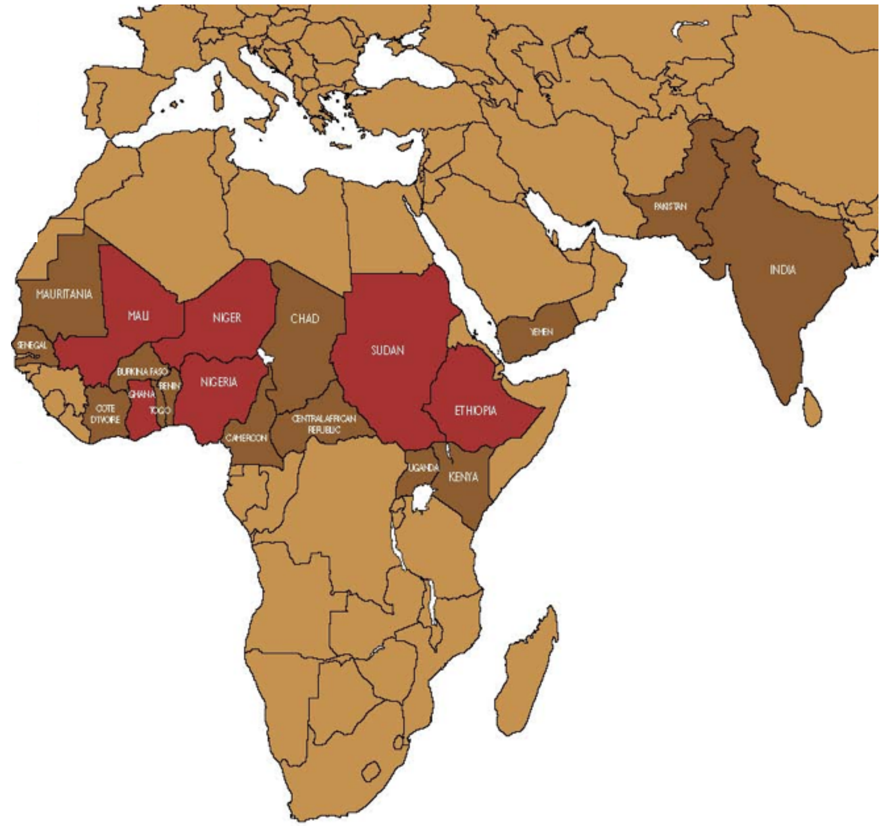

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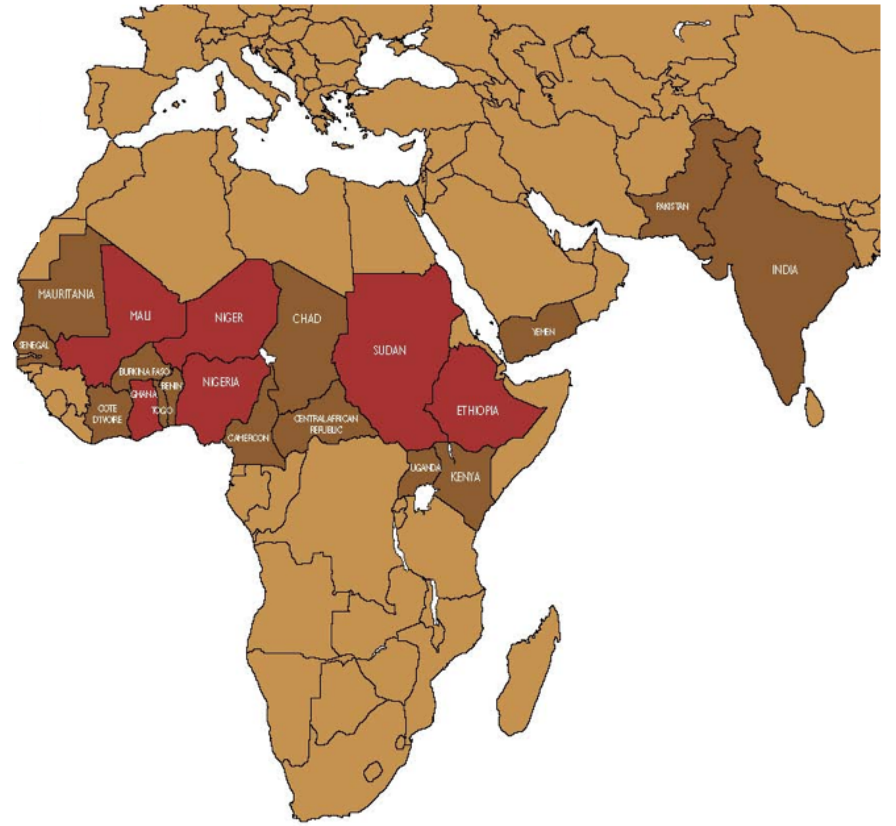

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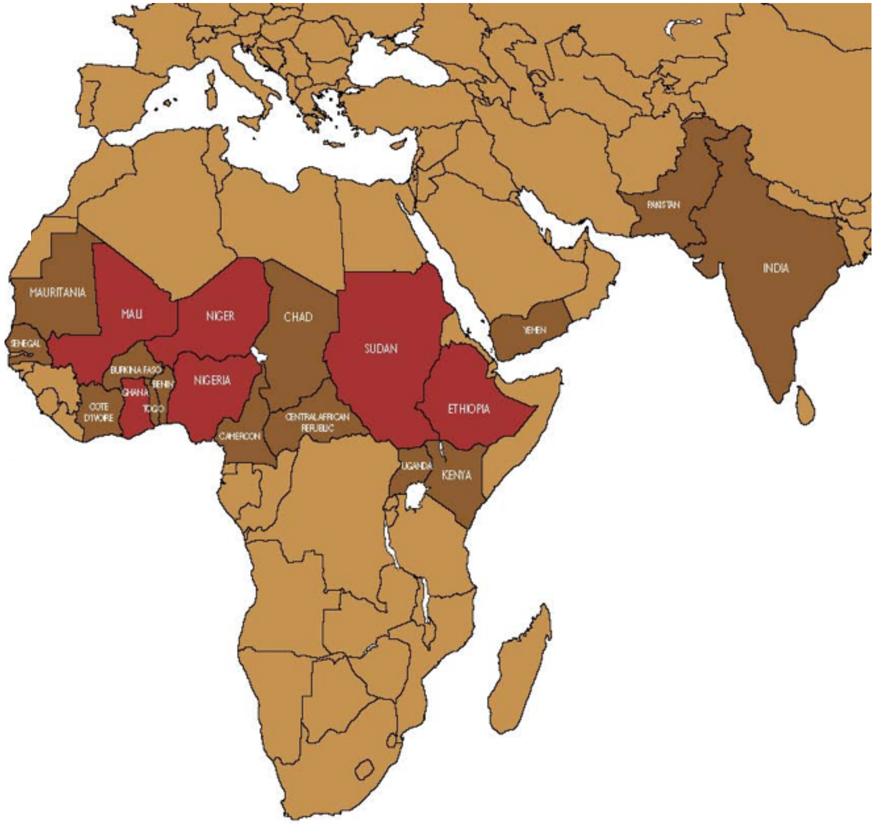

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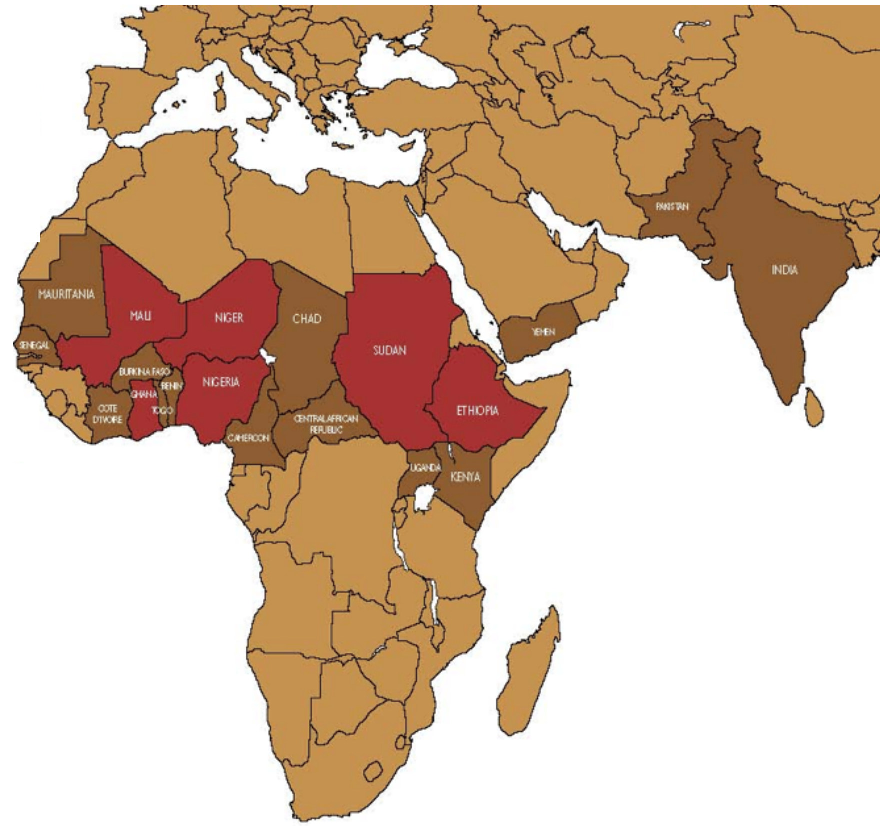

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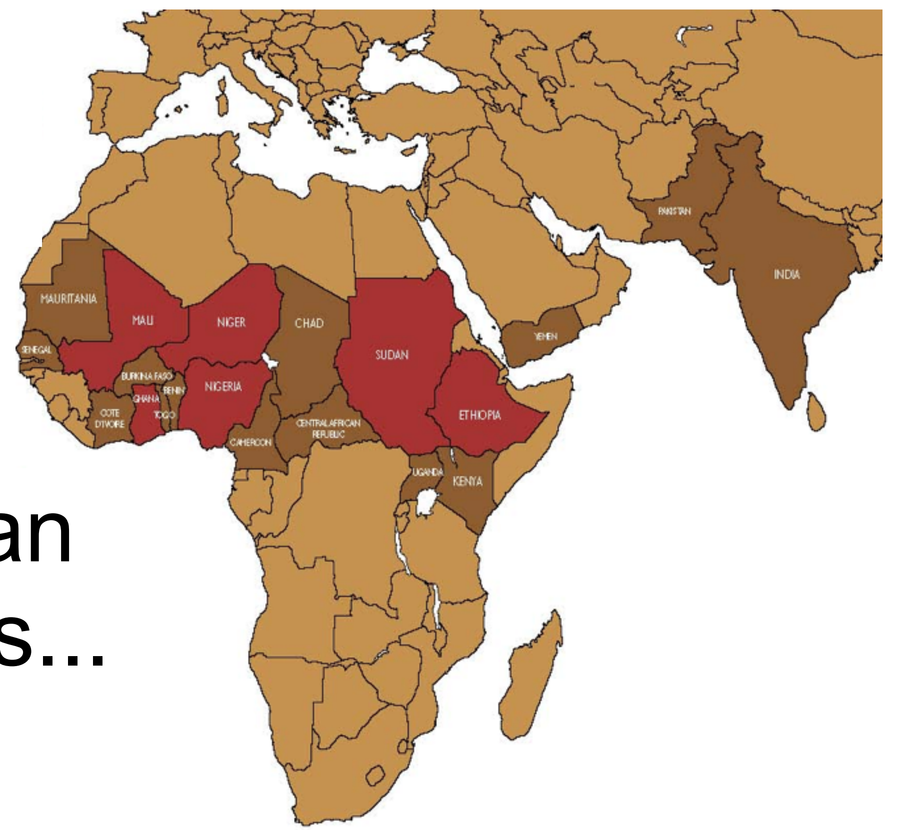

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- In the 1950s, there were an estimated 50 million cases...
- ...however, today it is almost eradicated.

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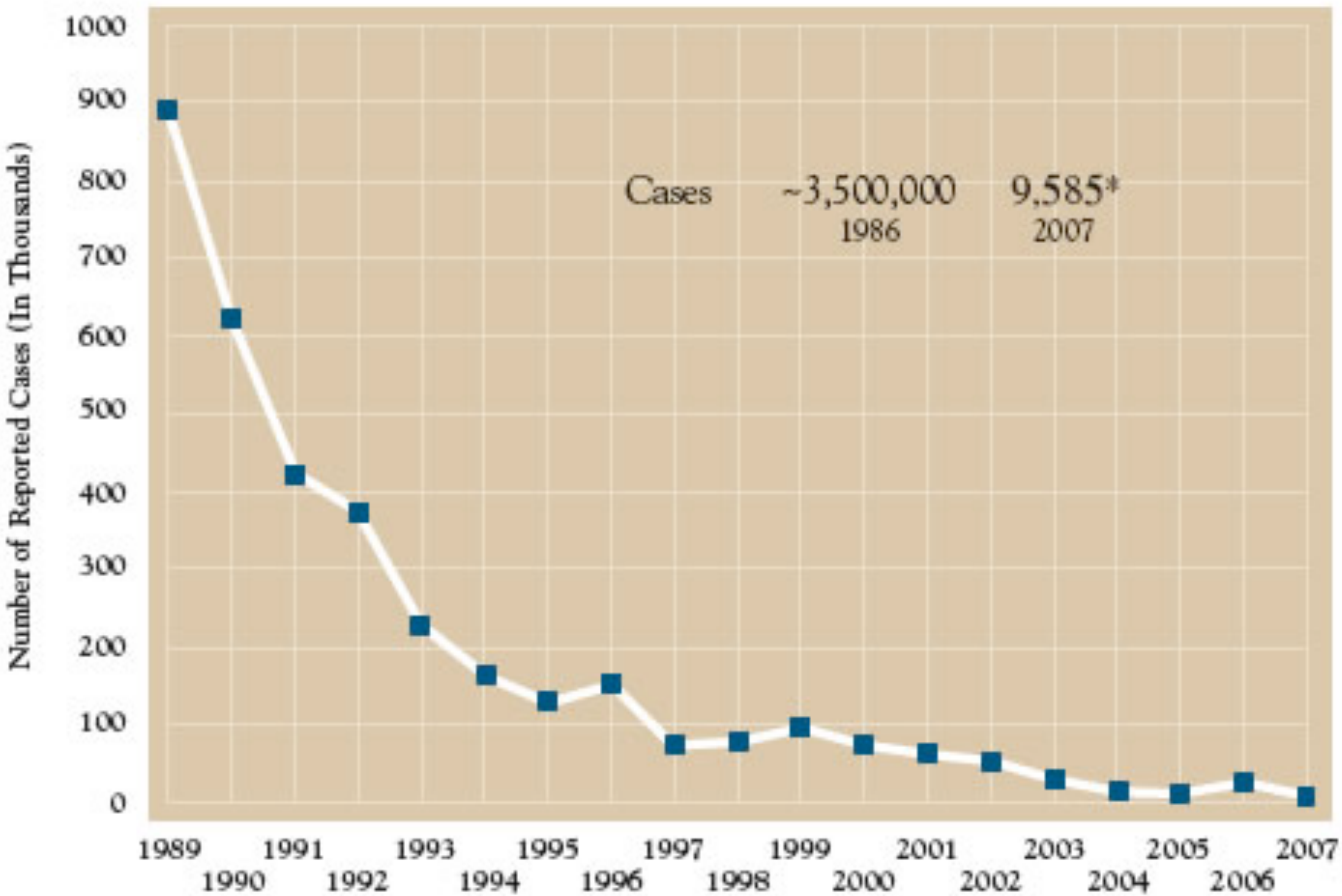
  - Ghana
- If eradicated, it will be the first parasitic disease and also the first to be eradicated using behaviour changes alone.

Significant decline



Prevention

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- Infected individuals can be educated about not submerging wounds in drinking water
- Cloth filters that fit over pots and pans can be distributed to villages
- Nomadic people have received personal-use cloths fitted over pipes, worn around the neck
- Chemical larvacides can be added to stagnant water supplies.

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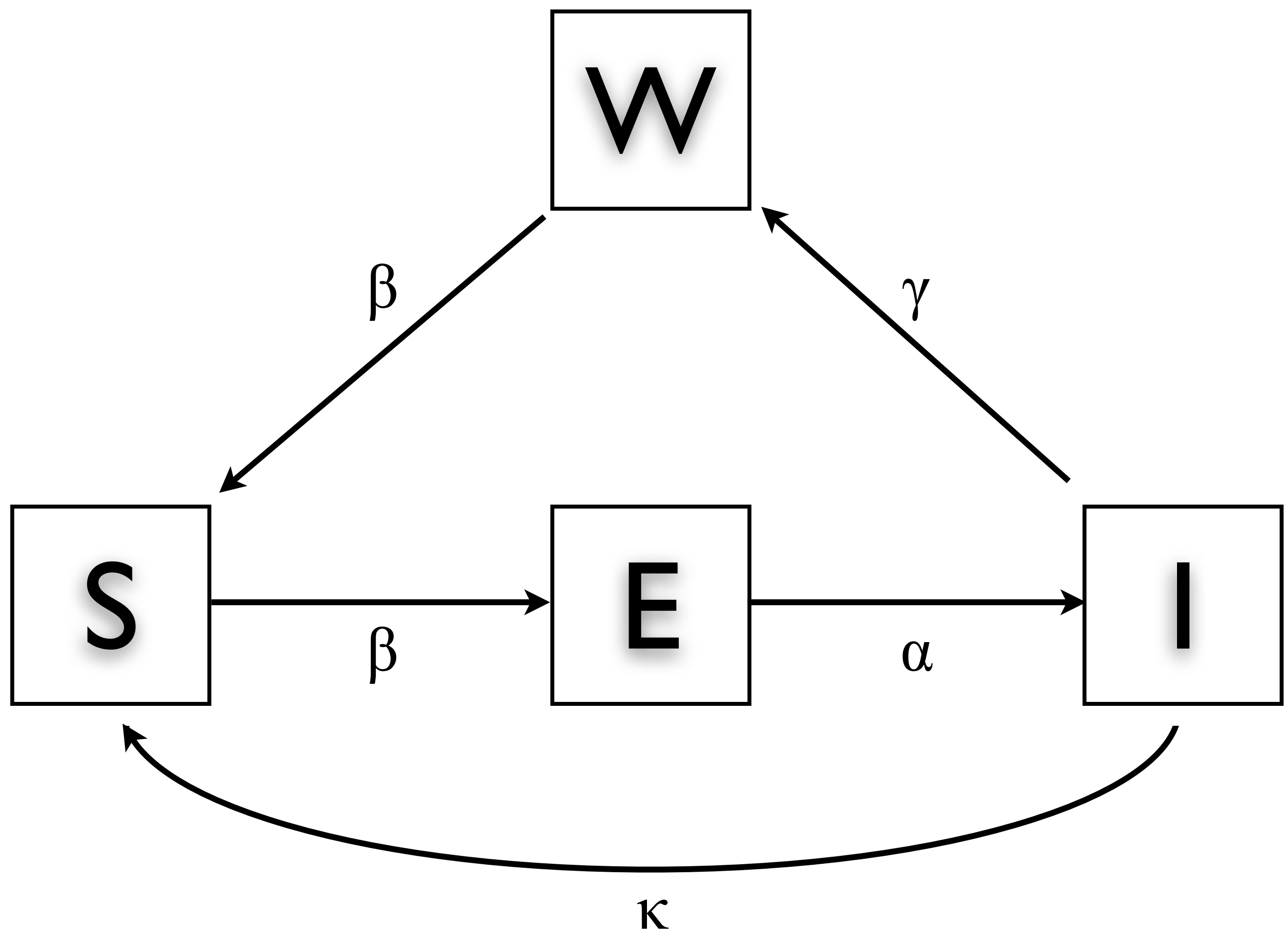
- There are environmental and toxicity issues
- Also limited supplies of resources
- Thus, we consider chlorination at discrete times.

The model



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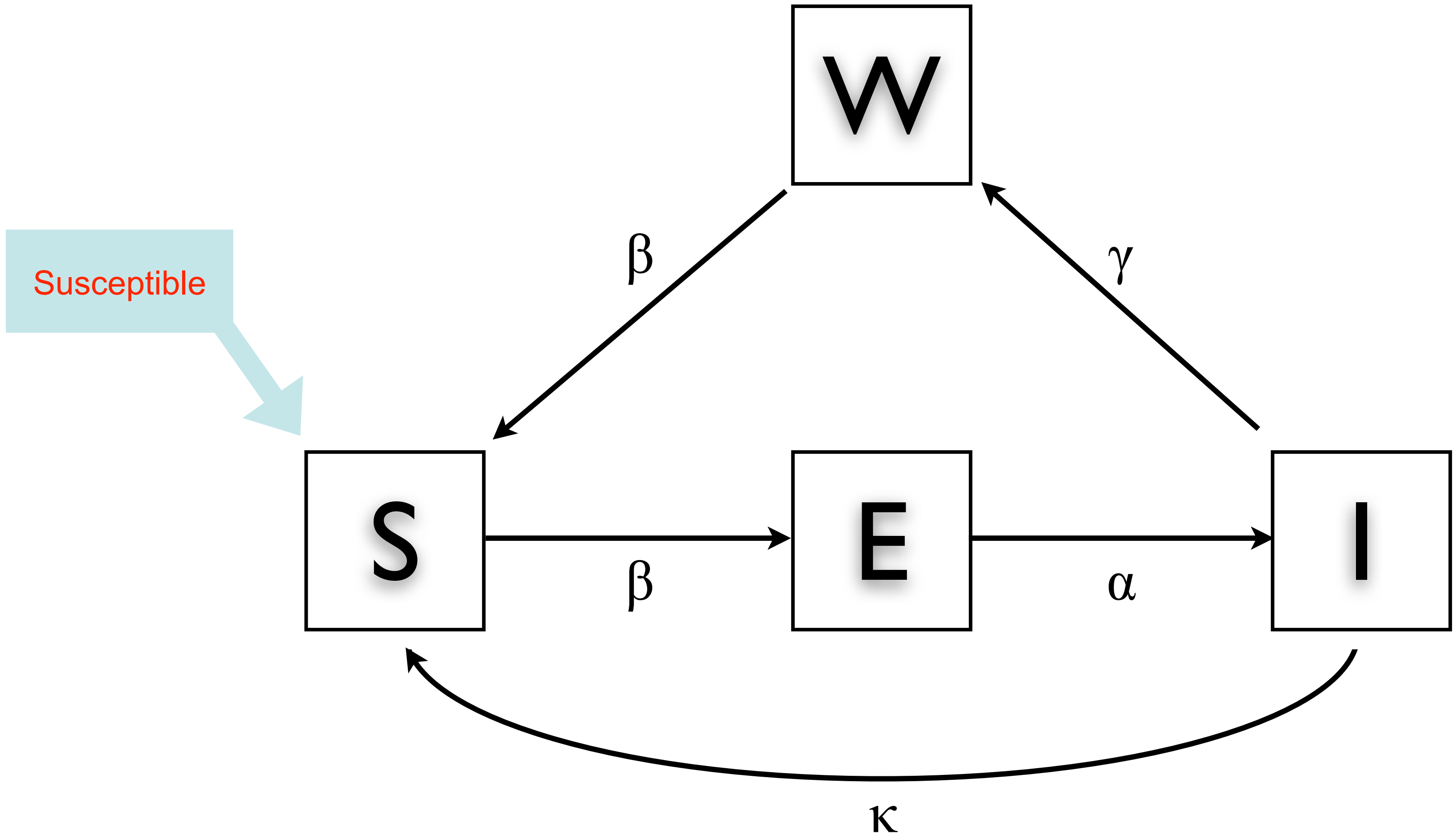

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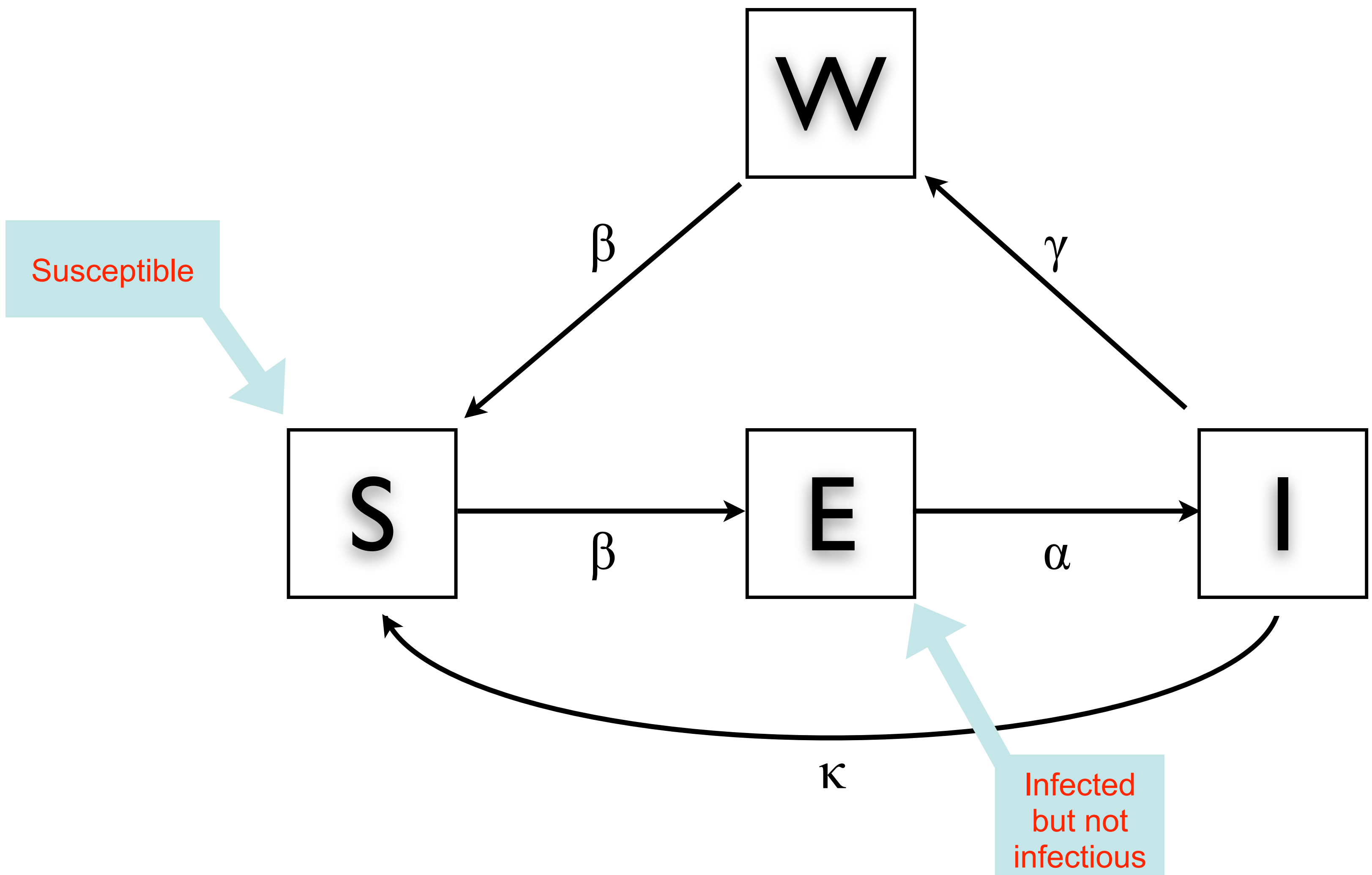

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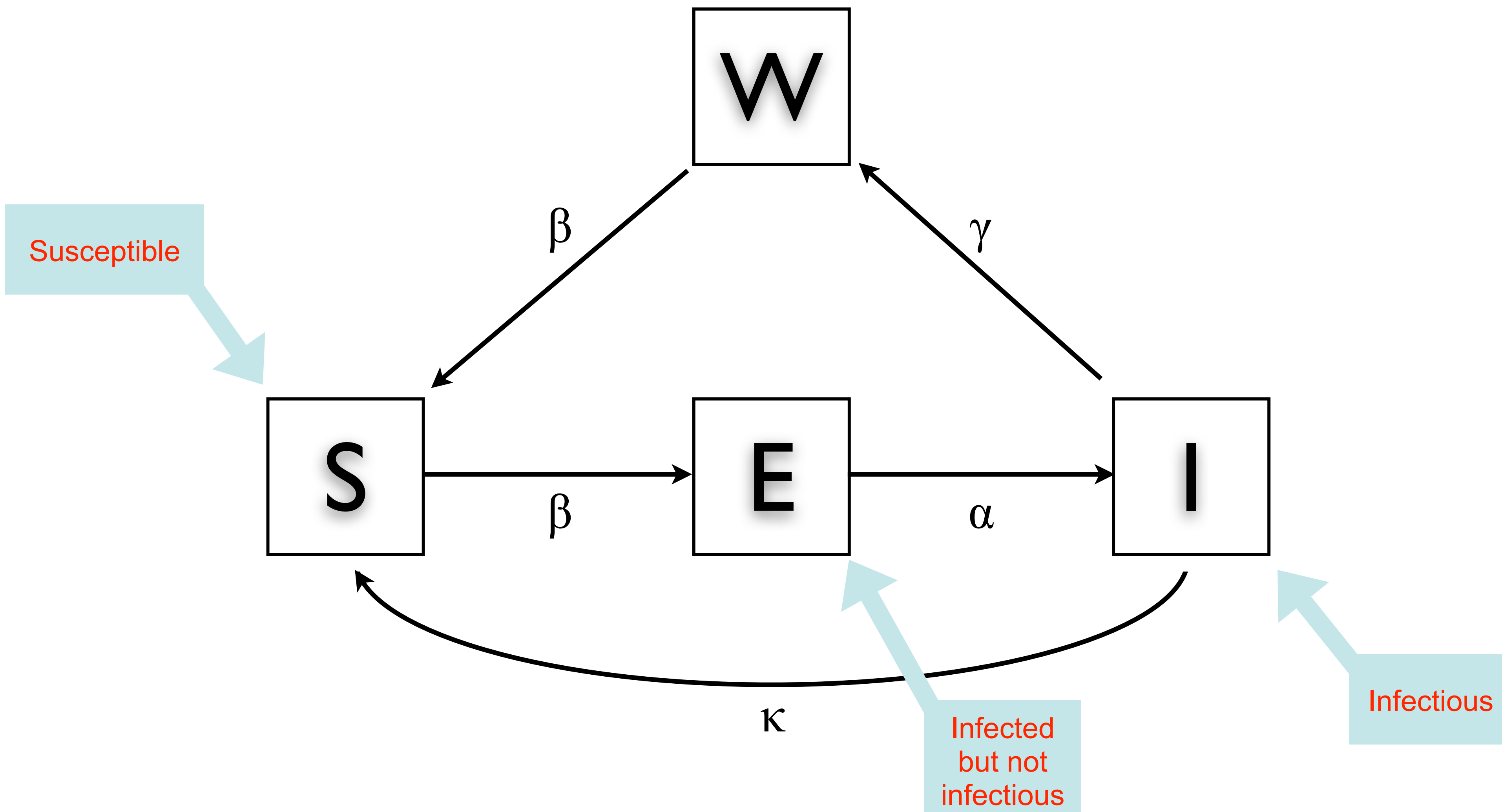
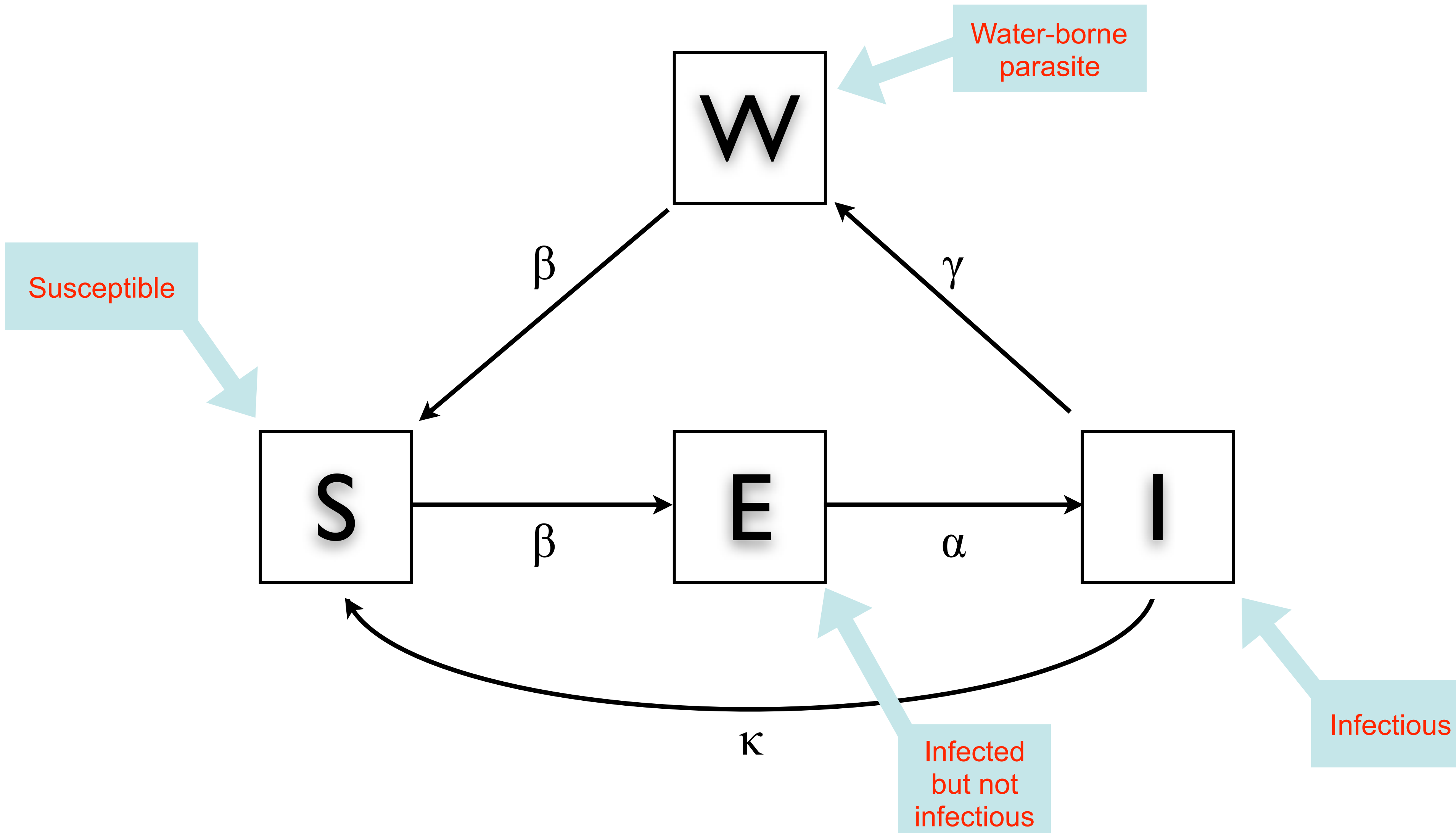

W
β
γ
Susceptible
S
β
E
α
I
κ
Infected but not infectious
Infectious

The model



Water-borne parasite
W
Susceptible
β
γ
S
E
I
β
α
κ
Infected but not infectious
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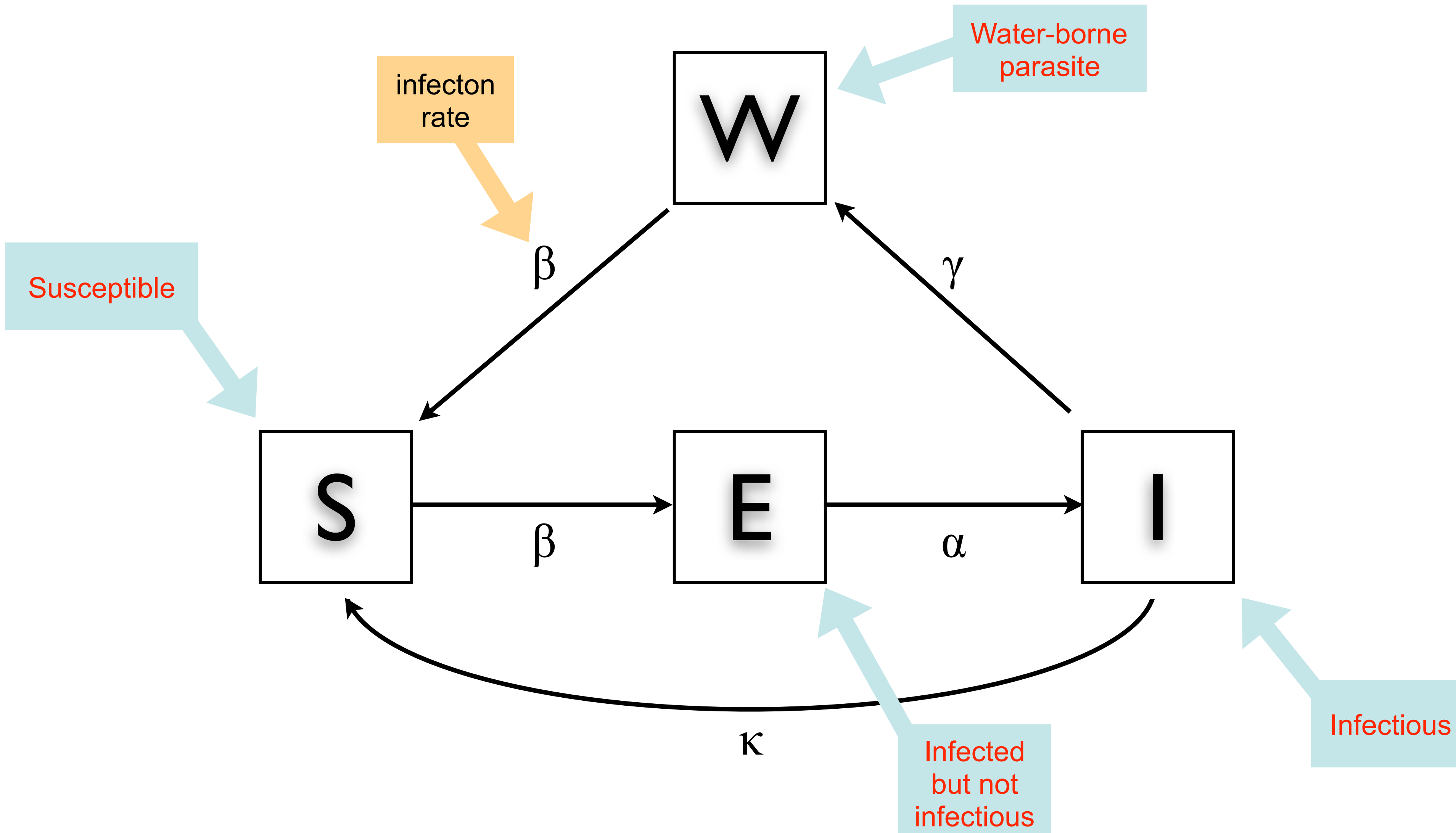
The model


infecton
rate
Water-borne
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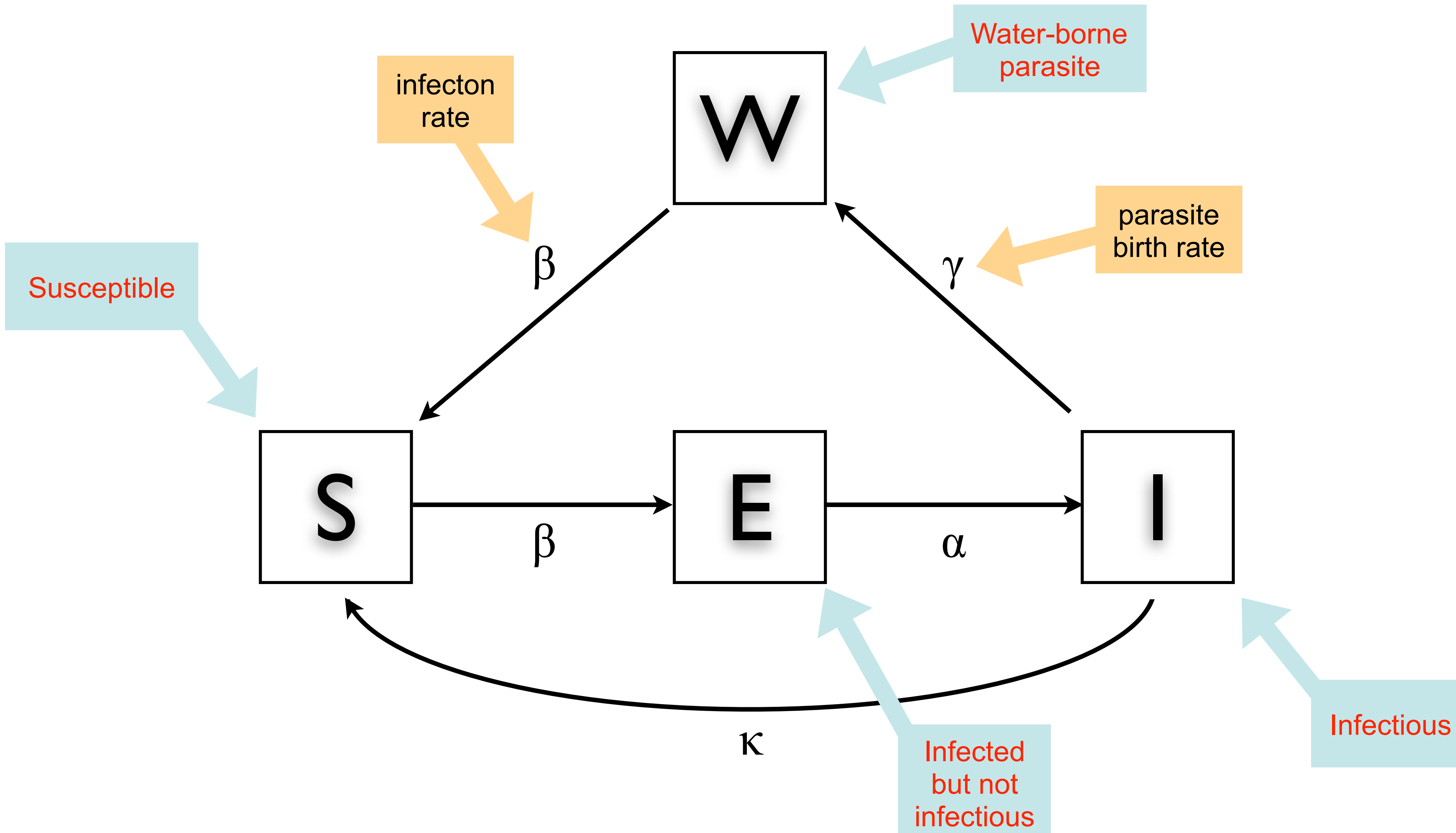
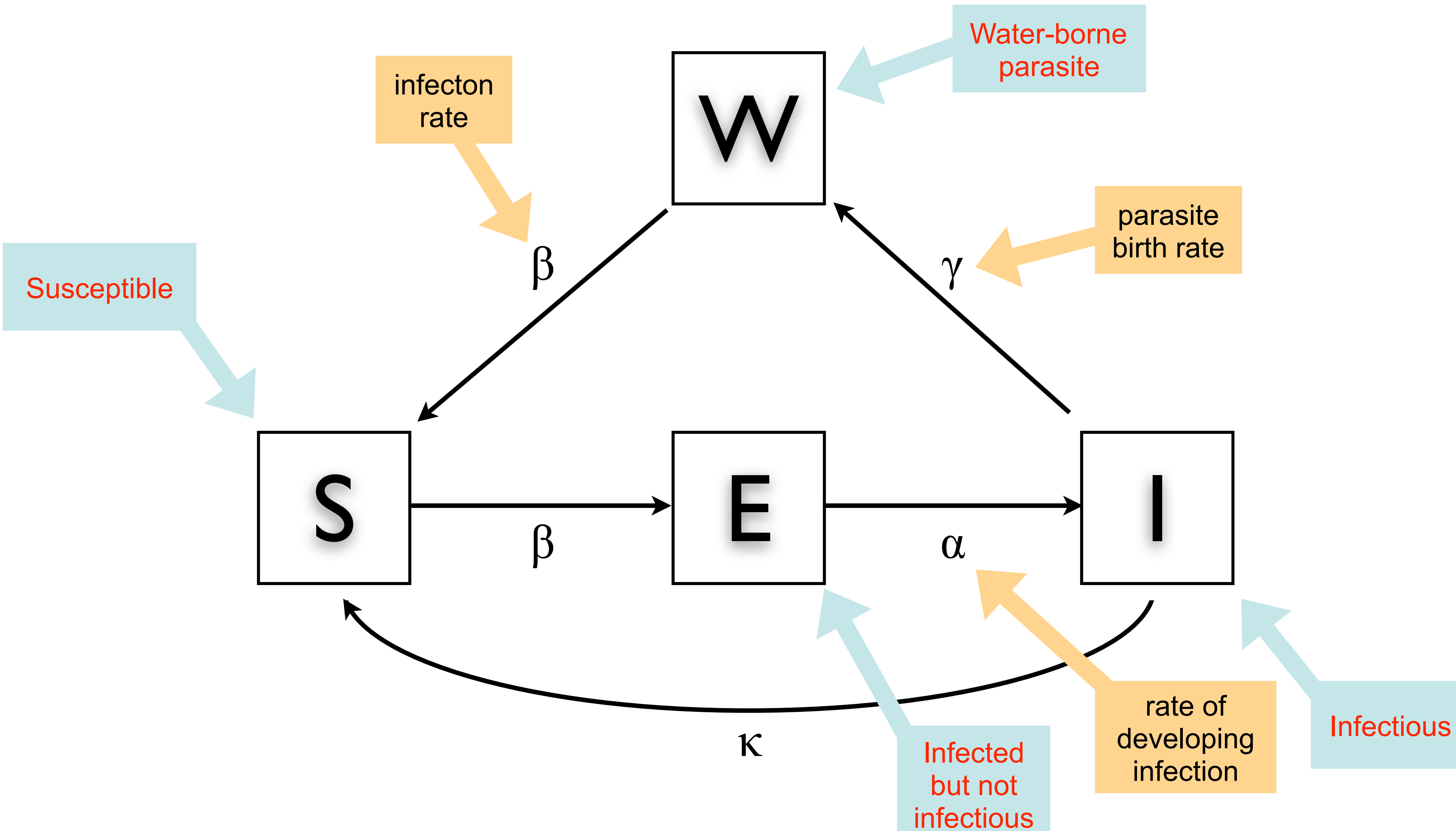


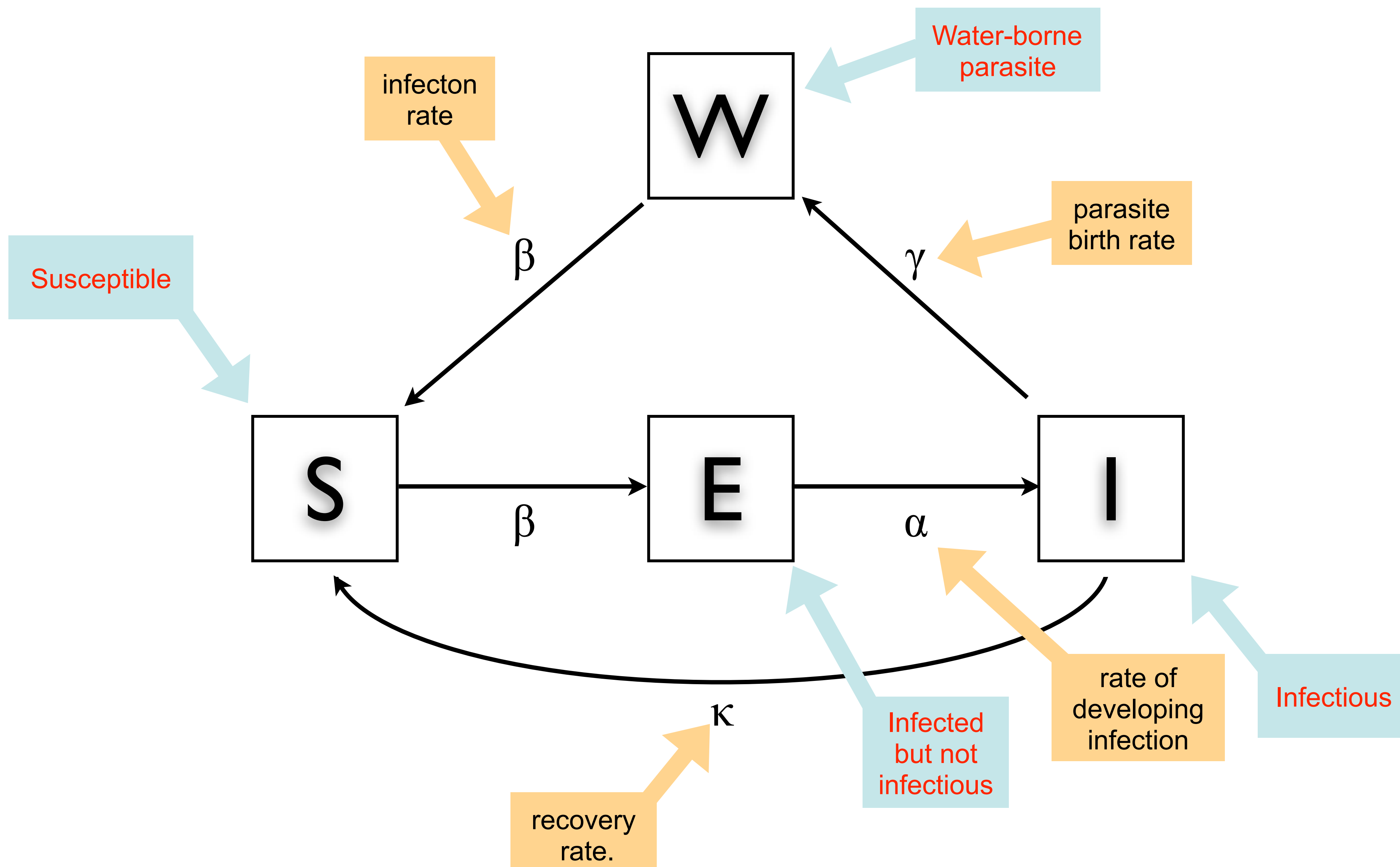
Water-borne
parasite
infecton
rate
W
parasite
birth rate
β
γ
Susceptible
S
E
I
β
α
κ
Infected
but not
infectious
Infectious

The model



Water-borne parasite
infecton rate
W
parasite birth rate
β
γ
Susceptible
S
E
I
β
α
κ
Infected but not infectious
rate of developing infection
Infectious

The model



Water-borne parasite
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rate of developing infection
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recovery rate.

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- Impulsive differential equations are a useful formulation for systems that undergo rapid changes in their state
- The approximation is reasonable when the time between impulses is large compared to the duration of the rapid change.

Putting it together

- The model thus consists of a system of ODEs (humans) together with an ODE and a difference equation (parasite).

Equations

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$$
\begin{aligned}
S' &= \Pi - \beta SW - \mu S + \kappa I & t \neq t_k \\
E' &= \beta SW - \alpha E - \mu E & t \neq t_k \\
I' &= \alpha E - \kappa I - \mu I & t \neq t_k \\
W' &= \gamma I - \mu_W W & t \neq t_k \\
\Delta W &= -rW & t = t_k
\end{aligned}
$$

S=susceptibles Π=birth rate β=transmissability
μ=background death rate E=exposed I=infectious
W=parasite-infested water κ=recovery rate
α=incubation period γ=parasite birth rate
μ_W=parasite death rate r=chlorine effectiveness

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- t_k is the chlorination time
- Chlorination may occur at regular intervals or not.

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- Two equilibria: disease free and endemic

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$$\left(\frac{\Pi}{\mu}, 0, 0, 0\right) \text{ and } (\hat{S}, \hat{E}, \hat{I}, \hat{W})$$

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- The former always exists
- The latter only exists for some parameters.

S=susceptibles Π=birth rate
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The basic reproductive ratio

$$R_0 = \frac{\Pi \alpha \gamma \beta}{\mu(\alpha + \mu)(\kappa + \mu)\mu_W}$$

Π=*birth rate* β=*transmissability* μ=*background death rate* κ=*recovery rate* α=*incubation period* γ=*parasite birth rate* μ_W=*parasite death rate*

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- Thus, R_0 is our eradication threshold.

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Effect of interventions

- Education discourages infected individuals from putting infected limbs in the drinking water

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$$R_0 = \frac{\Pi\alpha\gamma\beta}{\mu(\alpha+\mu)(\kappa+\mu)\mu_W}$$

- This decreases γ and hence R_0
- Filtration decreases β and hence R_0
- (Continuous) chlorination increases μ_W and hence decreases R_0.

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The system with impulses

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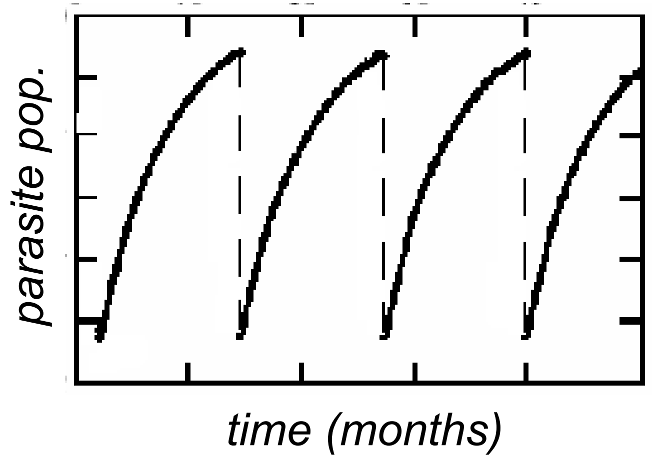

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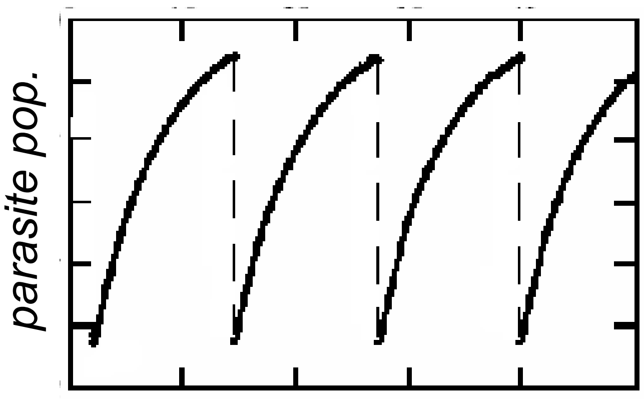
$$W' = \frac{\alpha\Pi\gamma}{\mu(\kappa+\mu)} - \mu_W W \qquad t \neq t_k$$



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W=parasite-infected water

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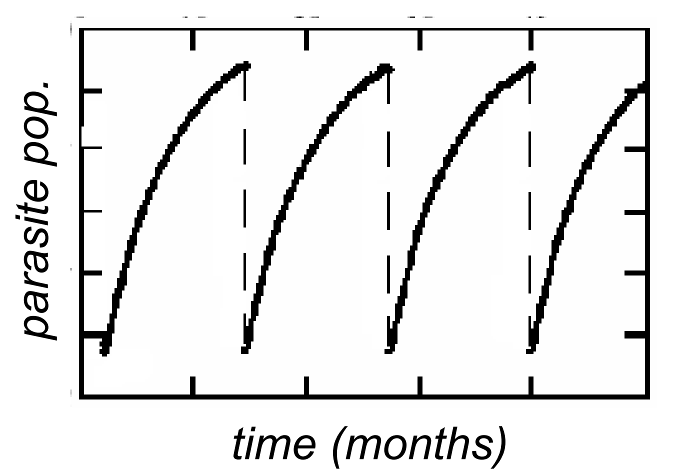
- The endpoints of the impulsive system satisfy the recurrence relation



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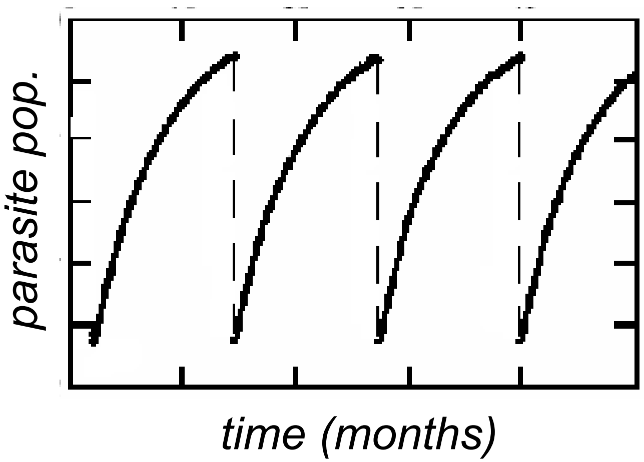

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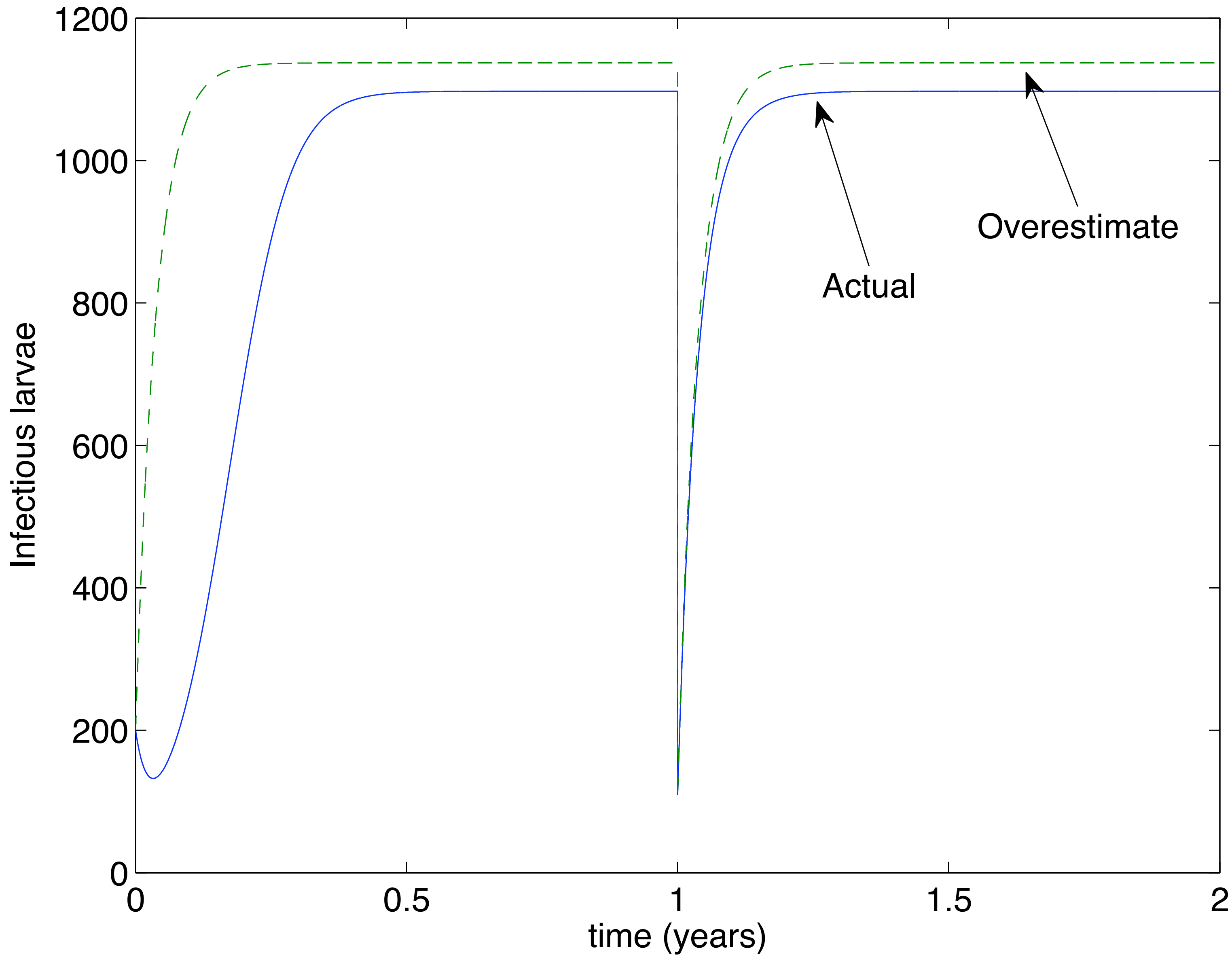
The degree of overestimation



An explicit solution

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$$W_n^- = \frac{\alpha\Pi\gamma}{\mu\mu_W(\kappa+\mu)}\Big[(1-r)^{n-1}e^{-\mu_W(t_n-t_1)} + (1-r)^{n-1}e^{-\mu_W(t_n-t_2)}$$
$$+\cdots+(1-r)e^{-\mu_W(t_n-t_{n-1})}+1$$
$$-(1-r)^{n-2}e^{-\mu_W(t_n-t_1)} - (1-r)^{n-3}e^{-\mu_W(t_n-t_2)}$$
$$-\cdots-e^{-\mu_W(t_n-t_{n-1})}\Big].$$

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Fixed chlorination

- If chlorination occurs at fixed intervals, then $t_n - t_{n-1} = \tau$ is constant

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- This is highly unlikely.

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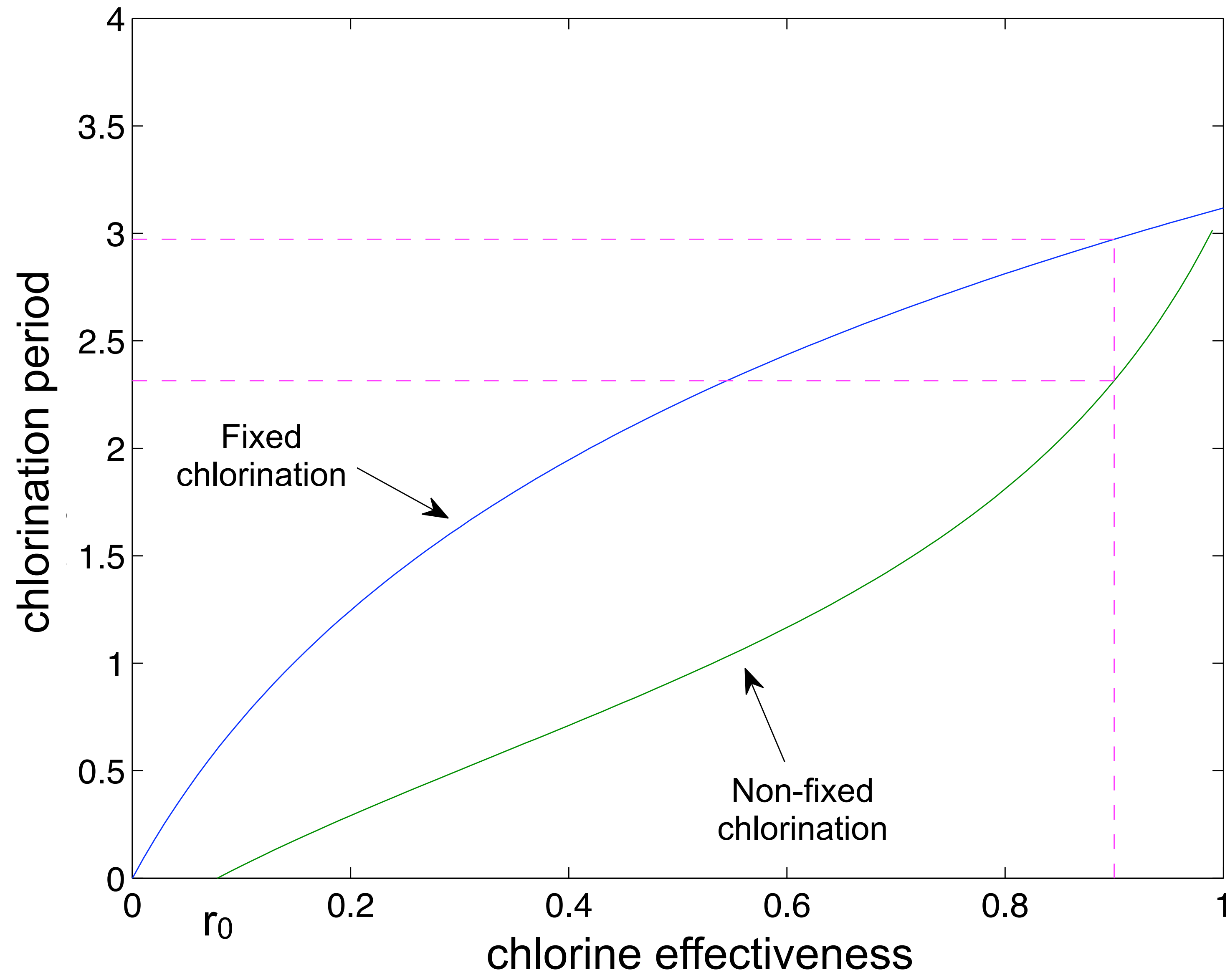
r=chlorination effectiveness

Fixed chlorination is always better



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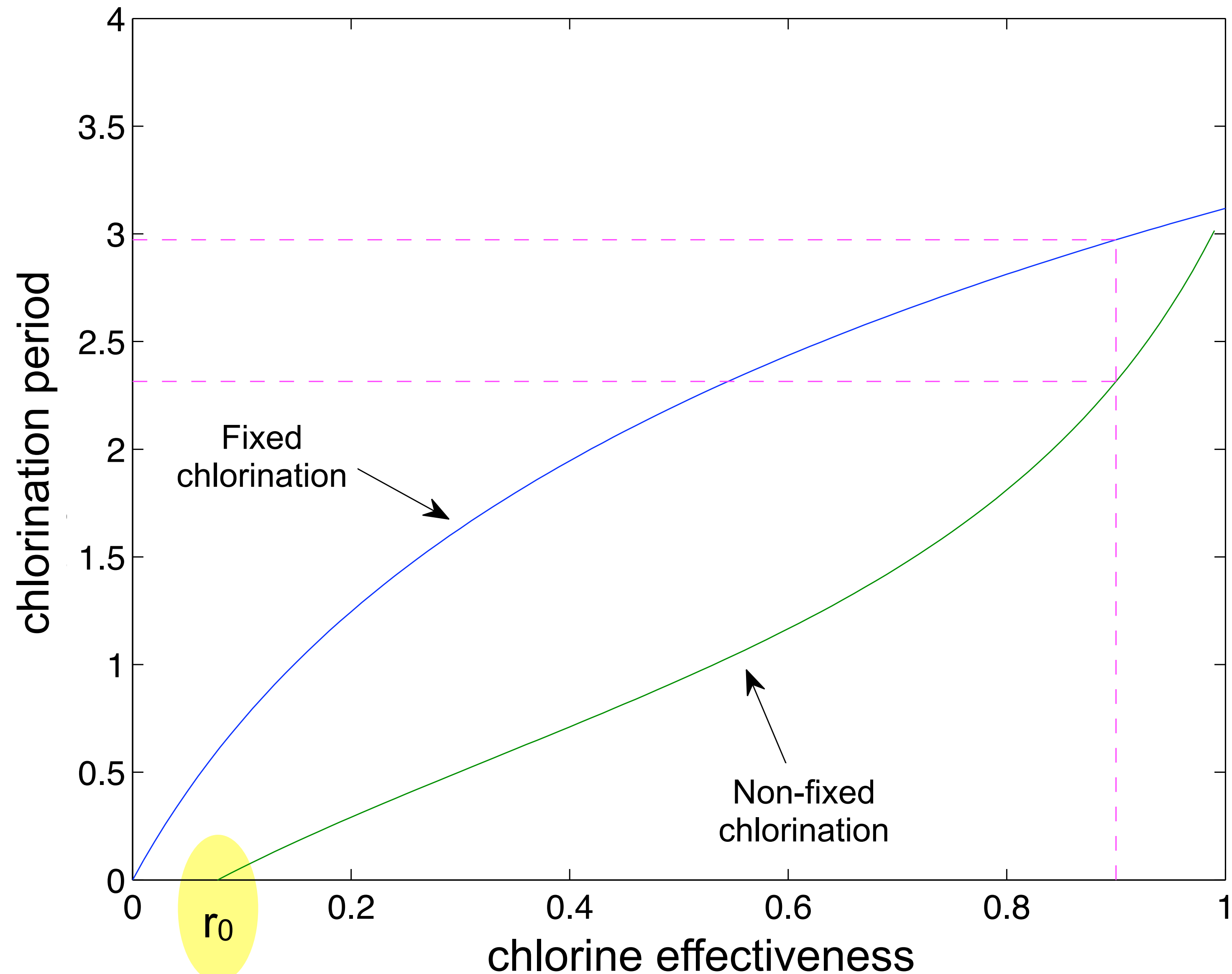

Latin Hypercube Sampling

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  - runs 1,000 simulations.

Example

Example

	✓	

Example

✗	✓	✗
	✗	
	✗	

Example

✗	✓	✗
	✗	✓
	✗	

Example

✗	✓	✗
✗	✗	✓
	✗	✗

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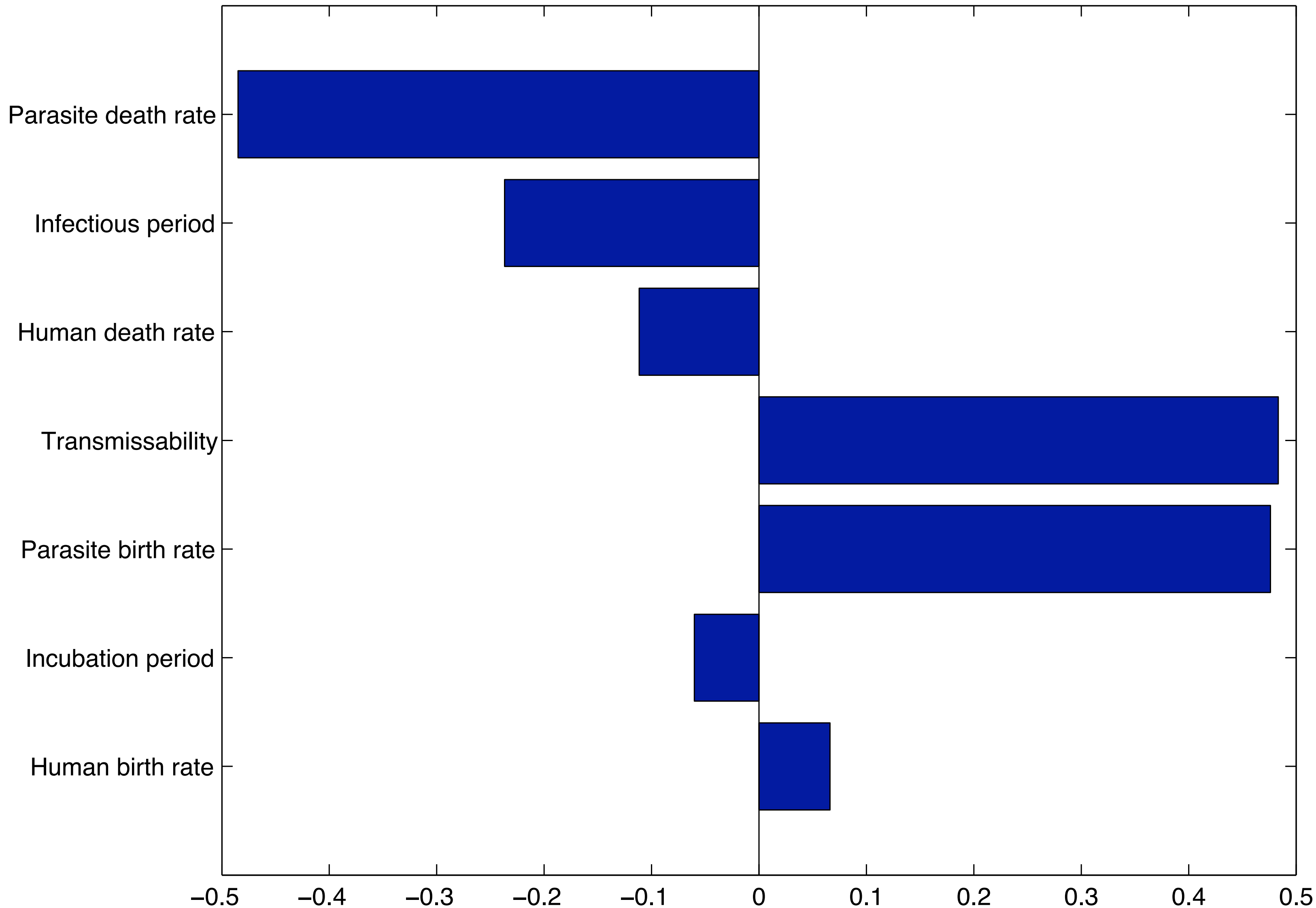
  - test individual parameters while holding all other parameters at median values
  - rank parameters by the amount of effect on the outcome
- PRCCs > 0 will increase R_0 when they are increased
- PRCCs < 0 will decrease R_0 when they are increased.

R_0=basic reproductive ratio

PRCCs



Parasite death rate
Infectious period
Human death rate
Transmissability
Parasite birth rate
Incubation period
Human birth rate
−0.5
−0.4
−0.3
−0.2
−0.1
0
0.1
0.2
0.3
0.4
0.5

Most important parameters

- The three parameters with the most impact on R_0 are

R_0=*basic reproductive ratio*

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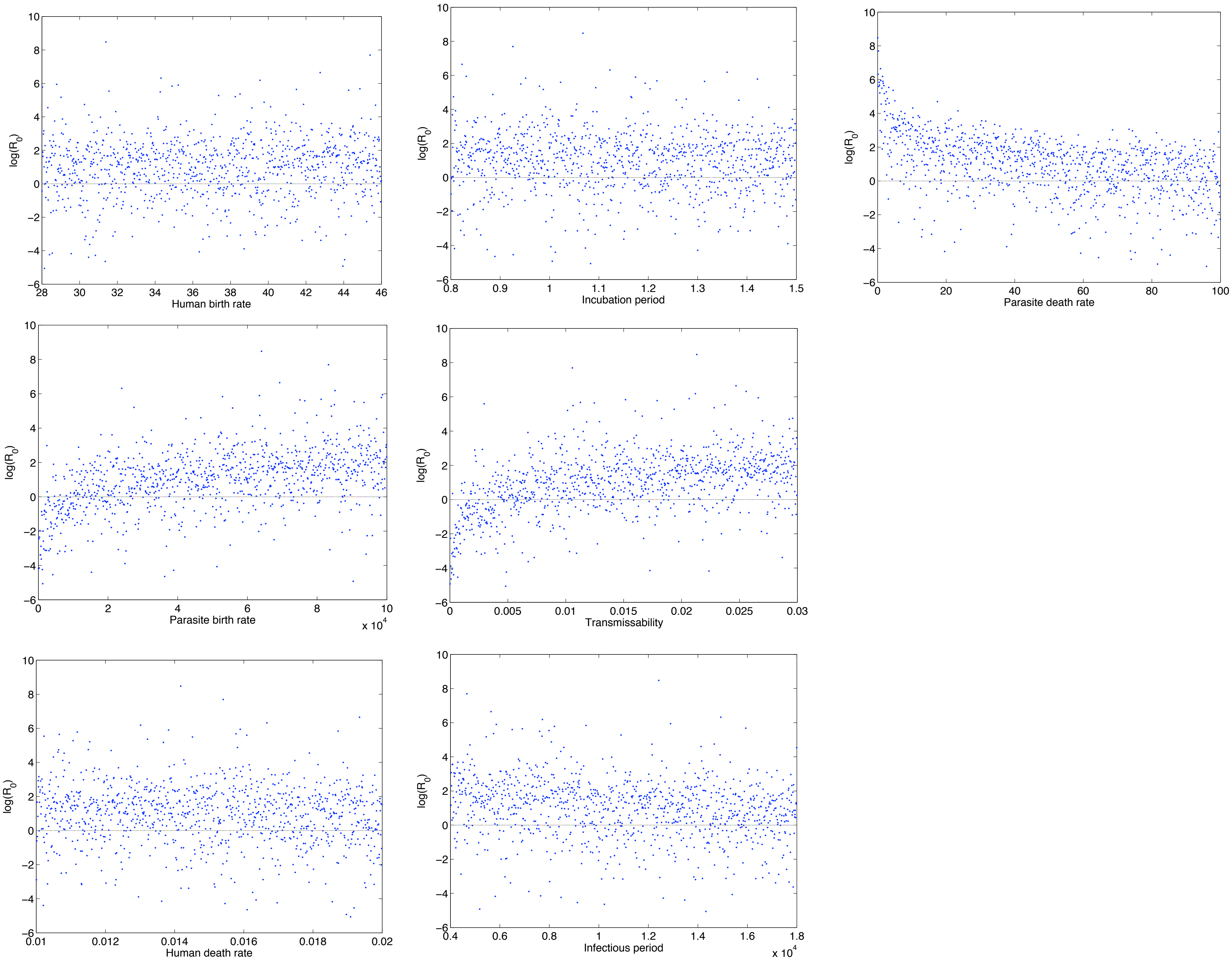
  - education.

R_0=basic reproductive ratio


log(R_0)
Human birth rate
Incubation period
Parasite death rate
Parasite birth rate
x 10^4
Transmissability
Human death rate
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Variation of control parameters

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Variation of control parameters

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- However, increasing μ_W (eg via continuous chlorination) is unlikely to lead to eradication
- Conversely, sufficiently decreasing γ (via education) is likely to bring R_0 below 1.

γ=parasite birth rate μ_W=parasite death rate R_0=basic reproductive ratio

Eradication threshold

- For R_0=1, we can plot the threshold surface for our three control parameters

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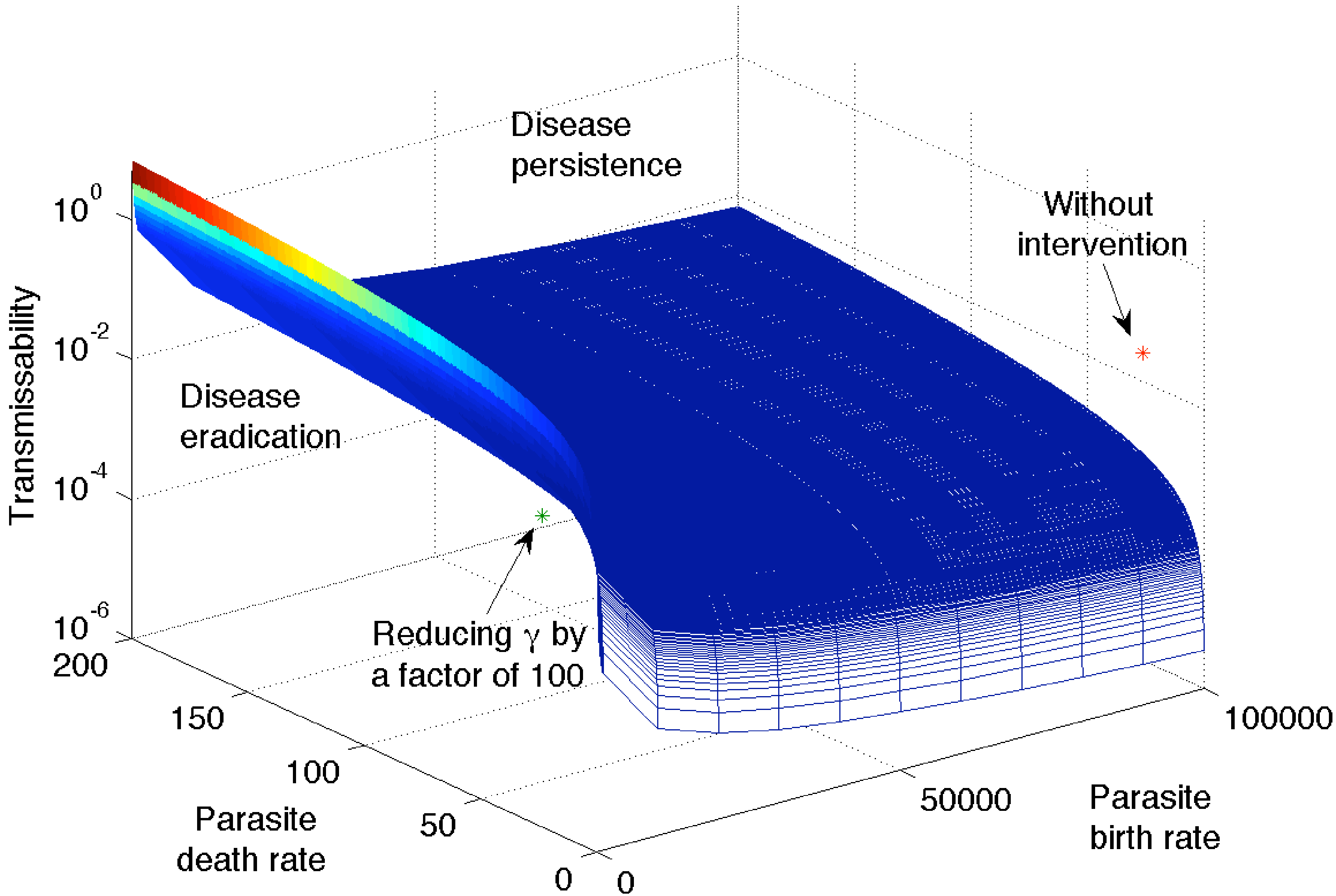
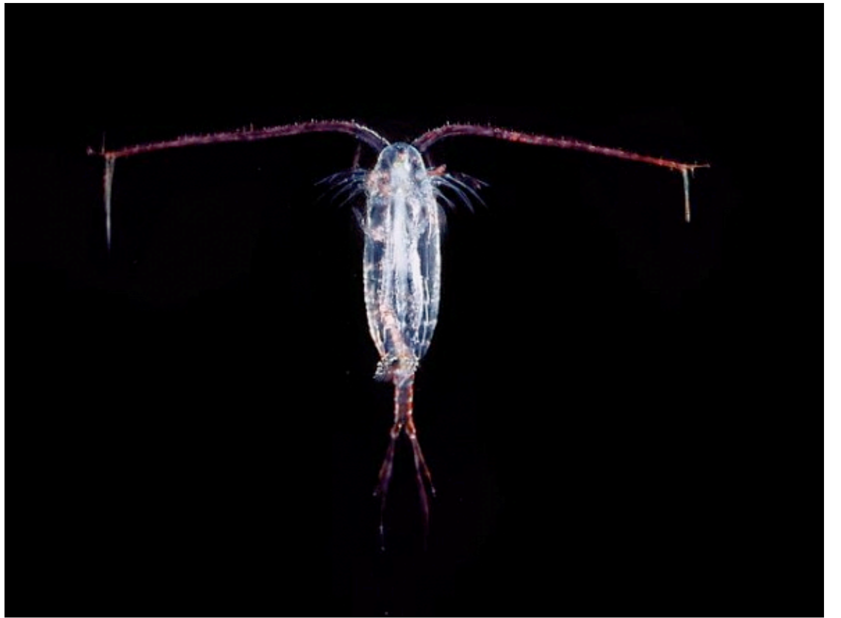
Eradication surface



Effect of control parameters

- The outcome is significantly dependent on changes in γ



β=transmissability
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μ_W=parasite death rate

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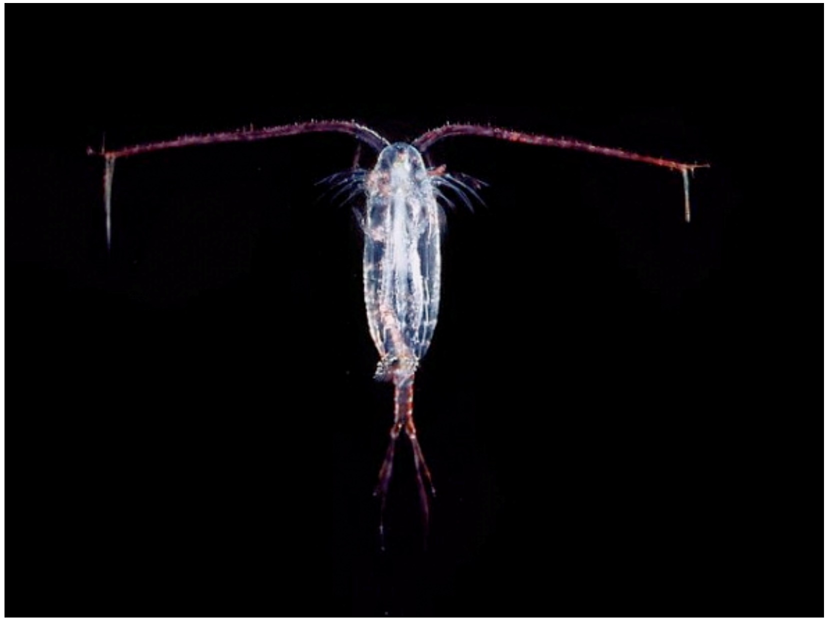

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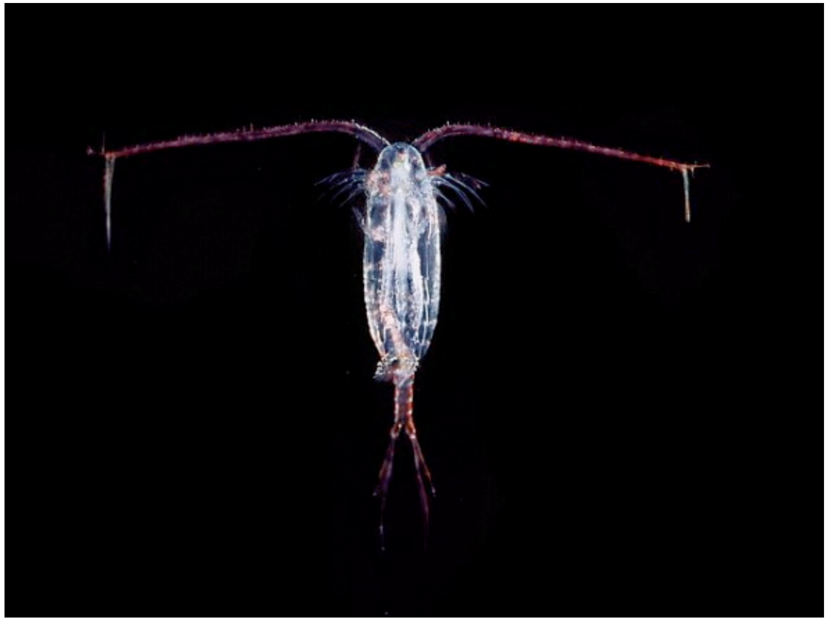
- β would have to be reduced to extremely low levels.



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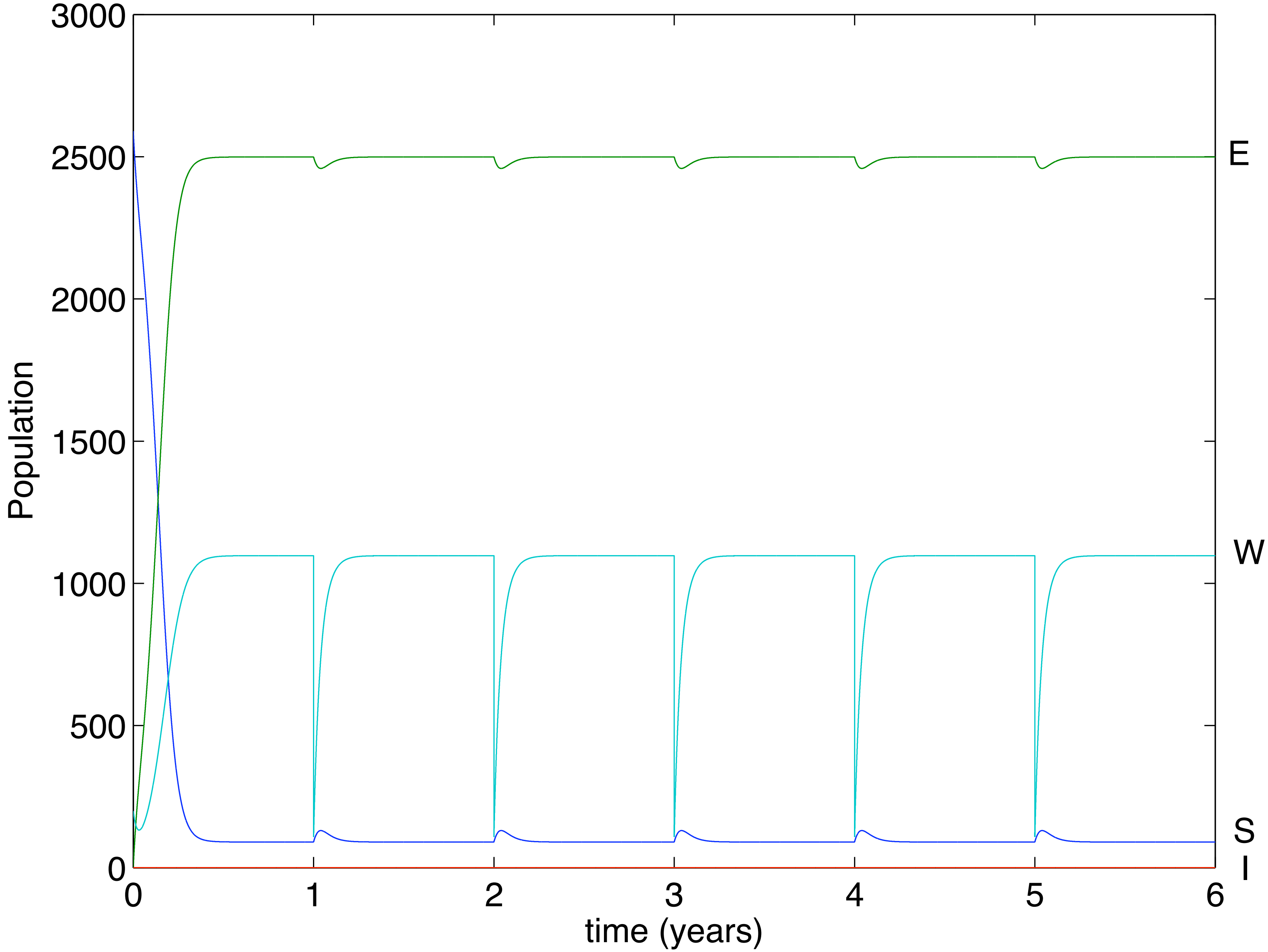
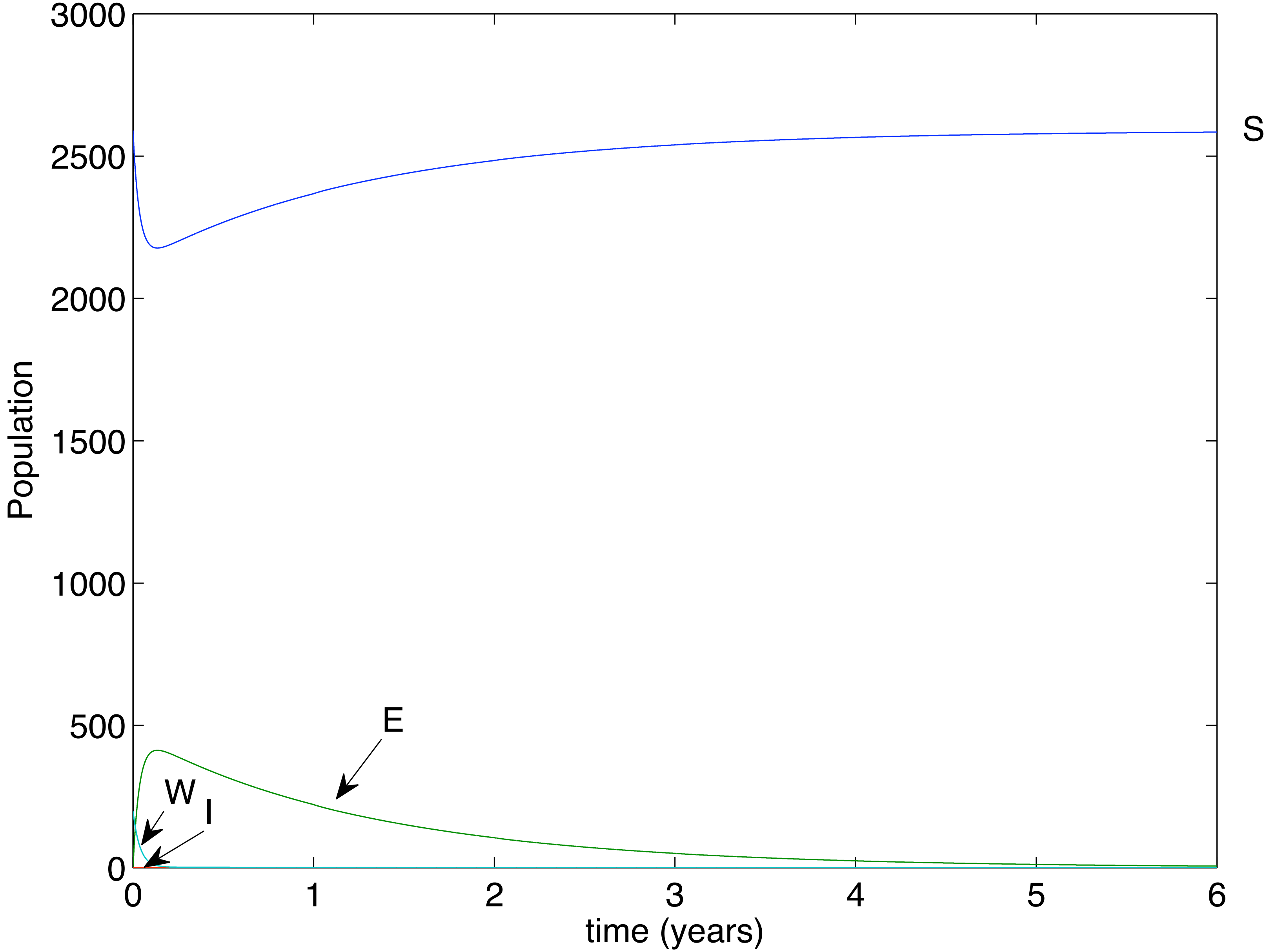
Annual chlorination



Reducing the parasite birthrate by 99%



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- The population quickly returns to high levels following chlorination
- Reducing the parasite birth rate by 99% (eg via education) can lead to eradication
- The entire population becomes uninfected.

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- Guinea worm disease satisfies all three.

Comparison with smallpox

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  - however, ongoing efforts mean India is about to be declared yaws-free.

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- Of course, a combination of education, chlorination and filtration is most desirable
- Efforts should be focussed on reaching remote communities.

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- This may reshape our understanding of what it takes to eradicate a disease
- By mustering both scientific and cultural resources, we can successfully defeat one of the oldest diseases in human history.

Key references

1. P. Cloutier, J. Harrison, A. Desforges and R.J. Smith? *A mathematical model for the eradication of Guinea worm disease* (under review)
2. A. Kealey and R.J. Smith? (2010) *Neglected Tropical Diseases: Infection Modeling and Control.* Journal of Healthcare for the Poor and Underserved 21, 53-69.

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