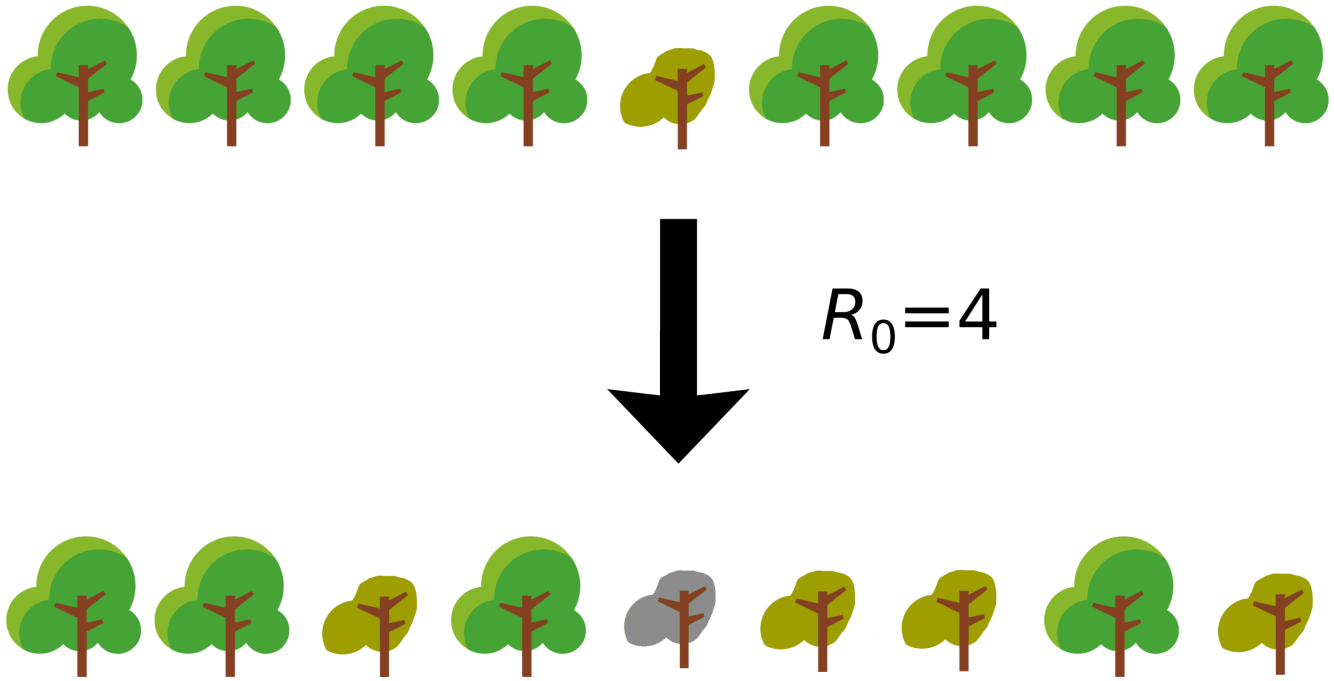
Epidemiological modelling and the basic reproduction number, R_0



Alexey Mikaberidze[1] and Nik Cunniffe[2]

[1]University of Reading, UK; [2]University of Cambridge, UK

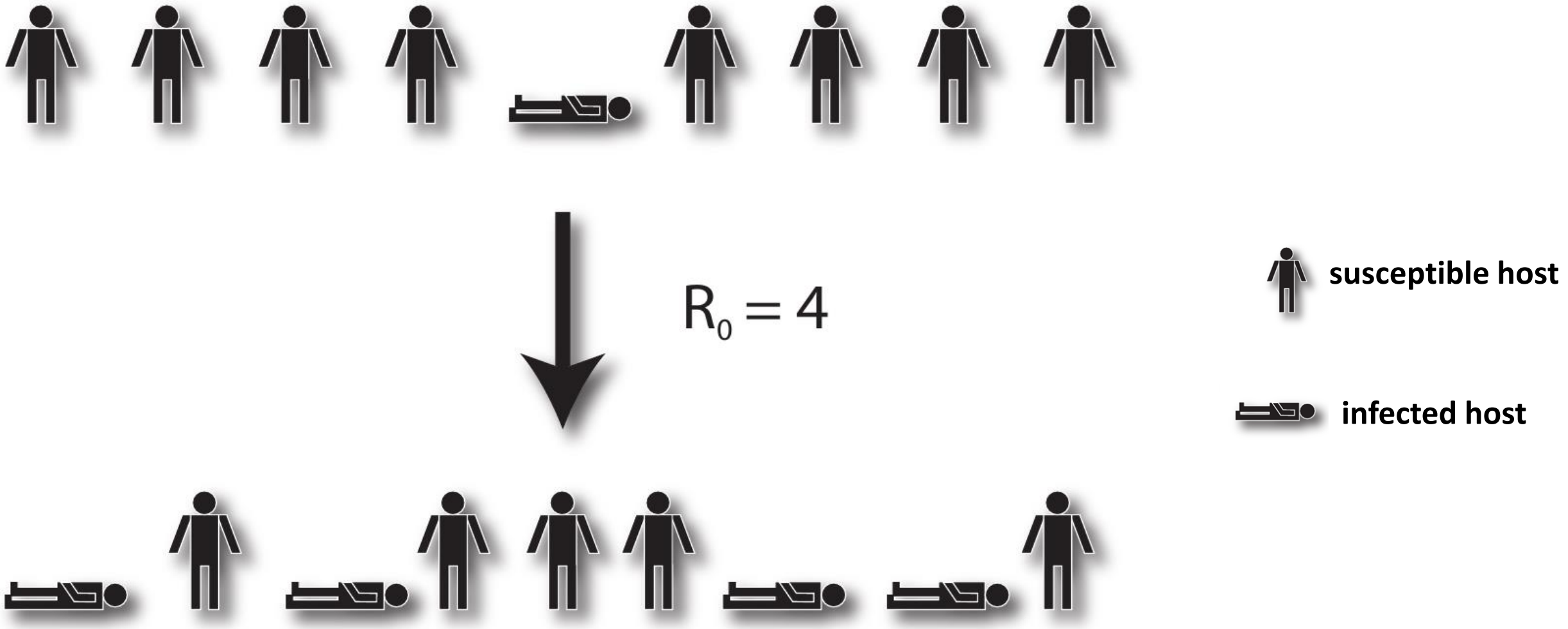
What is the basic reproduction number, R_0?

susceptible host

infected host

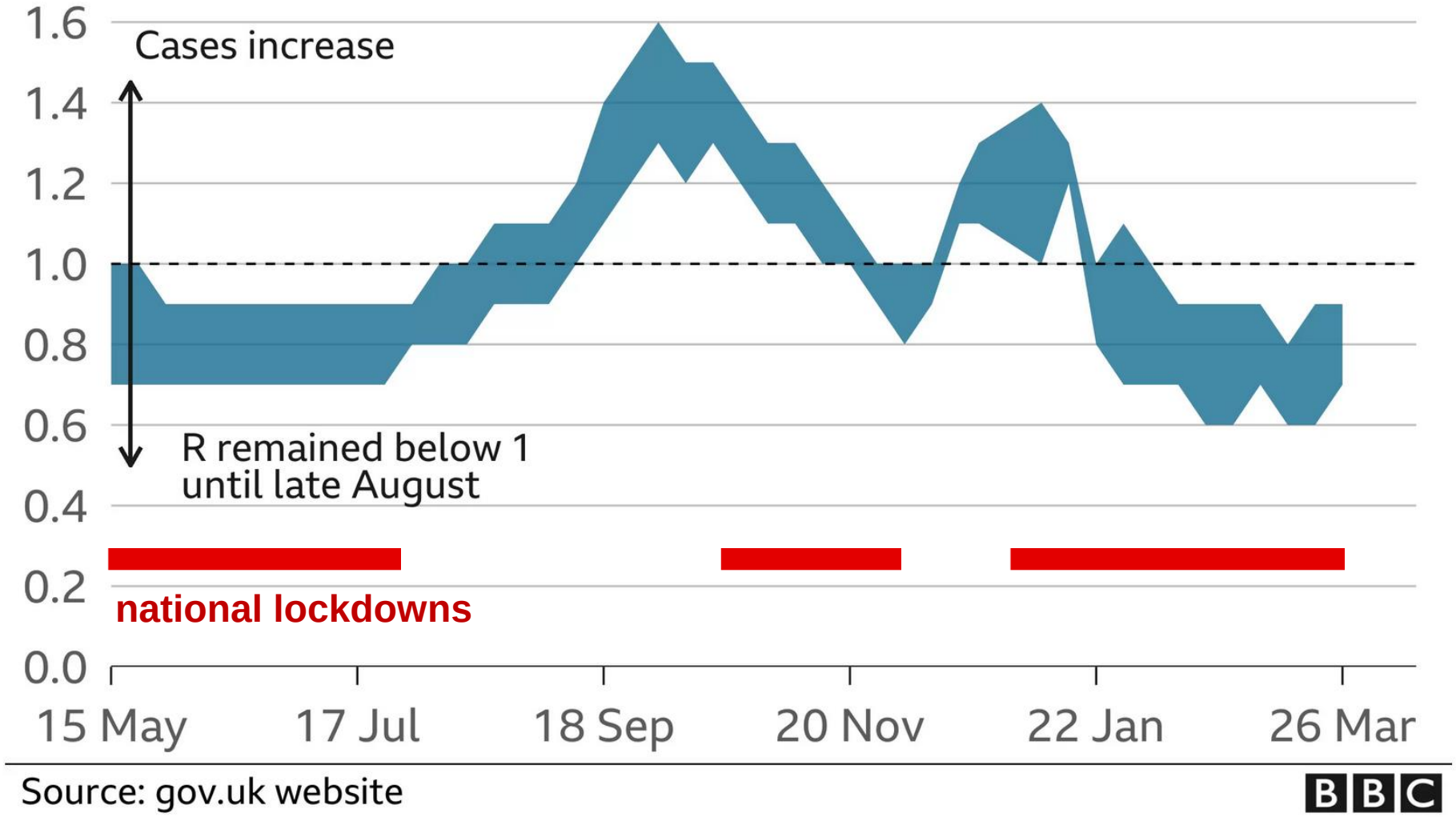
Anderson & May 1986

What is the basic reproduction number, R_0?



Anderson & May 1986

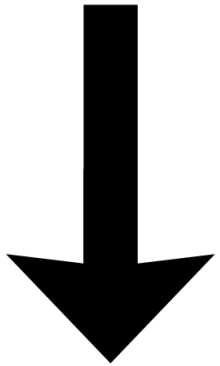
"R number" for COVID-19 in 2020-2021 in the UK



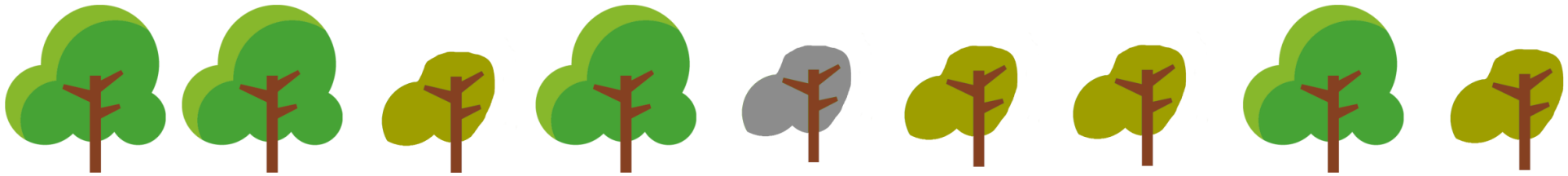
Outline

1. What is R_0 and what it can be used for?
2. Estimating R_0 for potato late blight
3. Methods of calculating R_0
4. R_0 across space: from fields to landscapes
5. Epidemiological modelling <-> remote sensing

What is the basic reproduction number R_0 for plant diseases?



$R_0=4$



susceptible host

infected host

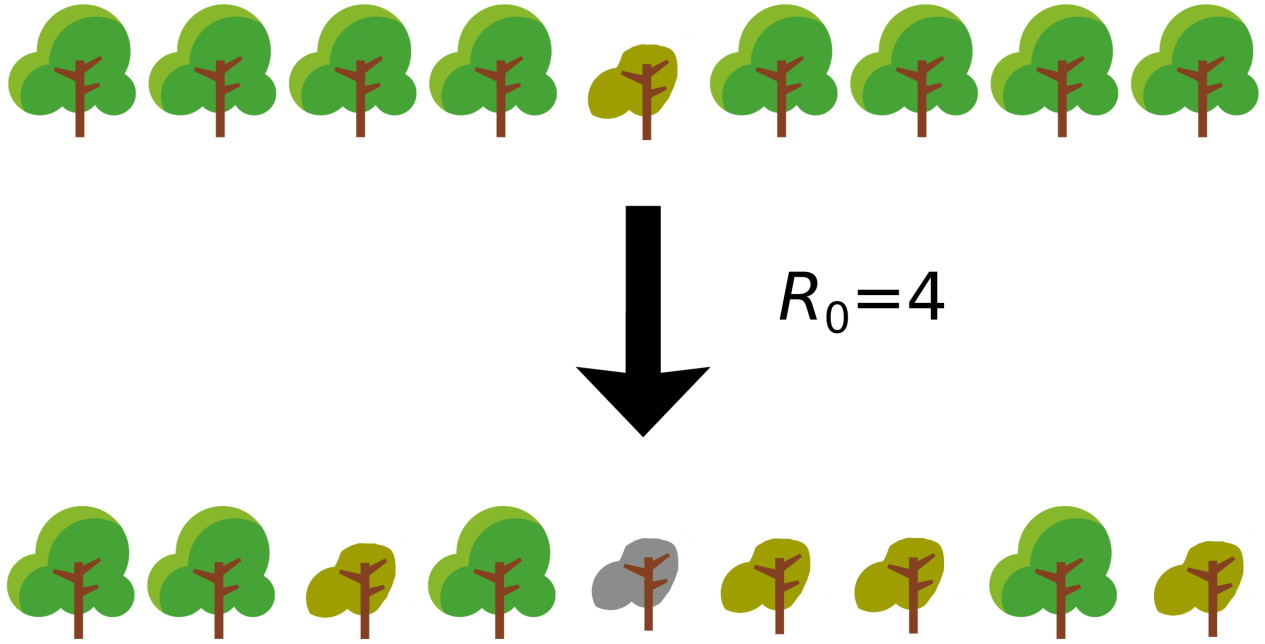
removed host

What is the basic reproduction number R_0 for plant diseases?

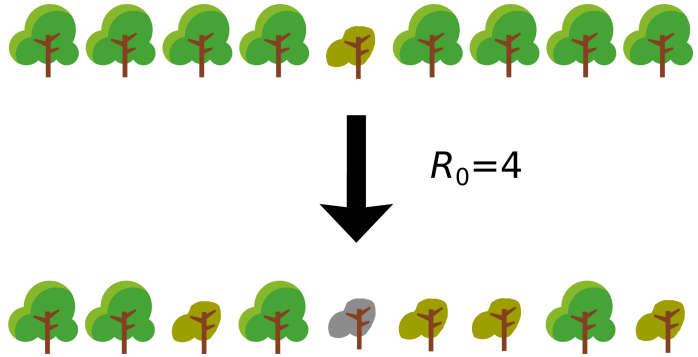
1. What are host units?

2. Space is important

3. Plants do not (usually) recover



How modelling and R_0 can be used to improve disease management



Gain a mechanistic understanding of how diseases spread

- R_0 as epidemic threshold
- R_0 as measure of pathogen fitness

Understand how pathogens adapt to control measures

- R_0 as measure of competitive capacity

Devise mathematical models to inform disease management

- R_0 as metric for monitoring
- R_0 as indication of success

R_0 across space

3. cultivated landscapes

2. fields (or orchards)

1. plants/leaves

What is R_0 for potato late blight?

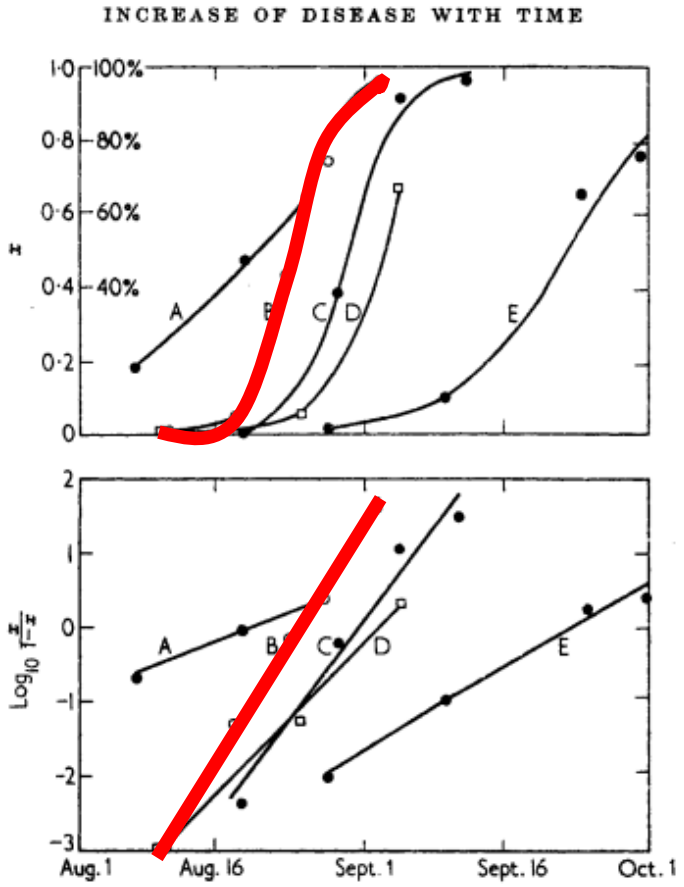
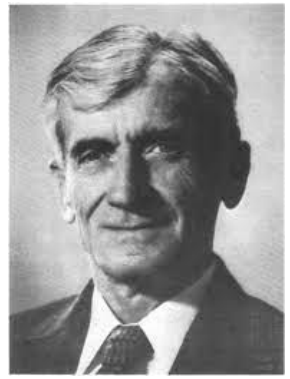


FIG. 4.1. Progress of blight on potatoes caused by *Phytophthora infestans*. The top half shows the increase of x, and the bottom half the increase of $\log_{10}[x/(1-x)]$, with time. Data of Large (1945). A, variety Majestic, Dartington, 1943; B, variety Majestic, Dartington, 1942; C, variety Majestic, Kentisbeare, 1942; D, variety Majestic, Durnsford, 1944; E, variety Arran Consul, Dartington, 1941.

Question

Can we fit an SIR type model to van der Plank's Epidemic B to find R_0?



van der Plank (1963) Plant Diseases: Epidemics & Control

Potato late blight. Classical approach

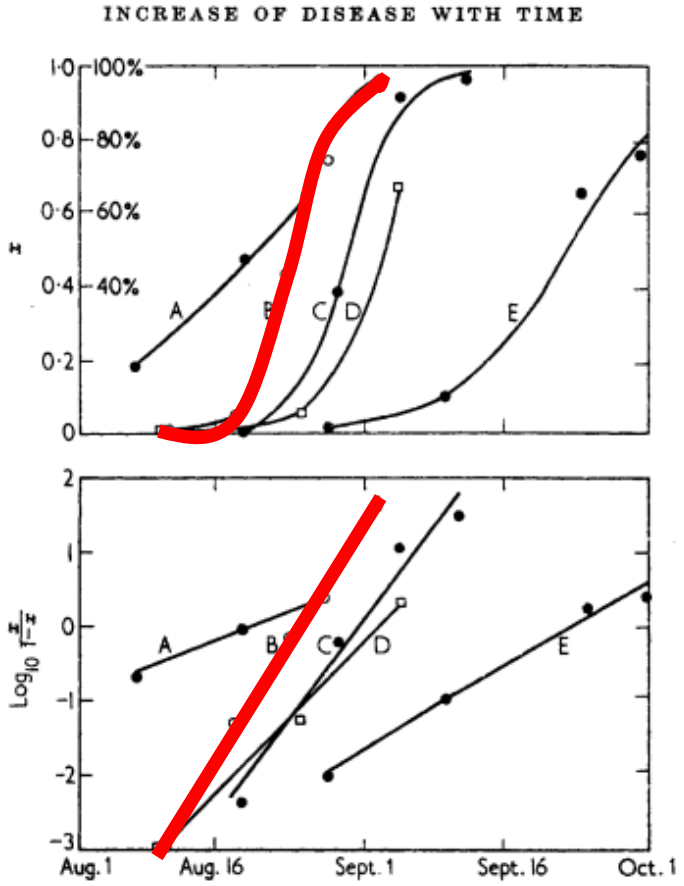


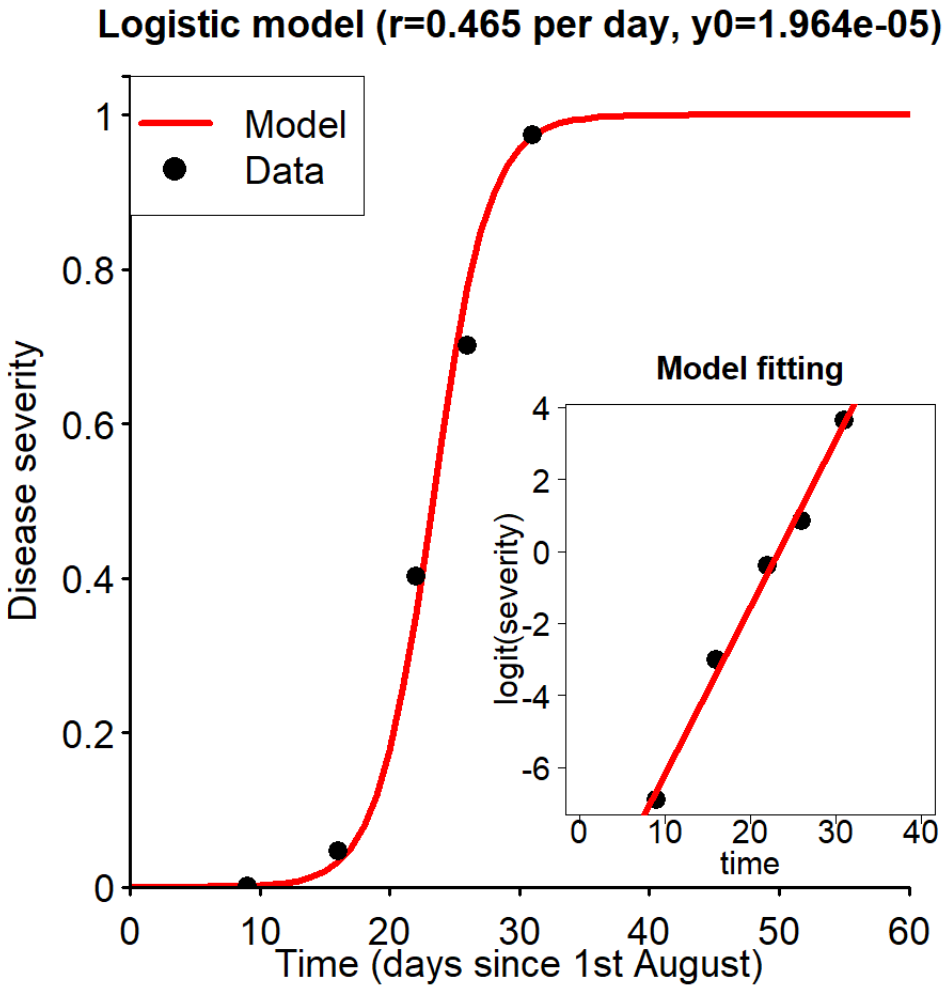
FIG. 4.1. Progress of blight on potatoes caused by *Phytophthora infestans*. The top half shows the increase of x, and the bottom half the increase of $\log_{10}[x/(1-x)]$, with time. Data of Large (1945). A, variety Majestic, Dartington, 1943; B, variety Majestic, Dartington, 1942; C, variety Majestic, Kentisbeare, 1942; D, variety Majestic, Durnsford, 1944; E, variety Arran Consul, Dartington, 1941.

Polycyclic epidemic

Try logistic growth

$$y = \frac{1}{1+(1/y_0 - 1)\exp(-rt)}$$

Various ways to find y_0 and r, e.g., regression of logit



A compartmental model

Susceptible
S

Infected
I

Removed
R

Divide population into classes according to disease status

(S)usceptible Healthy (& not infected)

(I)nfected Infected (& actively infecting others)

(R)emoved Dead/post-infectious

Must decide on a scale; use “infectable site” (area of leaf covered by lesion)

Omit latent period for now (could be added easily; see later)

Assume total population is constant (no birth/death; could be relaxed easily)

A compartmental model

Infection

A single susceptible site becomes infected

Net rate depends on numbers of susceptible and infected sites

Removal

A single infected site becomes removed (dead/post-infectious)

Net rate depends on number of infected sites only

A compartmental model

β = rate of infection
(per susceptible,
per infected)

μ = rate of removal
(infectious period is 1/μ)

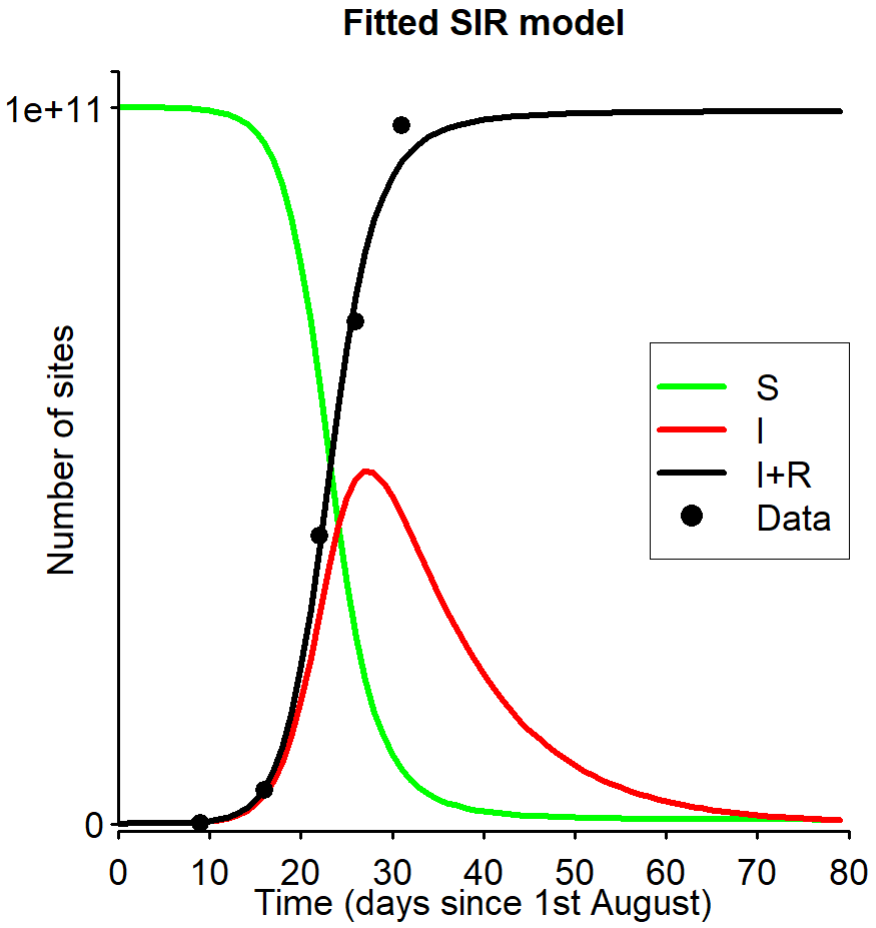
$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta IS - \mu I$$

$$\frac{dR}{dt} = \mu I$$

Fitting the model

Experiment	Time	Severity
B	9	0.001
B	16	0.047
B	22	0.402
B	26	0.701
B	31	0.975



- Fit $I + R$ from model to Severity by least squares
- Assume $N = 1 \times 10^{11}$ and $\mu = 0.1\ day^{-1}$
- Free parameters to fit are β and $I(0)$

So, what is R_0 for potato late blight?

- R_0 = Number of new infections caused by a single infected individual introduced into a totally susceptible population

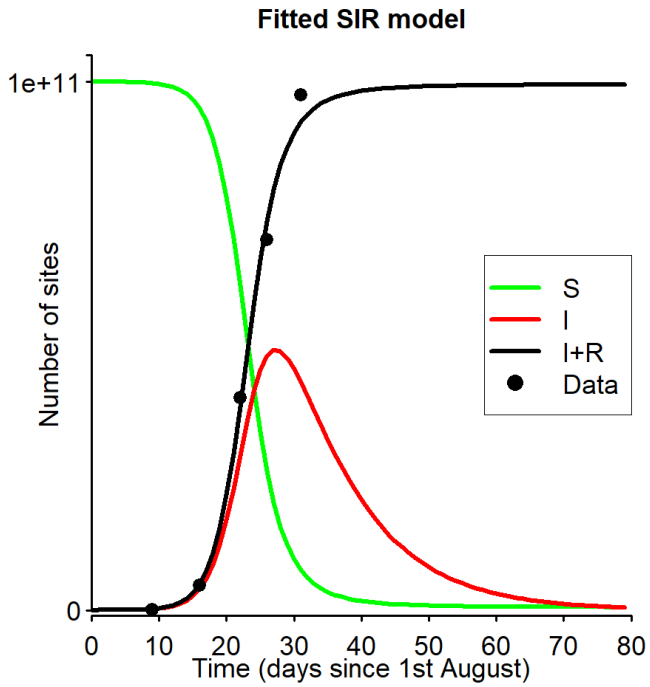
- R_0 = Infection Rate x Population Size x Infectious Period $= \beta \times N \times \frac{1}{\mu} = \frac{\beta N}{\mu}$

- For van der Plank's Epidemic B (assuming N and μ and fitting β and $I(0)$)

$$R_0 \approx \frac{1 \times 10^{11} \times 5.24 \times 10^{-12}}{0.1} \approx 5.24$$

Do assumptions matter?

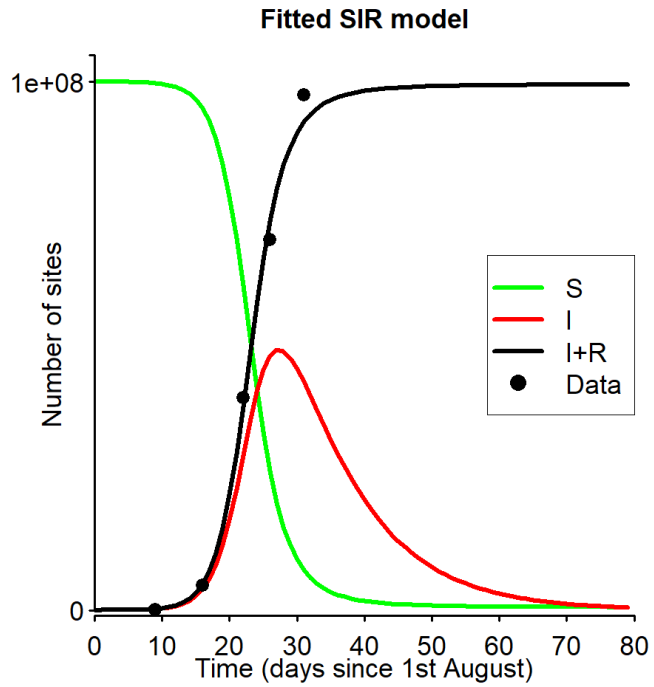
Original Fit



$N = 1x10^{11}$, $\beta \sim 5.24x10^{-12}$, $\mu = 0.1$

$R_0 \sim 5.24$

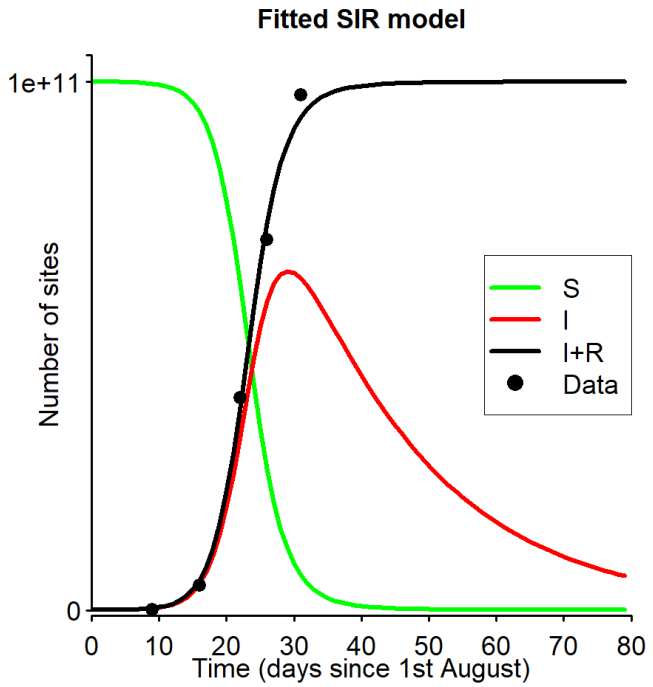
Alter number of sites (N)



$N = 1x10^{8}$, $\beta \sim 5.24x10^{-9}$, $\mu = 0.1$

$R_0 \sim 5.24$

Alter infectious period (1/μ)



$N = 1x10^{11}$, $\beta \sim 4.44x10^{-12}$, $\mu = 0.05$

$R_0 \sim 8.88$

A simple way of finding R_0 you may see

A threshold for initial spread extracted from dI/dt (0)

$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta IS - \mu I$$

$$\frac{dR}{dt} = \mu I$$

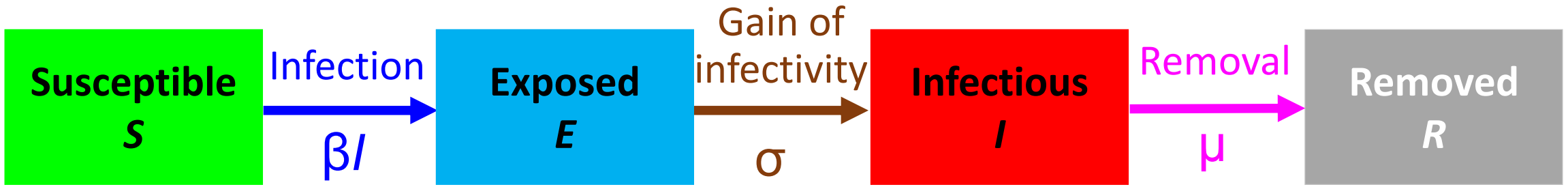
At $t = 0$ $\quad \frac{dI}{dt} \approx \beta IN - \mu I$

And R_0 is just the quantity that needs to be greater than one to make dI/dt(0) > 0, i.e. $R_0 = \frac{\beta N}{\mu}$

Very simple, but only easy when models have single infectious class; true R_0 can also be ambiguous

In practice we use Next Generation Matrix; see later

Extension. SEIR model (adding latent period)



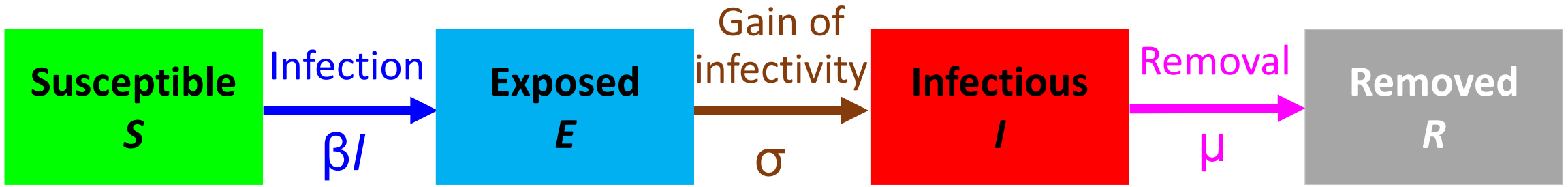
Rate of change of Susceptible sites = − Infection

Rate of change of Exposed sites = + Infection − Gain of infectivity

Rate of change of Infectious sites = + Gain of infectivity − Removal

Rate of change of Removed sites = + Removal

Extension. SEIR model (adding latent period)



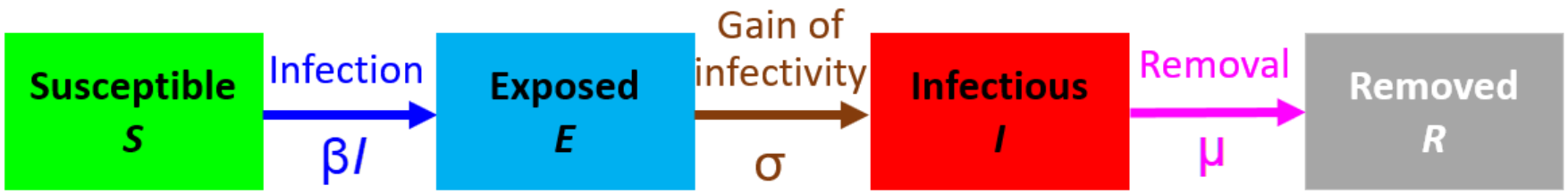
$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dE}{dt} = \beta SI - \sigma E$$

$$\frac{dI}{dt} = \sigma E - \mu I$$

$$\frac{dR}{dt} = \mu I$$

Finding R_0



$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dE}{dt} = \beta SI - \sigma E$$

$$\frac{dI}{dt} = \sigma E - \mu I$$

$$\frac{dR}{dt} = \mu I$$

Introduce an infectious host to population of size N

Exposed (i.e., latent) for $1/\sigma$; Infectious for $1/\mu$

Causes no new infections while Exposed

Causes infections at net rate βN while Infectious

$$R_0 = 0 \times \frac{1}{\sigma} + \beta N \times \frac{1}{\mu} = \frac{\beta N}{\mu}$$ (precisely as before)

Finding R_0 in practice

JOURNAL OF THE ROYAL SOCIETY Interface
J. R. Soc. Interface (2010) 7, 873–885
doi:10.1098/rsif.2009.0386
Published online 5 November 2009

The construction of next-generation matrices for compartmental epidemic models

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[2]Faculty of Veterinary Medicine, Utrecht University, Yalelaan 7, 3584 CL, Utrecht, The Netherlands
[3]Centre for Mathematical Biology, Institute of Information & Mathematical Sciences, Massey University, Private Bag 102 904, North Shore Mail Centre, Auckland, New Zealand

- These models were simple enough to reason out the form of R_0
- But this can be hard, particularly if "generation" is unclear, e.g., multiple host types
- Gold standard is "Next Generation Method"
- Embeds discrete time model in the (continuous time) compartmental model
- Underlying maths looks (is!) frightening, but boils down to just a calculation
- Tutorial introduction in Diekmann *et al.* (2010) *J. Roy. Soc. Interface*: 7:873-885.

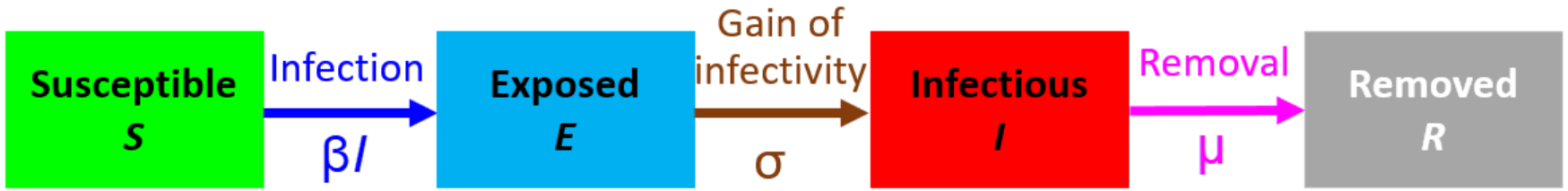
Next generation method for SEIR model

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dE}{dt} = \beta SI - \sigma E$$

$$\frac{dI}{dt} = \sigma E - \mu I$$

$$\frac{dR}{dt} = \mu I$$



Next generation method for SEIR model

$$\frac{dS}{dt} = -\beta SI$$

$$\frac{dE}{dt} = \beta SI - \sigma E$$

$$\frac{dI}{dt} = \sigma E - \mu I$$

$$\frac{dR}{dt} = \mu I$$

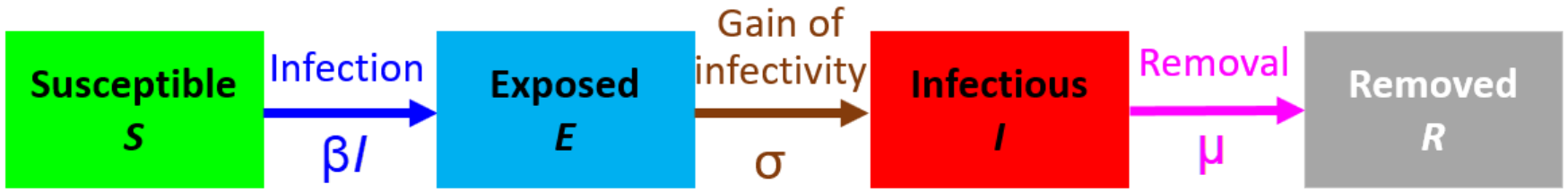
Focus on vector of infected hosts: $\mathbf{x} = (E, I)^T$

Model is $\frac{d\mathbf{x}}{dt} = \mathbf{F}(\mathbf{x}) - \mathbf{V}(\mathbf{x})$ where

$\mathbf{F}(\mathbf{x}) = (\beta SI, 0)^T$ New infections

$\mathbf{V}(\mathbf{x}) = (\sigma E, \mu I - \sigma E)^T$ Transfers out

R_0 is largest eigenvalue ("spectral radius") of $\mathcal{F}\mathcal{V}^{-1}$ where $\mathcal{F}$ and $\mathcal{V}$ are Jacobians of **F** and **V**



Next generation method for SEIR model

$$\boldsymbol{F}(\boldsymbol{x}) = (F_E, F_I)^T = (\beta SI, 0)^T$$

$$\boldsymbol{V}(\boldsymbol{x}) = (V_E, V_I)^T = (\sigma E, \mu I - \sigma E)^T$$

At DFE

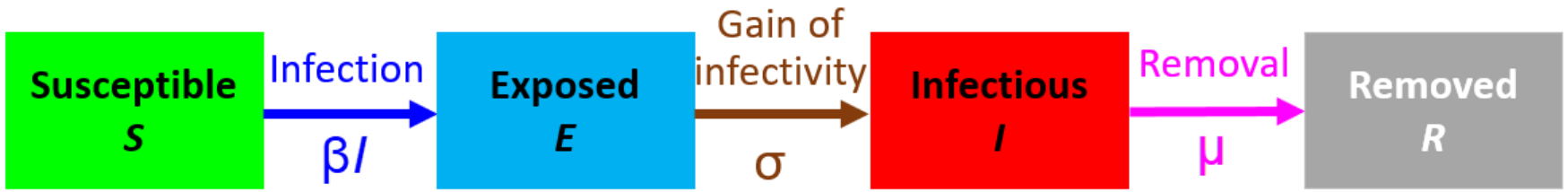
$$\boldsymbol{x} = (E, I)^T$$

$$\mathcal{F} = \frac{\partial F_i}{\partial x_j} = \begin{pmatrix} \frac{\partial F_E}{\partial E} & \frac{\partial F_E}{\partial I} \\ \frac{\partial F_I}{\partial E} & \frac{\partial F_I}{\partial I} \end{pmatrix}$$

$$\mathcal{V} = \frac{\partial V_i}{\partial x_j} = \begin{pmatrix} \frac{\partial V_E}{\partial E} & \frac{\partial V_E}{\partial I} \\ \frac{\partial V_I}{\partial E} & \frac{\partial V_I}{\partial I} \end{pmatrix}$$

Matrix inversion →

$$\mathcal{V}^{-1} = \begin{pmatrix} 1/\sigma & 0 \\ 1/\mu & 1/\mu \end{pmatrix}$$



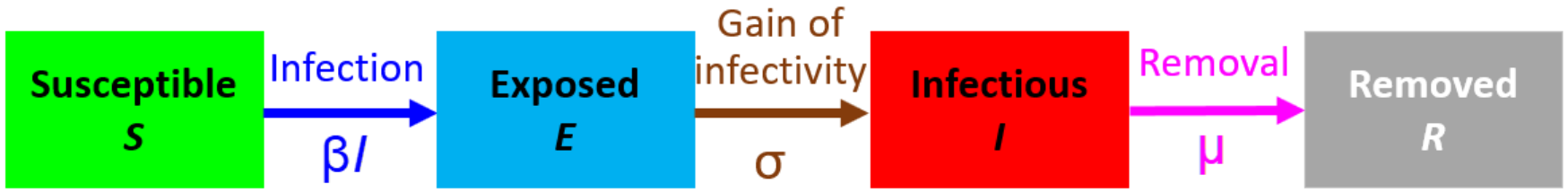
Next generation method for SEIR model

R_0 is the largest eigenvalue ("spectral radius") of $\mathcal{F}\mathcal{V}^{-1}$

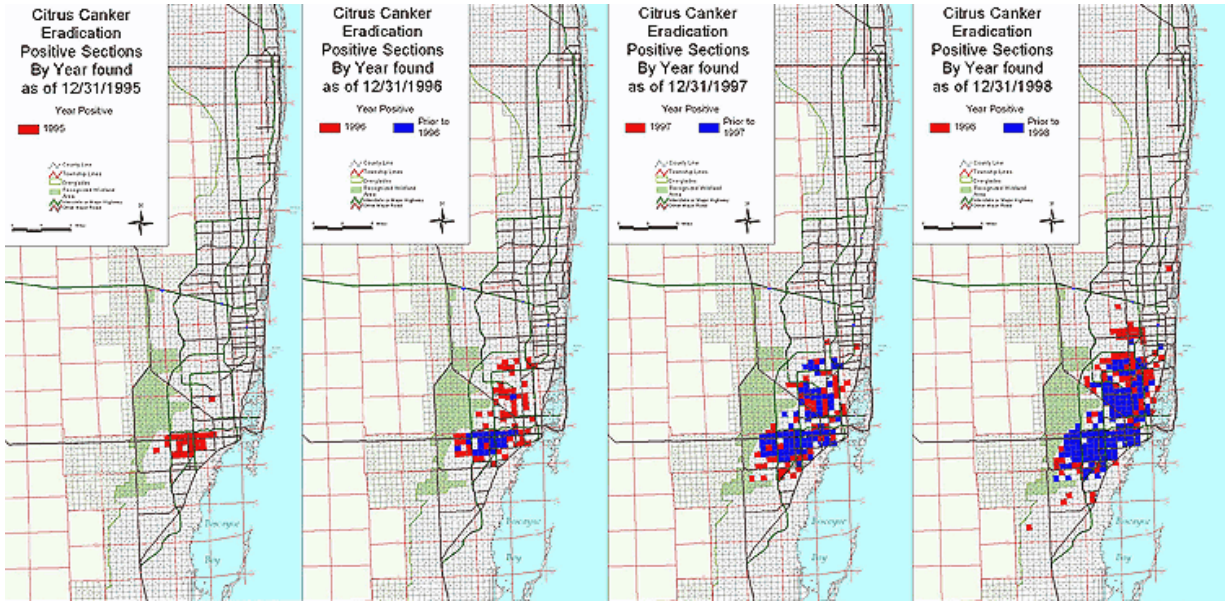
$$\mathcal{F}\mathcal{V}^{-1} = \begin{pmatrix} 0 & \beta N \\ 0 & 0 \end{pmatrix} \begin{pmatrix} 1/\sigma & 0 \\ 1/\mu & 1/\mu \end{pmatrix}$$

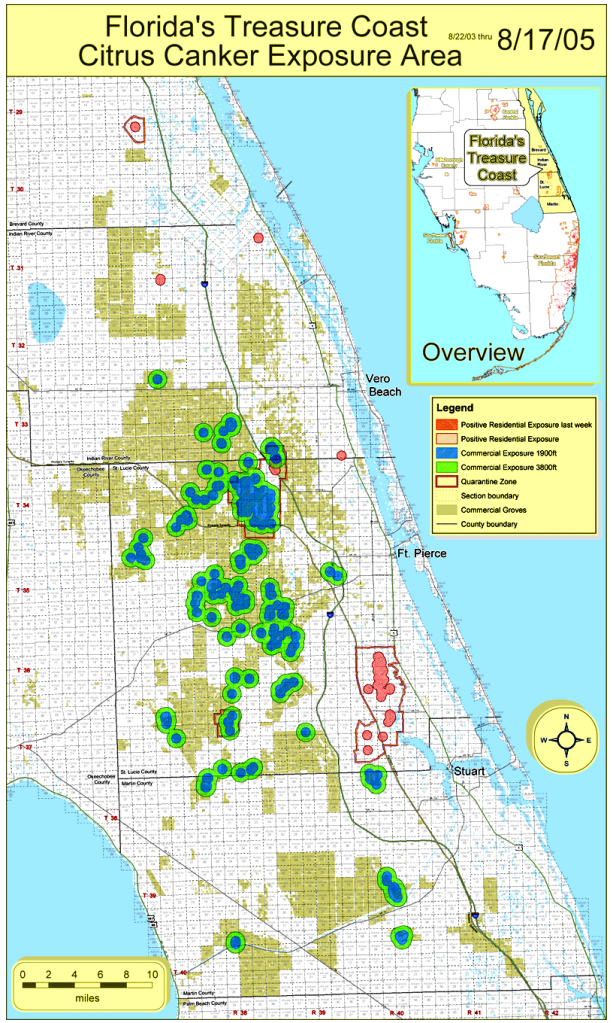
Eigenvalues are 0 and $R_0 = \dfrac{\beta N}{\mu}$

Same result, but no thinking required, instead just mindless (!) calculation



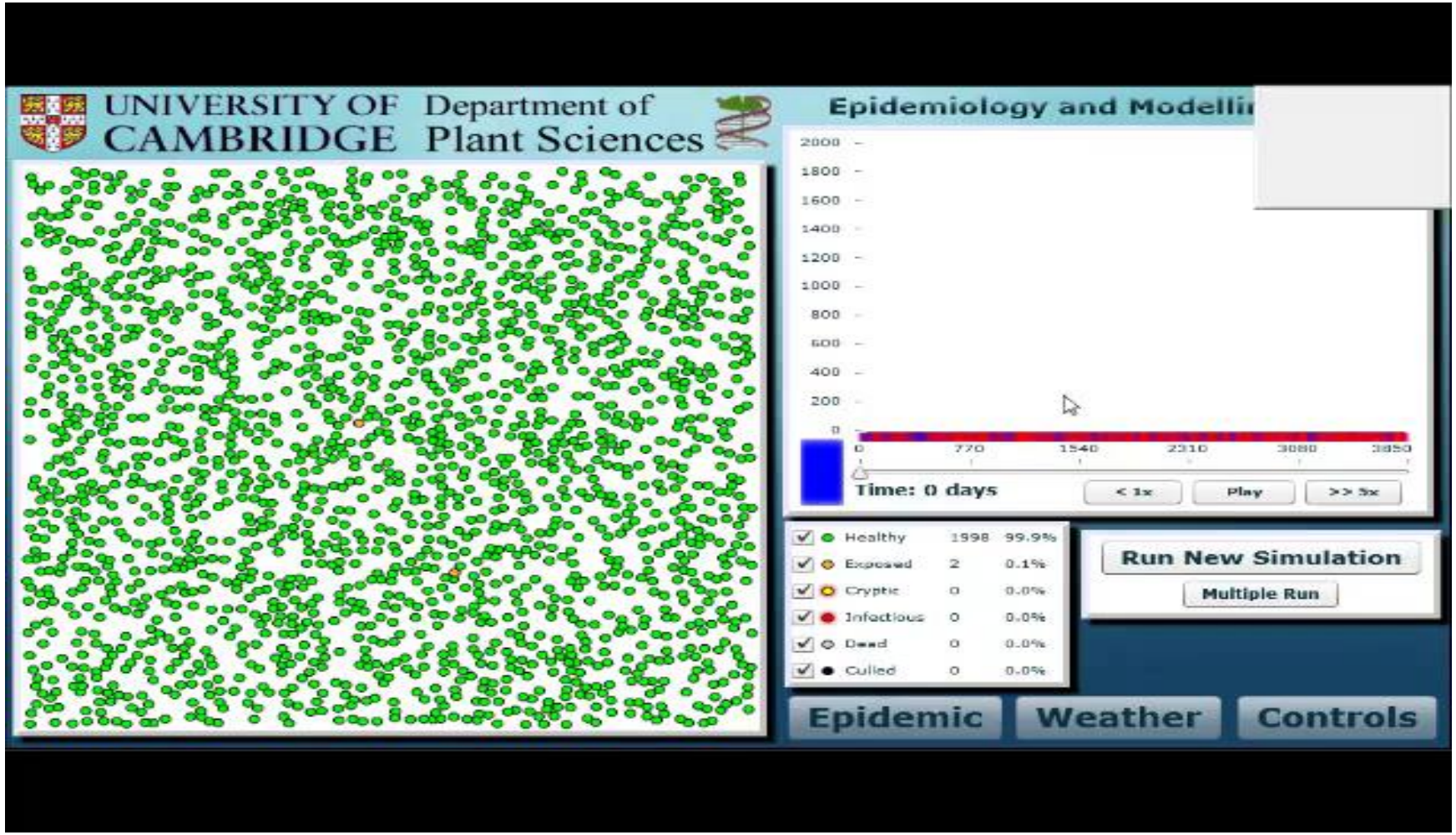
Using R_0 to understand control. Citrus canker





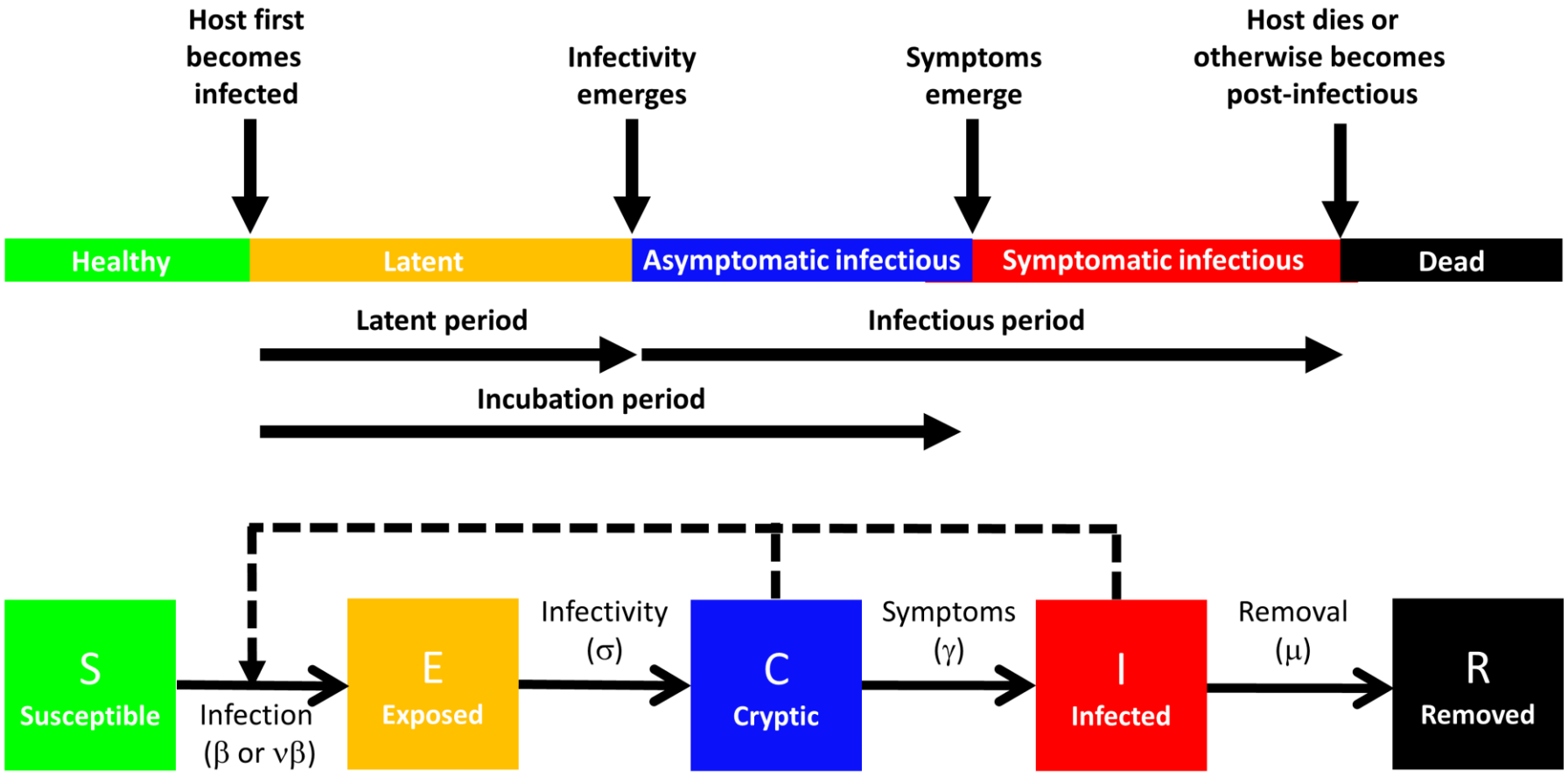
Cunniffe *et al.* (2015) *PLOS Computational Biology*. 11:e1004211

Using R_0 to understand control. Citrus canker



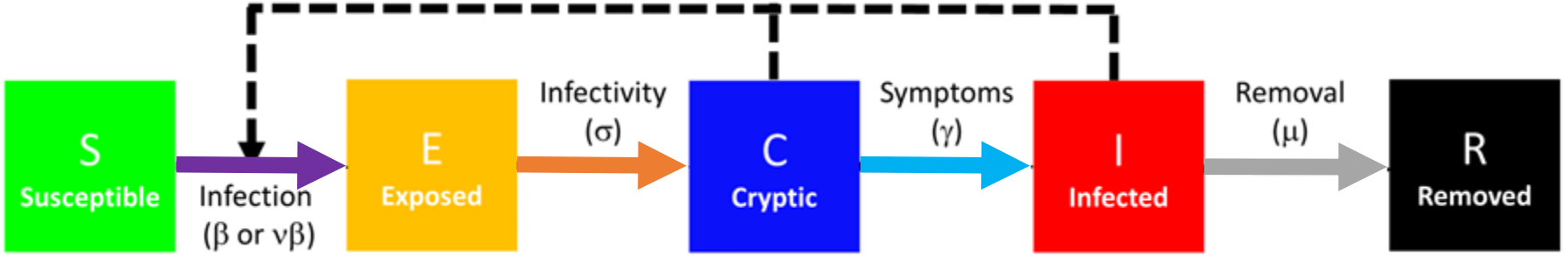
Cunniffe *et al.* (2015) *PLOS Computational Biology*. 11:e1004211

Can we use R_0 to see why culling is needed?



Cunniffe & Gilligan (2020) Chapter 12 in *Emerging Plant Diseases and Global Food Security* APS Press

Modelling



Rate of change of Susceptible trees = − Infection

Rate of change of Exposed trees = + Infection − Gain of infectivity

Rate of change of Cryptic trees = + Gain of infectivity − Emergence of symptoms

Rate of change of Infectious trees = + Emergence of symptoms – Removal (by roguing)

Rate of change of Removed trees = + Removal (by roguing)

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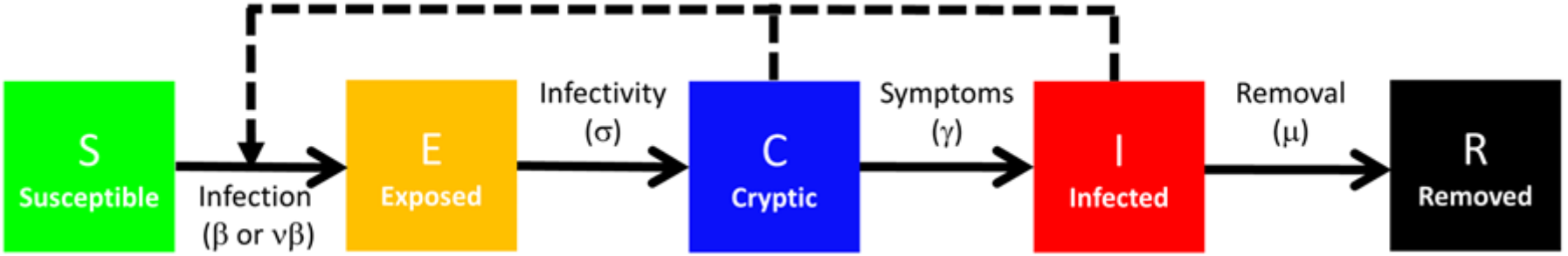
Modelling



$$\frac{dS}{dt} = -\nu\beta SC - \beta SI$$

$$\frac{dE}{dt} = \nu\beta SC + \beta SI - \sigma E$$

$$\frac{dC}{dt} = \sigma E - \gamma C$$

$$\frac{dI}{dt} = \gamma C - \mu I$$

$$\frac{dR}{dt} = \mu I$$

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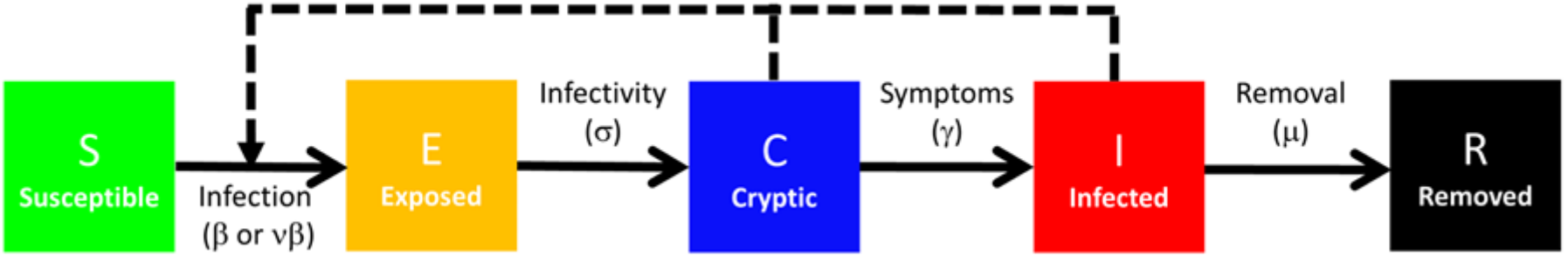
Finding R_0



$$\frac{dS}{dt} = -\nu\beta SC - \beta SI$$

$$\frac{dE}{dt} = \nu\beta SC + \beta SI - \sigma E$$

$$\frac{dC}{dt} = \sigma E - \gamma C$$

$$\frac{dI}{dt} = \gamma C - \mu I$$

$$\frac{dR}{dt} = \mu I$$

Introduce an infected host to population of size N

Exposed for $1/\sigma$; Cryptic for $1/\gamma$; Infected for $1/\mu$

Causes no infections while Exposed

infections at net rate $\nu\beta N$ while Cryptic

infections at net rate βN while Infected

$$R_0 = 0\times\frac{1}{\sigma} + \nu\beta N\times\frac{1}{\gamma} + \beta N\times\frac{1}{\mu}$$

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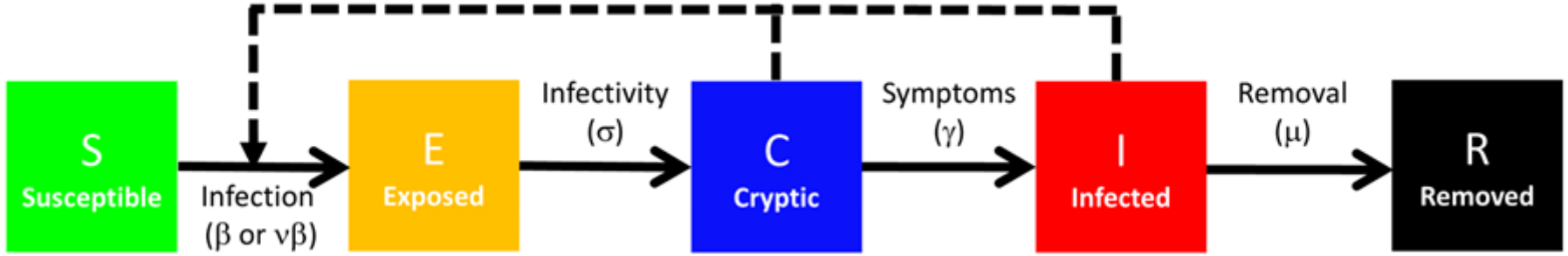
What does this mean?



We have found $R_0 = \frac{\nu\beta N}{\gamma} + \frac{\beta N}{\mu}$

But if we only rogue, all we can affect is μ (roguing rate)

Even if $\mu \to \infty$ (very frequent roguing), $R_0 \to \frac{\nu\beta N}{\gamma} > 1$

And so cryptic infection means culling is necessary

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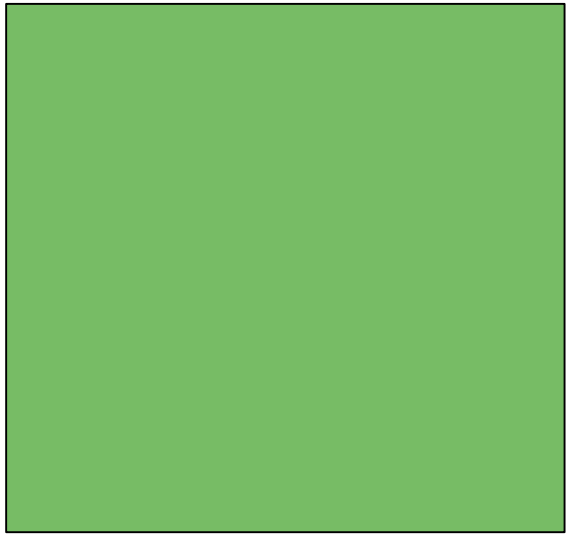
R_0 across space

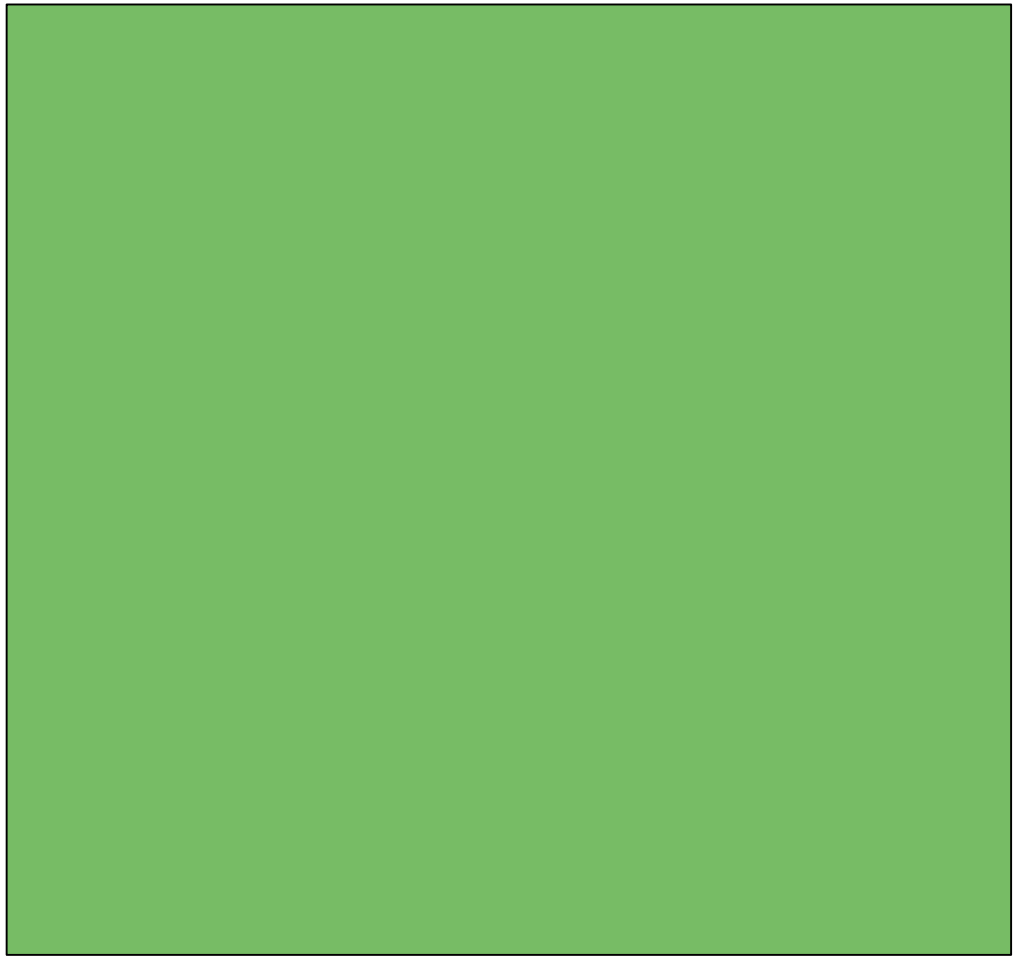
3. cultivated landscapes

2. fields (or orchards)

1. plants/leaves

Is the pathogen more invasive in smaller or larger fields?





Mikaberidze, Mundt, & Bonhoeffer,
Ecological Applications 2016

SIR model

$$\frac{dS}{dt} = -\beta IS$$

$$\frac{dI}{dt} = \beta IS - \mu I$$

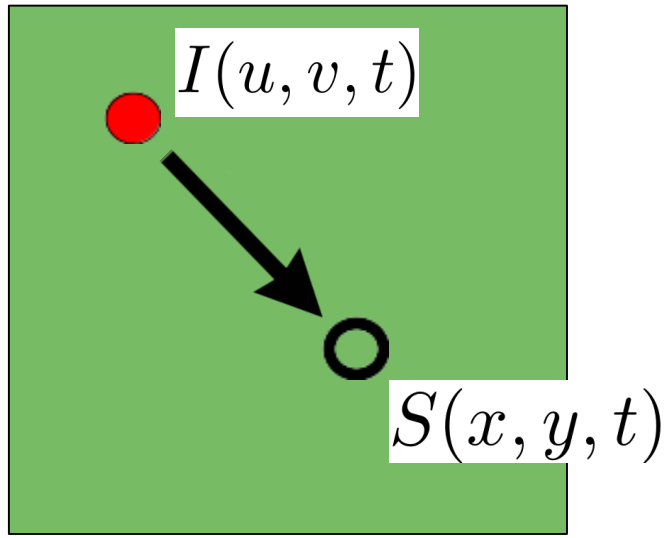
SIR model, now with space

$$\frac{\partial S(x,y,t)}{\partial t} = -\beta\lambda(x,y)S(x,y,t)$$

$$\frac{\partial I(x,y,t)}{\partial t} = \beta\lambda(x,y)S(x,y,t) - \mu I(x,y,t)$$

Mikaberidze, Mundt, & Bonhoeffer,
Ecological Applications 2016

Spatially explicit transmission



$$\frac{\partial S(x,y,t)}{\partial t} = -\beta\ \lambda(x,y)\ S(x,y,t)$$

$$\frac{\partial I(x,y,t)}{\partial t} = \beta\ \lambda(x,y)\ S(x,y,t) - \mu I(x,y,t)$$

force of infection

$= \kappa(r)$ dispersal kernel

$$\lambda(x,y) = \int_0^{d_x} du \int_0^{d_y} dv\ \kappa(x,y,u,v)\ I(u,v,t).$$

Mikaberidze, Mundt, & Bonhoeffer,
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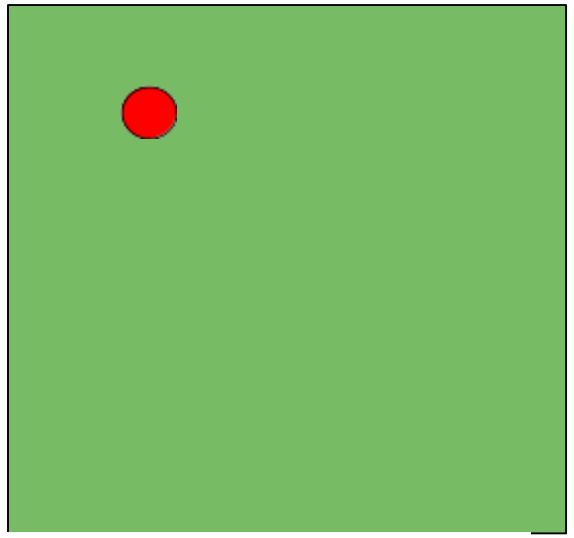
How to calculate R_0 : linear stability of disease-free equilibrium



$$I(x, y, t) = 0$$

$$\frac{\partial I(x, y, t)}{\partial t} = \beta \int_0^{d_x} du \int_0^{d_y} dv\, \kappa(x, y, u, v) I(u, v, t) \cancel{S(x, y, t)}\, K - \mu I(x, y, t)$$

Mikaberidze, Mundt, & Bonhoeffer,
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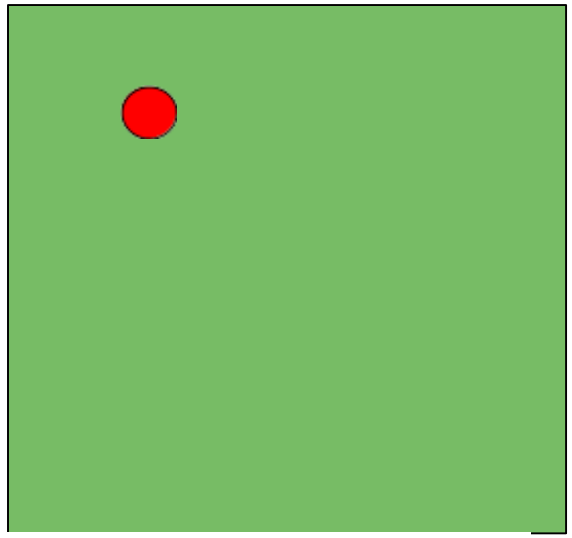
How to calculate R_0 : linear stability of disease-free equilibrium



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↓

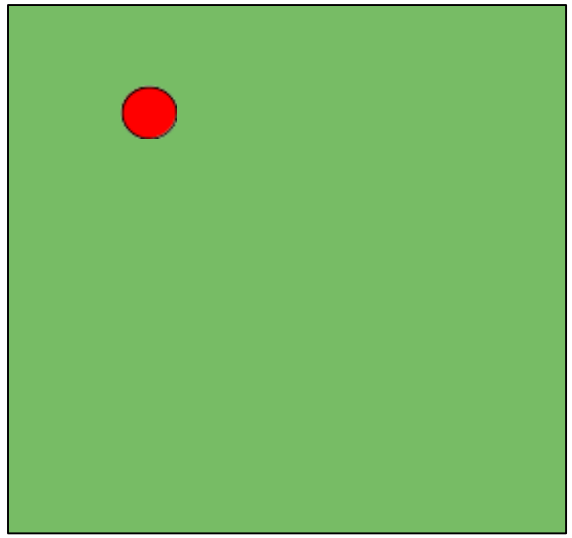
solve the eigenvalue problem

↓

R_0

Mikaberidze, Mundt, & Bonhoeffer, *Ecological Applications* 2016

How to calculate R_0 : linear stability of disease-free equilibrium



$$I(x, y, t) = 0$$

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$$I(x,\, y,\, t) = w(x,\, y) e^{\lambda t} \quad \rightarrow \quad \frac{\beta K}{\mu} \int_0^{d_x} du \int_0^{d_y} dv\, \kappa(r) w(u,v) = \sigma w(x,y)$$

$$\sigma = 1 + \lambda/\mu$$

$$R_0$$

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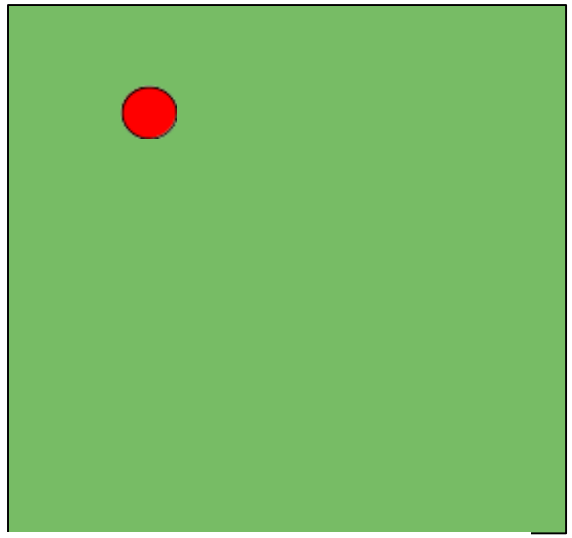
How to calculate R_0 : linear stability of disease-free equilibrium



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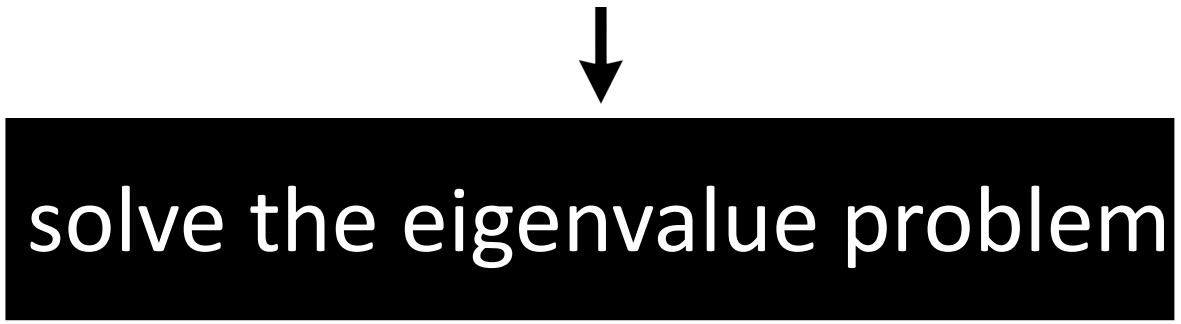

R_0

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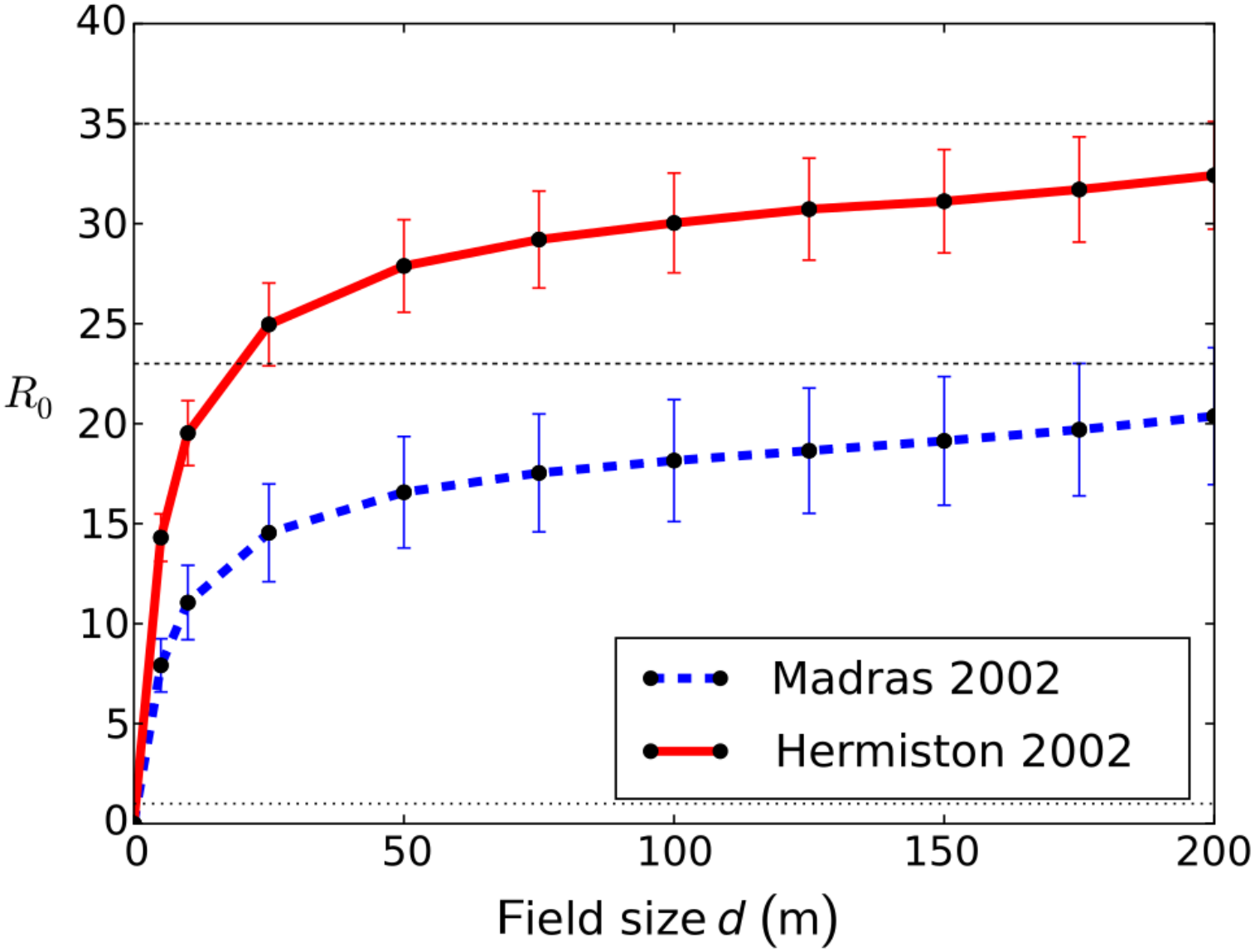
Smaller, more elongated wheat fields suppress the invasiveness of the pathogen (R_0) *Puccinia striiformis*



Mikaberidze, Mundt, & Bonhoeffer, *Ecological Applications* 2016

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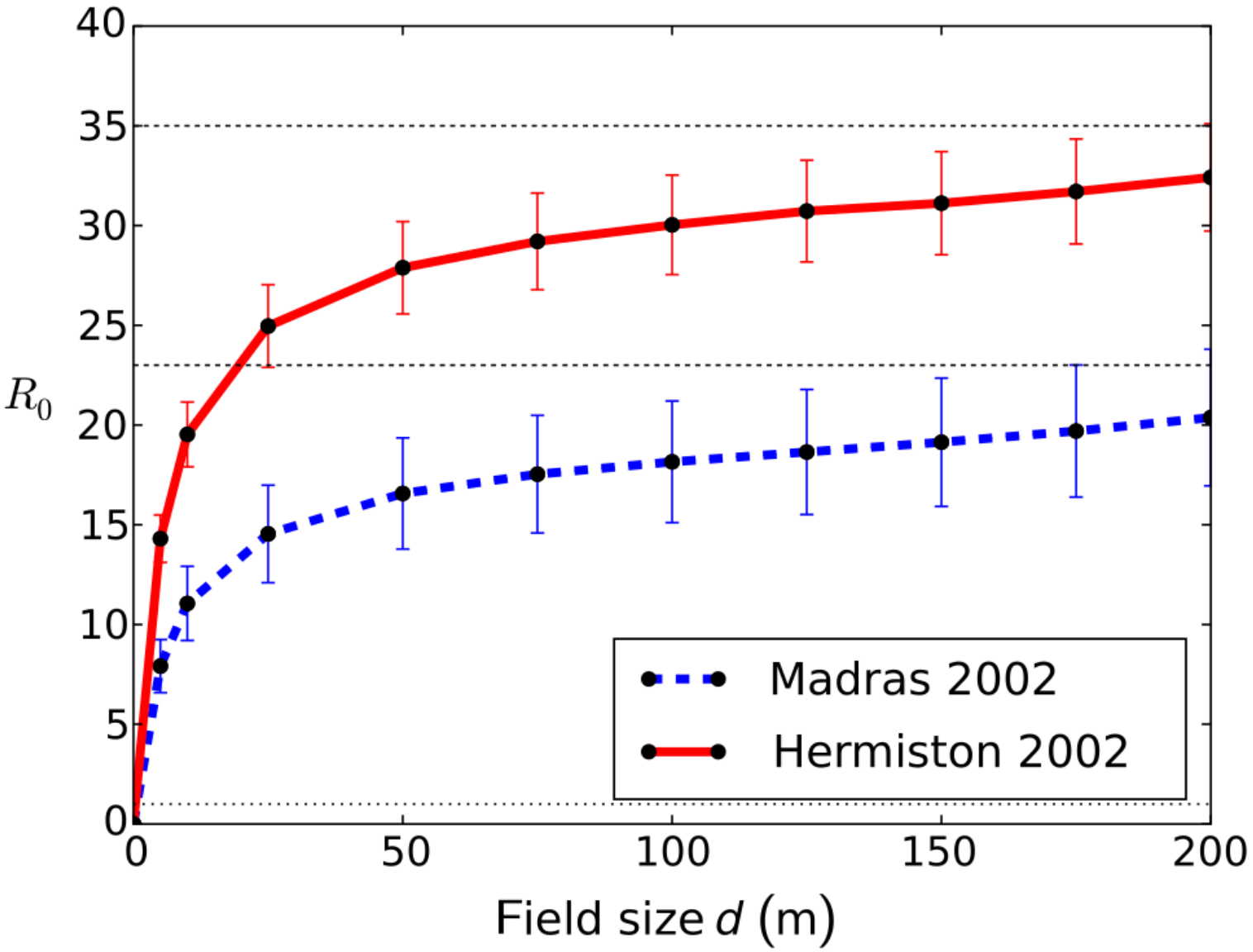

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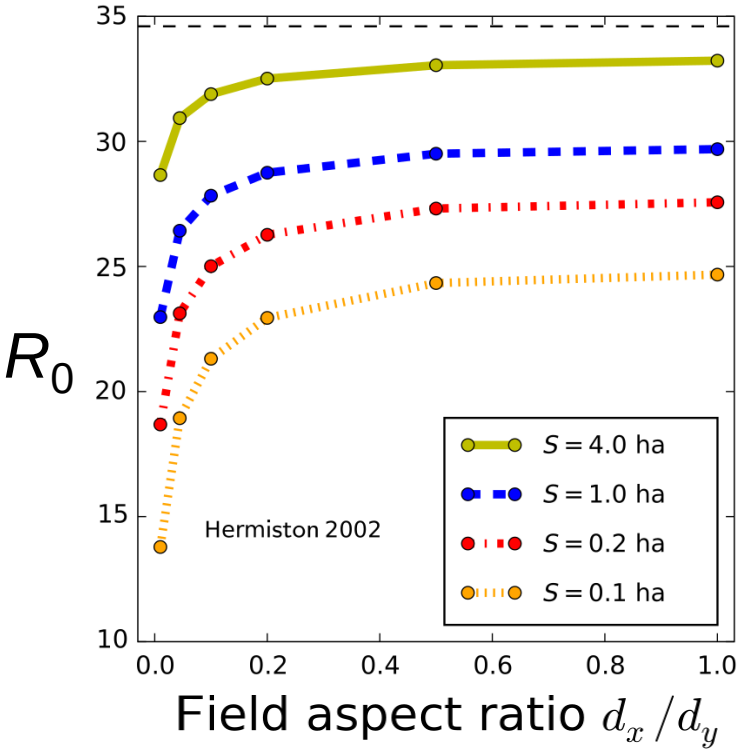
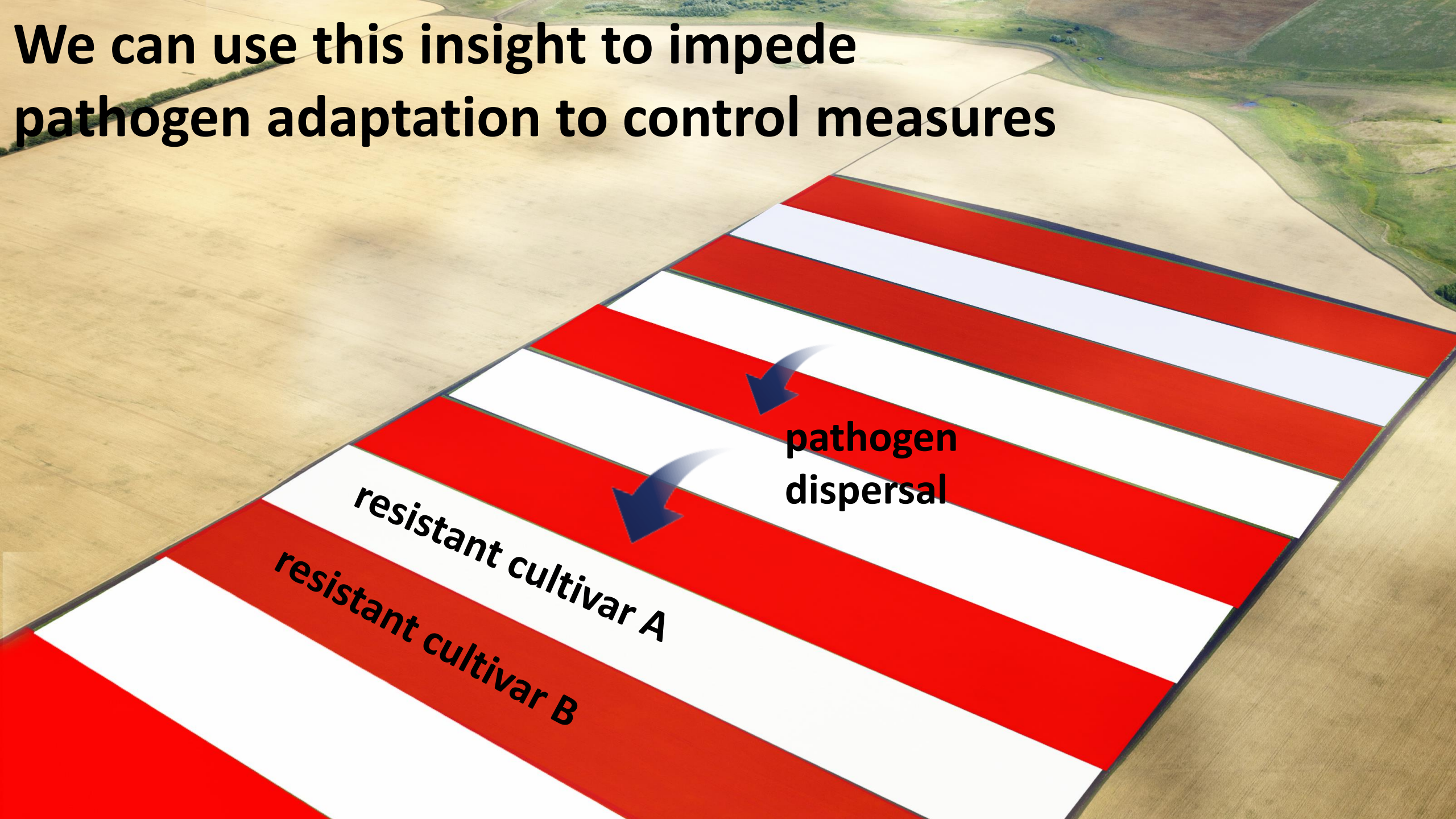


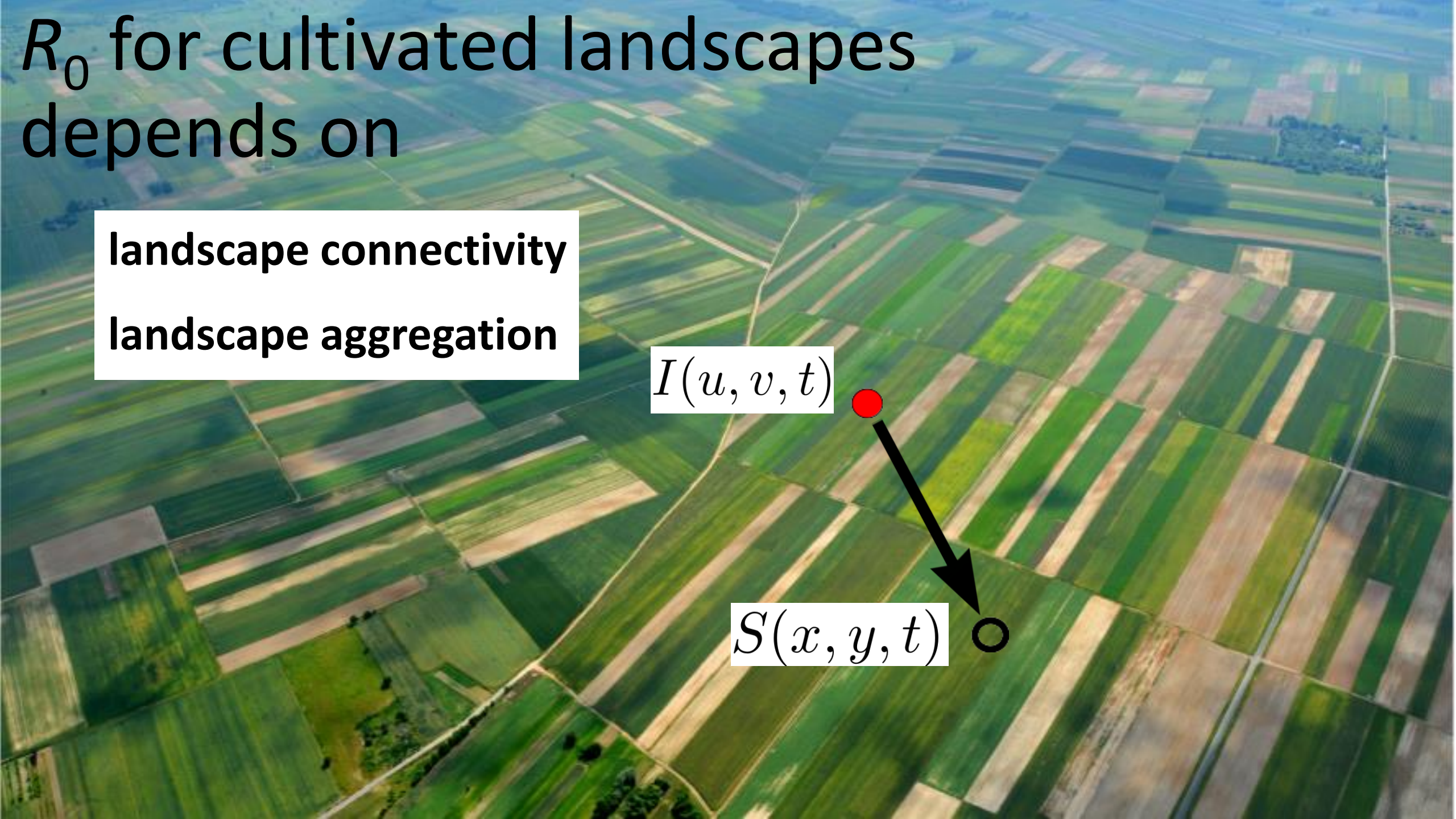
We can use this insight to impede pathogen adaptation to control measures



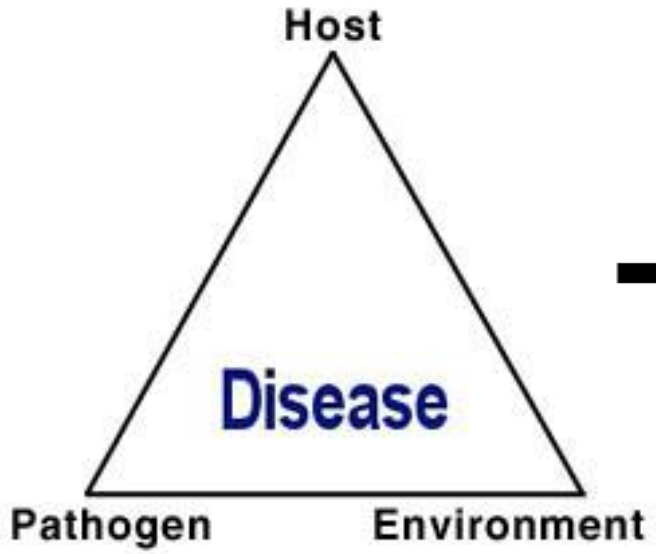
R_0 for cultivated landscapes depends on

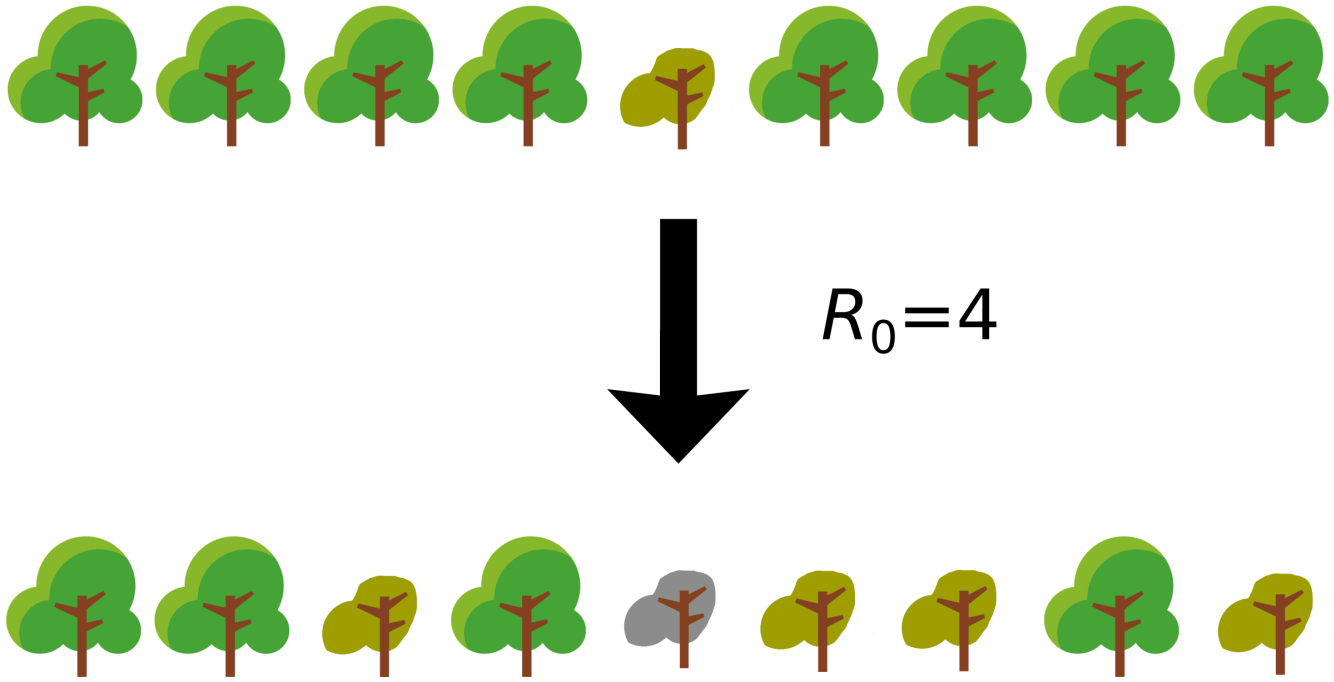
landscape connectivity

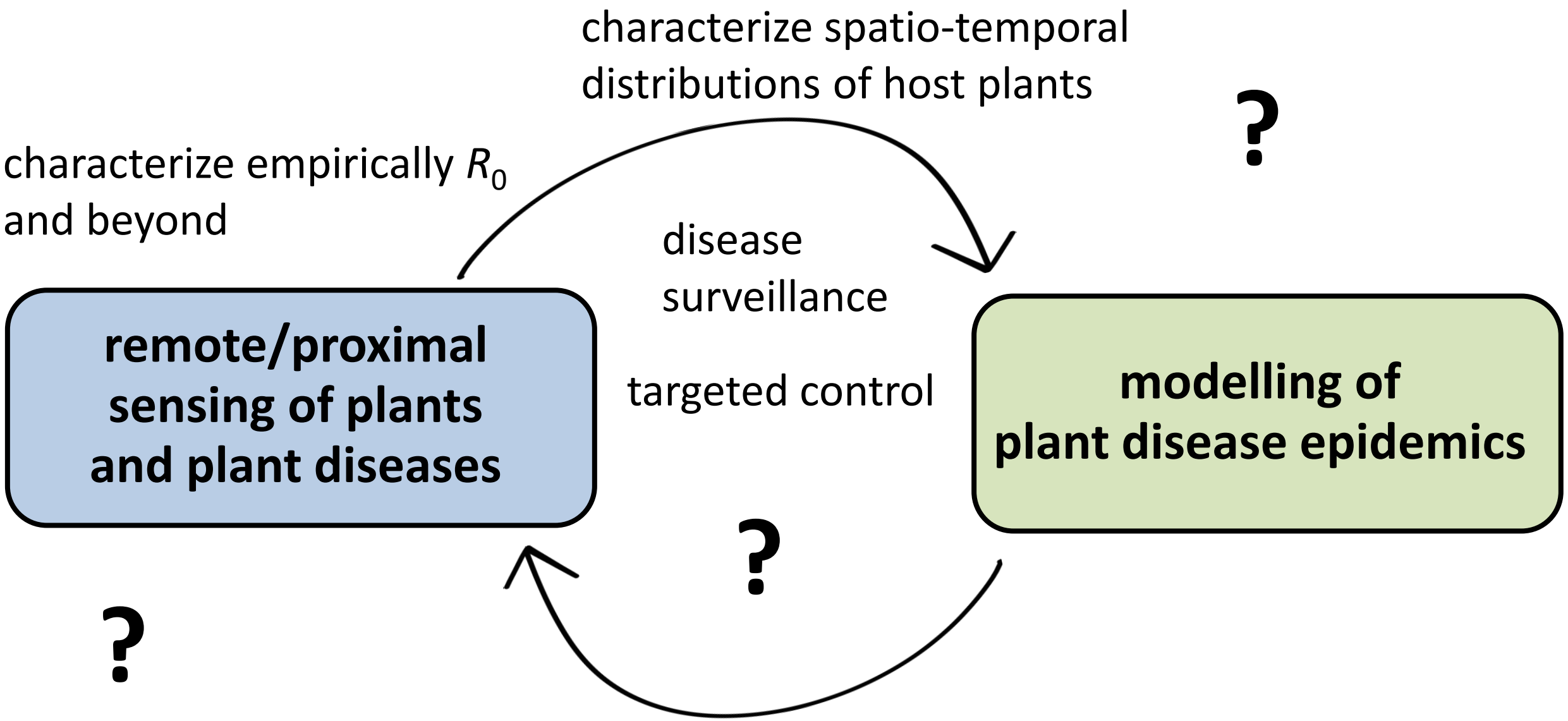
landscape aggregation



Basic reproduction number R_0 depends on disease triangle






characterize spatio-temporal distributions of host plants
?
characterize empirically R_0 and beyond
disease surveillance
targeted control
remote/proximal sensing of plants and plant diseases
modelling of plant disease epidemics
?
?
modelling to guide sensing data collection
reverse modelling for early measurement of diseases