Evolutionary escape and evolutionary suicide in host-pathogen evolution

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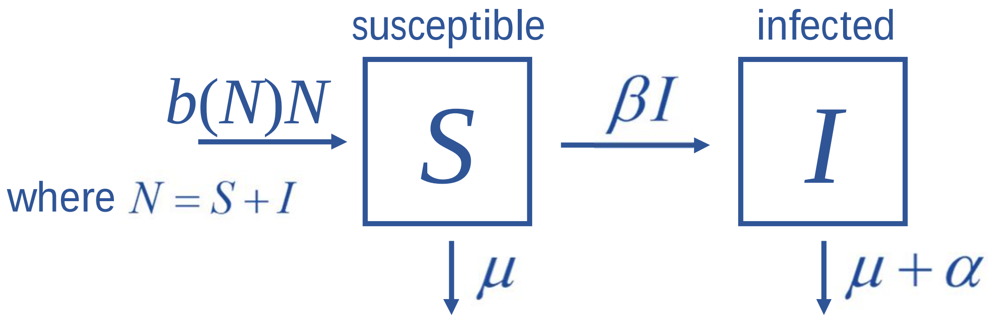
Population Dynamics, Ecology and Evolution (MPDEE21) CIRM online, 26-30 April 2021

SI-model



$$\dot{S} = b(N)N - \mu S - \beta SI$$

$$\dot{I} = [\beta S - (\mu + \alpha)] I$$

assuming that b is monotonically decreasing,

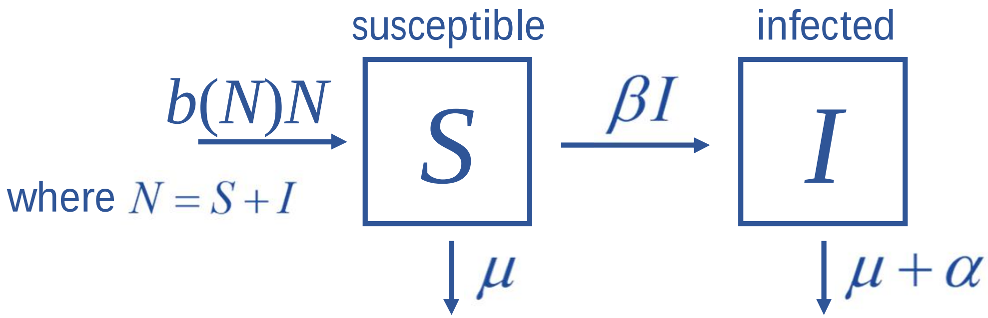
unique asymptotically stable interior equilibrium

when the pathogen is viable, $R_0 = \frac{\beta}{\mu + \alpha} N_0 > 1$

$b(N_0) = \mu$

Can the pathogen evolve to its own extinction?

SI-model

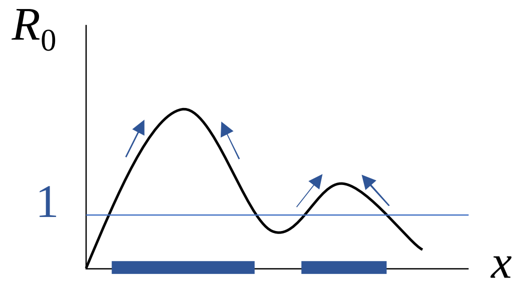


$$\dot{S} = b(N)N - \mu S - \beta(\alpha)SI$$

$$\dot{I} = [\beta(\alpha)S - (\mu + \alpha)]I$$

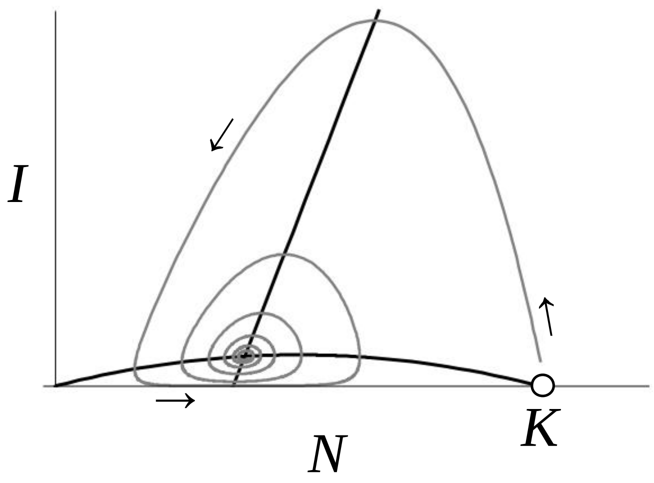
transmission – virulence trade-off

$R_0 = \frac{\beta(\alpha)}{\mu + \alpha} N_0$ is maximized



Can an epidemic drive the host extinct?

SI model, mass action,
logistic host



Decreasing host population

$\not\rightarrow$ few contacts per infected

$\rightarrow$ the epidemic (nearly) dies out

$\not\rightarrow$ the host population recovers

$\rightarrow$ the epidemic recovers

frequency-dependent transmission

Allee effect

Frequency-dependent transmission

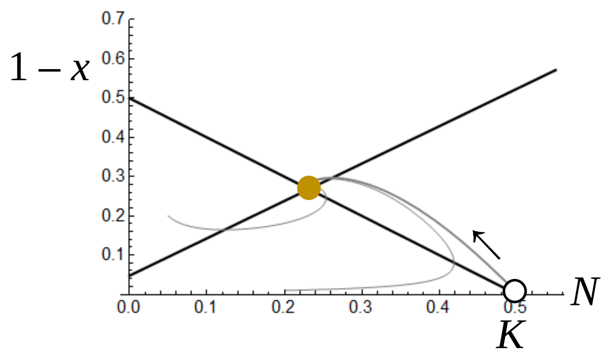
$$\dot{N} = b(N)N - \mu N - \alpha I$$

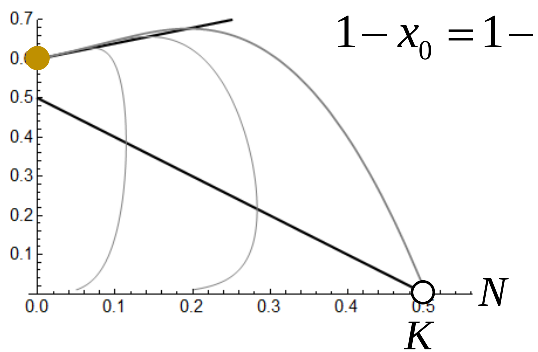
$$\dot{I} = \left[\beta \underbrace{\left(\frac{N-I}{N} \right)}_{O(1)} - (\mu + \alpha) \right] I$$

$1 - x = I / N$ freq of infecteds

$$\dot{N} = \left[b(N) - \mu - \alpha(1-x) \right] N$$

$$\dot{x} = (1-x)\left[b(N) - (\beta - \alpha)x \right]$$





$$1 - x_0 = 1 - \frac{b(0)}{\beta - \alpha}$$

increasing β: transcritical bifurcation

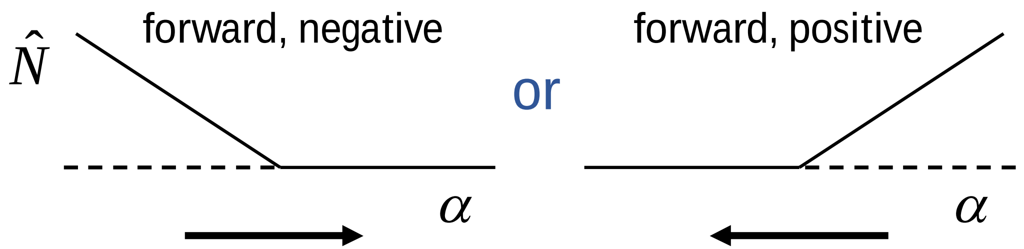
β evolves higher: evolutionary suicide (Boots & Sasaki 2003)

Frequency-dependent transmission

transmission-virulence trade-off $\beta(\alpha)$: $\frac{\partial R_0}{\partial \alpha} > 0 \Leftrightarrow \frac{\partial}{\partial \alpha} \frac{\beta(\alpha)}{\mu + \alpha} > 0 \Leftrightarrow \beta'(\alpha) > \frac{\beta}{\alpha + \mu}$

Inverse approach:

- choose $b(N)$ and $\beta(\alpha)$ to get a transcritical bifurcation



- choose $\beta(\alpha)$ to get evolution towards higher / lower α

Frequency-dependent transmission

$$\dot{N} = [b(N) - \mu - (1-x)\alpha]N$$
$$\dot{x} = (1-x)[b(N) - (\beta(\alpha) - \alpha)x]$$

① pick α_0 and $\beta_0 = \beta(\alpha_0)$ with $\beta_0/(\alpha_0 + \mu) > 1$ (viable pathogen)

② transcritical bifurcation: $b(0) = (\beta_0 - \alpha_0)(\alpha_0 + \mu)/\beta_0$

forward whenever $b'(0) < 0$ → choose the function b

③ the boundary is negative if $\beta'(\alpha_0) > \frac{\beta_0}{\alpha_0 + \mu}\left[1 - \underbrace{\frac{\beta_0 - (\mu + \alpha_0)}{\alpha_0}}_{\text{pos. if viable}}\right]$

⇑

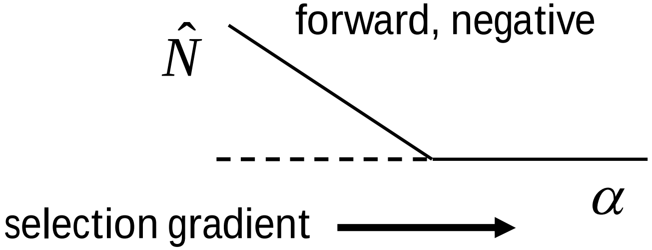
④ the selection gradient is positive if $\beta'(\alpha_0) > \frac{\beta_0}{\alpha_0 + \mu}$

Frequency-dependent transmission

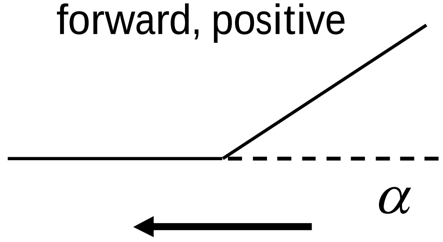
→ choose the function β such that $\beta(\alpha_0) = \beta_0$ and

$$\beta'(\alpha_0) > \frac{\beta_0}{\alpha_0 + \mu} \qquad\qquad \beta'(\alpha_0) < \frac{\beta_0}{\alpha_0 + \mu}\left[1 - \frac{\beta_0 - (\mu + \alpha_0)}{\alpha_0}\right]$$

forward, negative



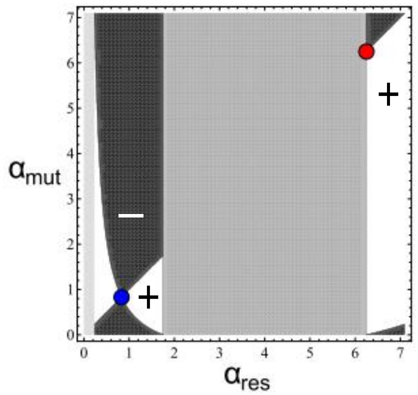
forward, positive

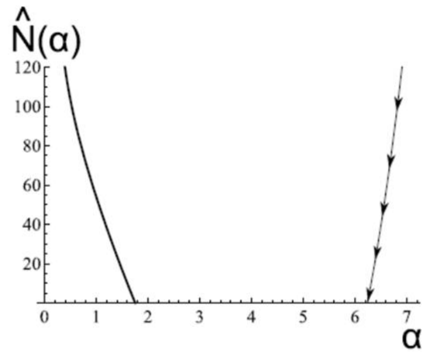


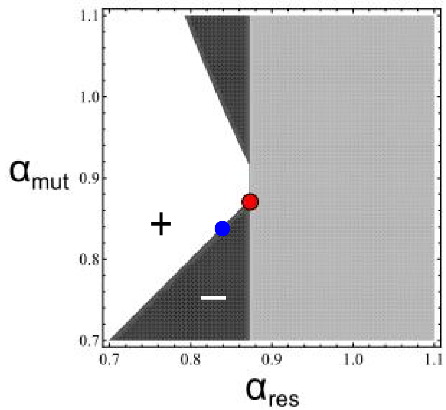
steeply increasing trade-off,
the pathogen evolves more aggressive

e.g. no trade-off,
the pathogen evolves more benign and yet kills the host

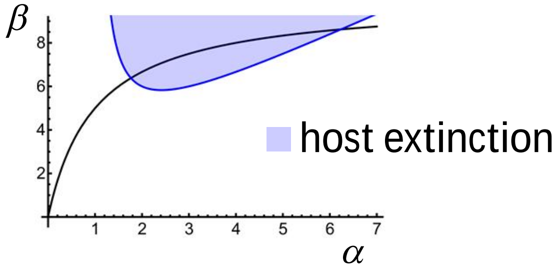
Frequency-dependent transmission







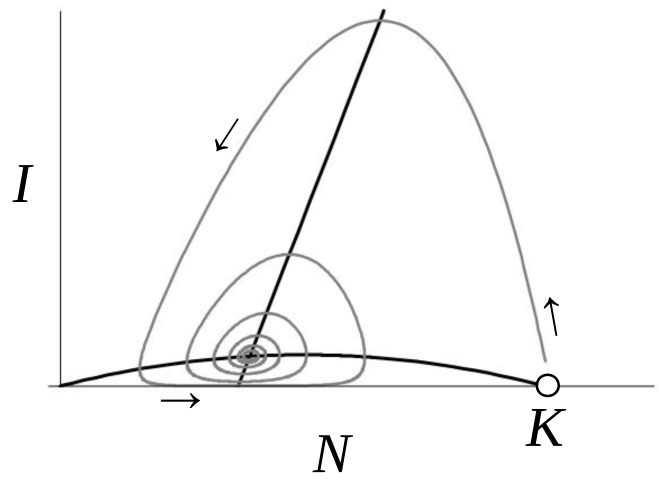
increasing μ



generalized model, Boldin & Kisdi (2016) JMB

Can an epidemic drive the host extinct?

SI model, mass action,
logistic host



Decreasing host population

↛ few contacts per infected

→ the epidemic (nearly) dies out

↛ the host population recovers

→ the epidemic recovers

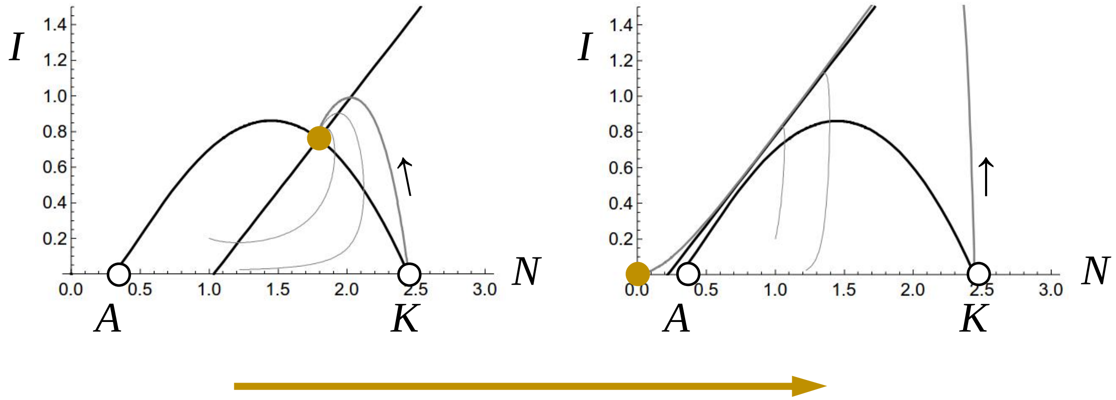
frequency-dependent transmission

Allee effect

Allee effect

$$\dot{N} = b(N)N - \mu N - \alpha I$$
$$\dot{I} = \left[\beta(N - I) - (\mu + \alpha)\right]I$$

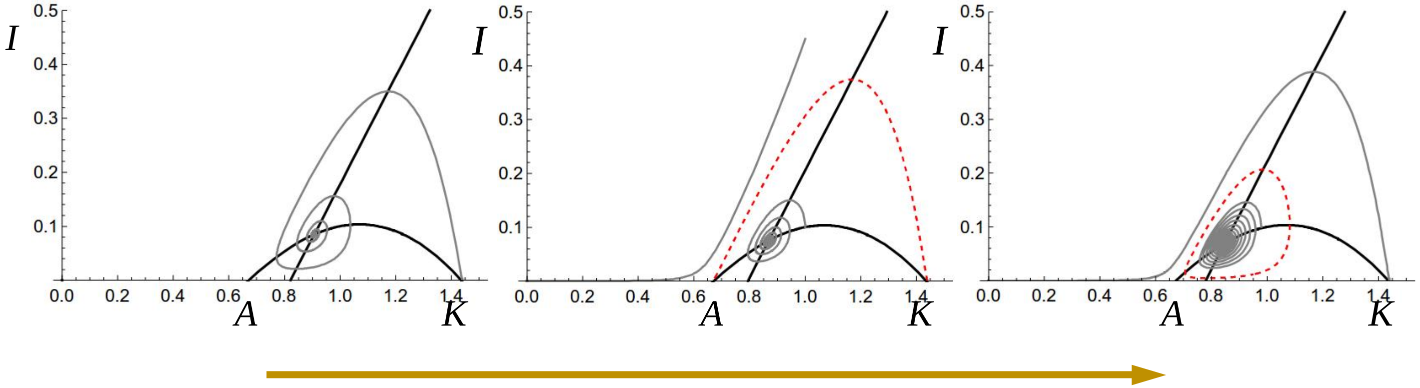
$$b(N) = \frac{b_0 N}{1 + cN}\left(1 - \frac{N}{M}\right)$$



increasing β: saddle-node bifurcation,
both host and pathogen go extinct

evolutionary suicide of the pathogen (cf Gandon & Day 2009)

Allee effect v2



increasing β: heteroclinic cycle $\longrightarrow$ unstable limit cycle
$\longrightarrow$ subcritical Hopf bifurcation destabilizes the equilibrium
(Thieme et al. 2009)

evolutionary suicide at the Hopf bifurcation

Evolution to host extinction through SN

$$\dot{N} = B(N) - \mu N - \alpha I$$
$$\dot{I} = \left[\beta(N - I) - (\mu + \alpha)\right] I$$

① pick α_0, β_0 and N_0 such that $\beta_0 N_0 > 2\,\alpha_0 + \mu$ (*)

② choose the function B to get a saddle-node bifurcation:

$B(N_0) = (N_0 - \alpha_0 / \beta_0)(\alpha_0 + \mu)$ for equilibrium

$B'(N_0) = \alpha_0 + \mu$ for $\mathrm{Det(J)} = 0$; $\mathrm{Tr(J)} < 0$ by (*)

$B''(N_0) < 0$ for extinction rather than blow-up

Evolution to host extinction through SN

③ the boundary is negative (the equilibria exist for $\alpha < \alpha_0$)

whenever $\beta'(\alpha_0) \geq 0$

④ the selection gradient is positive if $\dfrac{\partial R_0}{\partial \alpha} > 0 \iff \beta'(\alpha_0) > \dfrac{\beta_0}{\alpha_0 + \mu}$

→ choose $\beta(\alpha_0) = \beta_0$ and $\beta'(\alpha_0) > \beta_0/(\alpha_0 + \mu)$

for evolutionary suicide via increasing virulence

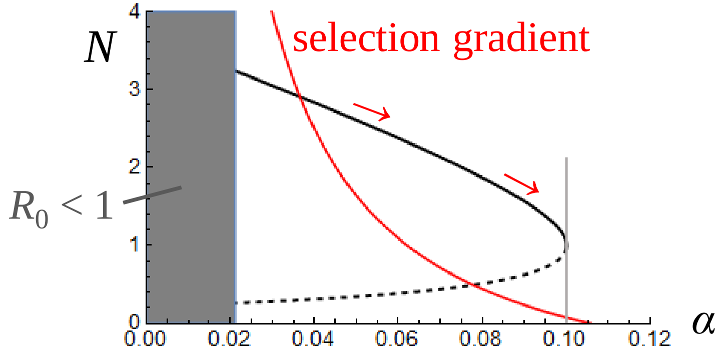
(suicide via decreasing virulence only if β decreases with α)

Evolution to host extinction through SN

Example: $B(N) = \frac{b_1 N}{1+b_2 N}(1-b_3 N)N, \quad \beta(\alpha) = \frac{c_1 \alpha}{1+c_2 \alpha}$

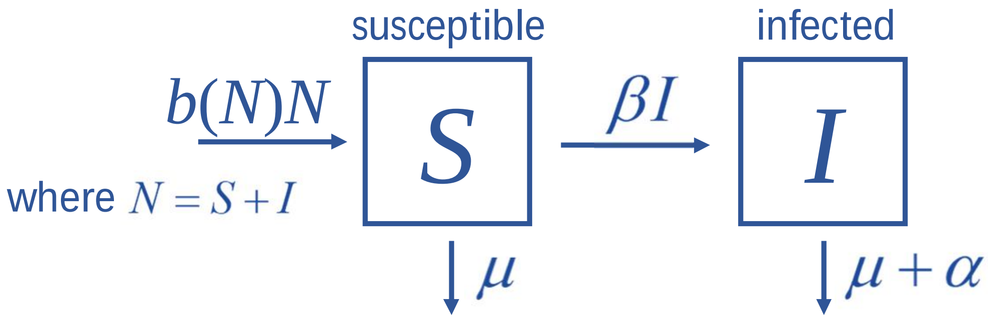
pick $\alpha_0 = 0.1$, $\beta_0 = 2$, $N_0 = 1$ and $\mu = 0.2$

solve for the parameters of B and β to satisfy the conditions for evolutionary suicide



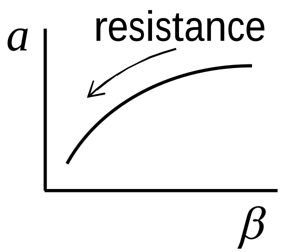
Can the host evolve high enough resistance to drive the pathogen extinct?

SI-model



$$\dot{S} = (a(\beta) - cN)N - \mu S - \beta SI$$

$$\dot{I} = [\beta S - (\mu + \alpha)]I$$



host trait: low β = high resistance

resistance – fecundity trade-off

unique asymptotically stable interior equilibrium

when the pathogen is viable, $R_0 = \dfrac{\beta}{\mu + \alpha} \dfrac{a(\beta) - \mu}{c} > 1$

high resistance (low β) + low fecundity (a): $R_0 < 1$

Can the host evolutionarily escape its pathogen?

$$\dot{S} = (a(\beta) - cN)N - \mu S - \beta SI$$

$$\dot{I} = \left[\beta S - (\mu + \alpha)\right] I$$

$$R_{mut}^{host} = \left[a(\beta_{mut}) - c\hat{N}\right]\left[\frac{1}{\mu + \beta_{mut}\hat{I}} + \frac{\beta_{mut}\hat{I}}{\mu + \beta_{mut}\hat{I}}\frac{1}{\mu + \alpha}\right]$$

$$\lim_{\hat{I} \to 0} \frac{\partial R_{mut}^{host}}{\partial \beta_{mut}}\bigg|_{\beta mut = \beta} = \frac{a'(\beta)}{a(\beta) - c\hat{N}} + 0 > 0$$

β increases, the host cannot escape the pathogen

High resistance of the host → low transmission

~~→~~ the pathogen is almost absent — Allee effect for the pathogen

~~→~~ no benefit from costly resistance — conditional strategy

→ resistance decreases and the pathogen survives

Allee effect for the pathogen

$$\dot{S} = (a(\beta) - cN)N - \mu S - \beta SI + \nu_E E$$

$$\dot{E} = \beta SI - \beta EI - (\mu + \nu_E)E$$

$$\dot{I} = \beta EI - (\mu + \alpha)I$$

exposed: need a second dose of the pathogen to become infectious

$$R_{mut}^{host} = (a(\beta_{mut}) - cN)L_{mut}$$

$$L_{mut} = \frac{1}{\mu + \beta_{mut}\hat{I}} + \frac{\beta_{mut}\hat{I}}{\mu + \beta_{mut}\hat{I}}\left(\frac{1}{\mu + \nu_E + \beta_{mut}\hat{I}} + \frac{\beta_{mut}\hat{I}}{\mu + \nu_E + \beta_{mut}\hat{I}}\frac{1}{\mu + \alpha} + \frac{\nu_E}{\mu + \nu_E + \beta_{mut}\hat{I}}L_{mut}\right)$$

$$\left.\frac{\partial R_{mut}^{host}}{\partial \beta_{mut}}\right|_{\beta mut = \beta} = \underbrace{a'(\beta)L}_{+} + \alpha\hat{I}\underbrace{[\ldots]}_{-}$$

Allee effect for the pathogen

$$\dot{N} = (a(\beta) - cN)N - \mu N - \alpha I$$

$$\dot{E} = \beta(N - E - I)I - \beta EI - (\mu + \nu_E)E$$

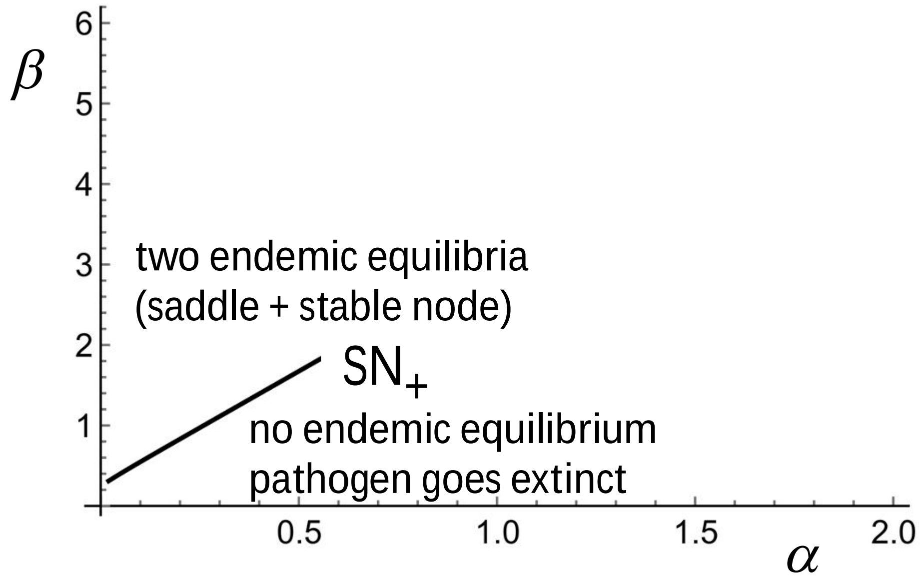
$$\dot{I} = \beta EI - (\mu + \alpha)I$$

Special case $\alpha = 0$: $\hat{N} = \frac{a(\beta) - \mu}{c}$, $\hat{E} = \frac{\mu + \alpha}{\beta}$, $\hat{I}_{1,2} = \frac{(\hat{N} - 2\hat{E}) \pm \sqrt{(\hat{N} - 2\hat{E})^2 - 4(\mu + \nu_E)\hat{E}/\beta}}{2}$

right-opening saddle-node bifurcation at $\beta = \frac{2}{\hat{N}}(\mu + \sqrt{\mu(\mu + \nu_E})$

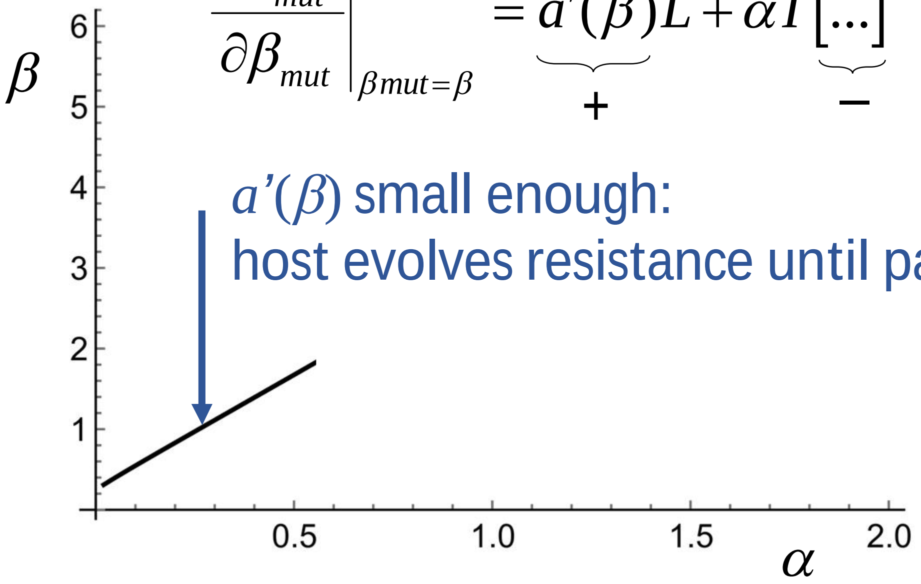
the pathogen goes extinct if the host evolves lower β – alas, not with $\alpha = 0$

Allee effect for the pathogen



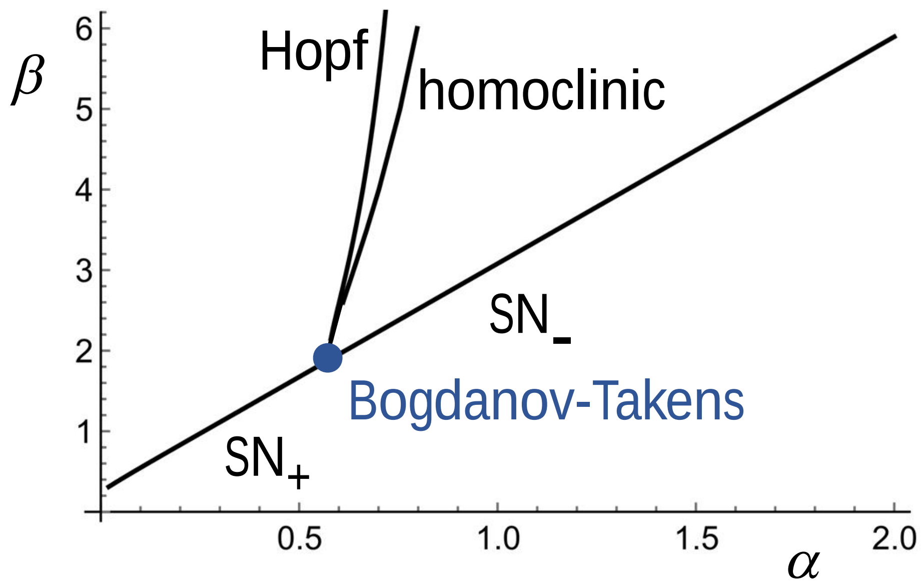
Allee effect for the pathogen

$$\left.\frac{\partial R_{mut}^{host}}{\partial \beta_{mut}}\right|_{\beta mut=\beta} = \underbrace{a'(\beta)L}_{+} + \alpha \hat{I} \underbrace{[\ldots]}_{-}$$



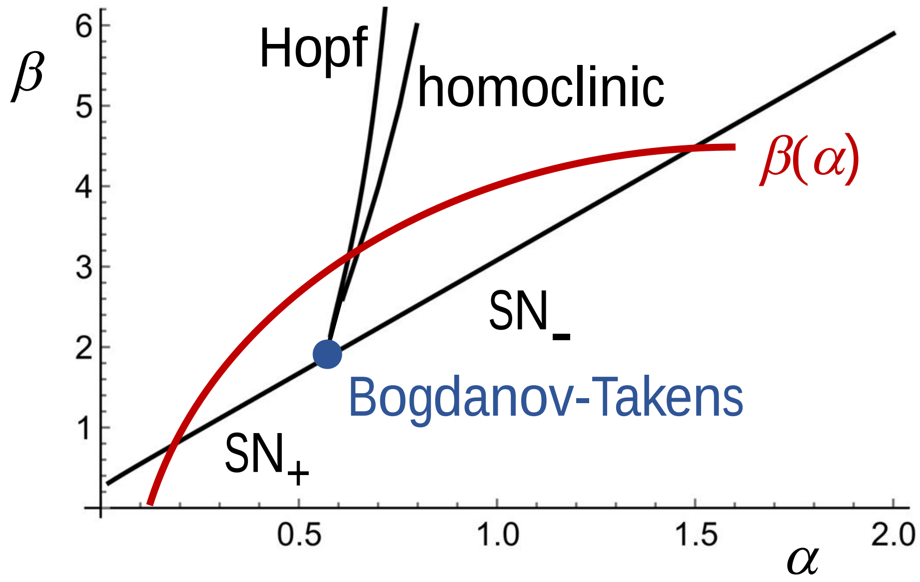
$a'(\beta)$ small enough:
host evolves resistance until pathogen extinct

Allee effect for the pathogen



Allee effect for the pathogen

Pathogen evolution



Allee effect for the pathogen

Pathogen evolution – cartoon models of double infections

1) The first infection only sensitizes the host; the second infection prevails

$$R_{mut} = \frac{\beta(\alpha_{mut})}{\mu + \alpha_{mut}} \hat{E} \qquad \Rightarrow \qquad \frac{\beta(\alpha)}{\mu + \alpha} \text{ maximized}$$

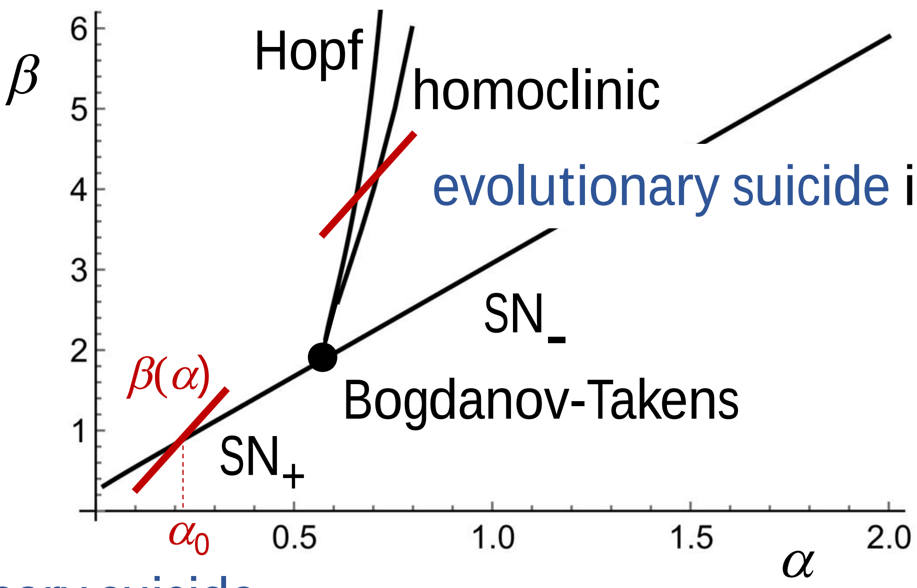
2) The first infection prevails

$$R_{mut} = \frac{\beta(\alpha_{mut})}{\mu + \alpha_{mut}} \hat{S} \cdot \frac{\beta(\alpha)\hat{I}}{\beta(\alpha)\hat{I} + \nu_E + \mu} \qquad \Rightarrow \qquad \frac{\beta(\alpha)}{\mu + \alpha} \text{ maximized}$$

α evolves lower when $\beta'(\alpha) < \dfrac{\beta(\alpha)}{\alpha + \mu}$

Allee effect for the pathogen

Pathogen evolution



evolutionary suicide if $\beta'(\alpha)$ high enough

evolutionary suicide

if slope of the SN line $< \beta'(\alpha_0) < \dfrac{\beta(\alpha_0)}{\alpha_0 + \mu}$

(nonempty interval for all α_0)

Allee effect for the pathogen

Mats Lindström (2020)

$$\dot{S} = (a(\beta) - cN)N - \mu S - \beta SI + \nu_E E$$
$$\dot{E} = (1-k)\beta SI - \beta EI - (\mu + \nu_E)E$$
$$\dot{I} = \beta(kS + E)I - (\mu + \alpha + \nu_I)I$$
$$\dot{R} = \nu_I I - \mu R$$

k = fraction of cases where a single dose makes full infection, $k = 1$ standard SI(R) model

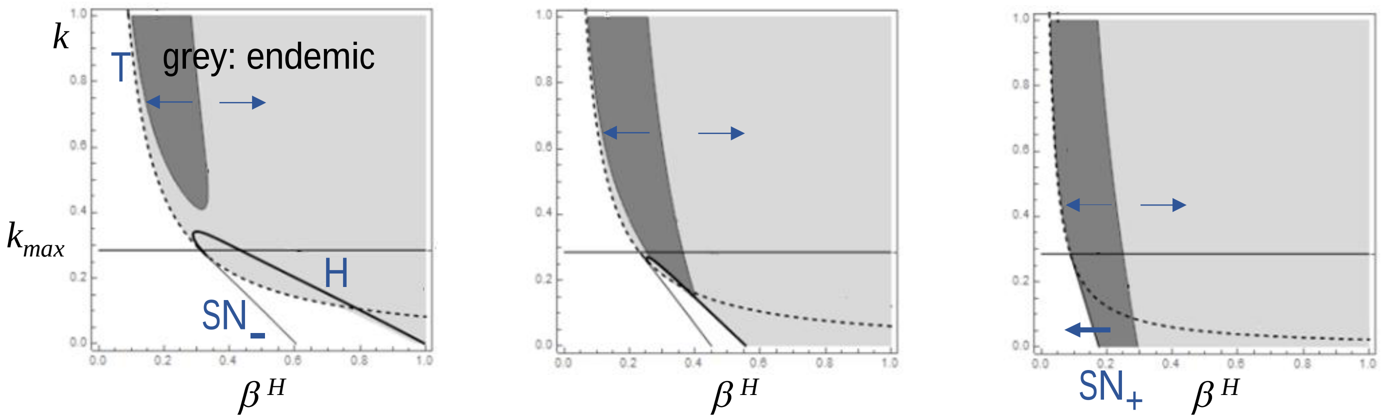
recovered with immunity

Host and pathogen coevolve: $\beta = \beta^H \beta^P$, β^H traded off with a, β^P traded off with α

pathogen maximizes $\dfrac{\beta^P(\alpha)}{\mu + \alpha + \nu_I} \;\Rightarrow\; \alpha,\ \beta^P(\alpha)$ fixed at the optimum

Allee effect for the pathogen

$k > k_{max}$: the transcritical bifurcation is forward, no SN bifurcation in $\mathbf{R}_+^4$



good chance to recover with immunity:
post-disease reproduction significant,
costly resistance does not evolve

no recovery from disease:
costly resistance evolves and
the host gets rid of the pathogen

Mats Lindström (2020)

Can the host evolutionarily escape its pathogen?

$$\dot{S} = (a(\beta) - cN)N - \mu S - \beta SI$$

$$\dot{I} = [\beta S - (\mu + \alpha)]I$$

$$R_{mut}^{host} = \left[a(\beta_{mut}) - c\hat{N}\right]\left[\frac{1}{\mu + \beta_{mut}\hat{I}} + \frac{\beta_{mut}\hat{I}}{\mu + \beta_{mut}\hat{I}}\frac{1}{\mu + \alpha}\right]$$

$$\lim_{\hat{I}\to 0} \frac{\partial R_{mut}^{host}}{\partial \beta_{mut}}\bigg|_{\beta mut=\beta} = \frac{a'(\beta)}{a(\beta) - c\hat{N}} + 0 > 0$$

β increases, the host cannot escape the pathogen

High resistance of the host $\longrightarrow$ low transmission

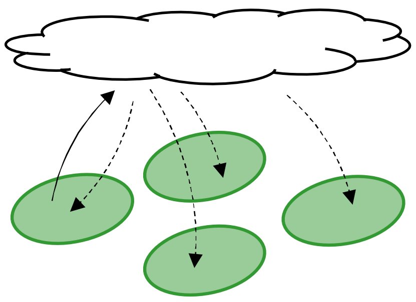
~~→~~ the pathogen is almost absent — Allee effect for the pathogen

~~→~~ no benefit from costly resistance — conditional strategy

$\longrightarrow$ resistance decreases and the pathogen survives

Disease-dependent dispersal

A large number of microsites each occupied by one parent (S / I)
Offspring of an infected parent is infected with probability *p*



Dispersal with probability
d (healthy) vs δ (infected)

with survival probability
s (healthy) vs σs (infected)

Disease dynamics within site for time T
Competition for the site, healthy at an advantage (biased lottery),
winner is the parent of the next generation

Disease-dependent dispersal

Why disperse?
- Do not compete with your siblings

Why stay at home?
- Dispersal is risky

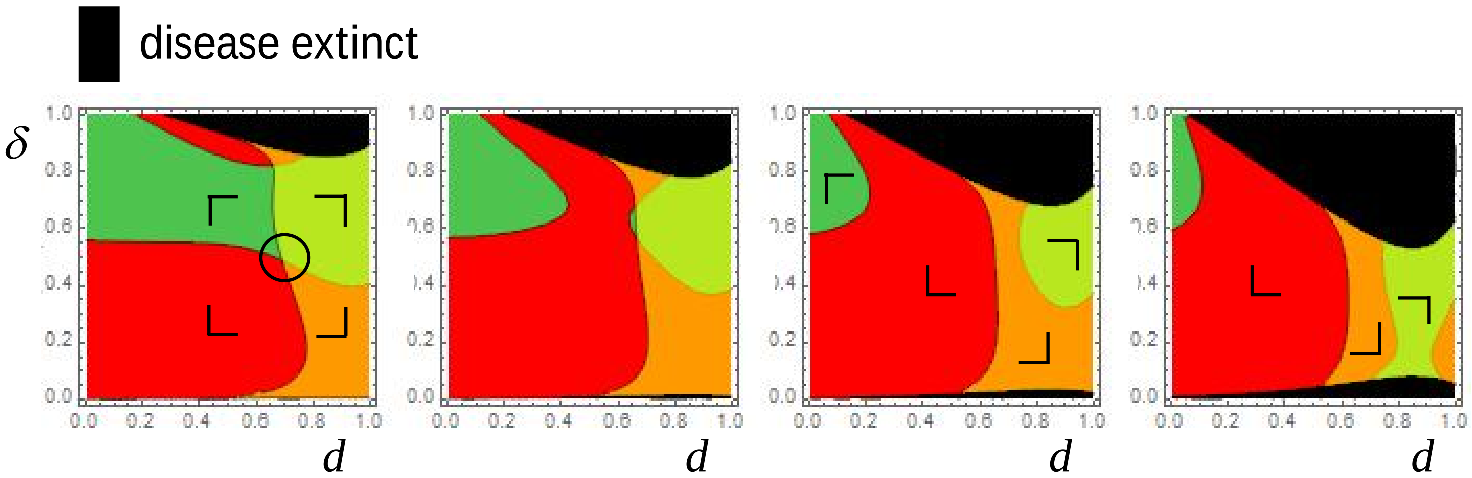
evolutionarily stable dispersal $0.5 < d^* < 1$ (Hamilton & May 1977)

Why disperse if infected?
- Do not infect your siblings

Why disperse if healthy?
- Dispersal is less risky for you

(Janne Sirén MSc thesis)

Disease-dependent dispersal



Host evolution can drive the disease extinct because

- infected disperse much, and die due to dispersal risk
- infected disperse little, the pathogen cannot spread to infect new sites

Summary

- Can the pathogen evolve to its own extinction under optimization (R_0 max)?

  yes, by driving the host extinct:
  1. frequency-dependent transmission: the disease spreads also at low host density
  2. Allee effect in the host dynamics: the host does not recover from the epidemic

  yes, leaving the host extant: Allee effect in the disease dynamics (double infection)
  ! R_0 maximization is not the same as maximizing infected density

- Can the host evolve to drive the pathogen extinct?

  yes, if resistance does not become superfluous near extinction (double infection)
  yes, if the host does not pay the price when there is no disease (conditional strategy)

Direct method: specify the functions (trade-offs, density dependence), hope for the outcome
Inverse method: choose the functions to make it happen