Modeling Host-Parasite Coevolution: A Limited, Extremely Biased Perspective

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Modeling Host-Parasite Coevolution

Overview

Previous Work

Current Work

Future Work

Modeling Host-Parasite Coevolution: Overview

Need intuitive, evolvable parameters to describe H-P interaction

Evolvable Parasite Parameters

- Antigen Type
- Replication rate
  - Within-Host (Bacteria, fungi, metazoans)
  - Within-Cell (Viruses)
- Target resource
  - Cell type
  - Tissue type

Modeling Host-Parasite Coevolution: Overview

Evolvable Host Parameters

- Behavior

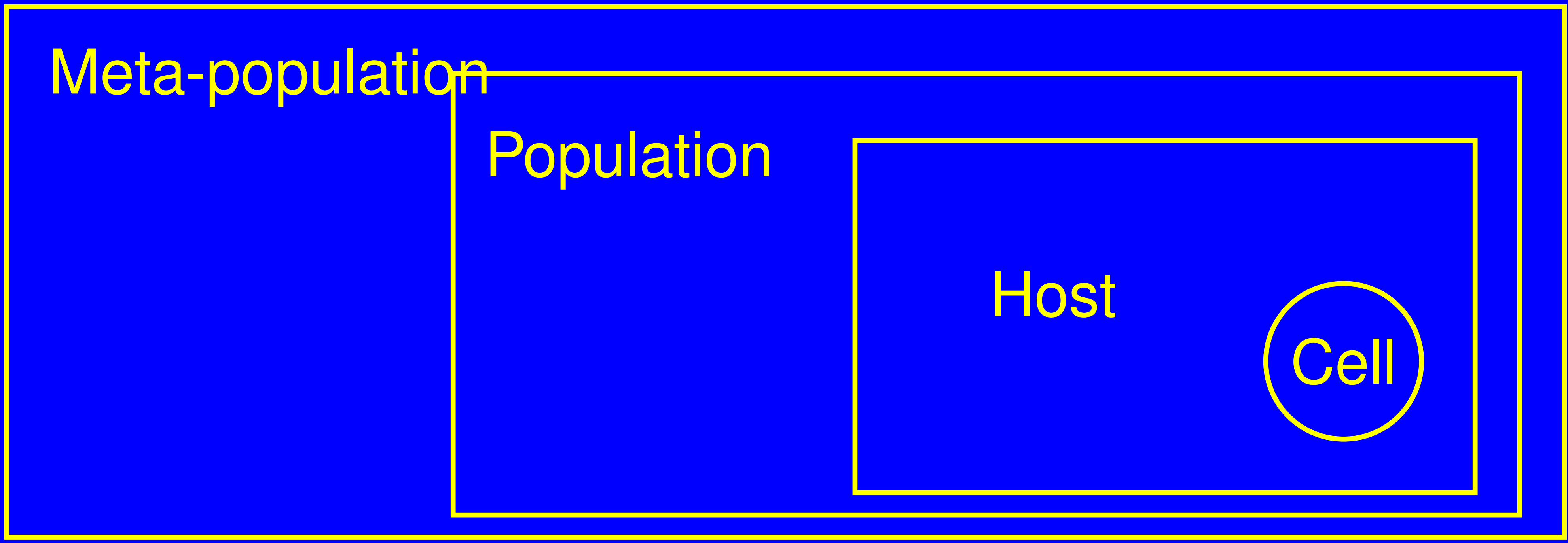
  Can affect mechanism and rate of exposure

- Immune Response
  - Background level (inate immunity, naive CTL density)
  - Sensitivity (ability to detect non-self vs. accidential triggering)
  - Proliferation rate (activation of specific & non-specific IR)

- Sensitivity to resource/target cell loss

Modeling Host-Parasite Coevolution: Overview

Nested Model Approach



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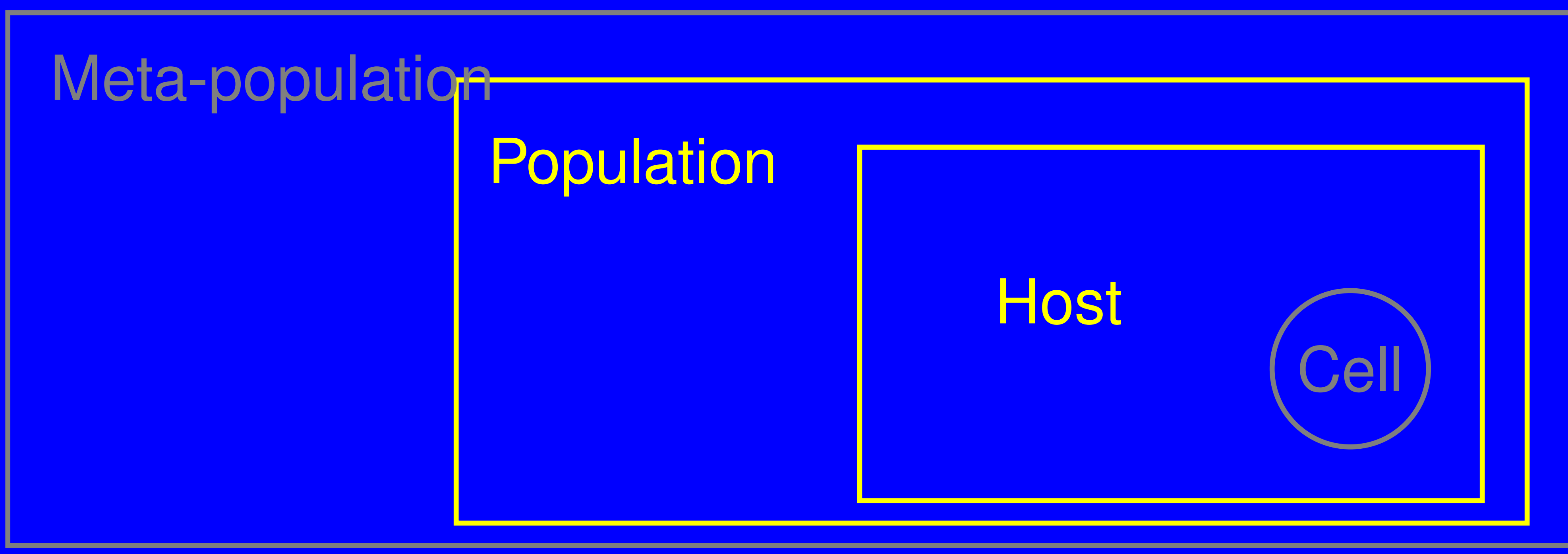

Modeling Host-Parasite Coevolution

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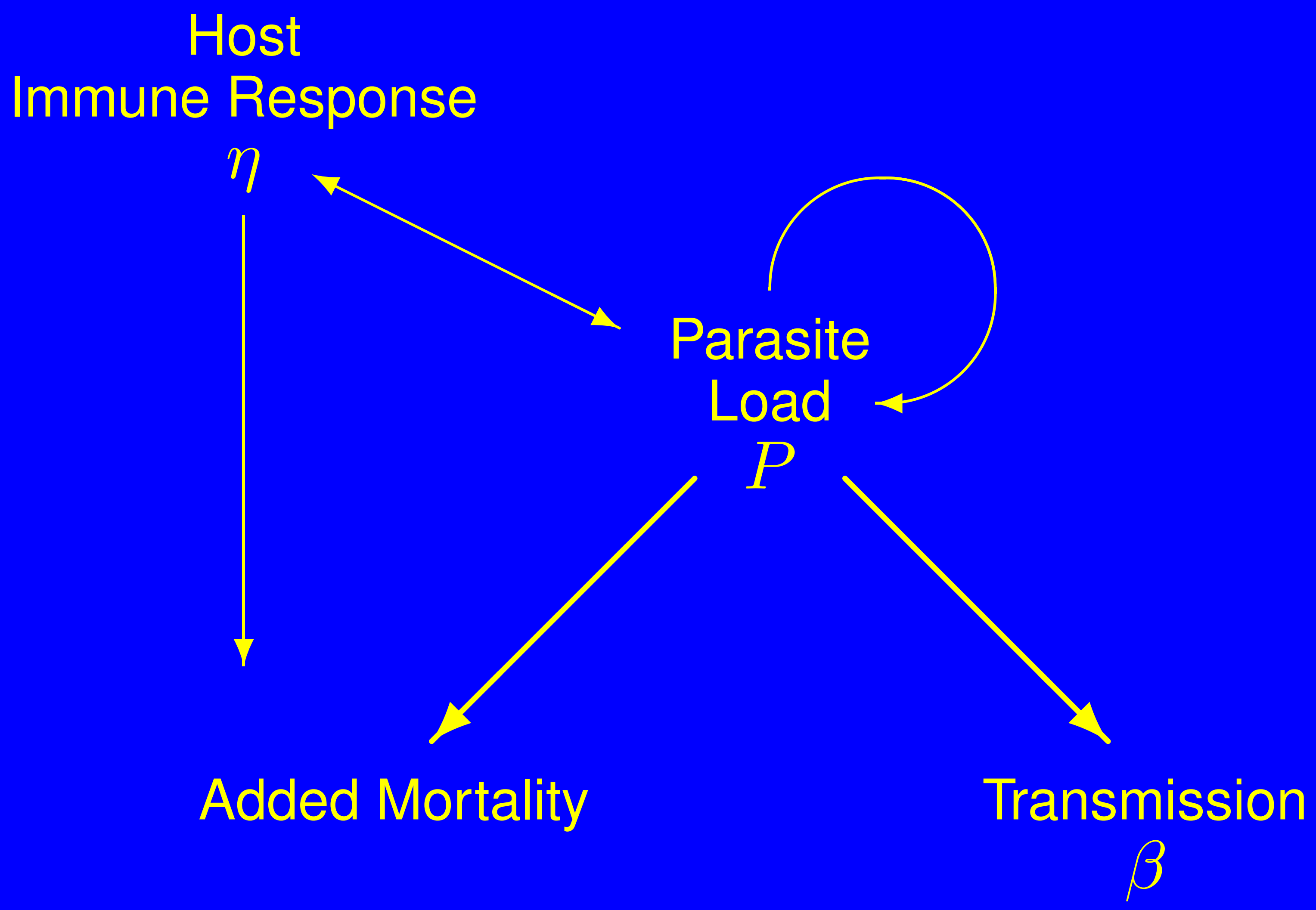
Previous Work: Host-Parasite Coevolution*



*Gilchrist & Sasaki (2002)

Immune response η

$$\frac{d\eta}{dt} = a\eta P$$

$a =$ Activation rate

Parasite Load P

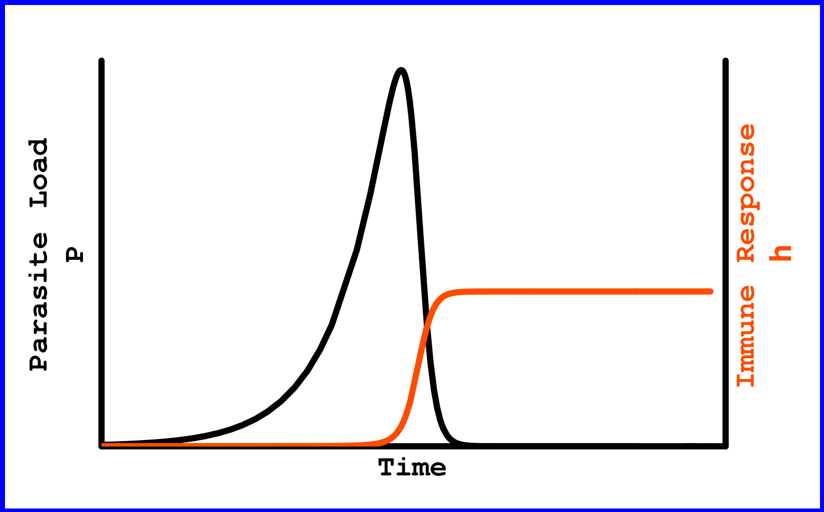
$$\frac{dP}{dt} = (b - \eta)P$$

$b =$ Parasite birth rate

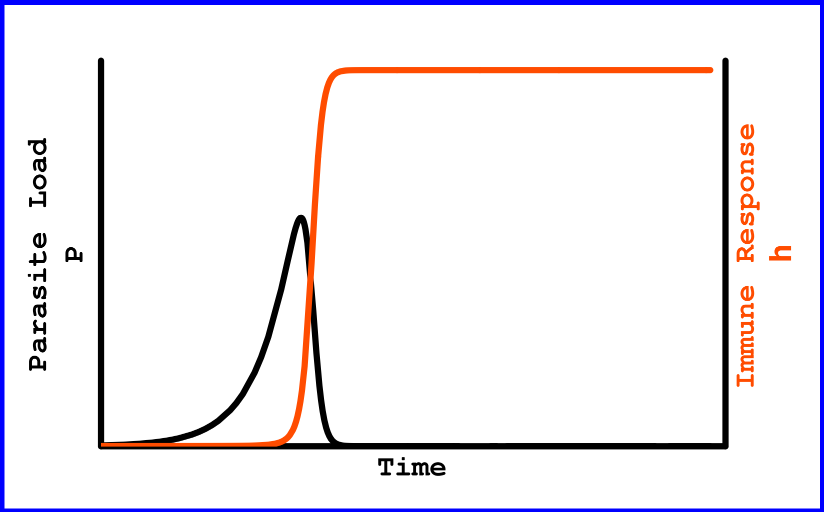
$\eta =$ Host immune response

Within-Host Dynamics

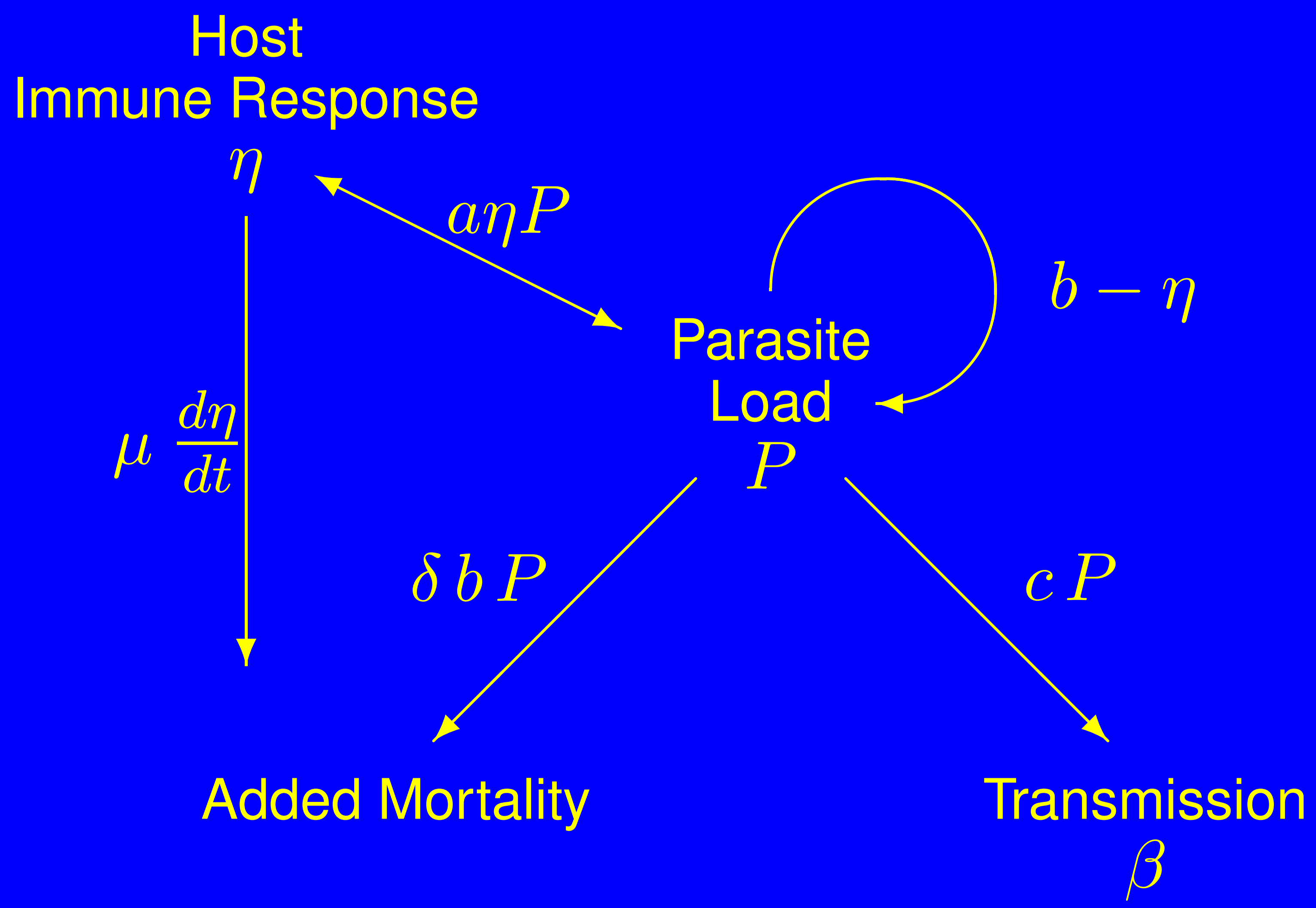
Low Activation/Replication



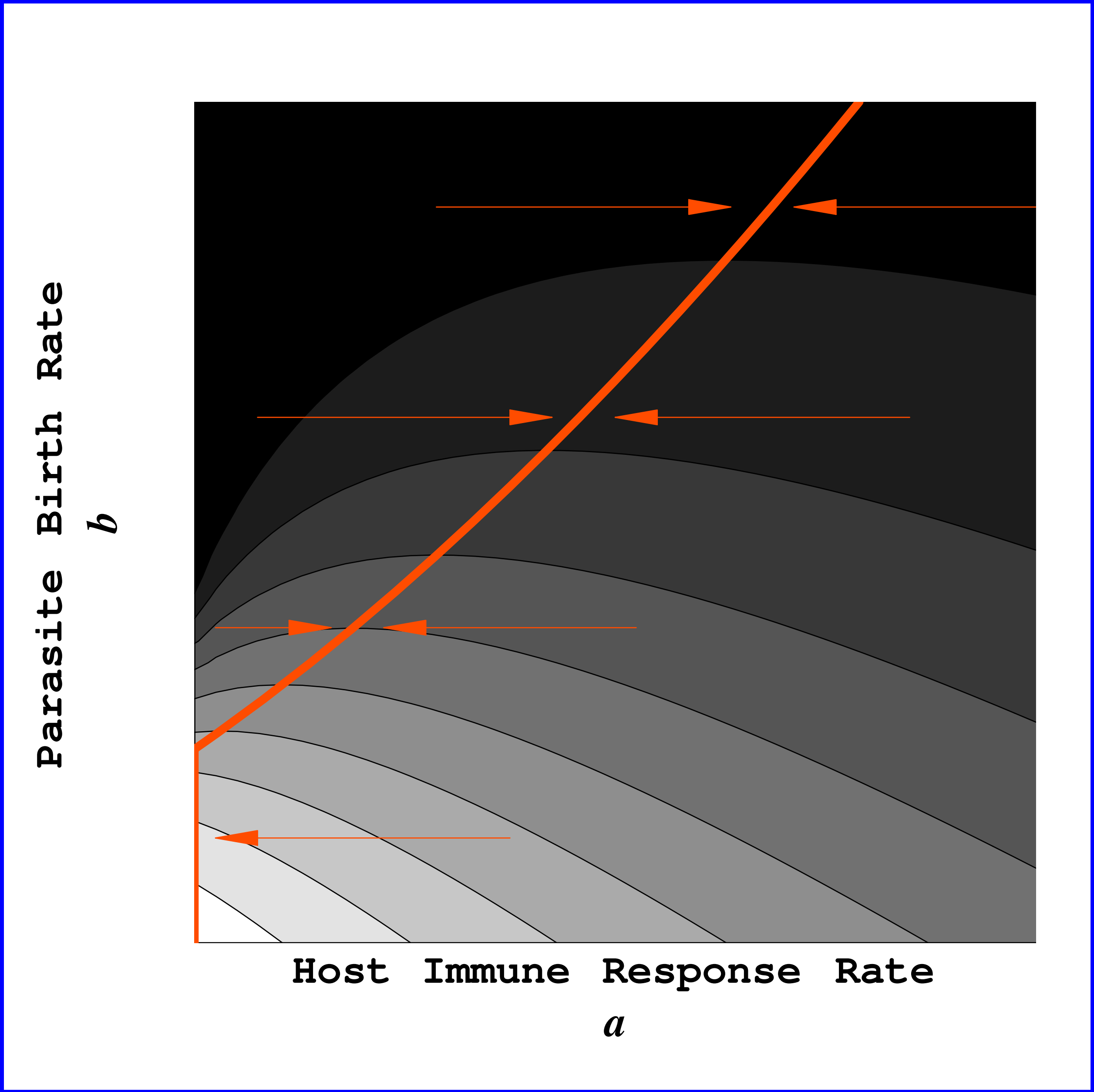
High Activation/Replication



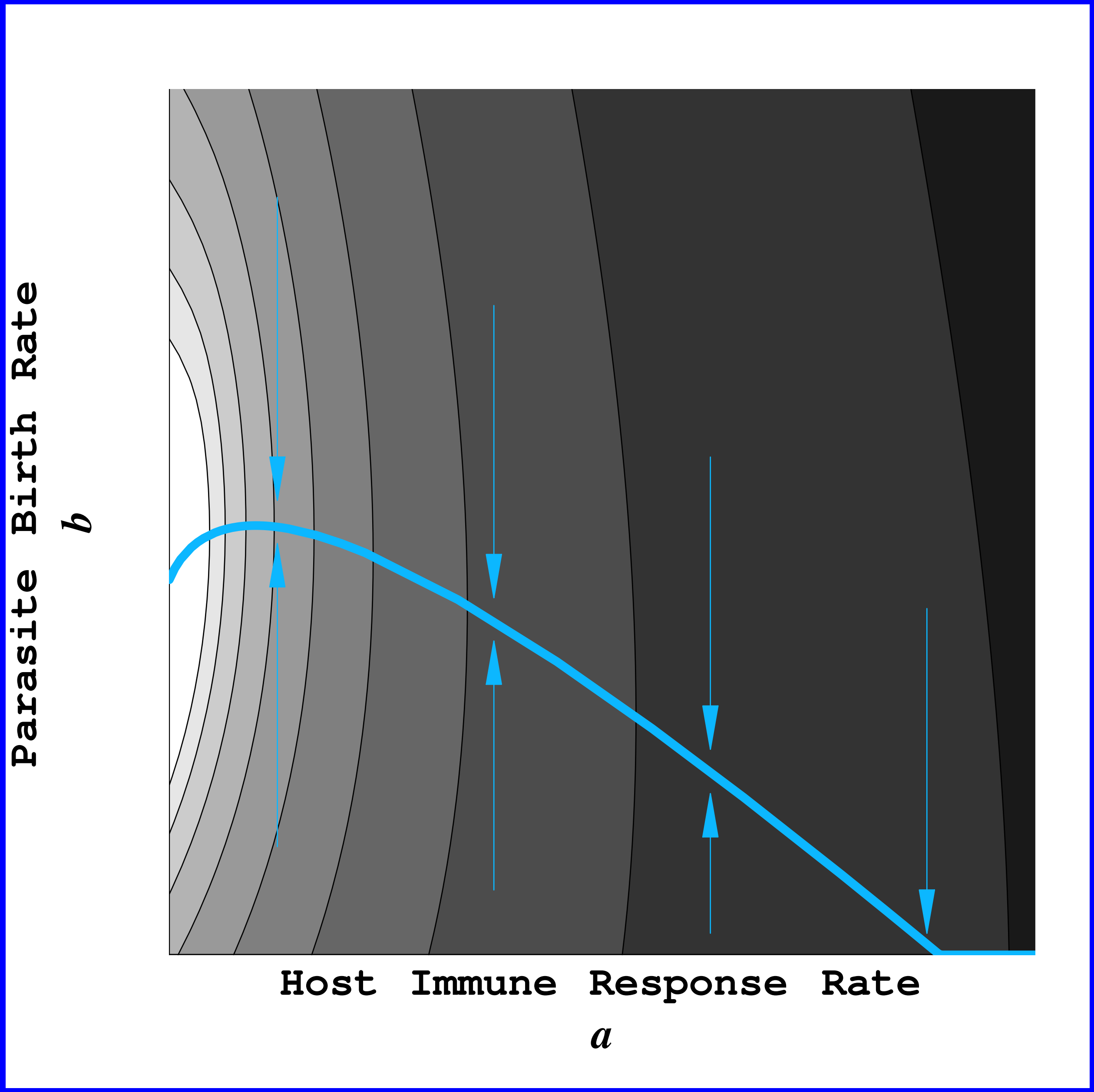
Link Within-Host Dynamics to Between-Host Parameters



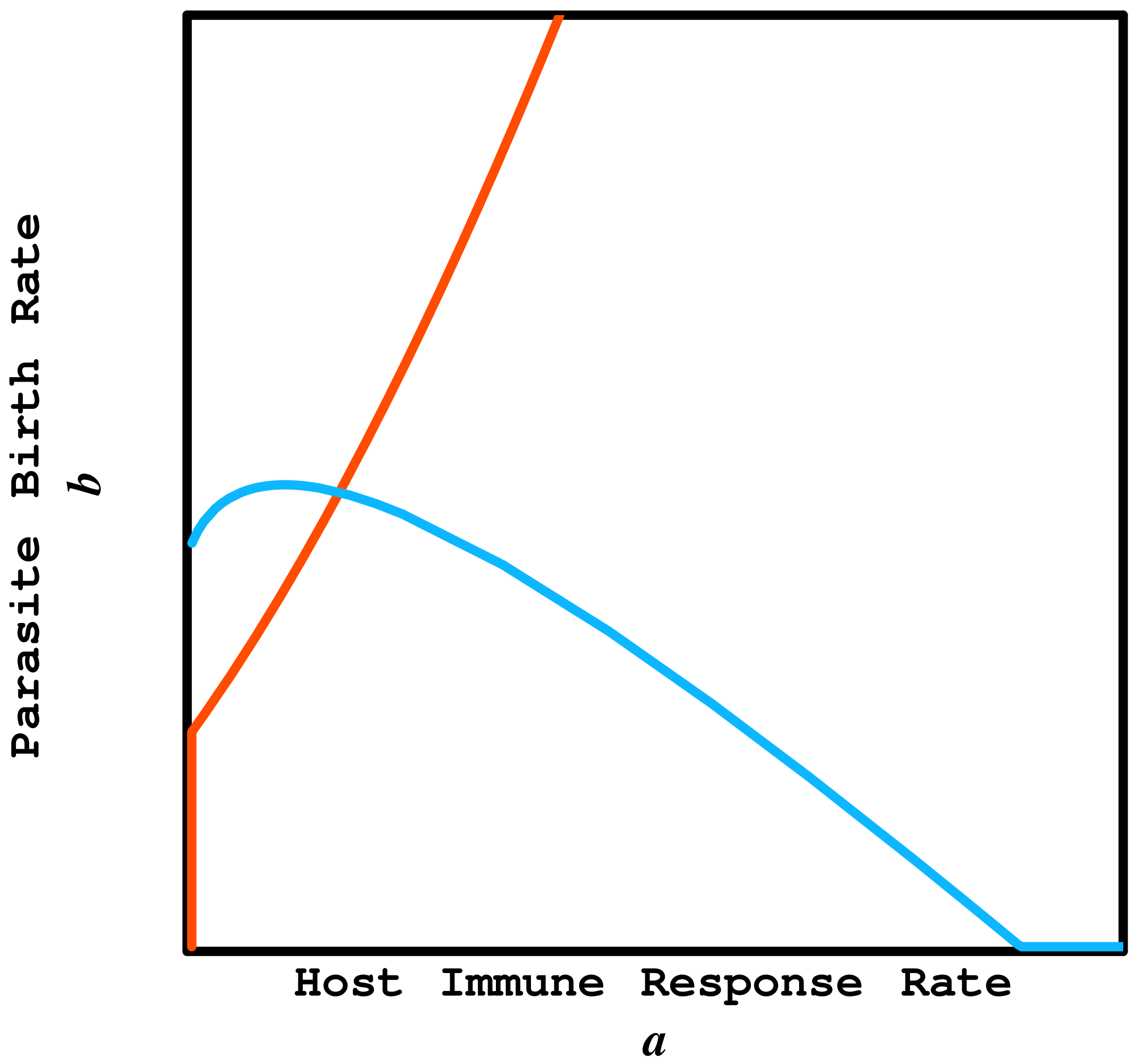
Host Fitness Landscape and Optimal a vs. b



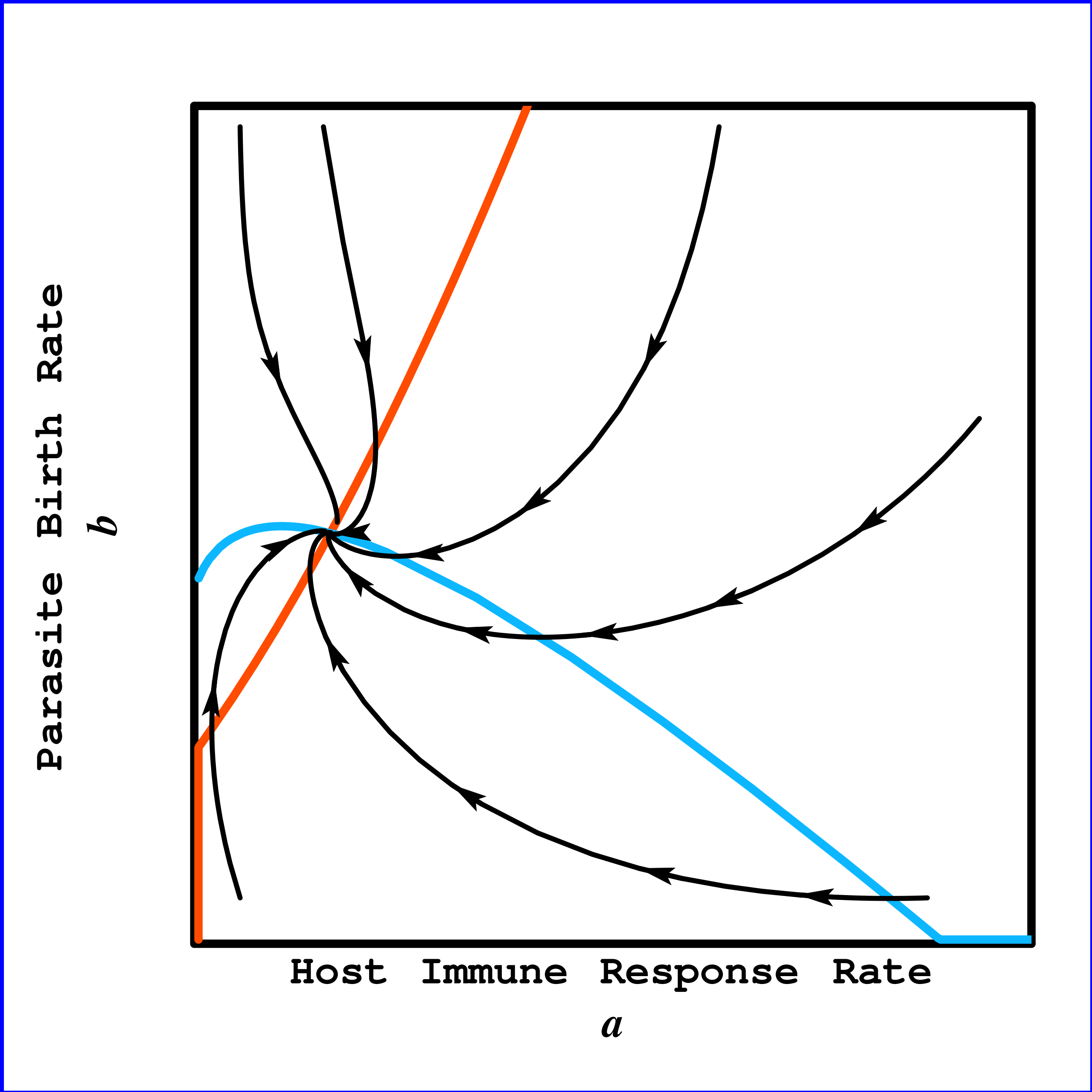
Parasite Fitness Landscape and Optimal a vs. b



Host-Parasite Coevolution



Host-Parasite Coevolution



Modeling Host-Parasite Coevolution

Overview

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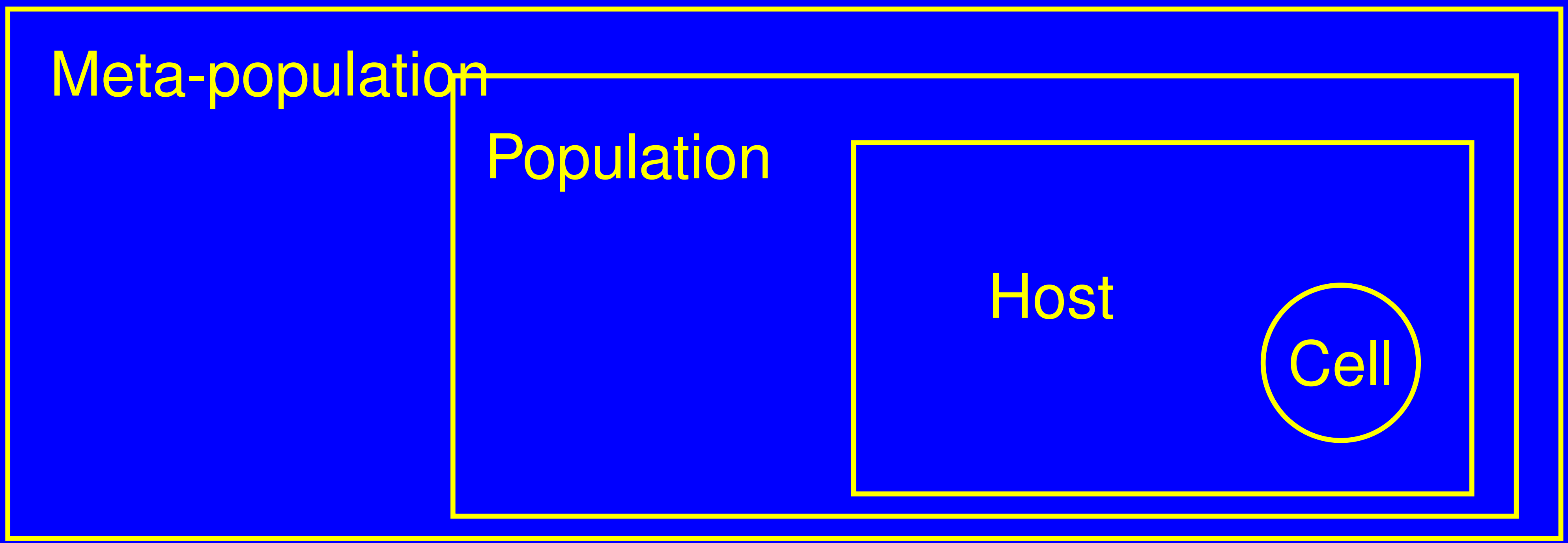
Current Work: Levels of Selection

With Dan Coombs and Collen Ball



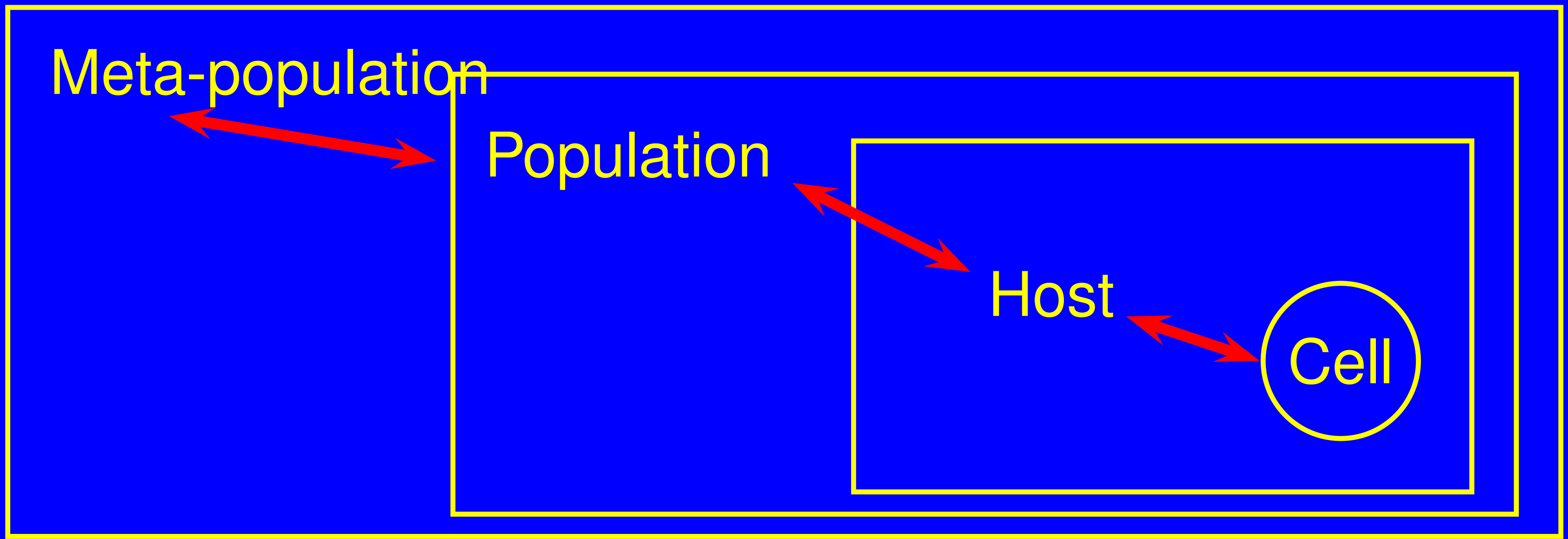
Levels of Selection: Conflict?

Meta-population: low virulence

Population: intermediate virulence

Host: high virulence

Cell: low virulence



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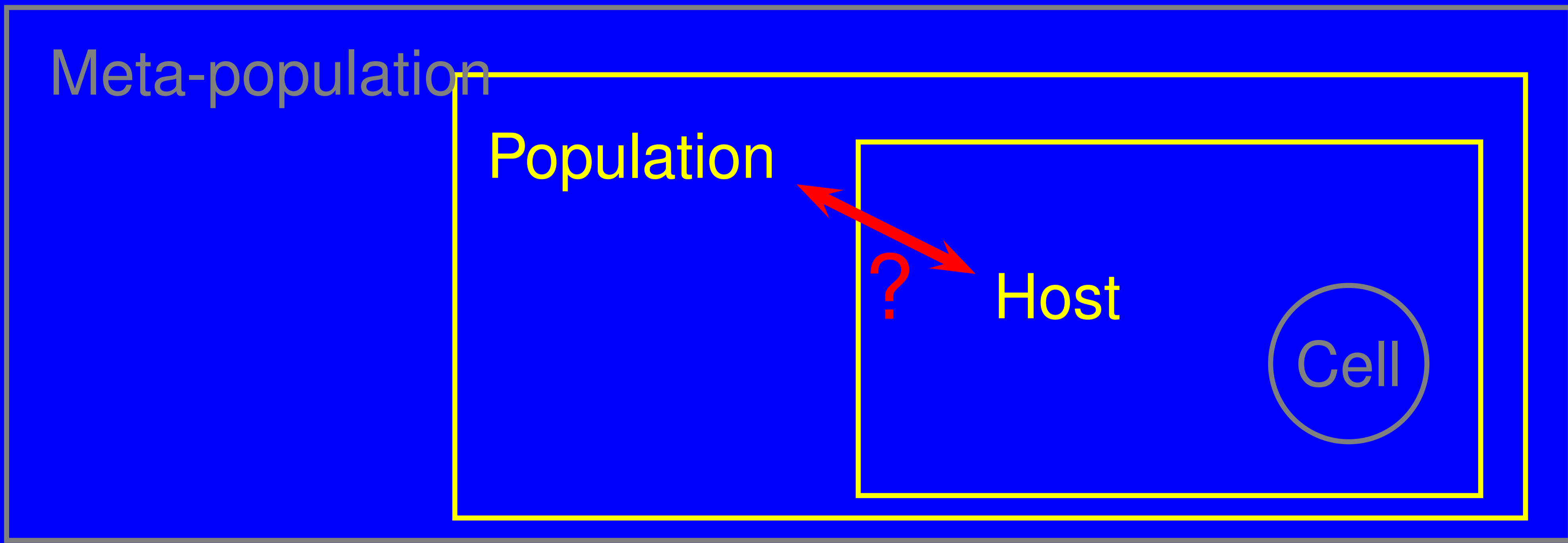
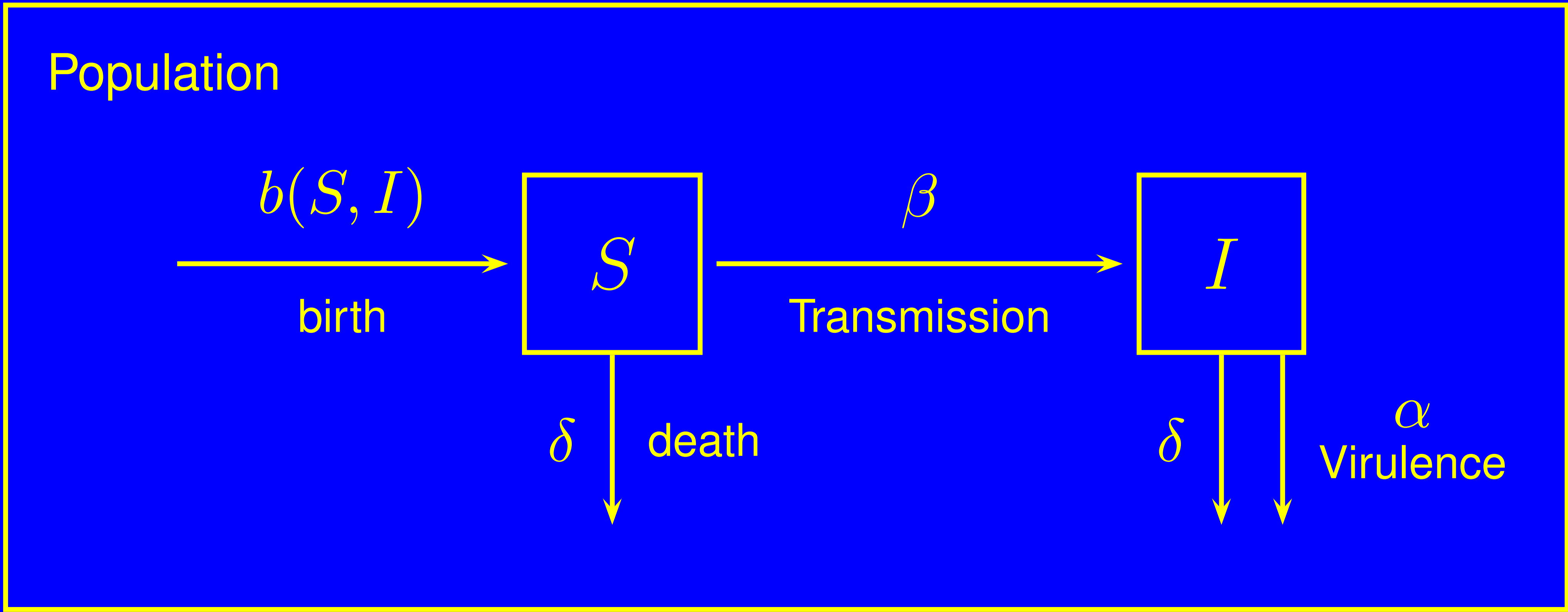


Between-Host Model & Selection

- Epidemiological model of Susceptible and Infectious hosts

$$dS/dt = b(S,I) - \beta SI - \delta S$$
$$dI/dt = \beta SI - (\alpha + \delta)I$$



Host Population: Between-Host Selection

- Natural selection favors the maximization of the reproductive ratio R:

$$R = \frac{\beta}{\alpha + \delta}$$
$$= \frac{1}{\hat{S}}$$

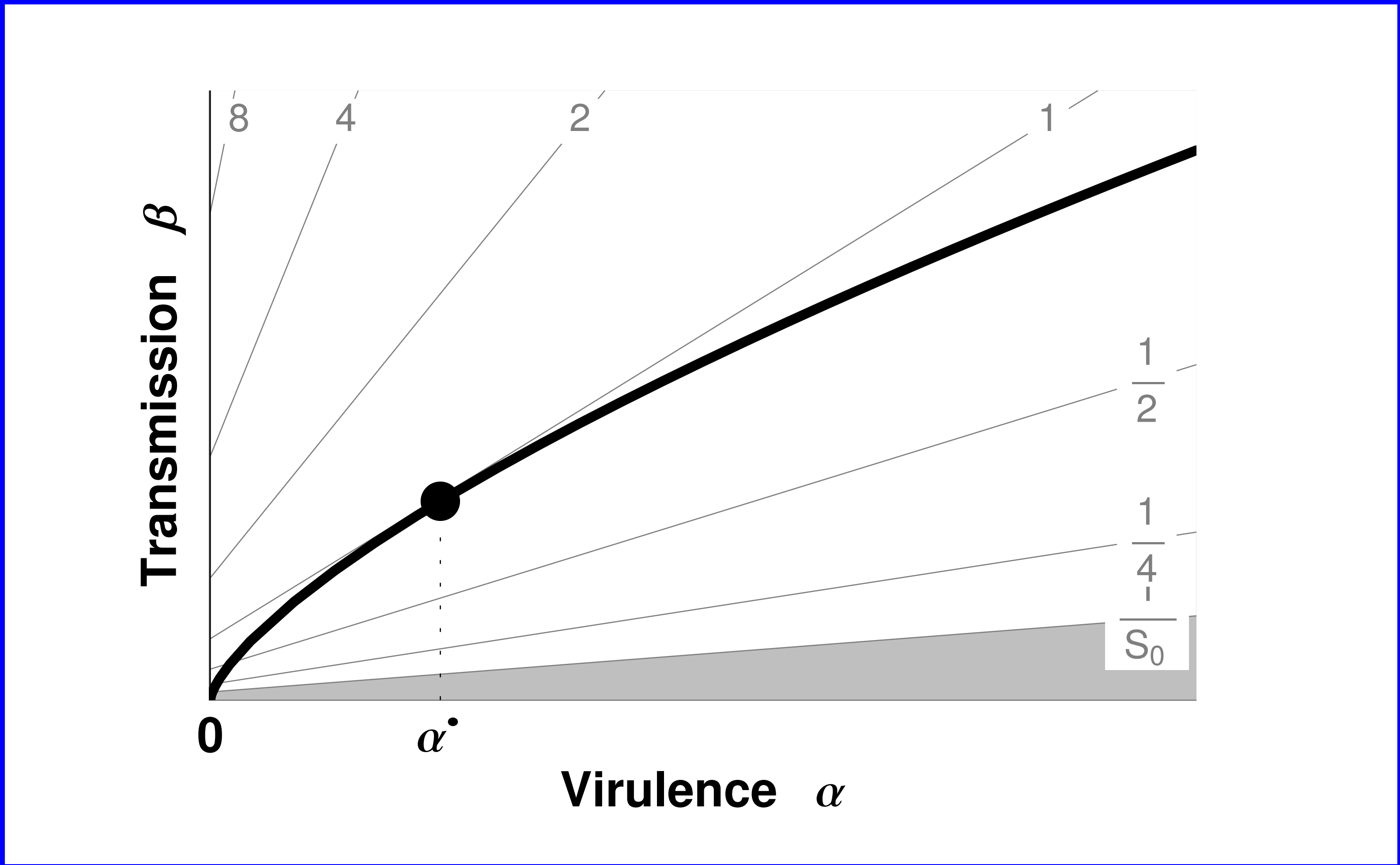
- Strain which maximizes R
  - Minimizes $\hat{S}$
  - Will competitively exclude other competitors.

Bremermann & Pickering (1982), Anderson & May (1983)

Between-Host Model & Selection

Maximizing R depends on relationship between β and α.

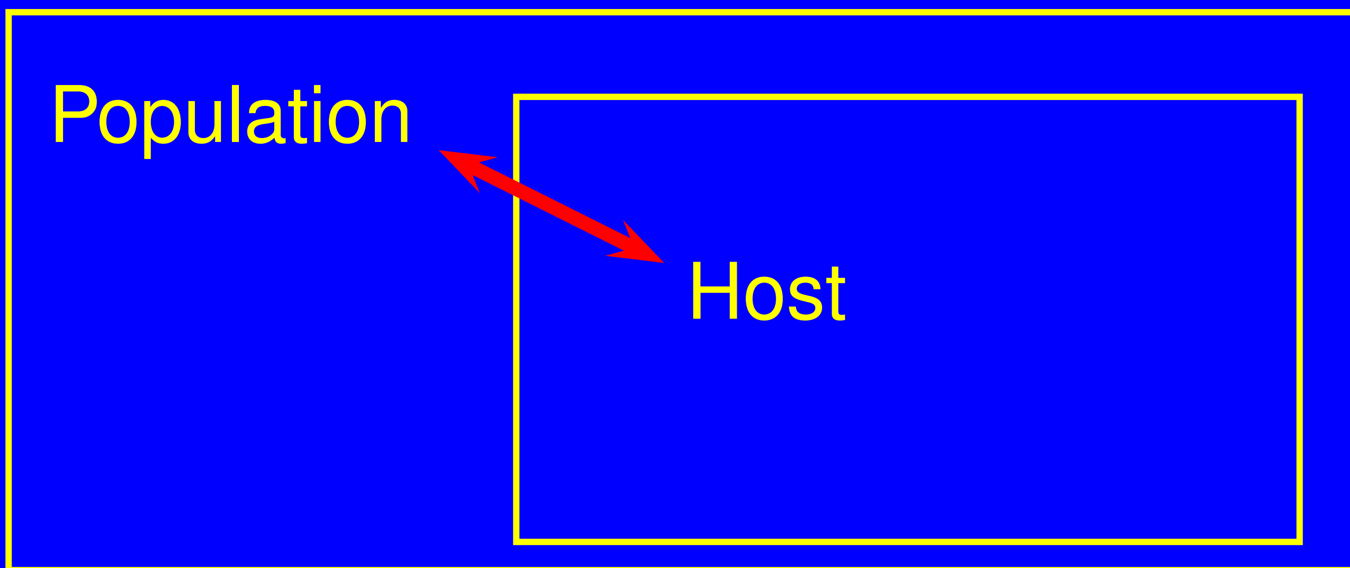
Bremermann & Pickering (1982), Lenski & May (1994), Frank (1996)



Levels of Selection

Between-Host Selection: Favors maximization of R

Within-Host Selection: ?

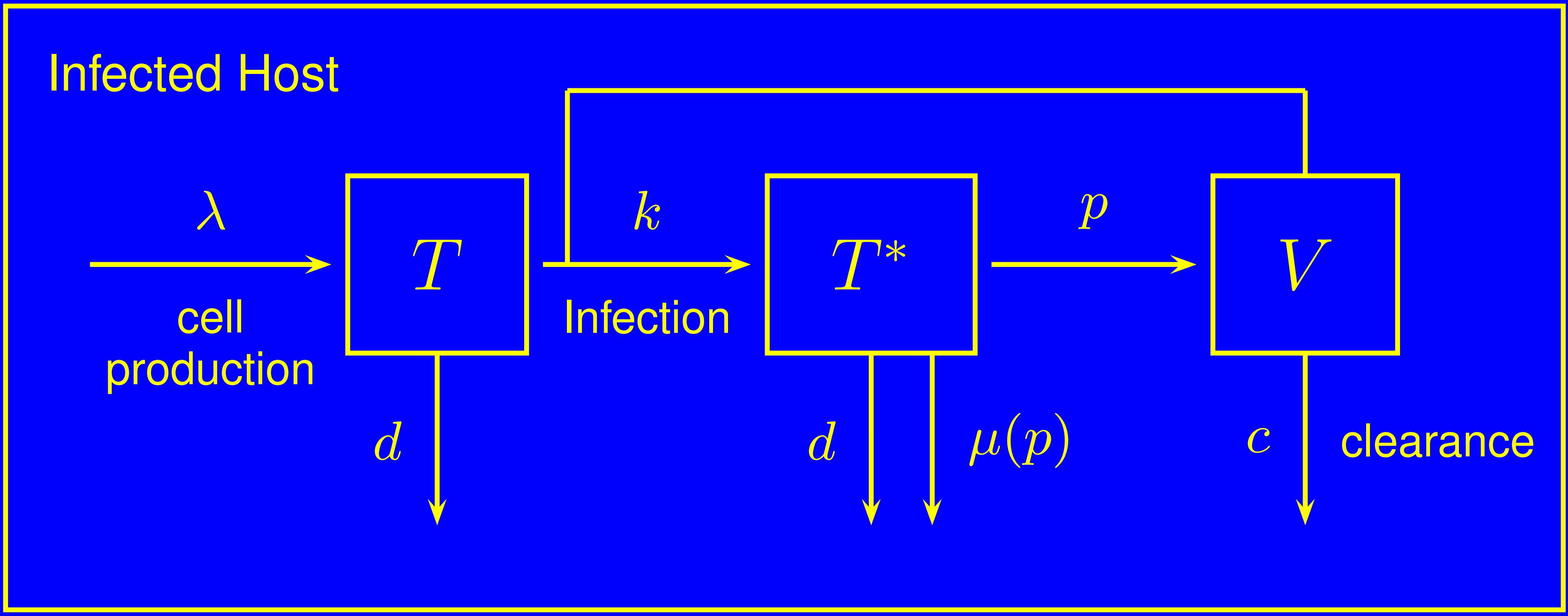


Within-Host Model & Selection

$$dT/dt = \lambda - k\,V\,T - d\,T$$

$$dT^*/dt = k\,V\,T\; - (\mu(p) + d)T^*$$

$$dV/dt = p\,T^* - c\,V,$$



Within-Host Model: Two Strains

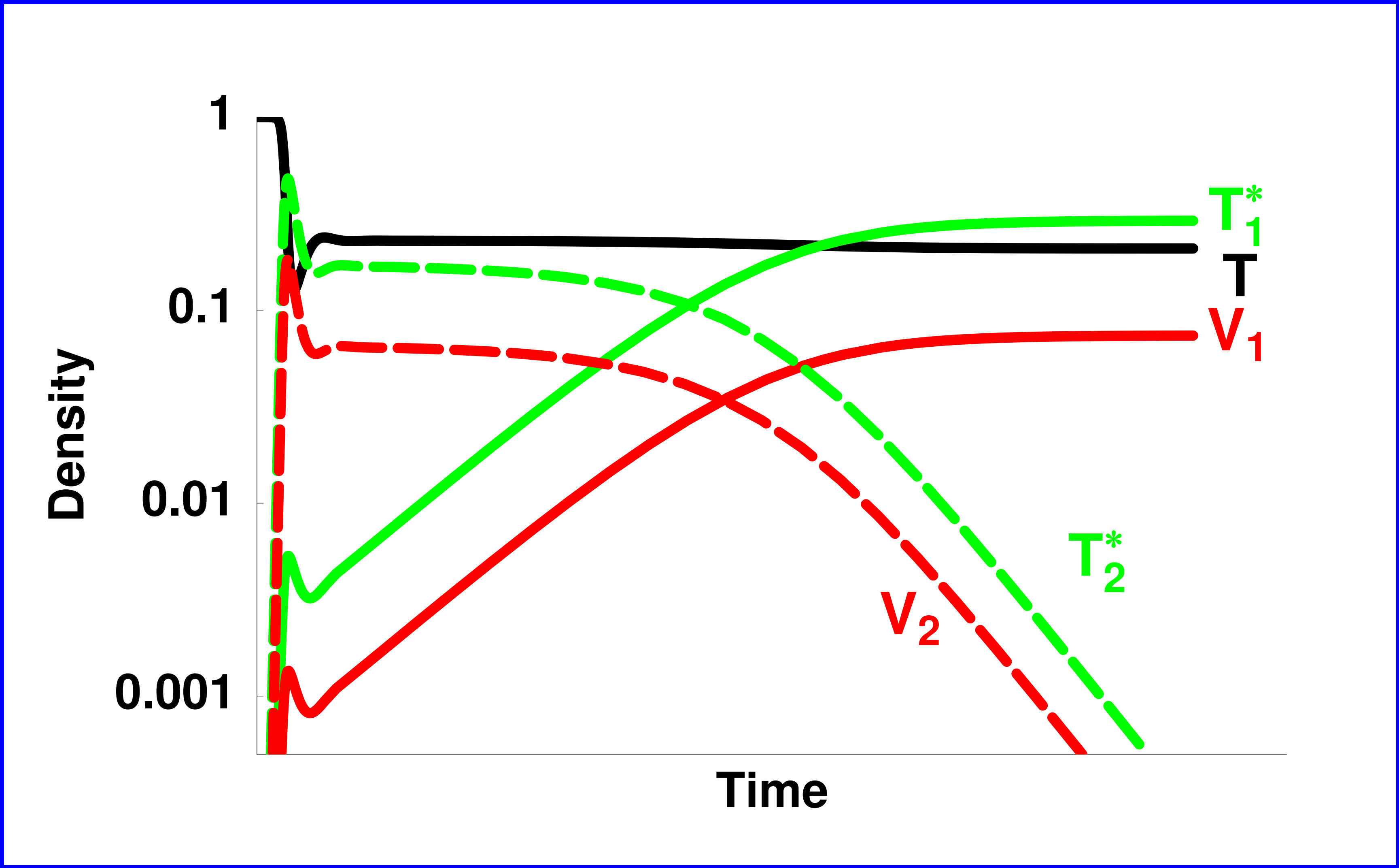
Expand model to include second strain within a host

$$dT/dt = \lambda - k\,(V_1 + V_2)\,T - d\,T$$
$$dT_i^*/dt = k\,V_i\,T\, - (\mu(p_i) + d)T_i^*$$
$$dV_i/dt = p_i\,T_i^* - c\,V_i$$

$$\begin{aligned} V_T(0) &= \text{Inoculum Size} \\ &= V_1(0) + V_2(0) \\ x(0) &= \text{Initial Strain Mix} \\ &= \frac{V_1(0)}{V_T(0)} \end{aligned}$$

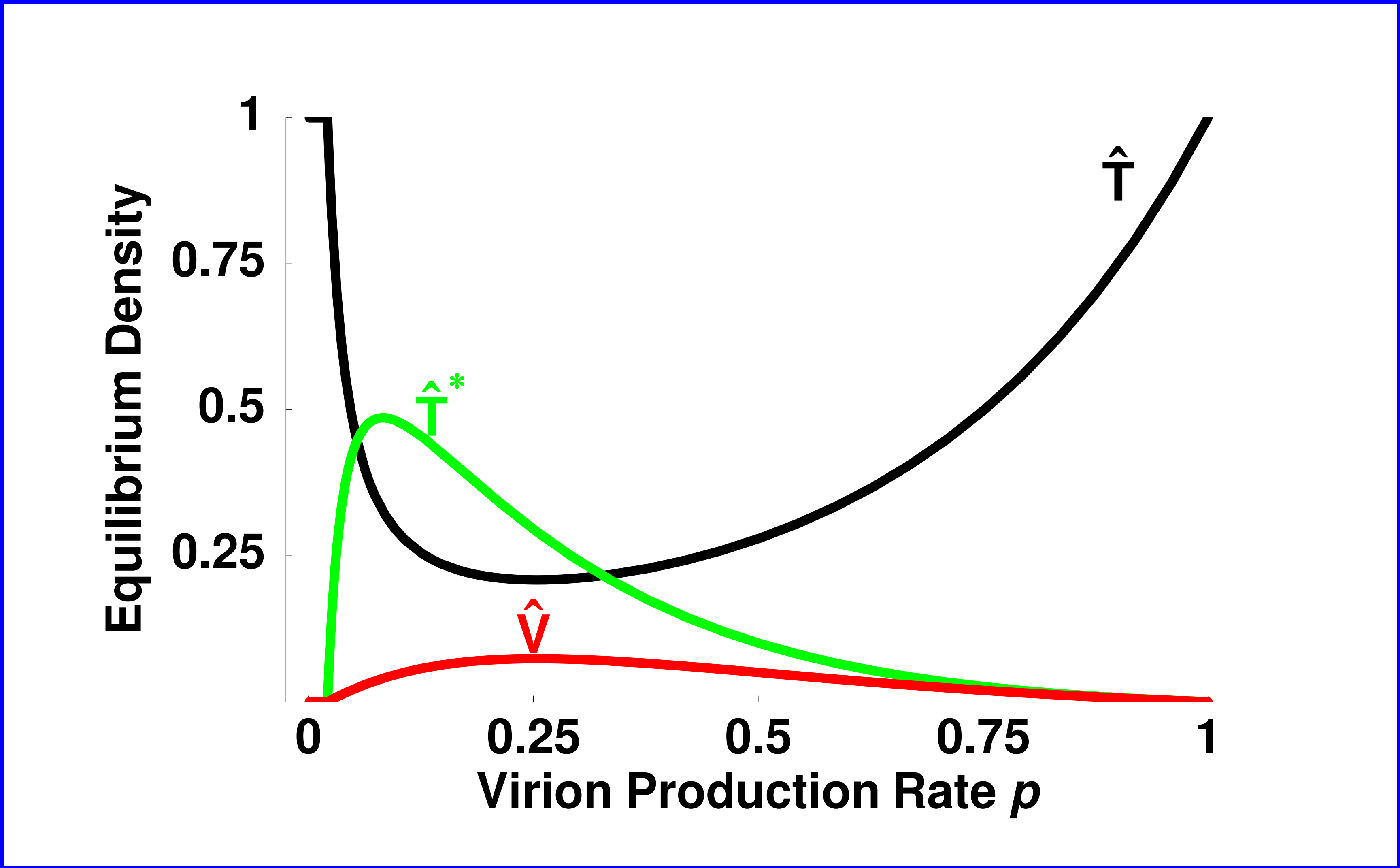
Within-Host Model: Two Strains

Model Behavior



Within-Host Model & Selection

Equilibrium Behavior



Within-Host Model & Selection

- Within-host selection favors the maximization of the *within-host* reproductive ratio ρ:

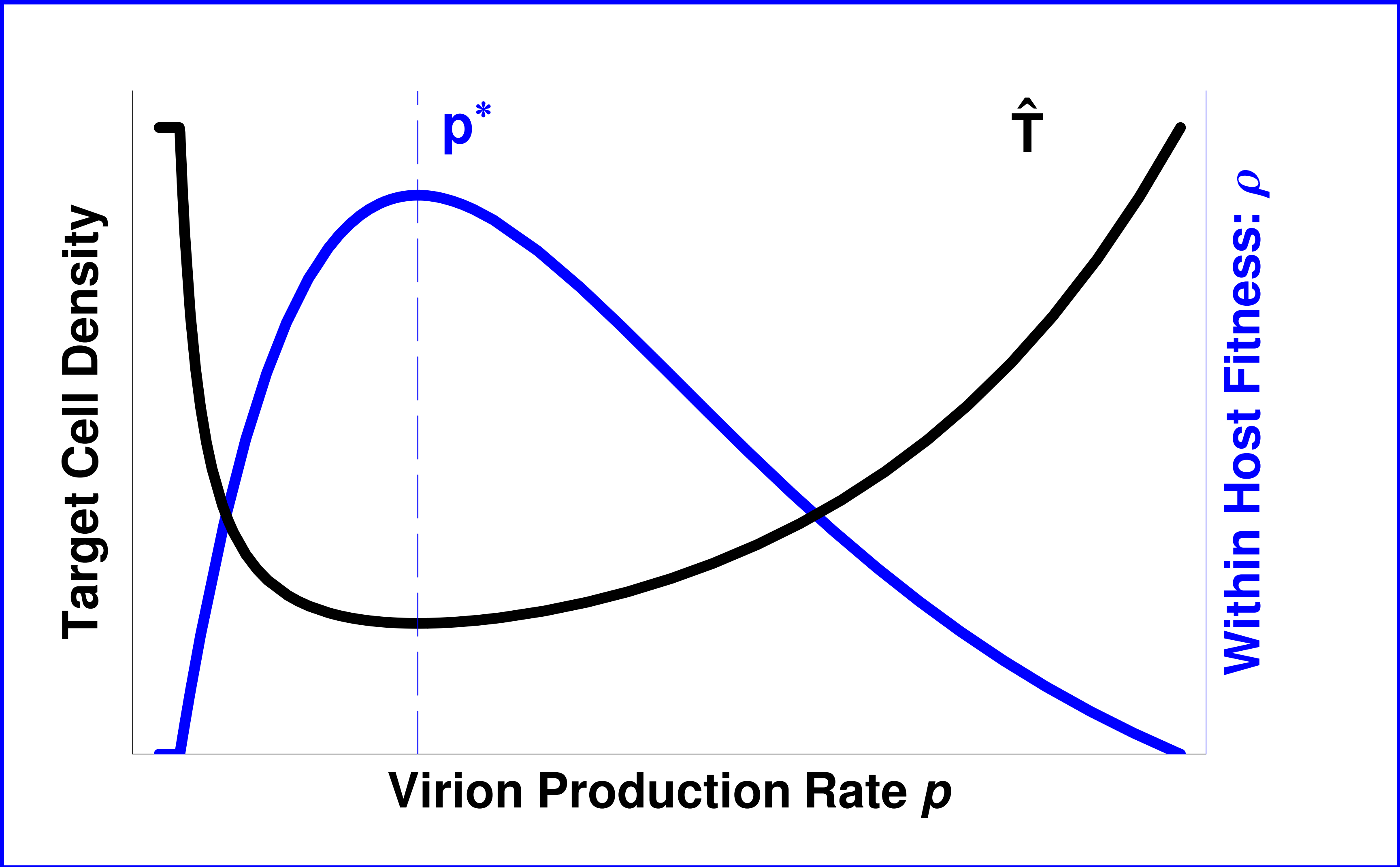
$$\begin{aligned}\rho &= \frac{k}{c}\frac{p}{\mu(p)+d} \\ &= \frac{1}{\hat{T}}\end{aligned}$$

- Strain which maximizes $\rho(p)$
  - Minimizes $\hat{T}(p)$
  - Will competitively exclude other competitors within the host.

Gilchrist *et al.* (2004)

Within-Host Model & Selection

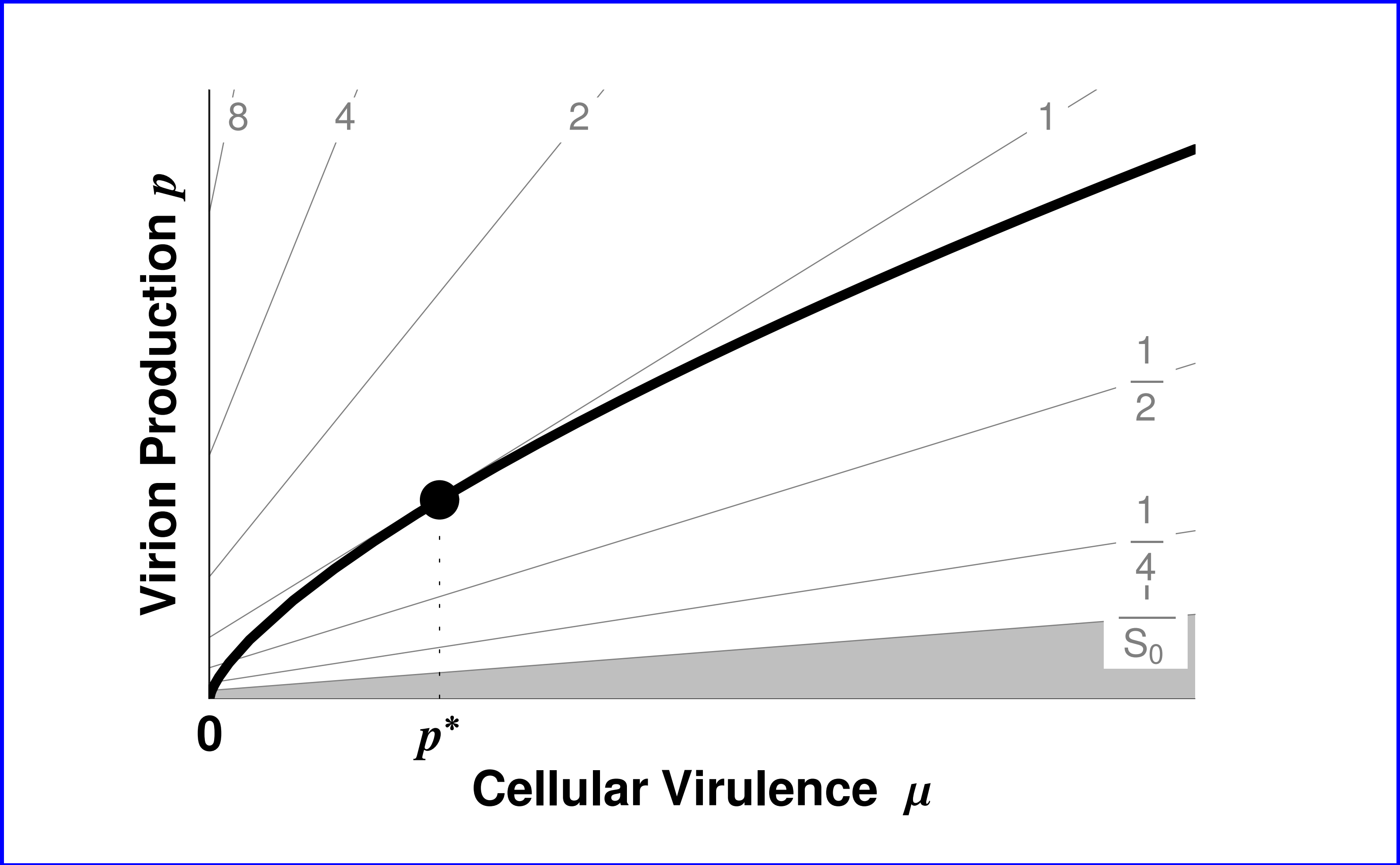
Min($\hat{T}(p^*)$) = Within-Host Optimum



Within-Host Model & Selection

Maximizing ρ depends on relationship between μ & p.

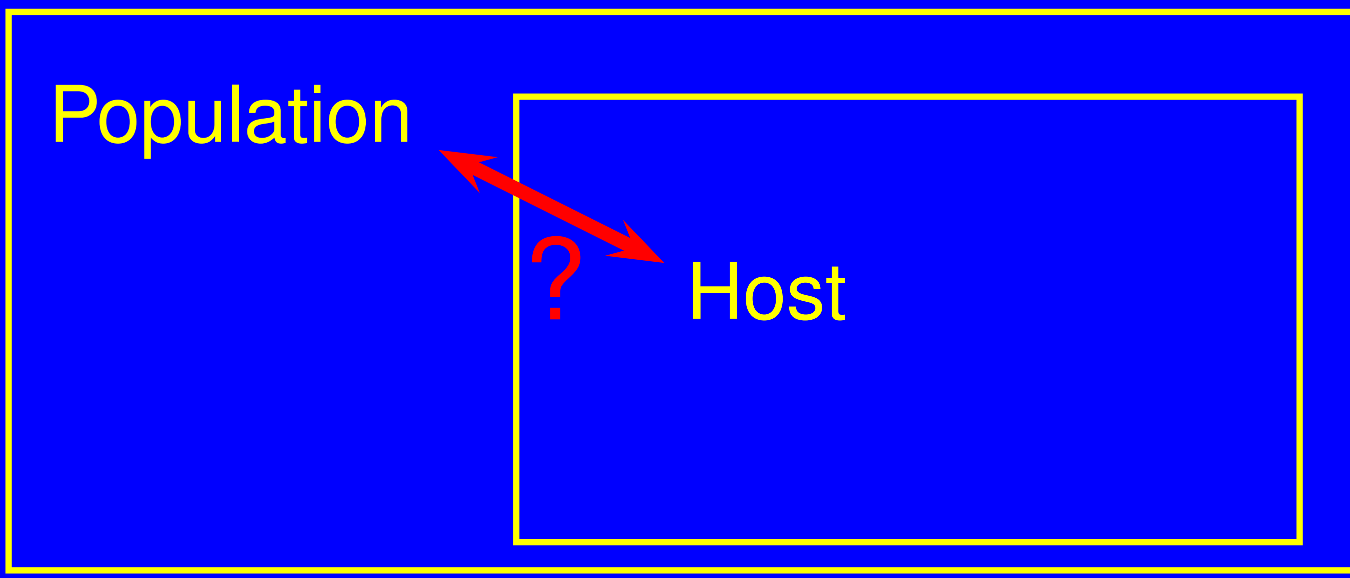
Coombs *et al.*(2003)



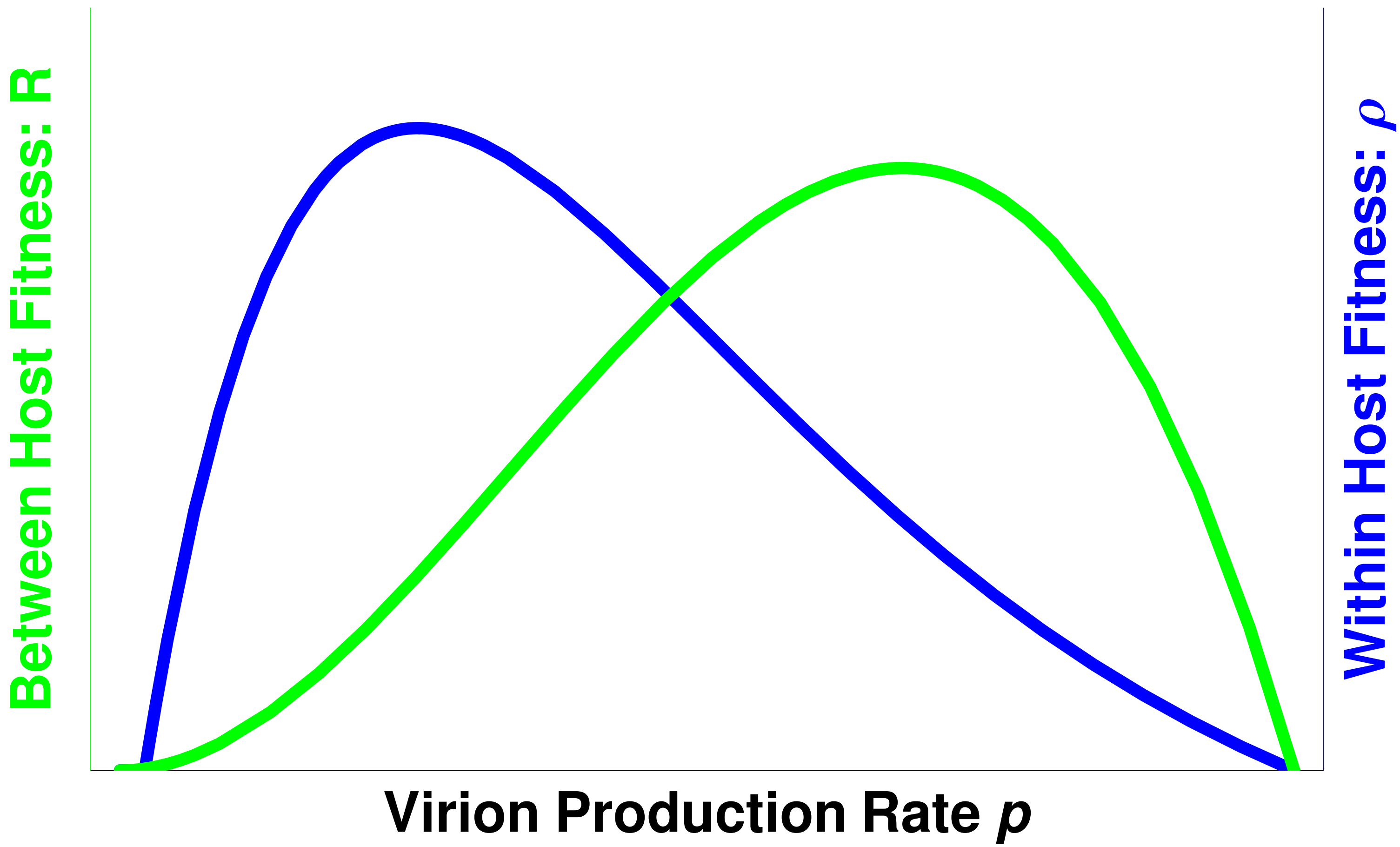
Levels of Selection

Between-Host Selection: Favors maximization of R

Within-Host Selection: Favors maximization of ρ

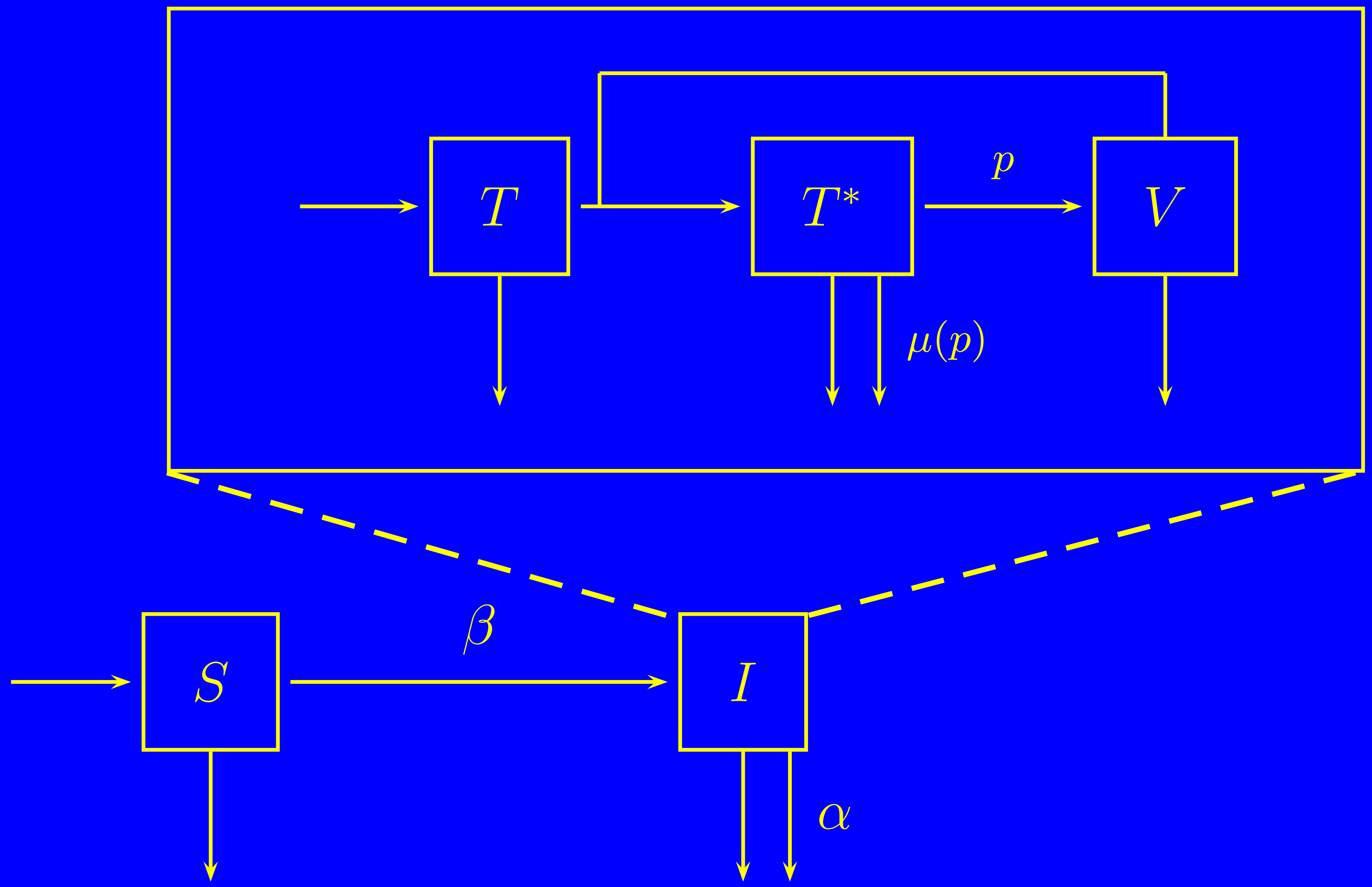


Possible Conflict?



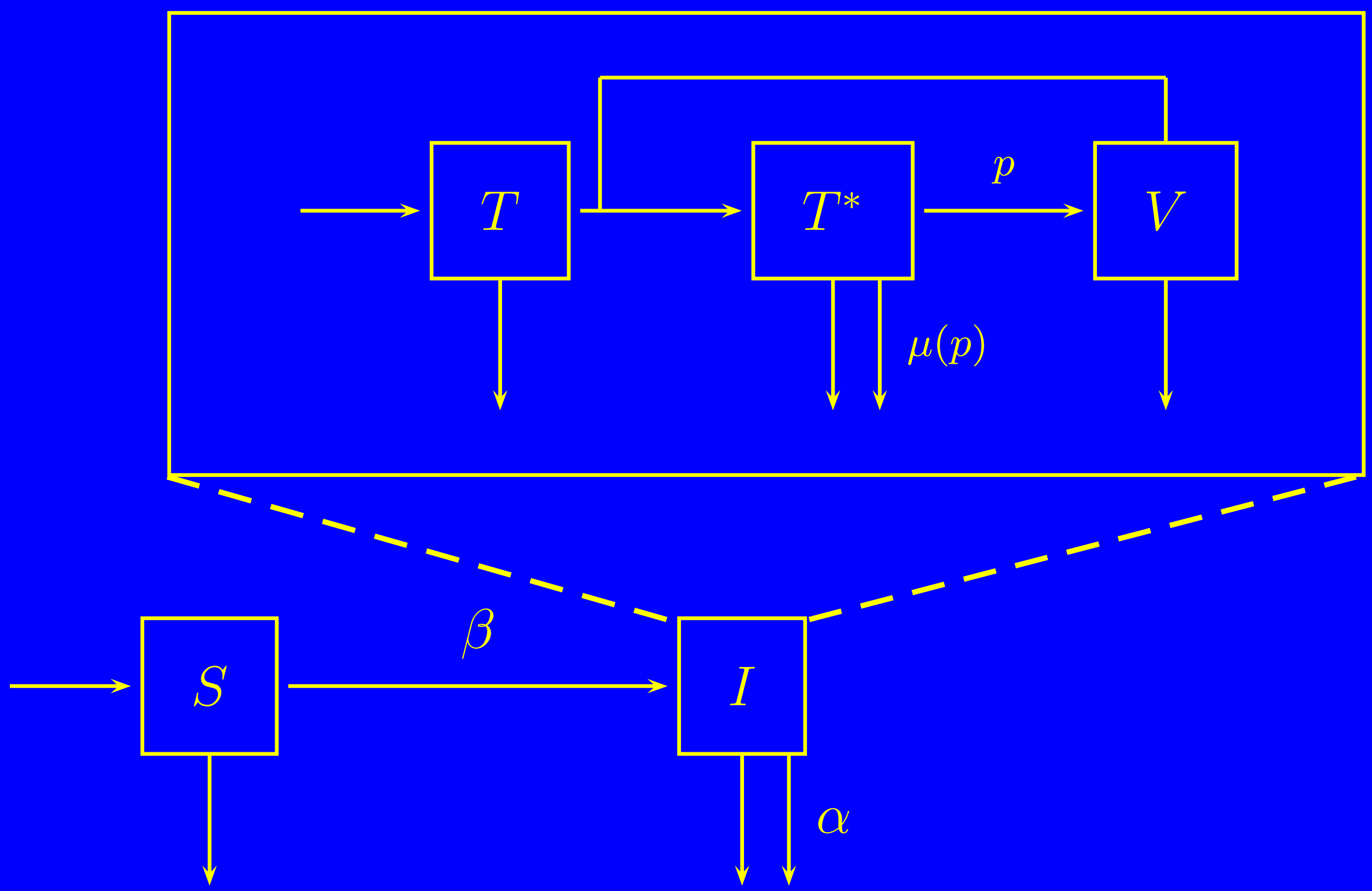
Nesting Models: Linking Within & Between-Host

Nest model of **within-host** processes inside a model of **between-host** processes



Nesting Models: Linking Within & Between-Host

$$\alpha(T) = a_1\,(T_0 - T) \qquad\qquad \beta(V) = b_1 V$$

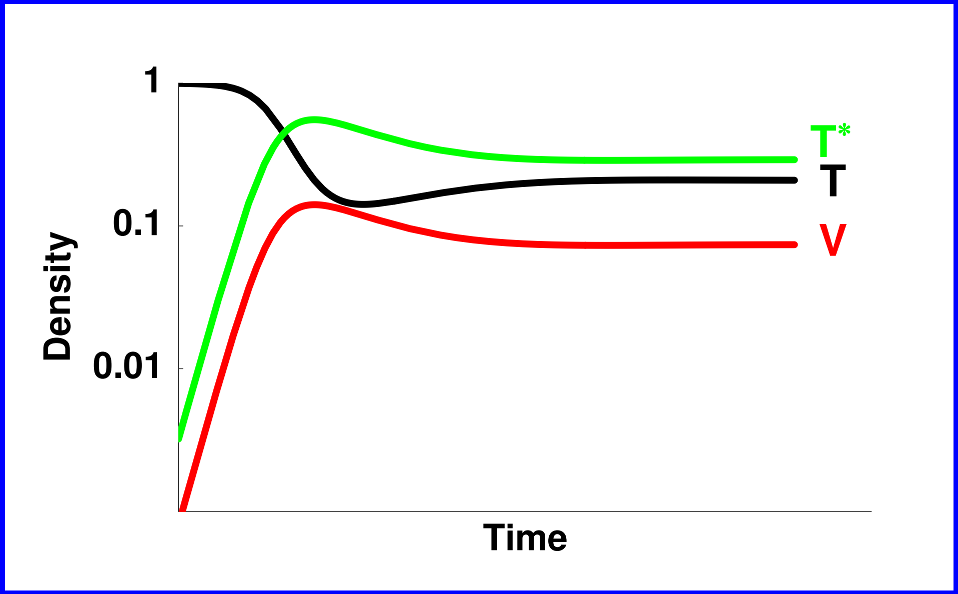


Nesting Models: Linking Within & Between-Host

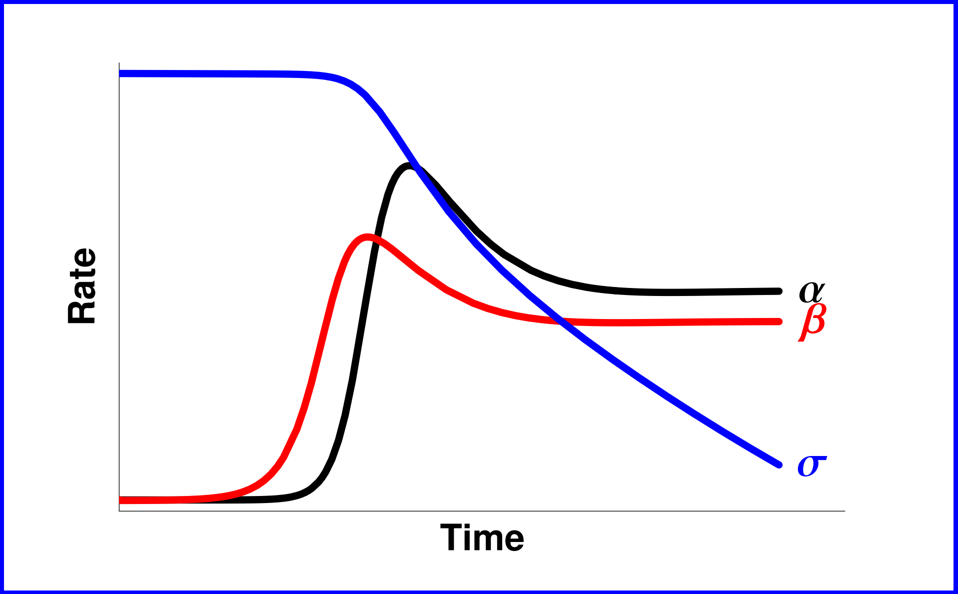
Behavior

Framework allows within-host virion production rate p and intial parasite mix x_0 to drive system

Within-Host Dynamics



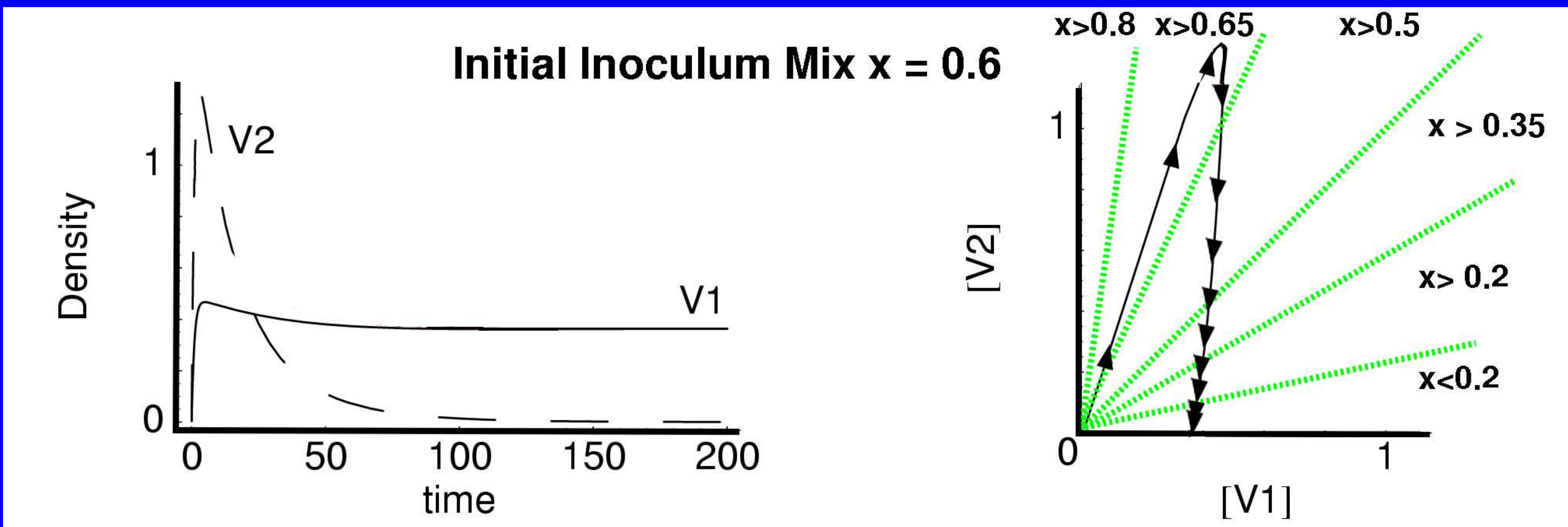
Between-Host Parameters



Nesting Models: Transmission

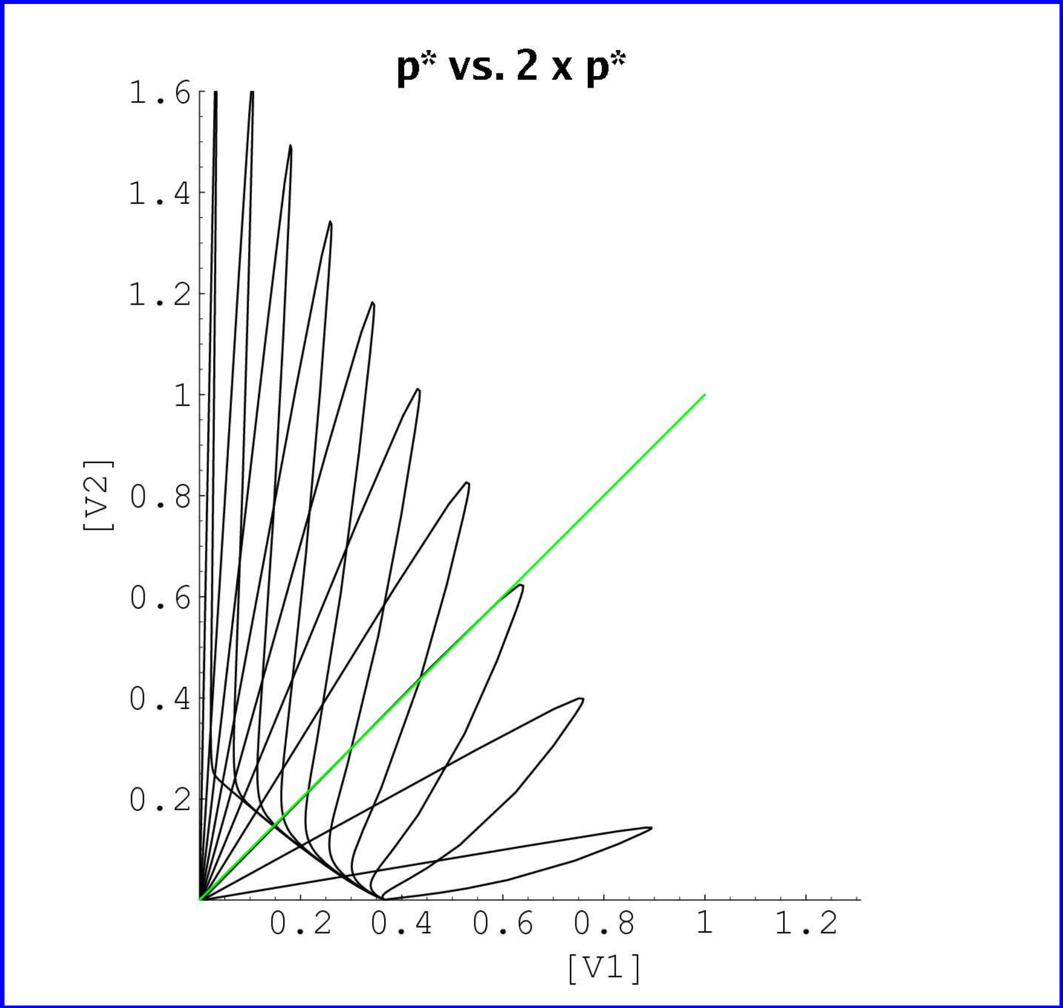
Assume inoculum reflects parasite mix at time of transmission

$$x(a) = \frac{V_1(a)}{V_1(a) + V_2(a)}$$



Nesting Models: Between-Host Fitness

Dynamics depends on virion production rates p_1 and p_2 as well as inoculum mix x_0.



Nesting Models: Between-Host Fitness

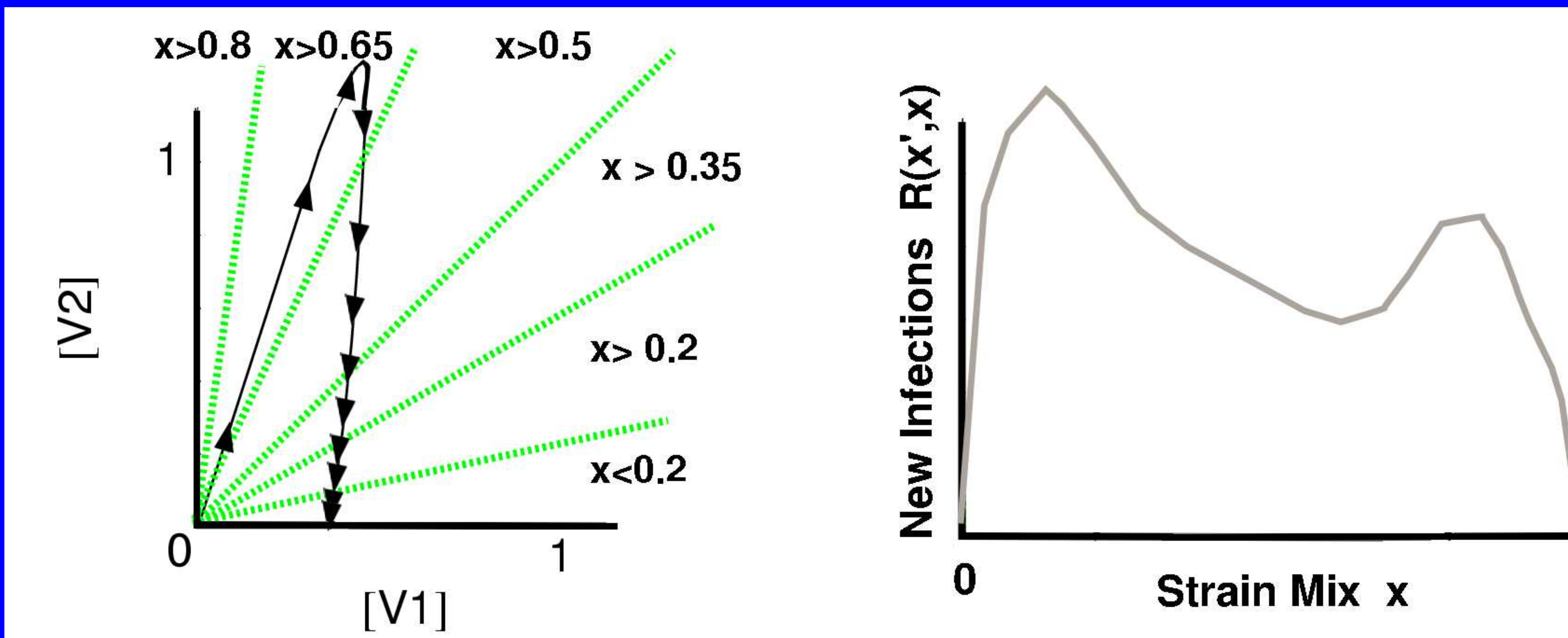
Keep track of number of new infections ($'$) with inoculum mixture $x'(0) = x(a)$

$$R\left(x_0' \left| x_0\right.\right) = \int_0^\infty \delta\left(x_0' - x(a)\right)$$

$$\times\, \beta(V_1(a), V_2(a)) \exp\left[-\int_0^a \alpha(T(z))dz + \delta a\right] da$$

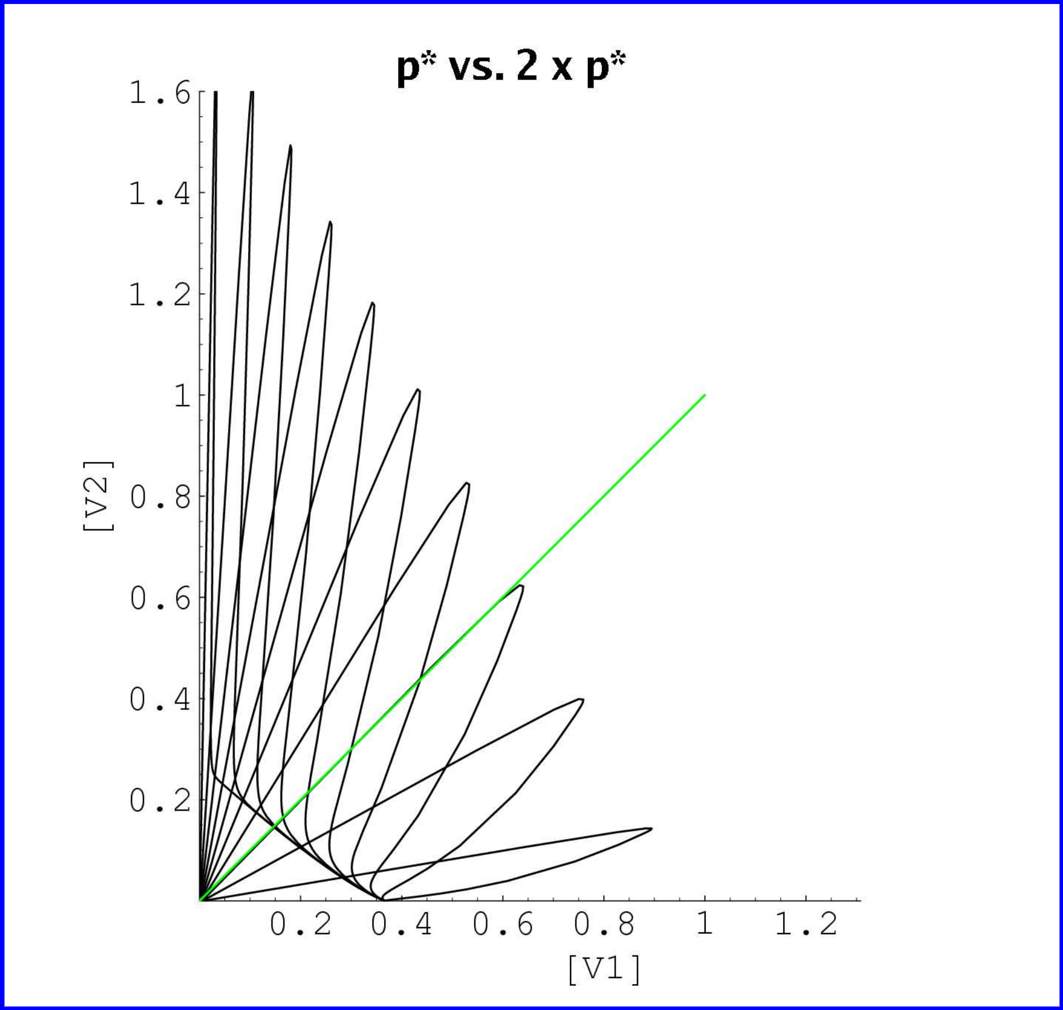
Nesting Models: Between-Host Fitness

$$R\left(x_0' \,|x_0\,\right) = \int_0^\infty \delta\left(x_0' - x(a)\right)\beta(V_1, V_2)e^{\left[- \int_0^a \alpha(T(z))dz + \delta a\right.}$$



Nesting Models: Between-Host Fitness

NB: Dynamics depends on virion production rates p_1 and p_2 as well as inoculum mix x_0.



Nesting Models: Between- & Within-Host Fitness

1. Discretize inoculum mixes $\vec{\mathbf{x}} = \{x_1, x_2, \ldots x_n\}$

2. Calculate next generation operator $\mathbf{R}$

$$\vec{\mathbf{x}}(t+1) = \mathbf{R}\vec{\mathbf{x}}(t)$$

   where,

$$R_{i,j} = \int_{x_i}^{x_{i+x}} R(x', x)dx$$

3. Calculate equilibrium distribution of inocula $\vec{\mathbf{x}}$ (dominant eigenvector)

Resolving Within & Between-Host Selection

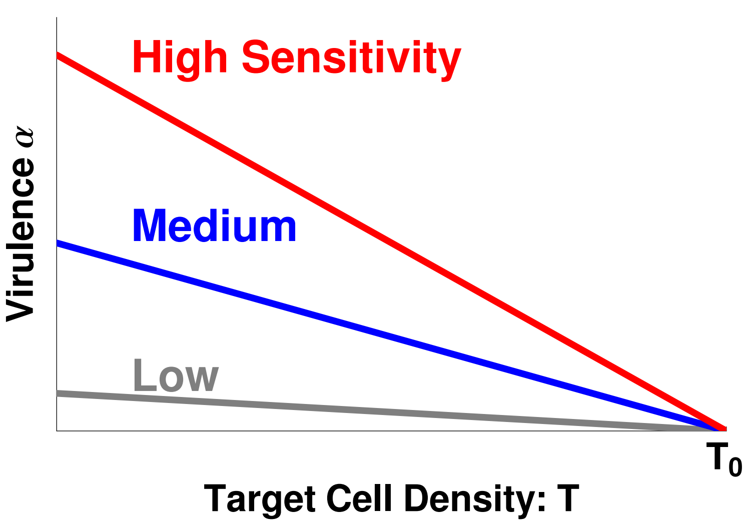
Examine three scenarios:

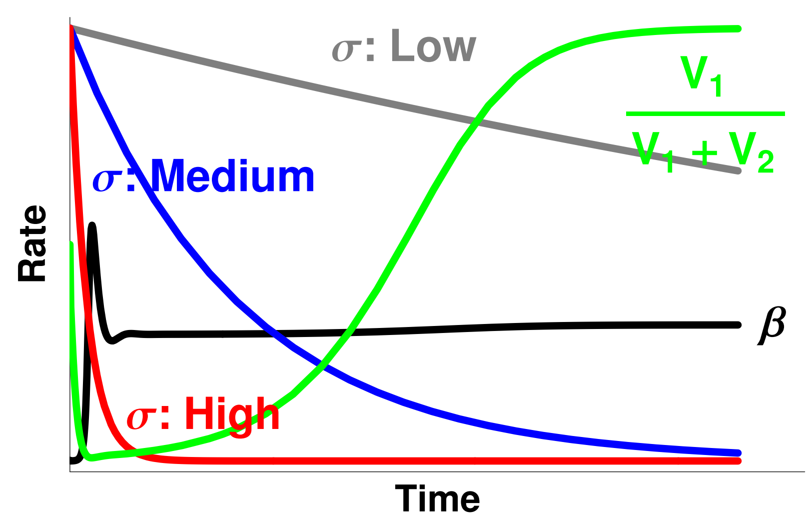
Low: Exculsion $>$ Spike

Medium: Exclusion $<=>$ Spike

High: Exclusion $<$ Spike

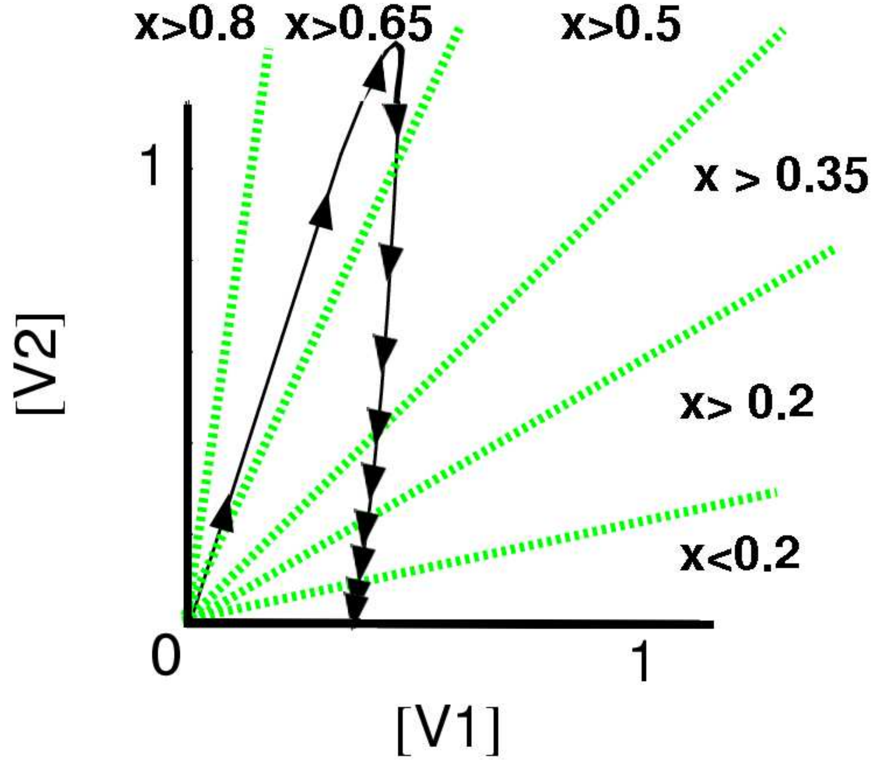
sensitivity of virulence α to target cell T depletion

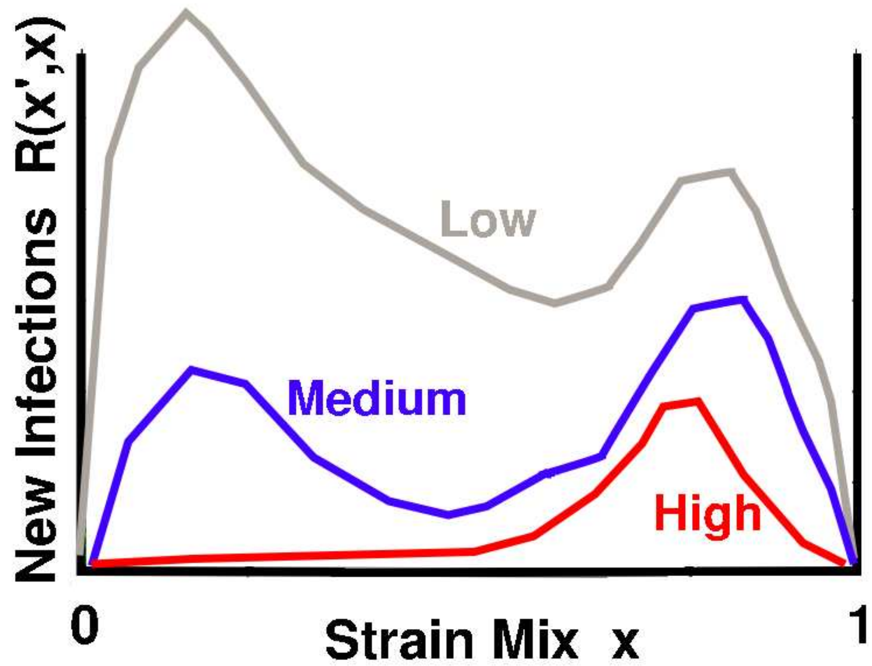




Dynamic Infection: Between Host Fitness

Examine for different host sensitivities to resource loss (reduction in target cell density T)





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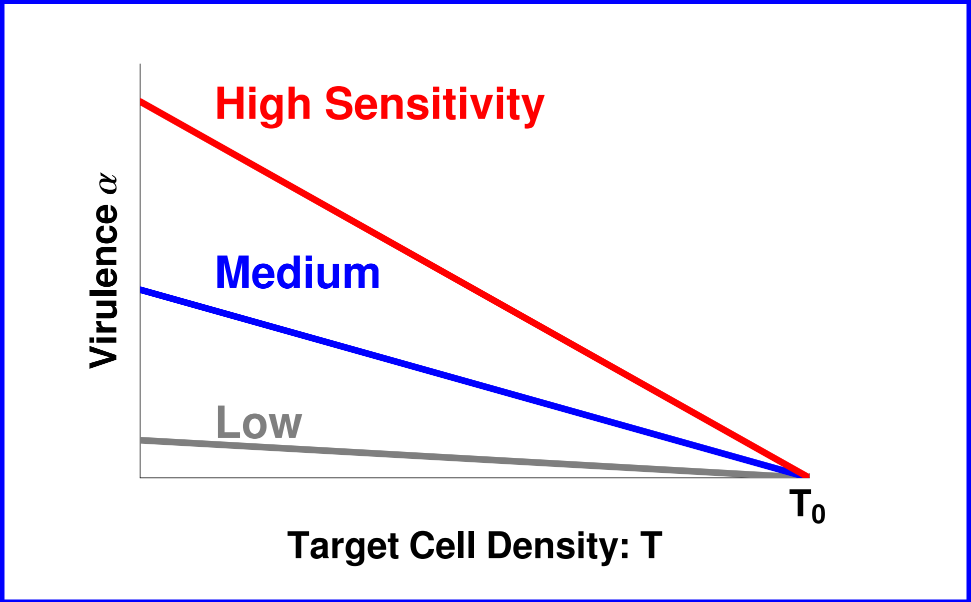
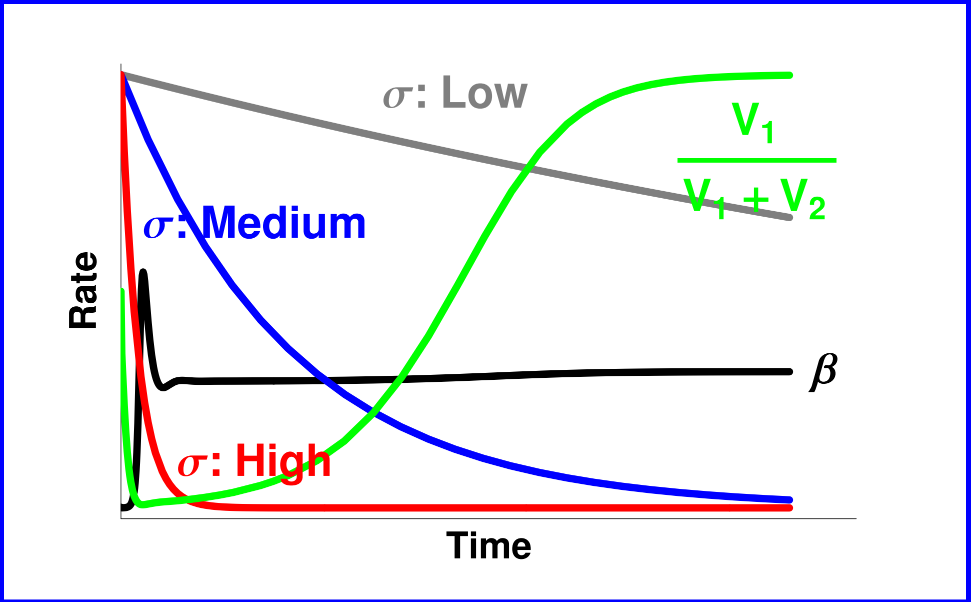
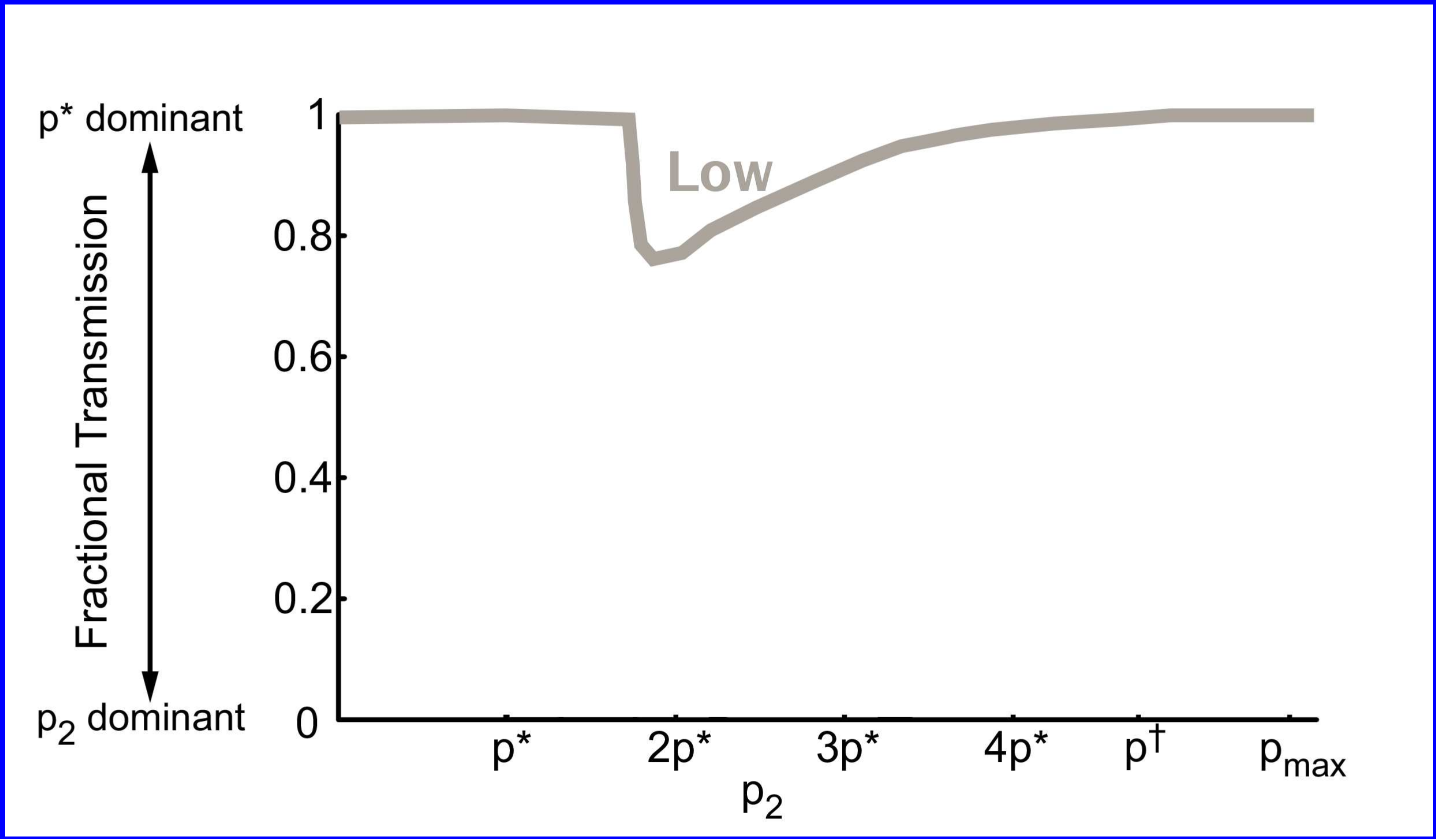




Resolving Within & Between-Host Selection

Scenario: Low sensitivity to target cell T depletion

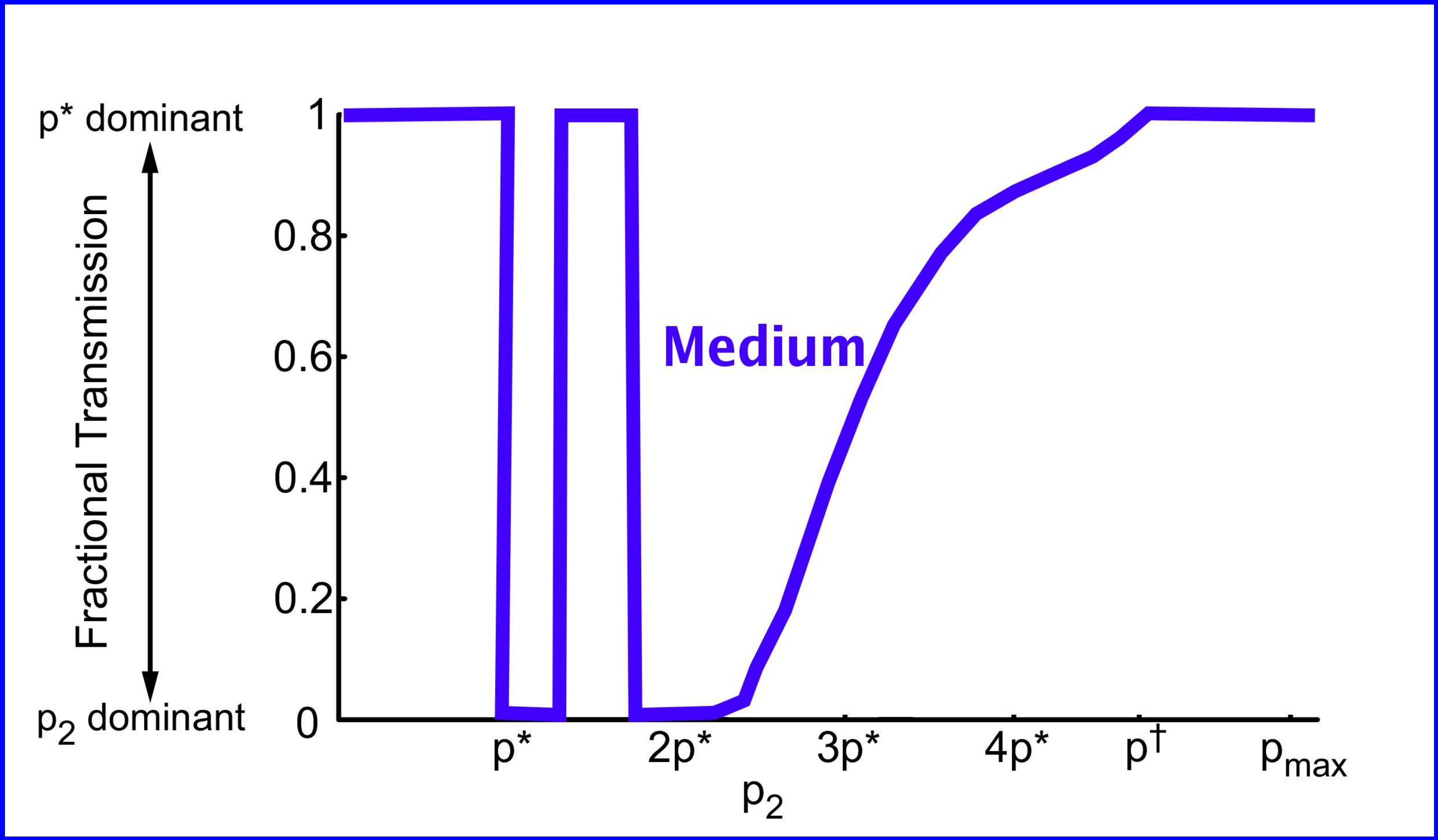
Result: One limited region of coexistence



Resolving Within & Between-Host Selection

Scenario: Medium sensitivity to target cell T depletion

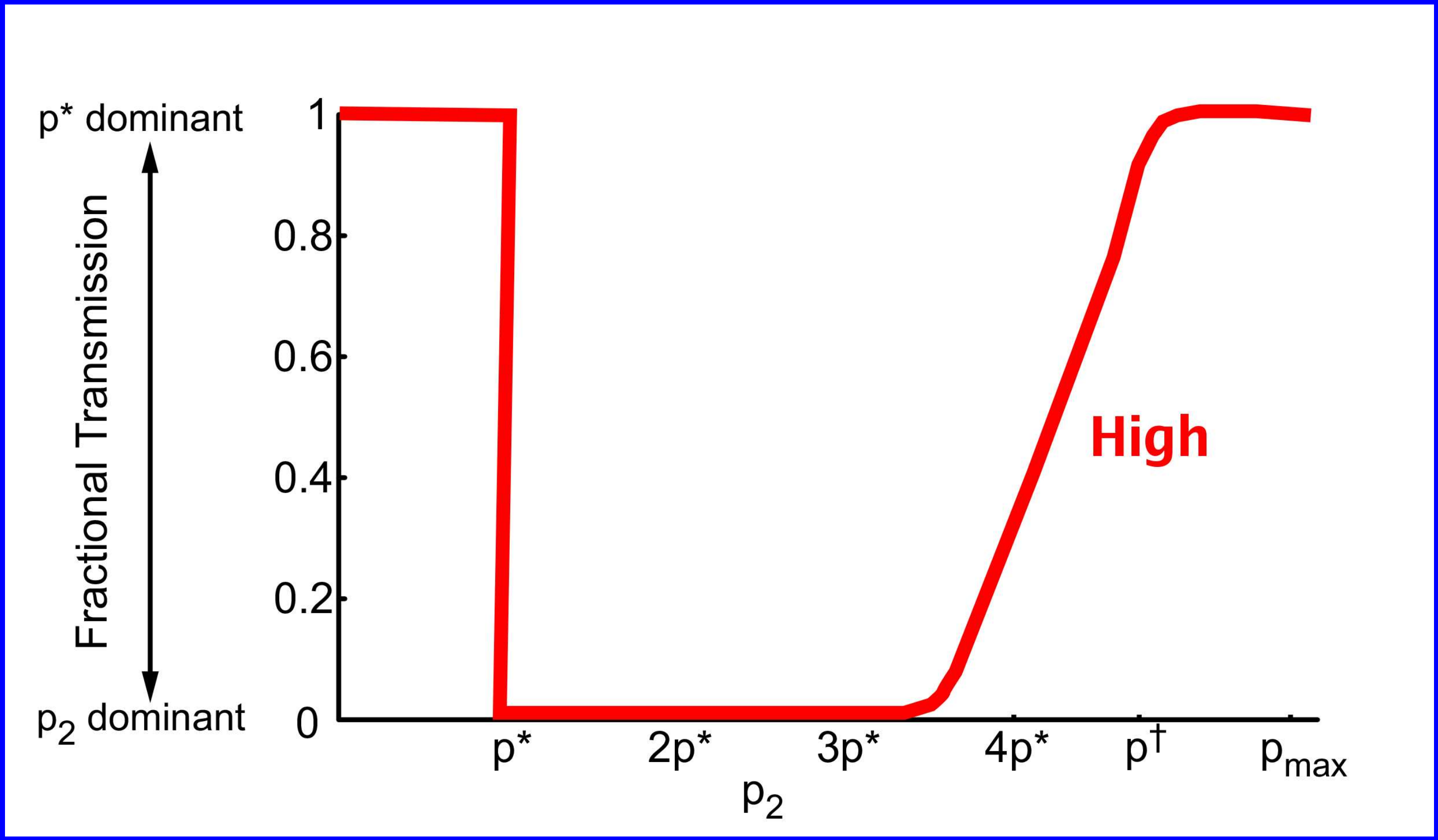
Result: Two distinct regions of coexistence



Resolving Within & Between-Host Selection

Scenario: High sensitivity to target cell T depletion

Result: One large region of coexistence



Resolving Within & Between-Host Selection

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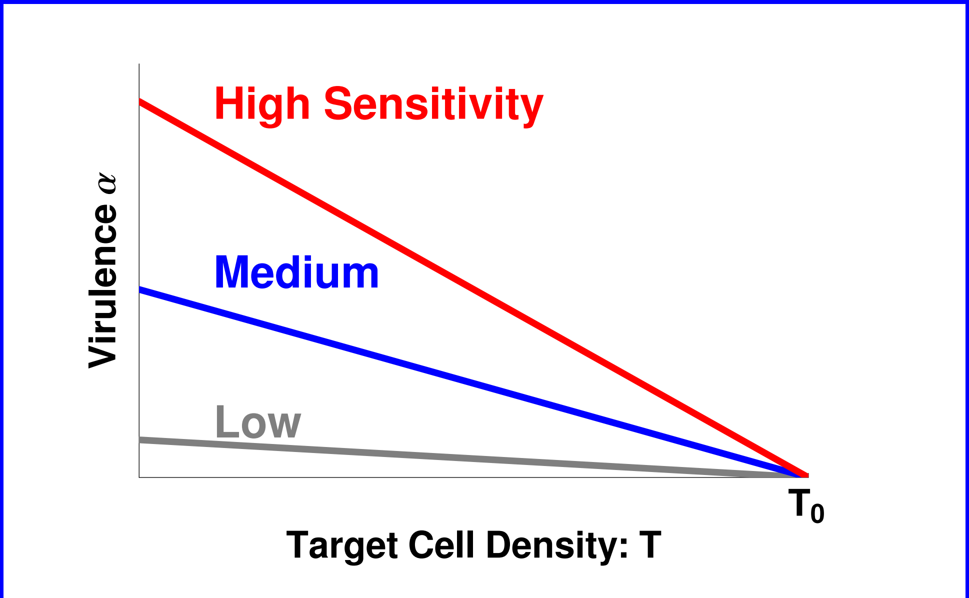
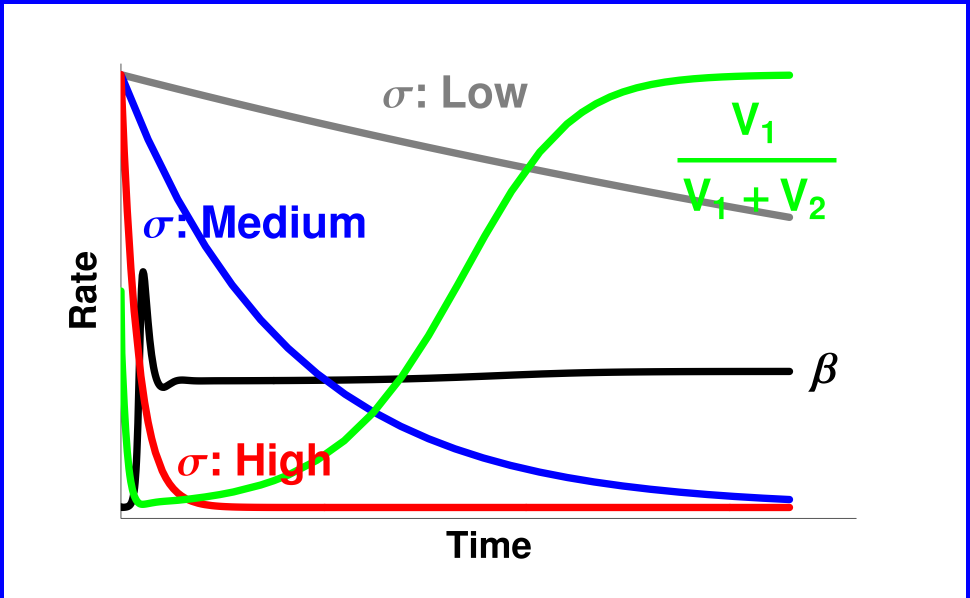
sensitivity of virulence α to target cell T depletion

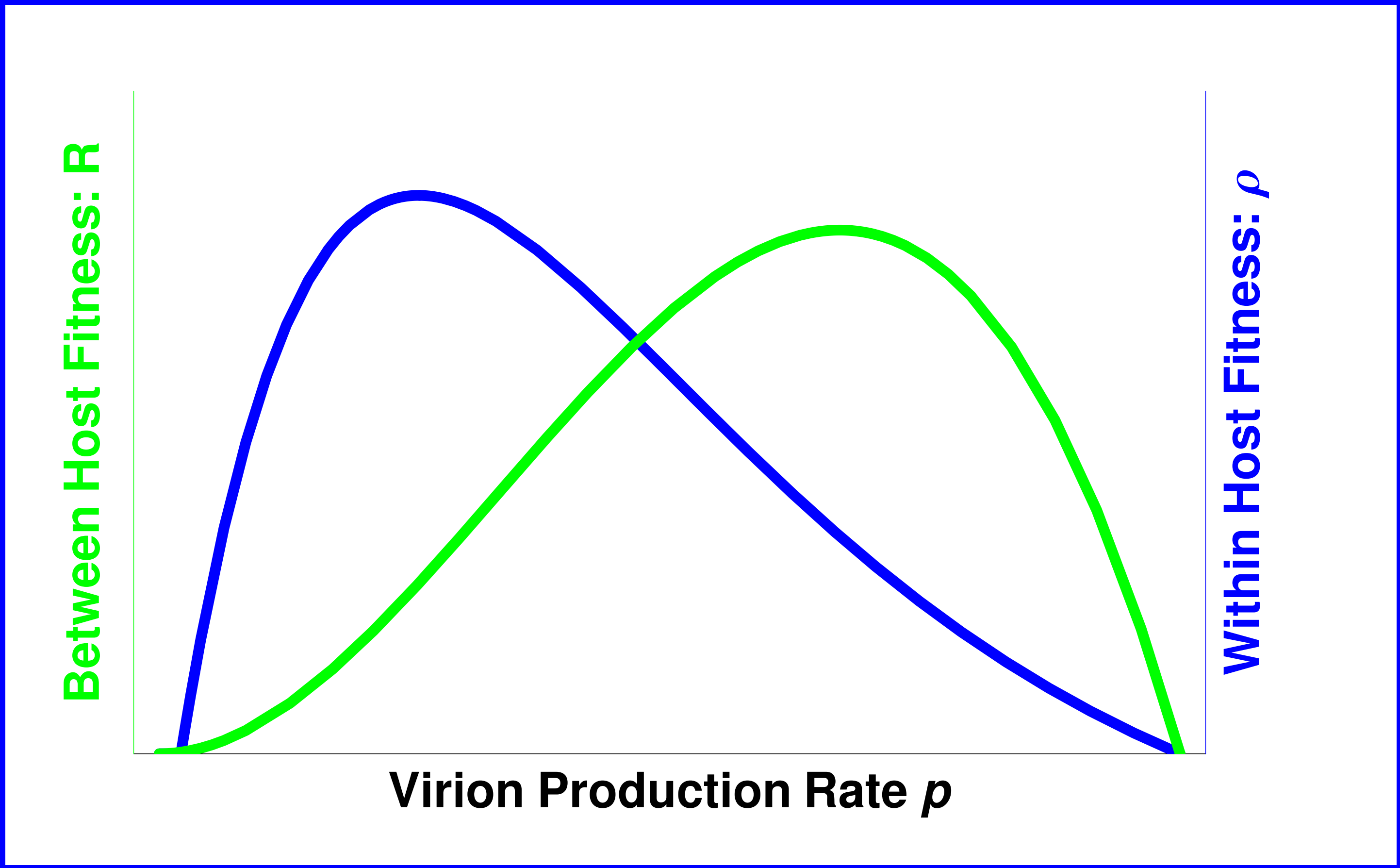




Resolving Within & Between-Host Selection

Conclusions

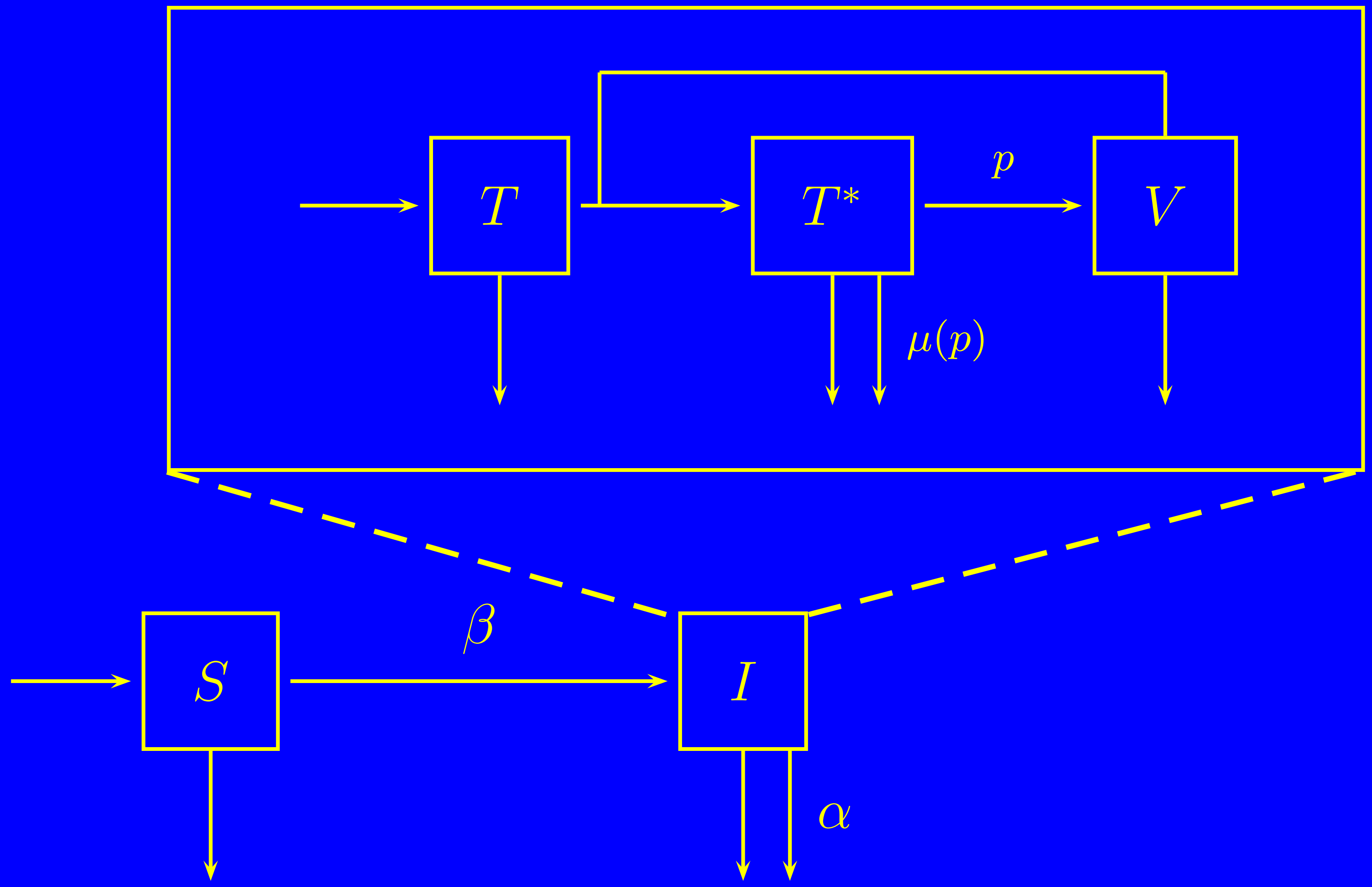
Conflict in selection at Within- and Between Host scales



Resolving Within & Between-Host Selection

Conclusions

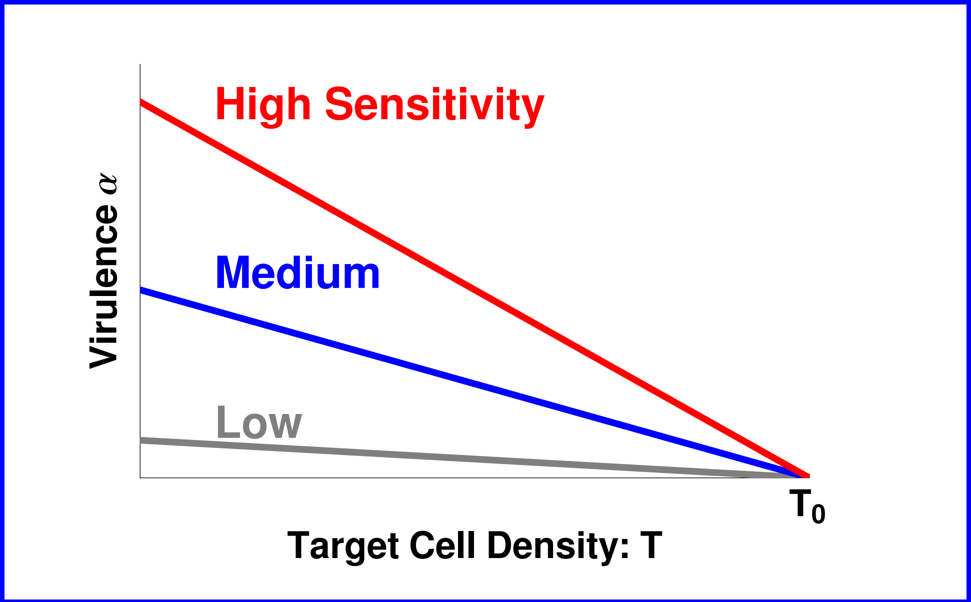
Nesting models allows us to examine conflict

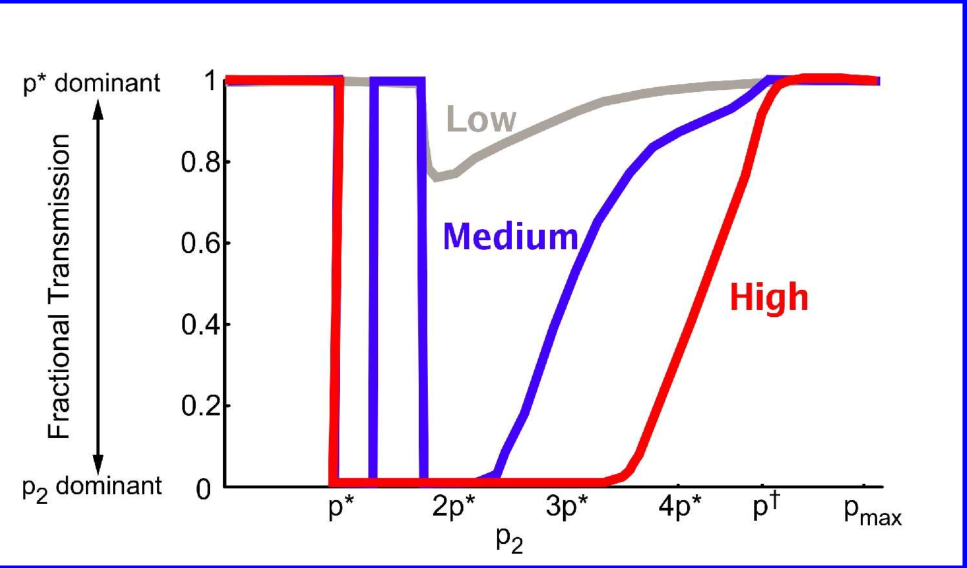


Resolving Within & Between-Host Selection

Conclusions

Range & behavior of coexistence depends on host sensitivity





Modeling Host-Parasite Coevolution

Overview

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Current Work

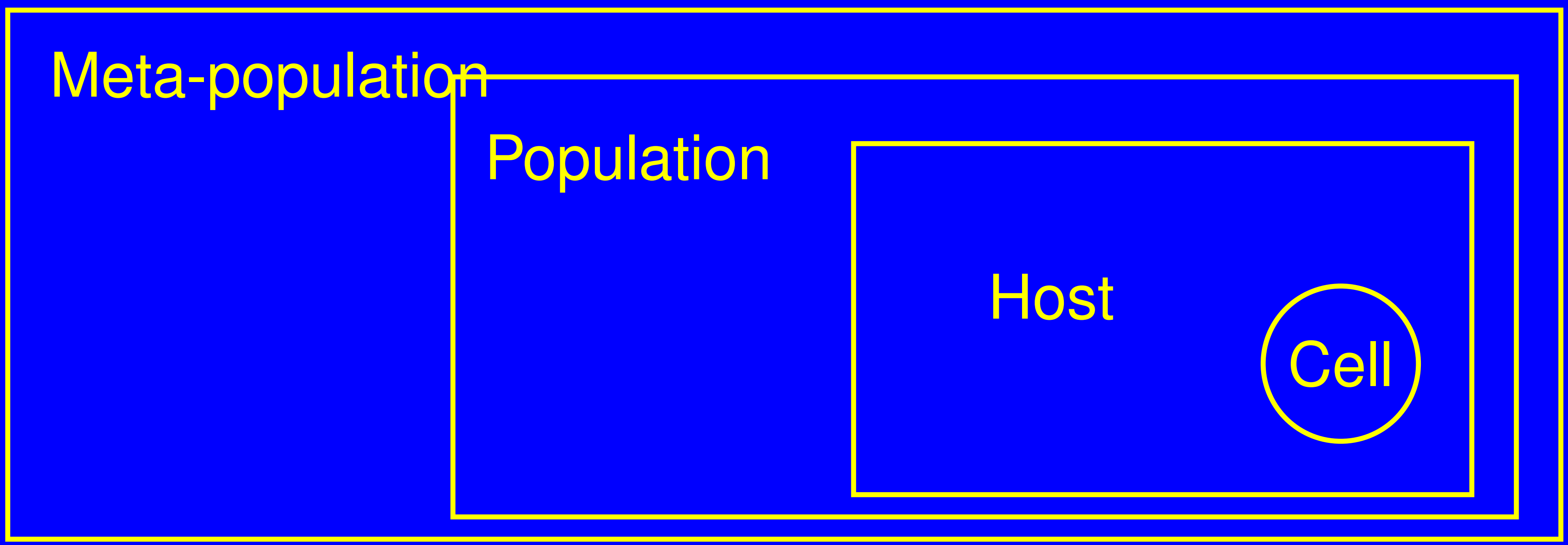
Future Work

Future Work

With Dan Coombs

- Add host immune response to model
- IR Trade-offs
  - Proliferation vs. Time lag
  - Sensitivity vs. Range of IR detection vs. Auto-immunity

Current Work: Levels of Selection



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