

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

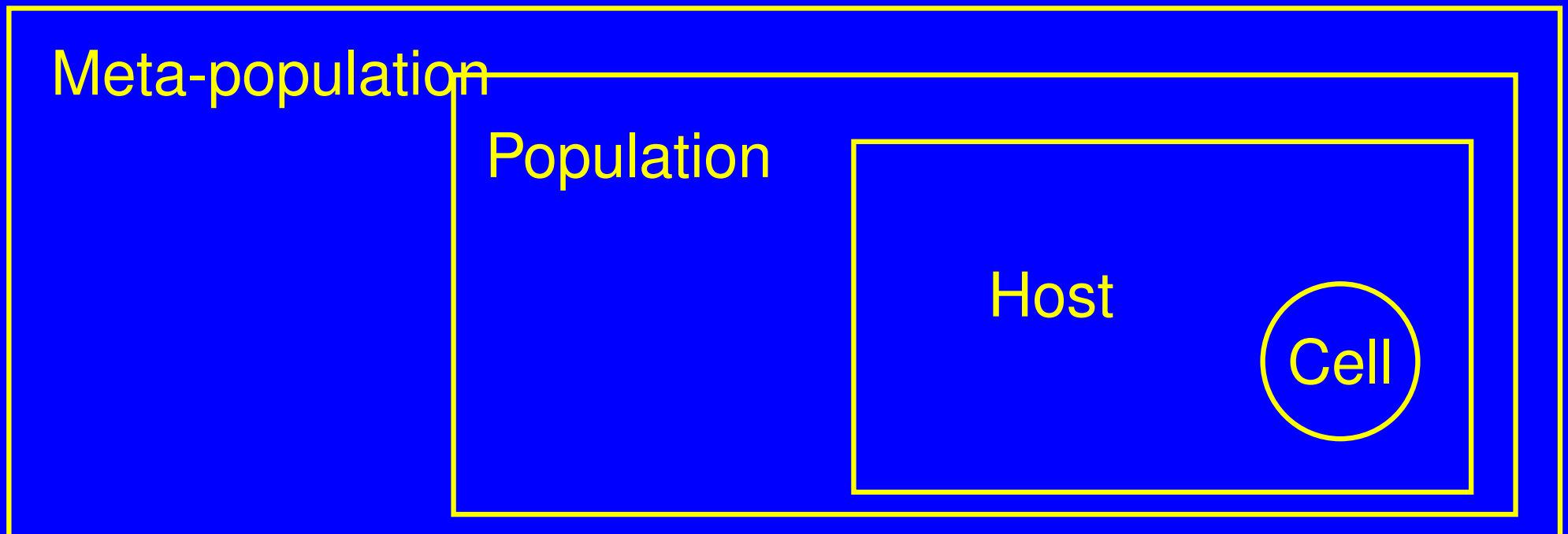
Modeling Host-Parasite Coevolution: Overview

Evolvable Host Parameters

- Behavior
 - Can affect mechanism and rate of exposure
- Immune Response
 - Background level (inade immunity, naive CTL density)
 - Sensitivity (ability to detect non-self vs. accidental triggering)
 - Proliferation rate (activation of specific & non-specific IR)
- Sensitivity to resource/target cell loss

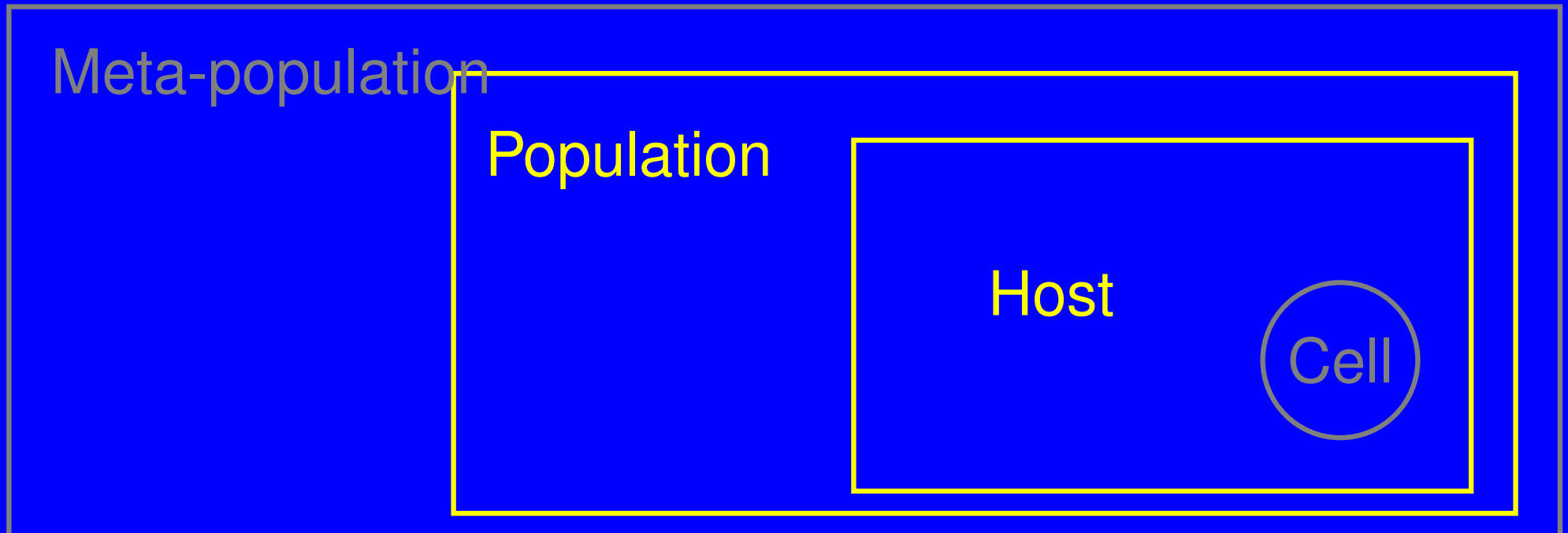
Modeling Host-Parasite Coevolution: Overview

Nested Model Approach



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Nested Model Approach



Modeling Host-Parasite Coevolution

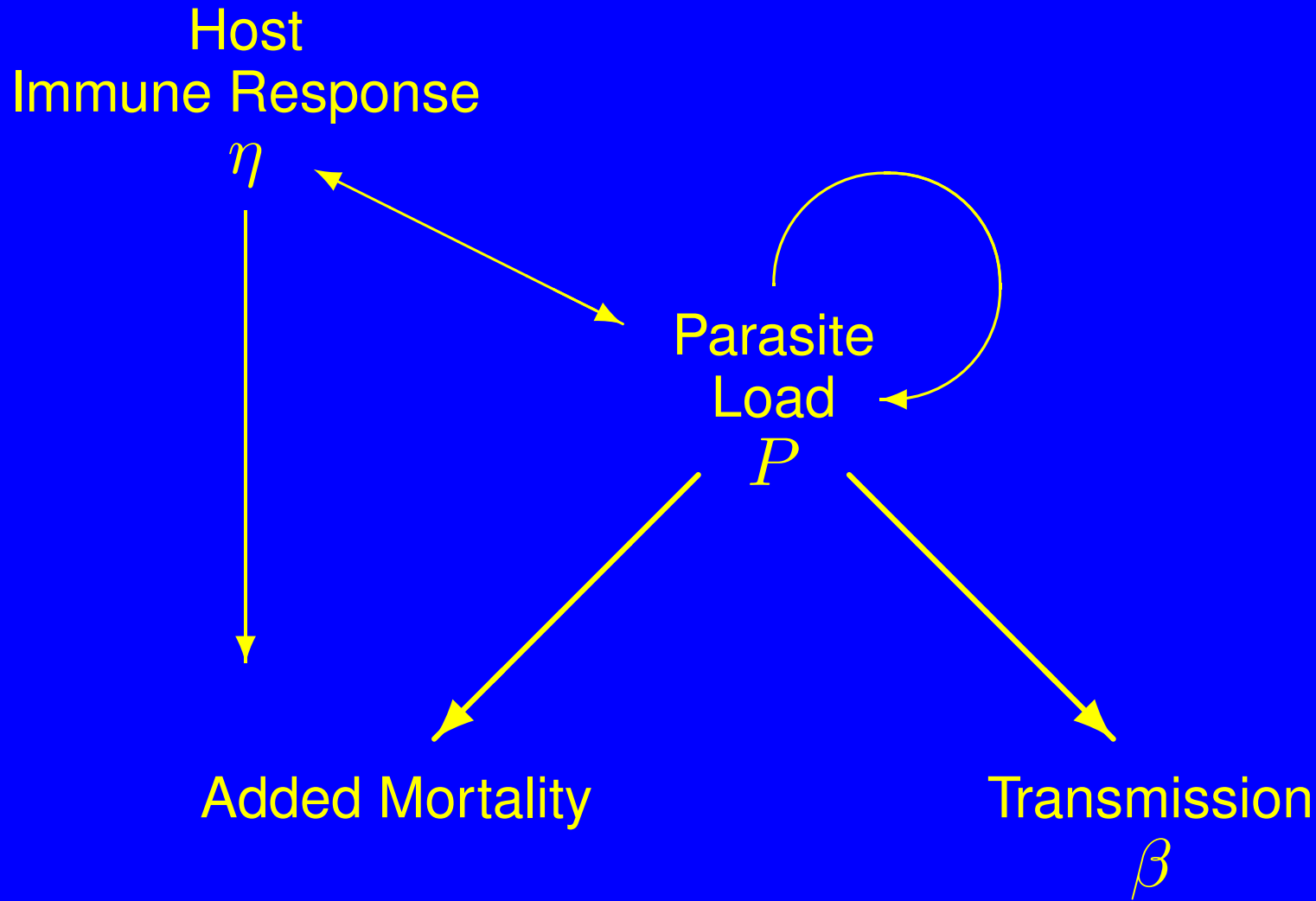
Overview

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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

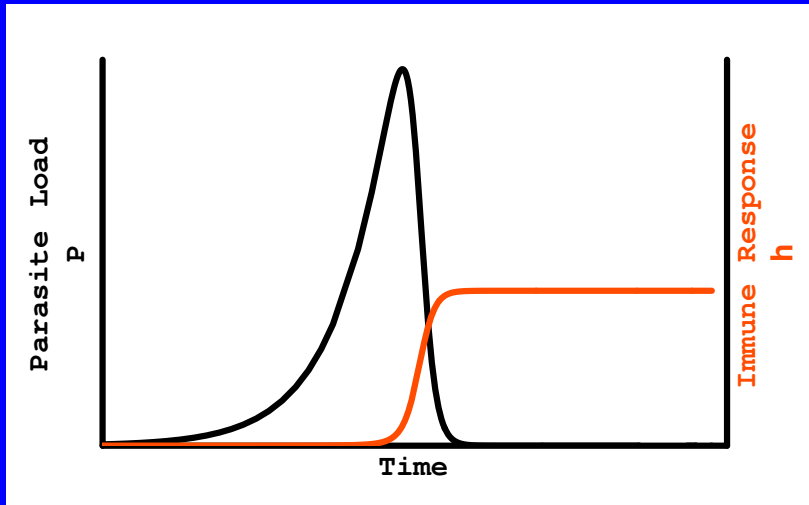
$$\frac{dP}{dt} = (b - \eta)P$$

b = Parasite birth rate

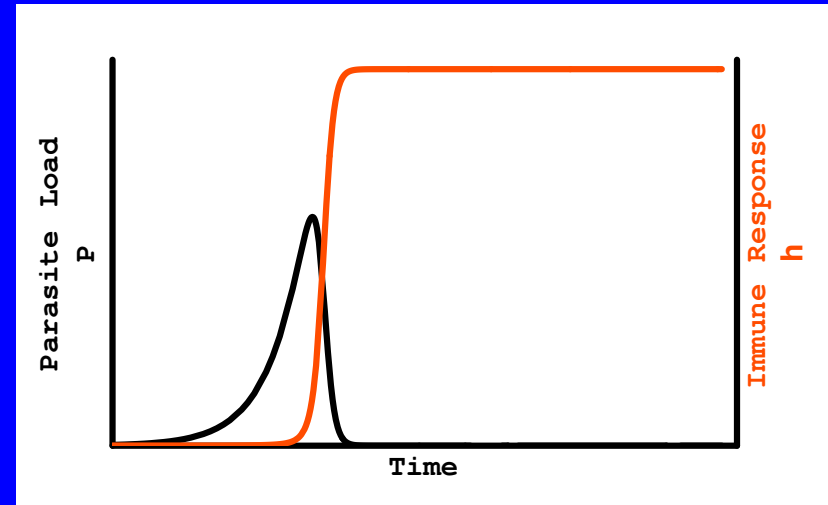
η = Host immune response

Within-Host Dynamics

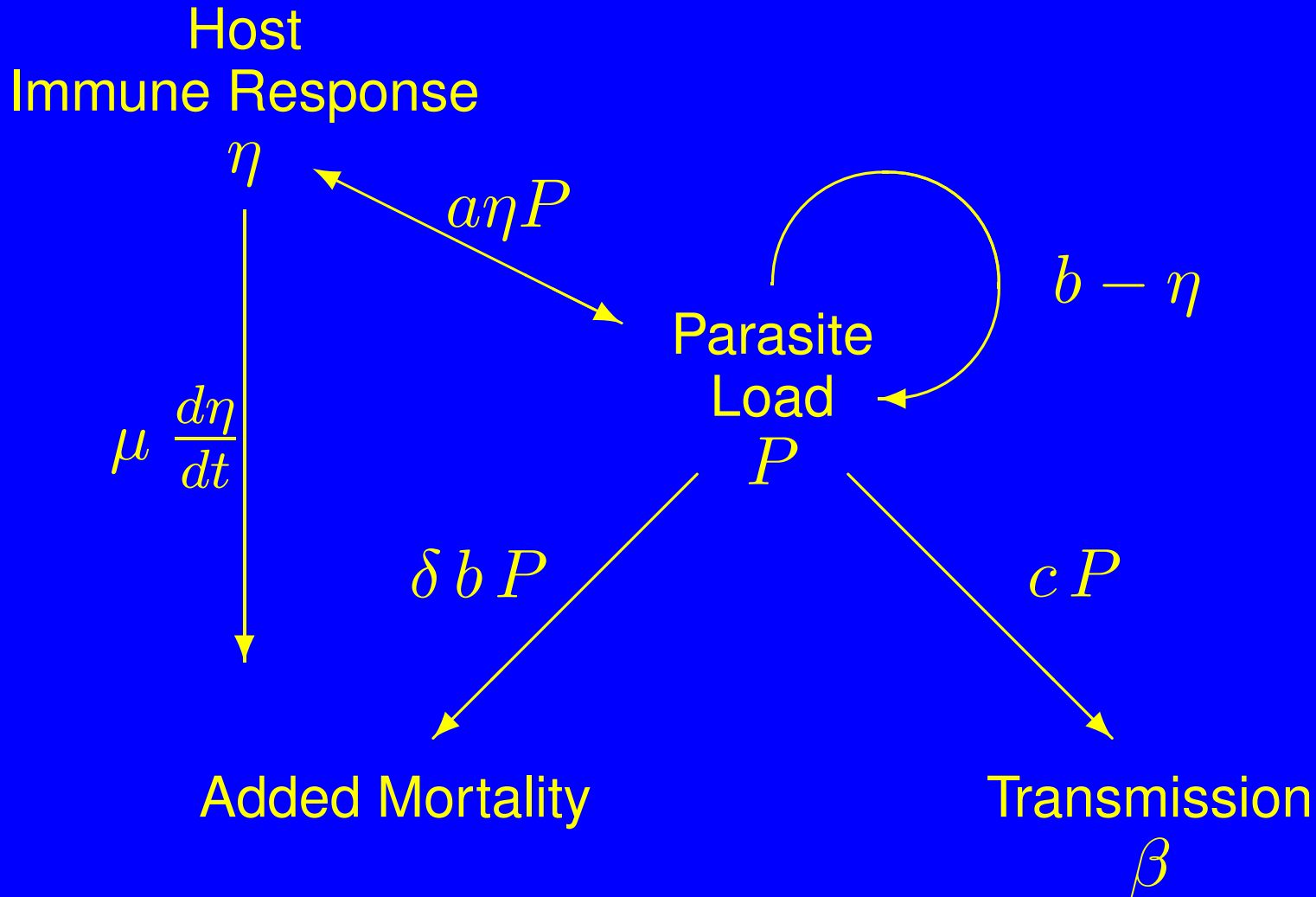
Low Activation/Replication



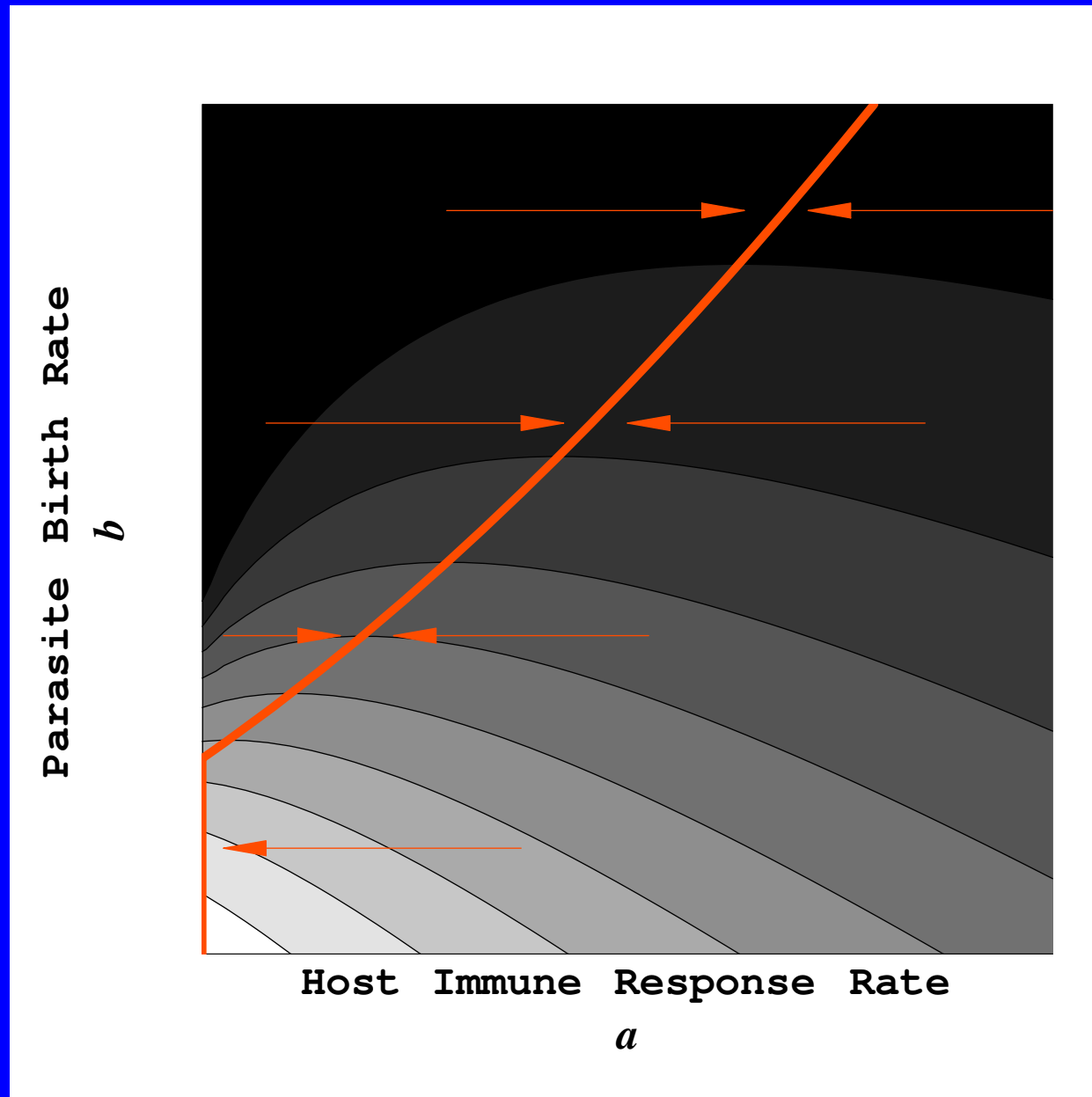
High Activation/Replication



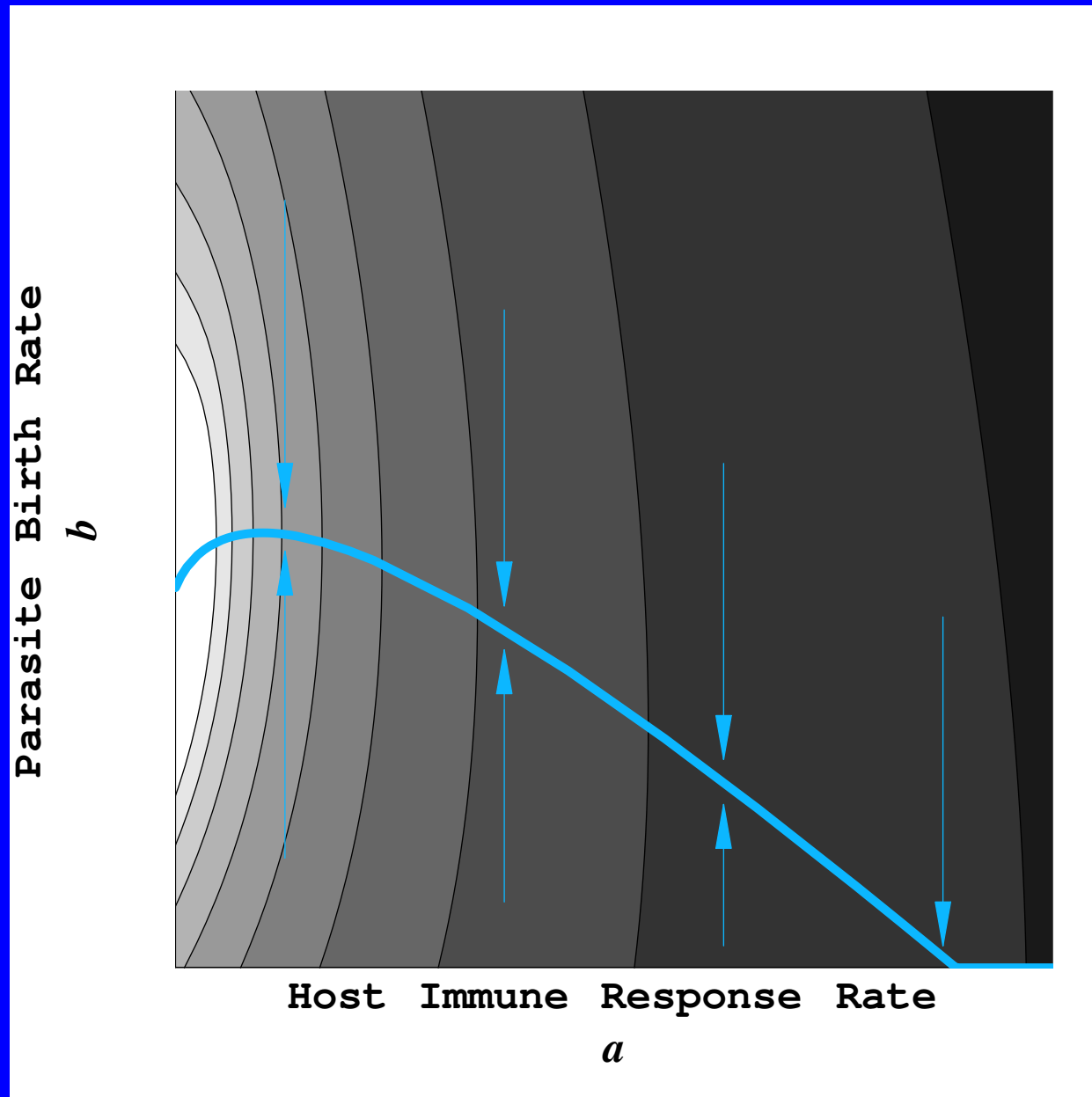
Link Within-Host Dynamics to Between-Host Parameters



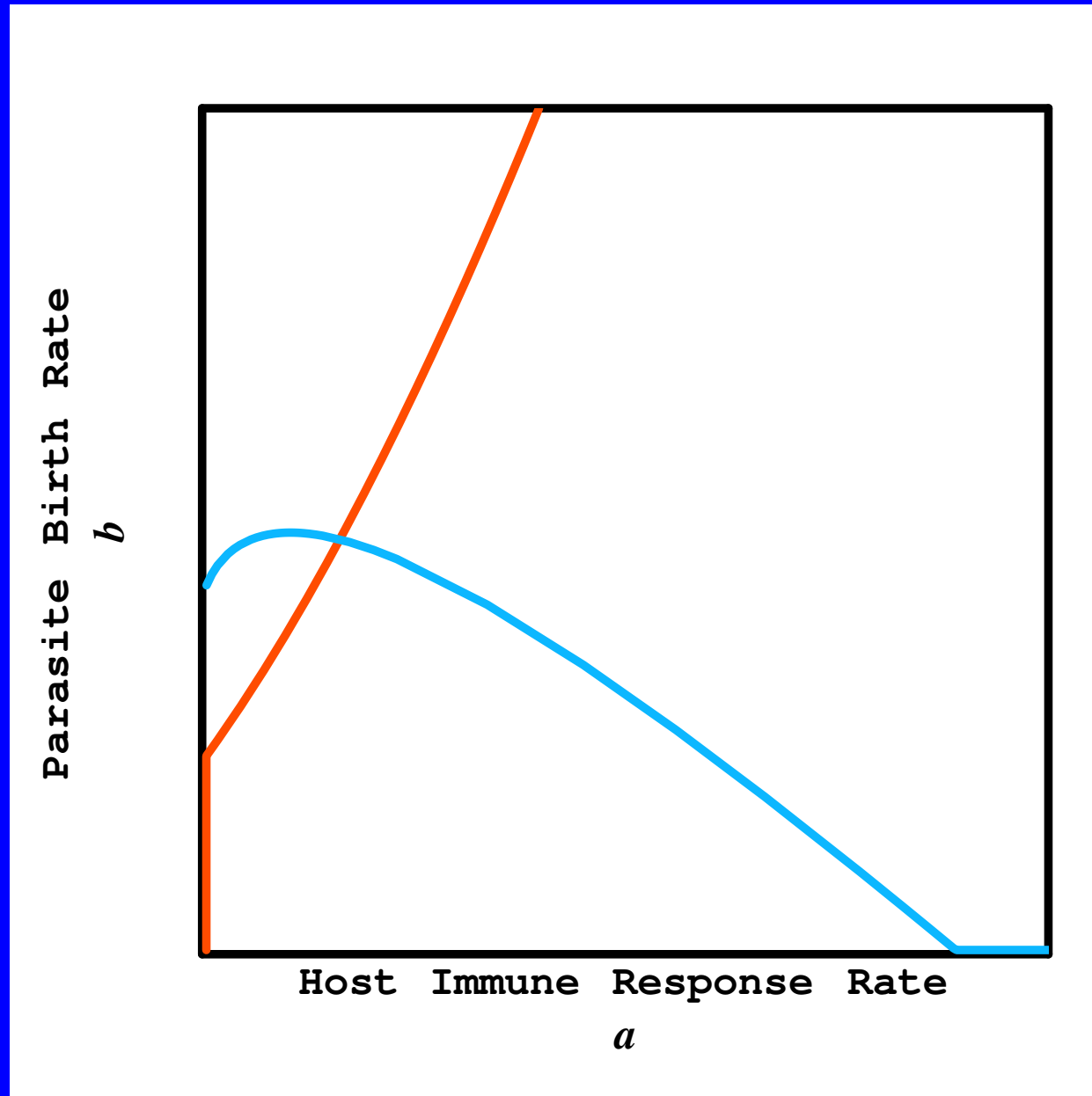
Host Fitness Landscape and Optimal a vs. b



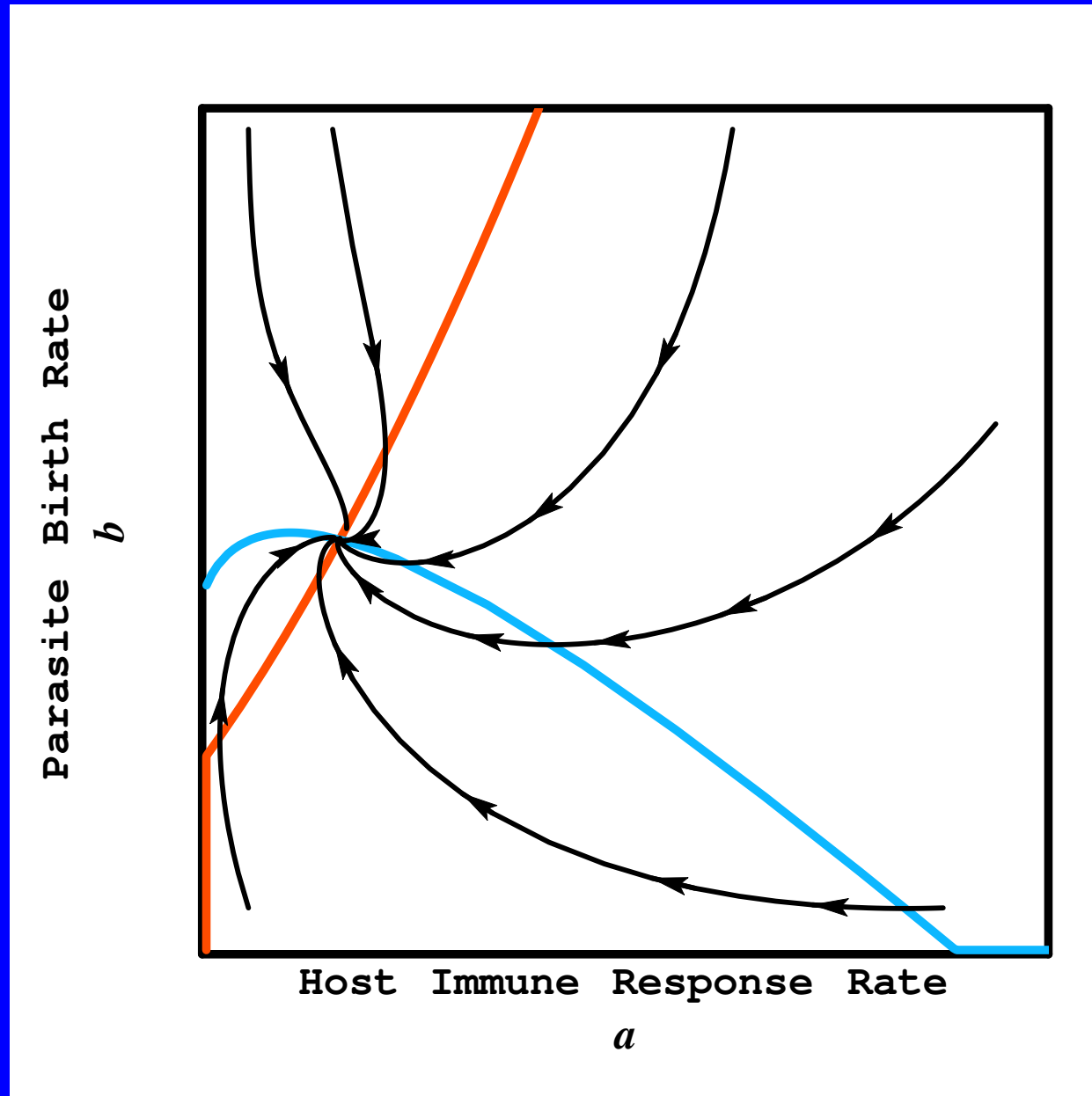
Parasite Fitness Landscape and Optimal a vs. b



Host-Parasite Coevolution



Host-Parasite Coevolution



Modeling Host-Parasite Coevolution

Overview

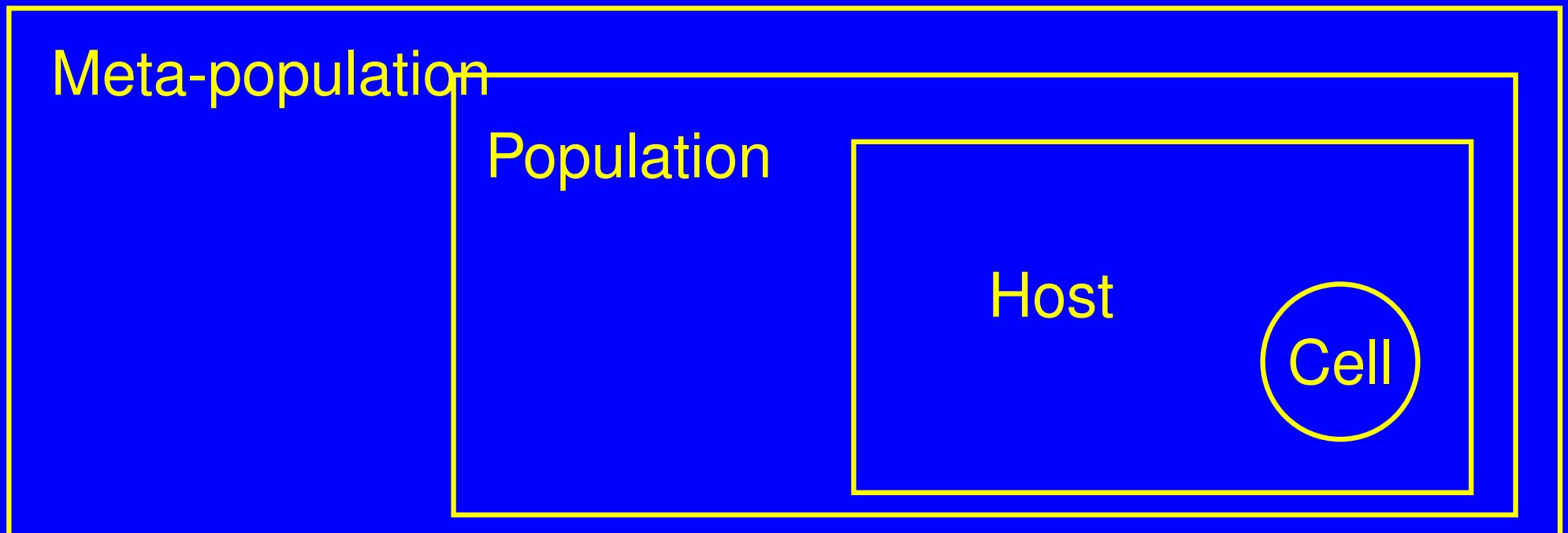
Previous Work

Current Work

Future Work

Current Work: Levels of Selection

With Dan Coombs and Collen Ball



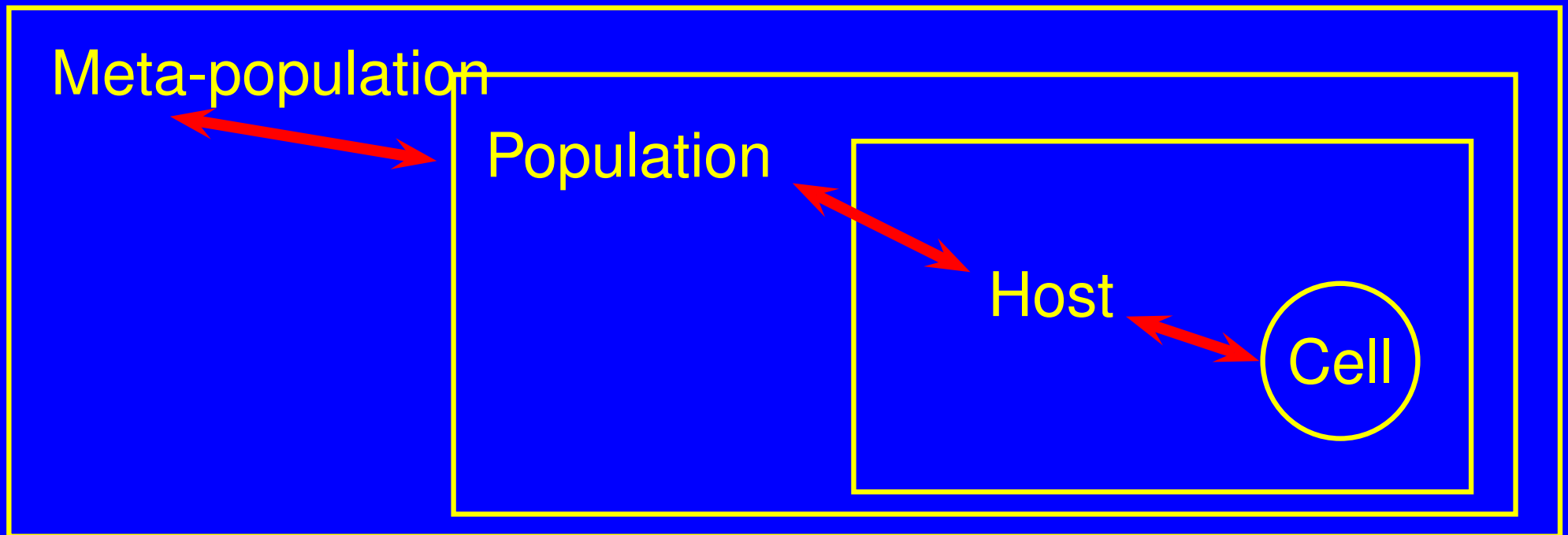
Levels of Selection: Conflict?

Meta-population: low virulence

Population: intermediate virulence

Host: high virulence

Cell: low virulence



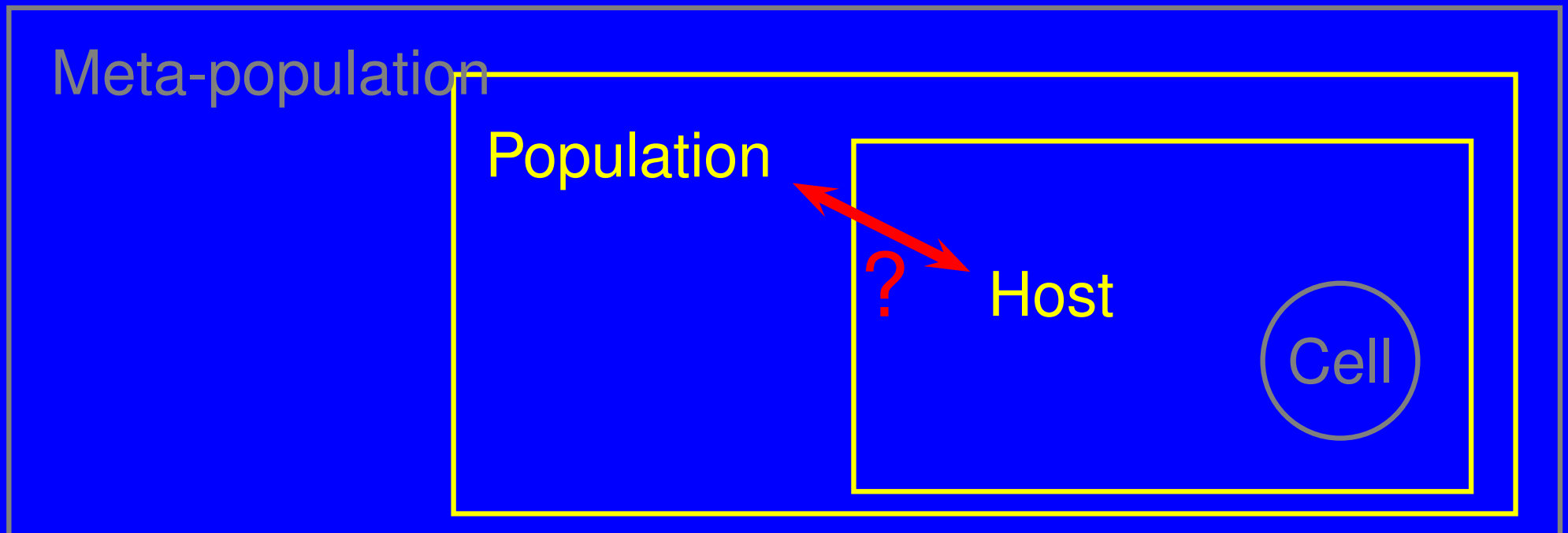
Levels of Selection: Conflict?

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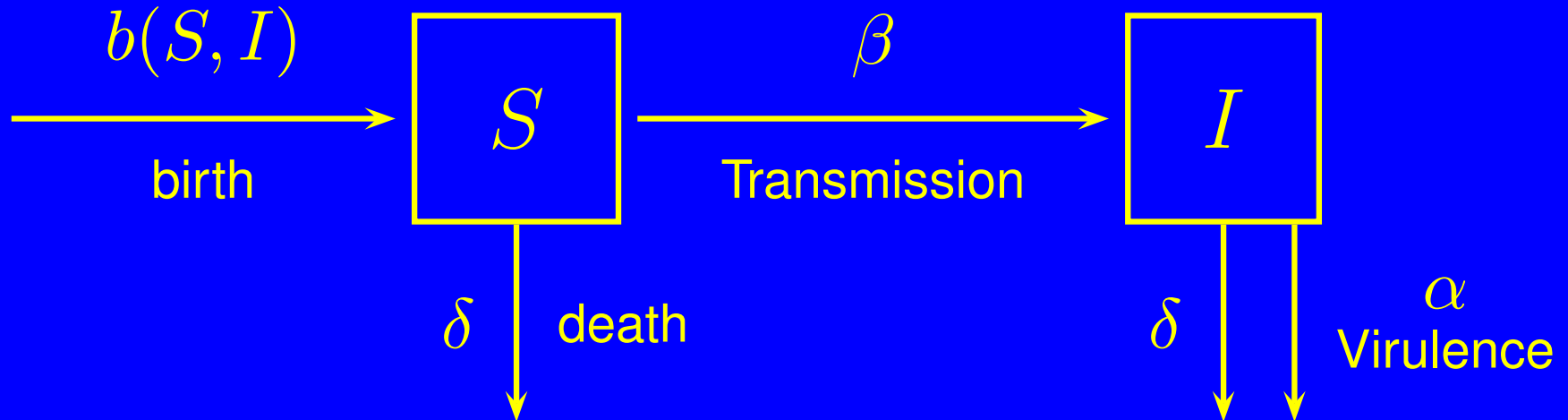
Between-Host Model & Selection

- Epidemiological model of Susceptible and Infectious hosts

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

$$dI/dt = \beta SI - (\alpha + \delta)I$$

Population



Host Population: Between-Host Selection

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

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

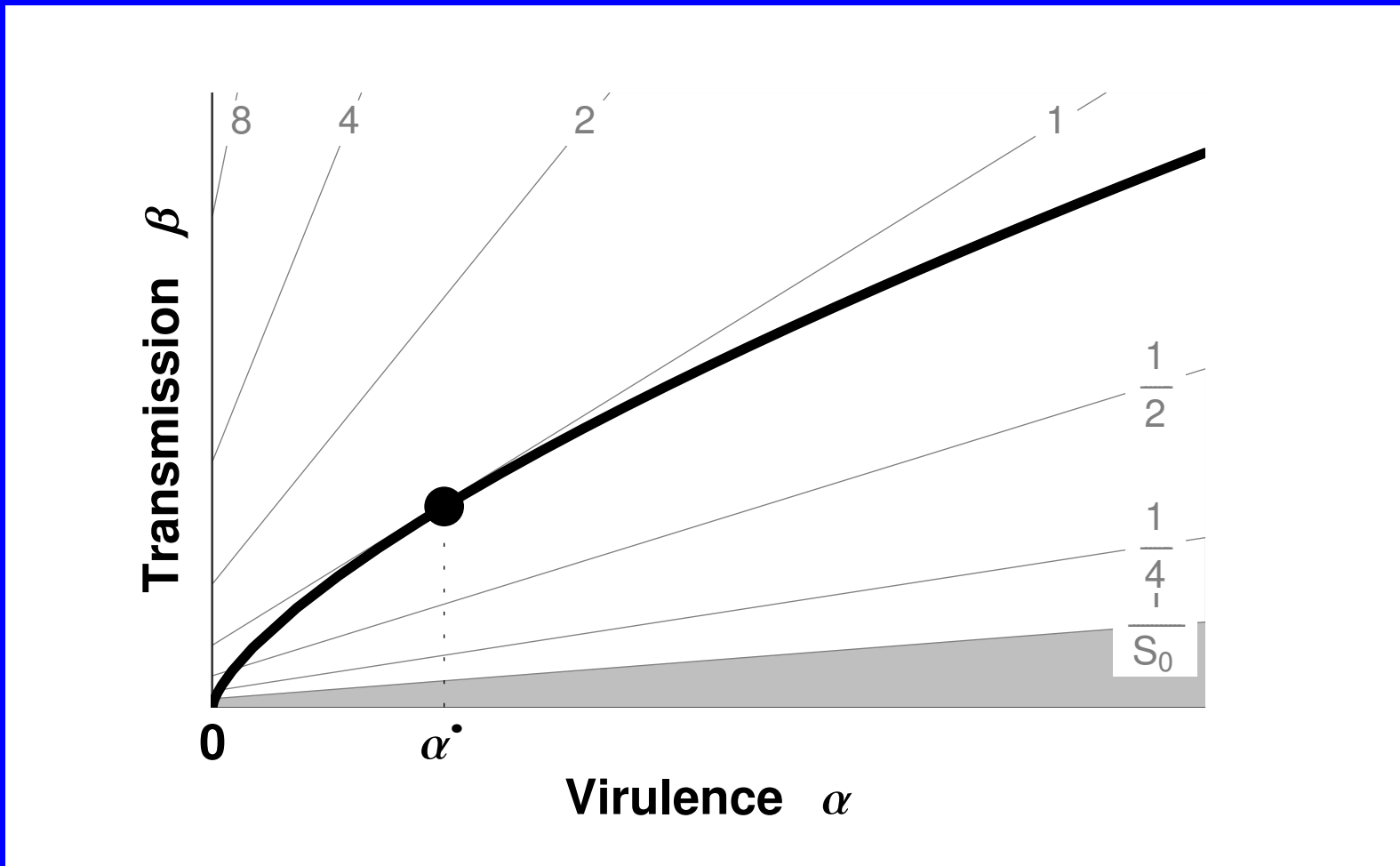
- Strain which maximizes R
 - Minimizes \hat{S}
 - Will competitively exclude other competitors.

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

Between-Host Model & Selection

Maximizing R depends on relationship between β and α .

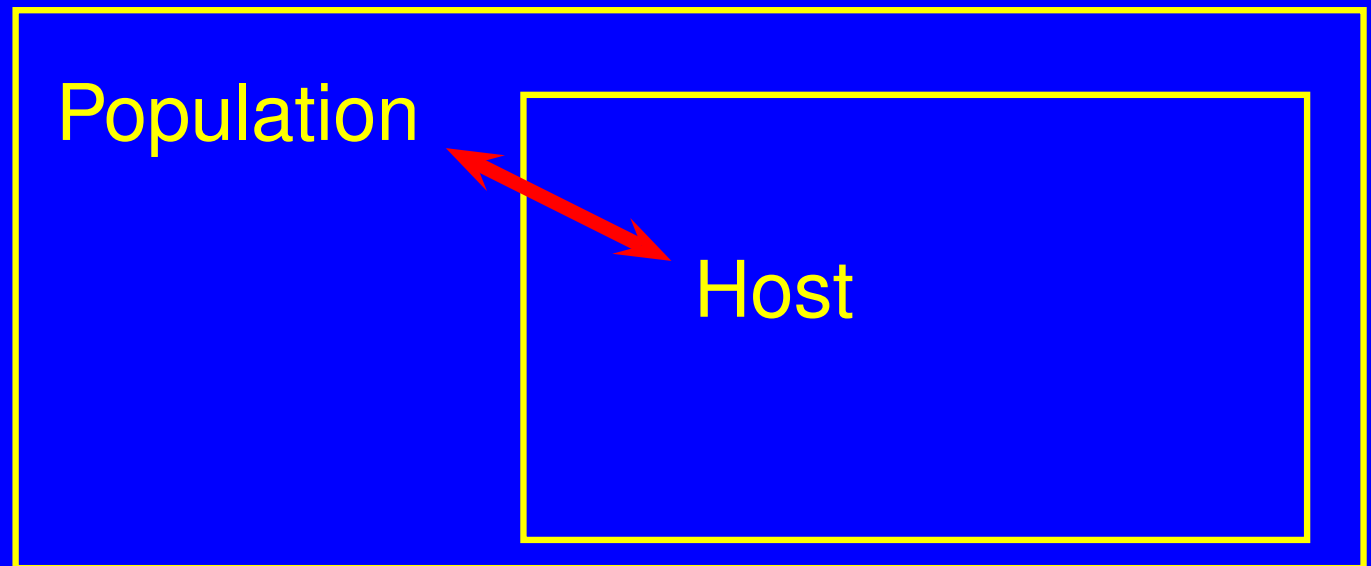
Bremermann & Pickering (1982), Lenski & May (1994), Frank (1996)



Levels of Selection

Between-Host Selection: Favors maximization of R

Within-Host Selection: ?



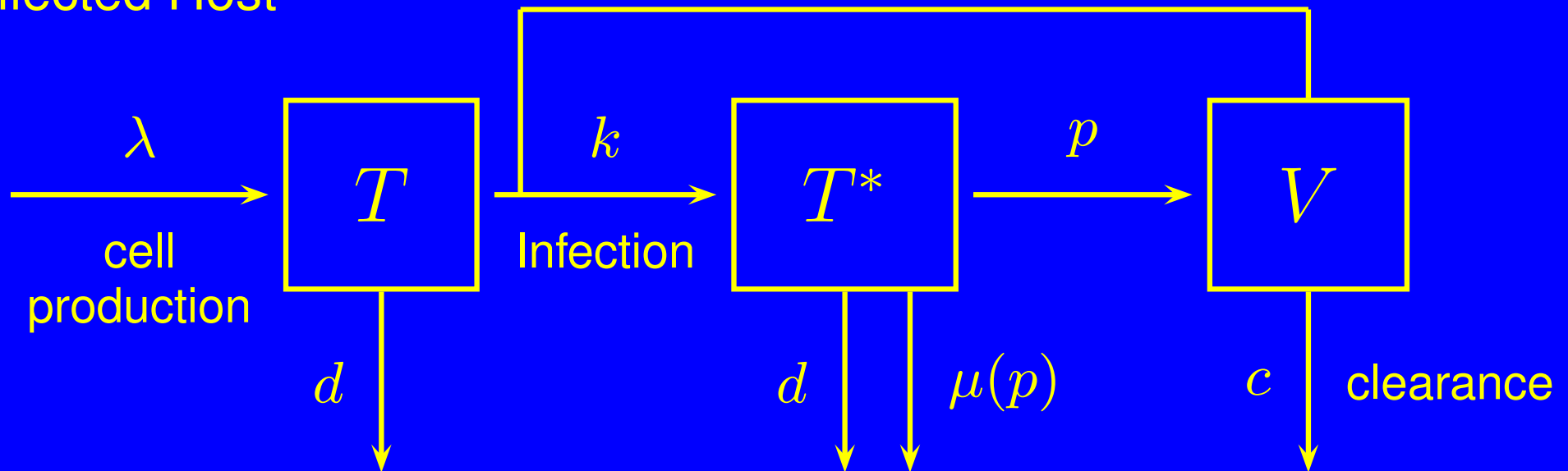
Within-Host Model & Selection

$$dT/dt = \lambda - kVT - dT$$

$$dT^*/dt = kVT - (\mu(p) + d)T^*$$

$$dV/dt = pT^* - cV,$$

Infected Host



Within-Host Model: Two Strains

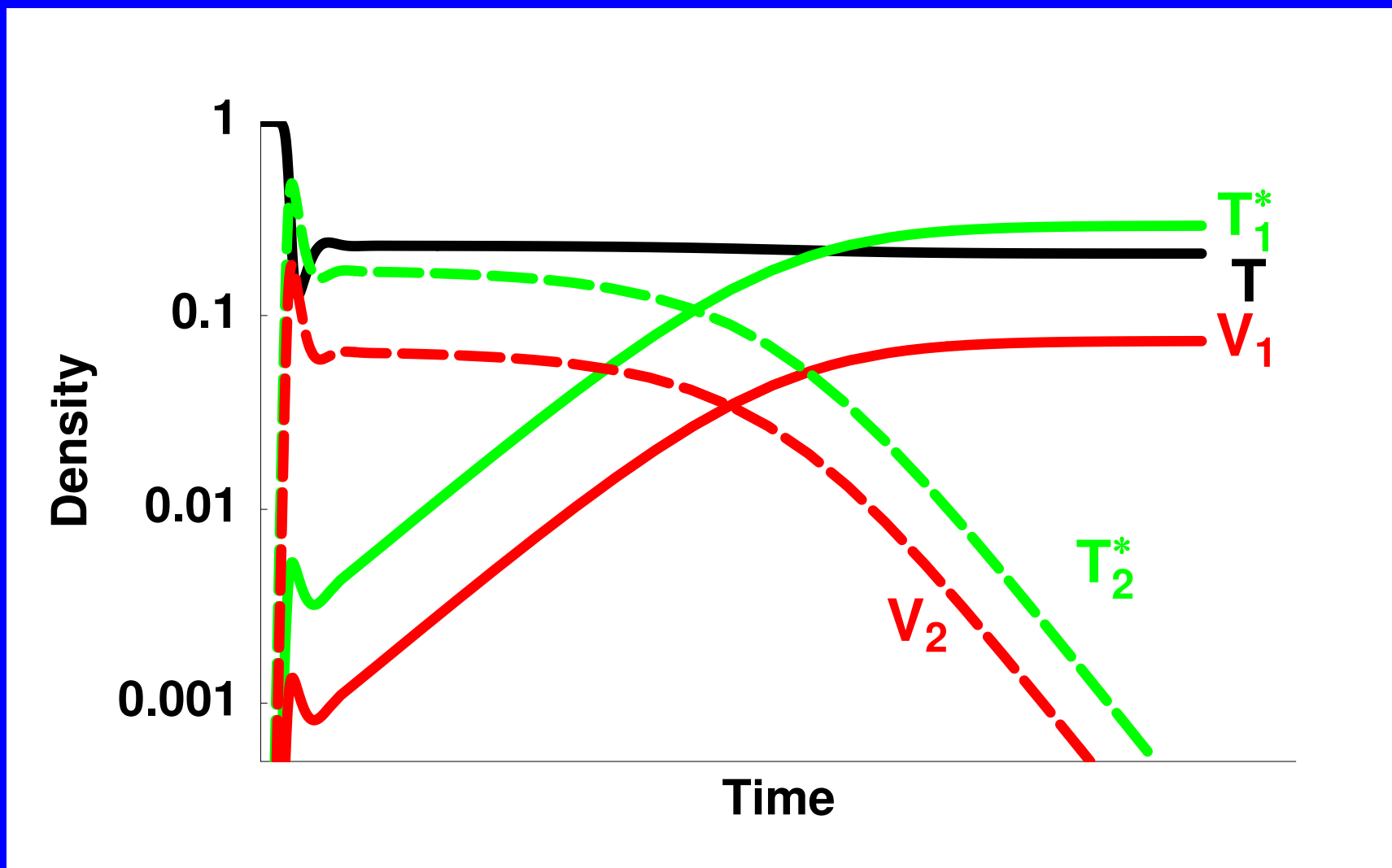
Expand model to include second strain within a host

$$\begin{aligned}dT/dt &= \lambda - k(V_1 + V_2)T - dT \\dT_i^*/dt &= kV_iT - (\mu(p_i) + d)T_i^* \\dV_i/dt &= p_iT_i^* - cV_i\end{aligned}$$

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

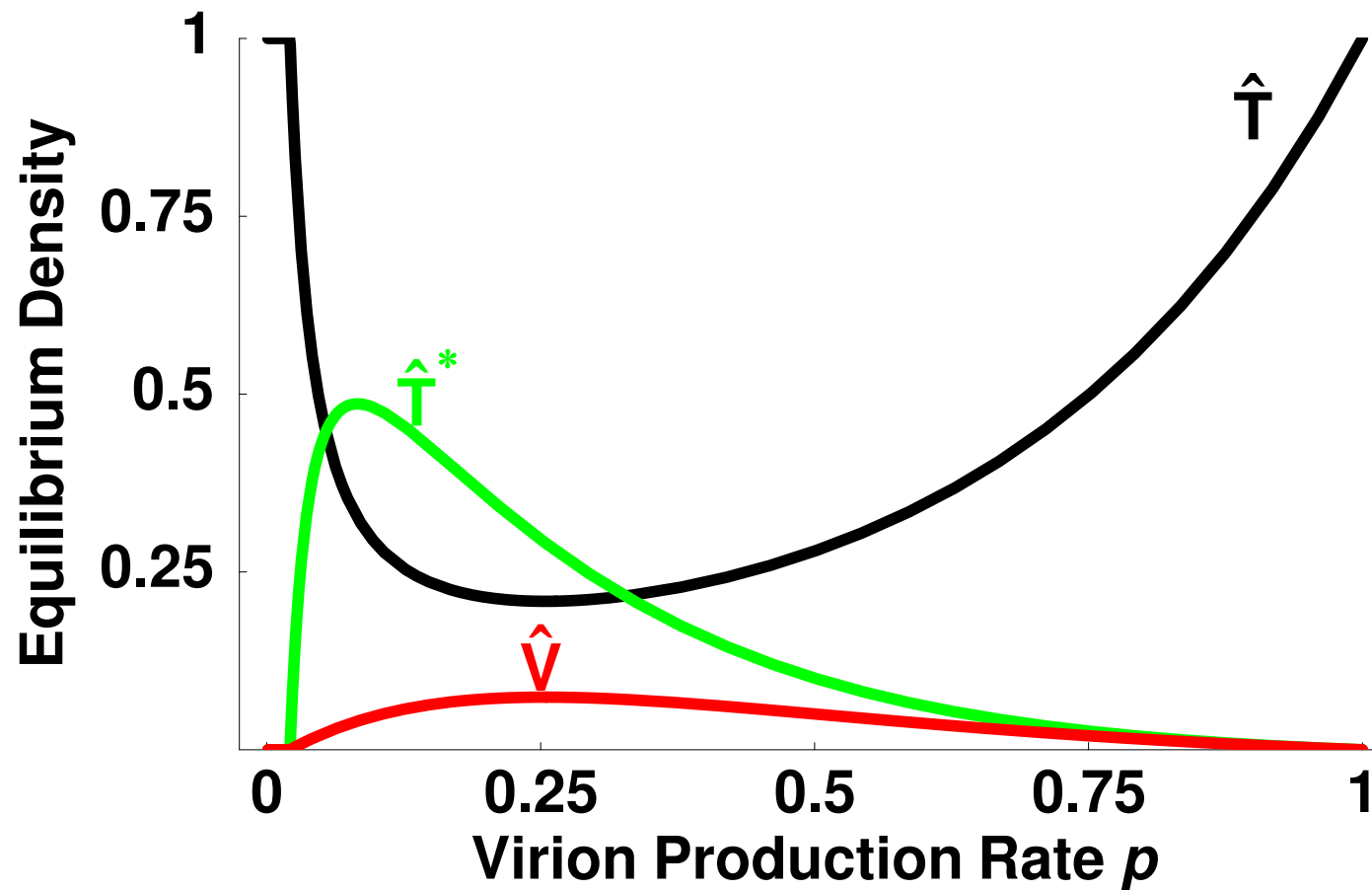
Within-Host Model: Two Strains

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 :

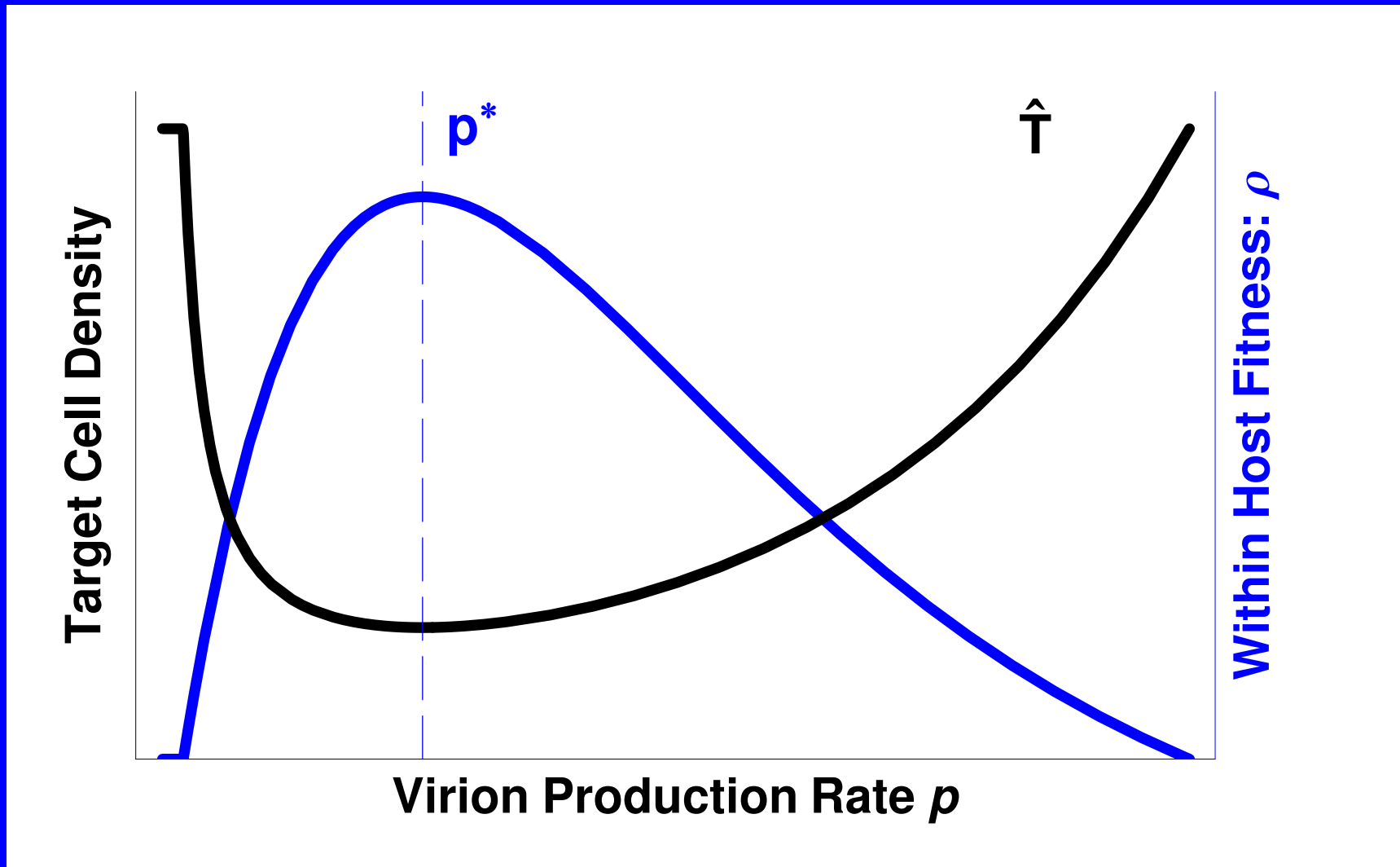
$$\begin{aligned}\rho &= \frac{k}{c} \frac{p}{\mu(p) + d} \\ &= \frac{1}{\hat{T}}\end{aligned}$$

- 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

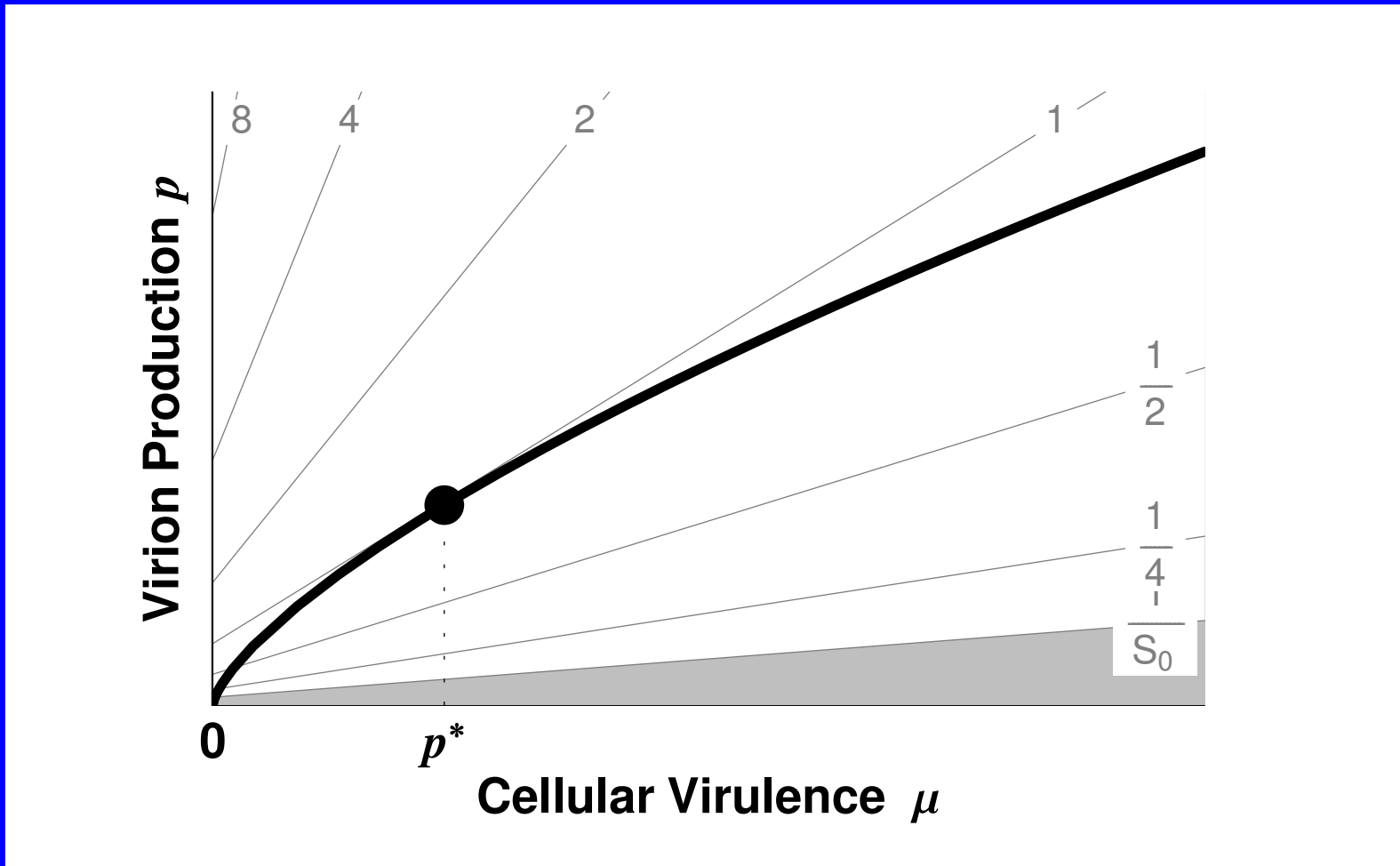
$\text{Min}(\hat{T}(p^*)) = \text{Within-Host Optimum}$



Within-Host Model & Selection

Maximizing ρ depends on relationship between μ & p .

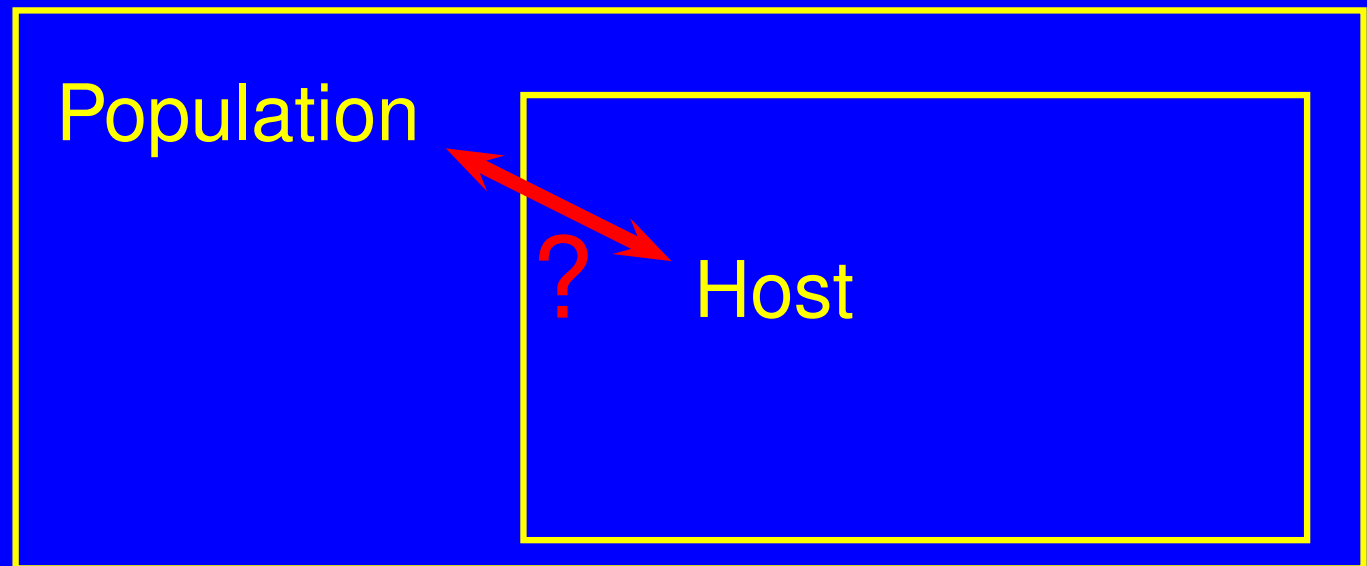
Coombs *et al.*(2003)



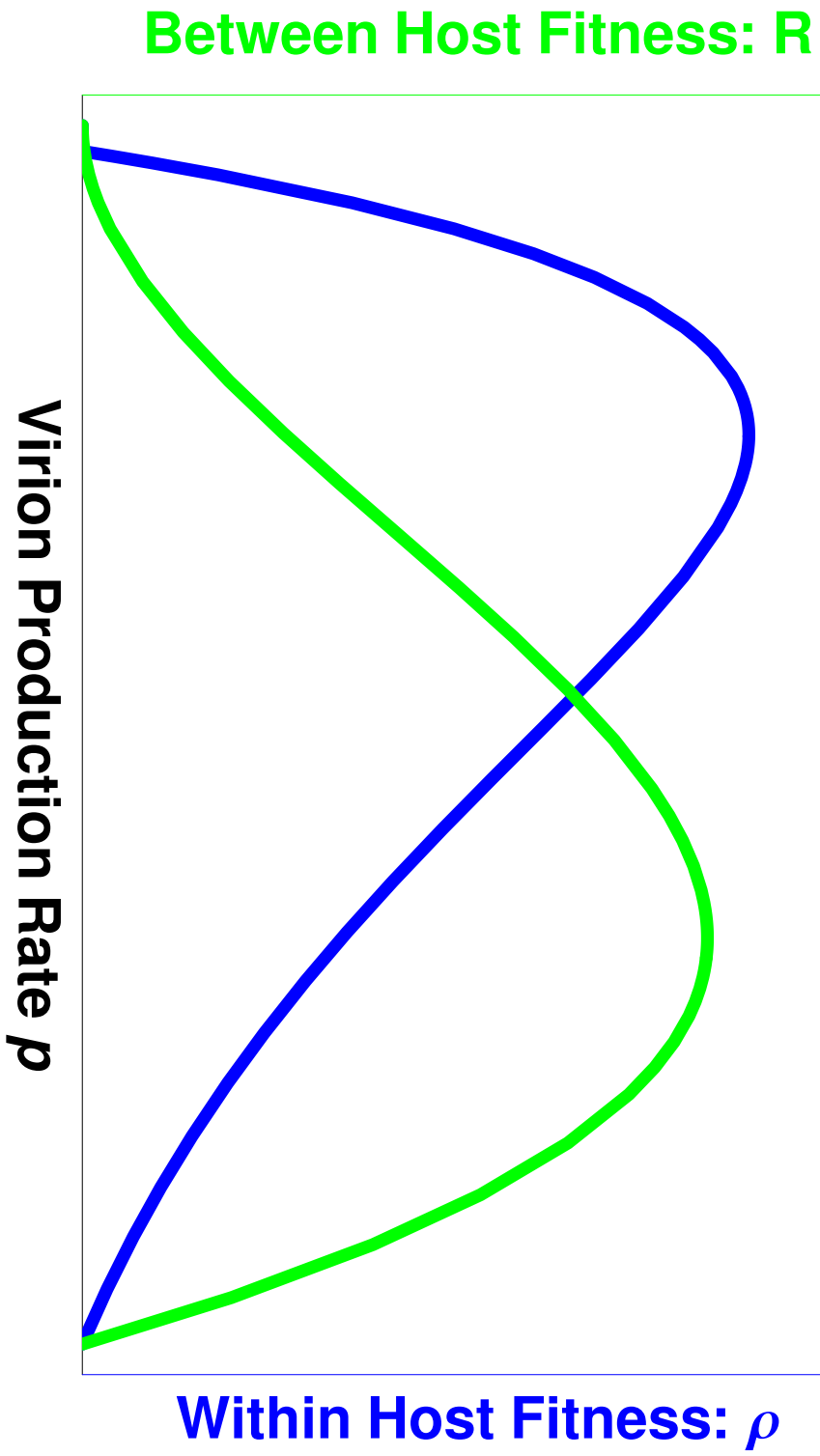
Levels of Selection

Between-Host Selection: Favors maximization of R

Within-Host Selection: Favors maximization of ρ

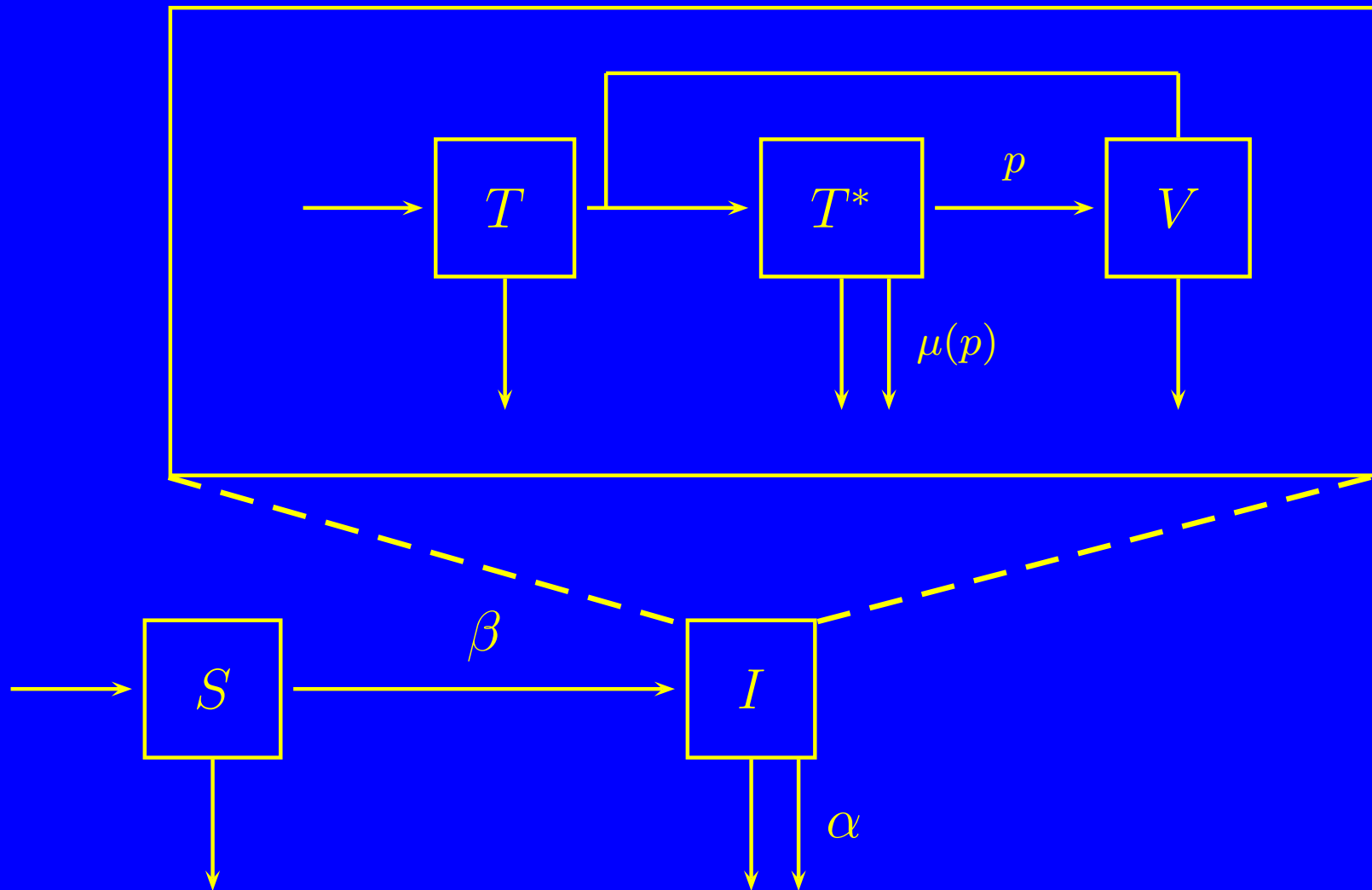


Possible Conflict?



Nesting Models: Linking Within & Between-Host

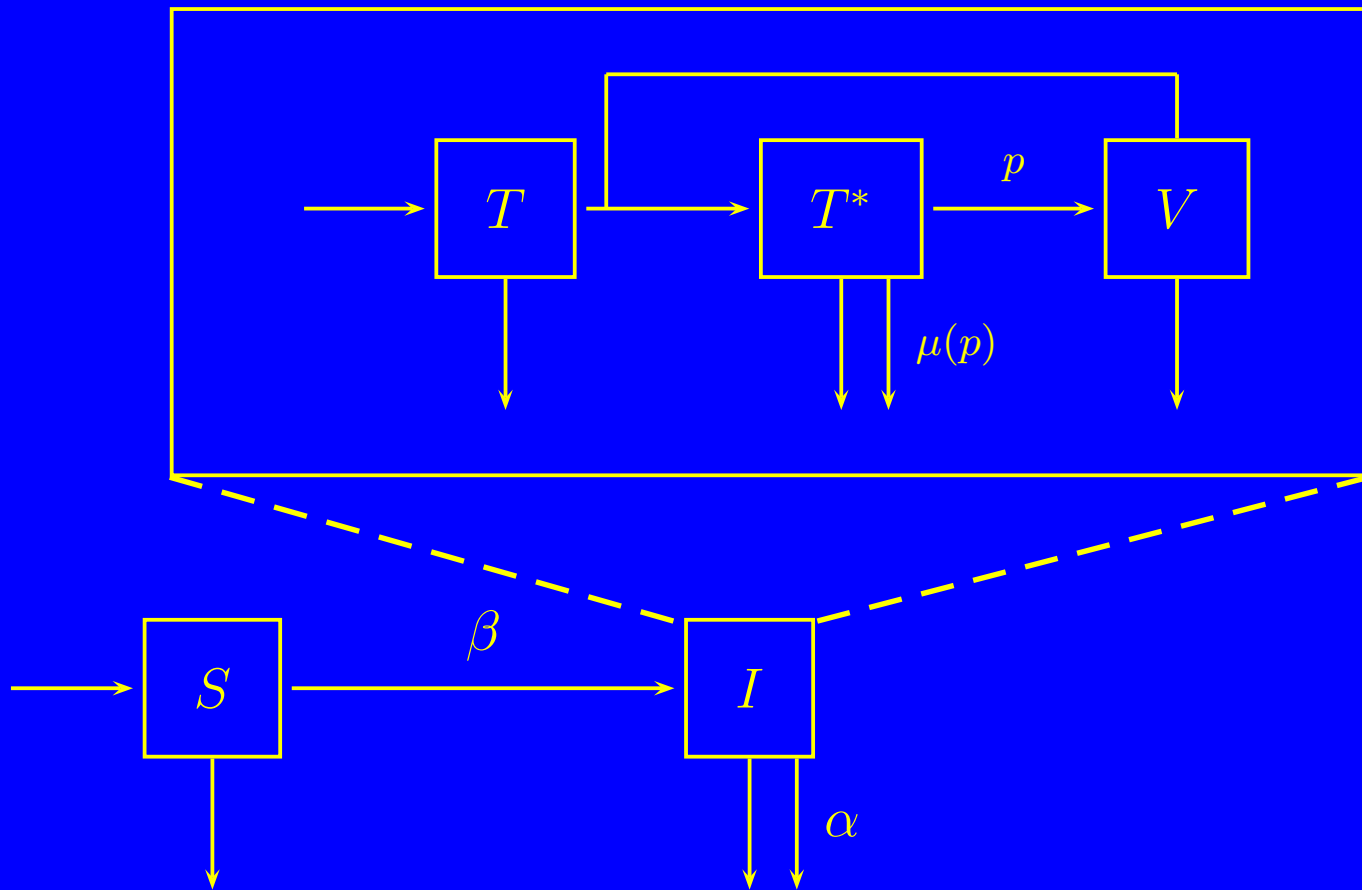
Nest model of **within-host** processes inside a model of **between-host** processes



Nesting Models: Linking Within & Between-Host

$$\alpha(T) = a_1 (T_0 - T)$$

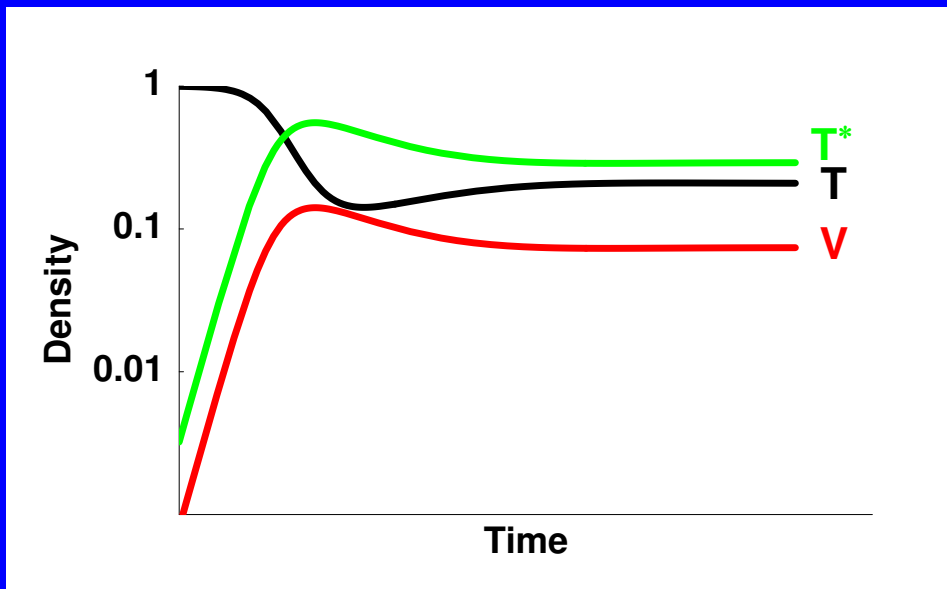
$$\beta(V) = b_1 V$$



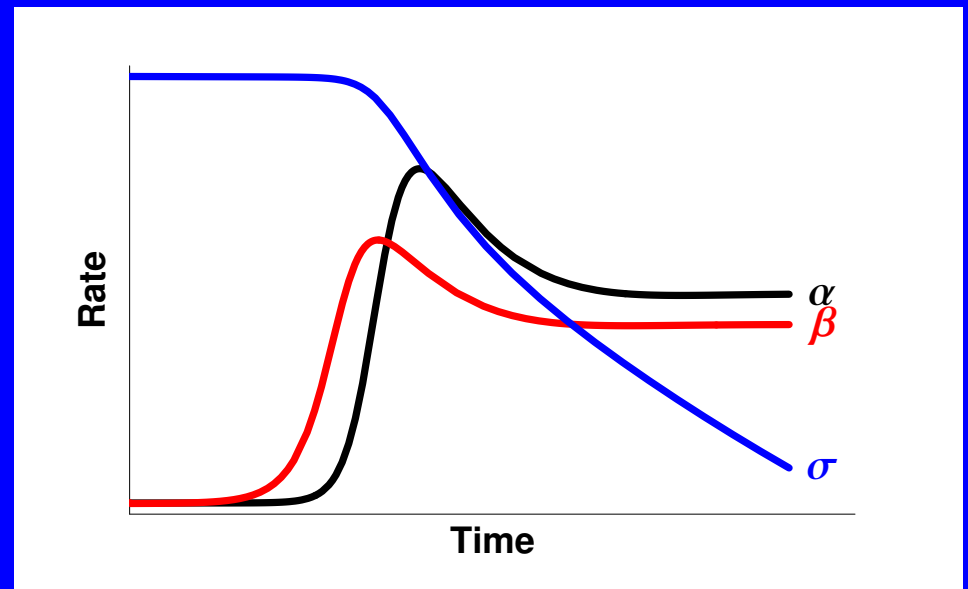
Nesting Models: Linking Within & Between-Host Behavior

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

Within-Host Dynamics



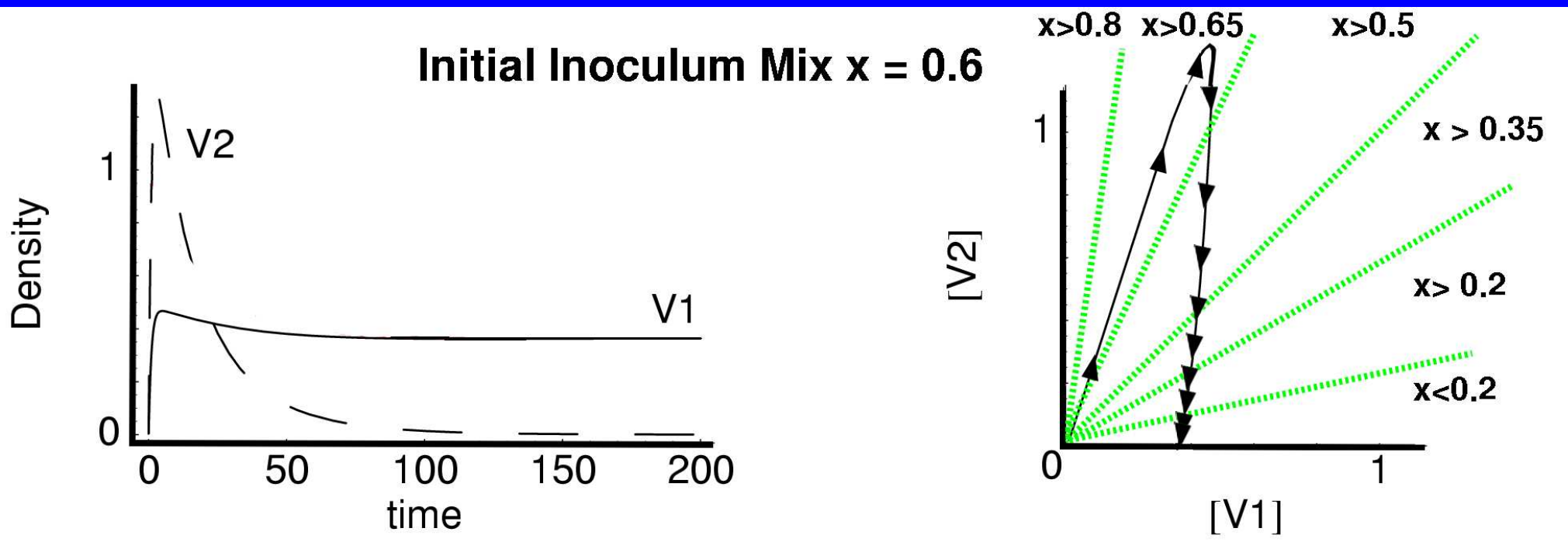
Between-Host Parameters



Nesting Models: Transmission

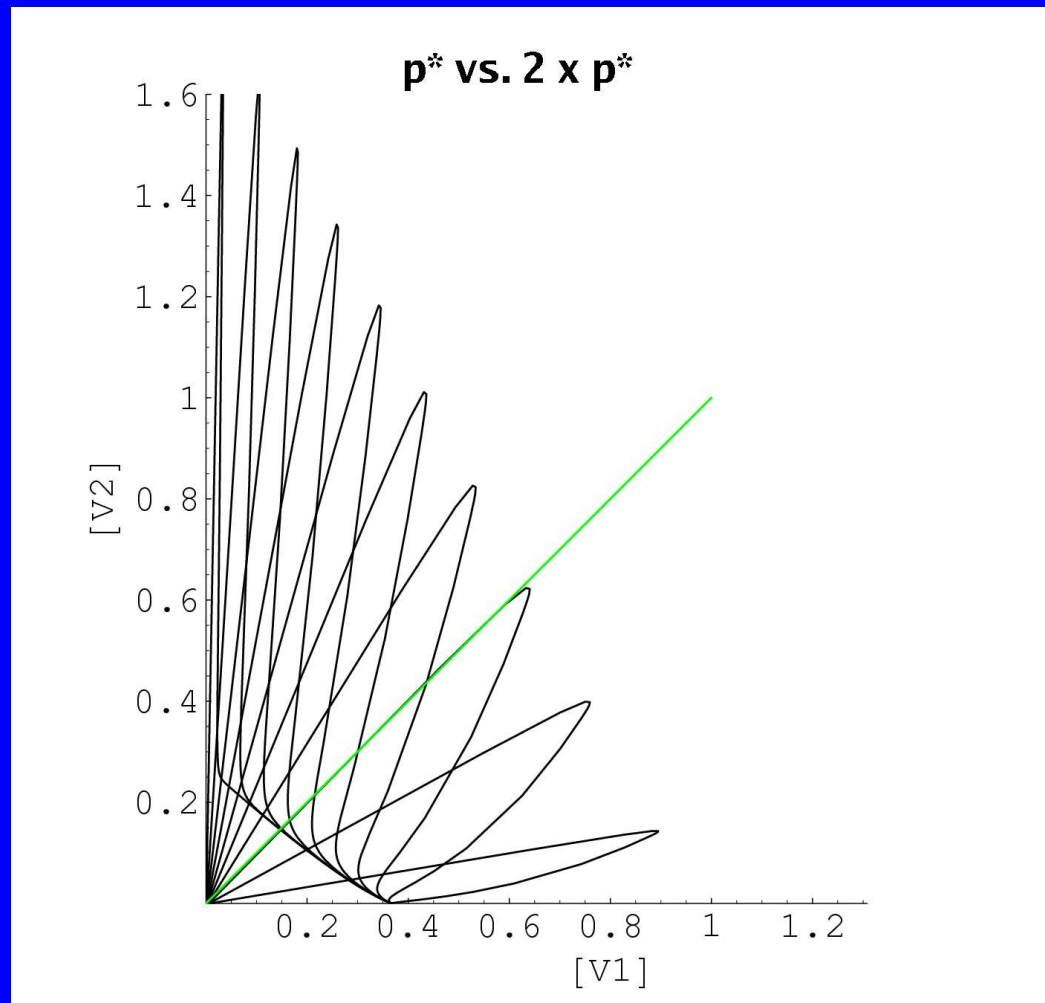
Assume inoculum reflects parasite mix at time of transmission

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



Nesting Models: Between-Host Fitness

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



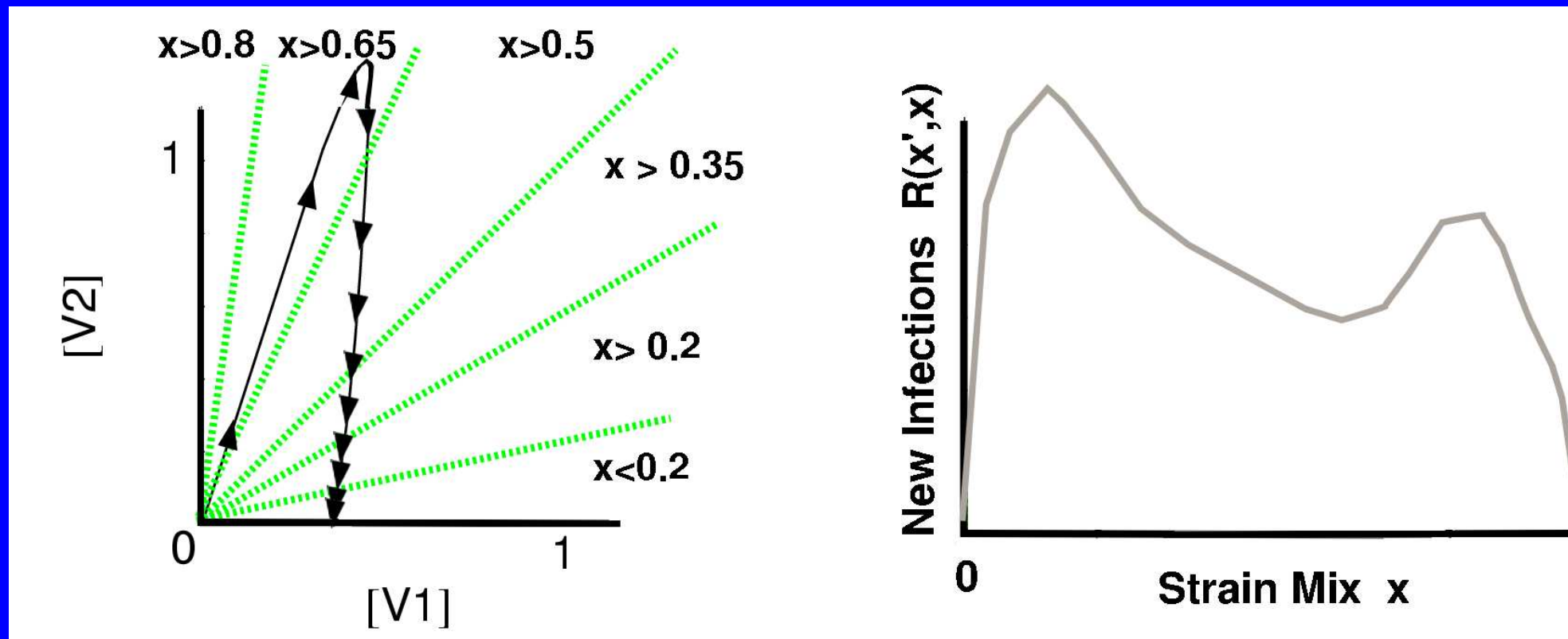
Nesting Models: Between-Host Fitness

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

$$R(x'_0 | x_0) = \int_0^\infty \delta(x'_0 - x(a)) \times \beta(V_1(a), V_2(a)) \exp \left[- \int_0^a \alpha(T(z)) dz + \delta a \right] da$$

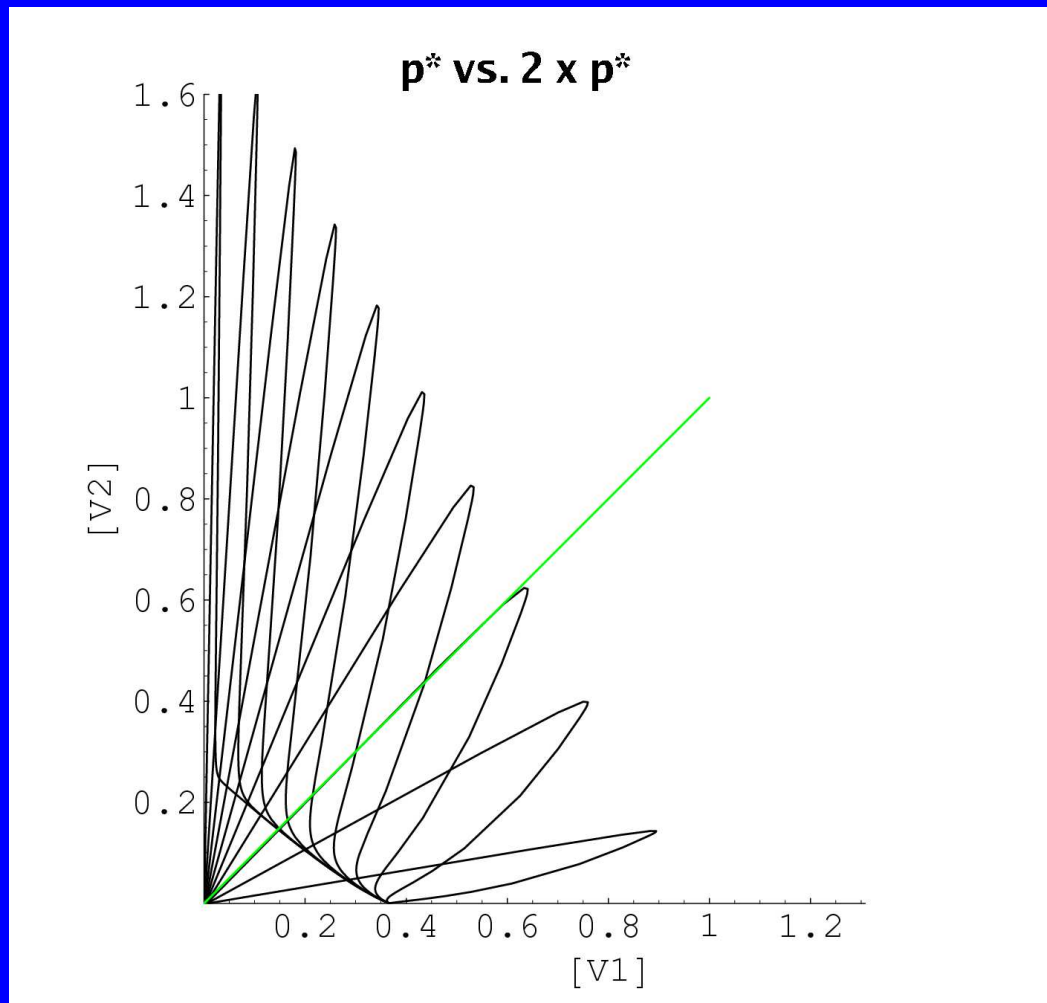
Nesting Models: Between-Host Fitness

$$R(x'_0 | x_0) = \int_0^\infty \delta(x'_0 - x(a)) \beta(V_1, V_2) e^{-\int_0^a \alpha(T(z)) dz + \delta a} dz$$



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 $\vec{x} = \{x_1, x_2, \dots, x_n\}$
2. Calculate next generation operator \mathbf{R}

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

where,

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

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

Resolving Within & Between-Host Selection

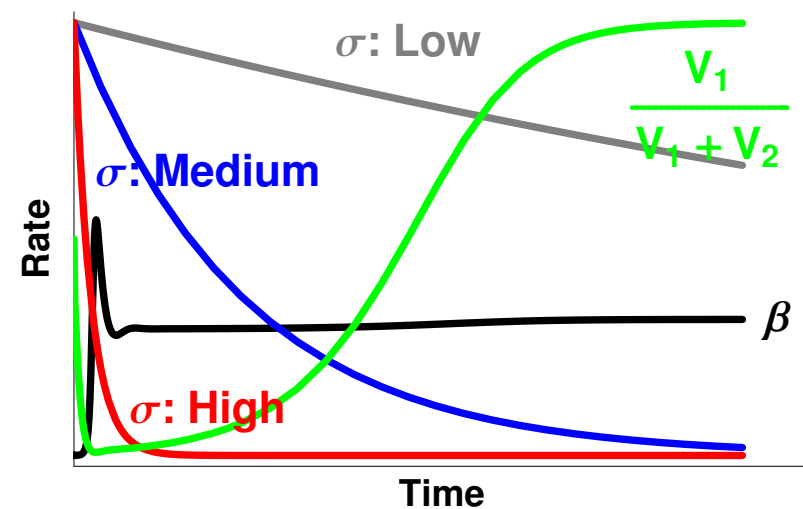
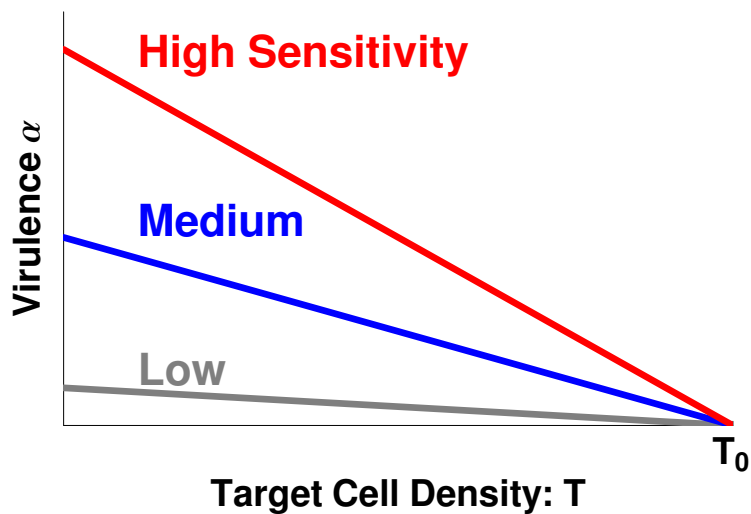
Examine three scenarios:

Low: Exclusion $>$ Spike

Medium: Exclusion \leq Spike

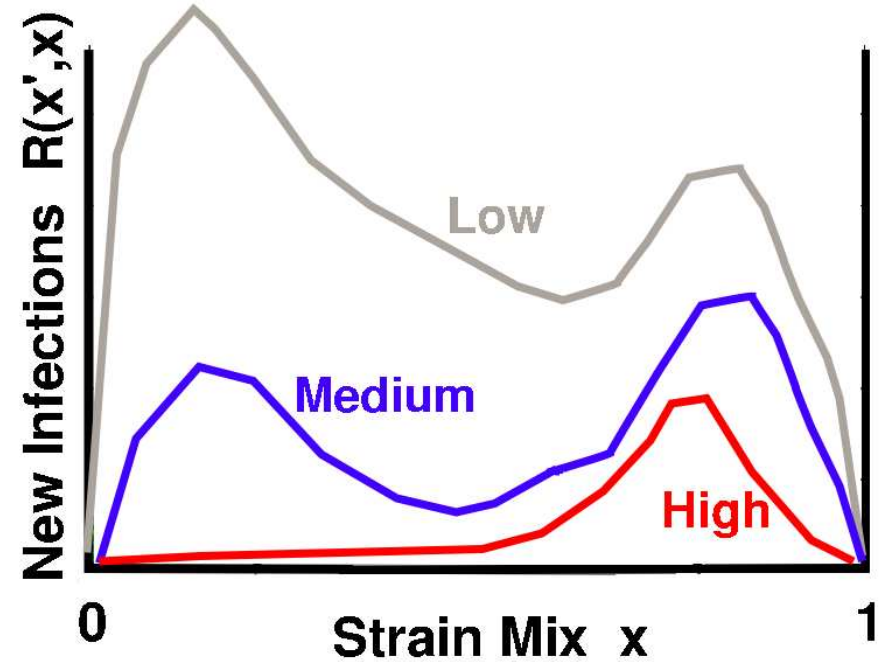
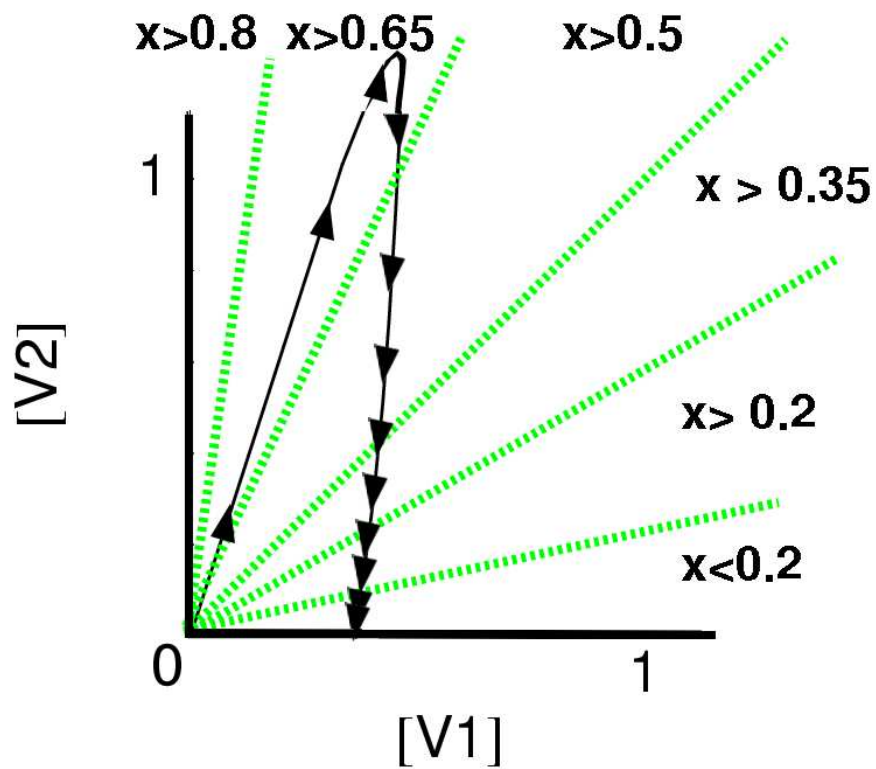
High: Exclusion $<$ Spike

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)



Resolving Within & Between-Host Selection

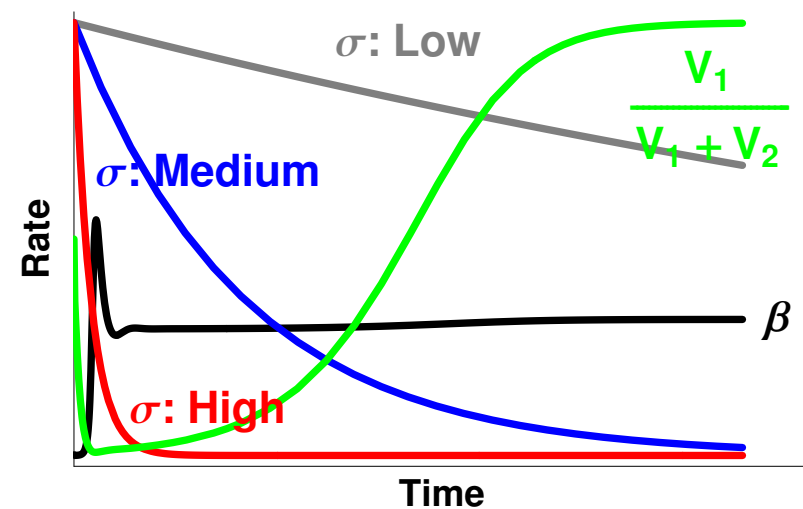
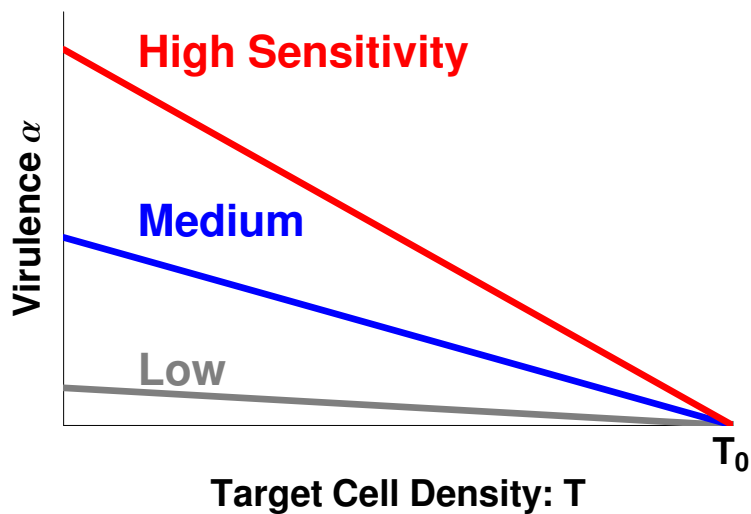
Examine three scenarios:

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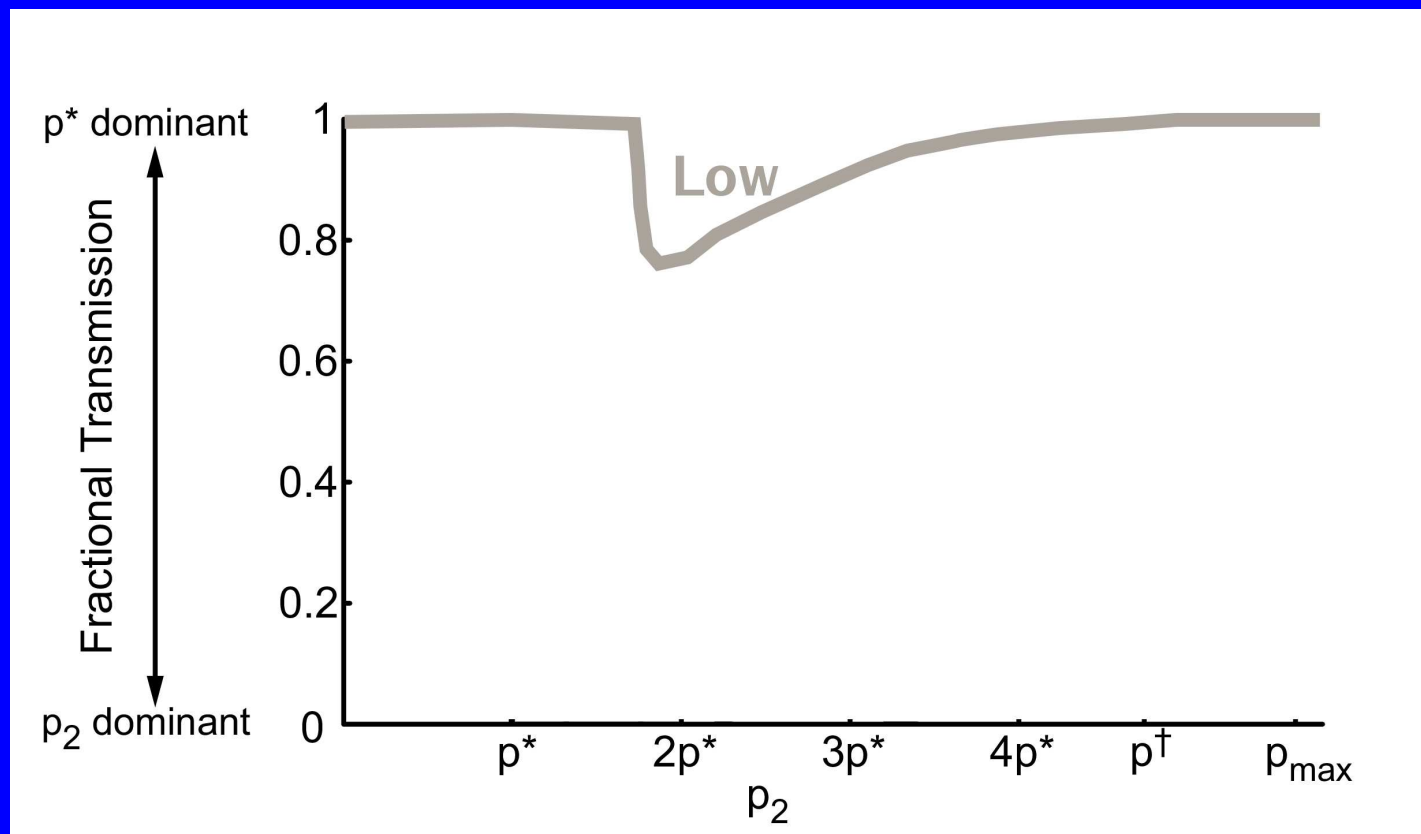
sensitivity of virulence α to target cell T depletion



Resolving Within & Between-Host Selection

Scenario: Low sensitivity to target cell T depletion

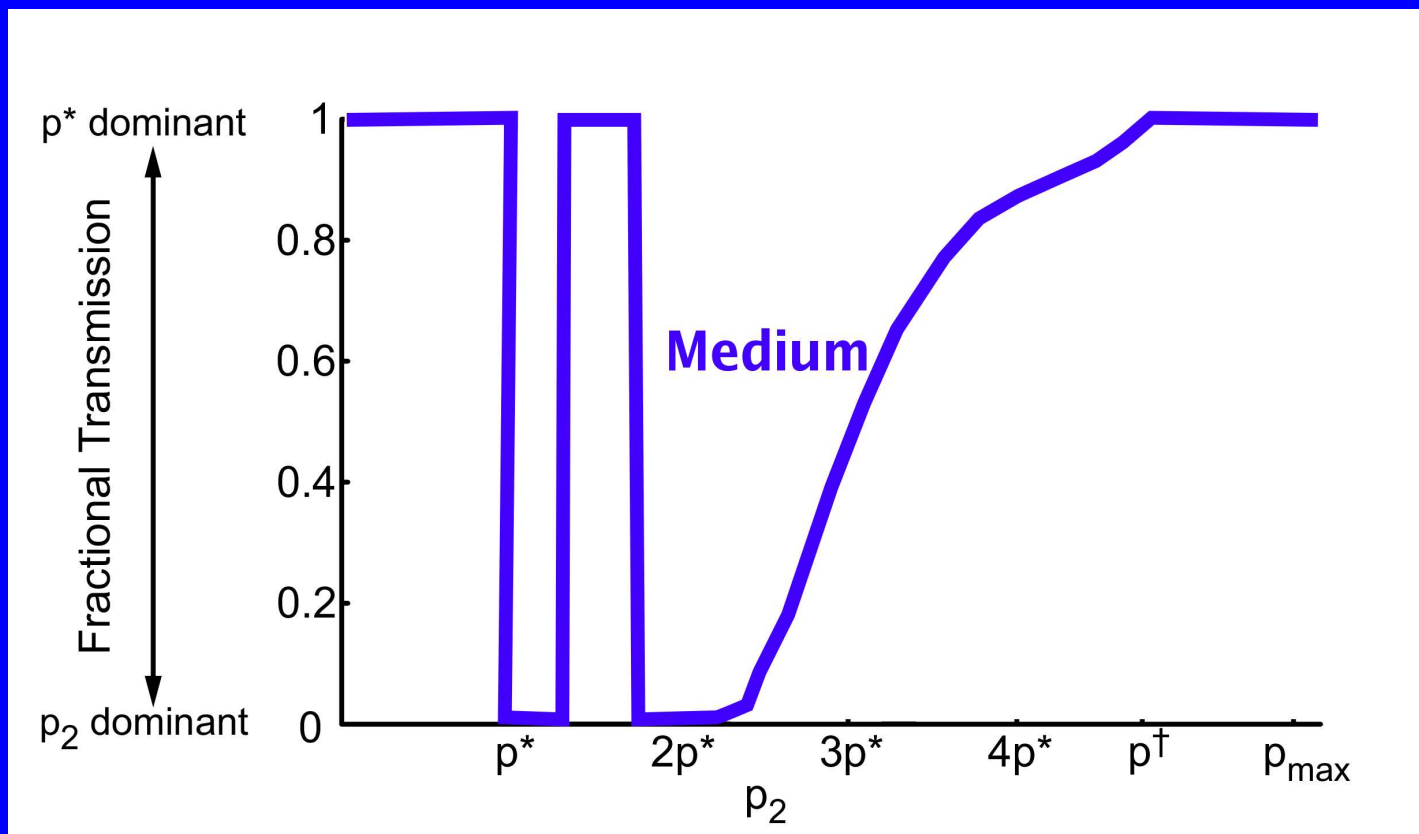
Result: One limited region of coexistence



Resolving Within & Between-Host Selection

Scenario: Medium sensitivity to target cell T depletion

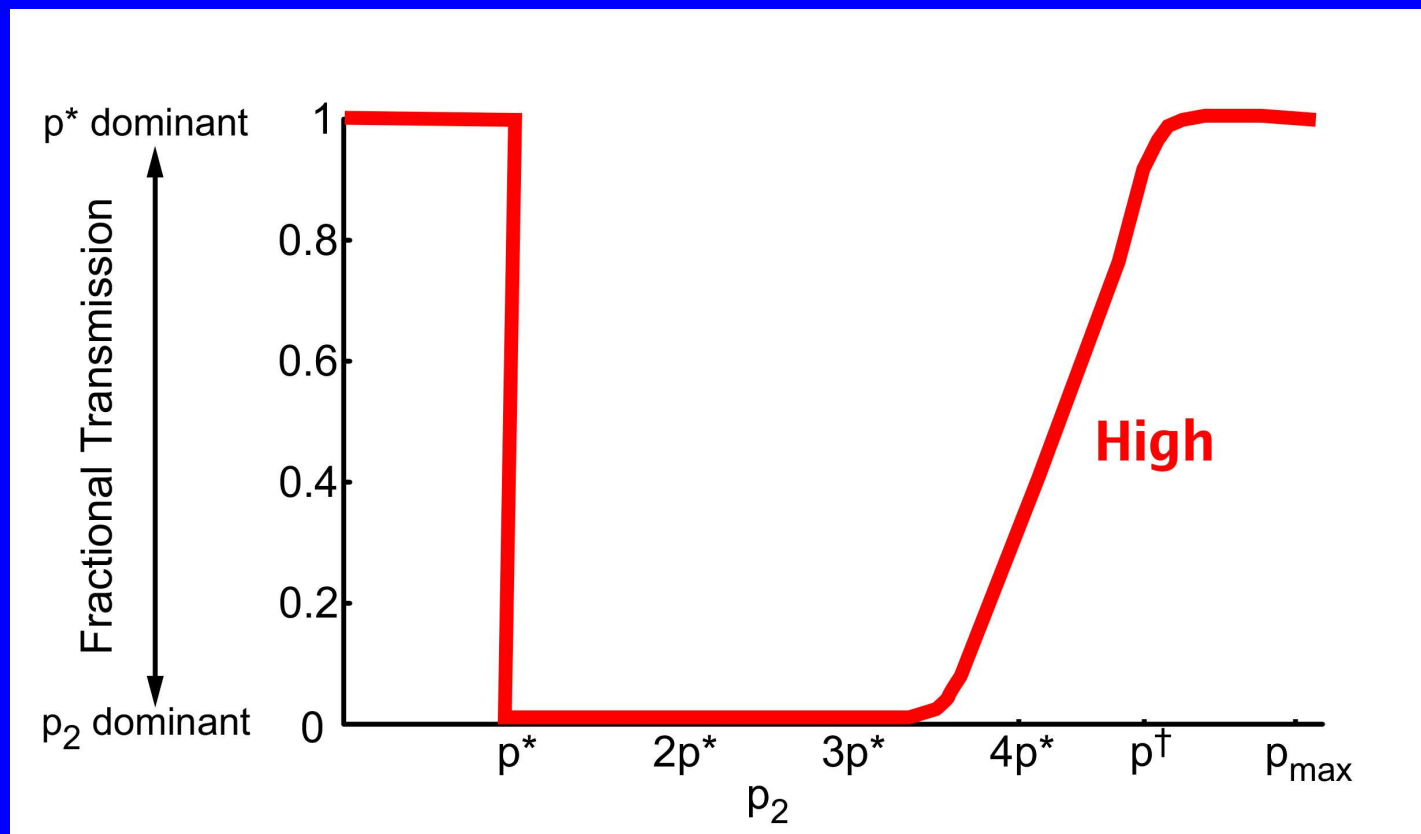
Result: Two distinct regions of coexistence



Resolving Within & Between-Host Selection

Scenario: High sensitivity to target cell T depletion

Result: One large region of coexistence



Resolving Within & Between-Host Selection

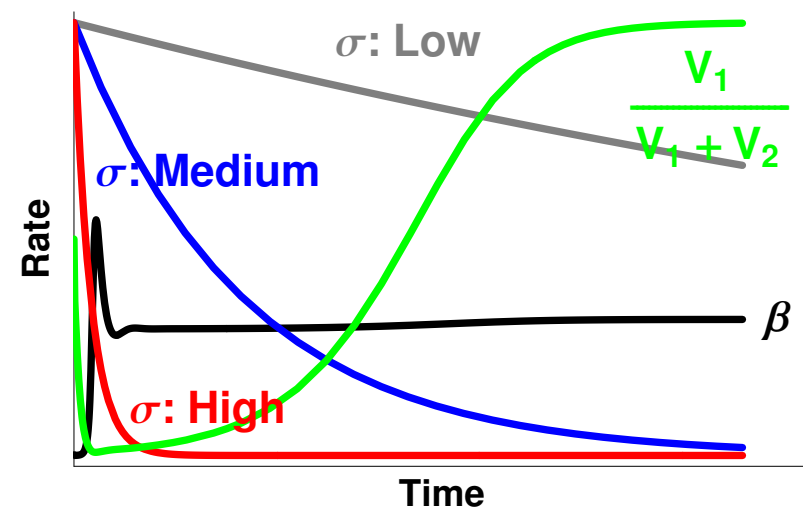
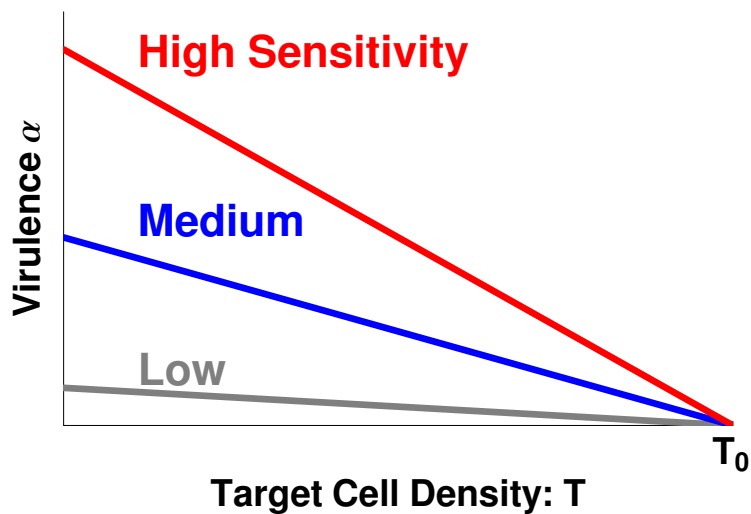
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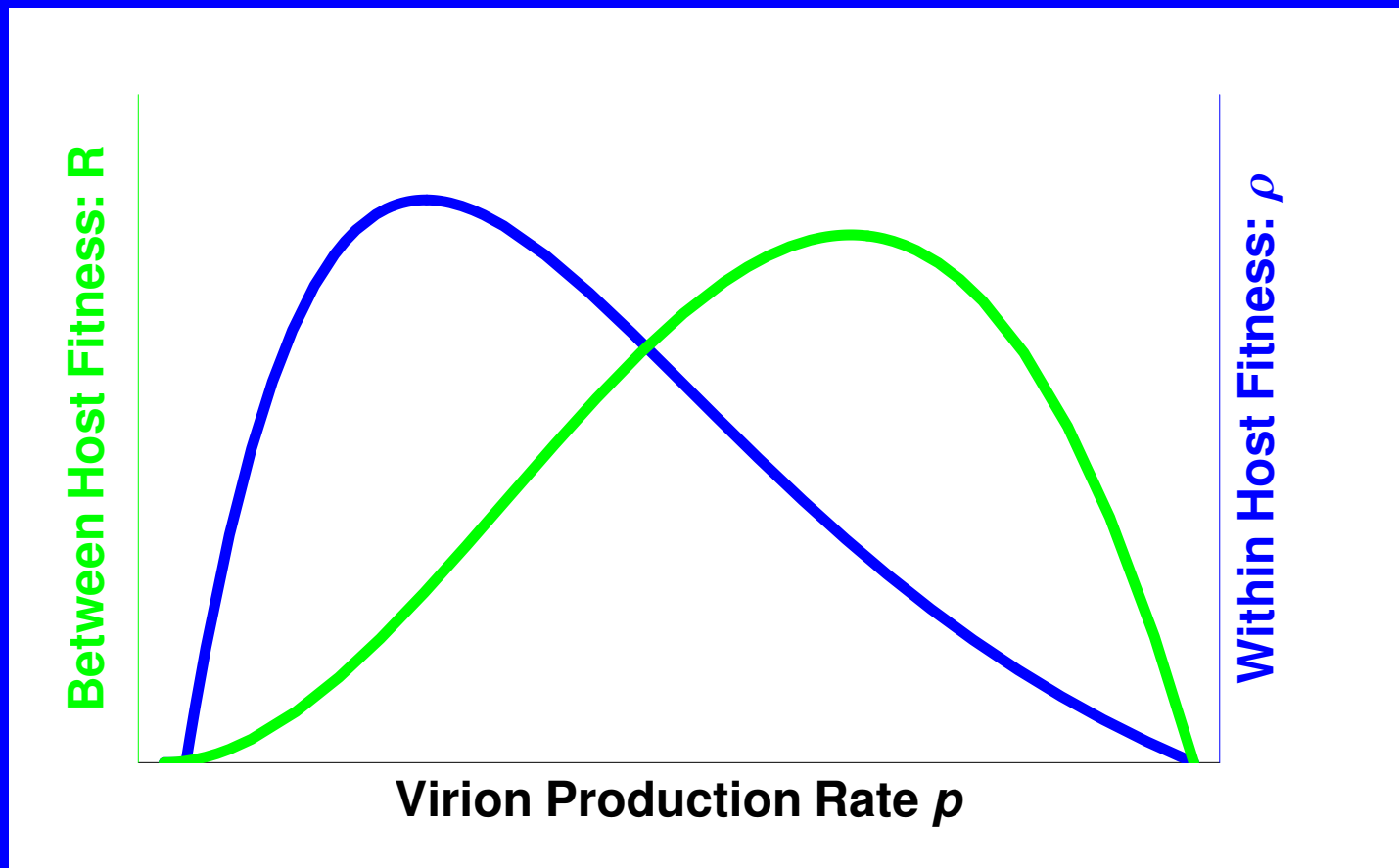
sensitivity of virulence α to target cell T depletion



Resolving Within & Between-Host Selection

Conclusions

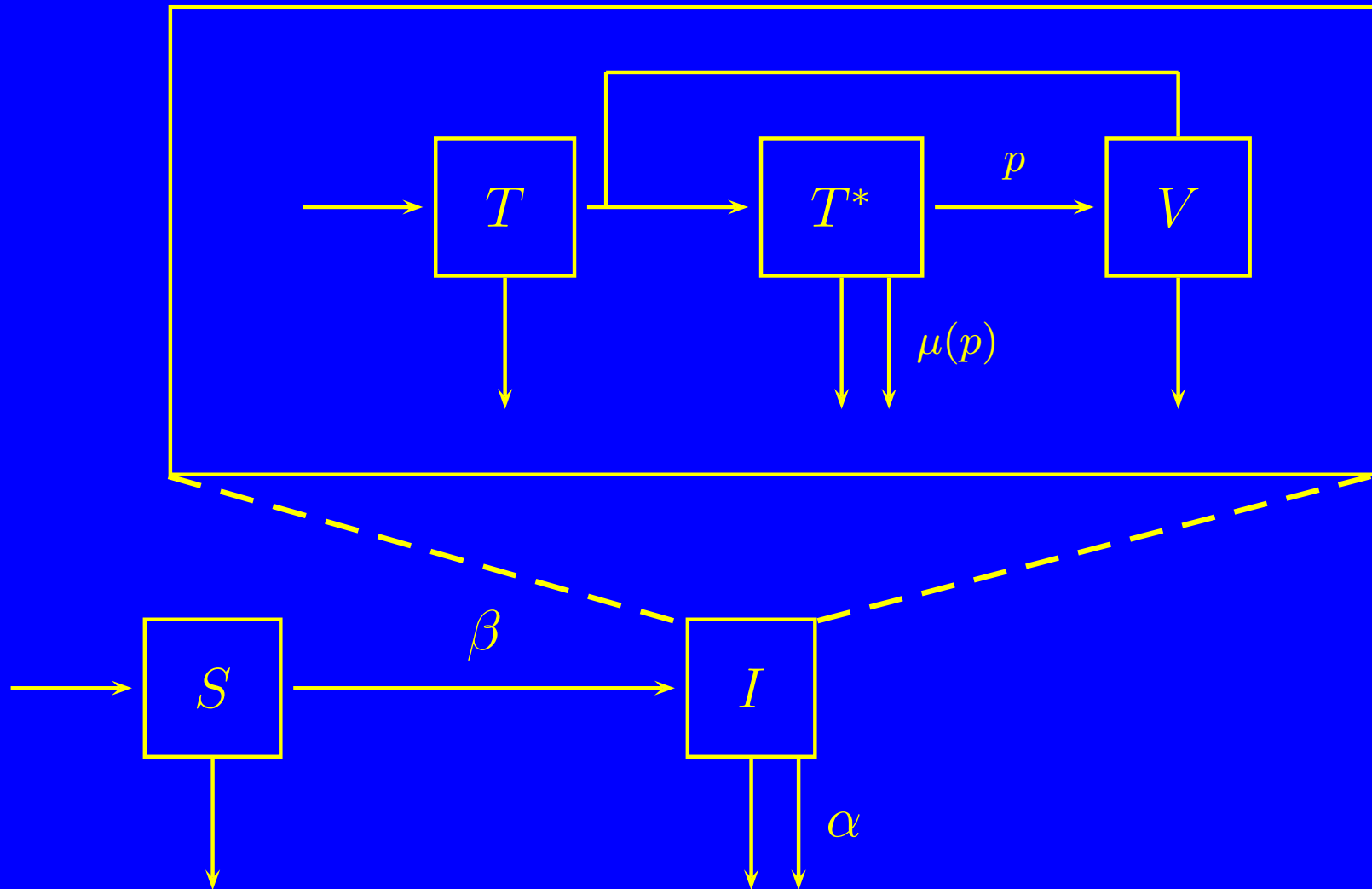
Conflict in selection at Within- and Between Host scales



Resolving Within & Between-Host Selection

Conclusions

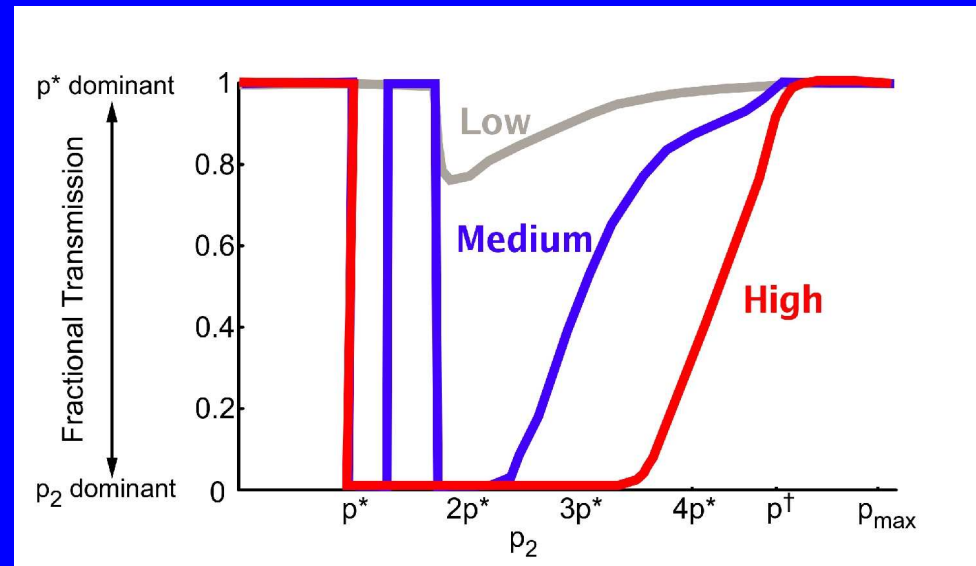
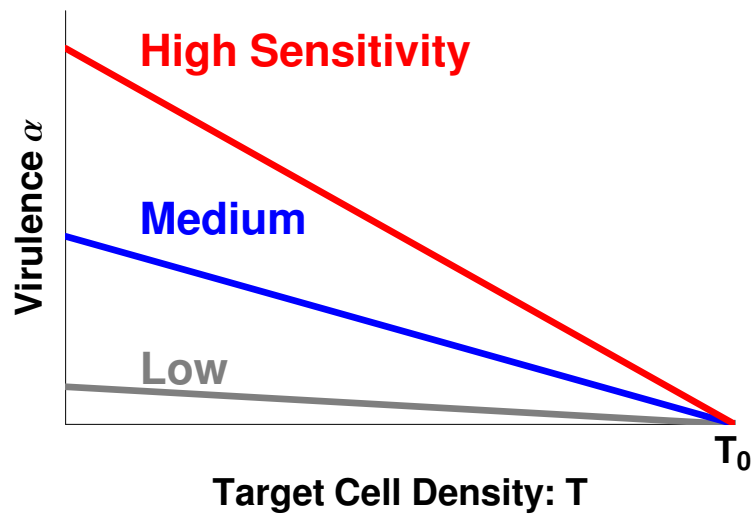
Nesting models allows us to examine conflict



Resolving Within & Between-Host Selection

Conclusions

Range & behavior of coexistence depends on host sensitivity



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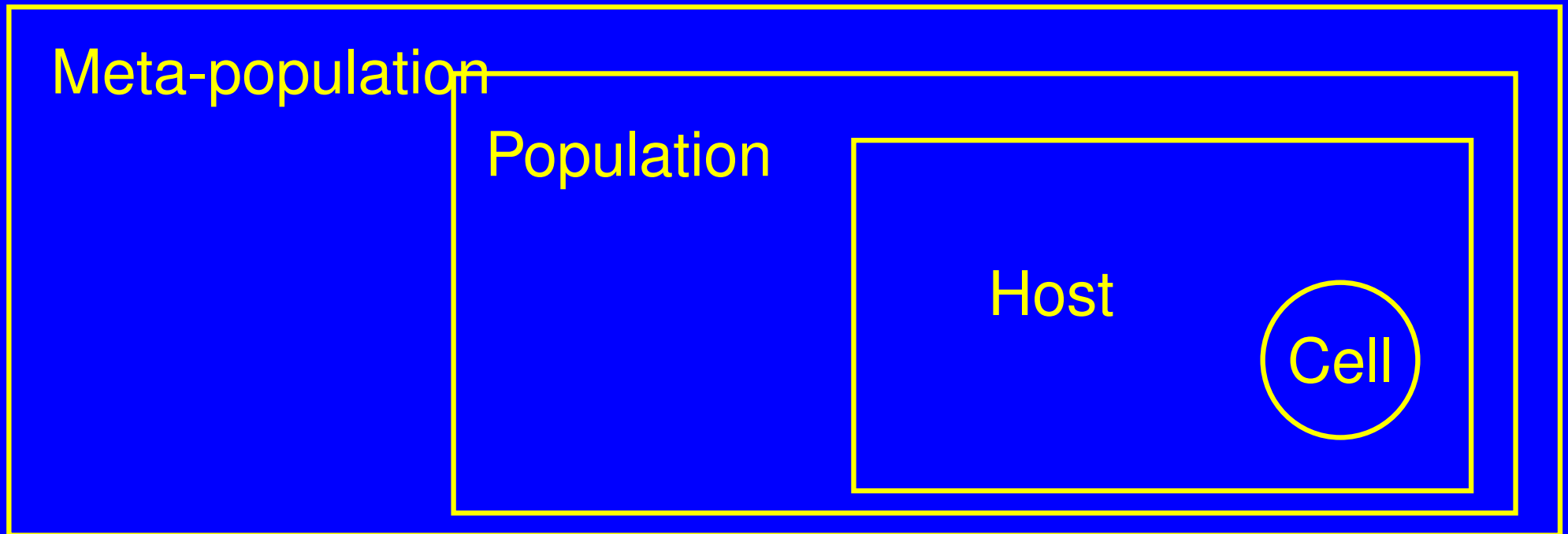
Future Work

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



Financial Support

Mike Gilchrist: University of Tennessee

Dan Coombs & Collen Ball: NSERC & MITACS NCE.