

Goldstein Model Overview

Canan Karakoç

July 2025

Concept

Evolved interaction (EI) model

Hosts and pathogens evolve their actual trait values directly:

- Host evolves: \tilde{c}
- Pathogen evolves: \tilde{v}
- Evolution proceeds through independent trait changes on static fitness landscapes.

Evolved strategy (ES) model

Organisms evolve **response strategies**:

- Host strategy: $c(v) = \max(0, \min(1, c_0 + m_c v)) = \max(0, \min(1, c_0 + \tan\theta_c v))$
- Pathogen strategy: $v(c) = \max(0, \min(1, v_0 + m_v c)) = \max(0, \min(1, v_0 + \tan\theta_v c))$
- Trait values are determined by mutual responses; coevolutionary feedback is present.

Acute vs. Chronic Infections

- **Acute infections:** Short-term, high-intensity. Immune activity aims to clear the pathogen rapidly.
 - **Chronic infections:** Long-term persistence. The immune system suppresses but does not eliminate the pathogen. Mortality and transmission depend on partial suppression and allow coexistence.
-

Hypotheses

- **EI vs. ES:**
 - EI: slow, stable evolution
 - ES: bursts of rapid evolution (punctuated equilibrium)
 - Transitions shaped by fitness landscape geometry
 - **Acute vs. Chronic:**
 - Acute: selection may favor rapid clearance or high virulence tradeoffs
 - Chronic: selection may favor coexistence, strategic suppression, and dynamic plasticity
-

Original Model Equations (Goldstein et al.)

Shared Trait Space

$$0 \leq v, c \leq 1$$

Where v is pathogen virulence and c is host immune activity.

Acute Infection Model

Transmission:

$$r(v) = v^\beta$$

Mortality: Note that ϵ is a small number preventing infinite mortality rates.

$$d(c, v) = d_0 + m_c \cdot \frac{(1 + \epsilon)c}{(1 + \epsilon) - c} + m_v \cdot \frac{(1 + \epsilon)v}{(1 + \epsilon) - v}$$

Host Fitness:

$$f_H = \frac{c}{c + d}$$

Pathogen Fitness:

$$f_P = \frac{v^\beta}{c + d}$$

Chronic Infection Model

Transmission:

$$r(v, c) = (1 - c)v^\beta$$

Mortality:

$$d(c, v) = d_0 + m_c \cdot \frac{(1 + \epsilon)c}{(1 + \epsilon) - c} + (1 - c)m_v \cdot \frac{(1 + \epsilon)v}{(1 + \epsilon) - v}$$

Host Fitness:

$$f_H = \frac{1}{d}$$

Pathogen Fitness:

$$f_P = \frac{(1 - c)v^\beta}{d}$$

Simulation Types

Evolved Interaction (EI)

- Traits mutate directly
- Fitness-based selection and fixation

Steps

1. Generate candidate mutations c' , v'
2. Compute fitness change and selection coefficient s
3. Calculate fixation probability p_{fix}
4. Apply mutation with rate $\propto p_{\text{fix}}$
5. Advance time stochastically

Evolved Strategy (ES)

- Traits determined by opponent-based functions

Steps

1. Mutate $c_0, \theta_c, v_0, \theta_v$
2. Find equilibrium (c, v) by mutual response
3. Evaluate selection and fixation
4. Apply mutation and update time

Probability of Mutations for the EI scenario

Probability of host mutation:

$$p(c' - c) = \gamma \mathcal{N}_{0,0.1}(c' - c)$$

Probability of pathogen mutation:

$$p(v' - v) = \gamma \mathcal{N}_{0,0.1}(v' - v)$$

γ is the relative likelihood of a mutation.

Probability of Mutations for the ES scenario

$$p([c - \theta_c] - [c' - \theta'_c]) = \gamma \mathcal{N}_{0,0.1}(c' - c) \mathcal{N}_{0,0.1} \pi(\theta'_c - \theta_c)$$

$$p([v - \theta_v] - [v' - \theta'_v]) = (1 - \gamma) \mathcal{N}_{0,0.1}(v' - v) \mathcal{N}_{0,0.1} \pi(\theta'_v - \theta_v)$$

Probability of Fixation

$$p_{fix} = \frac{1 - \exp(-2s)}{1 - \exp(-4N_e s)}$$

Selection coefficient

$$s = \frac{F_X(c', v') - F_X(c, v)}{F_X(c, v)}$$

Substitution Rate Comparison

$$\omega = \frac{\text{observed substitution rate}}{1/N_e}$$

Parameter Table

Parameter	Symbol	Description	Default Value	Biological?
Baseline mortality	d_0	Background mortality	0.1	Yes
Immune cost	m_c	Cost of immune activity	0.1	Yes
Virulence cost	m_v	Cost of pathogen virulence	1.0	Yes
Stabilizing term	ε	Numerical stabilizer (prevents division by zero)	10^{-4}	Technical
Transmission scaling	β	Controls steepness of transmission curve	1.0	Yes
Host mutation prob	γ	Probability that a mutation affects host	0.01	Algorithmic
Host pop size	N_e^H	Effective population size of host	10^4	Yes
Pathogen pop size	N_e^P	Effective population size of pathogen	10^6	Yes
Mutation step	c_0, v_0	Intercept mutation step size	0.01	Algorithmic
Mutations slope	θ_c, θ_v	Strategy slope mutation step size	0.314 (0.01 π)	Algorithmic

Parameter	Symbol	Description	Default Value	Biological?
Candidate mutations	—	Number of candidate mutations per generation	10000	Algorithmic
Max dwell time	—	Max evolutionary time allowed per fixation event	100	Algorithmic
Max evolutionary time	—	Total simulation time	1×10^6 with 1×10^4 burn-in	Algorithmic

Theory Notes

Fitness Landscapes

This section only evaluates fitness equations over a trait grid and plots them, no simulations involved. Probably best to start with this.

(Yellow highest fitness)

EI Host Fitness (Acute)

- The host benefits from increasing control c , especially when pathogen virulence v is low or moderate.
- The best response curve (blue) shows hosts evolve higher c as v increases. Increased immune control is beneficial under more virulent infection.

EI Pathogen Fitness (Acute)

- The pathogen's fitness increases with v , but peaks at an intermediate level due to the cost imposed by host control c .
- The red curve is the pathogen's best response: it evolves to reduce v when host control is high, and increase v when host control is low.

EI Joint Fitness (Acute)

- Shows fitness contours (product of host \times pathogen fitness).
- Intersection of blue and red curves marks a Nash equilibrium (black dot) — neither player can improve fitness by changing strategy unilaterally.
- In acute infections, the equilibrium lies at moderate v , high c . Consistent with host investing in strong immunity to offset pathogen aggressiveness.

ES Host Fitness (Chronic)

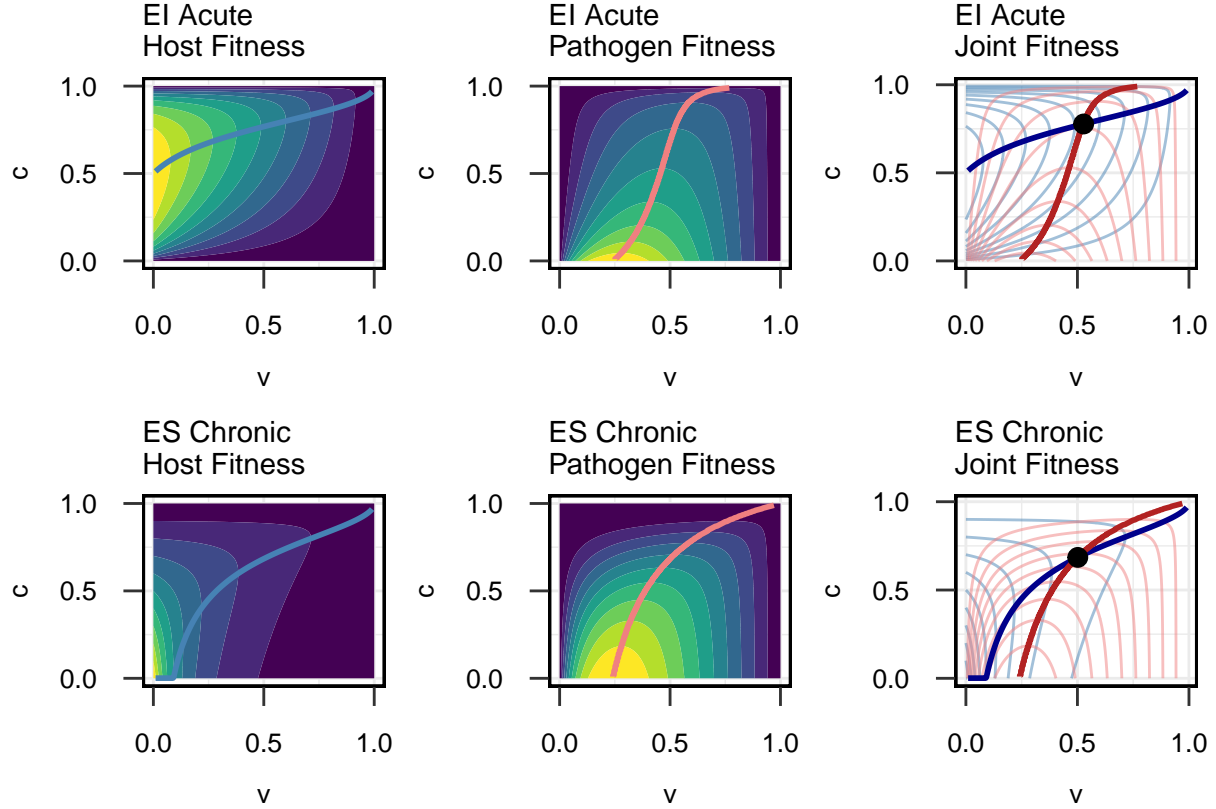
- Host fitness improves by suppressing pathogen virulence (v), and lowering immune control (c), especially since chronic immune activation is costly.
- The blue best response line bends downward: lower c is favored when v is low (and vice versa).

ES Pathogen Fitness (Chronic)

- Pathogen fitness is maximized at intermediate v , but now also increases when the host's immune control c is low.
- The red best response curve flattens out as the pathogen finds a compromise: enough virulence to transmit, but not so much to trigger strong immunity.

ES Joint Fitness (Chronic)

- Nash equilibrium here lies at moderate virulence and intermediate-low control:
- Host tolerates some pathogen presence.
- Pathogen “learns” not to kill host, stable chronic coexistence emerges.



Simulation results

1. Host Trait (c) Evolution

Acute-EI:

- Rapid stable convergence, with higher c and lower v .
- This reflects the classical co-adaptation to a static Nash equilibrium.

Chronic-EI:

- c stabilizes around a slightly lower value, consistent with reduced pressure on clearance when infections are persistent.
- v again stabilizes near 0.5, but possibly with slightly dampened evolution.
- Expected for equilibrium-focused dynamics where mutual strategies are fixed traits.

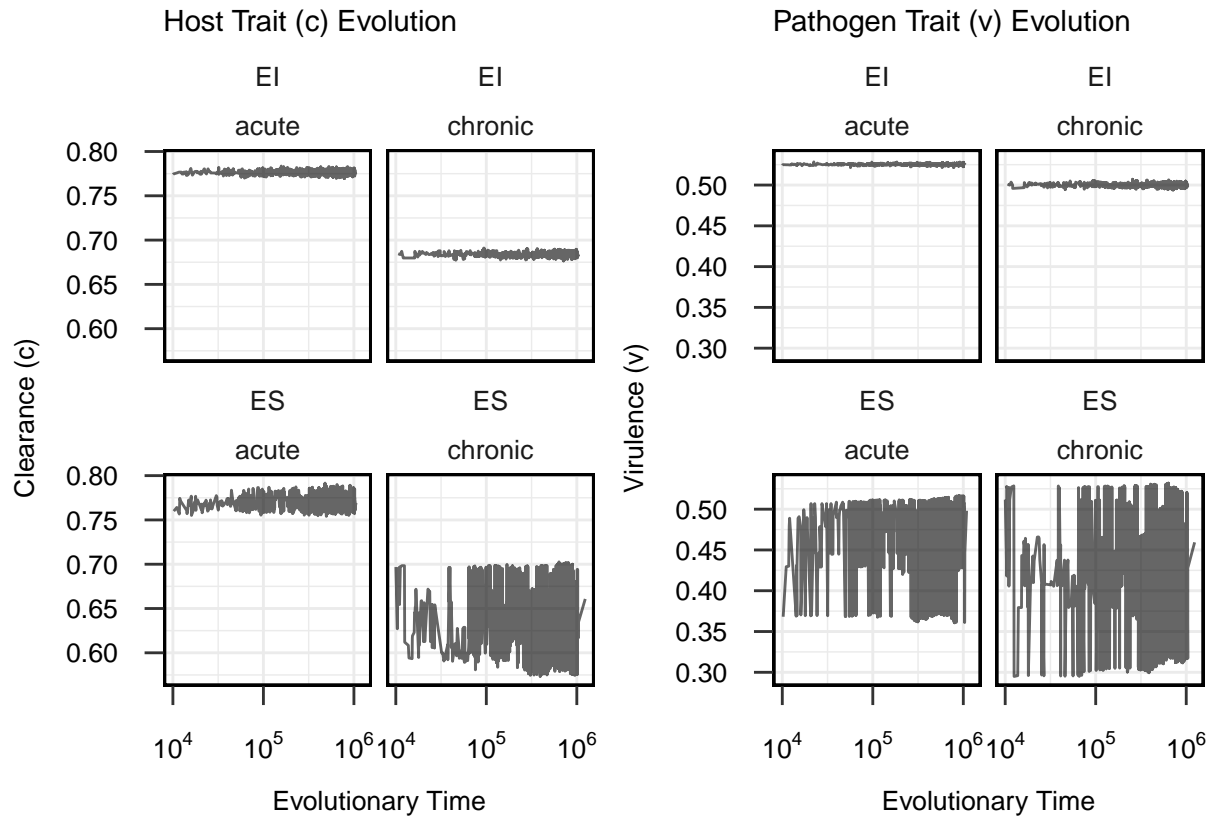
Acute-ES:

- c increases over time with moderate noise, stabilizing ~ 0.8 .
- v shows more variability, fluctuating around a slightly lower average (~ 0.4 – 0.5).

- In this model, both trait values and response slopes evolve, allowing more feedback and noise. Still, it converges to similar endpoints.

Chronic-ES:

- c stays below acute values, non monotonic.
- v shows non-monotonic, drifting dynamics, dipping and then rebounding over evolutionary time.
- This suggests instability or continual adaptation — possibly due to context-dependent strategies creating feedback loops in chronic environments.



3. Fitness over Time - Notes

Host fitness

EI-Acute:

- Fitness converges quickly to a low but stable value.
- This reflects the cost of high clearance in acute infection, which yields modest returns under strong pressure to eliminate infection.

EI-Chronic:

- Host fitness stabilizes at a much higher level (~ 1.6).
- Suggests a more favorable trade-off: hosts evolve clearance levels that allow coexistence with lower cost, yielding higher net payoff.

ES–Acute:

- Very similar to EI–Acute but noisy.
- Because ES models allow evolving responsiveness, the host may fine-tune clearance for a small advantage.

ES–Chronic:

- Even noisier, host leverages the co-evolutionary feedback in chronic infection to optimize strategy?

Pathogen Fitness

EI–Acute:

- Pathogen fitness converges to ~ 0.2 , low but stable.
- Reflects a controlled pathogen population; the host successfully constrains pathogen fitness via clearance.

EI–Chronic:

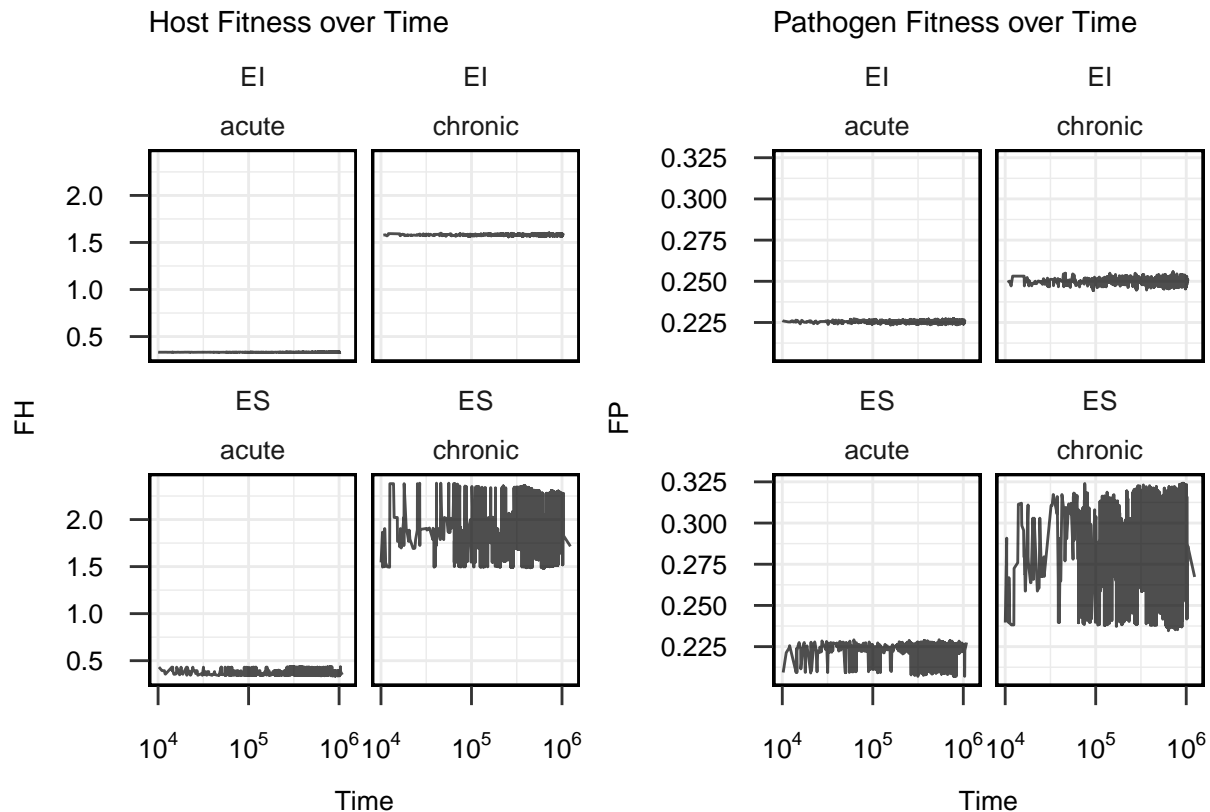
- Slightly higher fitness due to longer infection duration, maybe giving pathogens more room to replicate despite host defenses?

ES–Acute:

- Similar to EI–Acute, slightly more variability but no major divergence.
- Pathogen strategies adjust dynamically, but host control remains effective.

ES–Chronic:

- Looks like arms-race dynamics and delayed host counter-adaptations?



5. Relative Substitution Rates

Host

EI–Acute vs. Chronic:

- Acute vs. chronic scenarios are very similar.
- Most host adaptive changes occur early (possibly a single directional sweep), then selection pressure relaxes or equilibrium is reached.

ES–Acute vs. Chronic:

- Slightly more variable early on, especially in chronic ES.
- Substitution rates converge to similar values as EI.
- Context-dependent traits may delay convergence slightly, but the overall tempo is similar. Chronic ES has persistent pathogen turnover, unlike the stasis seen in EI.

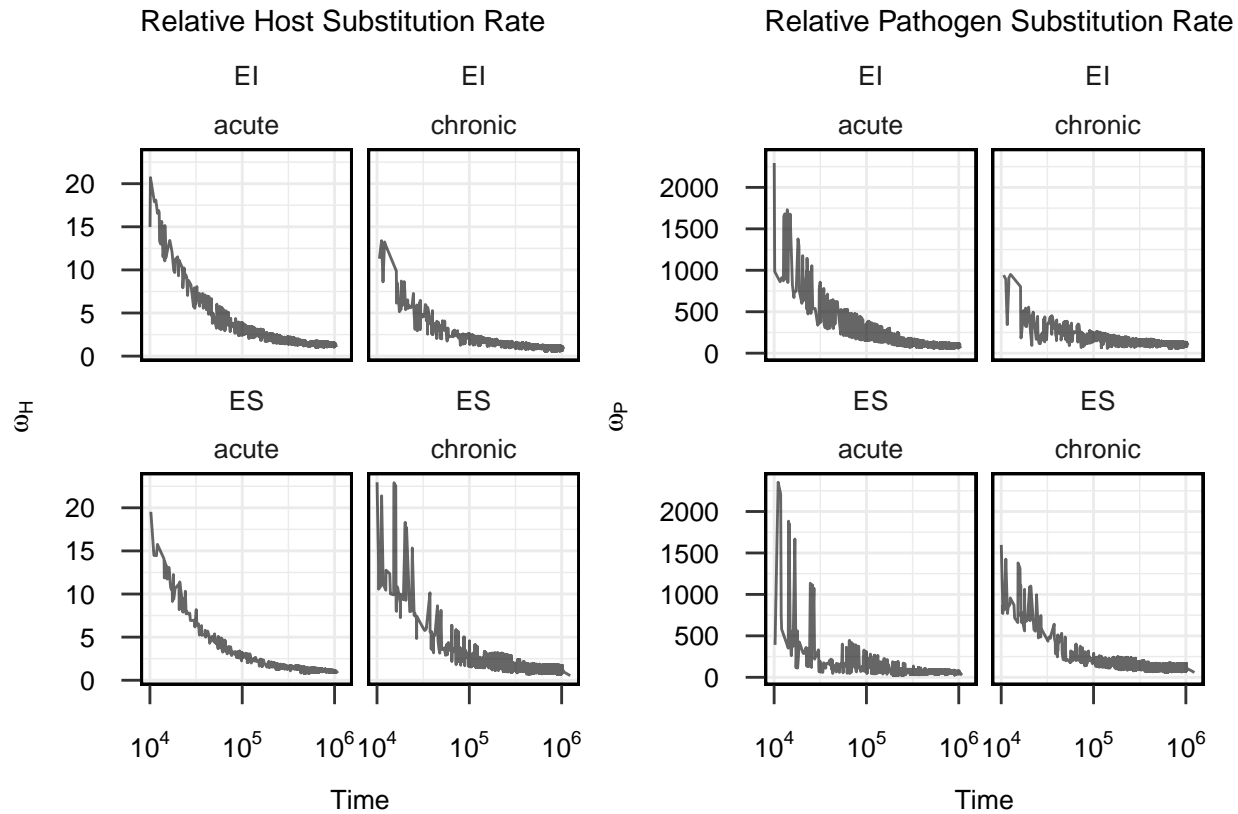
Pathogen

EI–Acute vs. Chronic:

- Pathogens evolve faster than hosts, consistent with smaller N_e and higher mutation effect.

ES–Acute vs. Chronic:

- Slightly elevated initial rate in acute, with greater early variability in chronic.
- Still converges to rates similar to EI—pathogen evolution slows as equilibrium is approached.
- ES dynamics don't fundamentally change the overall tempo, but they introduce more noise (especially in chronic infections where co-evolution is stronger).



Distribution plots

EI Acute:

- Rapid convergence to a single joint optimum with very little variance.
- Reflects the fixed-strategy nature of EI; dynamics settle into a stable evolutionary attractor.

EI Chronic:

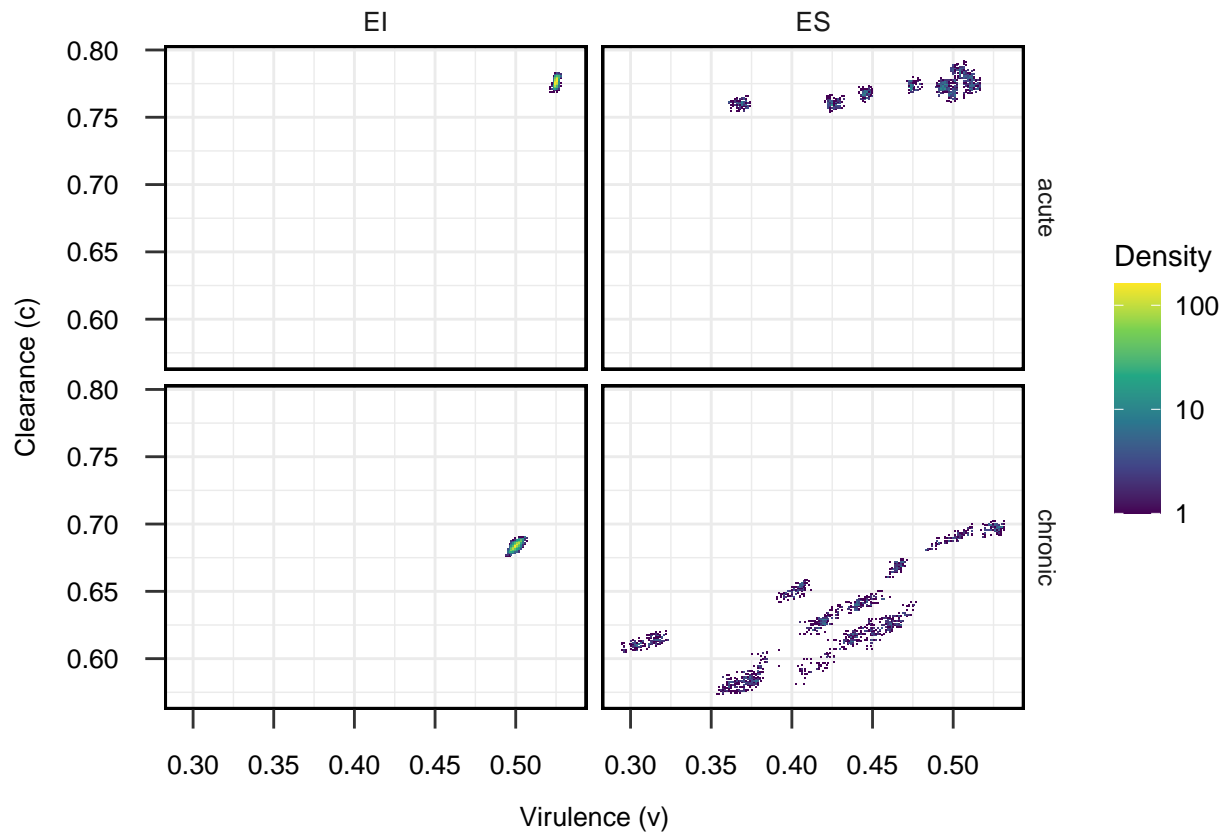
- Very narrow and stable peak, implying strong selection and low evolutionary flexibility.

ES Acute:

- Still fairly localized near high cc , intermediate vv , but notably more spread.
- Multiple small peaks: evolutionary branching or slow drift in trait space.
- This reflects co-evolutionary feedback loops—host and pathogen traits co-adapt, creating local attractors.

ES Chronic:

- Broad distribution, sloping positively: as v increases, so does c .
- Suggests trait correlation under ES dynamics: coevolution aligns clearance with virulence.
- Also shows much greater variance—suggesting sustained arms-race dynamics or polymorphism, especially in chronic infections where co-adaptation is prolonged and nonlinear.

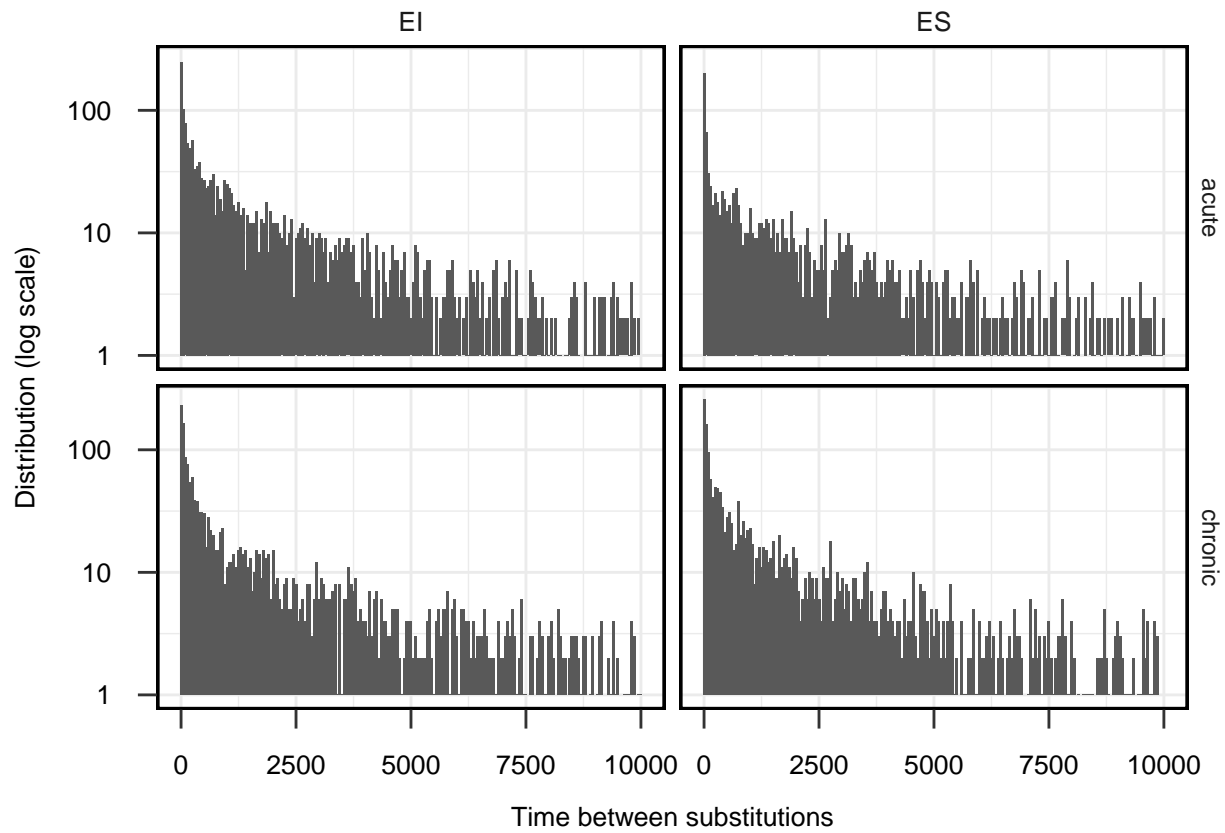


Dwell times

If substitution events are memoryless, the time between substitutions should follow an exponential distribution.

In the simulation, the waiting time until the next event is drawn from an exponential distribution with rate equal to the sum of all possible event rates (here: substitutions).

###EI (acute/chronic):



Overall, theory well coded. Simulations are qualitatively make sense. We have to double check that the steps and parameters are well implemented and biologically makes sense.