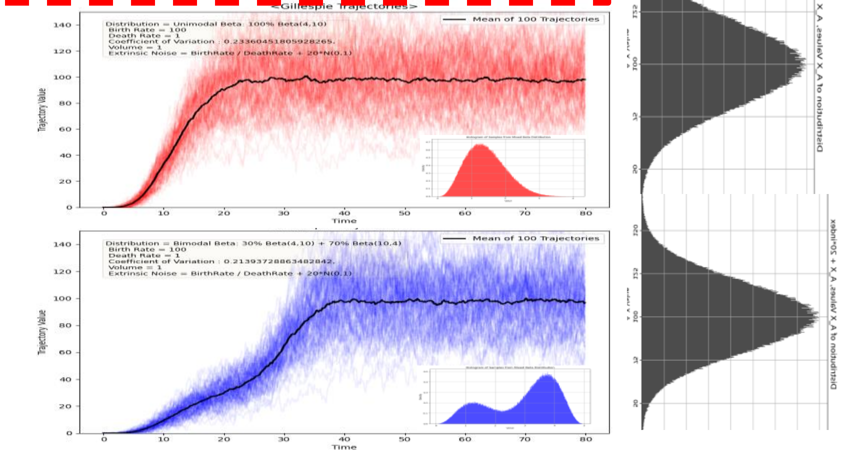
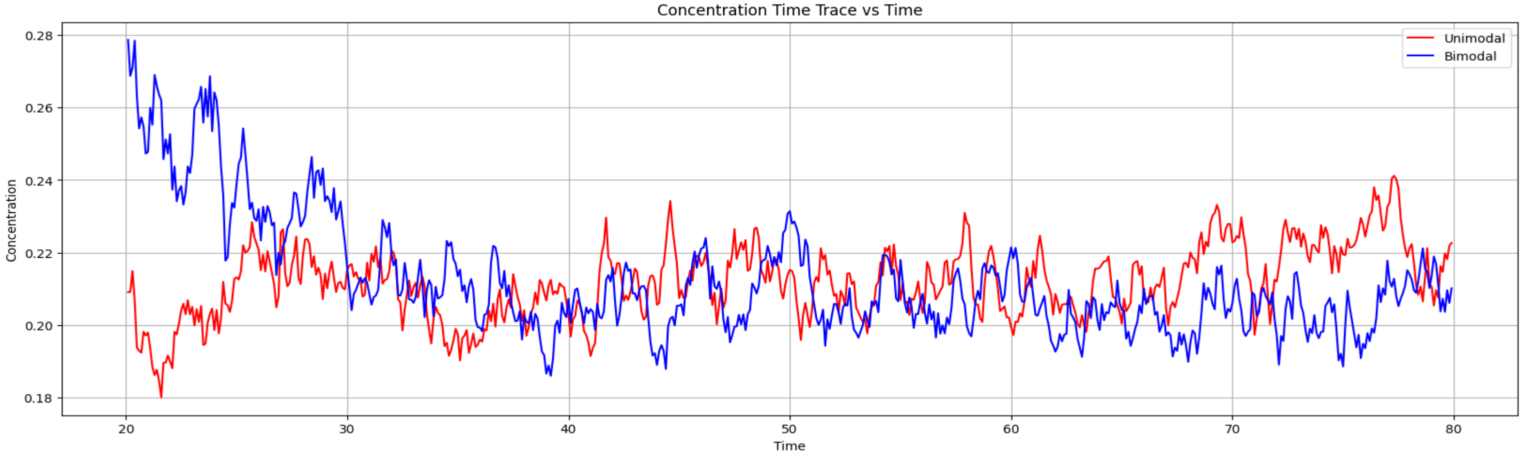
Review: No clear CV difference is observed after the same extrinsic noise is applied to both unimodal and bimodal delay Gillespie.

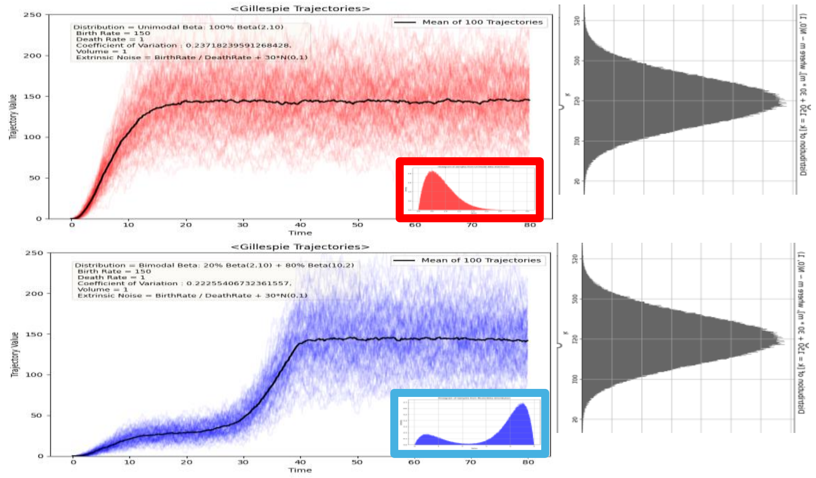
$$\lambda_b = 100 + 20 \cdot k, \quad k \sim N(0,1)$$
$$\lambda_d = 1$$



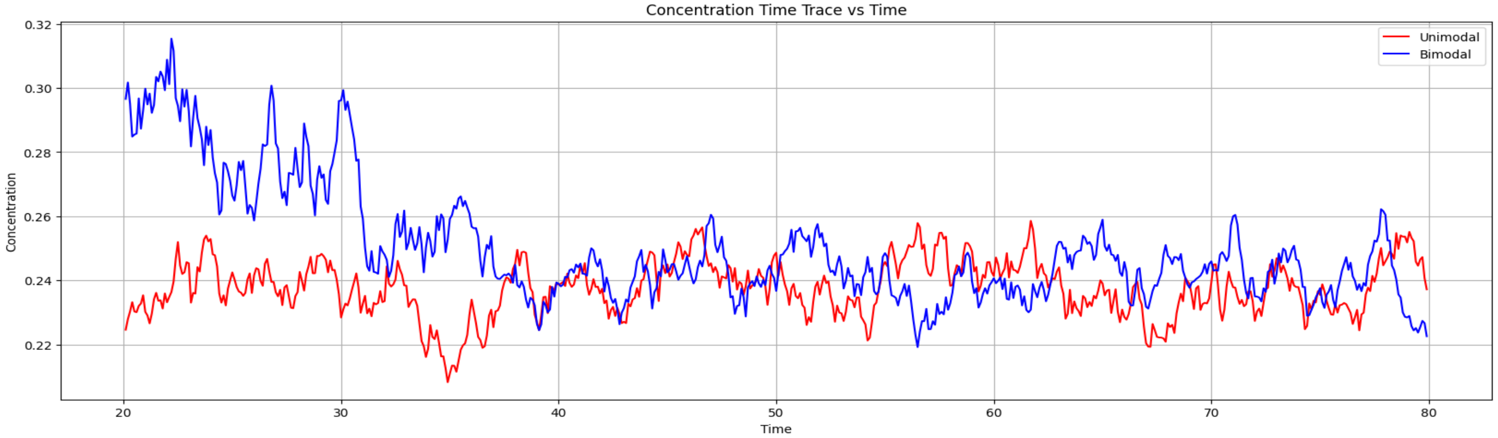
Steady-State:



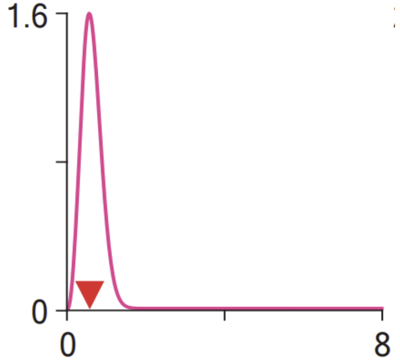
$$\lambda_b = 150 + 30 \cdot k, \quad k \sim N(0,1)$$
$$\lambda_d = 1$$

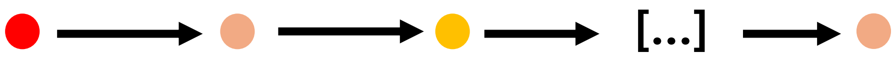


Steady-State:



Negative feedback-loop mediated birth/growth inhibition can be modeled by Hill-type birth rate function on X (popul.) and Gamma delay distribution with increasing scale parameter function.





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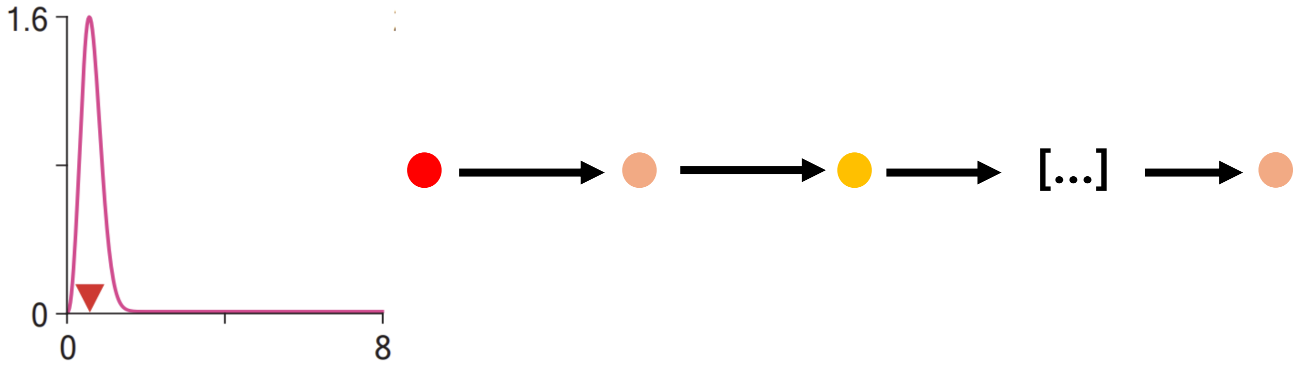

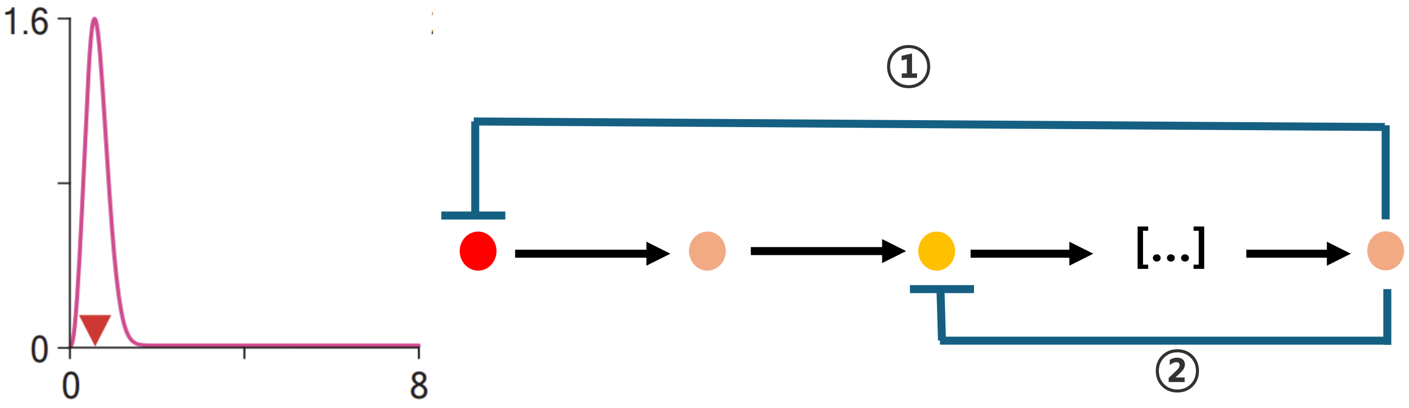

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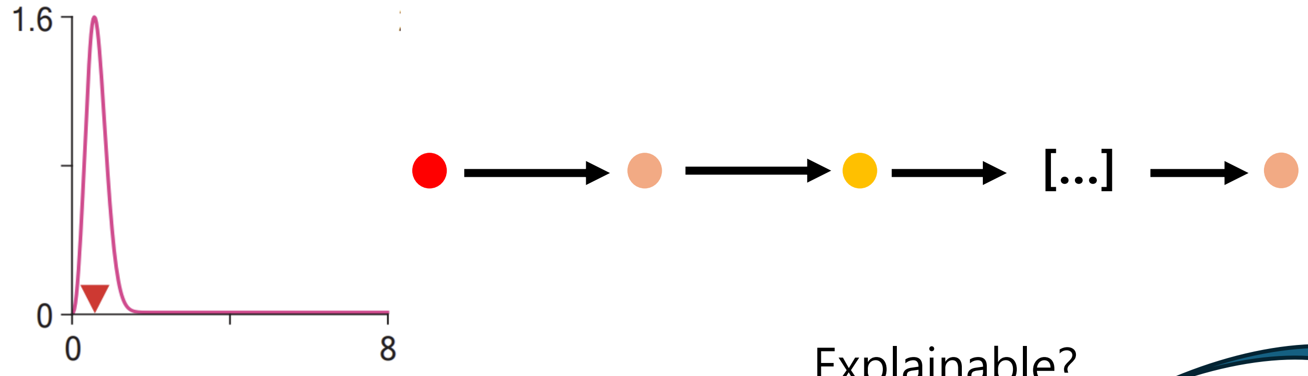
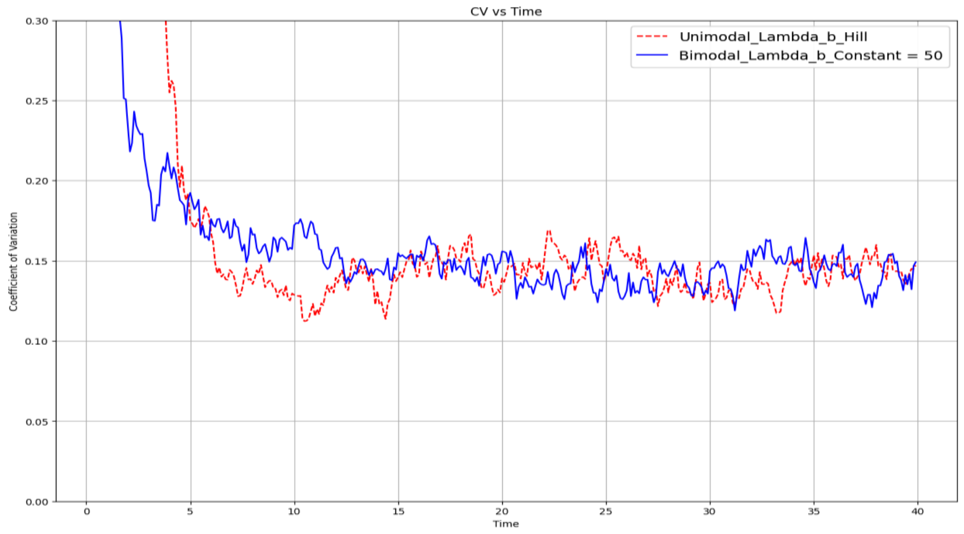
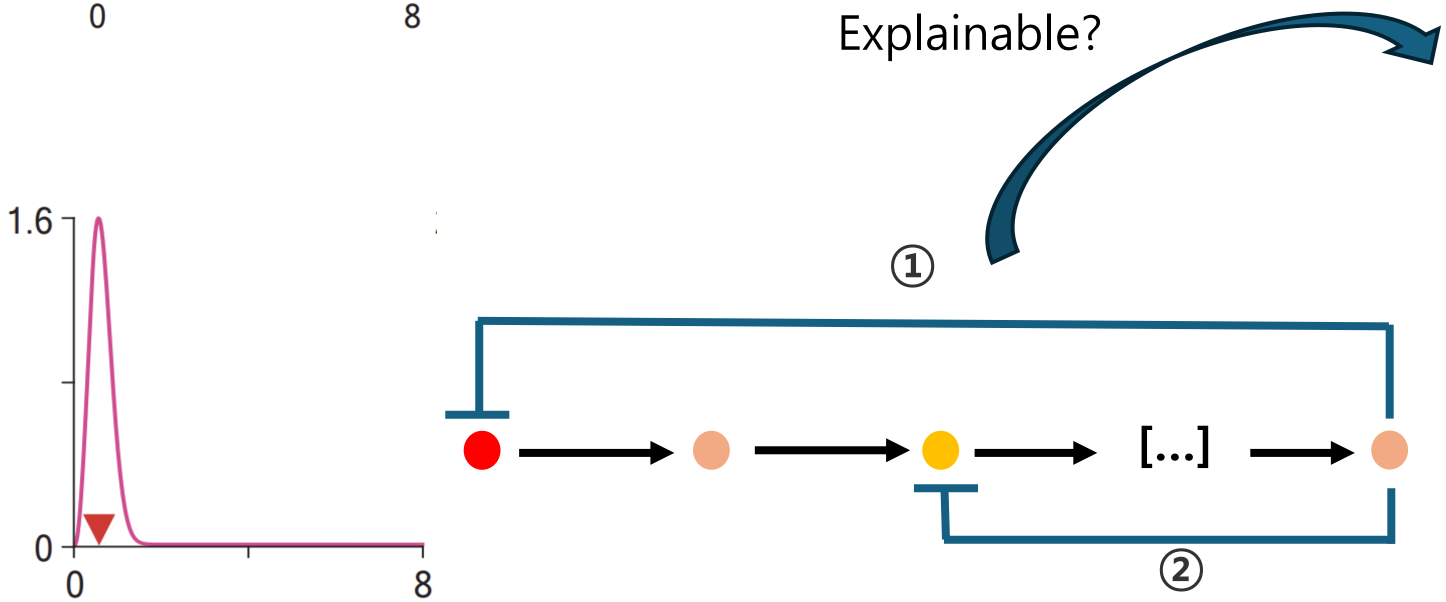




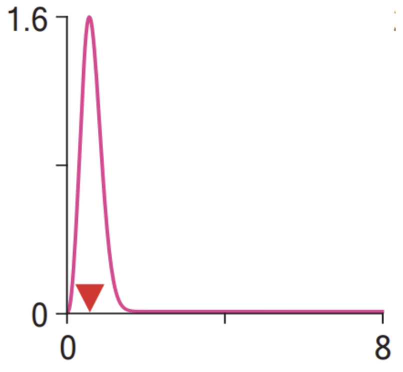


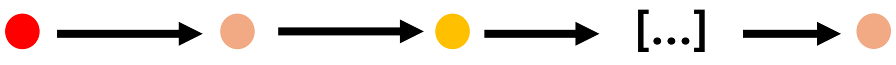
Unimodal + Feedback

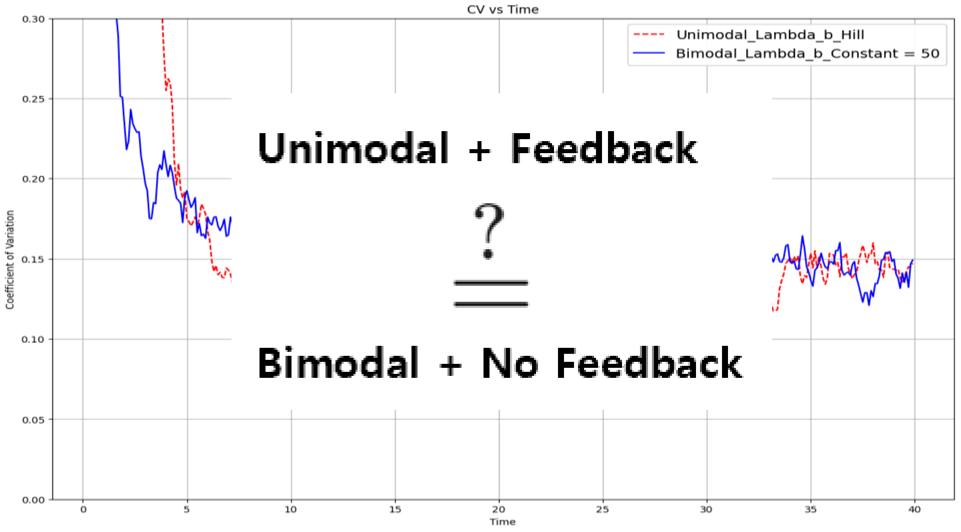
$\stackrel{?}{=}$

Bimodal + No Feedback

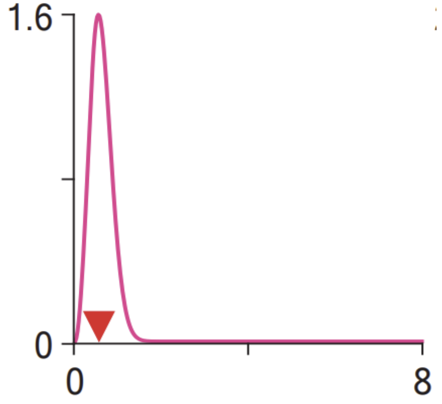
Negative feedback-loop mediated birth/growth inhibition can be modeled by Hill-type birth rate function on X (popul.) and Gamma delay distribution with increasing scale parameter function.

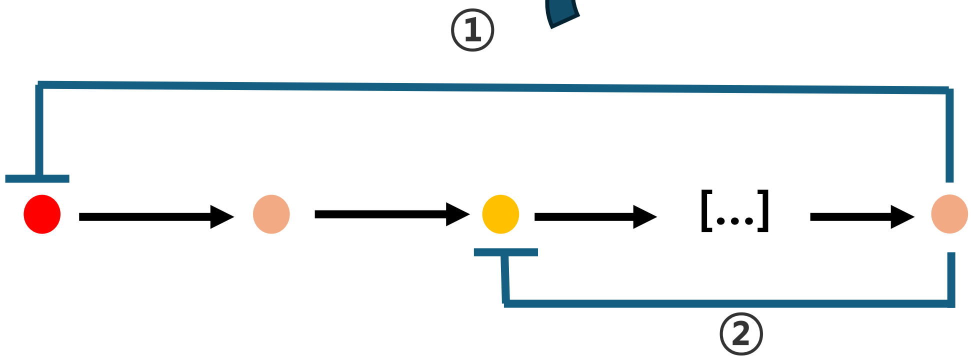






Explainable?





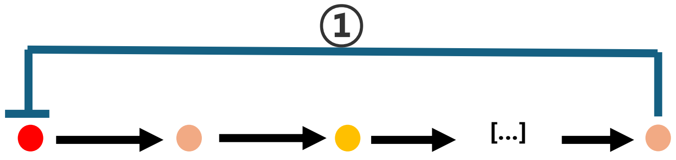
① Birth Inhibition:

$$\lambda_B\left(X(t),\tau\right) = \lambda_B \cdot \frac{1}{1+\left(\dfrac{X(t-\tau)}{C}\right)^n}$$

② Growth Inhibition:

$$\tau \sim \begin{cases} \Gamma(\alpha + kX(t-\tau),\ \beta) \\ \text{or} \\ \Gamma(\alpha,\ \beta) + kX(t-\tau) \end{cases}$$

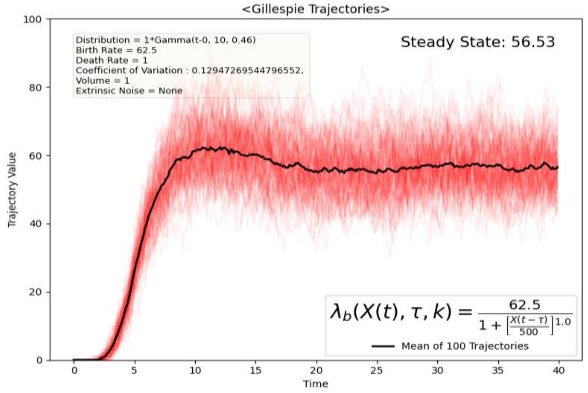
Increasing the influence of negative feedback (Hill-type birth rate, linear scale parameter) causes unstable oscillations in output population.

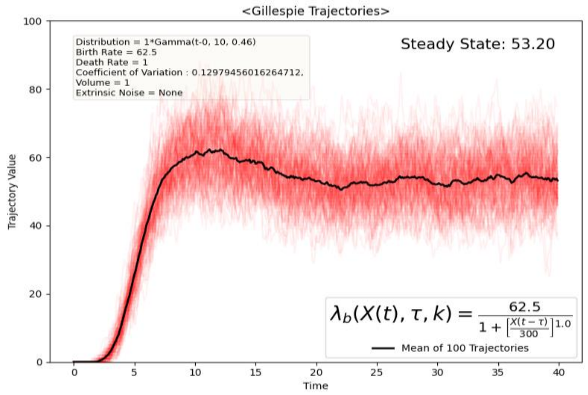


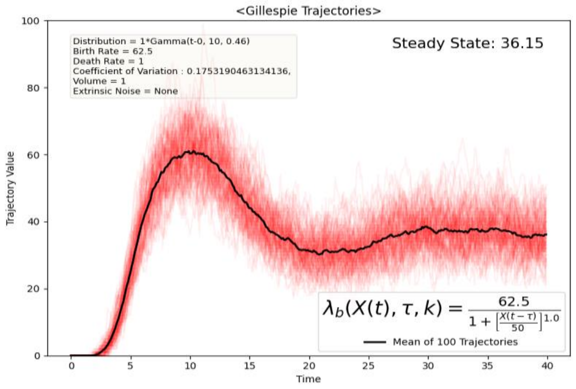
① Birth Inhibition:

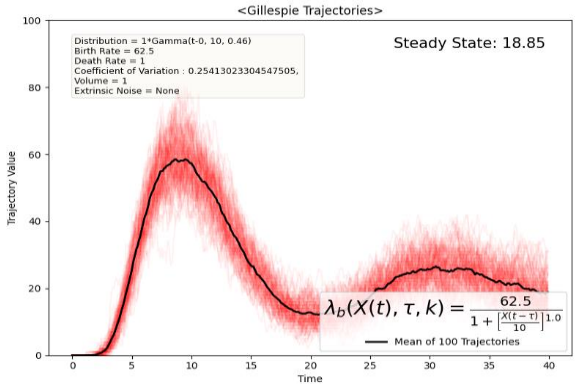
$$\lambda_B = \text{constant} \longrightarrow \lambda_B\left(X(t),\tau\right) = \lambda_B \cdot \frac{1}{1+\left(\frac{X(t-\tau)}{C}\right)^n}$$

$$\lambda_B\left(X(t),\tau\right) = \frac{62.5}{1+\left(\frac{X(t-\tau)}{500}\right)} > \lambda_B\left(X(t),\tau\right) = \frac{62.5}{1+\left(\frac{X(t-\tau)}{300}\right)} > \lambda_B\left(X(t),\tau\right) = \frac{62.5}{1+\left(\frac{X(t-\tau)}{50}\right)} > \lambda_B\left(X(t),\tau\right) = \frac{62.5}{1+\left(\frac{X(t-\tau)}{10}\right)}$$



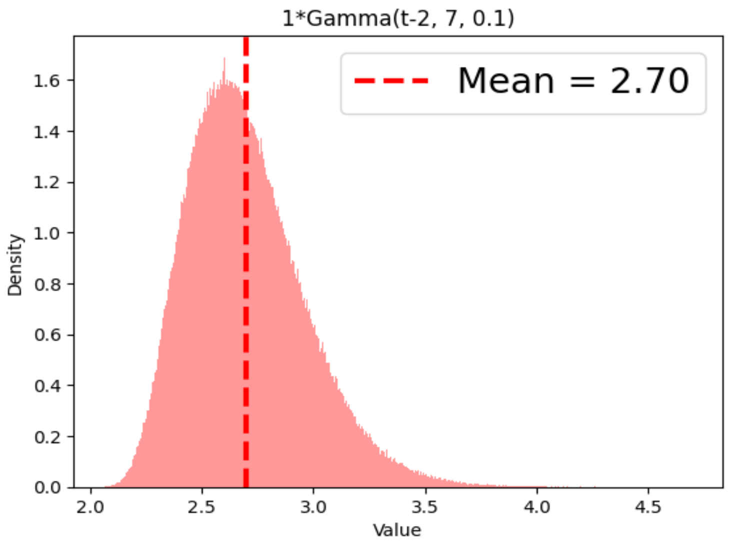


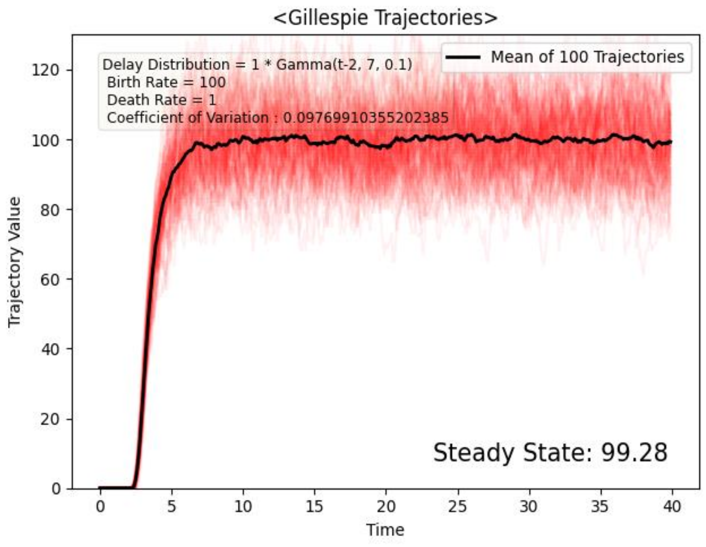




Significant overlap between unimodal + feedback & bimodal trajectories is observed at the same steady states and distribution mean.

$$\lambda_B = 100$$

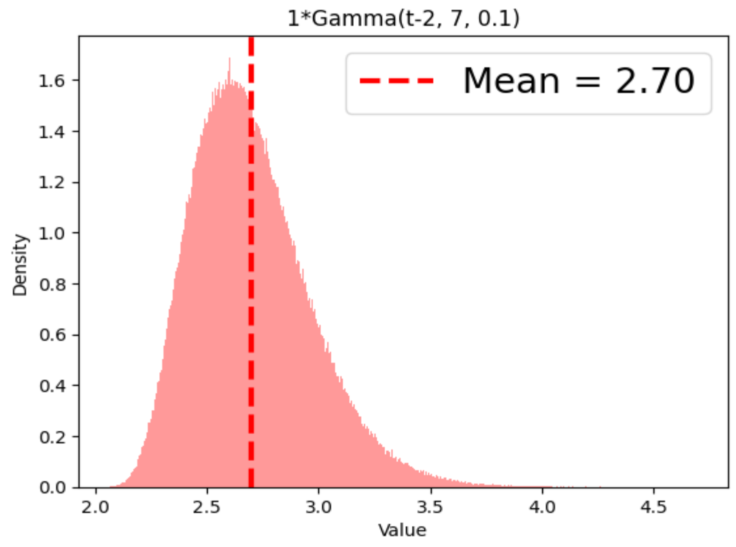


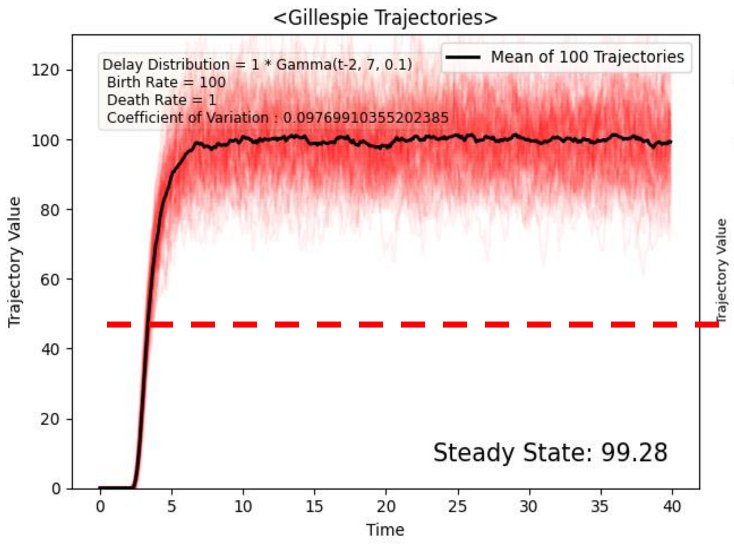


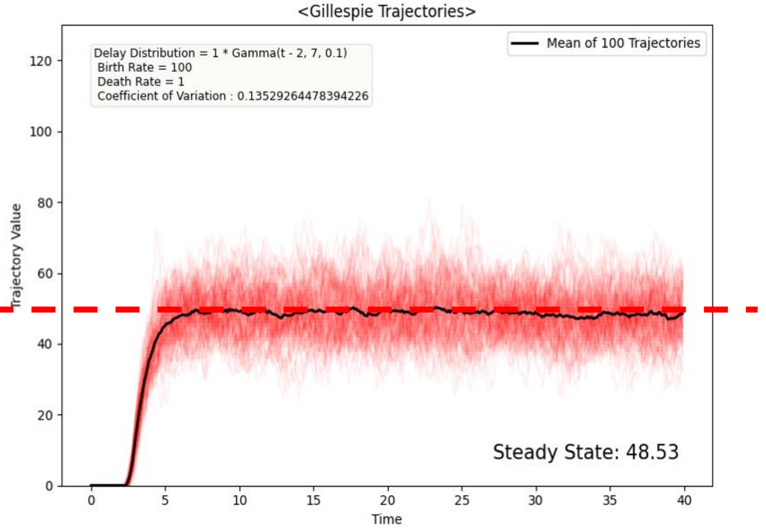
Significant overlap between unimodal + feedback & bimodal trajectories is observed at the same steady states and distribution mean.

$$\lambda_B = 100$$

$$\lambda_B\left(X(t), \tau\right) = \frac{100}{2 + \left(\frac{X(t-\tau)}{500}\right)}$$







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$$\lambda_B\left(X(t),\tau\right) = \frac{100}{2 + \left(\frac{X(t-\tau)}{500}\right)}$$

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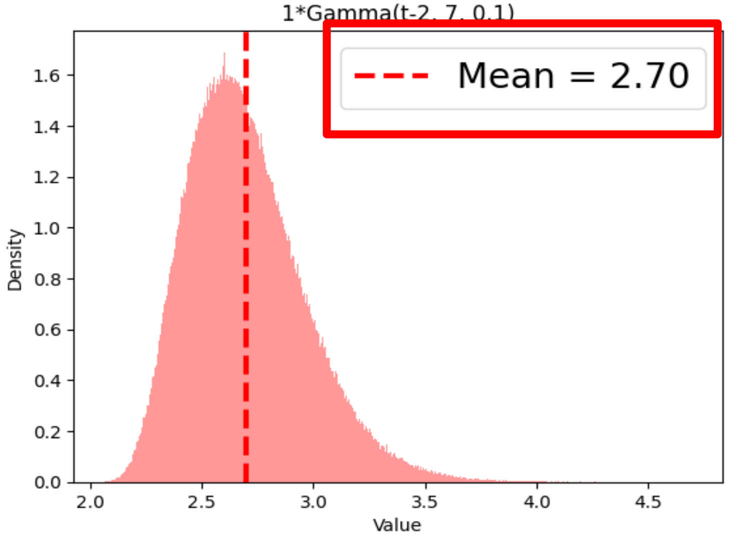
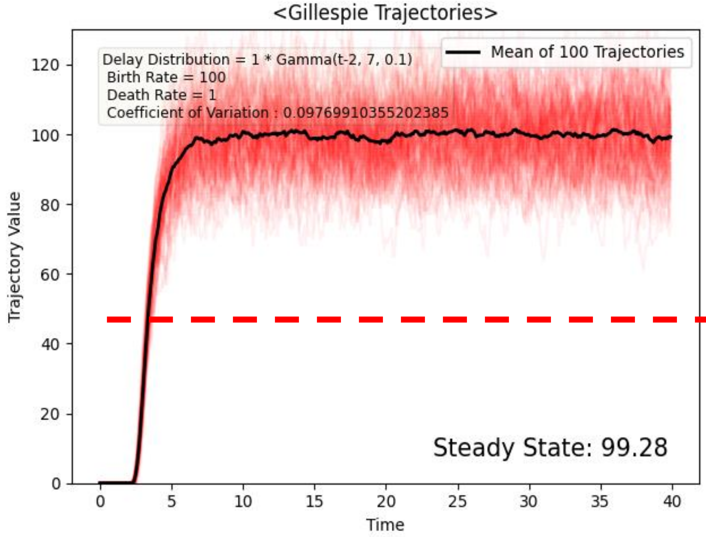
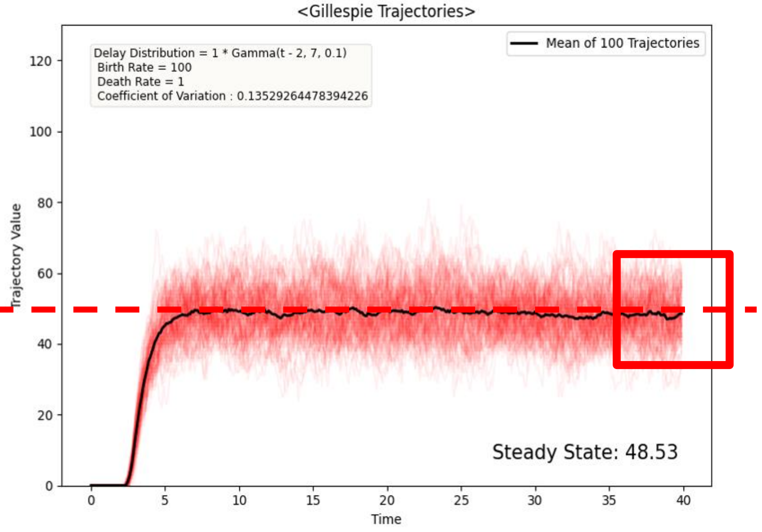
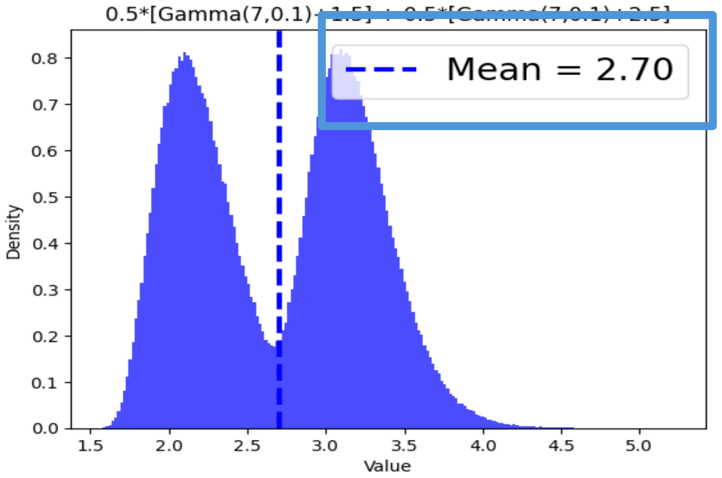
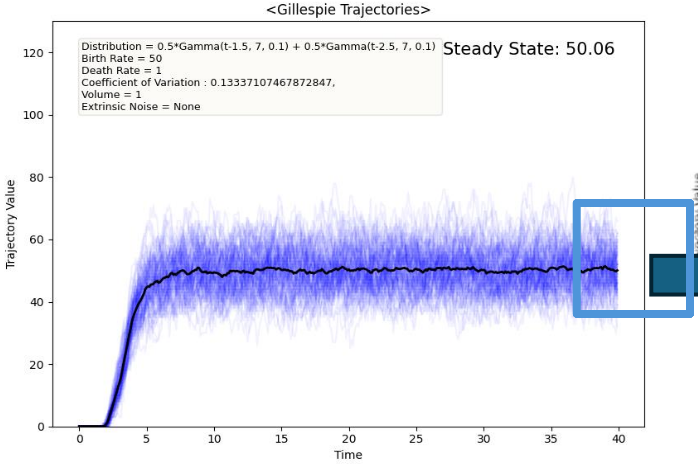


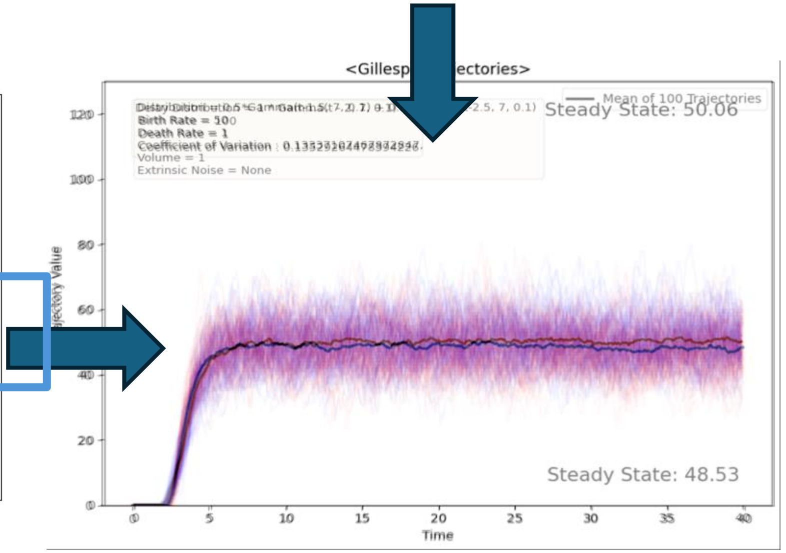




$$\lambda_B = 50$$







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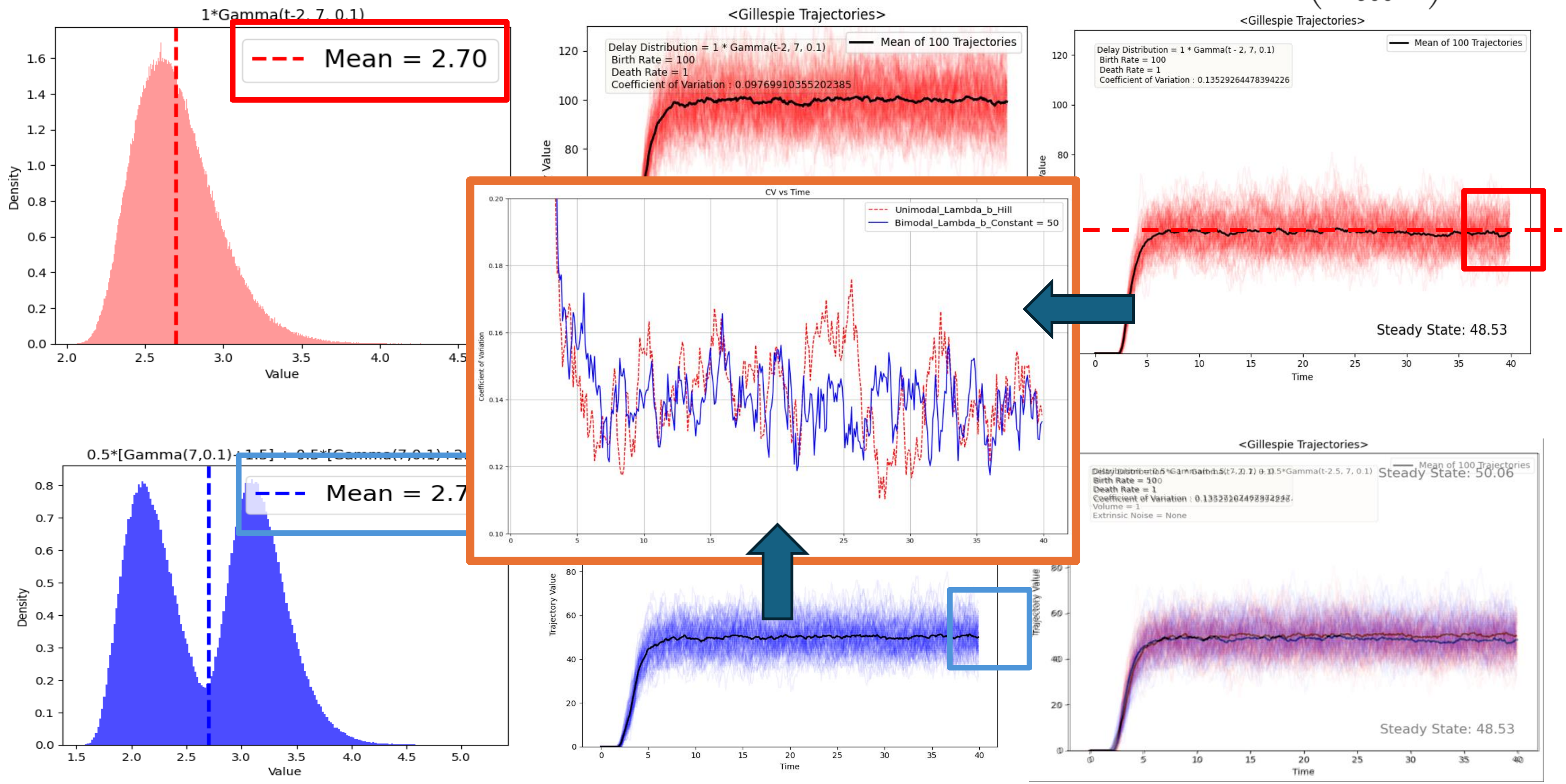
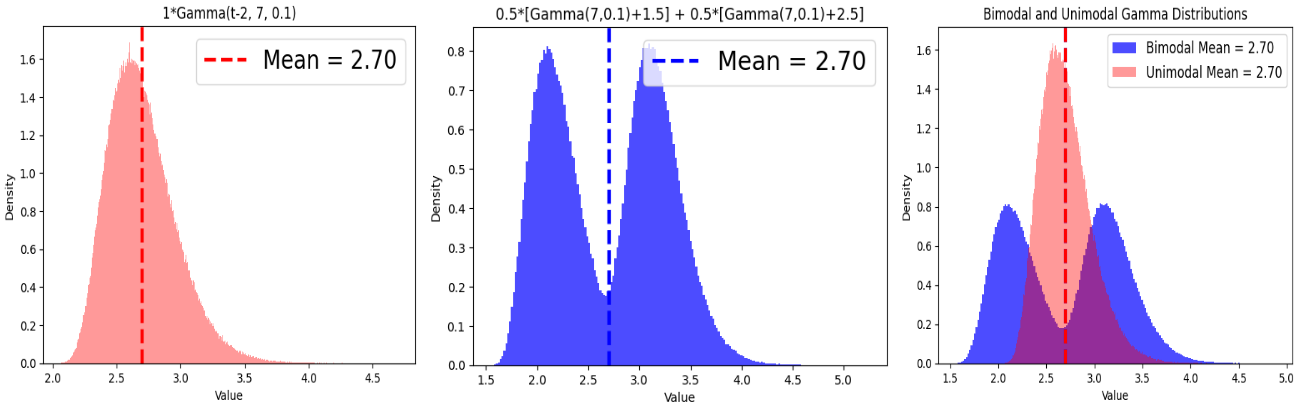
$$\lambda_B\left(X(t),\tau\right) = \frac{100}{2 + \left(\frac{X(t-\tau)}{500}\right)}$$



Trajectories' alignment depends on the bimodal distribution shape, and the constant added in the denominator in the negative feedback term.



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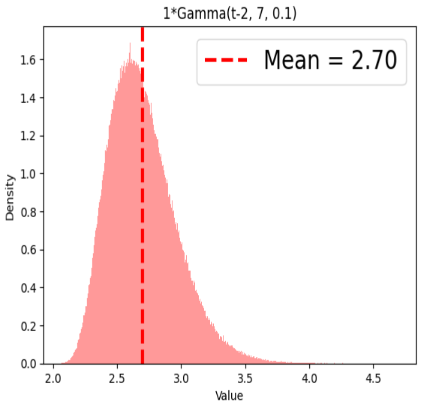

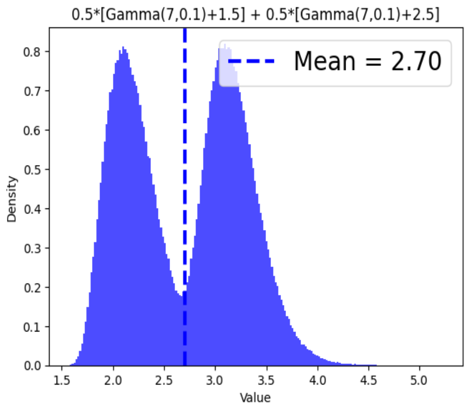

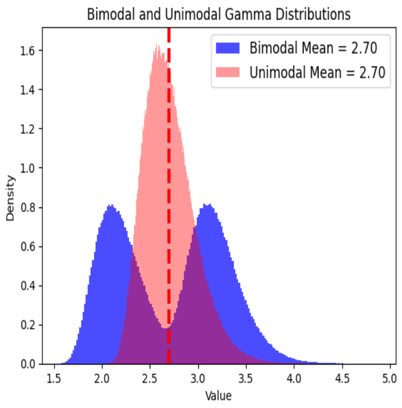

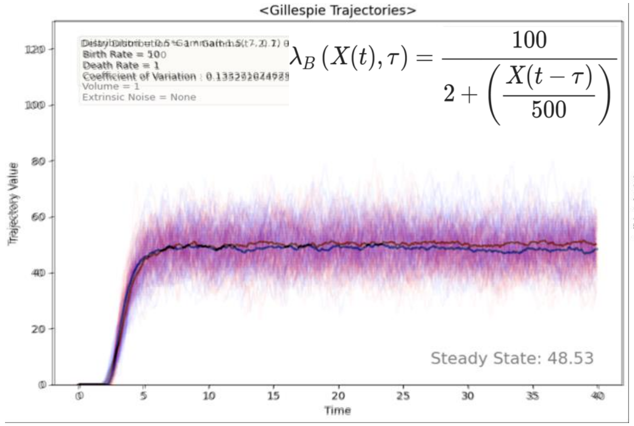

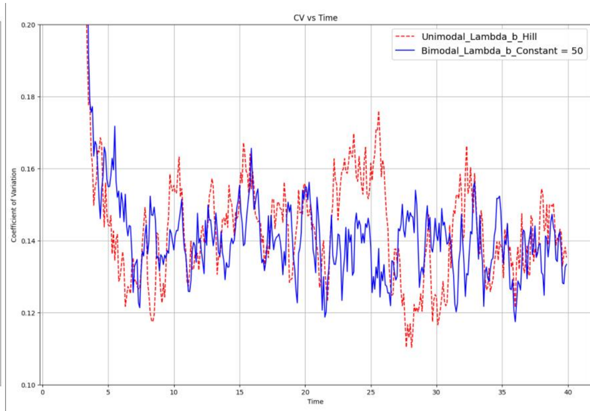

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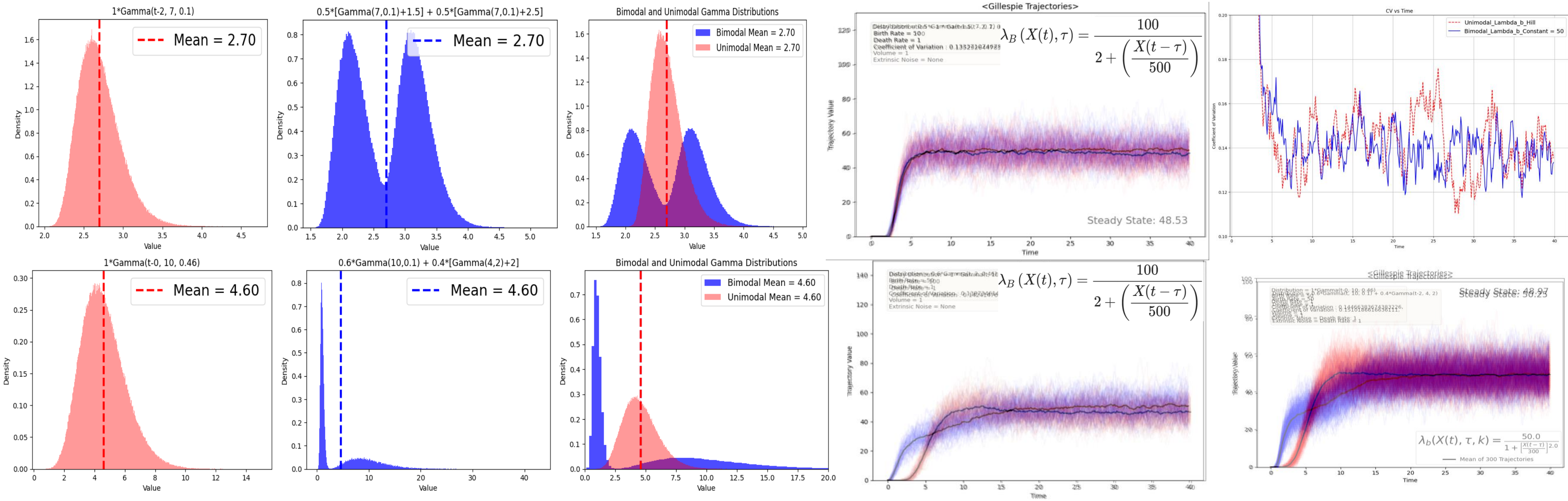

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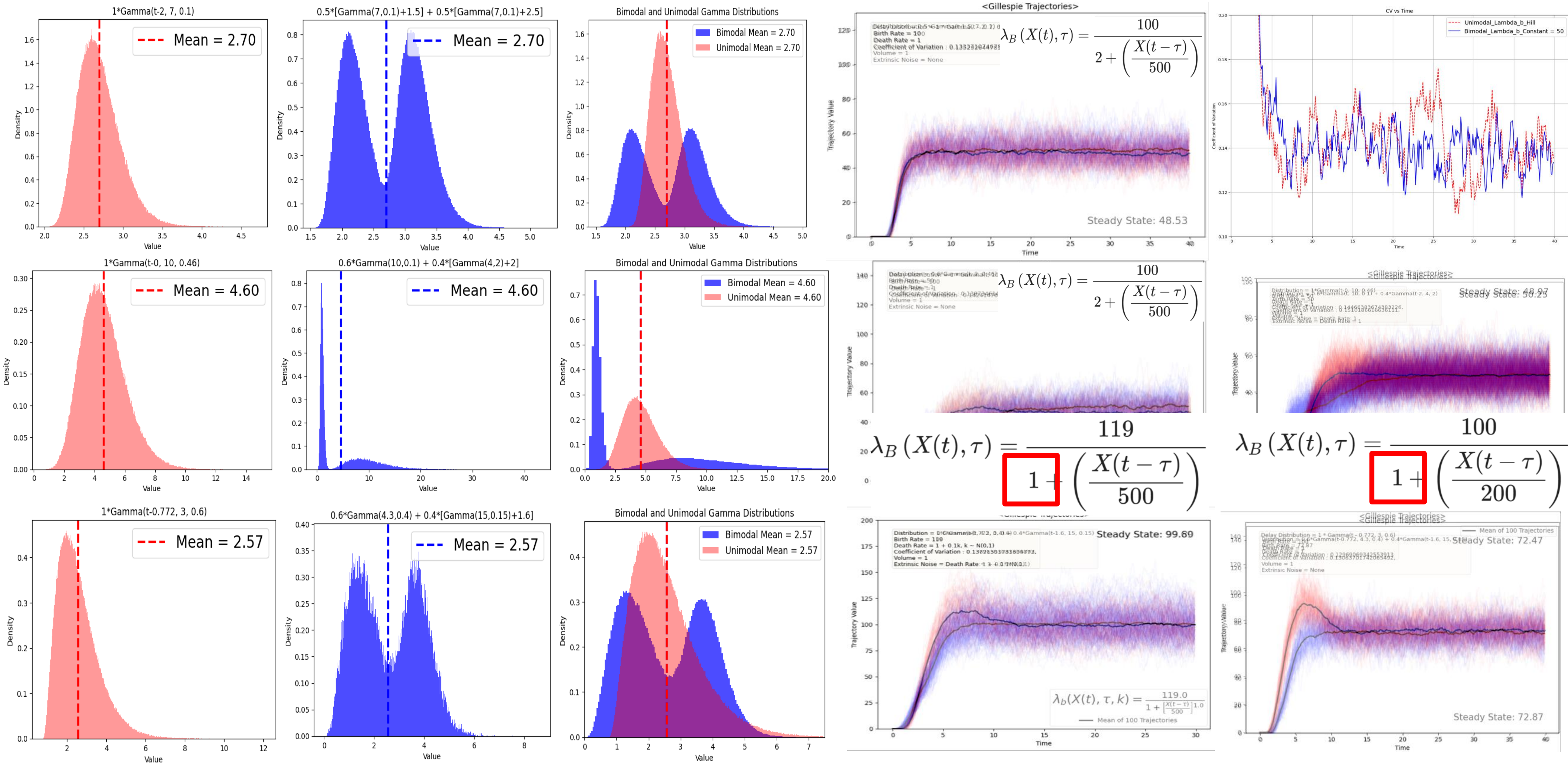
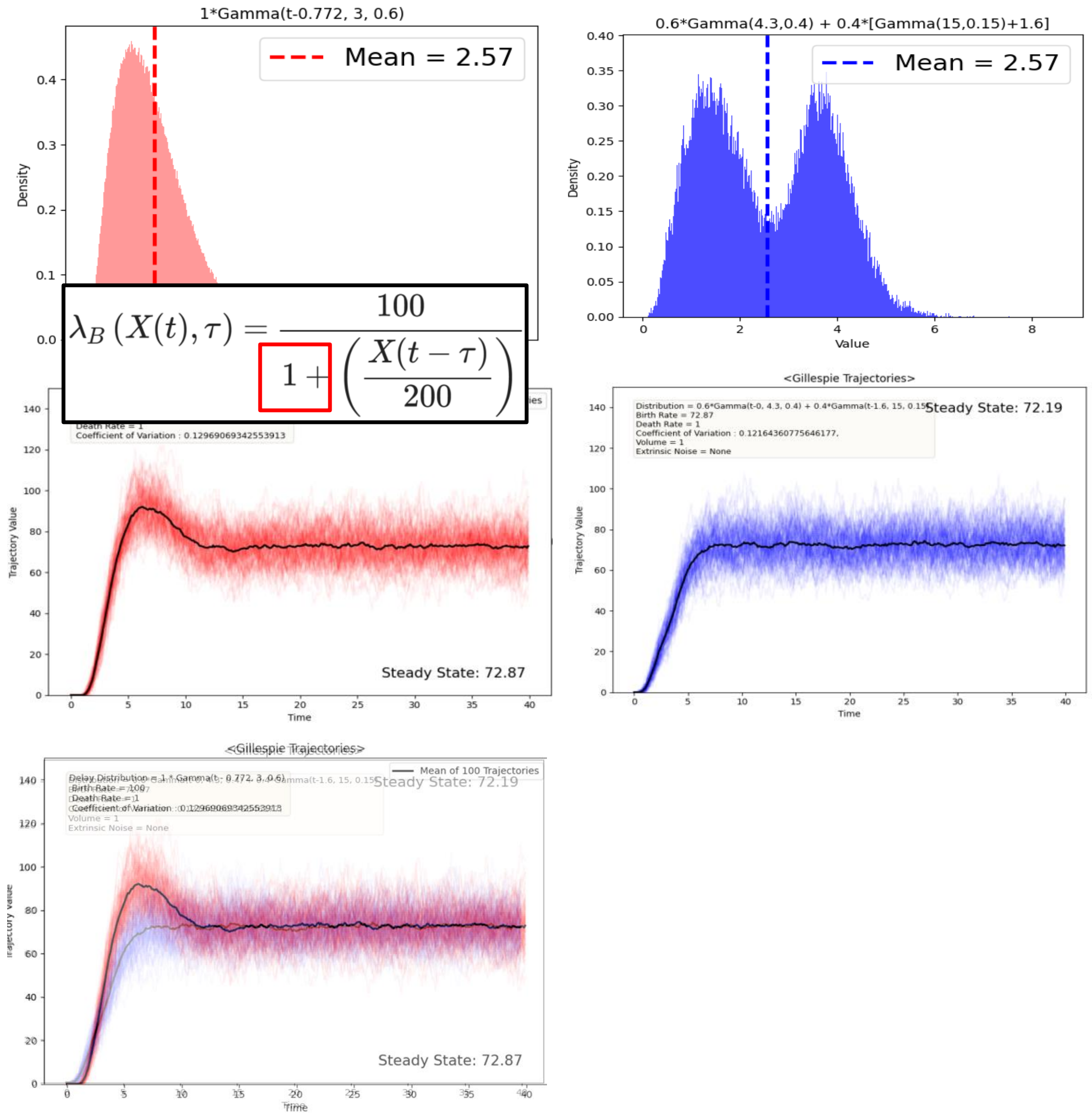
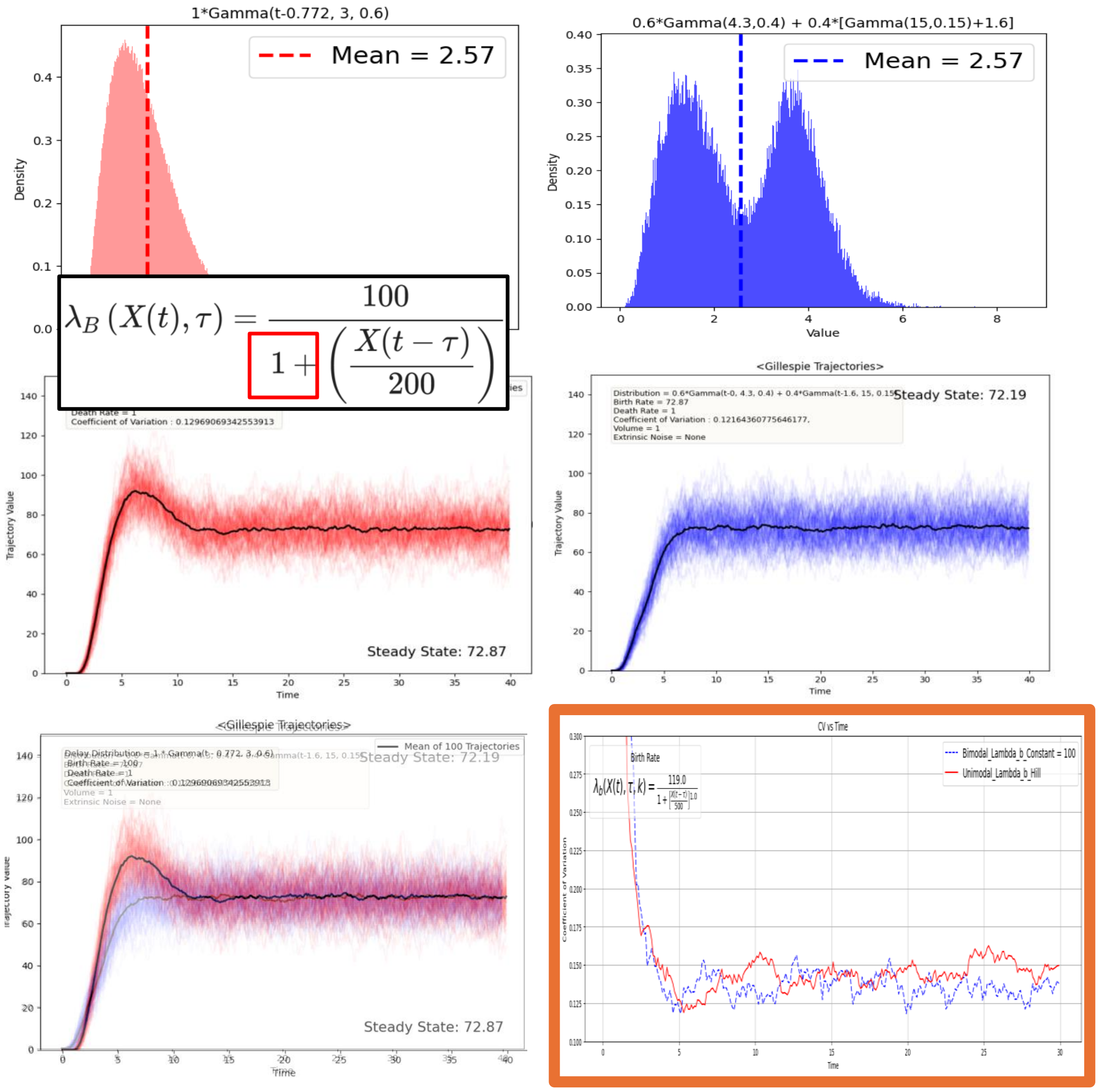


Bimodal delay Gillespie shows no CV difference with unimodal delay/negative feedback, at same distribution mean and steady state.



$$\lambda_B\left(X(t),\tau\right)=\frac{100}{\boxed{1+}\left(\frac{X(t-\tau)}{200}\right)}$$

Bimodal delay Gillespie shows no CV difference with unimodal delay/negative feedback, at same distribution mean and steady state.



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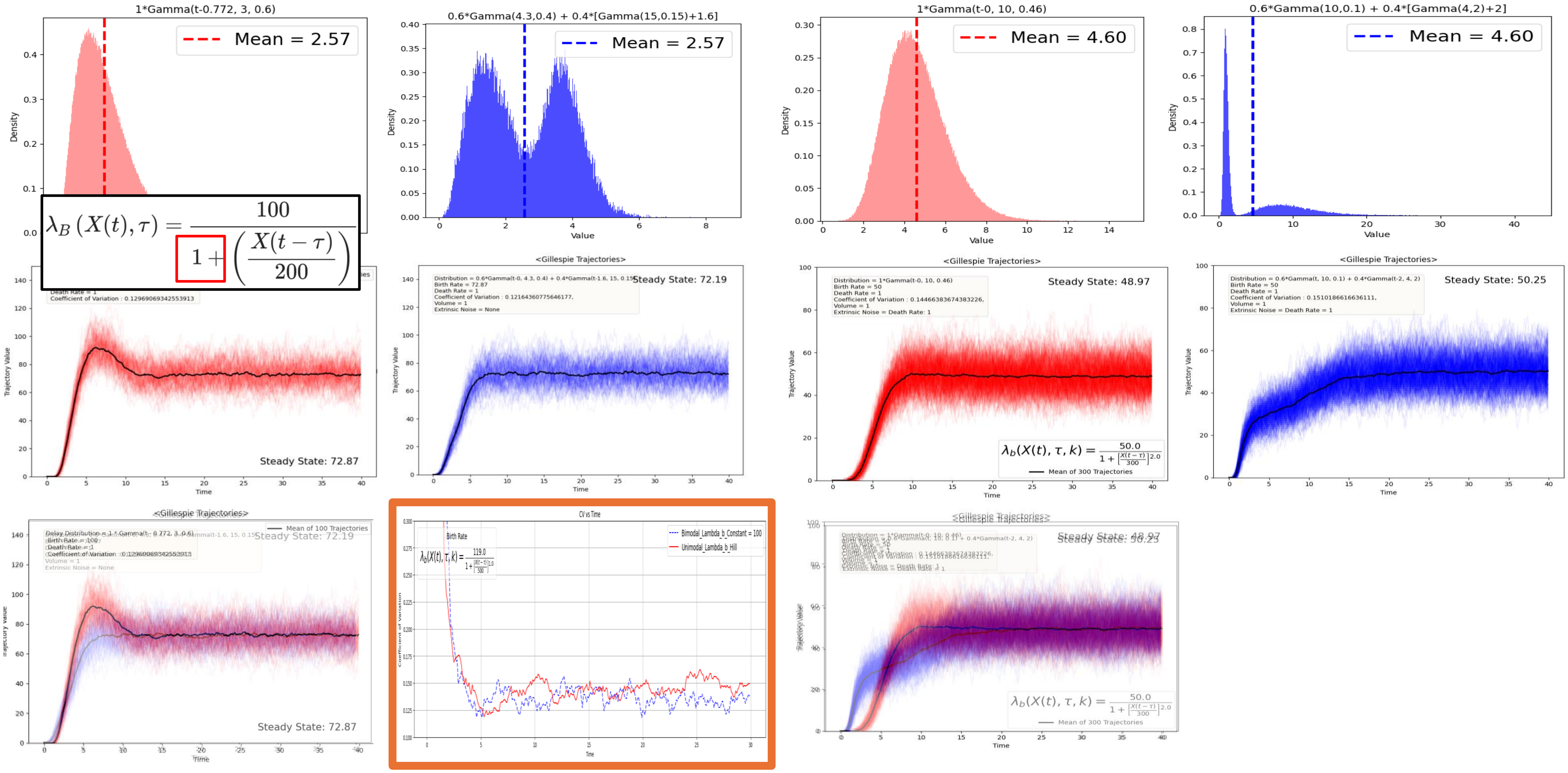

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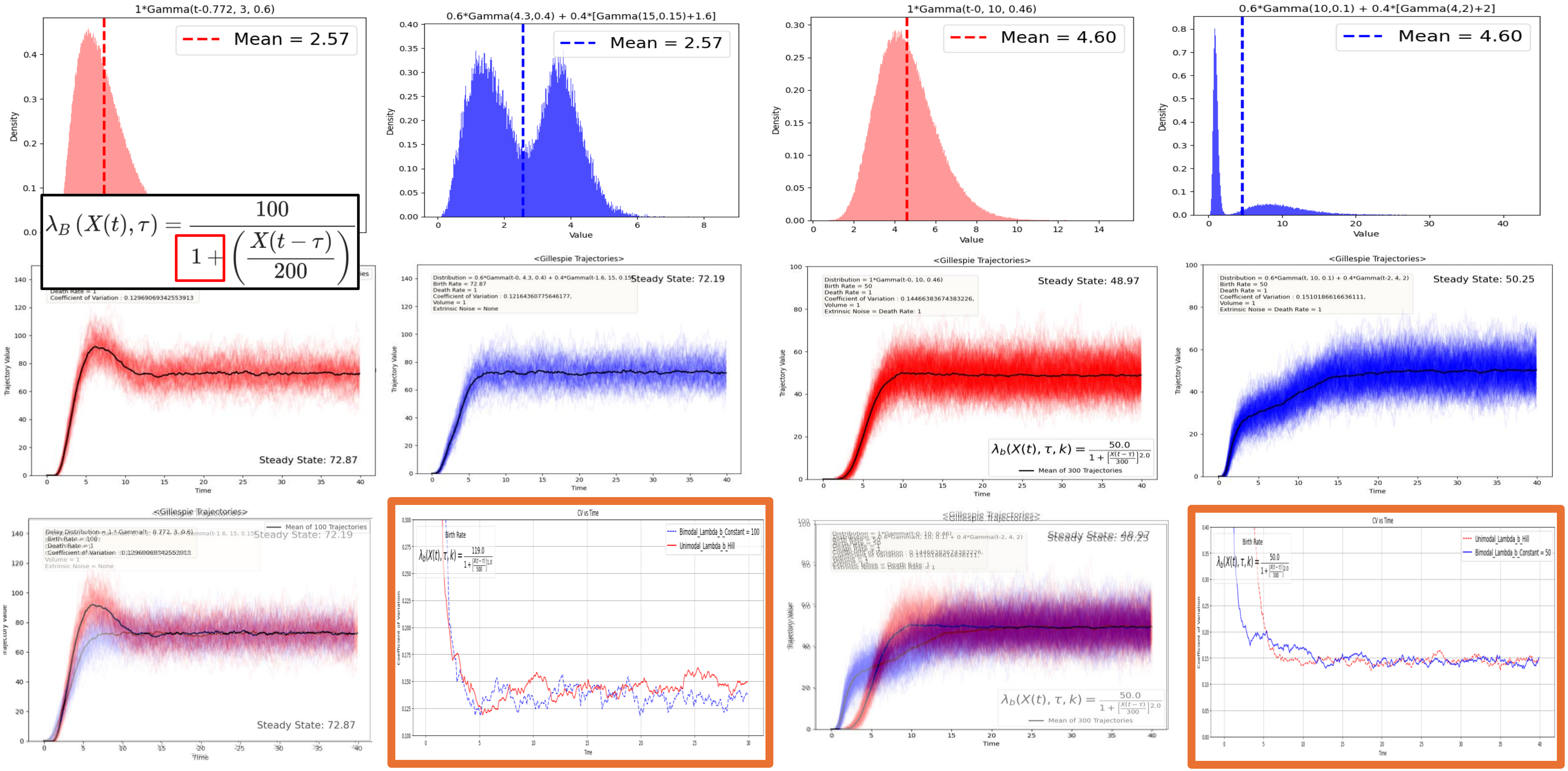
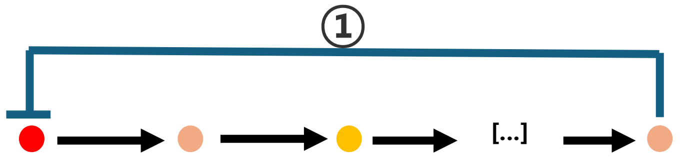


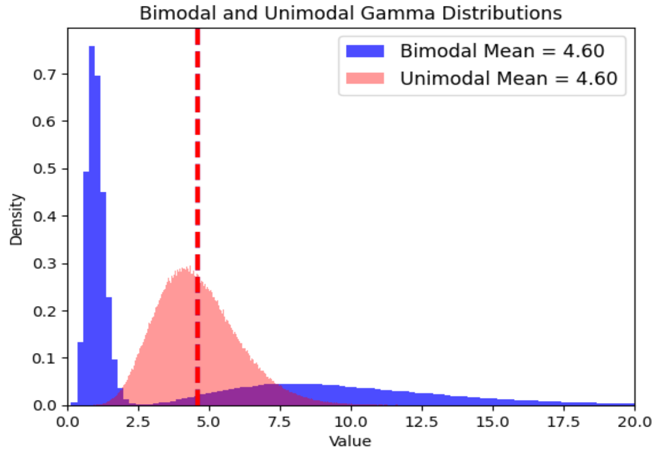
Bimodal delay Gillespie can be modeled with unimodal delay with negative feedback, but no CV difference is observed when compared with unimodal delay with same steady state.



① Birth Inhibition:

Steady State

$$\lambda_B\left(X(t),\tau\right) = 62.5 \longrightarrow \lambda_B\left(X(t),\tau\right) = \frac{62.5}{\boxed{1+}\left(\frac{X(t-\tau)}{168}\right)} \Rightarrow$$ **50**



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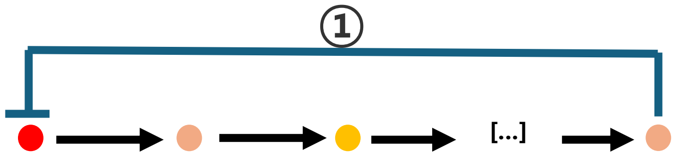

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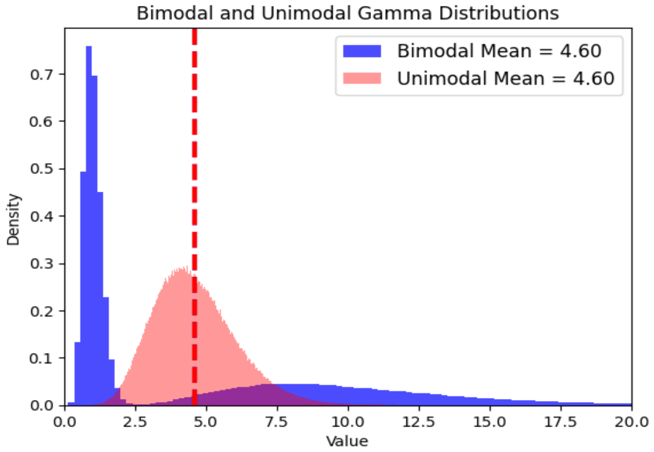
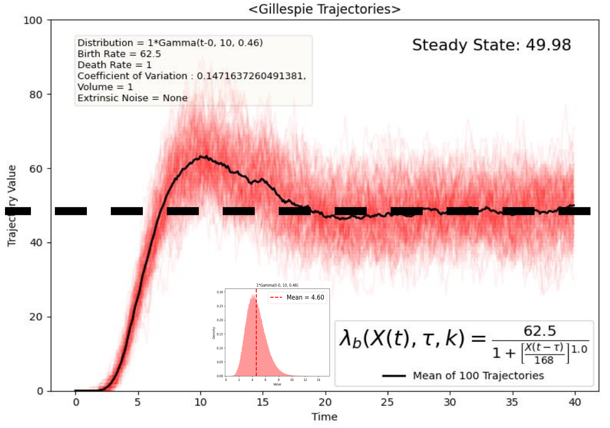
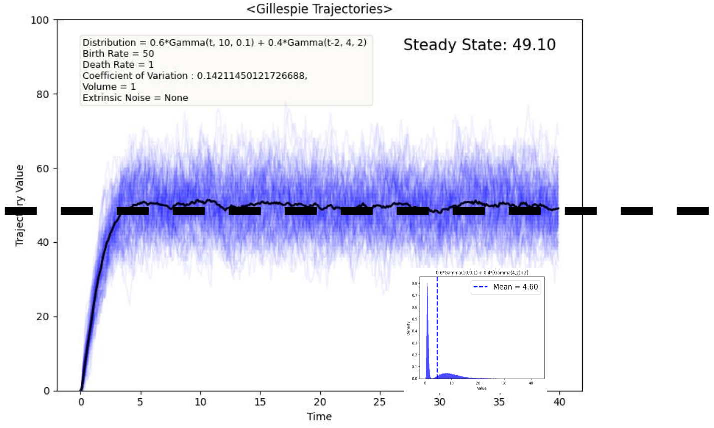
Steady State

50







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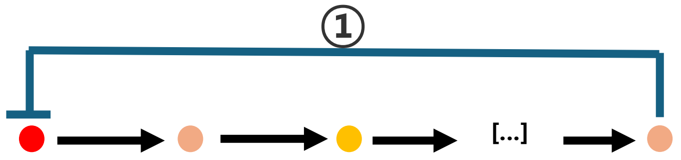

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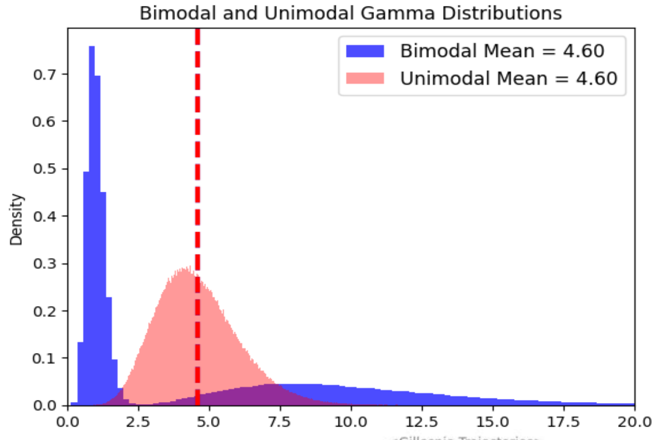
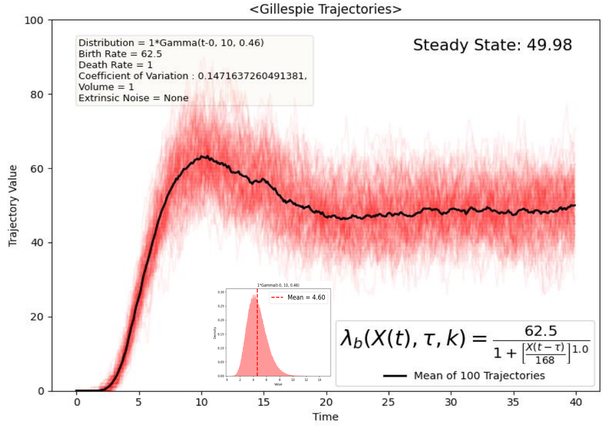
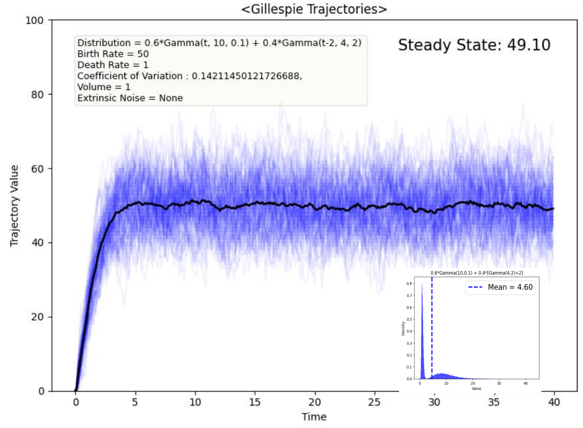
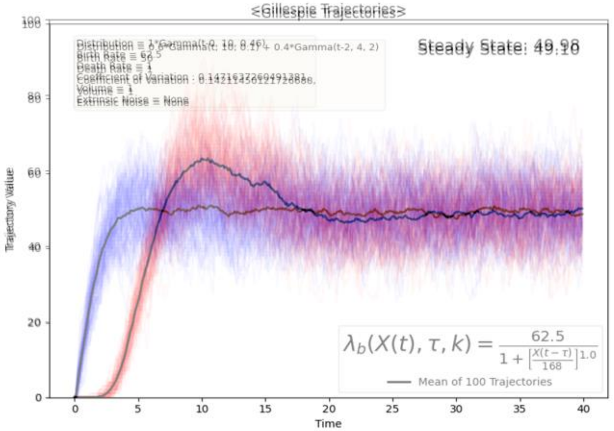
Steady State

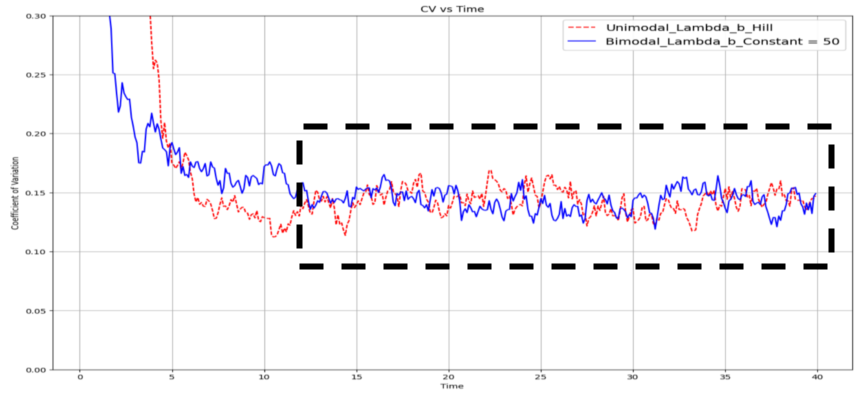
50











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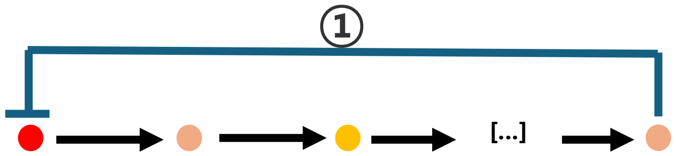

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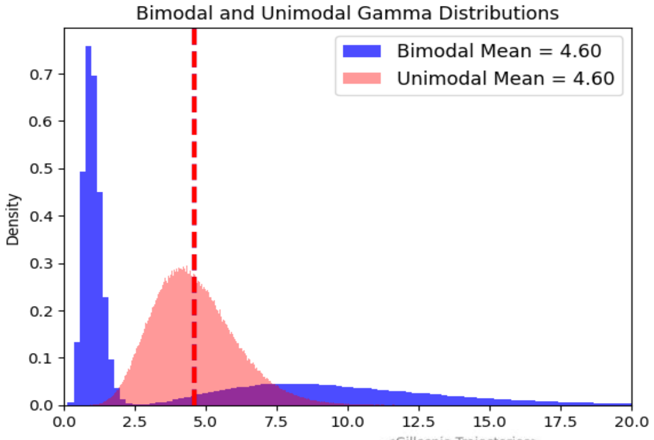
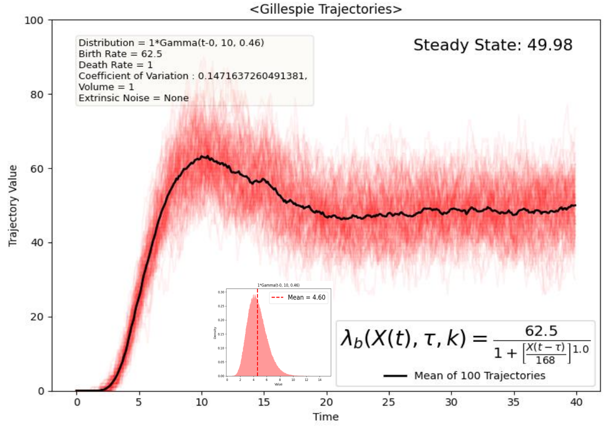
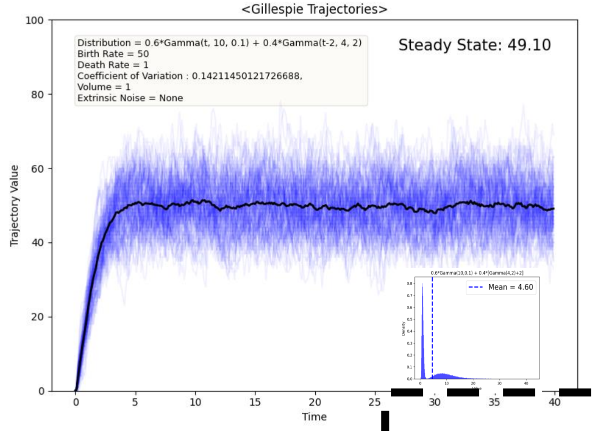
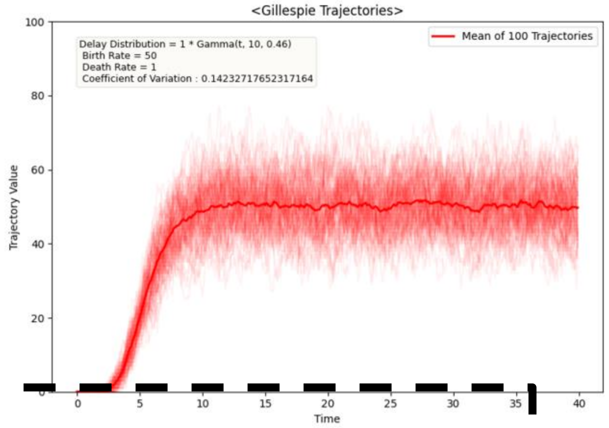
Steady State

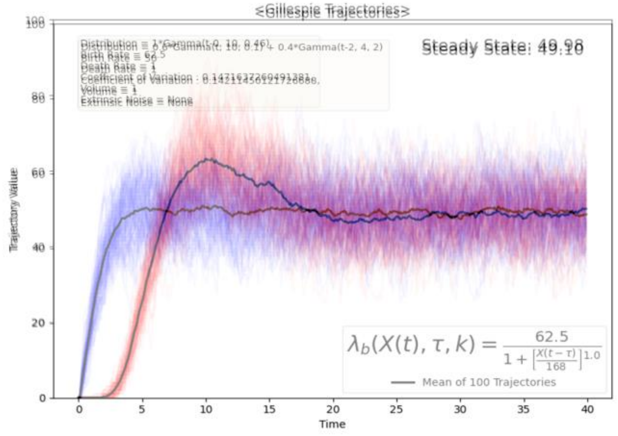
50

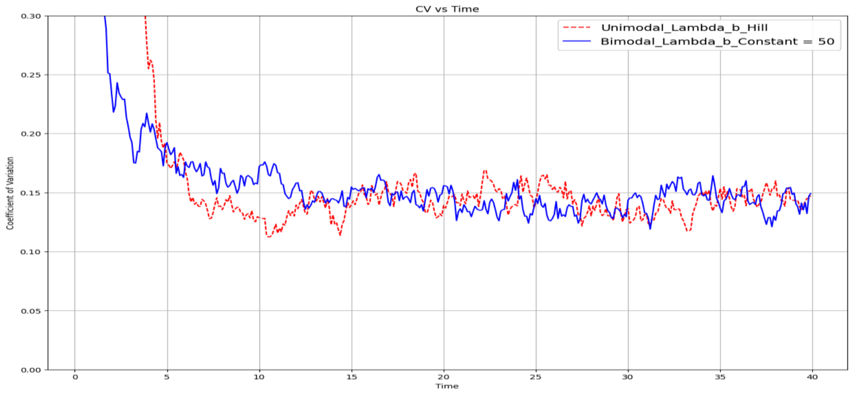


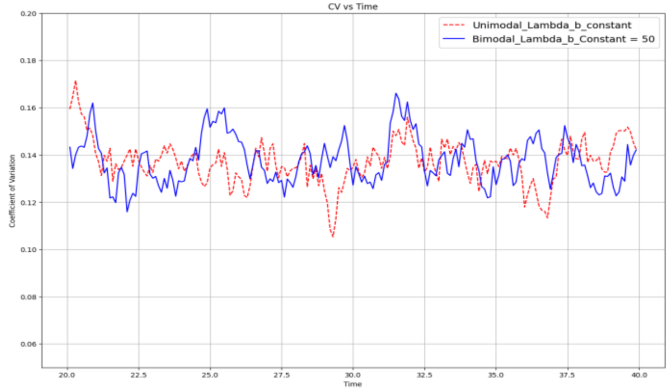




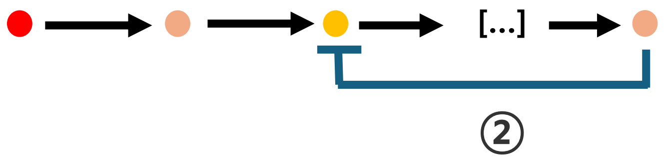






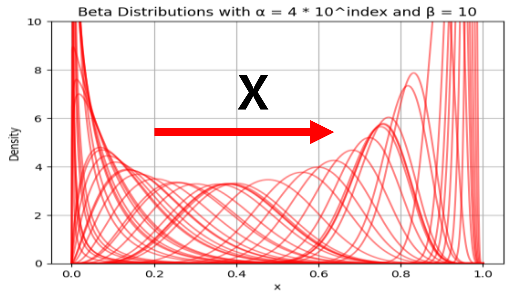


Increasing the influence of negative feedback (Hill-type birth rate, linear scale parameter) causes unstable oscillations in output population.



② Growth Inhibition:

$$\tau \sim \Gamma(\alpha, \beta) \longrightarrow \tau \sim \begin{cases} \Gamma(\alpha + kX(t-\tau),\ \beta) \\ \text{or} \\ \Gamma(\alpha,\ \beta) + kX(t-\tau) \end{cases}$$



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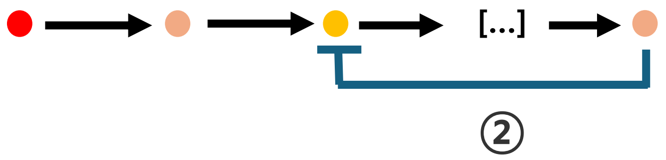

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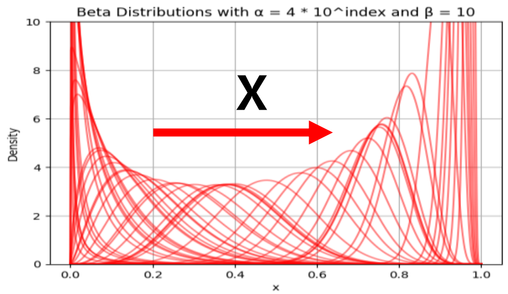
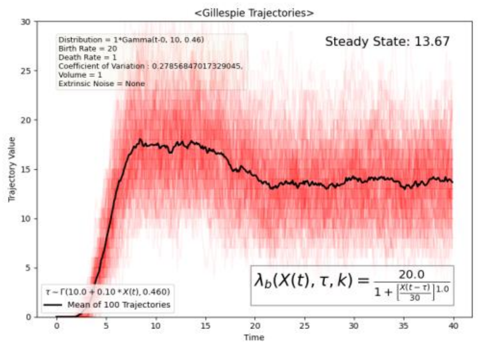
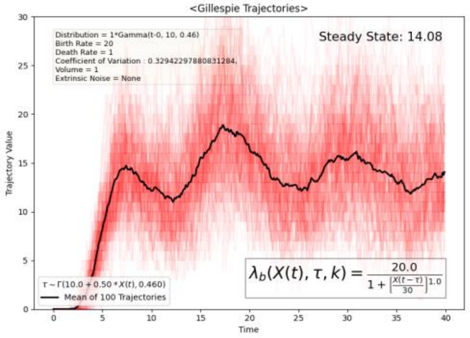


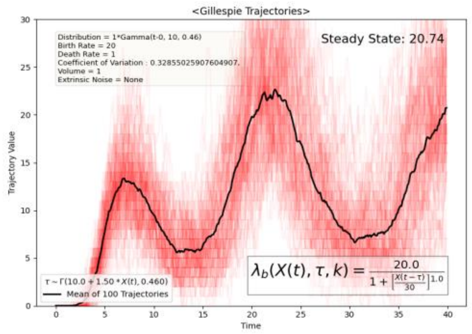
$$\Gamma(10 + 0.1 \cdot X(t), 0.46)$$



$$\Gamma(10 + 0.5 \cdot X(t), 0.46)$$



$$\Gamma(10 + 1.5 \cdot X(t), 0.46)$$



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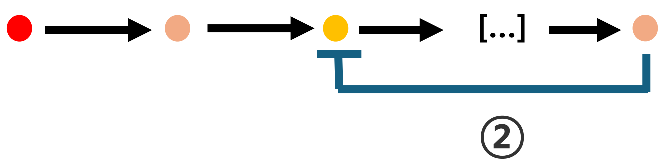

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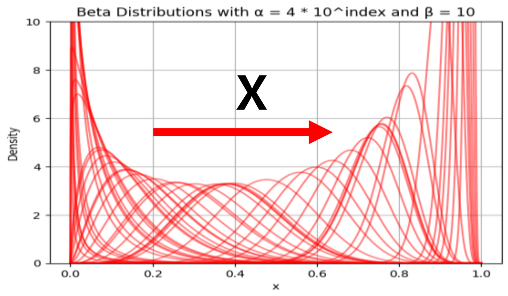

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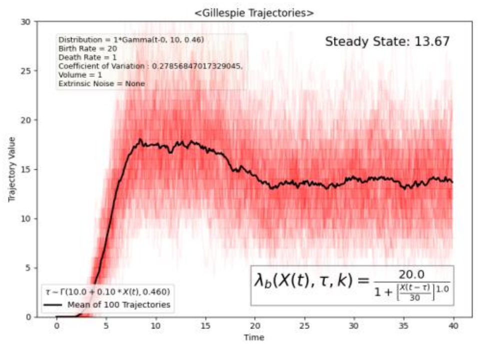

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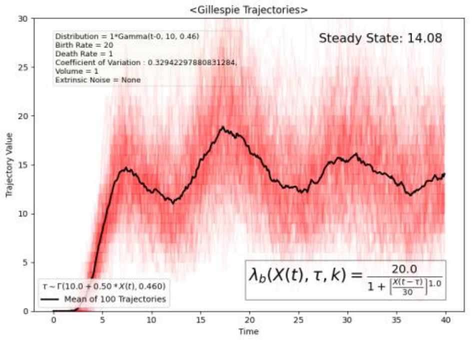
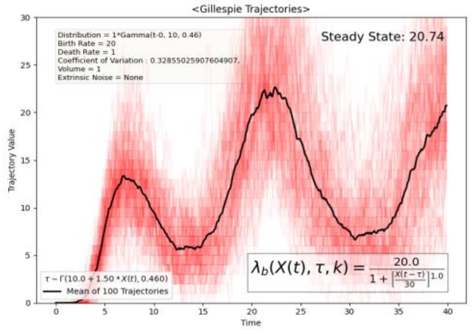
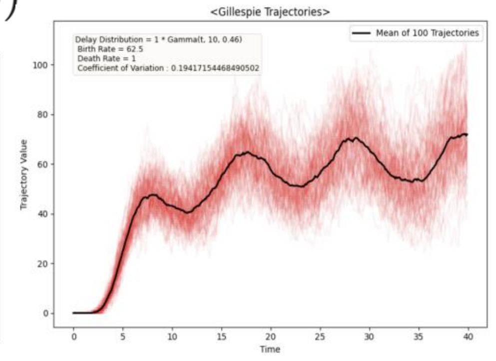


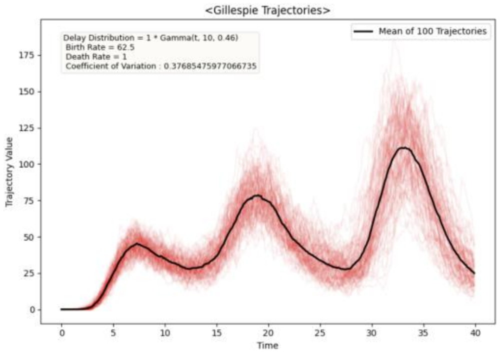
$\Gamma(10 + 1.5 \cdot X(t), 0.46)$



$\Gamma(10, 0.46) + 0.05 \cdot X(t)$



$\Gamma(10, 0.46) + 0.1 \cdot X(t)$



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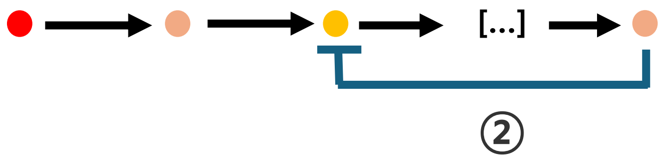

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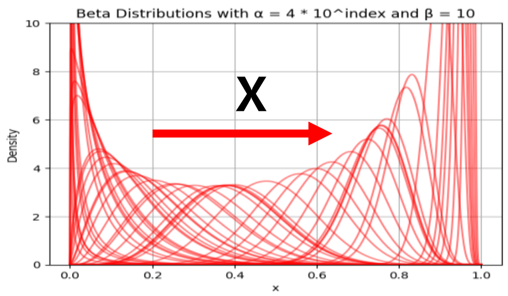
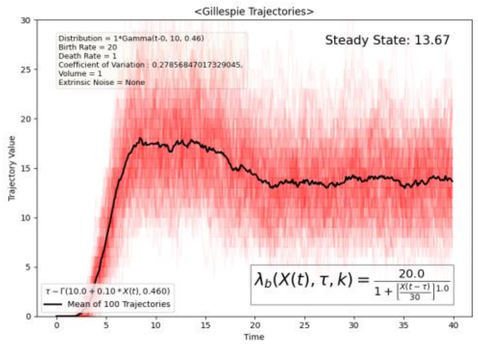
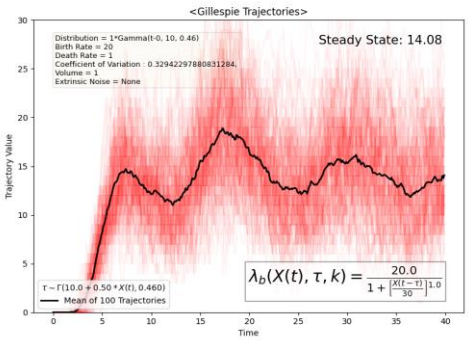


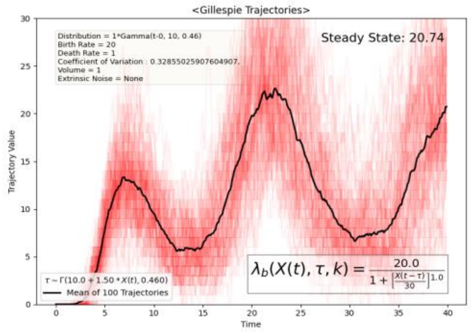
$\Gamma(10 + 0.1 \cdot X(t), 0.46)$



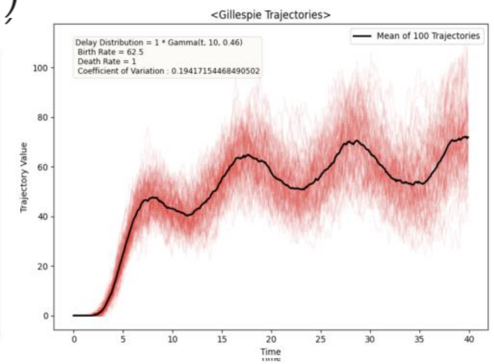
$\Gamma(10 + 0.5 \cdot X(t), 0.46)$



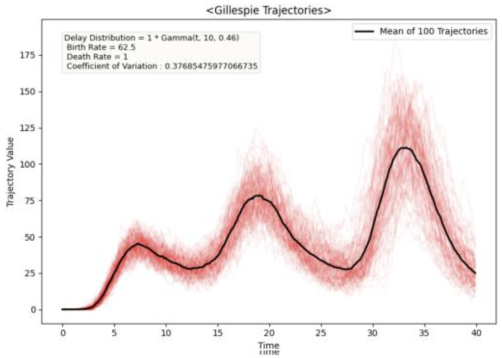
$\Gamma(10 + 1.5 \cdot X(t), 0.46)$



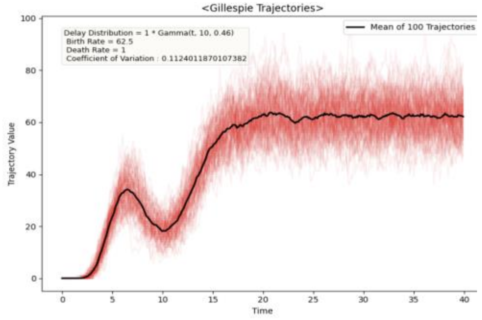
$\Gamma(10, 0.46) + 0.05 \cdot X(t)$



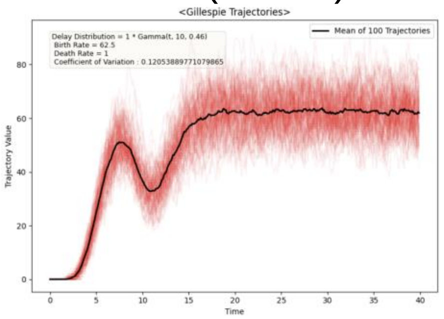
$\Gamma(10, 0.46) + 0.1 \cdot X(t)$



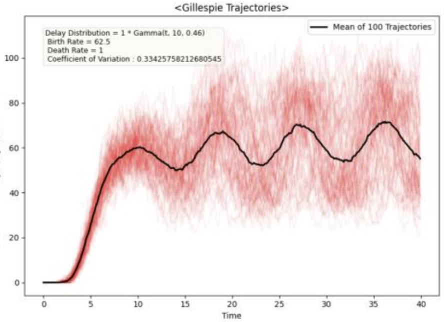
$\Gamma(\frac{20}{1+e^{-X}}, 0.46)$



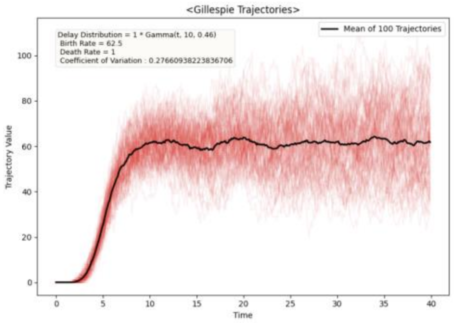
α= 10 (X<20)
α= 20 (X>20)



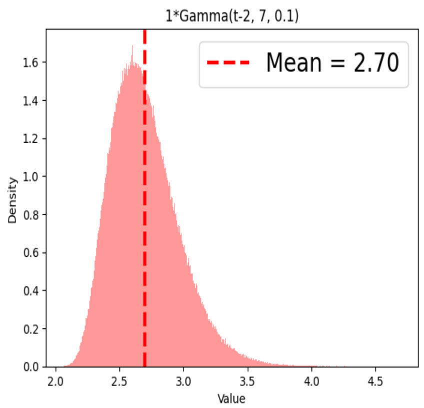
α = 10 (X<40)
α = 20 (X>40)

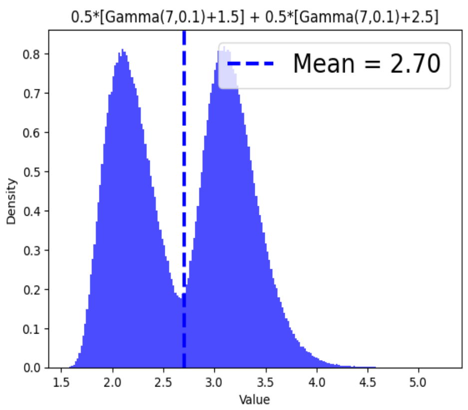


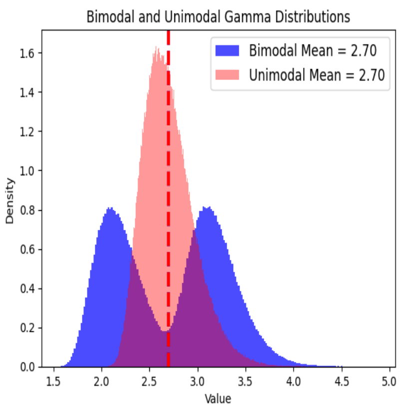
α = 10 (X<70)
α = 20 (X>70)

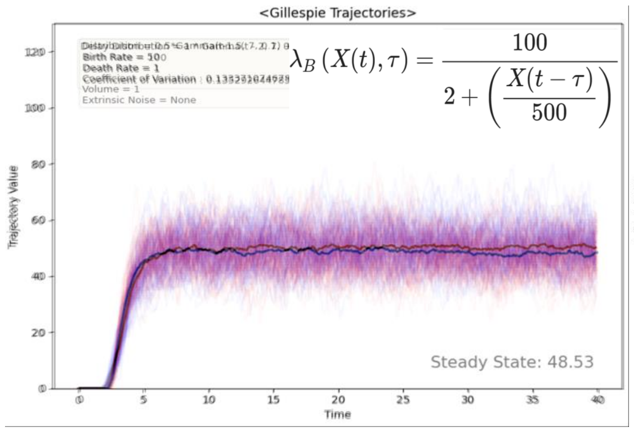


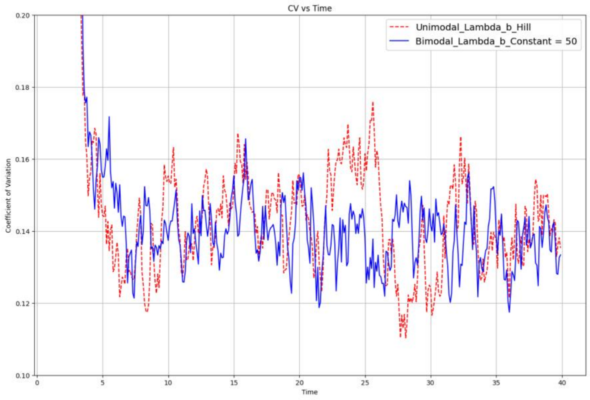
Future Directions: Apply D-PINN to Unimodal + Feedback











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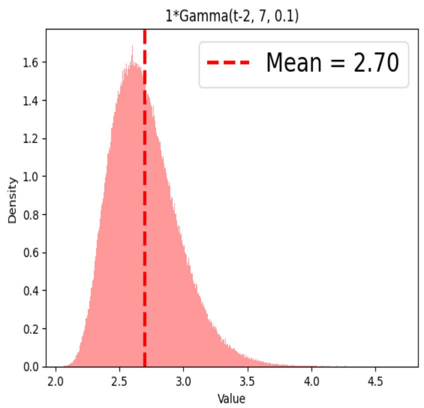

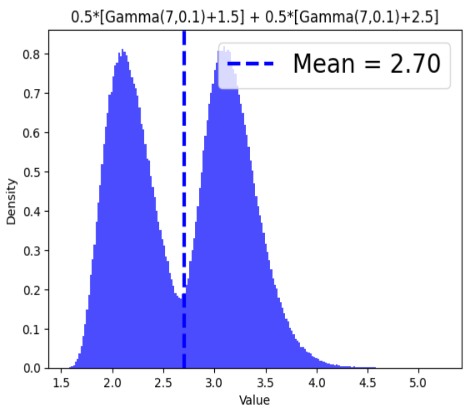

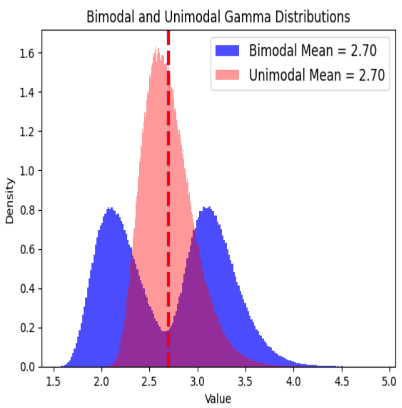

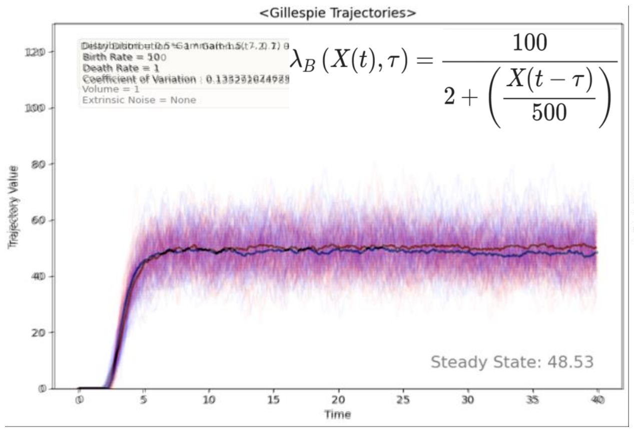

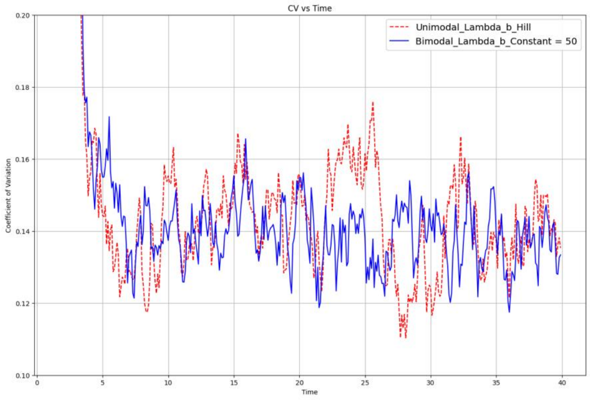

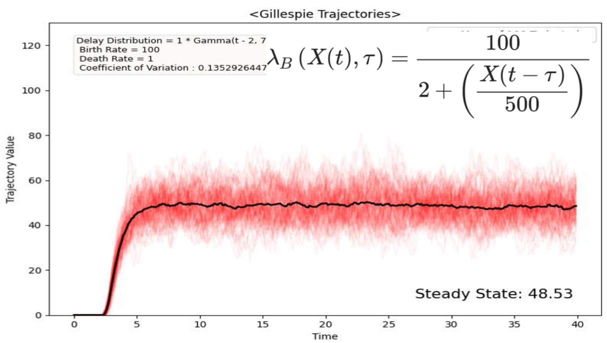

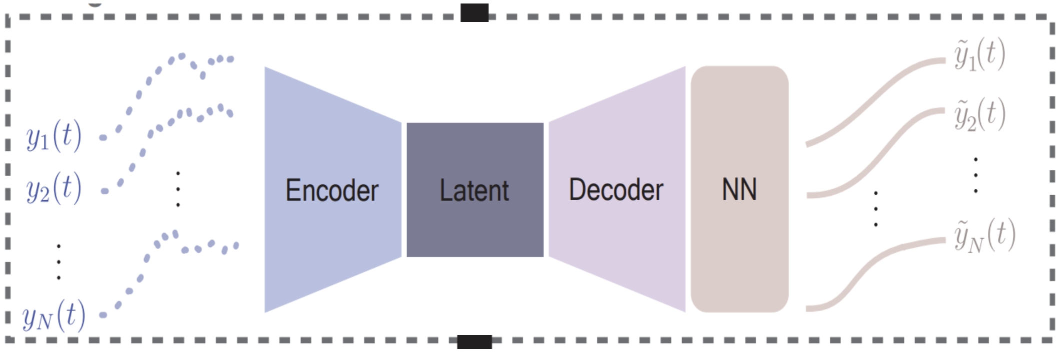

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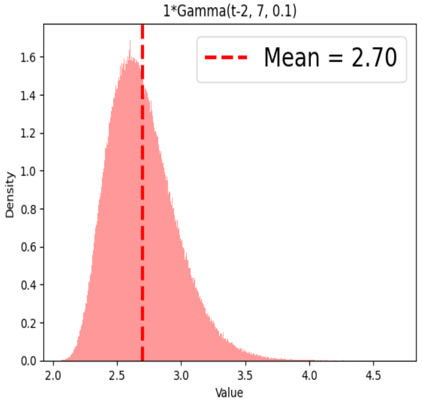

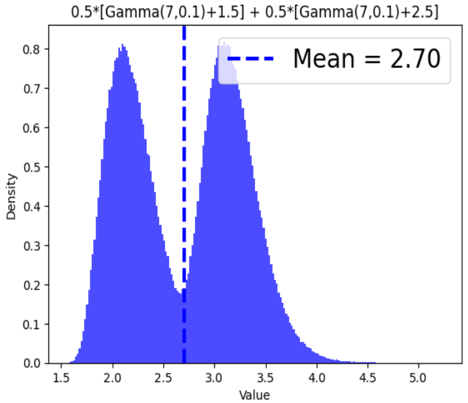

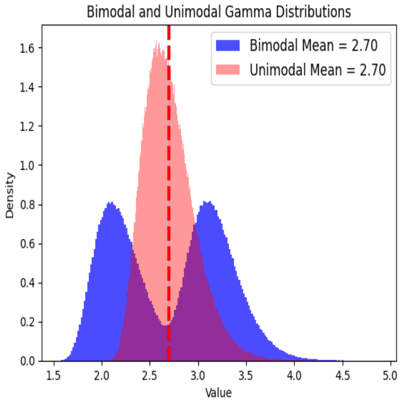

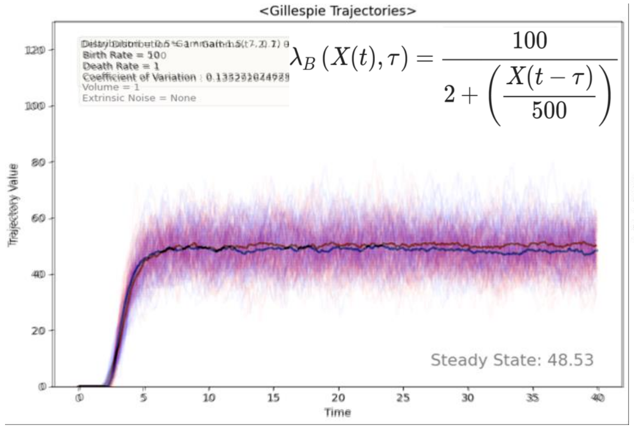

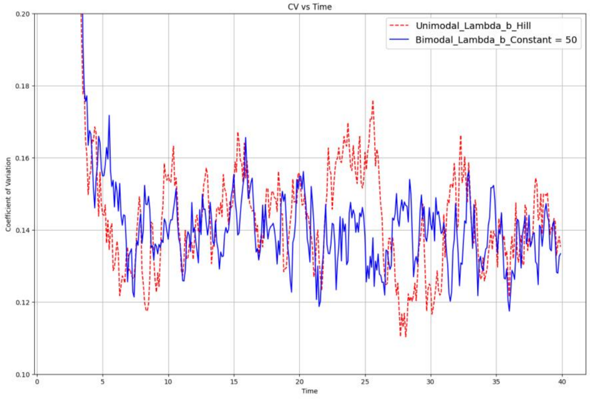

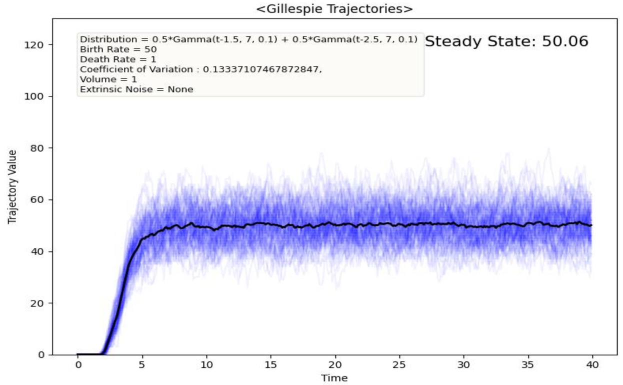

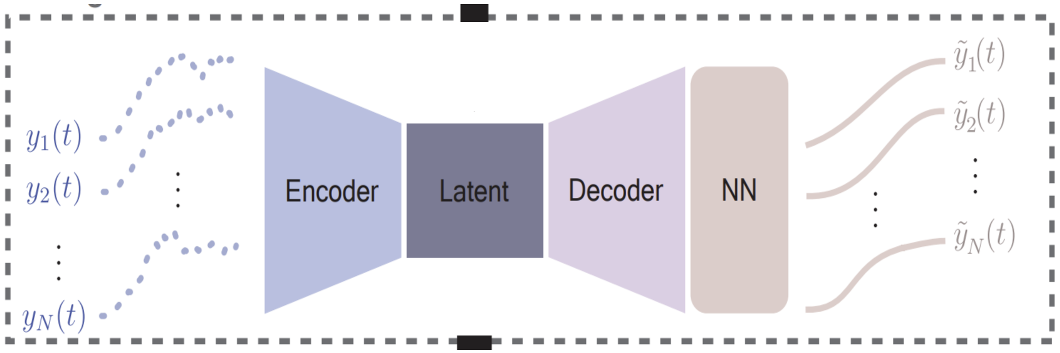

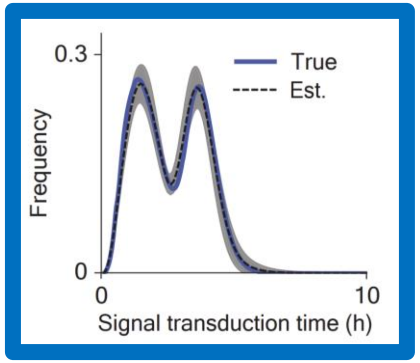

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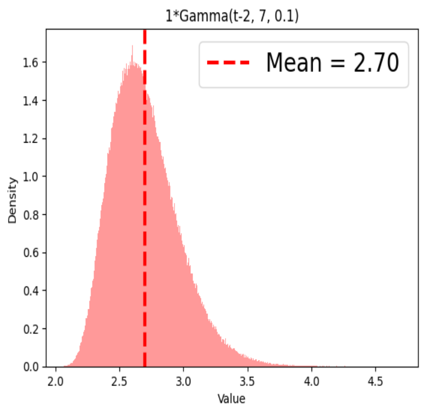
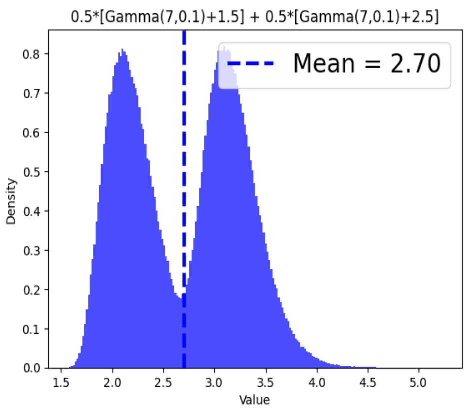
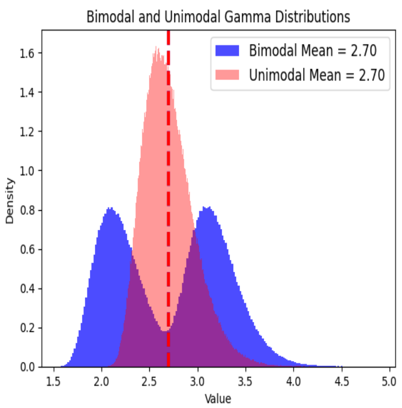
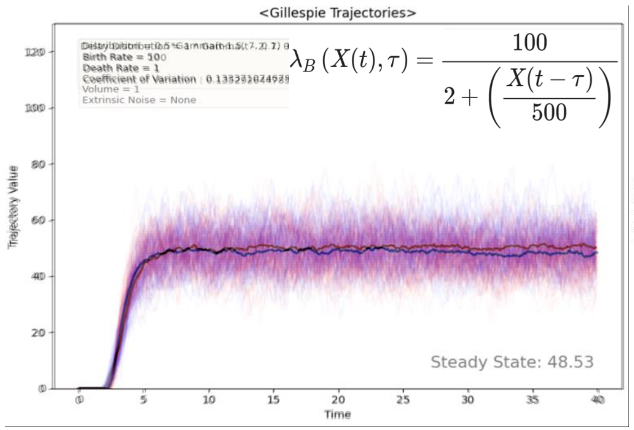
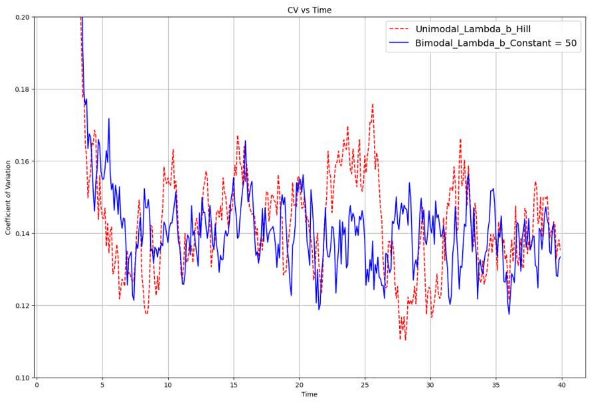
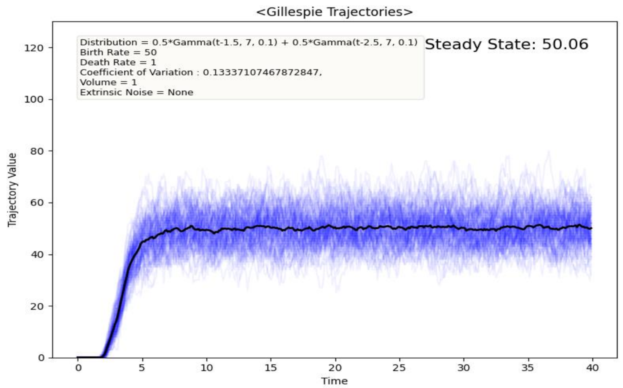


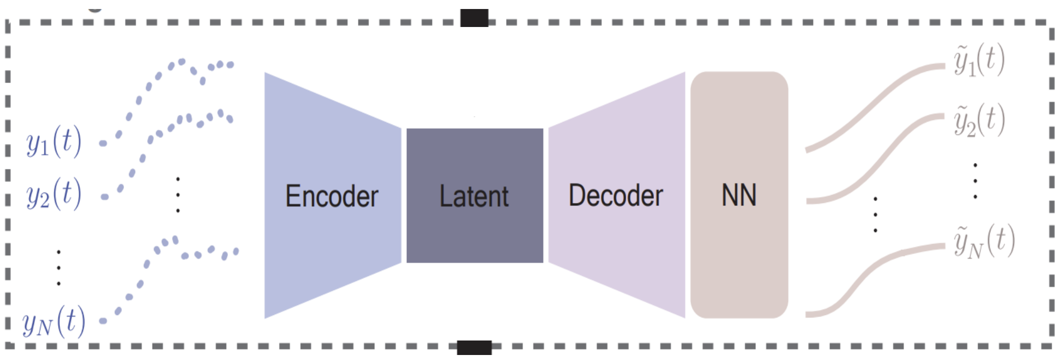


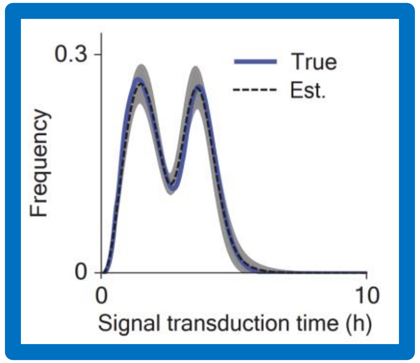


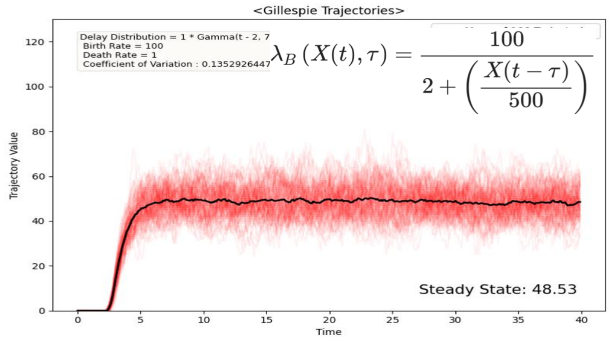


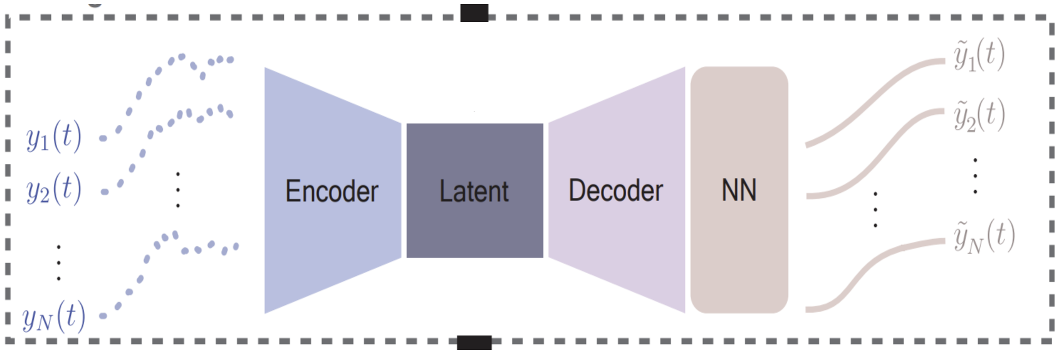


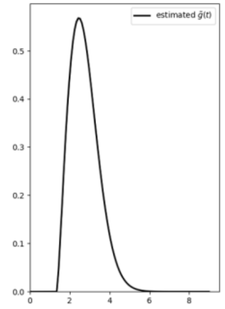


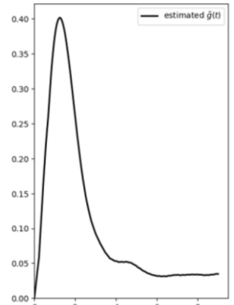






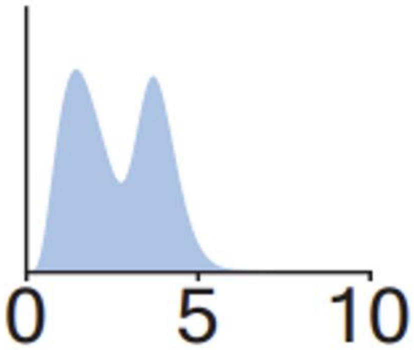


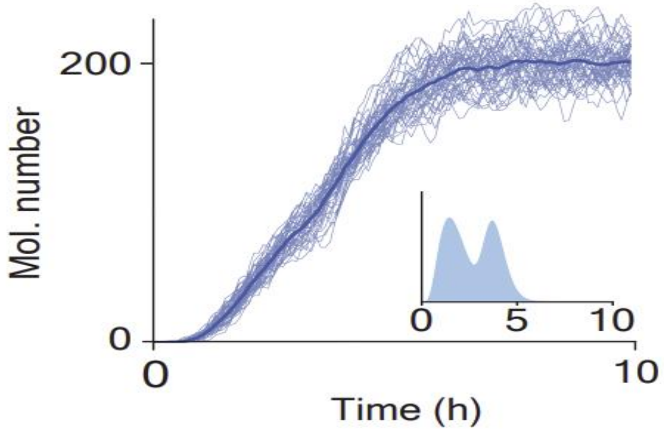


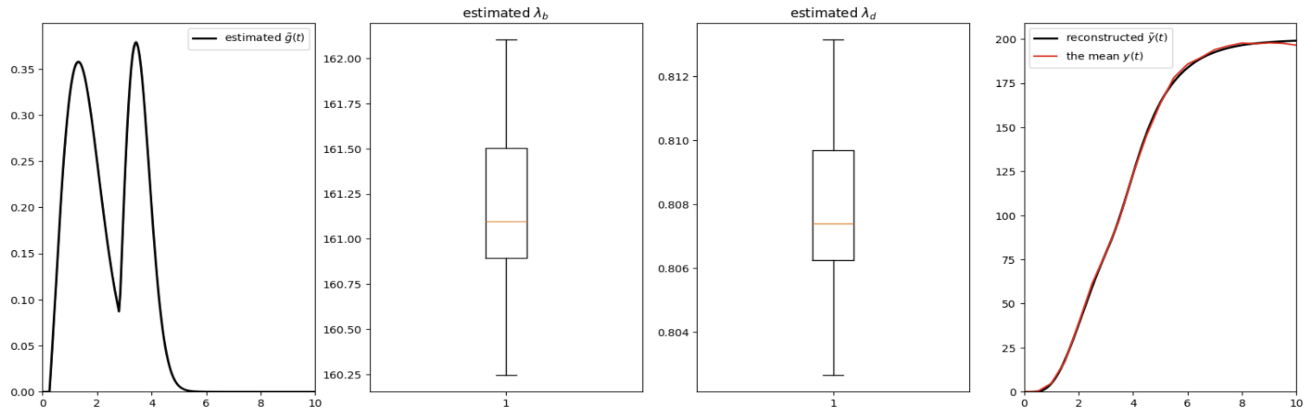


D-PINN

Unimodal delay with feedback shows as unimodal (single-timescale pathway) in D-PINN







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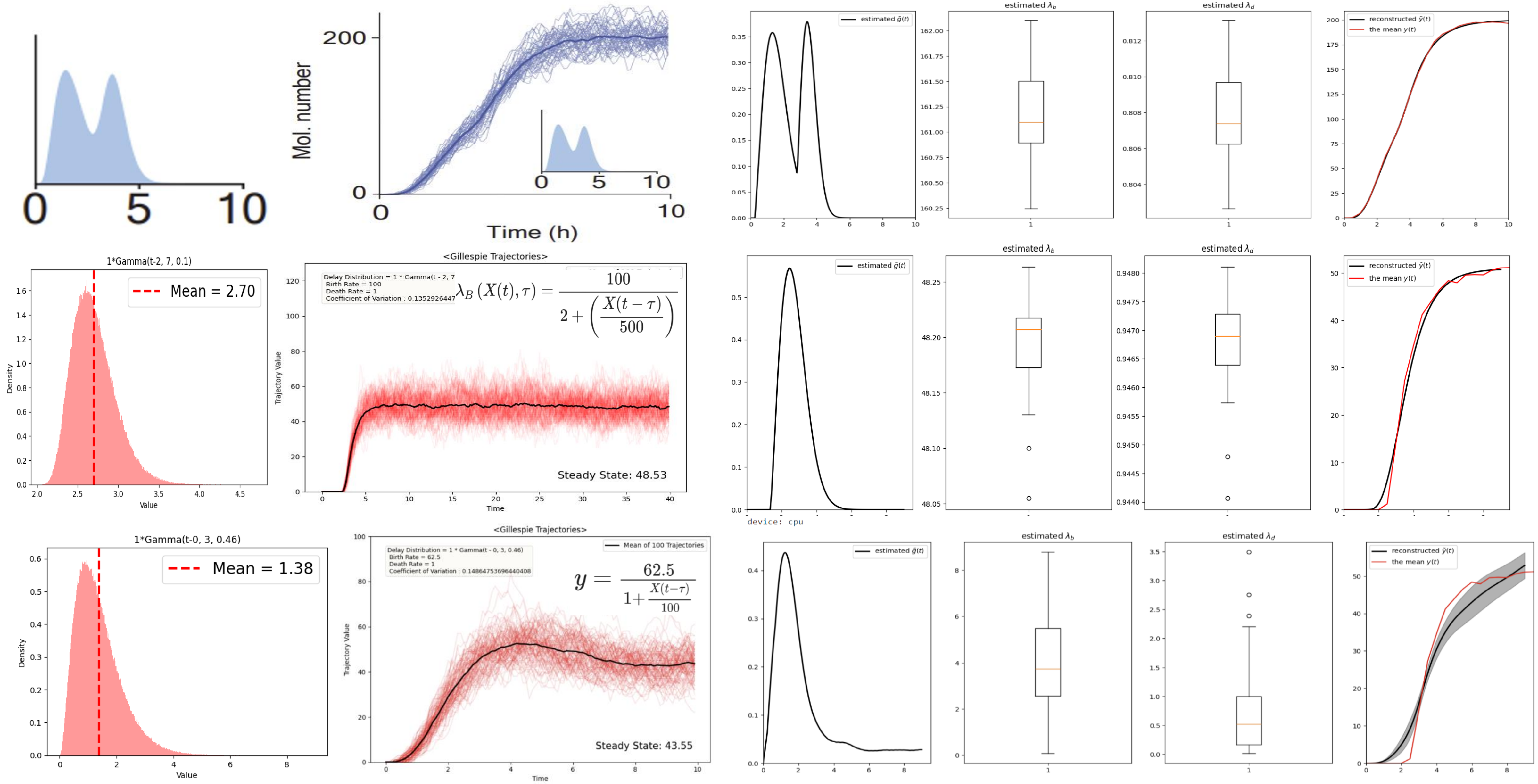
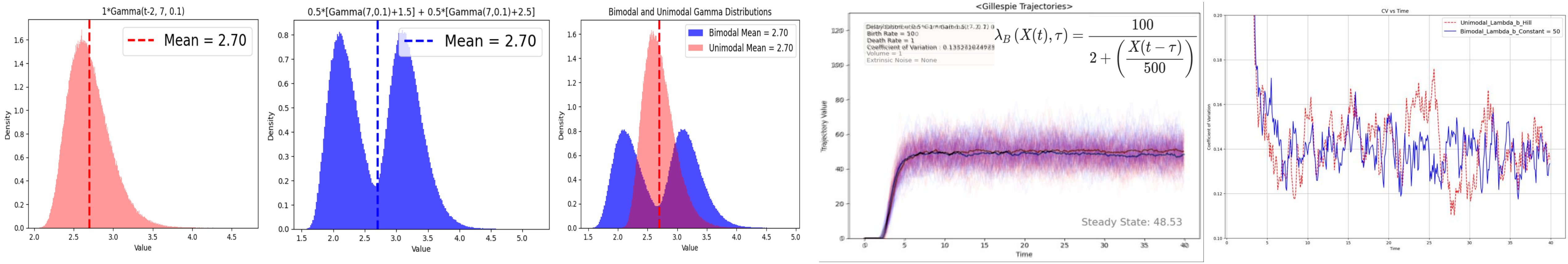
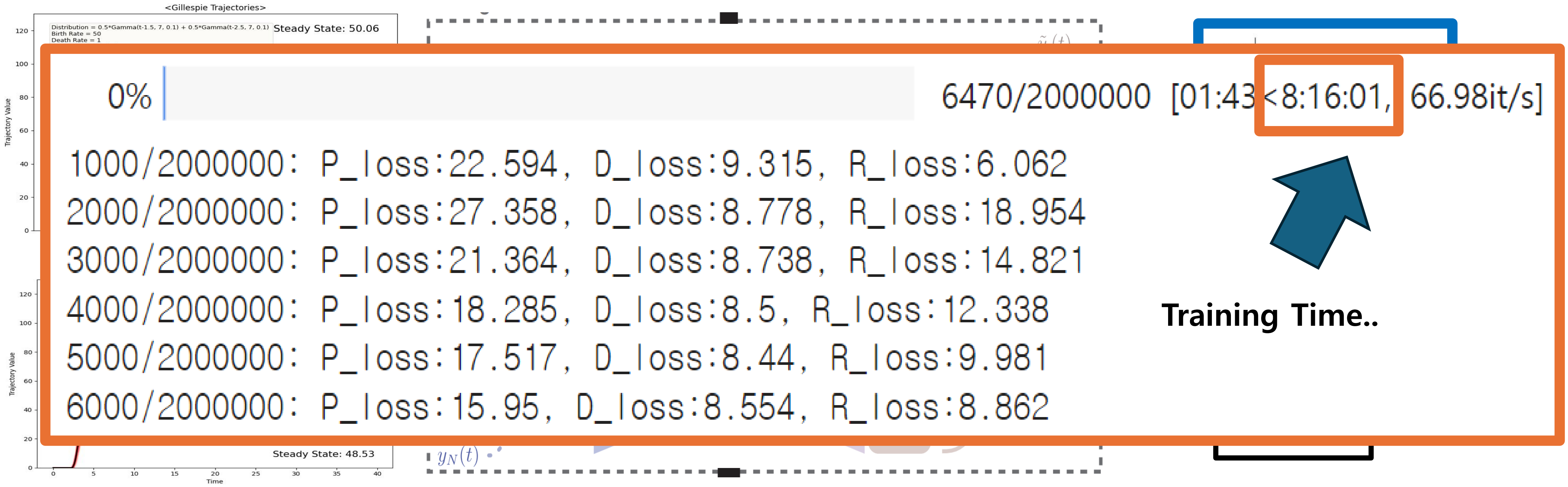
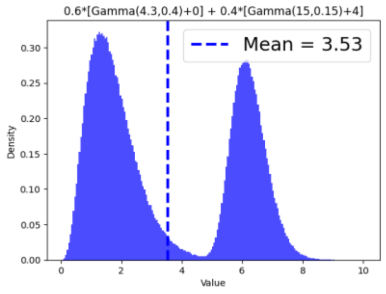


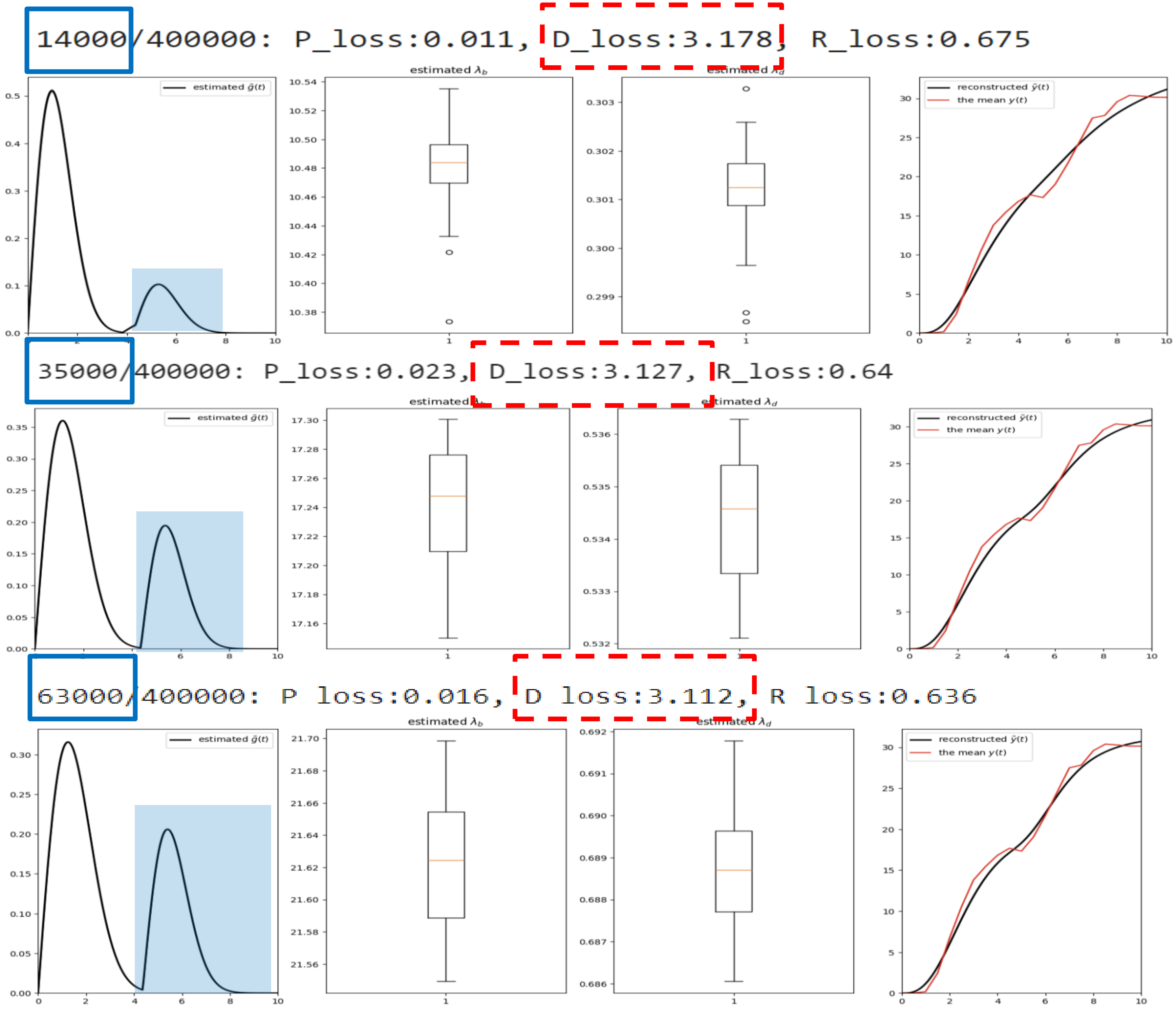
Training time is a problem.





Raising the training epoch/time and reducing the physics/data loss leads to closer-to-true distributions.

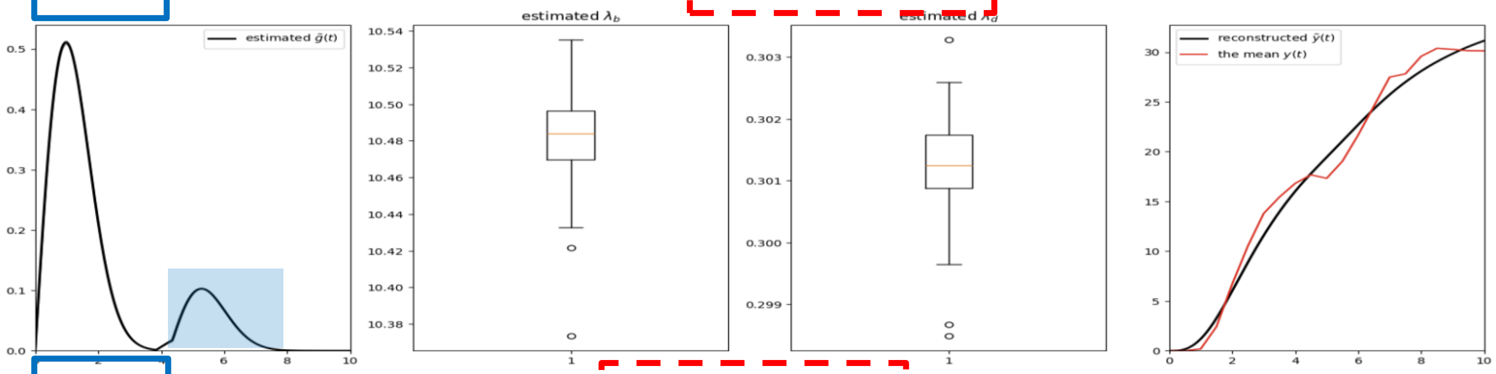


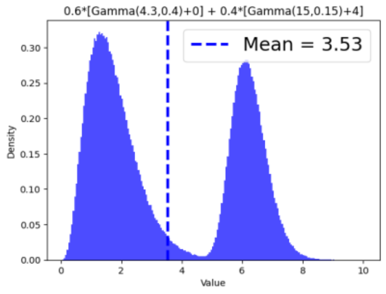


bimodal_test_selected_v7.csv

Raising the training epoch/time and reducing the physics/data loss leads to closer-to-true distributions.

14000/400000: P_loss:0.011, D_loss:3.178, R_loss:0.675

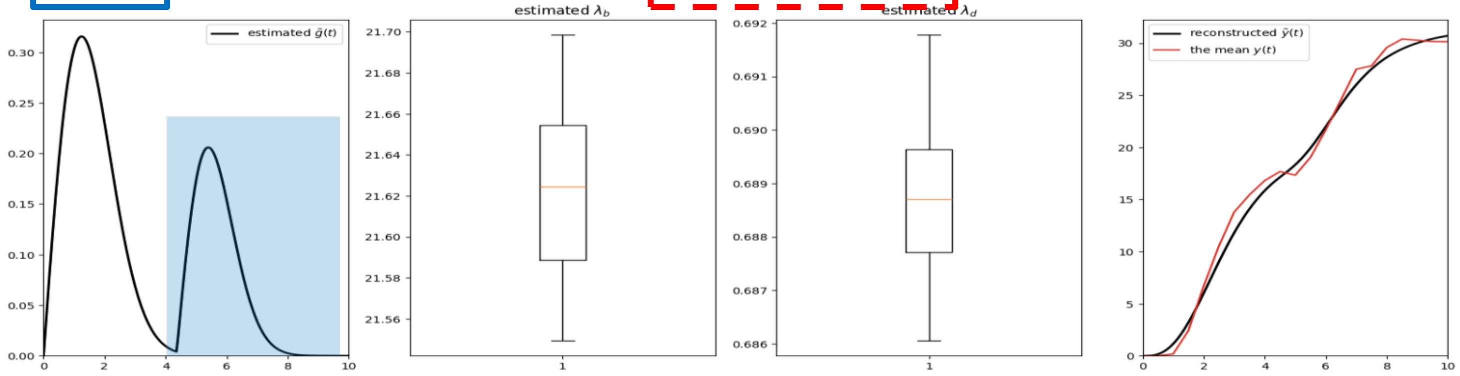




Note S2. Minimizing the data and physics losses ensures the convergence of an approximated transduction-time distribution, $\tilde{g}(t)$, to the true transduction-time distribution, $g(t)$.

and its limit converges to y'. In summary, if $\tilde{y}_{ex}$ converges to y during the training step, $\int_0^t \tilde{g}(u)$ converges to $\int_0^t g(u)du$. Consequently, $\tilde{g}(t)$ converges to $g(t)$ by differentiating Equation 1 and repeating same procedure.

63000/400000: P loss:0.016, D loss:3.112, R loss:0.636



bimodal_test_selected_v7.csv