Problem Set 11: Quasi-Steady-State in Reaction Dynamics

The mass-action enzyme-substrate system

$$\frac{\mathrm{d}[S]}{\mathrm{d}t} = -k_1[S][E] + k_{-1}[SE]$$
$$\frac{\mathrm{d}[E]}{\mathrm{d}t} = -k_1[S][E] + k_{-1}[SE] + k_2[SE]$$
$$\frac{\mathrm{d}[SE]}{\mathrm{d}t} = k_1[S][E] - k_{-1}[SE] - k_2[SE]$$
$$\frac{\mathrm{d}[P]}{\mathrm{d}t} = k_2[SE]$$

can be transformed to the dimensionless system

$$\dot{x} = -\epsilon x + \delta xy + y, \quad x(0) = 1,$$
$$\dot{y} = \epsilon x - \delta xy - y - \gamma y, \quad y(0) = 0.$$

where $\epsilon = k_1[E]_0/k_{-1}$, $\delta = k_1[S]_0/k_{-1}$, and $\gamma = k_2/k_{-1}$.

1. In class, we assumed γ was sufficiently small as to be ignored, and derived the approximation $\dot{y}_u = -\gamma y_u$ under the assumption

   $$0 = -\epsilon x_u(t) + \delta x_u(t) y_u(t) + y_u(t).$$

   Show that if this condition holds, $x_u(t)$ must satisfy

   $$\dot{x}_u = -\gamma x_u(1 + \delta x_u).$$

   Answer:
   Taking our quasi-steady-state assumption and differentiating, we find

   $$0 = -\epsilon \dot{x}_u(t) + \delta \dot{x}_u(t) y_u(t) + \delta x_u(t) \dot{y}_u(t) + \dot{y}_u(t).$$

   We use the conditions $y = \epsilon x/(\delta x + 1)$ and $\dot{y} = -\gamma y$ to eliminate y from the equation. Expanding and simplifying, we find

   $$\dot{x}_u = -\gamma x_u(1 + \delta x_u).$$

2. An alternative hypothesis would be that $\dot{y} \approx 0$, so

   $$0 = \epsilon x_V(t) - \delta x_V(t) y_V(t) - (1 + \gamma) y_V(t).$$

Derive a scalar ODE for $x_V(t)$ under this condition.

Answer:
Under this condition, we find $y = \epsilon x/(\delta x + 1 + \gamma)$. Substiting into the $\dot{x}$-equation, we obtain

$$\dot{x}_v = -\epsilon x_v + \frac{(\delta x_v + 1)\epsilon x_v}{\delta x_v + 1 + \gamma}$$

Simplify, and we find

$$\dot{x}_v = \frac{-\gamma \epsilon x_v}{\delta x_v + 1 + \gamma}$$

This is the standard quasi-steady-state approximation.

3. A third approximation can be obtained is given by the linearization around the stationary solution $(x, y) = (0, 0)$ when $\delta \ll 1$. Show that if $\delta = 0$, then the outer solution for $x(t)$ can be approximated by $x_L(t)$ where $\dot{x}_L = -\gamma x_L/2$ when γ is sufficiently small.

Answer:
The Jacobian of our original system at $(x, y) = (0, 0)$ is

$$\begin{bmatrix} -\epsilon & 1 \\ \epsilon & -(1+\gamma) \end{bmatrix}$$

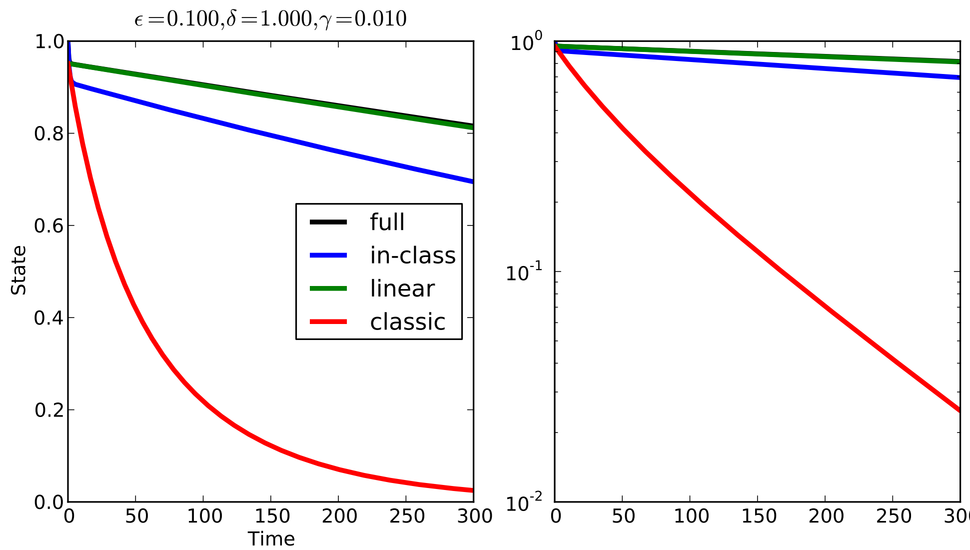
The characteristic equation is then $(\epsilon + z)(1 + \gamma + z) - \epsilon = 0$. We look for solutions to this in terms of power-series in γ rather than using the quadratic formula: $z = a_0 + a_1\gamma + a_2\gamma^2 \ldots$. Collecting like-terms, we find $a_0 \in 0, -1 - \epsilon$. The 0 is the slowest decaying term, so that's the one we expect to control the asymptotic dynamics. Solving for higher-order terms, we find $z \approx -\gamma\epsilon/(1 + \epsilon) + \gamma^2\epsilon/(1 + \epsilon)^3 + O(\gamma^3)$. I don't know where the two came from above. It looks like a typo to me.

4. Determine which of the three outer approximations described above is best (if any) in each of the following cases:

   (a) $\epsilon = 0.1$, $\delta = 1$, $\gamma = 0.01$.

   Answer:

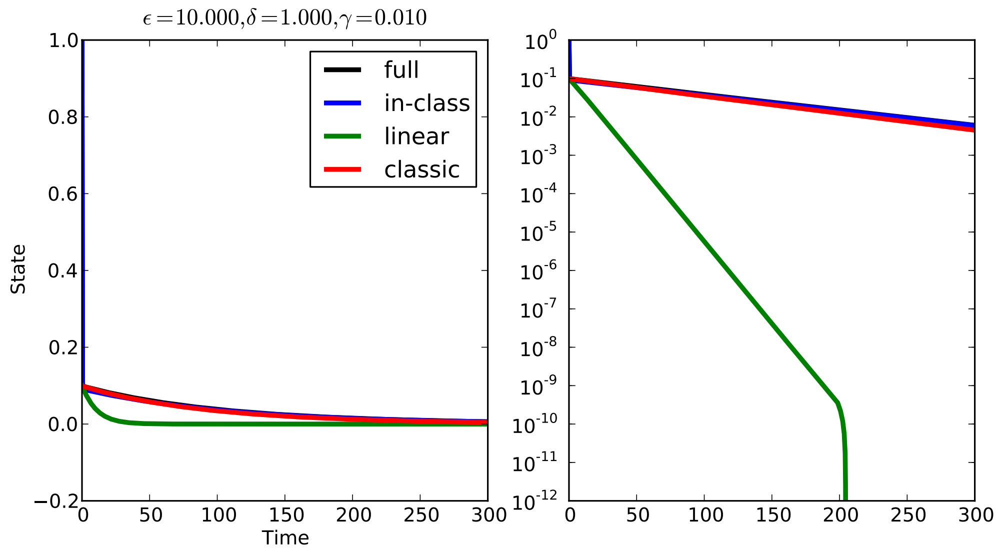
   The linear model matches the full model most closely. In this and all subsequent graphs, the full Jacobian is used to approximate the dynamics, rather than just the slowest eigenvalue.



   (b) $\epsilon = 10$, $\delta = 1$, $\gamma = 0.01$.

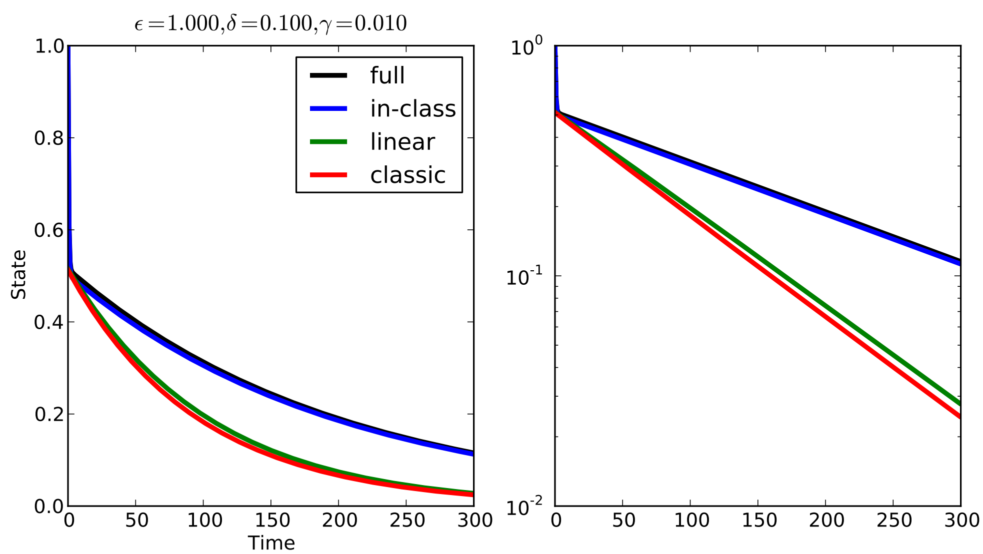
   Answer:

   The classic quasi-steady-state and the asymptotic approximation derived in class both fit the observed-dynamics well.



(c) $\epsilon = 1$, $\delta = 0.1$, $\gamma = 0.01$.

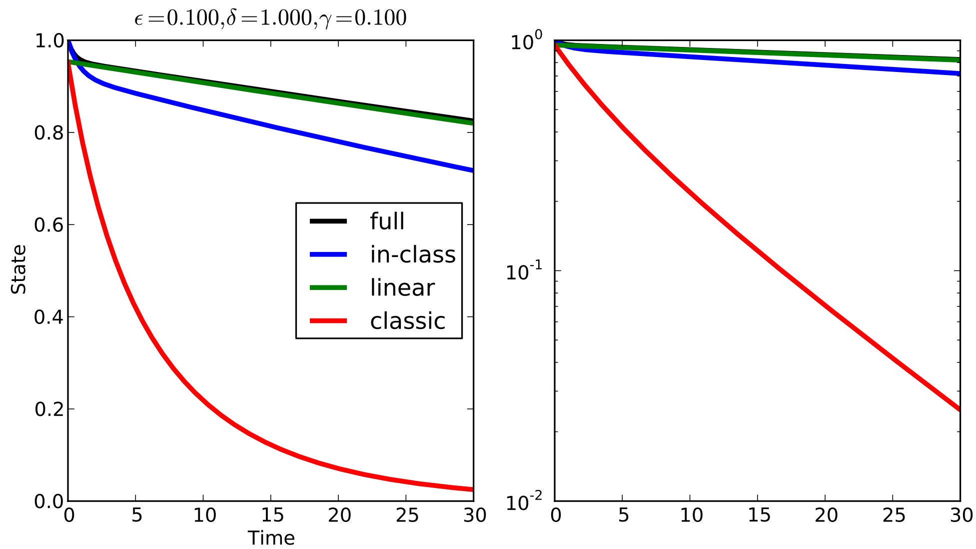
Answer:
The asymptotic approximation derived in class fits the observed-dynamics best.



(d) $\epsilon = 0.1$, $\delta = 1$, $\gamma = 0.1$.

Answer:
The linear model matches the observed dynamics best. fits the observed-

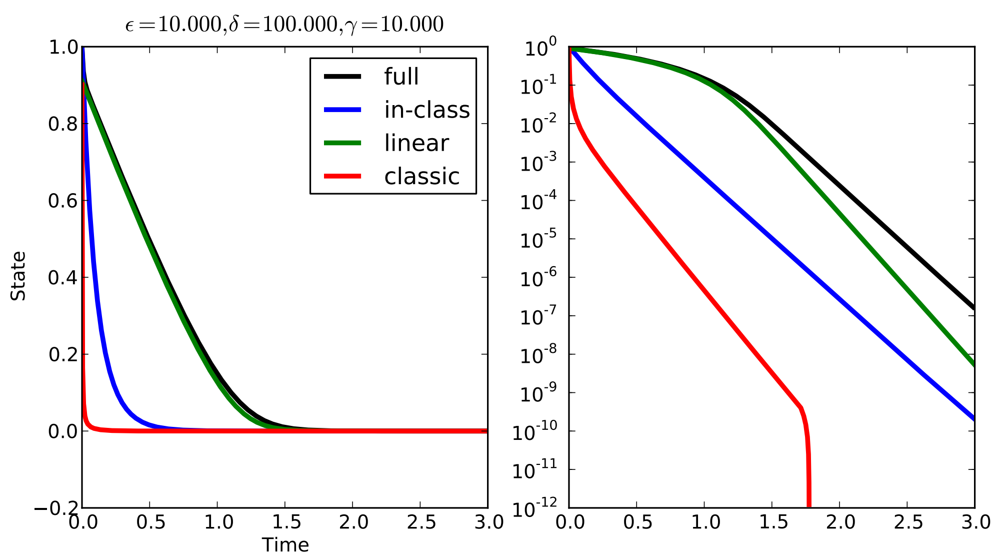
dynamics best.



(e) $\epsilon = 10$, $\delta = 100$, $\gamma = 10$.

Answer:

The linear model catches the first part of the dynamics well, but the final slope is best matched by the in-class model.



(numerical illustrations may be the most convenient)