

$$\dot{\vec{g}}(\vec{\eta}, \vec{\eta}, t, \vec{\beta}, \vec{v}) = \vec{0}_{g \times p} \quad (\text{ODEs})$$

$$\frac{d\vec{g}}{d\vec{\beta}} = \frac{\partial \vec{g}}{\partial \vec{\eta}} \frac{\partial \vec{\eta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{\eta}} \frac{\partial \vec{\eta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial t} \frac{\partial t}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{\beta}} \frac{\partial \vec{\beta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{v}} \frac{\partial \vec{v}}{\partial \vec{\beta}} = \vec{0}_{g \times p}$$

$$\Rightarrow \vec{0} = \frac{\partial \vec{g}}{\partial \vec{\eta}} \frac{\partial \vec{\eta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{\eta}} \frac{\partial \vec{\eta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{\beta}}$$

$$\frac{\partial \vec{g}}{\partial \vec{\eta}} \frac{\partial \vec{\eta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{\eta}} \frac{\partial \vec{\eta}}{\partial \vec{\beta}} + \frac{\partial \vec{g}}{\partial \vec{\beta}} = \vec{0}_{g \times p}$$

$$(n_g \times n_\eta) (n_\eta \times n_p) + (n_g \times n_\eta) (n_\eta \times n_p) + (n_g \times n_p) = (n_g \times n_p)$$

$$\vec{g} = \begin{bmatrix} \frac{dC_A}{dt} - F_{in}C_{A,in} - V_A^{(1)}r_1 - V_A^{(2)}r_2 \\ \frac{dC_B}{dt} - F_{in}C_{B,in} - V_B^{(1)}r_1 - V_B^{(2)}r_2 \\ \frac{dC_C}{dt} - F_{in}C_{C,in} - V_C^{(1)}r_1 - V_C^{(2)}r_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \\ 0 \end{bmatrix}$$

$$\vec{\eta}^T = [C_A, C_B, C_C]; \quad \vec{\eta}^T = \left[ \frac{dC_A}{dt}, \frac{dC_B}{dt}, \frac{dC_C}{dt} \right] \quad V = \begin{bmatrix} V_A^{(1)} & V_A^{(2)} \\ V_B^{(1)} & V_B^{(2)} \\ V_C^{(1)} & V_C^{(2)} \end{bmatrix} = \begin{bmatrix} -1 & 0 \\ 1 & -1 \\ 0 & 1 \end{bmatrix}$$

$$r_1 = k_1 C_A, \quad r_2 = k_2 C_B$$

$$\vec{g} = \begin{bmatrix} \frac{dC_A}{dt} - F_{in}C_{A,in} + k_1 C_A \\ \frac{dC_B}{dt} - F_{in}C_{B,in} - k_1 C_A + k_2 C_B \\ \frac{dC_C}{dt} - F_{in}C_{C,in} - k_2 C_B \end{bmatrix}$$

$$\frac{\partial \vec{g}}{\partial \vec{\eta}} = \begin{bmatrix} \frac{\partial g_1}{\partial C_A} & \frac{\partial g_1}{\partial C_B} & \frac{\partial g_1}{\partial C_C} \\ \frac{\partial g_2}{\partial C_A} & \frac{\partial g_2}{\partial C_B} & \frac{\partial g_2}{\partial C_C} \\ \frac{\partial g_3}{\partial C_A} & \frac{\partial g_3}{\partial C_B} & \frac{\partial g_3}{\partial C_C} \end{bmatrix} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

$$\frac{\partial \vec{g}}{\partial \vec{\eta}} = \begin{bmatrix} \frac{\partial g_1}{\partial C_A} & \frac{\partial g_1}{\partial C_B} & \frac{\partial g_1}{\partial C_C} \\ \frac{\partial g_2}{\partial C_A} & \frac{\partial g_2}{\partial C_B} & \frac{\partial g_2}{\partial C_C} \\ \frac{\partial g_3}{\partial C_A} & \frac{\partial g_3}{\partial C_B} & \frac{\partial g_3}{\partial C_C} \end{bmatrix} = \begin{bmatrix} k_1 & 0 & 0 \\ -k_1 & k_2 & 0 \\ 0 & -k_2 & 0 \end{bmatrix}$$

$$\frac{\partial \vec{g}}{\partial \vec{\beta}} = \begin{bmatrix} \frac{\partial g_1}{\partial k_1} & \frac{\partial g_1}{\partial k_2} \\ \frac{\partial g_2}{\partial k_1} & \frac{\partial g_2}{\partial k_2} \\ \frac{\partial g_3}{\partial k_1} & \frac{\partial g_3}{\partial k_2} \end{bmatrix} = \begin{bmatrix} C_A & 0 \\ -C_A & C_B \\ 0 & -C_B \end{bmatrix}$$

Putting things together:

$$\begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_2} \right) \\ \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_2} \right) \\ \frac{d}{dt} \left( \frac{\partial C_C}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_C}{\partial k_2} \right) \end{bmatrix} + \begin{bmatrix} k_1 & 0 & 0 \\ -k_1 & k_2 & 0 \\ 0 & -k_2 & 0 \end{bmatrix} \begin{bmatrix} \frac{\partial C_A}{\partial k_1} & \frac{\partial C_A}{\partial k_2} \\ \frac{\partial C_B}{\partial k_1} & \frac{\partial C_B}{\partial k_2} \\ \frac{\partial C_C}{\partial k_1} & \frac{\partial C_C}{\partial k_2} \end{bmatrix} + \begin{bmatrix} C_A & 0 \\ -C_A & C_B \\ 0 & -C_B \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\begin{bmatrix} \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_2} \right) \\ \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_2} \right) \end{bmatrix} + \begin{bmatrix} k_1 & 0 & 0 \\ -k_1 & k_2 & 0 \end{bmatrix} \begin{bmatrix} \frac{\partial C_A}{\partial k_1} & \frac{\partial C_A}{\partial k_2} \\ \frac{\partial C_B}{\partial k_1} & \frac{\partial C_B}{\partial k_2} \end{bmatrix} + \begin{bmatrix} C_A & 0 \\ -C_A & C_B \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$g$  differential equations / number of eqs.

$\eta$  state variable

$t$  time

$\beta$  model parameters

$v$  control variables

$\vec{x}$  vector

$\dot{x}$  time derivative

$x^T$  transpose

$$\begin{aligned}
 & \left[ \begin{array}{cc} \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_2} \right) \\ \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_2} \right) \\ \frac{d}{dt} \left( \frac{\partial C_C}{\partial k_1} \right) & \frac{d}{dt} \left( \frac{\partial C_C}{\partial k_2} \right) \end{array} \right] + \begin{bmatrix} K_1 & 0 & 0 \\ -k_1 & k_2 & 0 \\ 0 & -k_2 & 0 \end{bmatrix} \begin{bmatrix} \frac{\partial C_A}{\partial k_1} & \frac{\partial C_A}{\partial k_2} \\ \frac{\partial C_B}{\partial k_1} & \frac{\partial C_B}{\partial k_2} \\ \frac{\partial C_C}{\partial k_1} & \frac{\partial C_C}{\partial k_2} \end{bmatrix} + \begin{bmatrix} C_A & 0 \\ -C_A & C_B \\ 0 & -C_B \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix} \\
 & \left[ \begin{array}{cc} k_1 \frac{\partial C_A}{\partial k_1} & k_1 \frac{\partial C_A}{\partial k_2} \\ -k_1 \frac{\partial C_A}{\partial k_1} + k_2 \frac{\partial C_B}{\partial k_1} & -k_1 \frac{\partial C_A}{\partial k_2} + k_2 \frac{\partial C_B}{\partial k_2} \\ -k_2 \frac{\partial C_B}{\partial k_1} & -k_2 \frac{\partial C_B}{\partial k_2} \end{array} \right] + \begin{bmatrix} C_A & 0 \\ -C_A & C_B \\ 0 & -C_B \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}
 \end{aligned}$$

$$\left. \begin{aligned}
 & \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_1} \right) + k_1 \frac{\partial C_A}{\partial k_1} + C_A = 0 \\
 & \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_1} \right) - k_1 \frac{\partial C_A}{\partial k_1} + k_2 \frac{\partial C_B}{\partial k_1} - C_A = 0 \\
 & \frac{d}{dt} \left( \frac{\partial C_C}{\partial k_1} \right) - k_2 \frac{\partial C_B}{\partial k_1} = 0 \\
 & \frac{d}{dt} \left( \frac{\partial C_A}{\partial k_2} \right) + k_1 \frac{\partial C_A}{\partial k_2} = 0 \\
 & \frac{d}{dt} \left( \frac{\partial C_B}{\partial k_2} \right) - k_1 \frac{\partial C_A}{\partial k_2} + k_2 \frac{\partial C_B}{\partial k_2} + C_B = 0 \\
 & \frac{d}{dt} \left( \frac{\partial C_C}{\partial k_2} \right) - k_2 \frac{\partial C_B}{\partial k_2} - C_B = 0
 \end{aligned} \right\} \text{ sensitivity equations.}$$