Μοντέλο De Pillis - Radunskaya

$$\dot N = r_2 N(1-b_2 N) - c_4 TN - a_3 MN$$

$$\dot T = r_1 T(1-b_1 T) - c_2 IT - c_3 TN - a_2 MT$$

$$\dot I = s + \frac{\rho I T}{a+T} - c_1 IT - d_1 I - a_1 MI$$

$$\dot M = -d_2 M + u(t)$$

The system can be rewritten by shifting the tumor-free equilibrium point $(1/b_2, 0, s/d_1, 0)$ to the origin in terms of the following error states:

$x_1 = N - \frac{1}{b_2} \Leftrightarrow N = x_1 + \frac{1}{b_2}$

$x_2 = T \Leftrightarrow T = x_2$

$x_3 = I - \frac{s}{d_2} \Leftrightarrow I = x_3 + \frac{s}{d_1}$

$x_4 = M \Leftrightarrow M = x_4$

where $x = [x_1 \; x_2 \; x_3 \; x_4]^T$ denotes the error states.

The system in the new coordinates is:

- $\dot N = r_2 N(1-b_2 N) - c_4 TN - a_3 MN \Rightarrow$

$$\Rightarrow \dot x_1 = r_2\left(x_1 + \frac{1}{b_2}\right)\left(1 - b_2 x_1 - b_2 \frac{1}{b_2}\right) - c_4 x_2 \left(x_1 + \frac{1}{b_2}\right) - a_3 x_4 \left(x_1 + \frac{1}{b_2}\right)$$

$$\Rightarrow \dot x_1 = r_2\left(x_1 + \frac{1}{b_2}\right)(-b_2 x_1) - c_4 x_2 x_1 - c_4 x_2 \frac{1}{b_2} - a_3 x_4 x_1 - a_3 x_4 \frac{1}{b_2}$$

$$\Rightarrow \dot x_1 = -r_2 x_1 (1 + b_2 x_1) - c_4/b_2 \, x_2 - \frac{a_3}{b_2} x_4 - c_4 x_2 x_1 - a_3 x_1 x_4 \quad (1)$$

- $\dot{T} = r_1 T(1-b_1 T) - c_2 IT - c_3 TN - a_2 MT \Rightarrow$

$$\Rightarrow r_1 x_2(1-b_1 x_2) - c_2\left(x_3+\frac{s}{d_1}\right)x_2 - c_3 x_2\left(x_1+\frac{1}{b_2}\right) - a_2 x_4 x_2$$

$$\Rightarrow r_1 x_2(1-b_1 x_2) - \left(c_2 x_3 x_2 + \frac{c_2 s}{d_1}x_2\right) - c_3 x_2 x_1 - \frac{c_3 x_2}{b_2} - a_2 x_4 x_2$$

$$\Rightarrow r_1 x_2(1-b_1 x_2) - \left(\frac{c_2 s}{d_1}+\frac{c_3}{b_2}\right)x_2 - c_3 x_1 x_2 - c_2 x_2 x_3 - a_2 x_2 x_4$$

- $I = s + \frac{\rho IT}{a+T} - c_1 IT - d_1 TI - d_1 I - a_2 MI \Rightarrow$

$$\Rightarrow \dot{x}_3 = s + \frac{\rho\left(x_3+\frac{s}{d_1}\right)x_2}{a+x_2} - c_1\left(x_3+\frac{s}{d_1}\right)x_2 - d_1\left(x_3+\frac{s}{d_1}\right) - \cancel{x_2 x_4 x_2} - a_2 x_4 x_3 - a_2 x_4 \frac{s}{d_1}$$

$$\Rightarrow \dot{x}_3 = \cancel{s} + \rho\frac{x_2 x_3}{a+x_2} + \rho\frac{\frac{s x_2}{d_1}}{a+x_2} - c_1 x_2 x_3 - \frac{c_1 s}{d_1}x_2 - d_1 x_3 - \cancel{s} \cancel{a_2 x_2 x_4}$$

$$\Rightarrow \dot{x}_3 = -\frac{c_1 s}{d_1}x_2 - d_1 x_3 - \frac{a_1 s}{d_1}x_4 + \frac{\rho\frac{s x_2}{d_1}}{a+x_2} + \rho\frac{x_2 x_3}{a+x_2} - c_1 x_2 x_3 - a_1 x_3 x_4$$

- $M = -d_2 M + u(t) \Rightarrow$

$$\Rightarrow \dot{x}_4 = -d_2 x_4 + u(t)$$

The system is the following:

$$\dot{x}_1 = -r_2 x_1(1+b_2 x_1) - \frac{c_4}{b_2}x_2 - \frac{a_3}{b_2}x_4 - c_4 x_1 x_2 - a_3 x_1 x_4$$

$$\dot{x}_2 = r_1 x_2(1-b_1 x_2) - \left(\frac{c_2 s}{d_1}+\frac{c_3}{b_2}\right)x_2 - c_3 x_1 x_2 - c_2 x_2 x_3 - a_2 x_2 x_4$$

$$\dot{x}_3 = -\frac{c_1 s}{d_1}x_2 - d_1 x_3 - \frac{a_1 s}{d_1}x_4 + \frac{\frac{\rho s x_2}{d_1}}{a+x_2} + \rho\frac{x_2 x_3}{a+x_2} - c_1 x_2 x_3 - a_1 x_3 x_4$$

$$\dot{x}_4 = -d_2 x_4 + u(t)$$

A pseudo-linear form of the system is the following:

$$\dot{x} = A(x)x + B(x)\cdot u$$

$$\dot{x}_1 = \left[-r_2(1+b_2x_1)\right]x_1 + \left[-\frac{c_4}{b_2} + -c_4x_1\right]x_2 + 0\cdot x_3 + \left[-\frac{a_3}{b_2} - a_3x_1\right]x_4$$

$$= \left[-r_2(1+b_2x_1)\right]x_1 + \left[-c_4\left(\frac{1}{b_2}+x_1\right)\right]x_2 + 0\cdot x_3 + \left[-a_3\left(\frac{1}{b_2}+x_1\right)\right]x_4$$

$$\dot{x}_2 = \left[-c_3x_2\right]x_1 + \left[\left[r_1(1-b_1x_2)\right] - \left[\frac{c_2 s}{d_1} + \frac{c_3}{b_2}\right]\right]x_2 + \left[-c_2x_2\right]x_3 + \left[-a_2x_2\right]x_4$$

$$\dot{x}_3 = 0x_1 + \left[\frac{\rho\frac{s_1}{d_1}}{a+x_2} + \rho\frac{x_3}{a+x_2} - \frac{c_1 s}{d_1} - c_1x_3\right]x_2 + \left[-d_1\right]x_3 + \left[-\frac{a_1 s}{d_1} - a_1x_3\right]x_4$$

$$= 0x_1 + \left[\frac{\rho\left(x_3+\frac{s_1}{d_1}\right)}{a+x_2} - c_1\left(x_3+\frac{s}{d_1}\right)\right]x_2 + \left[-d_1\right]x_3 + \left[-a_1\left(x_3+\frac{s}{d_1}\right)\right]x_4$$

$$= 0x_1 + \left[\frac{\rho\left(x_3+\frac{s_1}{d_1}\right)}{a+x_2} - c_1\left(x_3+\frac{s}{d_1}\right)\right]x_2 + \underline{\left[-x_4\right]x_2} + \left[-d_1\right]x_3 + \left[-a_1\left(x_3+\frac{s}{d_1}\right)\right]x_4 + \underline{\left[+x_2\right]x_4}$$

$$= 0x_1 + \left[\frac{\rho\left(x_3+\frac{s_1}{d_1}\right)}{a+x_2} - c_1\left(x_3+\frac{s}{d_1}\right) - x_4\right]x_2 + \left[-d_1\right]x_3 + \left[-a_1\left(x_3+\frac{s}{d_1}\right) + x_2\right]x_4$$

$$\dot{x}_4 = 0x_1 + 0x_2 + 0x_3 + \left[-d_2\right]x_4$$

$$A(x) = \begin{bmatrix} -r_2(1+b_2x_1) & -c_4\left(x_1+\frac{1}{b_2}\right) & 0 & -a_3\left(\frac{1}{b_2}+x_1\right) \\ -c_3x_2 & r_1(1-b_1x_2)-\left(\frac{c_2s}{d_1}+\frac{c_3}{b_2}\right) & -c_2x_2 & -a_2x_2 \\ 0 & \frac{\rho\left(x_3+\frac{s}{d_1}\right)}{(a+x_2)}-c_1\left(x_3+\frac{s}{d_1}\right)-x_4 & -d_1 & -a_1\left(x_3+\frac{s}{d_1}\right)+x_2 \\ 0 & 0 & 0 & -d_2 \end{bmatrix}$$

$$B(x) = [0 \; 0 \; 0 \; 1]^T$$