STABILITY ANALYSIS

Module 1:

We know that LacI is constitutively expressed, so in the absence of IPTG:

$$MlacI^* = \frac{k_{mlacI}}{d_{mlacI}}$$

$$PlacI^* = \frac{k_{mlacI}\ k_{placI}}{d_{mlacI}\ d_{placI}}$$

$$Mout^* = \frac{k_{mout}\, f(PlacI^*)}{d_{mout}}$$

$$Pout^* = \frac{k_{mout}\, k_{pout}\, f(PlacI^*)}{d_{mout}\, d_{pout}}$$

So considering the now simplified system, since we are assuming that steady state of PlacI has been reached:

$$\frac{dMout}{dt} = k_{mout}\, f(PlacI^*) - d_{mout}\, Mout$$

$$\frac{dPout}{dt} = k_{pout}\, Mout - d_{pout}\, Pout$$

To evaluate the stability of the equations, we first work out the Jacobian matrix (J), and then find the determinant of the matrix M =$|J - \lambda I|$ = 0, where I represents the identity matrix and λ contains the eigenvalues of the system.

$$M = \begin{bmatrix} -d_{mout\ -\lambda} & 0 \\ k_{pout} & -d_{pout} - \lambda \end{bmatrix}$$

$$(-d_{mout} - \lambda)(-d_{pout} - \lambda) = 0$$

So $\lambda = -d_{mout}\ and\ -d_{pout}$.

d_{mout} and d_{pout} are the degradation terms of Mout and Pout respectively. They are always positive constants, therefore the eigenvalues are always negative. Therefore, in the absence of IPTG the system can only exhibit fixed points.

Now, when IPTG is added to the system, we can modify the differential equations and obtain:

$$\frac{dPlacI}{dt} = \frac{k_{mlacI}\ k_{pla\ cI}}{d_{mlacI}} - d_{placI}\, PlacI - k_{b1}IPTG * PlacI + k_{b2}IPTG\_PLacI$$

$$\frac{dIPTG}{dt} = -k_{b1}IPTG * PlacI + k_{b2}IPTG\_PLacI$$

$$\frac{dIPTG\_PlacI}{dt} = k_{b1}IPTG * PlacI - k_{b2}IPTG\_PLacI$$

$$\frac{dMout}{dt} = k_{mout}\, f(PlacI^{*}) - d_{mout}\, Mout$$

$$\frac{dPout}{dt} = k_{pout}\, Mout - d_{pout}\, Pout$$

If we assume that the IPTG quantity is conserved in the system, at any given point in time:

$$IPTG + IPTG\_PlacI = I_o$$

So we can simplify the system and get rid of one of the differential equations by assuming that:

$$IPTG\_PlacI = I_o\text{-}\ IPTG$$

Also, assuming that mRNA production is at steady state, we can get rid of those equations and obtain the much simplified system below:

$$\frac{dPlacI}{dt} = \frac{k_{mlacI}\ \ k_{placI}}{d_{mlacI}} - d_{placI}\, PlacI - k_{b1}IPTG * PlacI + k_{b2}(I_o\text{-}\ IPTG)$$

$$\frac{dIPTG}{dt} = -k_{b1}IPTG * PlacI + k_{b2}(I_o\text{-}\ IPTG)$$

$$\frac{dPout}{dt} = k_{pout}\, Mout - d_{pout}\, Pout$$

So,

$$PlacI^{*} = \frac{\frac{k_{mla\ cI}\ \ k_{placI}}{d_{mlacI}} + k_{b2}(I_o - IPTG^{*})}{d_{placI} + k_{b1}IPTG^{*}}$$

$$IPTG^{*} = \frac{k_{b2}\, I_o}{k_{b2} + k_{b1}\, PlacI^{*}}$$

$$Pout^{*} = \frac{k_{mout}\, k_{pout}\, f(PlacI^{*})}{d_{mout}\, d_{pout}}$$

So, once again, calculate the Jacobian matrix (J) to linearize around the fixed point, and then find the determinant of the matrix M =$|J - \lambda I|$ to evaluate its stability.

$$M = \begin{bmatrix} -d_{placI} - k_{b1}IPTG^{*} - \lambda & -k_{b1}PlacI^{*} & 0 \\ -k_{b1}IPTG^{*} & -k_{b2}(I_o - IPTG^{*}) - \lambda & 0 \\ 0 & 0 & -d_{pout} - \lambda \end{bmatrix}$$

$$M = (-d_{placI} - k_{b1}IPTG^{*} - \lambda)(-k_{b2}(I_o - IPTG^{*}) - \lambda)(-d_{pout} - \lambda) + k_{b1}PlacI^{*}(-k_{b1}IPTG^{*})(-d_{pout} - \lambda) = 0$$

Simplify:

$$(-d_{pout} - \lambda)\Big((-d_{placI} - k_{b1}IPTG^* - \lambda)(- k_{b2}(I_o - IPTG^*) - \lambda) - PlacI^*(k_{b1}IPTG^*)\Big) = 0$$

This shows that all eigen-directions are negative, so the system can only exhibit fixed points and we can safely assume that this is the only type of behavior we will observe in the system.