2a) $$\frac{d\tilde{X}}{d\tilde{t}} = -\tilde{\delta}_x \tilde{X} + \frac{\tilde{\alpha}_x + \tilde{\beta}_x S}{1 + S + (\tilde{Z}/\tilde{z}_x)^{n_{zx}}}$$

$$\frac{d\tilde{Z}}{d\tilde{t}} = -\tilde{\delta}_z \tilde{Z} + \frac{\tilde{\alpha}_z}{1 + (\tilde{X}/\tilde{x}_z)^{n_{xz}}}$$

b) $$\frac{d\tilde{X}}{d\tilde{t}} = \tilde{\alpha}_z \frac{dX}{dt}$$

* note: error in eqn 3 $(t = \tilde{t}\delta_x)$
Correction: $t = \tilde{t}\delta_x$

$$\frac{d\tilde{Z}}{d\tilde{t}} = \tilde{\alpha}_z \frac{dZ}{dt}$$

$$\tilde{\alpha}_z \frac{dX}{dt} = -\tilde{\delta}_x \tilde{X} + \frac{\tilde{\alpha}_x + \tilde{\beta}_x S}{1 + S + (\tilde{Z}/\tilde{z}_x)^{n_{zx}}}$$

$$\frac{dX}{dt} = -\frac{\tilde{\delta}_x \tilde{X}}{\tilde{\alpha}_z} + \frac{\tilde{\alpha}_x/\tilde{\alpha}_z + (\tilde{\beta}_x/\tilde{\alpha}_z) S}{1 + S + \left[\frac{\tilde{Z}}{\tilde{z}_x} \cdot \frac{\tilde{\delta}_x/\tilde{\alpha}_z}{\tilde{\delta}_x/\tilde{\alpha}_z}\right]^{n_{zx}}} = -X + \frac{a_x + \beta_x S}{1 + S + \left(\frac{Z}{z_x}\right)^{n_{zx}}}$$

$$\tilde{\alpha}_z \frac{dZ}{dt} = -\tilde{\delta}_z \tilde{Z} + \frac{\tilde{\alpha}_z}{1 + (\tilde{X}/\tilde{x}_z)^{n_{xz}}}$$

$$\frac{dZ}{dt} = -\frac{\tilde{\delta}_z \tilde{Z} \cdot \tilde{\delta}_x}{\tilde{\alpha}_z \cdot \tilde{\delta}_x} + \frac{\tilde{\alpha}_z/\tilde{\alpha}_z}{1 + \left[\frac{\tilde{X}}{\tilde{x}_z} \cdot \frac{\tilde{\delta}_x/\tilde{\alpha}_z}{\tilde{\delta}_x/\tilde{\alpha}_z}\right]^{n_{xz}}} = -\delta_z Z + \frac{1}{1 + \left(\frac{X}{x_z}\right)^{n_{xz}}}$$

$$\boxed{\begin{aligned} \frac{dX}{dt} &= -X + \frac{a_x + \beta_x S}{1 + S + \left(\frac{Z}{z_x}\right)^{n_{zx}}} \\ \frac{dZ}{dt} &= -\delta_z Z + \frac{1}{1 + \left(\frac{X}{x_z}\right)^{n_{xz}}} \end{aligned}}$$

c) @ ss $\frac{dX}{dt} = 0$, $\frac{dZ}{dt} = 0$
(see excel)

d) Equation 1:

$$\frac{dX}{dt} = \frac{a_x + B_x S}{1 + S + (Z/z_x)^{n_{zx}}} - X$$

$$\frac{dY}{dt} = \frac{a_y + B_y S}{1 + S + (X/x_y)^{n_{xy}}} - \delta_y Y$$

$$\frac{dZ}{dt} = \frac{1}{1 + (X/x_z)^{n_{xz}} + (Y/y_z)^{n_{yz}}} - \delta_z Z$$

$S = 0.02,\ 10,\ 10^5$

$X_0 = Y_0 = Z_0 = 0$

e) From figure 2A)

S below Hopf bifurcation point: 0.3

S above saddle node bifurcation point: 12000 (only one SS)

SS values ± 25% ⇒ initial conditions

vastly different steady state expression levels

S = 0.3	1.25 SS	.75 SS
X_{ss} = 0.00186	0.00233	0.00140
Y_{ss} = 0.243	0.304	0.182
Z_{ss} = 0.00293	0.00366	0.00220

Small change in initial conditions affects final oscillation phase

S = 12000	1.25 SS	.75 SS
X_{ss} = 5.70	7.13	4.28
Y_{ss} = 0.00128	0.00160	0.000963
Z_{ss} = 0.000395	0.000494	0.000296

For S = 0.3, oscillations for 3 cells out of phase ⇒ incoherent (attracting spiral loses stability & becomes repulsing spiral)

For S = 12000, oscillations for 3 cells in phase → coherent because this oscillatory behavior originates from a stable steady state at high signal levels where a large limit cycle is already present. Cells passing through the saddle node have expression levels far from the unstable spiral center near the Hopf birufication point. Therefore expression levels remain in phase.

2f) The authors were very ambiguous when describing the results from figure 3E. It is not clear what the gene expressions were before decreasing the signal. It was never discussed whether the expressions were producing coherent oscillations when S=105. If not, it would be impossible to produce coherent oscillations from previously incoherent oscillations. Also, I am skeptical of this claim because again, S=105 does fall in the unstable regime so small perturbations to the system might not guarantee maintanence of coherent oscillations. From part e, we know that going through the Hopf bifurcation point leads to incoherent oscillations and going through the sadle point to S=100 leads to coherent oscillations: starting points/initial conditions matter!