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

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

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

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

† note: error in eqn 3 ($t = \tilde{t}\tilde{\delta}_x$)
Correction: $t = \tilde{t}\tilde{\delta}_x$

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

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

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

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

$$\boxed{\frac{dX}{dt} = -X + \frac{a_x + \beta_x S}{1 + S + \left(\frac{Z}{z_x}\right)^{n_{zx}}}}$$

$$\boxed{\frac{dZ}{dt} = -\delta_z Z + \frac{1}{1 + \left(\frac{X}{x_z}\right)^{n_{xz}}}}$$

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

(see excel)

d) Equation 1:

$$\frac{dX}{dt} = \frac{\alpha_x + \beta_x S}{1 + S + (Z/\varepsilon_x)^{n_{xz}}} - X$$

$$\frac{dY}{dt} = \frac{\alpha_y + \beta_y S}{1 + S + (X/\varepsilon_y)^{n_{xy}}} - \delta_y Y$$

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

$S = 0.02, 10, 10^5$

$X_0 = Y_0 = Z_0 = 0$

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

→ S = 0.3	1.25 SS	.75 SS	
X_{ss} = 0.00186	0.00233	0.00140	Small change in initial conditions affects final oscillation phase
Y_{ss} = 0.243	0.304	0.182	
Z_{ss} = 0.00293	0.00366	0.00220	

Vastly different steady state expression levels

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 bifurcation 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 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 incoherrent oscillations and going through the saddle point to S=100 leads to coherrent oscillations: starting points/initial conditions matter!