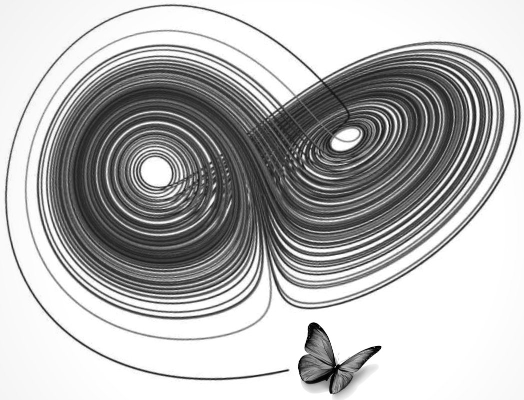
Biology and Dynamical Systems



Week 6: Explaining ever more complex systems

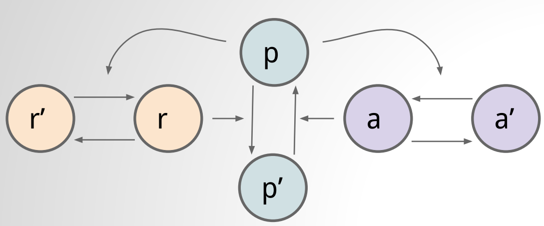
Today's aim is to get us working with systems that have 3 or more components

1. Quick review of the methods we learned for two component systems
2. Analyzing a 3 component system
3. We still need to boil down our models to focus on the key factors

What tools have we learned for building and analyzing mathematical models?

1. Converting reaction diagrams to equations
2. Graphing equilibrium points
3. Reducing the number of equations
4. Non-dimensionalization to remove extra constants
5. Running simulations and graphing output
6. Plotting nullclines and phase space plots

Looking at a three component system with feedback



activator and repressor

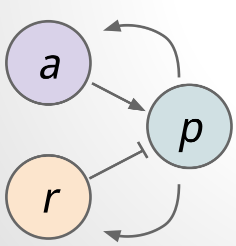
$$\frac{dr'}{dt} = k_1' r + k_1^p r p' - k_1' r' \qquad \frac{dr}{dt} = -k_1' r - k_1^p r p' + k_1' r'$$

$$\frac{da'}{dt} = k_2' a + k_2^p a p' - k_2 a' \qquad \frac{da}{dt} = -k_2' a - k_2^p a p' + k_2 a'$$

$$\frac{dp'}{dt} = k_3' p + k_3^a p a' - (k_3 + k_3^r r') p'$$

$$\frac{dp}{dt} = -k_3' p - k_3^a p a' + (k_3 + k_3^r r') p'$$

$$r' + r = r_T \qquad a' + a = a_T \qquad p' + p = p_T$$



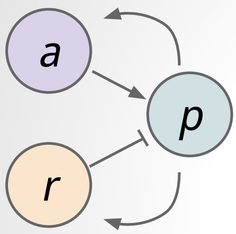
simplified diagram

$$\frac{dp}{dt} = k_{on}^p + k_{on}^{pa} a - (k_{off} + k_{off}^{pr} r) p$$

$$\frac{da}{dt} = k_{on}^a + k_{on}^{ap} p - k_{off}^a a$$

$$\frac{dr}{dt} = k_{on}^r + k_{on}^{rp} p - k_{off}^r r$$

We can reduce complexity by eliminating equations



$$\frac{dp}{dt} = k_{on}^{p} + k_{on}^{pa}a - (k_{off} + k_{off}^{pr}r)p$$

$$\frac{da}{dt} = k_{on}^{a} + k_{on}^{ap}p - k_{off}^{a}a$$

$$\frac{dr}{dt} = k_{on}^{r} + k_{on}^{rp}p - k_{off}^{r}r$$

start: 9 equations + 13 constants

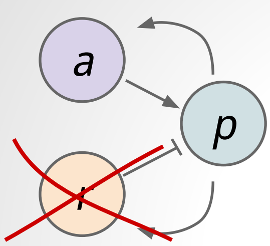
finish: 3 equations + 4 constants

$$\frac{dp}{dt} = 1 + \gamma_a a - (1 + \gamma_r r)p$$

$$\frac{da}{dt} = 1 + \beta_a p - \frac{a}{\kappa_a}$$

$$\frac{dr}{dt} = 1 + \beta_r p - \frac{r}{\kappa_r}$$

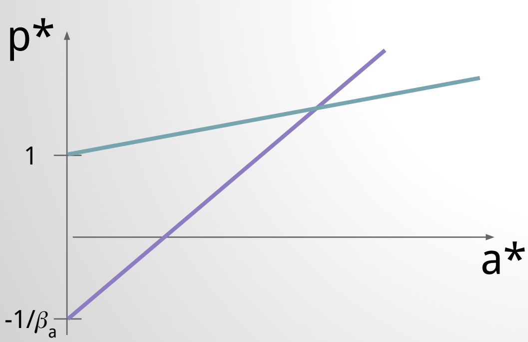
To start, let's see what happens if r = 0



$$\frac{dp}{dt} = 1 + \gamma_a a - (1 + \cancel{\gamma_r r})p$$

$$\frac{da}{dt} = 1 + \beta_a p - \frac{a}{\kappa_a}$$

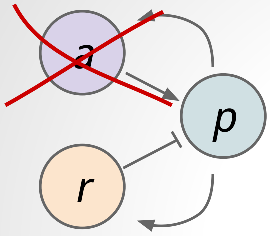
$$\cancel{\frac{dr}{dt} = 1 + \beta_r p - \frac{r}{\kappa_r}}$$



$$p^* = 1 + \gamma_a a^*$$

$$p^* = -\frac{1}{\beta_a} + \frac{a^*}{\kappa_a \beta_a}$$

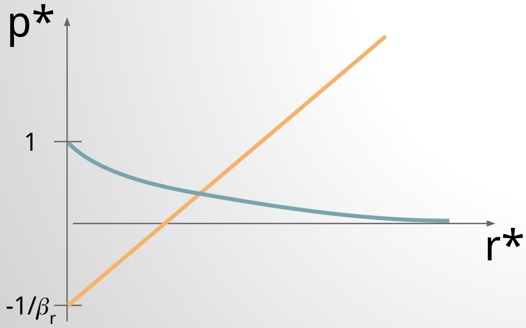
and what if a = 0



$$\frac{dp}{dt} = 1 + \cancel{\gamma_a a} - (1 + \gamma_r r)p$$

$$\cancel{\frac{da}{dt} = 1 + \beta_a p - \frac{a}{\kappa_a}}$$

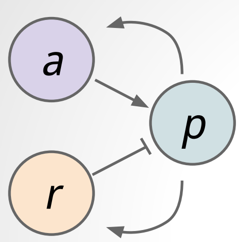
$$\frac{dr}{dt} = 1 + \beta_r p - \frac{r}{\kappa_r}$$



$$\boxed{p^* = \frac{1}{1 + \gamma_r r^*}}$$

$$\boxed{p^* = -\frac{1}{\beta_r} + \frac{r^*}{\kappa_r \beta_r}}$$

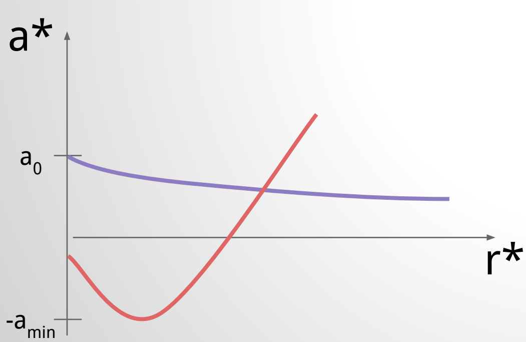
Let’s just see what this system looks like if p very close to its equilibrium value.



$$\frac{dp}{dt} \approx 0 \Rightarrow \quad p^* = \frac{1 + \gamma_a a^*}{1 + \gamma_r r^*}$$

$$\frac{da}{dt} = 1 + \beta_a \frac{1 + \gamma_a a}{1 + \gamma_r r} - \frac{a}{\kappa_a}$$

$$\frac{dr}{dt} = 1 + \beta_r \frac{1 + \gamma_a a}{1 + \gamma_r r} - \frac{r}{\kappa_r}$$



$$\boxed{a^* = \frac{a_0 + \omega_1 r^*}{1 + \omega_2 r^*}}$$

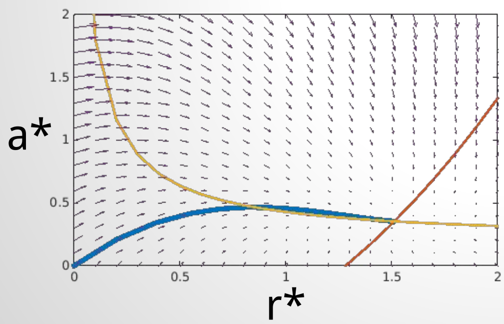
$$\boxed{a^* = \omega_r (r - r_0)^2 - a_{min}}$$

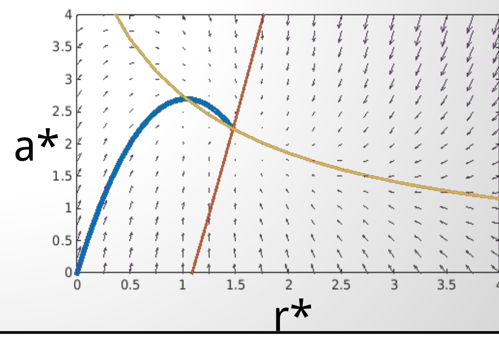
Now that we have simplified and gathered some intuition, we can start analyzing simulations

$$\frac{da}{dt} = 1 + \beta_a \frac{1+\gamma_a a}{1+\gamma_r r} - \frac{a}{\kappa_a}$$

$$\frac{dr}{dt} = 1 + \beta_r \frac{1+\gamma_a a}{1+\gamma_r r} - \frac{r}{\kappa_r}$$

```
function dc = myode2(t,c,ba,br,ya,yr,ka,kr)
	a = c(1);
	r = c(2);
	da = 1 +ba*(1+ya*a)/(1+yr*r) - a/ka;
	dr = 1 +br*(1+ya*a)/(1+yr*r) - r/kr;
	dc = [da;dr];
end
```





Discussion: Let’s finish this problem (40 pts)

1. Break into groups
2. Each group works on a simulation of the full 3 component system (10pts)
3. We’ll regroup after 15-20 minutes
4. Every group should present 5 minutes on one interesting finding (10 pts)
5. 10 pts will be awarded for the clearest explanation
6. 10 pts for giving good feedback to others

Project: Go forth and conquer

Keep working with your models! Solve your problem and present it clearly.