Lecture 9: Genetic Control System

Chapter 7.2.2, Strogatz ch. 8

11/11/24

$$\dot{x} = -ax + y \qquad x = [\text{Protein}]$$

$$\dot{y} = -by + \frac{x^2}{1+x^2} \qquad y = [\text{RNA}] \text{ coding for protein } x$$

$a, b > 0$ are parameters relating to decay/lifetime of protein/RNA

Identify the terms:

$-ax, -ay$ linear decay — NB First quadrant only

$+y$ production of protein from RNA

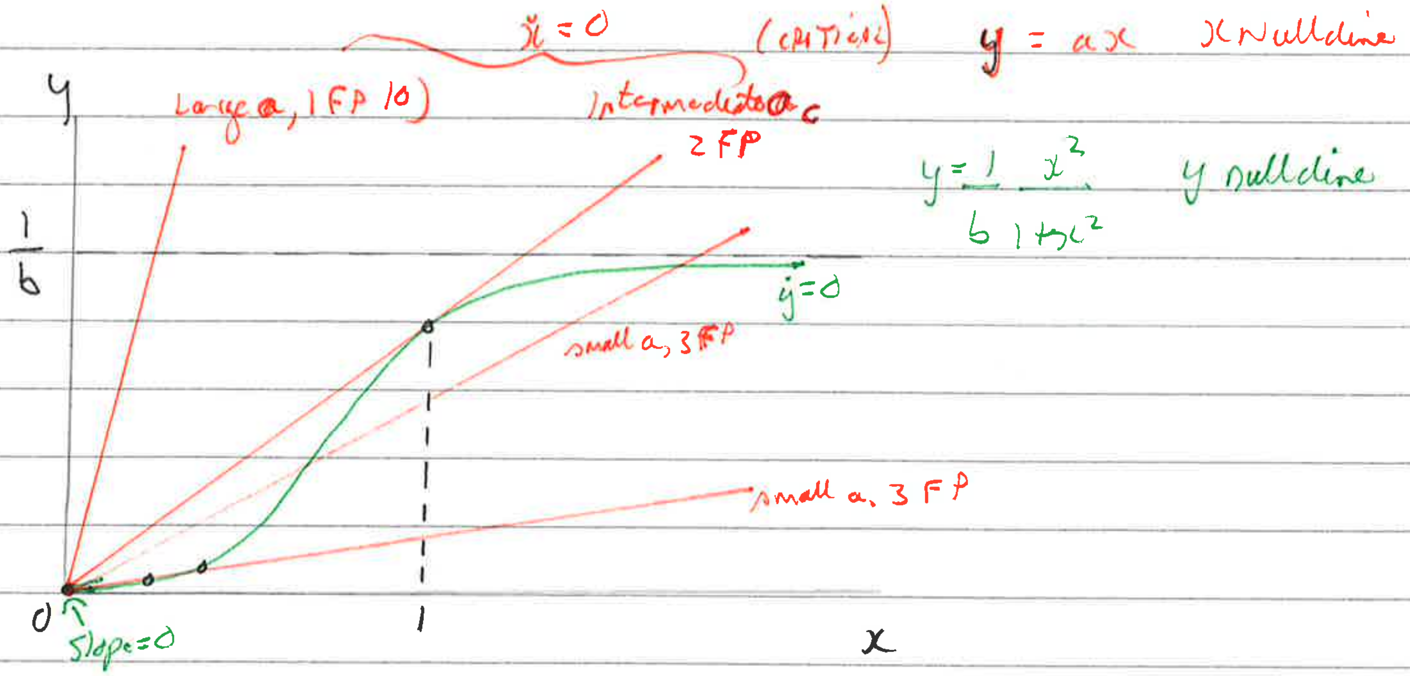
$\frac{x^2}{1+x^2}$ autocatalytic feed back from protein to RNA; it saturates because there is a limited number of binding sites for promoter.

cp. $\dot{g} = s - rg + \frac{g^2}{1+g^2}$ — But now we separate the RNA and protein dynamics.

Nullclines

$\dot{x} = 0 \Rightarrow \underline{\underline{y = ax}}$ i.e. linear

$$\dot{y} = 0 \Rightarrow \underline{\underline{by = \frac{x^2}{1+x^2}}}$$



As $x \to \infty$ $y \to 1/b$ What is $\frac{dy}{dx}(x=0)$? $= \frac{2x}{(1+x^2)^2} = 0$

Clearly, $(0,0)$ is always a fixed point.

For a less than a certain value, there are 3 FPs, and for a special value, there are two.

Where are the non-trivial FPs? Intersection of nullcline.

$$ax^* = \frac{1}{b}\frac{x^{*2}}{1+x^{*2}}$$

$\Rightarrow x^* = 0$ or $ab = \frac{x^*}{1+x^{*2}}$ i.e. a quadratic equation in x^* so possibly 0, 1 or 2 real roots.

(Drop the * on x) Non-trivial fixed points

$ab(1+x^2) = x$

$$\Rightarrow \quad x^2 - \frac{x}{ab} + 1 = 0$$

$$\therefore \; x = \frac{\frac{1}{ab} \pm \sqrt{\left(\frac{1}{ab}\right)^2 - 4}}{2} = \frac{1}{2ab}\left[1 \pm \left(1 - (2ab)^2\right)^{\frac{1}{2}}\right]$$

Non-zero fixed point

So, if $2ab < 1$, there are two non-trivial fixed points (as well as $0,0$)

$2ab = 1$, there is one non-trivial FP : $x^* = 1$
$y^* = a$

$2ab > 1$, only $(0,0)$ is a fixed point.

Jacobian

$$\underset{=}{J} = \begin{pmatrix} -a & 1 \\ \frac{2x}{(1+x^2)^2} & -b \end{pmatrix}$$

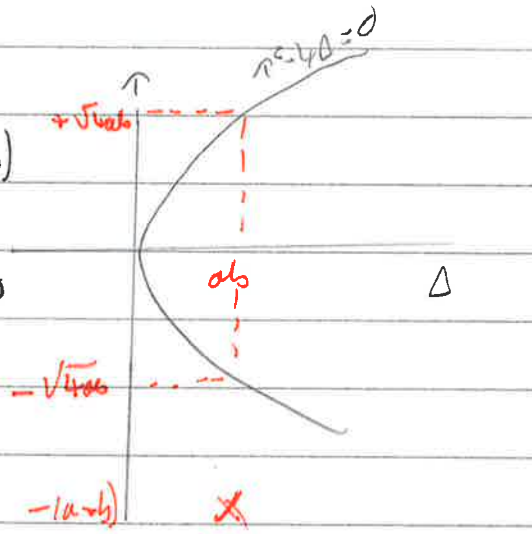
$\boxed{\therefore \; \tau = -(a+b) < 0}$ as $a, b > 0$ $\Rightarrow$ All fixed points are stable or saddlepoints

$$\boxed{\Delta = ab - \frac{2x}{(1+x^2)^2}}$$

Analyse each Fixed point

A) $(0,0)$ $\quad \underline{J} = \begin{pmatrix} -a & 1 \\ 0 & -b \end{pmatrix}$ $\quad \therefore \tau = -(a+b)$

$\Delta = ab > 0$



But $\tau^2 - 4\Delta = (a+b)^2 - 4ab$

$= (a-b)^2 > 0$

$\therefore$ $(0,0)$ is a stable node for all values of a, b. NB Ignoring $a=b$!

Before we look at the non-zero fixed points, we need some results.

For $a > a_c$, the origin is the only fixed point. When $a = a_c$, we have two fixed points, and for $a < a_c$, we have three.

The bifurcation occurs when the nullclines are tangent to each other.

1) $\Rightarrow$ Function values are equal

2) and Slope of functions (tangents) are equal

1) $\Rightarrow$ $\boxed{ab = \dfrac{x}{1+x^2} \quad \text{from before}}$

2) $\Rightarrow$ $a = \dfrac{1}{b}\left[\dfrac{(1+x^2).2x - x^2.2x}{(1+x^2)^2}\right] = \dfrac{2x}{b(1+x^2)^2}$

$\boxed{\therefore ab = \dfrac{2x}{(1+x^2)^2}}$

Divide one by the other.

$$1 = \frac{1+x^2}{2} \Rightarrow x = 1$$ (Draw this on phase portrait)

and so, also from $ab = \frac{x}{1+x^2} = 1/2$

$$\boxed{\therefore\ 2 a_c b = 1}$$ a_c = critical value of a

Where are the non-zero fixed points for $2ab < 1$?

B) $$x_1^* = \frac{1}{2ab}\left[1 - (1-(2ab)^2)^{\frac{1}{2}}\right]$$

we know that $T = -(a+b)$, what is Δ?

$$\Delta = ab - \frac{2x_1^*}{(1+x_1^{*2})^2}$$ This looks hard but we know $ab = \frac{x_1^*}{1+x_1^{*2}}$

$$\therefore \Delta = ab - \frac{2}{(1+x_1^{*2})} \cdot \frac{x_1^*}{(1+x_1^{*2})} \quad \equiv ab$$

$$= ab\left[1 - \frac{2}{(1+x_1^{*2})}\right] = ab\left[\frac{1+x_1^{*2}-2}{1+x_1^{*2}}\right] = ab\left[\frac{x_1^{*2}-1}{x_1^{*2}+1}\right] < 0$$

Q. why is $x_1^* < 1$?

$\therefore$ This is a saddle point as $\Delta < 0$.

How do we know $x_1^* < 1$ for $x \in [0,1]$

Consider $f(x) = \dfrac{1-(1-x^2)^{\frac{1}{2}}}{x}$ i.e. Let $x = 2ab$ in Eqn B

Consider the product: $\left(\dfrac{1-(1-x^2)^{\frac{1}{2}}}{x}\right) * \left(\dfrac{1+(1-x^2)^{\frac{1}{2}}}{x}\right)$

$$= \frac{1-(1-x^2)}{x^2}$$

$$= 1$$

If two numbers multiplied together give 1, one must be larger than 1, and the other smaller than 1.

Also $1-(1-x^2)^{\frac{1}{2}} < 1+(1-x^2)^{\frac{1}{2}}$

$$\therefore \frac{1-(1-x^2)^{\frac{1}{2}}}{x} \leq 1 \leq \frac{1+(1-x^2)^{\frac{1}{2}}}{x}$$

i.e. The two non-zero roots are on opposite sides of 1.

c) $x_2^* = \frac{1}{2ab}\left[1 + (1-(2ab)^2)^{\frac{1}{2}}\right]$

again, we know $\tau < 0$, what is Δ?

$\Delta = ab - \frac{2x_2^*}{(1+x_2^{*2})^2}$ but again $\frac{x_2^*}{1+x_2^{*2}} = ab$

$\therefore \Delta = ab\left(\frac{x_2^{*2}-1}{x_2^{*2}+1}\right)$ so numerator < denominator

$\therefore \Delta < ab$

$\Rightarrow \tau^2 - 4\Delta > (a+b)^2 - 4ab = (a-b)^2 > 0$

$\therefore x_2^*$ is a stable node

so, we have a stable node at $(0,0)$ and $(x_2^*, a x_2^*)$

and a saddlepoint at $(x_1^*, a x_1^*)$

if $2ab < 1$

What are the vector fields along the nullclines?

$\dot{x} = 0 \Rightarrow y = ax$ in the x nullcline

and $\dot{y} = -by + \frac{x^2}{1+x^2} = \frac{-abx + x^2}{1+x^2} = \frac{-abx(1+x^2) + x^2}{1+x^2}$

When does this change sign? only the numerator matters.

$x^2 - abx(1+x^2) = 0$

$\Rightarrow x = 0$ or $x - ab - abx^2 = 0$

$\Rightarrow x^2 - \frac{x}{ab} + 1 = 0$

which has solutions x_1^*, x_2^* as before.

$\Rightarrow \dot{y} \sim -\frac{abx(x - x_1^*)(x - x_2^*)}{1+x^2}$

NB cubic term must be negative because it is negative above in original equation for $\dot{y}$

$\boxed{\begin{array}{l} \therefore \dot{y} < 0 \text{ when } x < x_1^* \text{ and } x > x_2^* \\ \dot{y} > 0 \text{ when } x_1^* < x < x_2^* \end{array}}$

$\dot{y} = 0 \Rightarrow by = \dfrac{x^2}{1+x^2}$ is the y nullcline

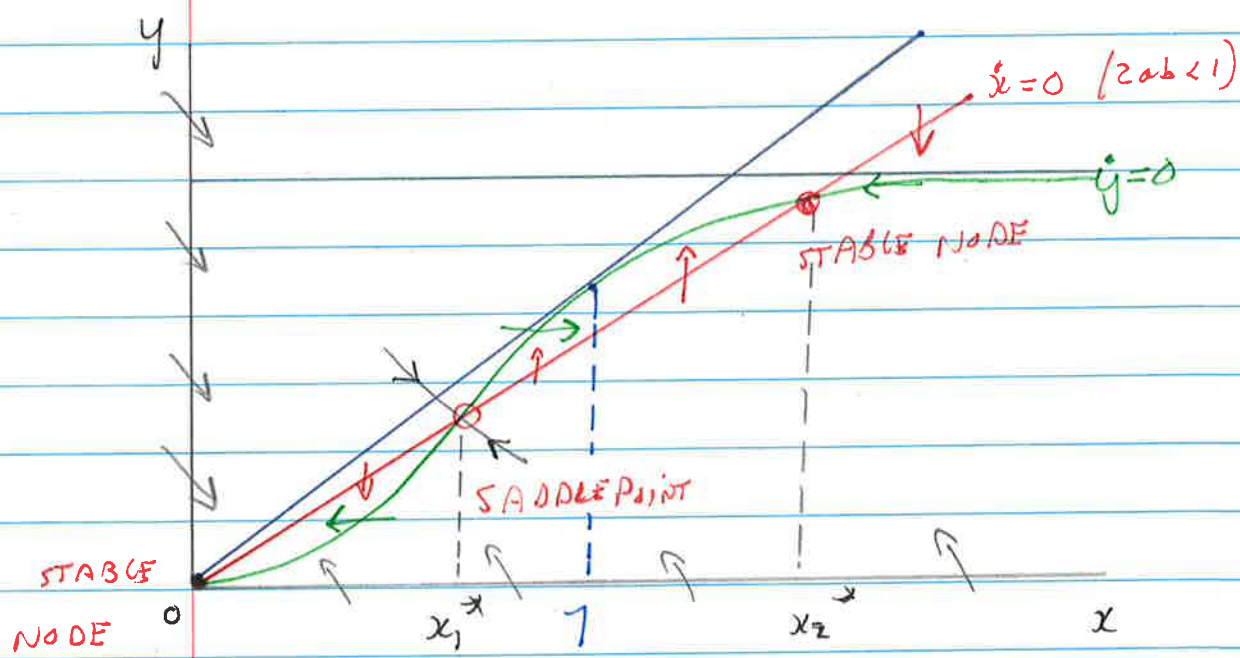
and so $\dot{x} = -ax + y = -ax + \dfrac{1}{b}\dfrac{x^2}{1+x^2}$

$$= \frac{1}{b}\left[\frac{-abx(1+x^2) + x^2}{1+x^2}\right]$$

Same roots x_1^*, x_2^* as before.

$\therefore$ $\dot{x} < 0$ along y nullcline when $x < x_1^*$ and $x > x_2^*$.

$\dot{x} > 0$ when $x_1^* < x < x_2^*$



Along x axis: $\dot{x} = -ax < 0 \ \forall x$
$\dot{y} = \dfrac{x^2}{1+x^2} > 0$

and along y axis: $\dot{x} = y > 0 \ \forall y$
$\dot{y} = -by < 0$

Numerical example

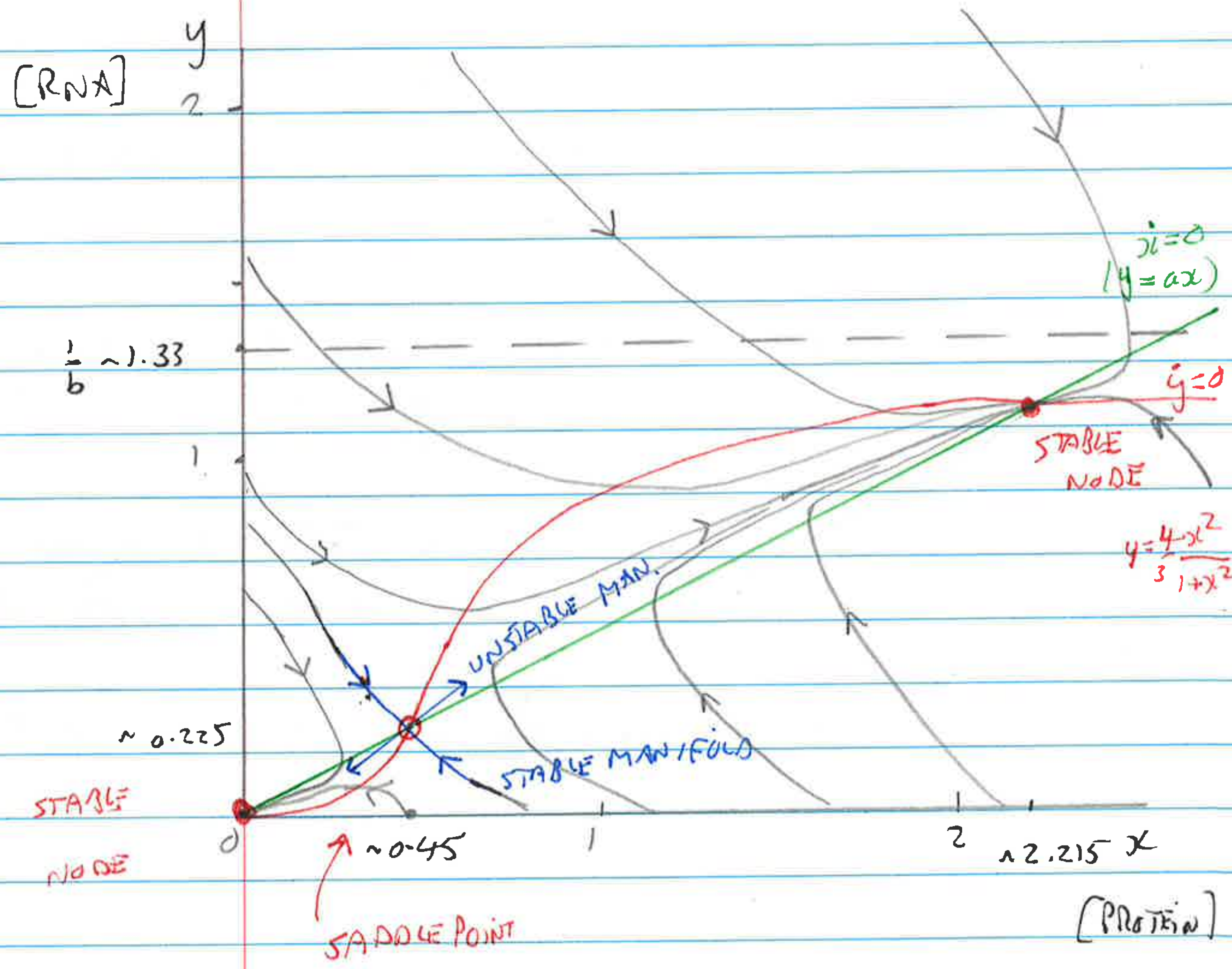
We need $2ab < 1$, try $a = 1/2$, $b = 3/4$ $\Rightarrow 2ab = 3/4$

$$x_1^* = \frac{1}{3/4}\left[1 - \left(1-(3/4)^2\right)^{\frac{1}{2}}\right] = \frac{4}{3}\left[1 - \left(1 - \frac{9}{16}\right)^{\frac{1}{2}}\right] \sim 0.45$$

$$\Rightarrow y_1^* = a x^* = 0.225$$

$$x_2^* = \frac{1}{3/4}\left[1 + \left(1-(3/4)^2\right)^{1/2}\right] \approx 2.215$$

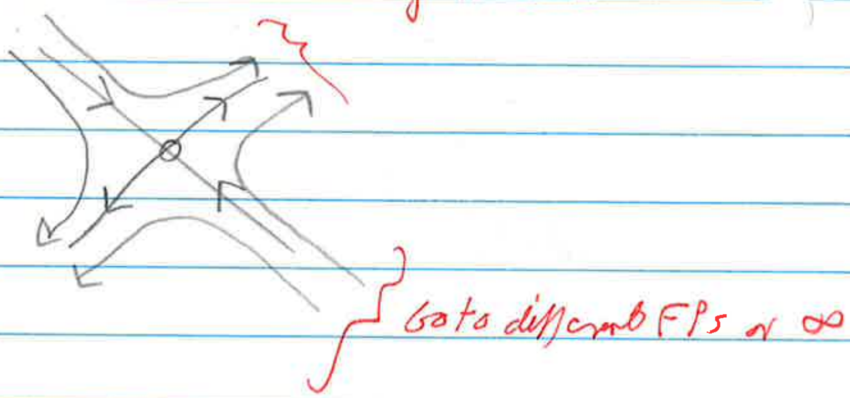
$$\Rightarrow y_2^* \sim 1.11$$



NOTES

1 The stable/unstable manifolds and slow/fast eigenvectors are only straight lines close to the fixed point. BUT they are trajectories, so they must continue somehow as curves.

2 The stable manifold divides the phase portrait into disjoint parts:



3 If $a > a_c$, only $(0,0)$ is a fixed point: gene is off

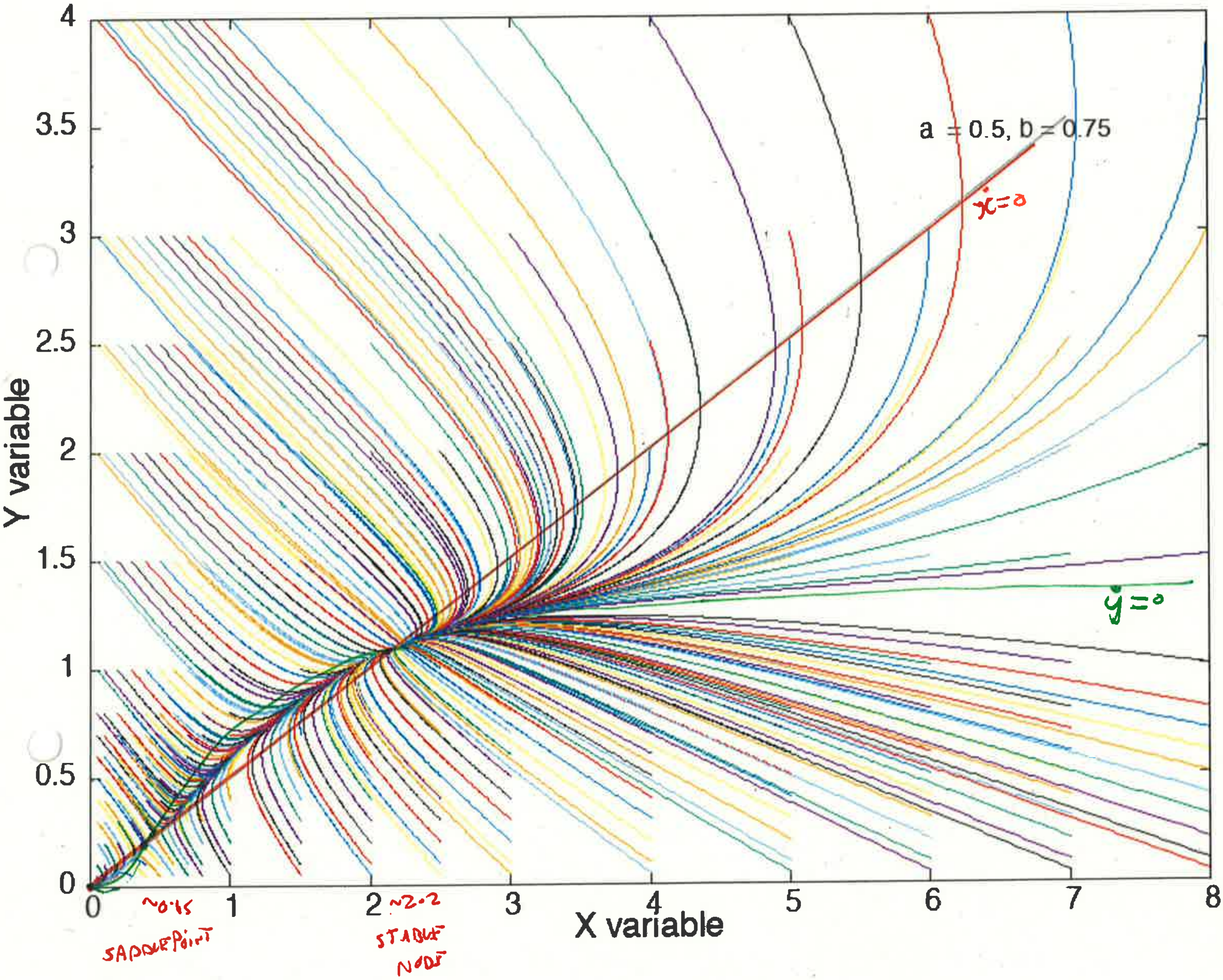
when $a < a_c$, a stable node appears at large [protein], separated by a saddlepoint.

There is a switch between two states.

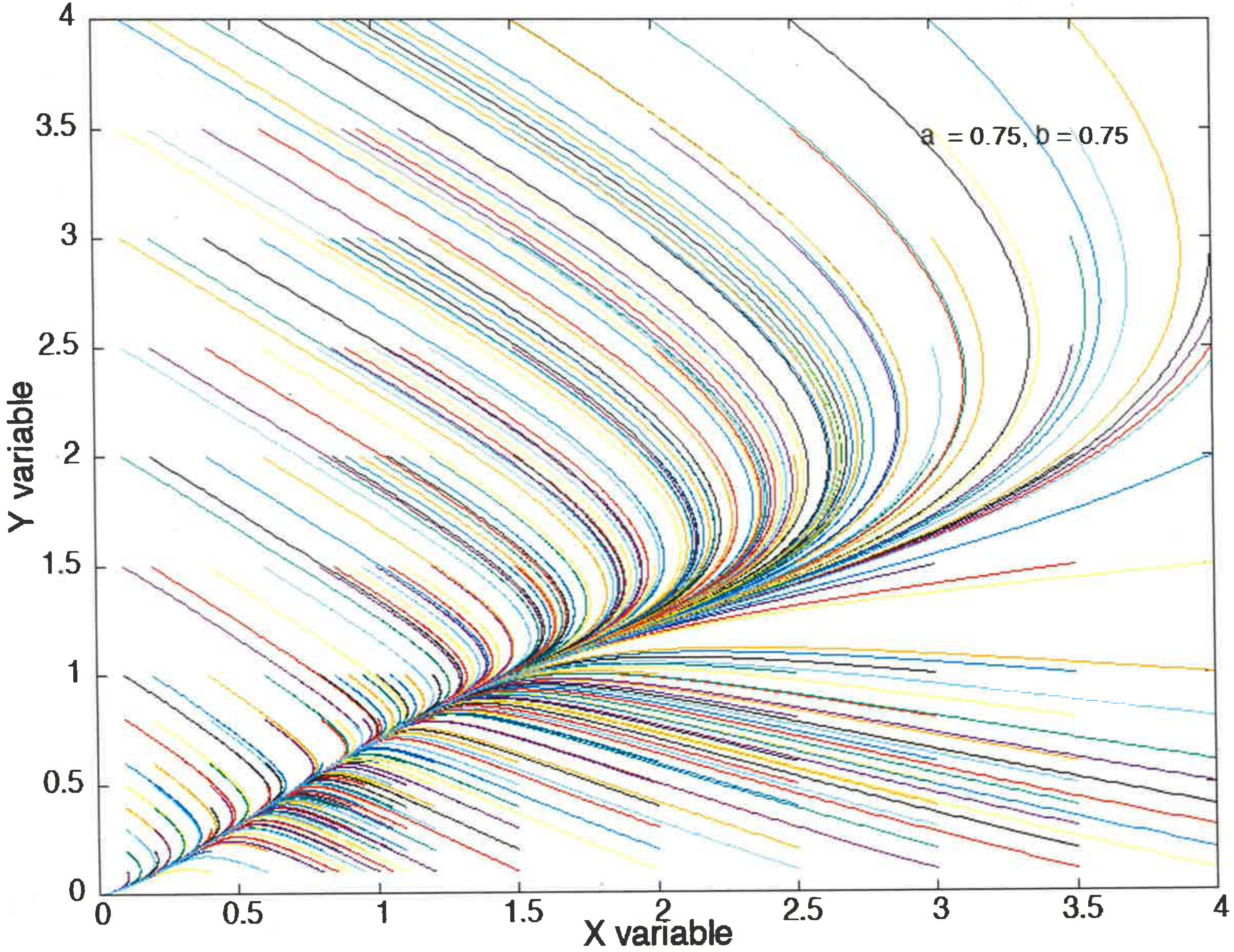
Lecture 9 GC5

Strogatz 8.1.1 (Example)

$2ab < 1$



(Misc 2ab 8)



Analysis of the saddle point

Set $a = 1/2$, $b = 3/4$ $\Rightarrow 2ab = 0.75$

$$x_1^* = \frac{4}{3}\left[1 - \sqrt{1 - 0.75^2}\right] = 0.451 \quad , \quad y^* = a x^* = 0.225$$

$\therefore$ FP is at $(0.45, 0.225)$

$$T = -(a+b) = -5/4 = -1.25$$

$$\Delta = ab - \frac{2x^*}{(1+x^{*2})^2} = 0.375 - \frac{2 \cdot 0.45}{(1+0.45^2)^2} = -0.25 < 0$$

$\therefore$ A saddlepoint.

Eigenvalues

$$\underline{\underline{J}} = \begin{pmatrix} -a & 1 \\ \frac{2x}{(1+x^2)^2} & -b \end{pmatrix}$$

$$\therefore \det(\underline{\underline{J}} - \lambda) = \begin{vmatrix} -0.5-\lambda & 1 \\ 0.62 & -0.75-\lambda \end{vmatrix} = (0.5+\lambda)(0.75+\lambda) - 0.62 = 0$$

$$\Rightarrow 0.375 + 1.25\lambda + \lambda^2 - 0.62 = 0$$

$$\therefore \lambda^2 + 1.25\lambda - 0.245 = 0$$

$$\Rightarrow \lambda = \frac{-1.25 \pm \sqrt{1.25^2 + 4.0.245}}{2}$$

$$= \frac{-1.25 \pm 1.59}{2} = 0.172, -1.422$$

$\therefore$ General trajectory is: $\underline{x}(t) = c_1 e^{0.172t} \underline{v_1} + c_2 e^{-1.422} \underline{v_2}$

Eigenvectors

$\underline{\lambda = 0.172}$ $\begin{pmatrix} -0.5-0.172 & 1 \\ 0.62 & -0.75-0.172 \end{pmatrix}\begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = 0$

$$= \begin{pmatrix} -0.672 & 1 \\ 0.62 & -0.922 \end{pmatrix}\begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = 0$$

$\Rightarrow -0.672 v_1 + v_2 = 0$

$0.62 v_1 - 0.922 v_2 = 0$

$\therefore \underline{v_1} = \begin{pmatrix} 1 \\ 0.672 \end{pmatrix}$

$\underline{\lambda = -1.422}$ $\begin{pmatrix} -0.5+1.422 & 1 \\ 0.62 & -0.75+1.422 \end{pmatrix}\begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = 0$

$\Rightarrow \begin{pmatrix} 0.922 & 1 \\ 0.62 & 0.672 \end{pmatrix}\begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = 0$

$\Rightarrow \quad 0.922 v_1 + v_2 = 0$

$\quad\; 0.62 v_1 + 0.672 v_2 = 0$

$\therefore \; v_2 = \begin{pmatrix} 1 \\ -0.922 \end{pmatrix}$

$$\therefore \; x(t) = c_1 e^{0.172t} \begin{pmatrix} 1 \\ 0.672 \end{pmatrix} + c_2 e^{-1.422t} \begin{pmatrix} 1 \\ -0.922 \end{pmatrix}$$

UNSTABLE MANIFOLD   STABLE MANIFOLD

! But only close to the saddlepoint!

17/11/23 On the other hand, if we have $a=1$, $b=0.75$, so $a > a_c = \frac{1}{2b} = 0.6\dot{6}$ $2a_cb = 1$

so there is only a stable node at $(0,0)$. Can any trajectories go to infinity?

Look at $\dot{x} = -ax + y \qquad = -x + y$

$\qquad\;\; \dot{y} = -by + \frac{x^2}{1+x^2} \qquad = -0.75y + \frac{x^2}{1+x^2}$

NB $\dot{y} < 0$ $\forall y$ except near 0, when $\frac{x^2}{1+x^2}$ might make it positive

If we let x, y both go to infinity, $\dot{y} < 0$ as $\frac{x^2}{1+x^2}$ is bounded. So y will decrease. If $x > y$, $\dot{x}$ will decrease until it reaches the nullcline $x = y$. Then y will decrease as y is still large, so $\dot{x} < 0$.

$\therefore$ All trajectories will end up at $(0,0)$.

3/4/24 What happens as $x \to \infty$? Trajectories above a certain y appear to curve around from smaller x, while those below a certain y seem to rise from the x axis?

$$\dot{x} = -ax + y$$

NB $y = ax$ must go through all fixed points; this nullcline is not a trajectory!

$$\dot{y} = -by + \frac{x^2}{1+x^2} \to 1 - by \text{ as } x \to \infty$$

$\therefore$ If $y < 1/b$ (1.33 here), $\dot{y} > 0$ as $x \to \infty$ while if $y > 1/b$, $\dot{y}$ is always negative. If $y = 1/b$, then $\dot{y} \to 0$ as $x \to \infty$.

When $\dot{y} = 0$ $\quad y = \frac{1}{b} \cdot \frac{x^2}{1+x^2}$

$$\Rightarrow \dot{x} = -ax + \frac{1}{b}\frac{x^2}{1+x^2}$$

Suppose we start at (x_0, y_0) that satisfy $y_0 = \frac{1}{b}\frac{x_0^2}{1+x_0^2}$, where does it go?

$\Rightarrow \dot{x} = -ax_0 + \frac{x_0^2}{b(1+x_0^2)}$ and assume x_0 is such that $(-ax_0) > \frac{x_0^2}{b(1+x_0^2)}$

$\dot{y} = \frac{-x_0^2}{1+x_0^2} + \frac{x_0^2}{1+x_0^2} = 0$ then $\dot{x} < 0$, and x decreases.

$$\Rightarrow \dot{y}(t+\delta t) \sim \frac{-x_0^2}{1+x_0^2} + \frac{(x_0 - \delta)^2}{1+(x_0-\delta)^2} < 0$$

$\{ < x_0^2 \}$ $\quad \{ \cancel{<} (1+x_0^2) \}$

Suppose $y_0 = 1/b$ and x_0 is larger than $1/ba$

$$\Rightarrow \dot{x} = \frac{1}{b} - ax_0 < 0$$

$$\dot{y} = -1 + \frac{x_0^2}{1+x_0^2} < 0$$

Eigenvalues of the stable fixed points in the GCS

5/7/24 At $(0,0)$ $\underset{=}{J} = \begin{pmatrix} -a & 1 \\ 0 & -b \end{pmatrix}$

Eigenvalues: $\Rightarrow \begin{vmatrix} -a-\lambda & 1 \\ 0 & -b-\lambda \end{vmatrix} = 0$

$\Rightarrow (a+\lambda)(b+\lambda) - 0 = 0$

$\therefore \lambda = -a, -b$

STABLE NODE

we have $x^*_{1,2} = \frac{1}{2ab}\left[1 \mp \left(1 - (2ab)^2\right)^{\frac{1}{2}}\right]$

and for $a = 0.5$, $b = 0.75 \Rightarrow 2ab = 0.75$

$x_1^* = 0.4514$, $y^* = ax^* = 0.2258$

$x_2^* = 2.2152$, $y^* = 1.108$

x_1^*

$\underset{=}{J} = \begin{pmatrix} -0.5 & 1 \\ 0.6230 & -0.75 \end{pmatrix}$

x_2^*

$\begin{pmatrix} -0.5 & 1 \\ 0.127 & -0.75 \end{pmatrix}$

Eigenvalues of the stable node at the origin

$\lambda = -0.5; 0.75$

$$\underset{\sim}{J} = \begin{pmatrix} -0.5 & 0 \\ 0 & -0.75 \end{pmatrix}$$

$\lambda = -0.5$ $\begin{pmatrix} 0 & 0 \\ 0 & -0.25 \end{pmatrix}\begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = 0 \quad \therefore \underline{v_1} = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$

$\lambda = -0.75$ $\begin{pmatrix} 0.25 & 0 \\ 0 & 0 \end{pmatrix}\begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = 0 \Rightarrow \underline{v_2} = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$

$$\therefore \underline{x}(t) = c_1 e^{-0.5t}\begin{pmatrix} 1 \\ 0 \end{pmatrix} + c_2 e^{-0.75t}\begin{pmatrix} 0 \\ 1 \end{pmatrix}$$

Slow EIGENVECTOR FAST EIGENVECTOR