Calculating Biological Quantities

CSCI 2897

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Last time on CSCI 2897

Definitions: An **Eigenvector** of a square matrix A is a vector x such that $Ax = \lambda x$ for some scalar λ . An **Eigenvalue** is that scalar, λ.

There can be at most n eigenvectors and n eigenvalues for an $n \times n$ matrix.

To compute eigenvalues, we:

1. Write $Ax = \lambda x$ as $Ax - \lambda x = 0$ and then as $(A - \lambda I)x = 0$.
2. If $(A - \lambda I)x = 0$ but $x \neq 0$, this means that $\det(A - \lambda I) = 0$.
3. Write out the characteristic equation: $(a - \lambda)(d - \lambda) - bc = 0$
4. Solve for λ.

To compute the eigenvectors, for each eigenvalue, we

1. Plug in the λ to $(A - \lambda I)x = 0$, and write out the equations.
2. The equations *should* be redundant. Pick one and determine the relationship between x_1 and x_2. That's your eigenvector!

Why do we care though?

$\dot{n} = \lambda n$

$$\frac{d\vec{n}}{dt} = A\vec{n} \qquad \text{Solution: } \vec{n}(t) = k_1\vec{x}_1 e^{\lambda_1 t} + k_2 \vec{x}_2 e^{\lambda_2 t}$$

$$\frac{dn}{dt} = \lambda n \longrightarrow n(t) = k_1 e^{\lambda t}$$

Example

$$\frac{dn_1}{dt} = 2n_1 + 3n_2$$

$$\frac{dn_2}{dt} = 2n_1 + n_2$$

rewrite system of ODEs in matrix form

$$\star \quad \frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix}$$

solution to ODEs is in terms of eigenvalues and eigenvectors

$$\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = k_1 \begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-t} + k_2 \begin{pmatrix} 3 \\ 2 \end{pmatrix} e^{4t}$$

we can check that this solves, by plugging into ★

Plug solution into LHS of ★

$$\frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = -1k_1 \begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-t} + 4k_2 \begin{pmatrix} 3 \\ 2 \end{pmatrix} e^{4t}$$

Plug solution into RHS of ★

$$\begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = k_1 \begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}\begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-t} + k_2 \begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}\begin{pmatrix} 3 \\ 2 \end{pmatrix} e^{4t}$$

$Ax_1 = \lambda_1 x_1$ $\qquad$ $Ax_2 = \lambda_2 x_2$

$$\begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = k_1(-1) \begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-t} + k_2(4) \begin{pmatrix} 3 \\ 2 \end{pmatrix} e^{4t}$$

Practice. Find the eigenvalues & eigenvectors of $A = \begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}$

$I = \begin{bmatrix} 1 & 0 \\ 0 & 1 \end{bmatrix}$

$\lambda_1, \lambda_2 = 1, 1$

② $A - \lambda I = \begin{pmatrix} 2-\lambda & 3 \\ 2 & 1-\lambda \end{pmatrix}$

so $\det(A - \lambda I) = (2-\lambda)(1-\lambda) - (3)(2)$

③ set $= 0 \longrightarrow 2 - 3\lambda + \lambda^2 - 6 = 0$

$\lambda^2 - 3\lambda - 4 = 0$

④ $(\lambda - 4)(\lambda + 1) = 0$

$\Rightarrow \boxed{\lambda = 4, \ \lambda = -1}$

Formula allows you to skip to step 4.

Recall: $\lambda_1, \lambda_2 = \dfrac{-tr(A) \pm \sqrt{tr^2(A) - 4\det(A)}}{2}$

$\lambda = 4$

① $\begin{pmatrix} 2-\lambda & 3 \\ 2 & 1-\lambda \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$

$\begin{pmatrix} -2 & 3 \\ 2 & -3 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$

$-2x_1 + 3x_2 = 0$

$2x_1 - 3x_2 = 0$

redundant

② $-2x_1 + 3x_2 = 0$

$3x_2 = 2x_1$

$\frac{3}{2} x_2 = x_1$

$x_2 = 1 \rightarrow x_1 = \frac{3}{2}$

$x = \begin{pmatrix} 3/2 \\ 1 \end{pmatrix}$

$\lambda = -1$

$\begin{pmatrix} 2--1 & 3 \\ 2 & 1--1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$

$3x_1 + 3x_2 = 0$

$2x_1 + 2x_2 = 0$

$x_1 = -x_2$

$x = \begin{pmatrix} 1 \\ -1 \end{pmatrix}$

To compute eigenvalues, we:

1. Write $Ax = \lambda x$ as $Ax - \lambda x = 0$ and then as $(A - \lambda I)x = 0$.
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To compute the eigenvectors, for each eigenvalue, we

1. Plug in the λ to $(A - \lambda I)x = 0$, and write out the equations.
2. The equations *should* be redundant. Pick one and determine the relationship between x_1 and x_2. That's your eigenvector!

Practice. Solve $\frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix}$, $\quad n_1(0) = 7,\ n_2(0) = 3$

Initial Conditions!

$$\begin{pmatrix} n_1 \\ n_2 \end{pmatrix}(t) = k_1 \vec{x}_1 e^{\lambda_1 t} + k_2 \vec{x}_2 e^{\lambda_2 t}$$

$$\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = k_1 \begin{pmatrix} 3/2 \\ 1 \end{pmatrix} e^{4t} + k_2 \begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-t}$$

Plug in initial conditions.

$t = 0,\ n_1 = 7,\ n_2 = 3$

$$\begin{pmatrix} 7 \\ 3 \end{pmatrix} = k_1 \begin{pmatrix} 3/2 \\ 1 \end{pmatrix} e^{4\cdot 0} + k_2 \begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-0}$$

solve for what the constants must be

$$\begin{pmatrix} 7 \\ 3 \end{pmatrix} = k_1 \begin{pmatrix} 3/2 \\ 1 \end{pmatrix} + k_2 \begin{pmatrix} 1 \\ -1 \end{pmatrix}$$

$$\begin{aligned} 7 &= \tfrac{3}{2} k_1 + k_2 \\ + \quad 3 &= k_1 - k_2 \\ \hline 10 &= \tfrac{5}{2} k_1 \end{aligned}$$

$20 = 5 k_1$

$\boxed{4 = k_1}$

$3 = 4 - k_2 \rightarrow \boxed{k_2 = 1}$

$$\boxed{\begin{pmatrix} n_1 \\ n_2 \end{pmatrix}(t) = 4 \begin{pmatrix} 3/2 \\ 1 \end{pmatrix} e^{4t} + \begin{pmatrix} 1 \\ -1 \end{pmatrix} e^{-t}}$$

Linear Multivariable Models

$\frac{dn}{dt} = \alpha n$ vs. $\frac{dn}{dt} = \alpha n + c$

S.O.V. I.F.

Linear model $\frac{d\vec{n}}{dt} = M\vec{n}$

Affine model $\frac{d\vec{n}}{dt} = M\vec{n} + \vec{c}$

Two dimensional case (individual equation form)

$$\frac{dn_1}{dt} = an_1 + bn_2$$

$$\frac{dn_2}{dt} = cn_1 + dn_2$$

$$\frac{dn_1}{dt} = an_1 + bn_2 + c_1$$

$$\frac{dn_2}{dt} = cn_1 + dn_2 + c_2$$

Two dimensional case (matrix vector form)

$$\frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix}$$

$$\frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} + \begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$$

Question: what are the equilibria of these systems?

Equilibria of linear multivariable models

Three methods:

1. **Solve individual equations.**
2. Solve matrix equation.
3. Nullclines.

too much work! Imagine if 3x3? 10x10?

$$\frac{dn_1}{dt} = an_1 + bn_2 = 0 \rightarrow an_1 = -bn_2$$

$$n_1 = \frac{-b}{a} n_2$$

$$\frac{dn_2}{dt} = cn_1 + dn_2 = 0$$

$$c\left(\frac{-b}{a}\right)n_2 + dn_2 = 0$$

$$\left[c\left(\frac{-b}{a}\right) + d\right] n_2 = 0$$

$$n_2 = 0$$

$$n_1 = 0$$

$$(n_1, n_2) = (0, 0)$$

$$\frac{dn_1}{dt} = an_1 + bn_2 + c_1 = 0$$

$$an_1 = -c_1 - bn_2$$

$$\boxed{n_1 = \frac{-c_1 - bn_2}{a}}$$

$$\frac{dn_2}{dt} = cn_1 + dn_2 + c_2 = 0$$

$$c\left(\frac{-c_1 - bn_2}{a}\right) + dn_2 + c_2 = 0$$

$$\frac{-cc_1}{a} - \frac{bcn_2}{a} + dn_2 + c_2 = 0$$

$$\left(-\frac{bc}{a} + d\right) n_2 = -c_2 + \frac{cc_1}{a}$$

$$\boxed{n_2 = \frac{-c_2 + \frac{cc_1}{a}}{-bc/a + d}}$$

Equilibria of linear multivariable models

Three methods:

1. Solve individual equations.
2. **Solve matrix equation.**
3. Nullclines.

$$\frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

$$M\vec{n} = \vec{0}$$

$$M^{-1}M\vec{n} = M^{-1}\vec{0}$$

$$\vec{n} = M^{-1}\vec{0}$$

$$\hat{\vec{n}} = \vec{0}$$

$\boxed{\text{If I can invert } M, \text{ then } \hat{\vec{n}} = \vec{0}}$

$$\frac{d}{dt}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix}\begin{pmatrix} n_1 \\ n_2 \end{pmatrix} + \begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$$

$$M\vec{n} + \vec{c} = 0$$

$$M\vec{n} = -\vec{c}$$

$$M^{-1}M\hat{\vec{n}} = M^{-1}(-\vec{c})$$

$$\boxed{\vec{n} = -M^{-1}\vec{c}}$$

(If I can invert M)

Equilibria of linear multivariable models

n_1, n_2 space

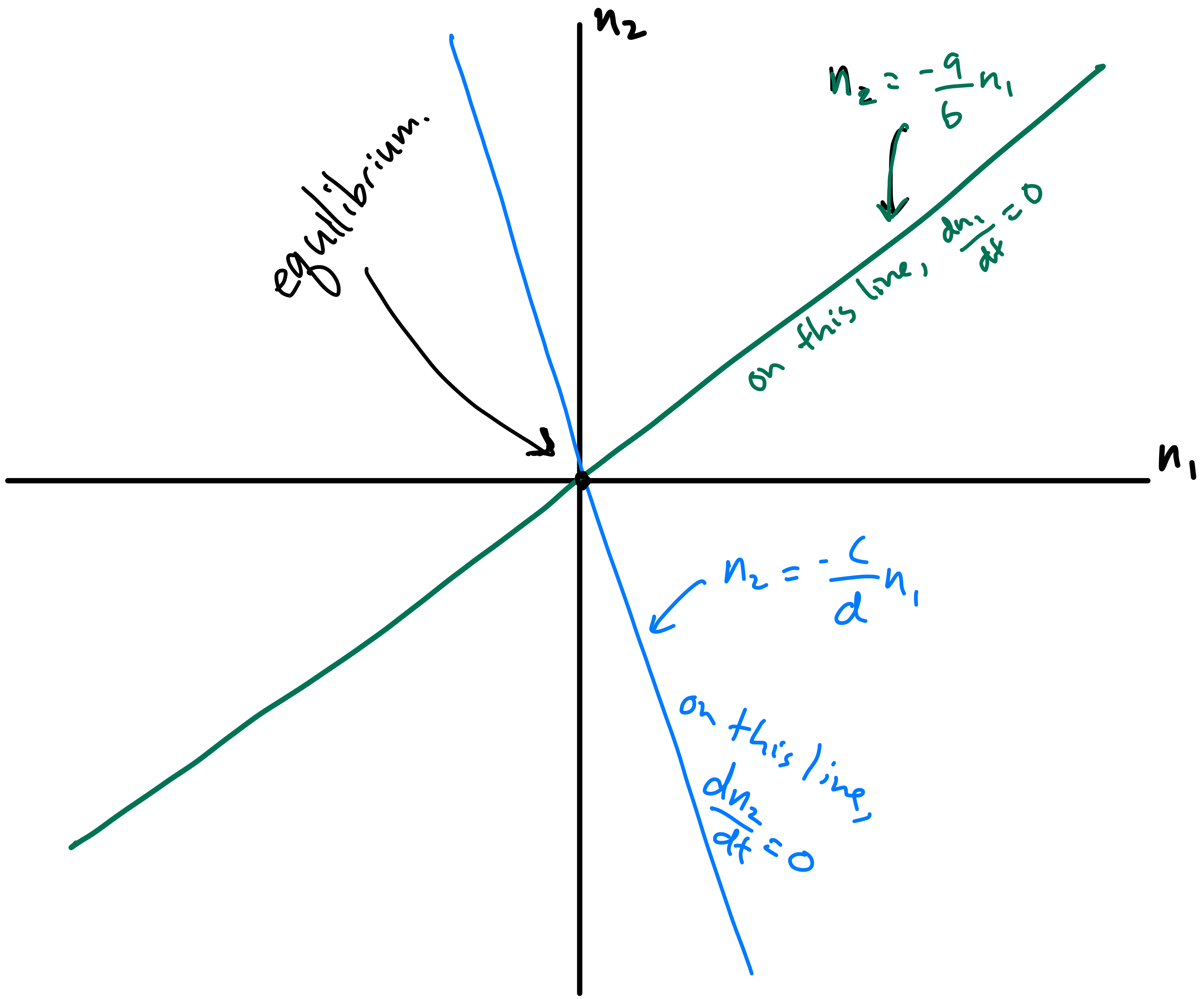
Three methods:

1. Solve individual equations.
2. Solve matrix equation.
3. **Nullclines.**

A **nullcline** is a line in phase space on which one of the variables is constant (unchanging).

$$\frac{dn_1}{dt} = an_1 + bn_2 = 0 \qquad n_2 = \frac{-a}{b} n_1$$

$$\frac{dn_2}{dt} = cn_1 + dn_2 = 0 \qquad n_2 = \frac{-c}{d} n_1$$



Equilibria of linear multivariable models

Three methods:

1. Solve individual equations.
2. Solve matrix equation.
3. **Nullclines.**

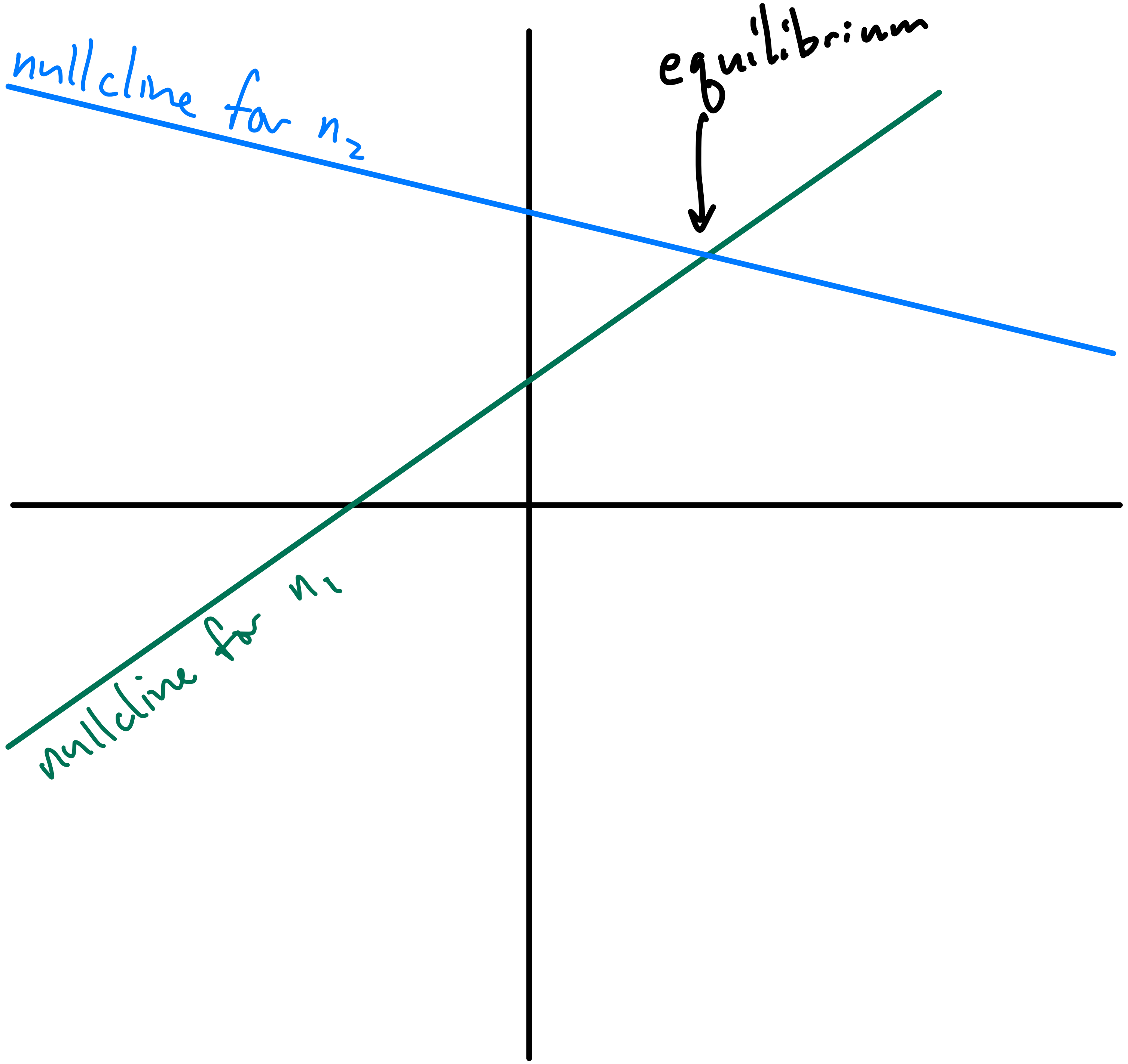
A **nullcline** is a line in phase space on which one of the variables is constant (unchanging).

$$\frac{dn_1}{dt} = an_1 + bn_2 + c_1 \qquad n_2 = -\frac{a}{b}n_1 - \frac{c_1}{b}$$

$$\frac{dn_2}{dt} = cn_1 + dn_2 + c_2 \qquad n_2 = -\frac{c}{d}n_1 - \frac{c_2}{d}$$

(affine)

$$y = mx + b$$



Equilibria of linear multivariable models

Rule: A linear or affine model in continuous time has only one equilibrium regardless of the number of variables, provided that the determinant of M is not zero.

↳ equivalent: M is invertible.

- If $\frac{d\vec{n}}{dt} = M\vec{n}$ then $\boxed{\hat{\vec{n}} = 0}$

see prev slides

- If $\frac{d\vec{n}}{dt} = M\vec{n} + \vec{c}$ then $\boxed{\hat{\vec{n}} = -M^{-1}\vec{c}}$

Is an affine model a type of linear model?

- A linear model is affine
- An affine model is only linear if $\vec{c} = \vec{0}$

If $\det(M) = 0$, there are an *infinite* number of equilibria.

Stability of Equilibria

Recall that a system grows or decays in the direction of an eigenvector at a rate given by its eigenvalue.

Rule: a system is unstable if it will move away from the equilibrium in at least one direction.

e^{4t}

Because moving away = positive eigenvalue, this leads us to conclude:

Stability of equilibria (real eigenvalues):

equilibrium

- If all eigenvalues are negative, the system is stable.
- If one or more eigenvalues are positive, the system is unstable.

e^{-t} e^{-3t}

as $t \to \infty$ $e^{-t} \to 0$ $e^{-3t} \to 0$

positive eigenvalues

$$A = \begin{pmatrix} 2 & 3 \\ 2 & 1 \end{pmatrix} \xrightarrow{\text{prev. slides}} \lambda_1 = 4, \quad \lambda_2 = -1$$

$\dot{n} = An$

$\dot{n} = \vec{0}$, and it is

a) stable

$\boxed{\text{b) unstable.}}$

Stability of Equilibria

book calls λ "r"

Stability of equilibria (real eigenvalues):

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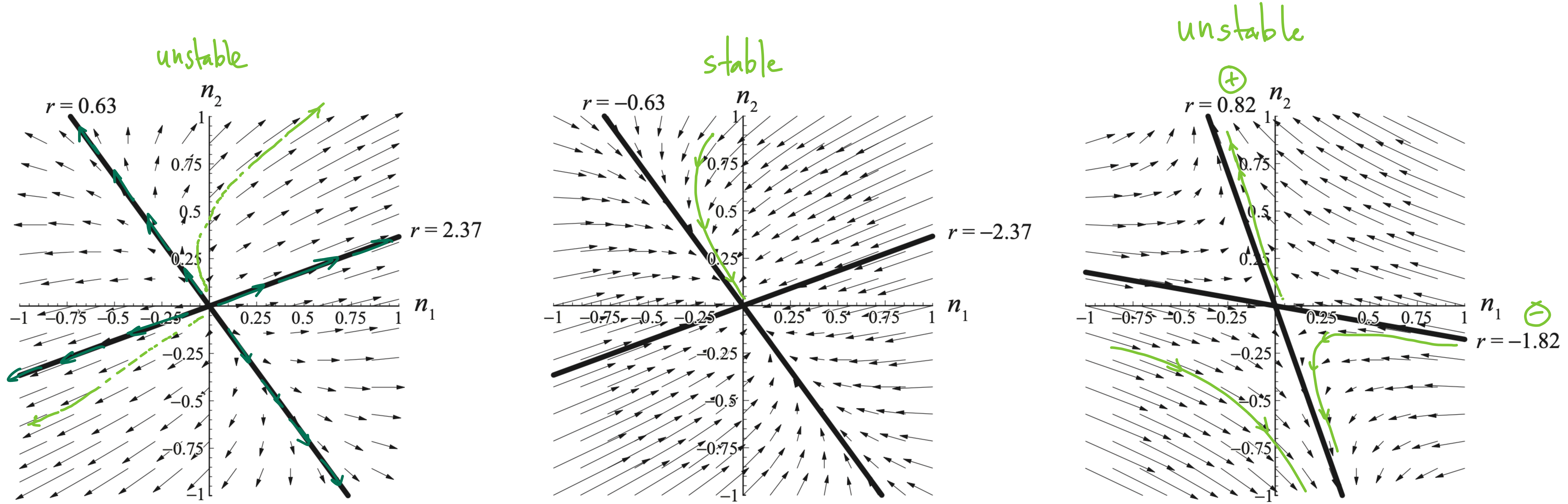
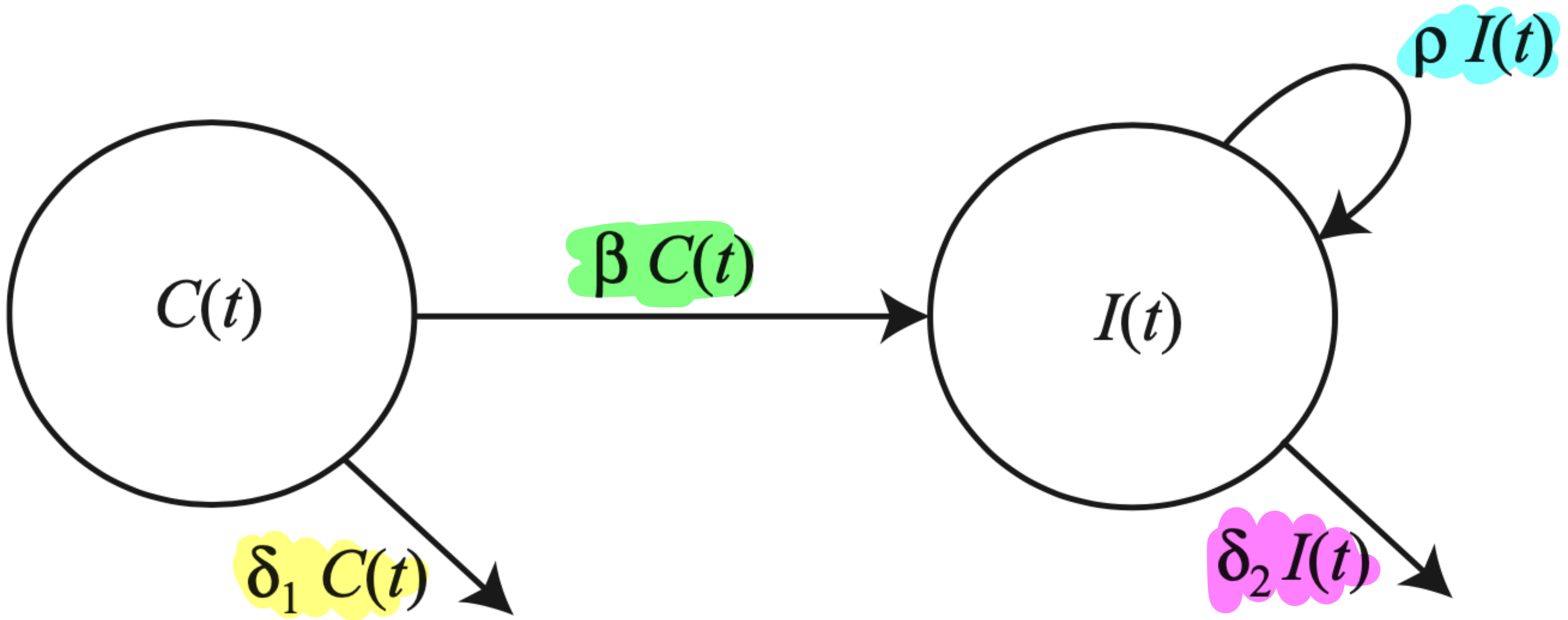


Metastasis of Malignant Tumors

A model for the dynamics of the number of cancer cells lodged in the capillaries of an organ, C, and the number of cancer cells that have actually invaded that organ, I.

Suppose that cells are lost from the capillaries by dislodgement or death at a per capita rate δ_1 and that they invade the organ from the capillaries at a per capita rate β. Once cells are in the organ they die at a per capita rate δ_2, and the cancer cells replicate at a per capita rate ρ.



$$\frac{dC}{dt} = -\delta_1 C - \beta C$$

$$\frac{dI}{dt} = \beta C + \rho I - \delta_2 I$$

Otto & Day — Adapted from Glass & Kaplan 1995

Metastasis of Malignant Tumors

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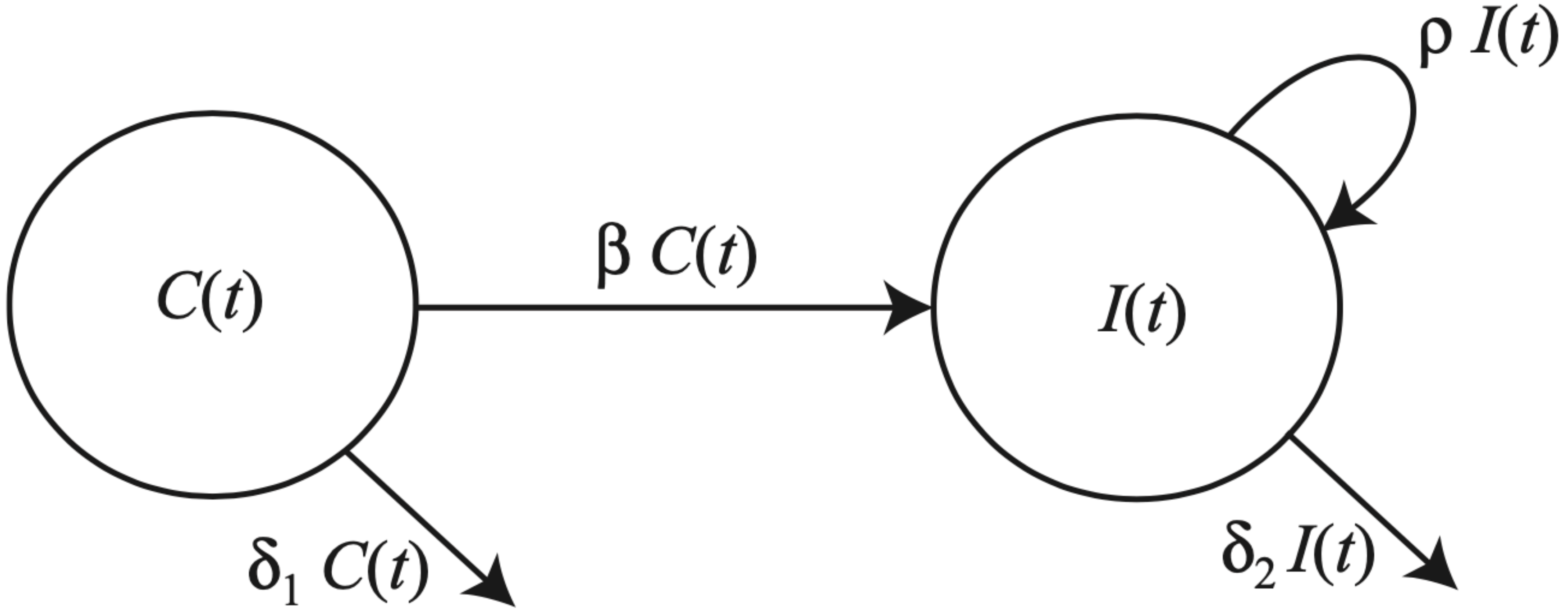

$$\frac{dC}{dt} = \delta_1 C - \beta C$$

$$\frac{dI}{dt} = \beta C - \delta_2 I + \rho I$$

matrix/vector notation

$$\begin{pmatrix} \frac{dC}{dt} \\ \frac{dI}{dt} \end{pmatrix} = M \begin{pmatrix} C \\ I \end{pmatrix} \qquad M = \begin{pmatrix} -(\delta_1 + \beta) & 0 \\ \beta & \rho - \delta_2 \end{pmatrix}$$

matrix is driving the dynamics!

Metastasis of Malignant Tumors

$$\begin{pmatrix} \frac{dC}{dt} \\ \frac{dI}{dt} \end{pmatrix} = M \begin{pmatrix} C \\ I \end{pmatrix} \qquad M = \begin{pmatrix} -(\delta_1 + \beta) & 0 \\ \beta & \rho - \delta_2 \end{pmatrix}$$

Suppose that cells are lost from the capillaries by dislodgement or death at a per capita rate δ_1 and that they invade the organ from the capillaries at a per capita rate β. Once cells are in the organ they die at a per capita rate δ_2, and the cancer cells replicate at a per capita rate ρ.

1. Identify the equilibrium or equilibria.
2. Determine the stability.

① If M^{-1} exists, then equilibrium at $\begin{pmatrix} C \\ I \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$

↓

If det(M) is not zero. $\det(M) = -(\delta_1 + \beta)(\rho - \delta_2) - 0$

All the coeffs are positive (in the text — none can be negative)

So det(M) can $= 0$ only if $(\rho - d_2) = 0 \rightarrow \rho = \delta_2$

Conclusion: Equilibrium at $\begin{pmatrix} 0 \\ 0 \end{pmatrix}$ as long as $\rho \neq \delta_2$

② stability depends on eigenvalues.

$$\lambda_1, \lambda_2 = \frac{-tr(A) \pm \sqrt{tr^2(A) - 4\det(A)}}{2}$$

$$\boxed{\begin{aligned} \lambda_1 &= -(\delta_1 + \beta) \\ \lambda_2 &= \rho - \delta_2 \end{aligned}}$$

$\lambda_1 < 0$ always. → cool! what happens in the capillaries doesn't affect stability!

stability if both are negative. $\lambda_2 < 0$ only when $\rho - \delta_2 < 0$ or $\rho < \delta_2$

growth rate < death rate