QUALITATIVE ANALYSIS

Overview

1. Simplified System of ODEs
2. Solution and Analysis Approaches
3. Graphical Analysis: Finding Nullclines and Equilibria
4. Determining Stability Analytically

Qualitative Analysis

Reduction to Two ODEs

Letting

$$\begin{aligned} p &= fk \\ m &= k(k_{-1}+k_2)-k_1 \\ n &= k(k_{-1}+k_3)-k_1 \end{aligned}$$

the new ODE system becomes

$$\frac{dE}{dt} = \underline{\hspace{8cm}} \quad (1)$$

$$\frac{dT}{dt} = \underline{\hspace{8cm}} \quad (2)$$

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Solution and Analysis Approaches

Question: What is the next step?

Answer: We want to “solve” this system. There are three main approaches to understanding the solutions of a system of ODEs:

1. Find the ______________________________ (1)
2. Do a ______________________________ (2)
3. Find a ______________________________ (3)

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Finding Nullclines

Step 1: Find nullclines algebraically.

1. Set

$$\frac{dE}{dt} = \underline{\hspace{3cm}} \quad (1)$$

$$\frac{dT}{dt} = \underline{\hspace{3cm}} \quad (2)$$

continue ⇒

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Finding Nullclines (continued)

2. Solve for E-nullcline:

$$E = \underline{\hspace{8cm}} \quad (3)$$

3. Solve for T-nullcline:

$$E = \underline{\hspace{8cm}} \quad (4)$$

$$\text{or} \quad T = \underline{\hspace{2cm}} \quad (5)$$

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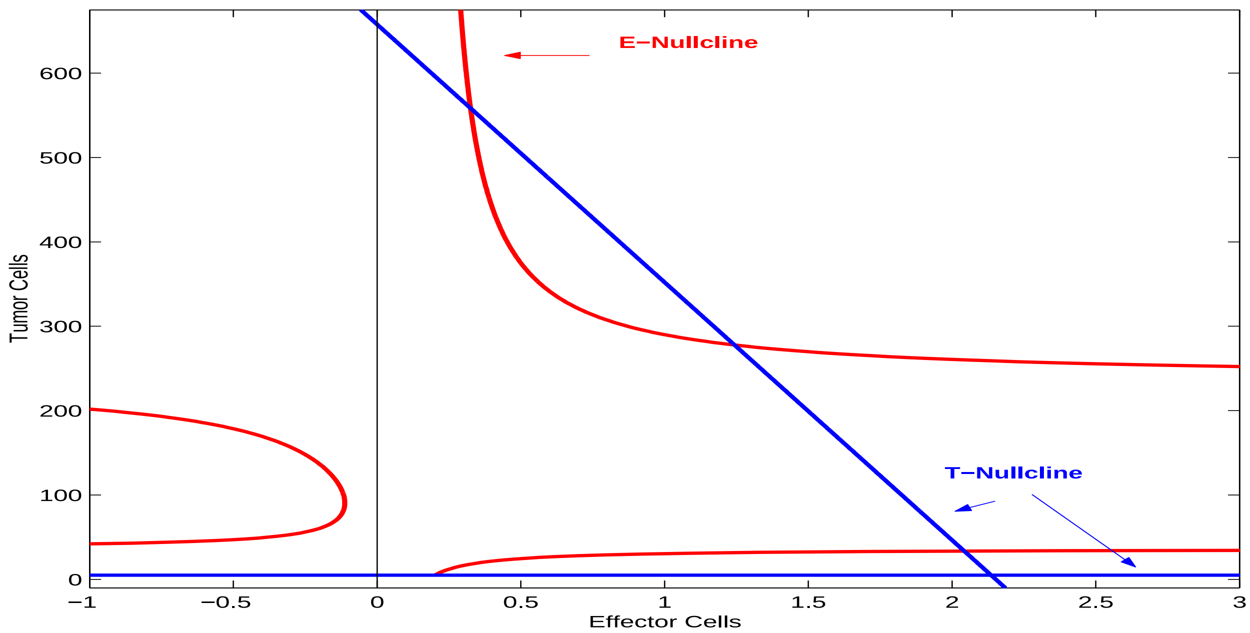
Finding Equilibria

Step 2: Find ______________________ (1) graphically.



Step 3: Determine the ____ (2) graphically.

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Summary of Graphical Analysis

From our *graphical* analysis of the equilibria we can conclude that **for the particular parameter set** used in the example:

- Point A (tumor-free) is an ____________________(1).
- Point B (low tumor burden) may be a ________________(2) or a ________________(3), and may be ________________(4) or ________________(5), in which case nearby points might converge to a ________________(6).
- Point C (non-zero tumor burden) is ________________(7) (and may be a ________________(8)).
- Point D (high tumor burden) is ________________(9).

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Analytic Determination of Stability

General Procedure

Step 1: Specify an ____________________$_{(1)}$ point to analyze. Call it (x_0, y_0).

Step 2: ____________________$_{(2)}$ the system about the equilibrium point by evaluating the Jacobian at that point.

Step 3: Find the ____________________$_{(3)}$ of the Jacobian to determine the stability properties of point (x_0, y_0).

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The Stability of a Nearly Linear System

Theorem: from Borrelli and Coleman [BC98] Suppose that $\mathbf{J}$ is an $n \times n$ matrix of real constants. Furthermore, suppose $\vec{\mathbf{P}}(\vec{\mathbf{x}})$ is a vector-valued function that is continuously differentiable in an open ball $B_r(\vec{\mathbf{p}})$, that $\vec{\mathbf{P}}(\vec{\mathbf{p}}) = 0$, and that $\vec{\mathbf{P}}(\vec{\mathbf{x}})$ has order at least 2 at $\vec{\mathbf{p}}$. Then the *nearly linear* system:

$$\frac{d\vec{\mathbf{x}}}{dt} = \mathbf{J}(\vec{\mathbf{x}} - \vec{\mathbf{p}}) + \vec{\mathbf{P}}(\vec{\mathbf{x}})$$

has the following properties:

1. The system is **asymptotically stable** at $\vec{\mathbf{p}}$ if all eigenvalues of $\mathbf{J}$ have negative real parts.

2. The system is **unstable** at $\vec{\mathbf{p}}$ if there is at least one eigenvalue of $\mathbf{J}$ with positive real part.

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The Stability of a Nearly Linear System (continued)

Note: The matrix, $\mathbf{J}$, is the ____________________ $_{(1)}$ of the nonlinear system, evaluated at the ____________________ $_{(2)}$ $\vec{\mathbf{p}}$.

Unfortunately, this theorem doesn't tell us anything about the equilibrium if all of the eigenvalues of $\mathbf{J}$ have real part ____________________ $_{(3)}$, but at least one of them has real part ______________________________ $_{(4)}$.

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Analytic Determination of Stability: General Example

Example: Given the ODE system

$$\begin{aligned} \frac{dx}{dt} &= F_1(x,y) \\ \frac{dy}{dt} &= F_2(x,y) \end{aligned}$$

the linearized system at a point (x_0, y_0) is

$$\begin{bmatrix} \frac{dx}{dt} \\ \frac{dy}{dt} \end{bmatrix} = \mathbf{J} \begin{bmatrix} x \\ y \end{bmatrix}, \quad \text{or with vector notation: } \dot{\vec{\mathbf{x}}} = \mathbf{J}\vec{\mathbf{x}}$$

where $\mathbf{J}$ is the Jacobian of the system evaluated at (x_0, y_0). continued ⇒

Qualitative Analysis

Analytic Determination of Stability: General Example (continued)

The Jacobian matrix $\mathbf{J}$ is given by

$$\mathbf{J} = \begin{bmatrix} \underline{\hspace{6cm}}(1) & \underline{\hspace{6cm}}(2) \\ & \\ \underline{\hspace{6cm}}(3) & \underline{\hspace{6cm}}(4) \end{bmatrix}$$

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Example: Jacobian for Point A

- Plug $T = 0$ into E-nullcline equation $\Rightarrow E = s/d$. Therefore, $(x_0, y_0) = (s/d, 0)$.
- Determine the Jacobian.

$$\mathbf{J} = \begin{bmatrix} \rule{4cm}{0.4pt}(1) & \rule{4cm}{0.4pt}(2) \\ \\ \rule{4cm}{0.4pt}(3) & \rule{4cm}{0.4pt}(4) \end{bmatrix}$$

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Example: Eigenvalues of Jacobian for Point A

Because $\mathbf{J}$ is a ____________________(1) matrix, the eigenvalues are on the ____________________(2). Therefore, eigenvalues λ_1 and λ_2 are

$$\lambda_1 = \underline{\hspace{4cm}}_{(3)}$$
$$\lambda_2 = \underline{\hspace{4cm}}_{(4)}$$

Note:

- λ_1 is always ____________________(5).
- λ_2 is ____________________(6) if and only if ____________________(7)