Introducción a los Sistemas Dinámicos y Aplicaciones en Medicina

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Hecho en Power Point

Índice

1.1 Introducción

$$\dot{x} = f(x)$$

$$e.g. \quad \dot{x} = cos(x)$$

$\dot{x} = f(x)$ e.g. $\dot{x} = cos(x)$

$\dot{x} = f(x, a_1, a_2, a_3 \dots)$ e.g. $\dot{x} = kx$

$\dot{x} = f(x)$ *e.g.* $\dot{x} = cos(x)$

$\dot{x} = f(x, a_1, a_2, a_3 \dots)$ *e.g.* $\dot{x} = kx$

$$\begin{cases} \dot{x}_1 = f_1(x_1, x_2, x_3, \dots, a_1, a_2, a_3, \dots) \\ \dot{x}_2 = f_2(x_1, x_2, x_3, \dots, a_1, a_2, a_3, \dots) \\ \dot{x}_3 = f_3(x_1, x_2, x_3, \dots, a_1, a_2, a_3, \dots) \\ \quad\quad\quad\quad . \\ \quad\quad\quad\quad . \\ \quad\quad\quad\quad . \end{cases}$$

e.g. $$\begin{cases} \dot{u} = f(u, v) + D_u \Delta u \\ \dot{v} = g(u, v) + D_v \Delta v \end{cases}$$

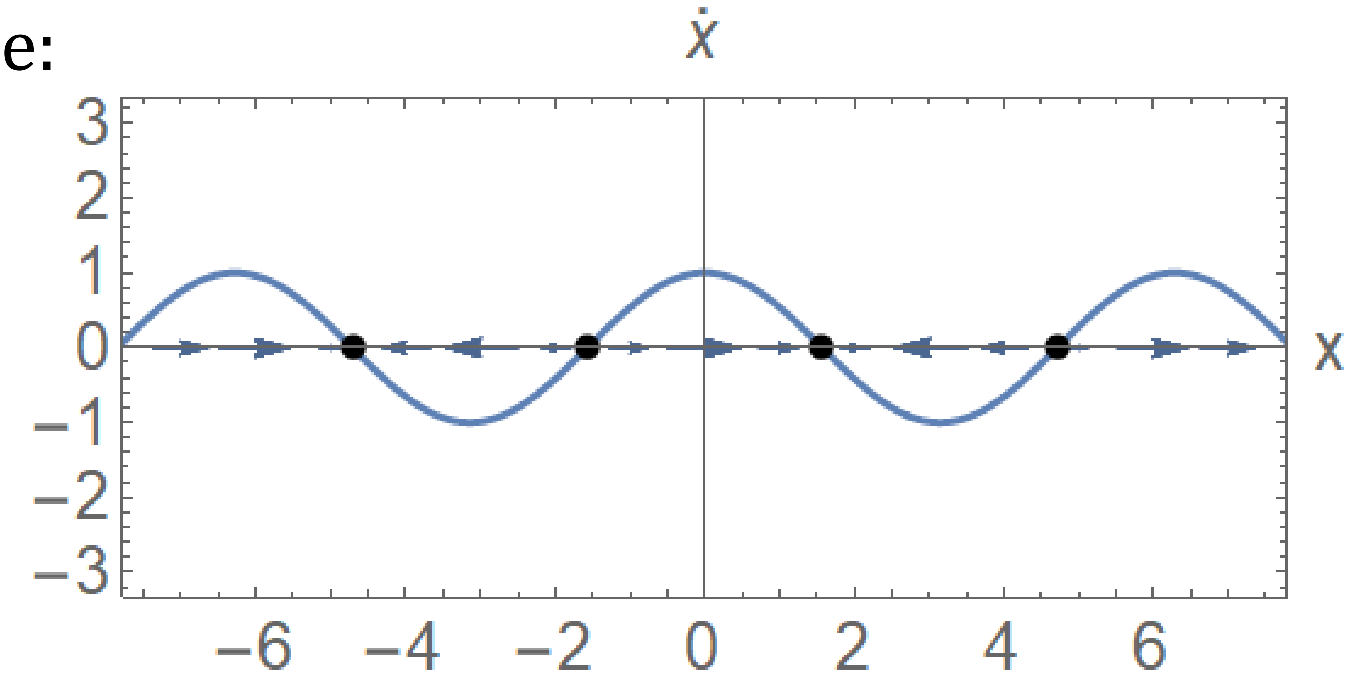
1.1 Introducción

$\dot{x} = cos(x)$

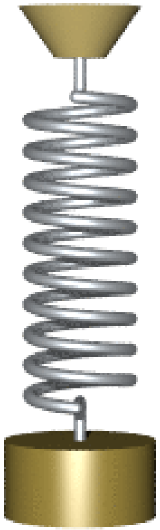
- Puntos fijos: $\dot{x} = 0 \rightarrow x(t) = \left(\frac{1}{2} + n\right)\pi \quad n \in \mathbb{Z}$

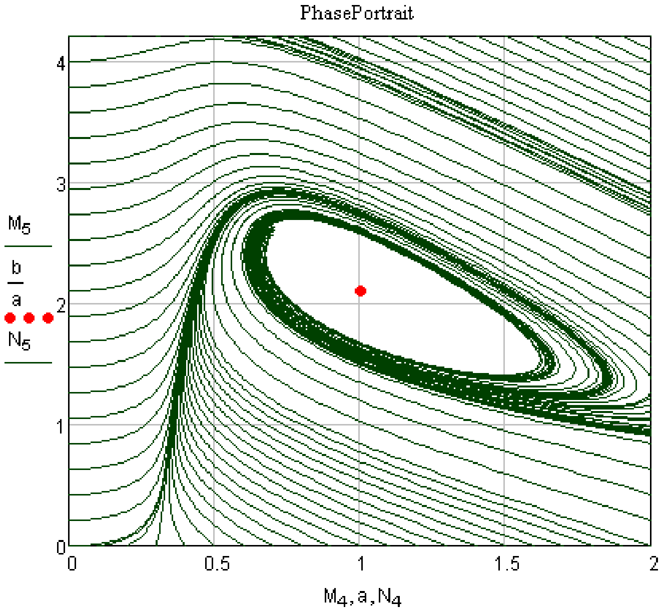
$\dot{x} = cos(x)$

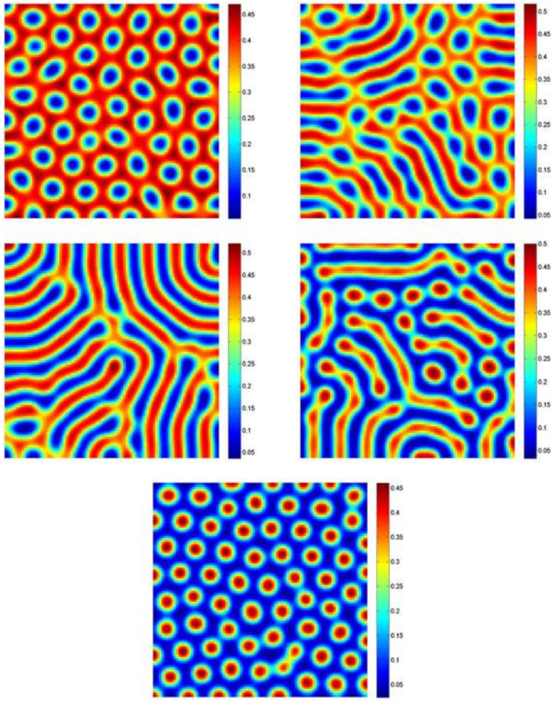
- Puntos fijos: $\dot{x} = 0 \rightarrow x(t) = \left(\frac{1}{2} + n\right)\pi \quad n \in \mathbb{Z}$
- Espacio de fase:



$$\begin{cases} \dot{x} = f_x(x, y, a_1, a_2, a_3, \dots) \\ \dot{y} = f_y(x, y, a_1, a_2, a_3, \dots) \end{cases}$$







1.2.1 Sistemas lineales

$$\begin{cases} \dot{x} = ax + by \\ \dot{y} = cx + dy \end{cases} \rightarrow \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix}$$

1.2.1 Sistemas lineales

$$\begin{cases} \dot{x} = ax + by \\ \dot{y} = cx + dy \end{cases} \rightarrow \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} a & b \\ c & d \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix}$$

$$\begin{pmatrix} x(t) \\ y(t) \end{pmatrix} = C_1 e^{\lambda_1 t} \vec{v}_{\lambda_1} + C_2 e^{\lambda_2 t} \vec{v}_{\lambda_2}$$

1.2.1 Sistemas lineales

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = A \begin{pmatrix} x \\ y \end{pmatrix} \qquad A = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$$

$$\begin{cases} \mathrm{Tr(A)} = \tau = a + d \\ \mathrm{Det(A)} = \Delta = ad - bc \end{cases}$$

$$\mathrm{Det}(A - \lambda I) = 0 \rightarrow (a\text{-}\lambda)(\mathrm{d}\text{-}\lambda)\text{-bc} = 0 \rightarrow$$

$$\rightarrow \lambda^2 - (a + d)\lambda + ad - bc = 0$$

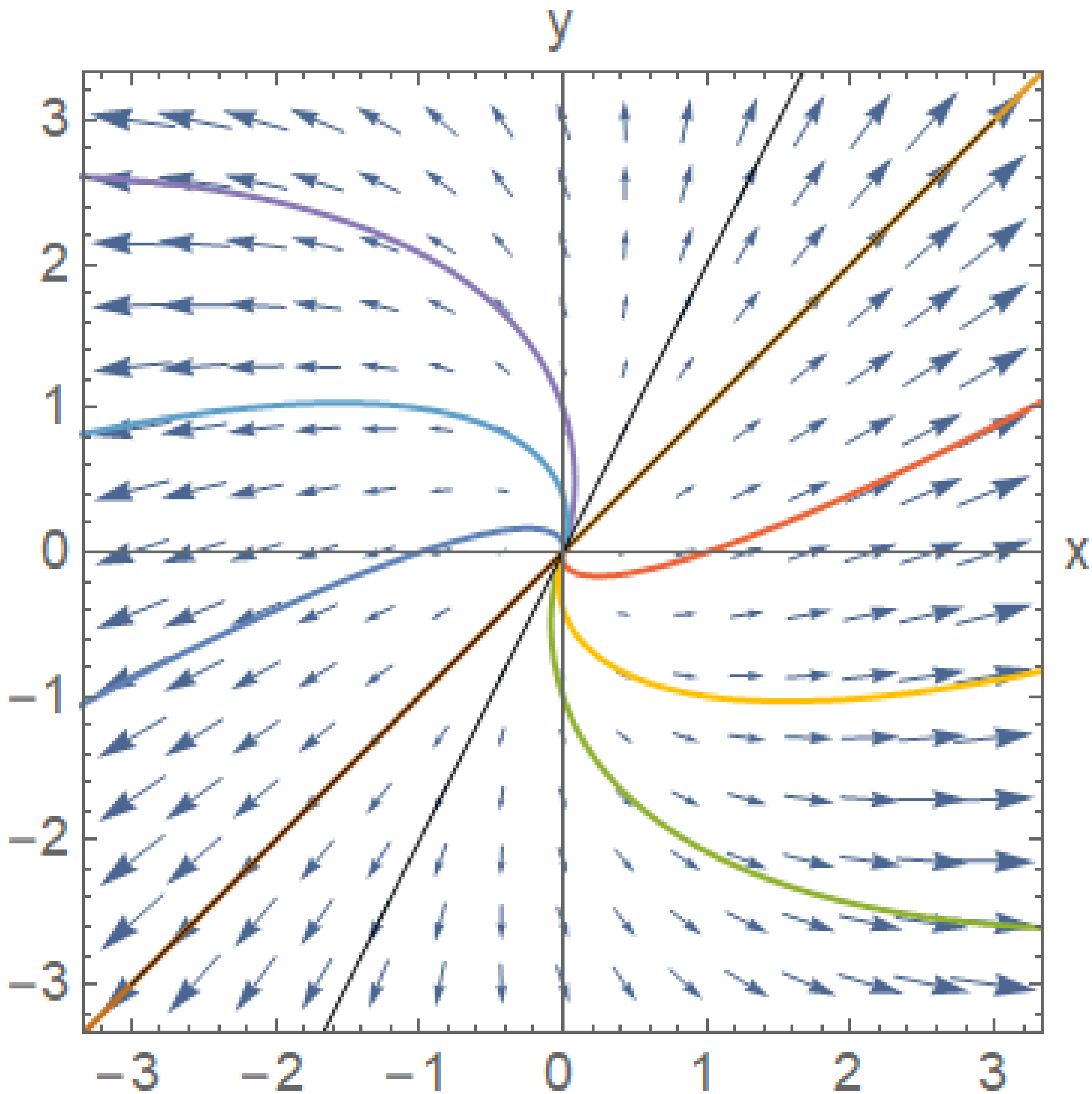
$$\lambda_1 = \frac{1}{2}(\tau + \sqrt{\tau^2 - 4\Delta}) \qquad \lambda_2 = \frac{1}{2}(\tau - \sqrt{\tau^2 - 4\Delta})$$

$\lambda_1, \lambda_2 \in \mathbb{R}$
$\lambda_1 > \lambda_2 > 0$

$e.g.$

$$A = \begin{pmatrix} 6 & -1 \\ 2 & 3 \end{pmatrix}$$

$\lambda_1 = 5$
$\lambda_2 = 4$

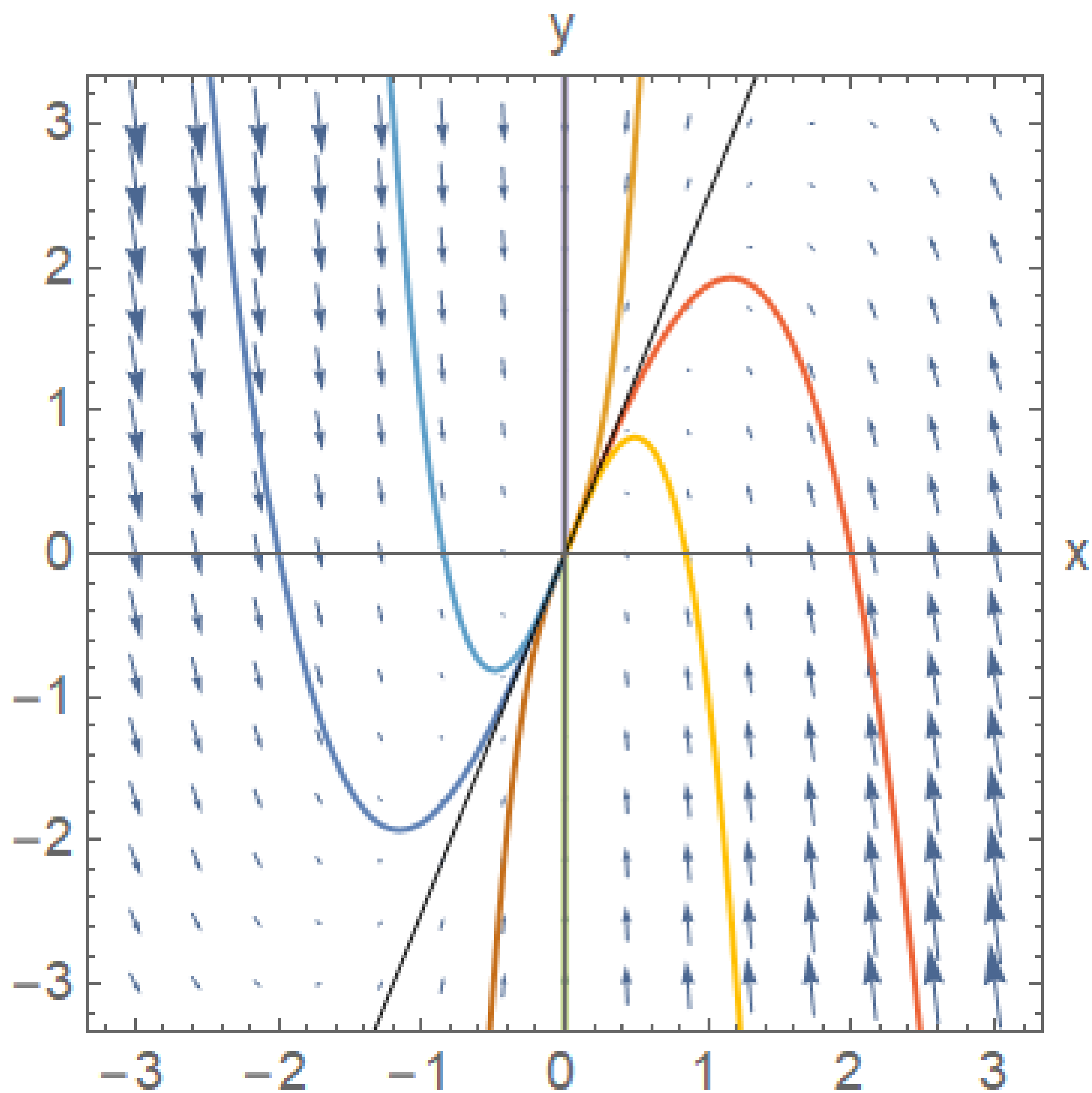


$\lambda_1, \lambda_2 \in \mathbb{R}$
$\lambda_1 < \lambda_2 < 0$

$e.g.$

$$A = \begin{pmatrix} -1 & 0 \\ 5 & -3 \end{pmatrix}$$

$\lambda_1 = -3$
$\lambda_2 = -1$

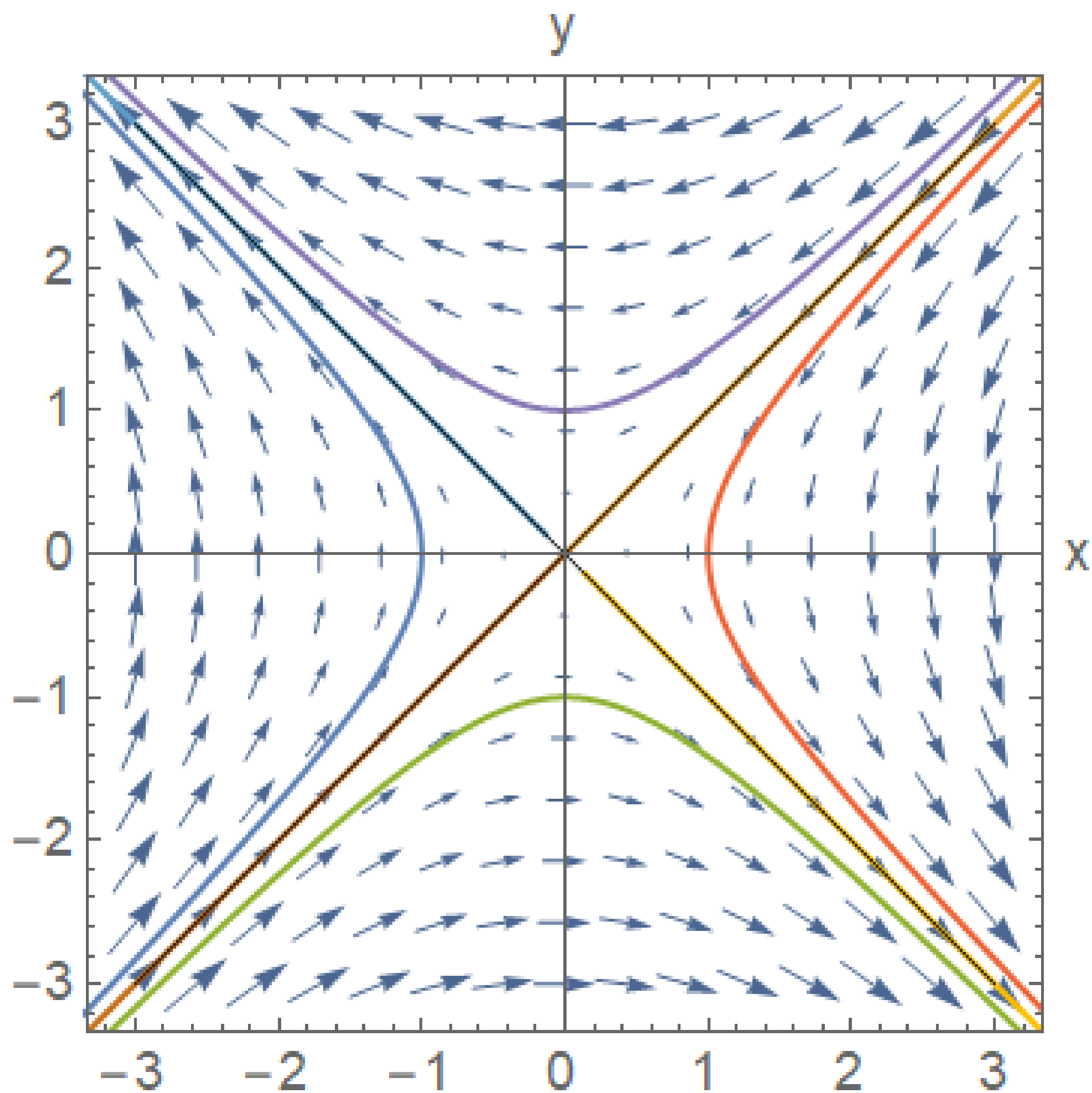


$\lambda_1, \lambda_2 \in \mathbb{R}$
$\lambda_1 > 0 > \lambda_2$

$e.g.$

$$A = \begin{pmatrix} 2 & 0 \\ 0 & -2 \end{pmatrix}$$

$\lambda_1 = 2$
$\lambda_2 = -2$



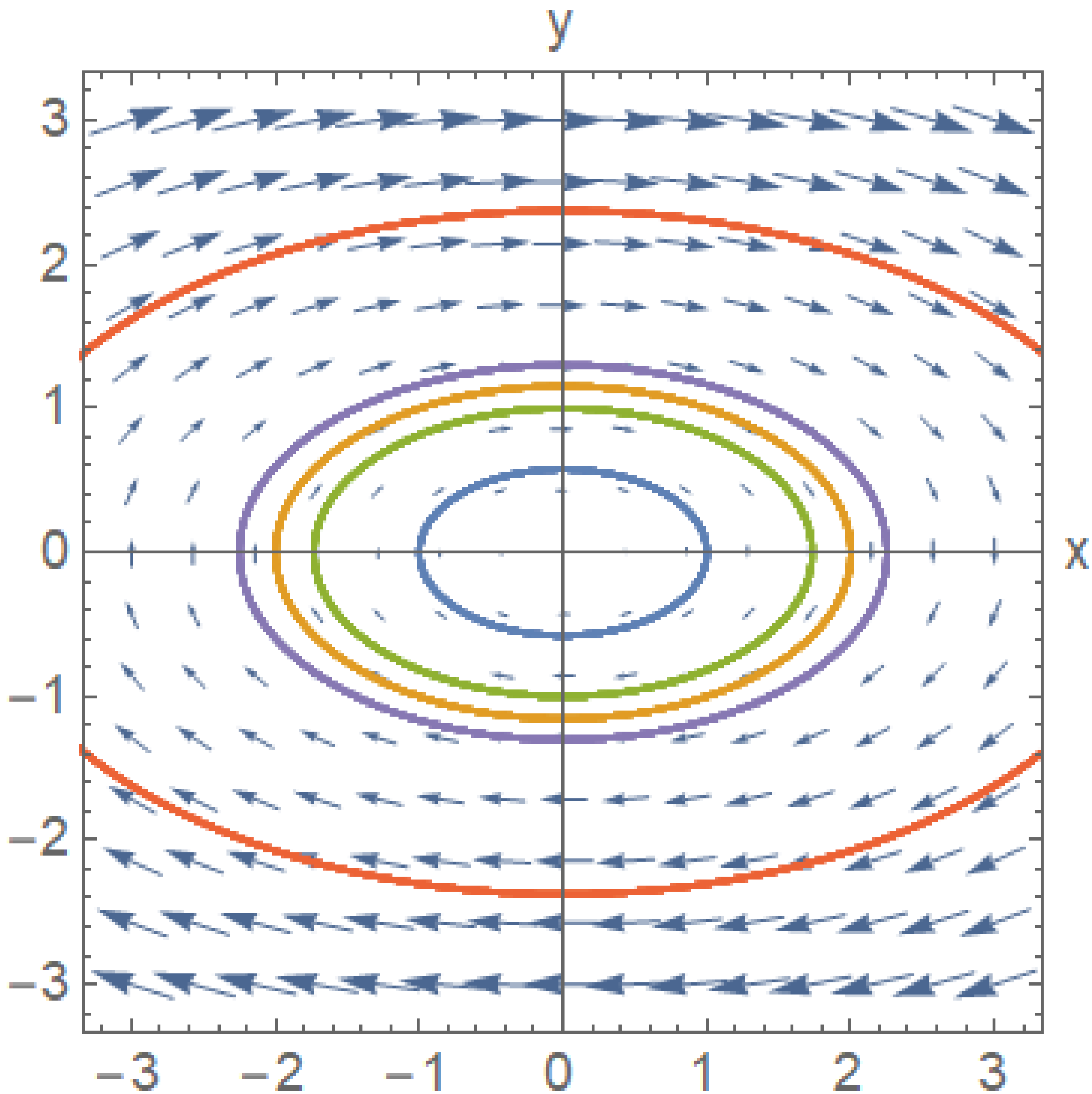
$\lambda_1, \lambda_2 \in \mathbb{C}$
$\lambda_1 = {\lambda_2}^*$
$\lambda_1 = \alpha + i\beta$

$\alpha = 0;\ \beta \neq 0$

$e.g.$

$$A = \begin{pmatrix} 0 & 3 \\ -1 & 0 \end{pmatrix}$$

$\lambda_1 = \sqrt{3}i$
$\lambda_2 = -\sqrt{3}i$



1.2.1 Sistemas lineales

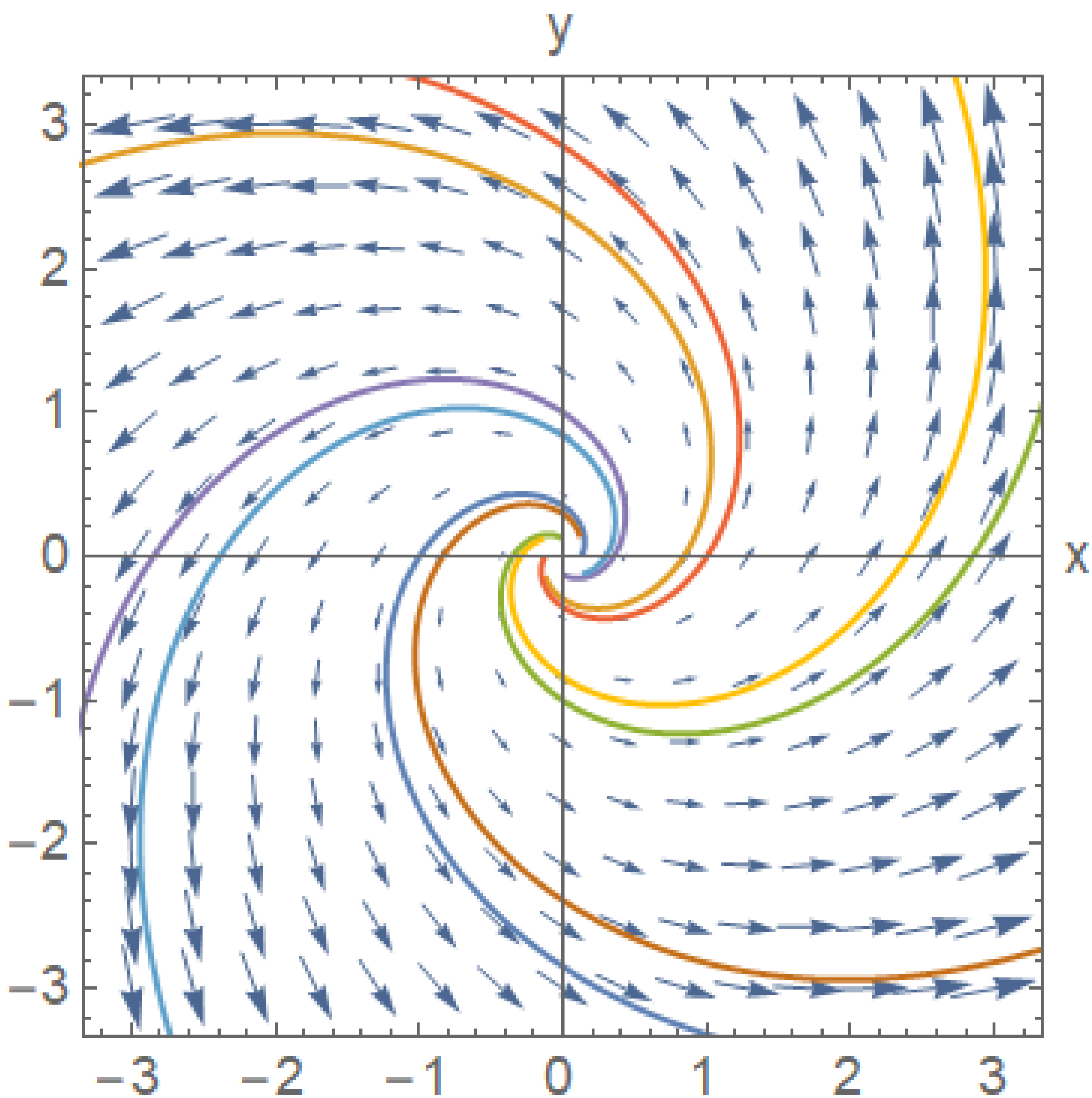
$\lambda_1, \lambda_2 \in \mathbb{C}$
$\lambda_1 = \lambda_2^*$
$\lambda_1 = \alpha + i\beta$

$\alpha > 0;\ \beta \neq 0$

$e.g.$

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

$\lambda_1 = 2 + 3i$
$\lambda_2 = 2 - 3i$



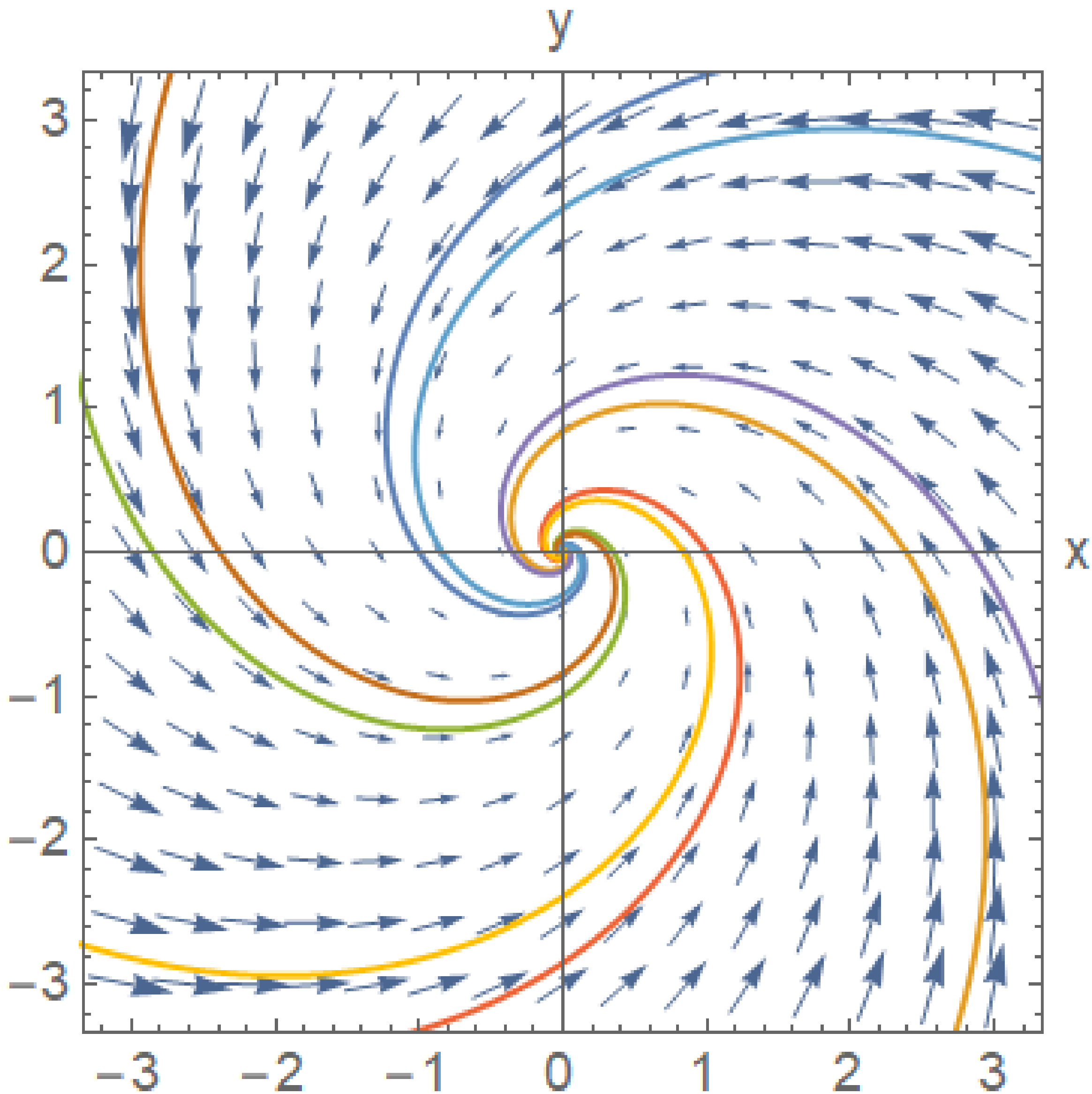
$\lambda_1, \lambda_2 \in \mathbb{C}$
$\lambda_1 = \lambda_2{}^*$
$\lambda_1 = \alpha + i\beta$

$\alpha < 0;\ \beta \neq 0$

$e.g.$

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

$\lambda_1 = -2 + 3i$
$\lambda_2 = -2 - 3i$

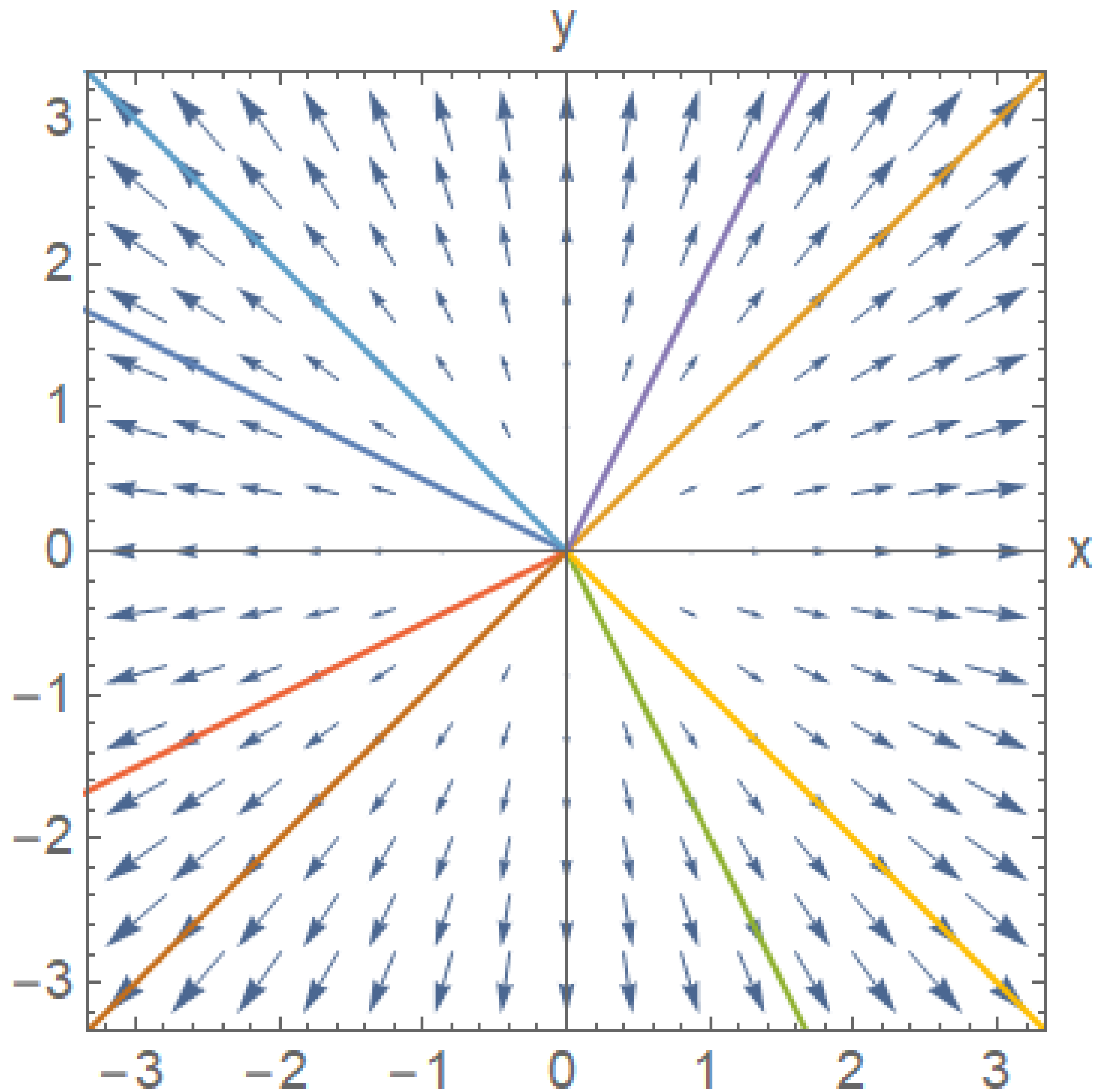


$\lambda_1 = \lambda_2$

$e.g.$

$$A = \begin{pmatrix} 2 & 0 \\ 0 & 2 \end{pmatrix}$$

$\lambda_1 = 2$
$\lambda_2 = 2$



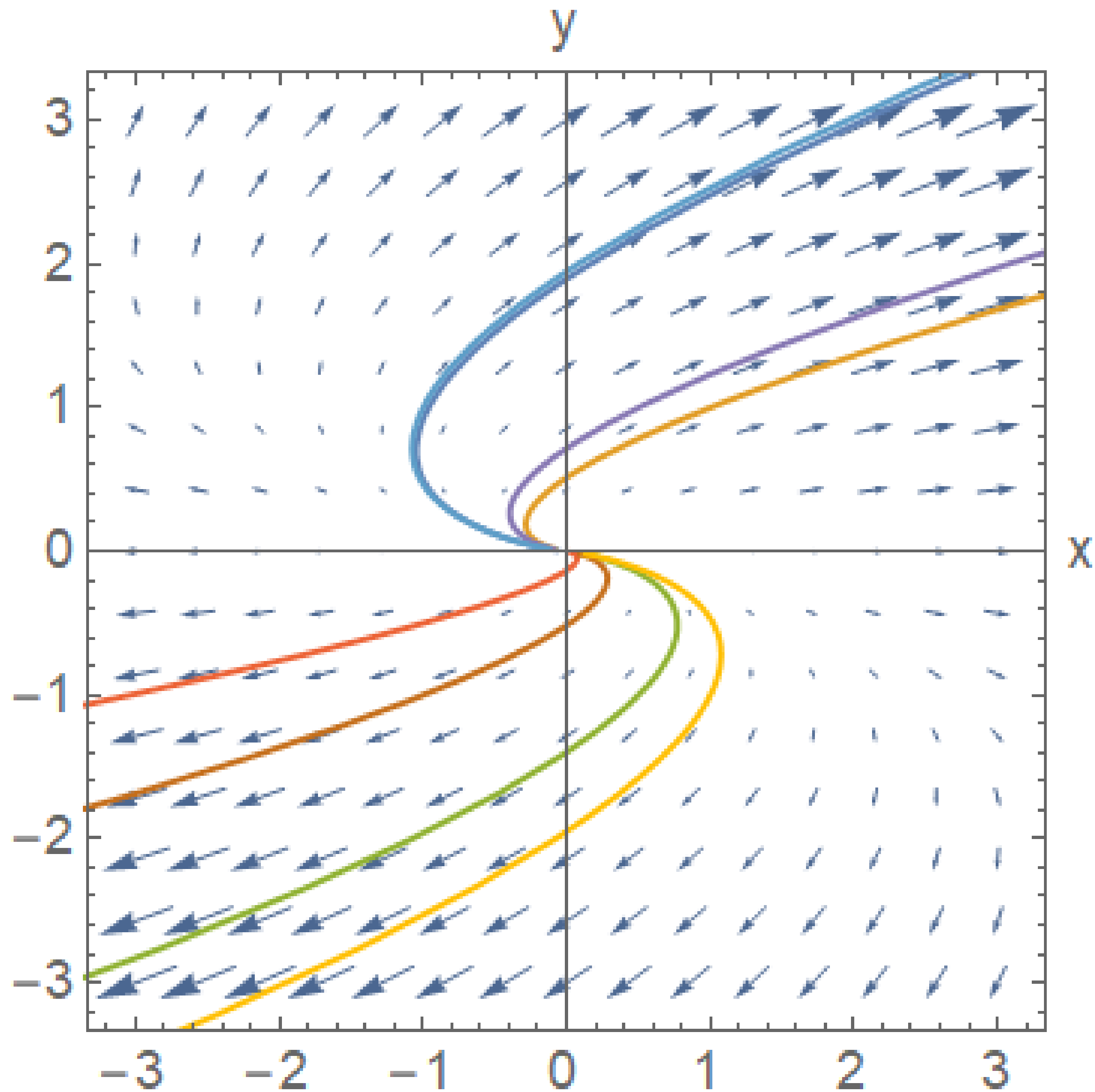
$\lambda_1 = \lambda_2$

$e.g.$

$A = \begin{pmatrix} 2 & 3 \\ 0 & 2 \end{pmatrix}$

$\lambda_1 = 2$
$\lambda_2 = 2$

$\vec{v}_\lambda = (1 \quad 0)$

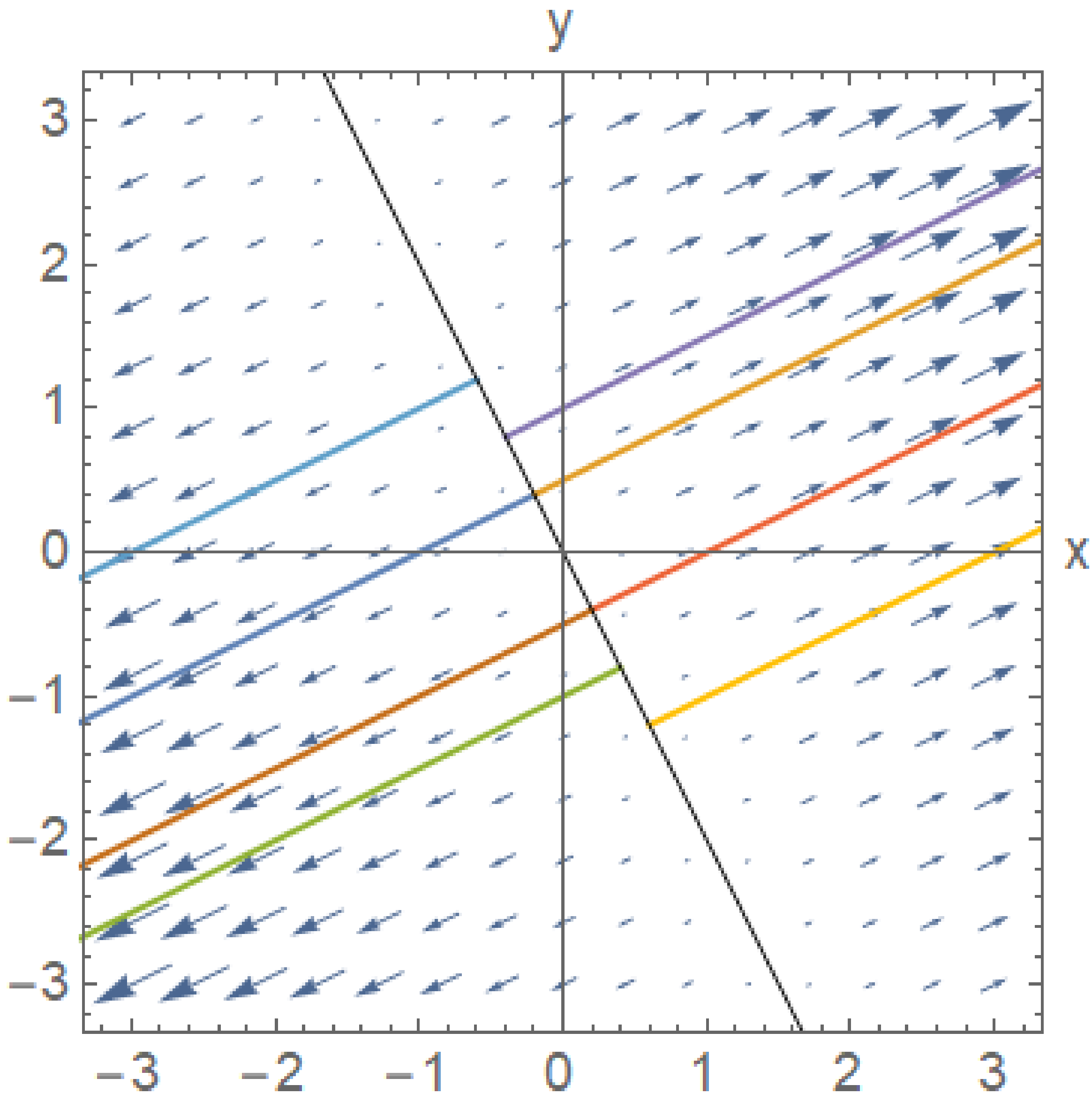


$\mathrm{Det}(A) = 0$

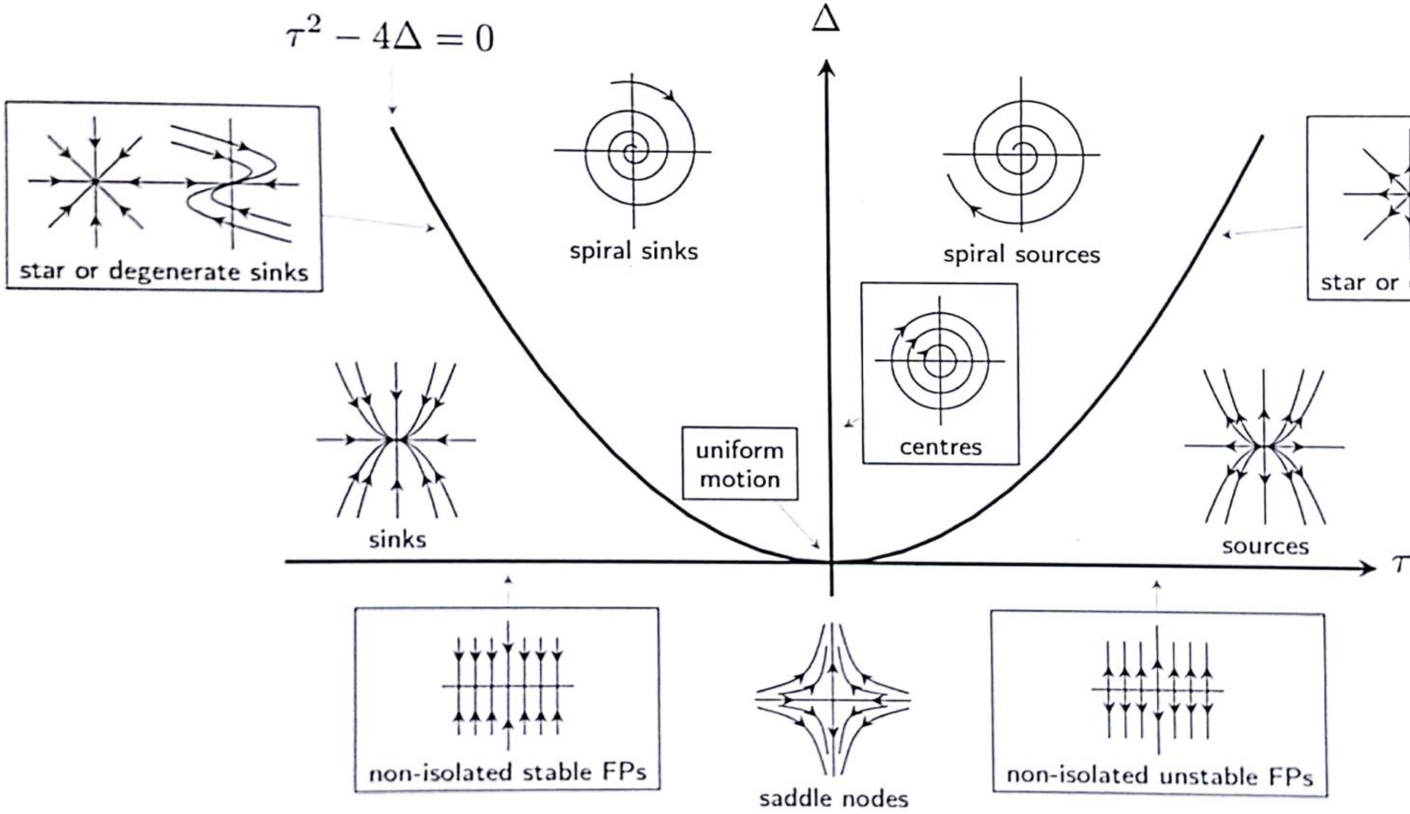
$e.g.$

$A = \begin{pmatrix} 4 & 2 \\ 2 & 1 \end{pmatrix}$

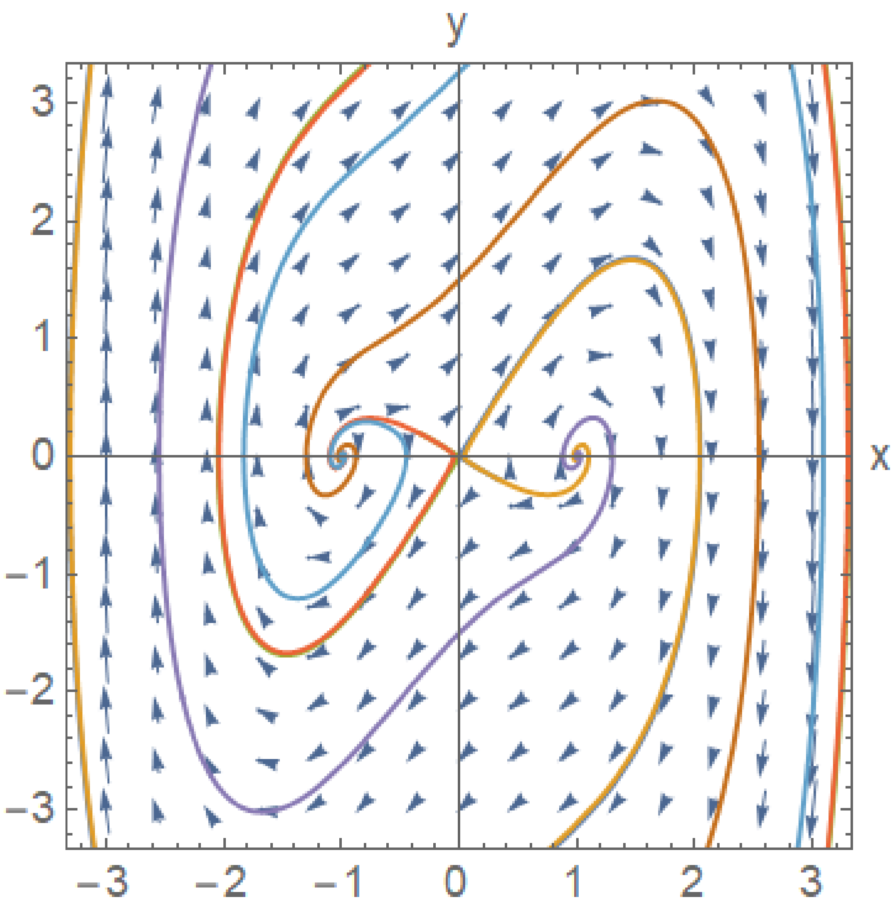
$\lambda_1 = 5$
$\lambda_2 = 0$

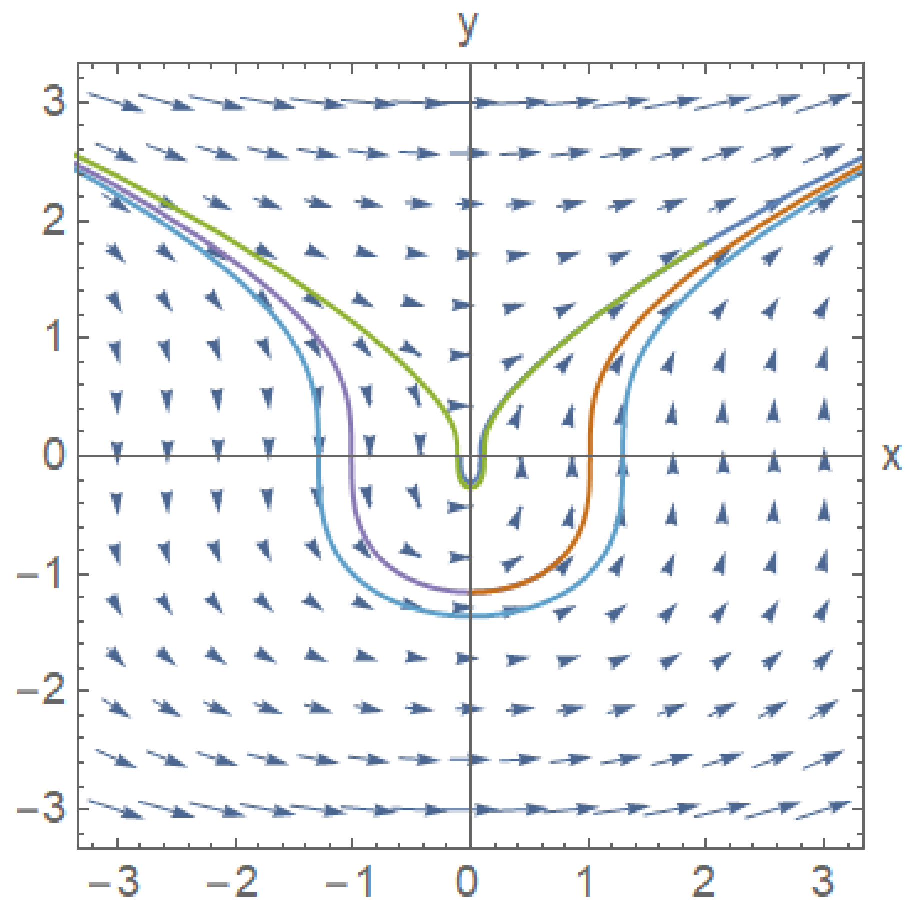


Cheatsheet: Classification of Phase Portaits



1.2.2 Sistemas no lineales





1.2.2 Sistemas no lineales

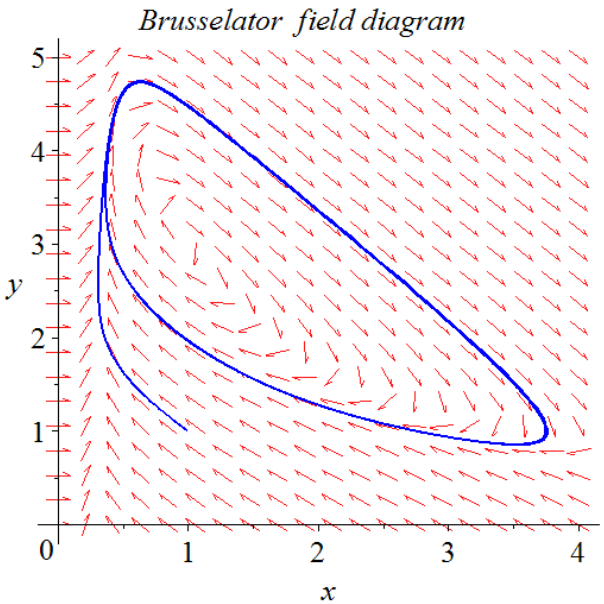
$$\begin{cases} \dot{x} = f_x(x, y, a_1, a_2, a_3, \dots) \\ \dot{y} = f_y(x, y, a_1, a_2, a_3, \dots) \end{cases}$$

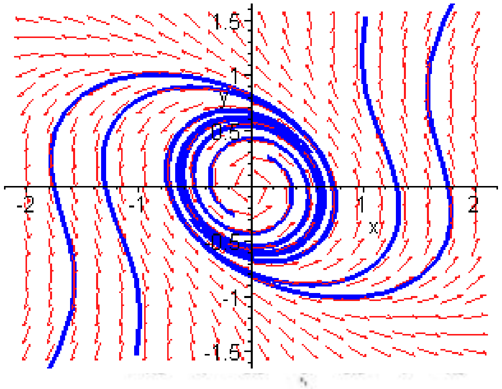
$$\boldsymbol{r}^* = (x^* \quad y^*)$$

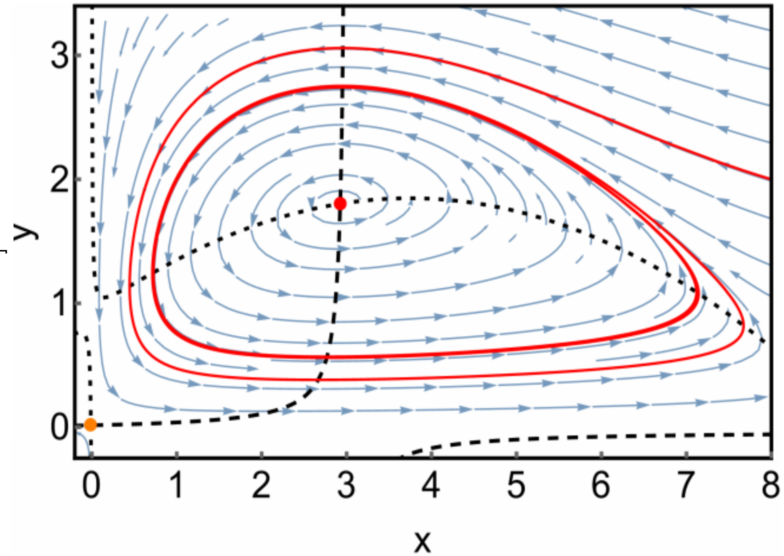
$$\begin{cases} \dot{x} = f_x(x^*, y^*) + x \dfrac{\partial f_x}{\partial x}\Big|_{\boldsymbol{r}^*} + y \dfrac{\partial f_x}{\partial y}\Big|_{\boldsymbol{r}^*} + \Theta(x^2, y^2) \\ \dot{y} = f_y(x^*, y^*) + x \dfrac{\partial f_y}{\partial x}\Big|_{\boldsymbol{r}^*} + y \dfrac{\partial f_y}{\partial y}\Big|_{\boldsymbol{r}^*} + \Theta(x^2, y^2) \end{cases}$$

$$\begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \begin{pmatrix} \dfrac{\partial f_x}{\partial x}\Big|_{\boldsymbol{r}^*} & \dfrac{\partial f_x}{\partial y}\Big|_{\boldsymbol{r}^*} \\ \dfrac{\partial f_y}{\partial x}\Big|_{\boldsymbol{r}^*} & \dfrac{\partial f_y}{\partial y}\Big|_{\boldsymbol{r}^*} \end{pmatrix} \begin{pmatrix} x \\ y \end{pmatrix} \rightarrow \begin{pmatrix} \dot{x} \\ \dot{y} \end{pmatrix} = \mathcal{J} \begin{pmatrix} x \\ y \end{pmatrix}$$

estable	inestable	semiestable







Fuente: Tallin university.
Java kursuse leht

Fuente: Marc Mendler, Johannes Falk, Barbara Drossel.
Analysis of stochastic bifurcations with phase portraits

Fuente: Wikimedia

Teorema de Poincare-Bendixon: Sea R una región finita del plano delimitada por el conjunto de curvas simples cerradas $(D_1, D_2, \ldots)$. Sea **F** el campo vectorial velocidad asociado a un sistema dinámico. De verificarse:

i) En cada punto de $(D_1, D_2, \ldots)$ **F** apunta al interior de R

ii) R no contiene puntos fijos del sistema

Entonces el sistema dinámico contiene una trayectoria cerrada en R

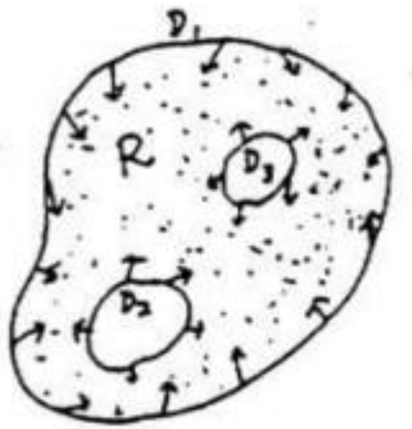


fig. 1

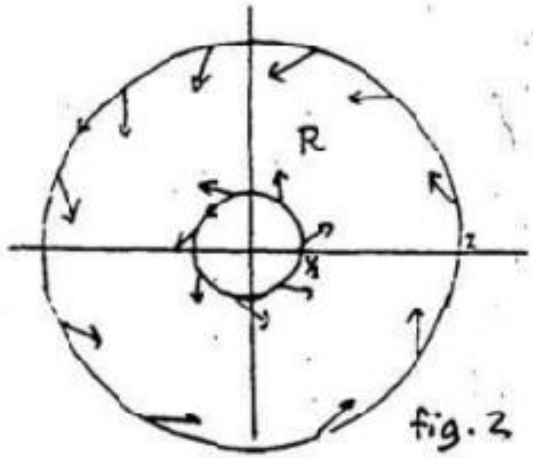


fig. 2

Imágenes tomadas de: Haynes Miller, Ordinary Differential Equations. https://math.mit.edu/~jorloff/suppnotes/suppnotes03/lc.pdf

1.2.2 Sistemas no lineales

Criterio de Bendixon: Sean $\dot{x} = P(x, y),\ \dot{y} = Q(x, y)$ el campo vectorial velocidad de un sistema dinámico. Si en un dominio simplemente conexo G la expresión $\frac{\partial P}{\partial x} + \frac{\partial Q}{\partial y}$ tiene un signo constante (pudiendo anularse sobre una curva o sobre puntos aislados), entonces el sistema no tiene trayectorias cerradas sobre el dominio G

$$A = \begin{pmatrix} a & b \\ c & d \end{pmatrix}$$

$$\begin{cases} \mathrm{Tr(A)} = \tau = a + d \\ \mathrm{Det(A)} = \Delta = ad - bc \end{cases}$$

$$\lambda_{1,2} = \frac{1}{2}\left(\tau \pm \sqrt{\tau^2 - 4\Delta}\right)$$

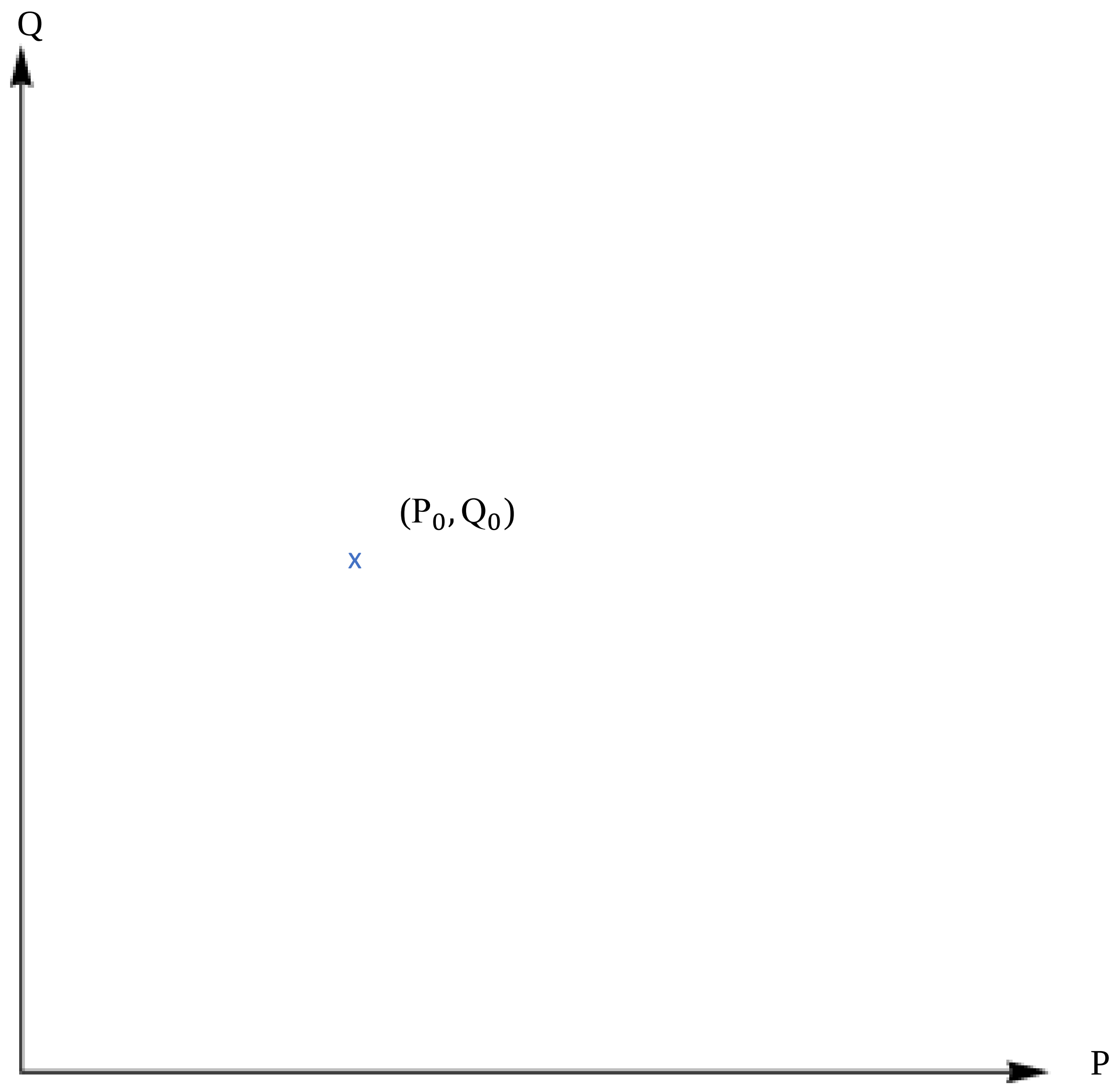
Teorema: $bc > 0 \;\rightarrow \lambda_1, \lambda_2 \in \mathbb{R}$

Modelo de crecimiento tumoral

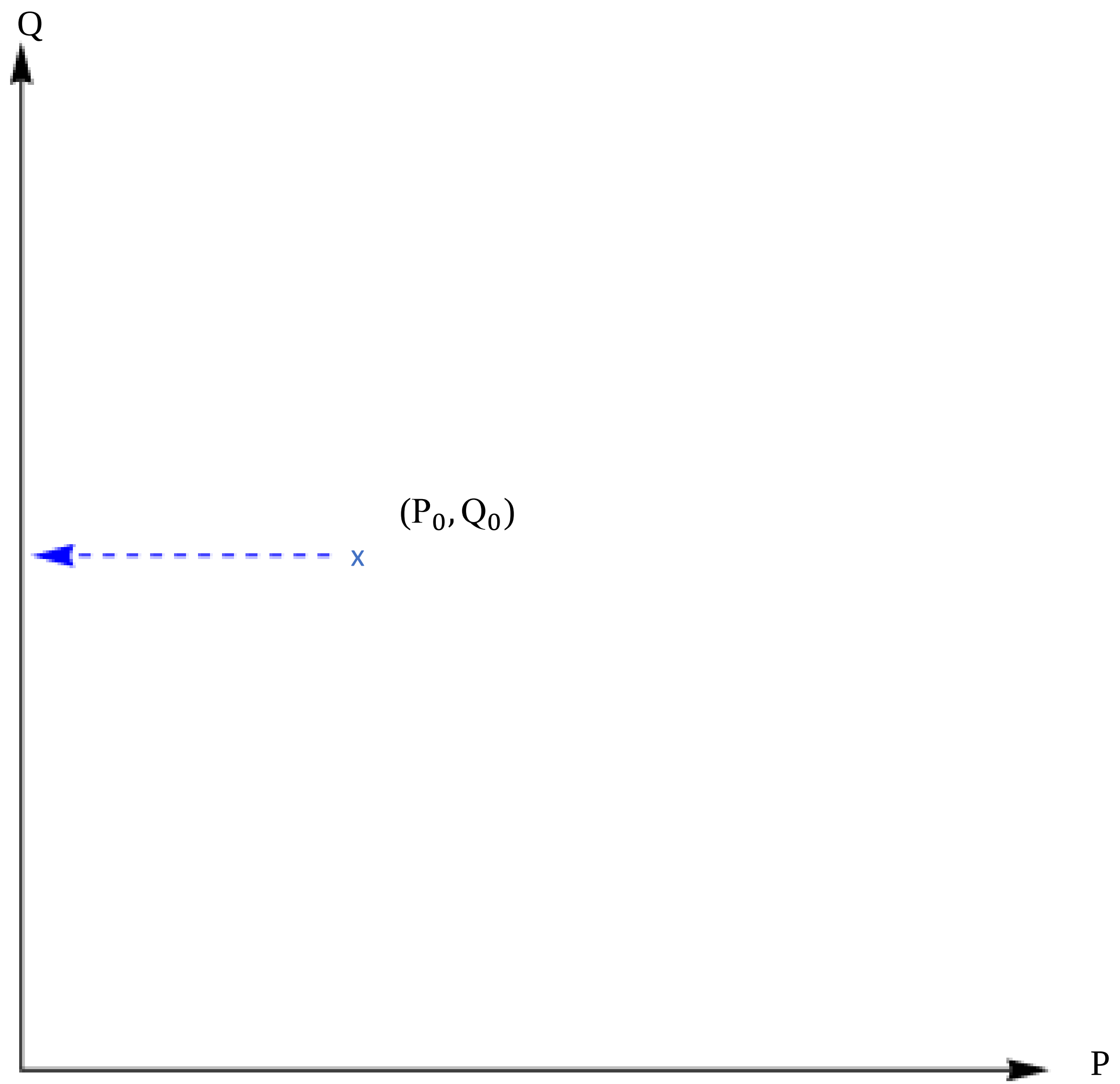
Bibliografía:

- Benoît Perthame. Some mathematical models of tumor growth. 2014.
- Elisabet Oter Perrote. Some simple mathematical models of tumor growth. 2015
- Benjamin Ribba et al. A Tumor Growth Inhibition Model for Low-Grade Glioma Treated with Chemotherapy or Radiotherapy. 2012

2.1. Modelo sin medicación



2.1. Modelo sin medicación



- Puntos fijos

$$\begin{cases} 0 = rP\left(1 - \left(\frac{P}{K}\right)^{a}\right) - bP + cQ \\ 0 = bP - cQ - dQ \end{cases} \rightarrow Q = \frac{bP}{c+d}$$

$$(P_0, Q_0) = (0,0)$$

$$(P_1, Q_1) = (K(1 - \frac{bd}{r(c+d)})^{1/a}, \frac{bK}{c+d}(1 - \frac{bd}{r(c+d)})^{1/a})$$

2.1. Modelo sin medicación

- Matriz Jacobiana

$$\mathcal{J} = \begin{pmatrix} \dfrac{\partial f_1}{\partial P} & \dfrac{\partial f_1}{\partial Q} \\ \dfrac{\partial f_2}{\partial P} & \dfrac{\partial f_2}{\partial Q} \end{pmatrix} = \begin{pmatrix} r\left(1 - \left(\dfrac{P}{K}\right)^a (1+a)\right) - b & c \\ \text{b} & -(c+d) \end{pmatrix}$$

2.1. Modelo sin medicación

$$(P_0, Q_0) = (0,0)$$

$$\mathcal{J}(0,0) = \begin{pmatrix} r - b & c \\ \mathrm{b} & -(c+d) \end{pmatrix}$$

$$\begin{cases} \tau = \mathrm{Tr}(\mathcal{J}) = r - b - c - d \\ \Delta = \mathrm{Det}(\mathcal{J}) = (b - r)(c + d) - bc \end{cases}$$

$$\lambda_1 = \frac{1}{2}\left(\tau + \sqrt{\tau^2 - 4\Delta}\right) \qquad \lambda_2 = \frac{1}{2}\left(\tau - \sqrt{\tau^2 - 4\Delta}\right)$$

2.1. Modelo sin medicación

$(P_0, Q_0) = (0,0)$ $\qquad$ $bd > (c+d)r$

$$\begin{cases} \tau = \mathrm{Tr}(\mathcal{J}) = r - b - c - d \\ \Delta = \mathrm{Det}(\mathcal{J}) = (b-r)(c+d) - bc = bd - cr - dr \end{cases}$$

$$bd > (c+d)r \ \leftrightarrow \Delta > 0 \leftrightarrow \sqrt{\tau^2 - 4\Delta} < |\tau|$$

$$bd > (c+d)r \ \leftrightarrow \tau < 0$$

$$\lambda_1 = \frac{1}{2}(\tau + \sqrt{\tau^2 - 4\Delta}) < 0 \qquad \lambda_2 = \frac{1}{2}\left(\tau - \sqrt{\tau^2 - 4\Delta}\right) < 0$$

2.1. Modelo sin medicación

$(P_0, Q_0) = (0,0)$ $\qquad$ $bd < (c+d)r$

$$\begin{cases} \tau = \mathrm{Tr}(\mathcal{J}) = r - b - c - d \\ \Delta = \mathrm{Det}(\mathcal{J}) = (b - r)(c + d) - bc \end{cases}$$

$$bd < (c+d)r \leftrightarrow \Delta < 0 \leftrightarrow \sqrt{\tau^2 - 4\Delta} > |\tau| \leftrightarrow \sqrt{\tau^2 - 4\Delta} > \tau$$

$$\lambda_1 = \frac{1}{2}(\tau + \sqrt{\tau^2 - 4\Delta}) > 0 \qquad \lambda_2 = \frac{1}{2}\left(\tau - \sqrt{\tau^2 - 4\Delta}\right) < 0$$

2.1. Modelo sin medicación

$(P_0, Q_0) = (0,0)$ $\qquad bd < (c+d)r$

$$\vec{v}_{\lambda_1} = (\frac{-b+c+d+r+\sqrt{(b+c+d-r)^2-4(bd-cr-dr)}}{2b}, 1)$$

$$\vec{v}_{\lambda_2} = (\frac{-b+c+d+r-\sqrt{(b+c+d-r)^2-4(bd-cr-dr)}}{2b}, 1)$$

$$\sqrt{(b+c+d-r)^2-4(bd-cr-dr)} = \sqrt{(-b+c+d-r)^2+4bc}$$

$$\sqrt{(-b+c+d-r)^2+4bc} > \sqrt{(-b+c+d-r)^2} = |-b+c+d-r|$$

2.1. Modelo sin medicación

$$(P_1, Q_1) = \left(K\left(1 - \frac{bd}{r(c+d)}\right)^{1/a}, \frac{bK}{c+d}\left(1 - \frac{bd}{r(c+d)}\right)^{1/a}\right)$$

$$\mathcal{J}(P_1, Q_1) = \begin{pmatrix} -ar + \frac{bd}{c+d}(1+a) - b & c \\ \mathrm{b} & -(c+d) \end{pmatrix}$$

$$\begin{cases} \tau = -\mathrm{ar} + \frac{\mathrm{bd}}{\mathrm{c+d}}(1+\mathrm{a}) - \mathrm{b} - \mathrm{c} - \mathrm{d} \\ \Delta = ar(c+d) - abd \end{cases}$$

2.1. Modelo sin medicación

$$(P_1, Q_1) = (K(1 - \frac{bd}{r(c+d)})^{1/a}, \frac{bK}{c+d}(1 - \frac{bd}{r(c+d)})^{1/a})$$

$$\begin{cases} \tau = -\mathrm{ar} + \frac{\mathrm{bd}}{\mathrm{c+d}}(1 + \mathrm{a}) - \mathrm{b} - \mathrm{c} - \mathrm{d} \\ \Delta = ar(c+d) - abd \end{cases}$$

$$bd < (c+d)r \leftrightarrow \Delta > 0 \leftrightarrow \sqrt{\tau^2 - 4\Delta} < |\tau|$$

$$bd < (c+d)r \leftrightarrow \tau < 0$$

$$\lambda_1 = \frac{1}{2}(\tau + \sqrt{\tau^2 - 4\Delta}) < 0 \qquad \lambda_2 = \frac{1}{2}\left(\tau - \sqrt{\tau^2 - 4\Delta}\right) < 0$$

2.1. Modelo sin medicación

Criterio de Bendixon: Sean $\dot{x} = P(x,y),\ \dot{y} = Q(x,y)$ el campo vectorial velocidad de un sistema dinámico. Si en un dominio simplemente conexo G la expresión $\frac{\partial P}{\partial x} + \frac{\partial Q}{\partial y}$ tiene un signo constante (pudiendo anularse sobre una curva o sobre puntos aislados), entonces el sistema no tiene trayectorias cerradas sobre el dominio G

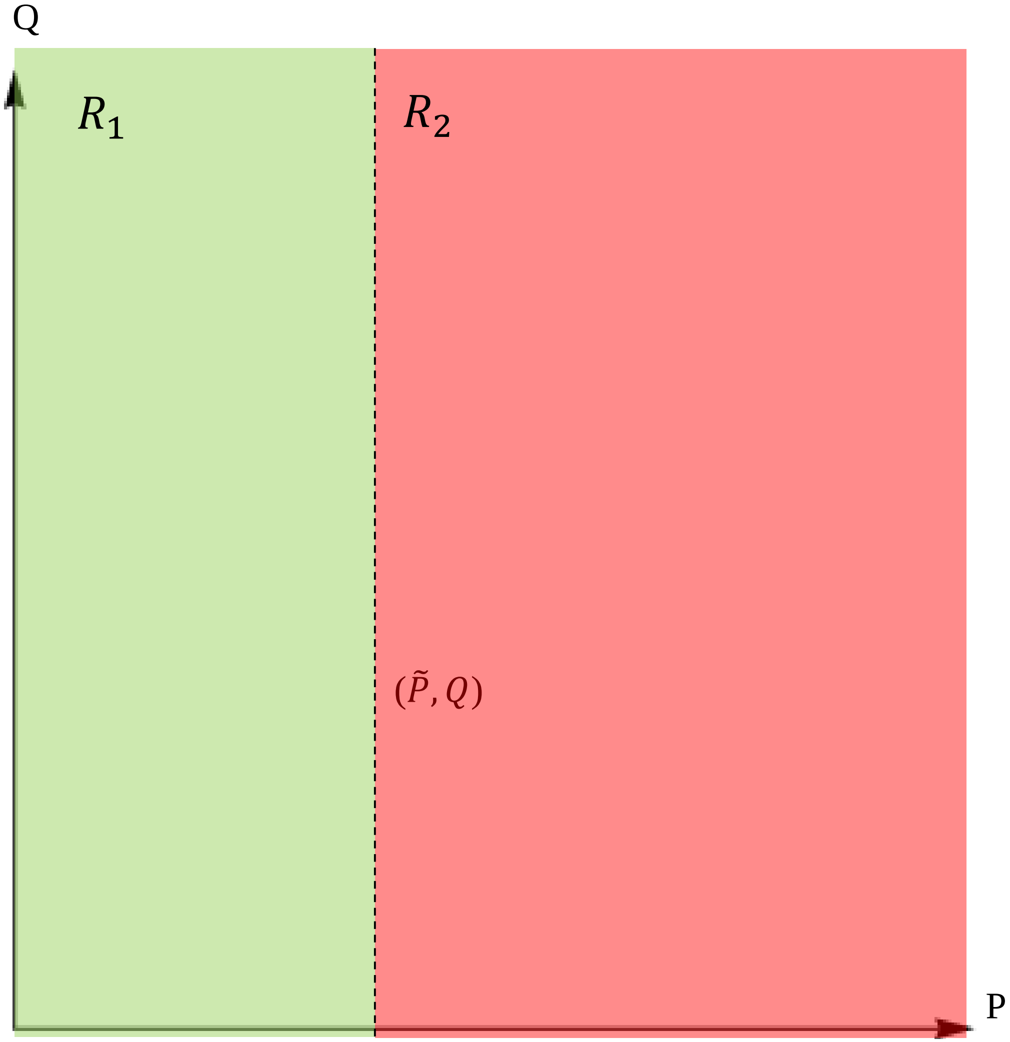
$$\nabla \cdot (\dot{P}, \dot{Q}) = \frac{\partial \dot{P}}{\partial P} + \frac{\partial \dot{Q}}{\partial Q} = r - b - c - d + (-(1+a)r\left(\frac{P}{K}\right)^a)$$

- $r - b - c - d \leq 0 \ \rightarrow \ \nabla \cdot (\dot{P}, \dot{Q}) < 0 \quad \forall (P,Q) \in \mathbb{R}^+ \times \mathbb{R}^+$
- $r - b - c - d > 0 \ \rightarrow \ \nabla \cdot (\dot{P}, \dot{Q}) = 0 \quad \leftrightarrow P = K \sqrt[a]{\frac{r-b-c-d}{(1+a)r}}$

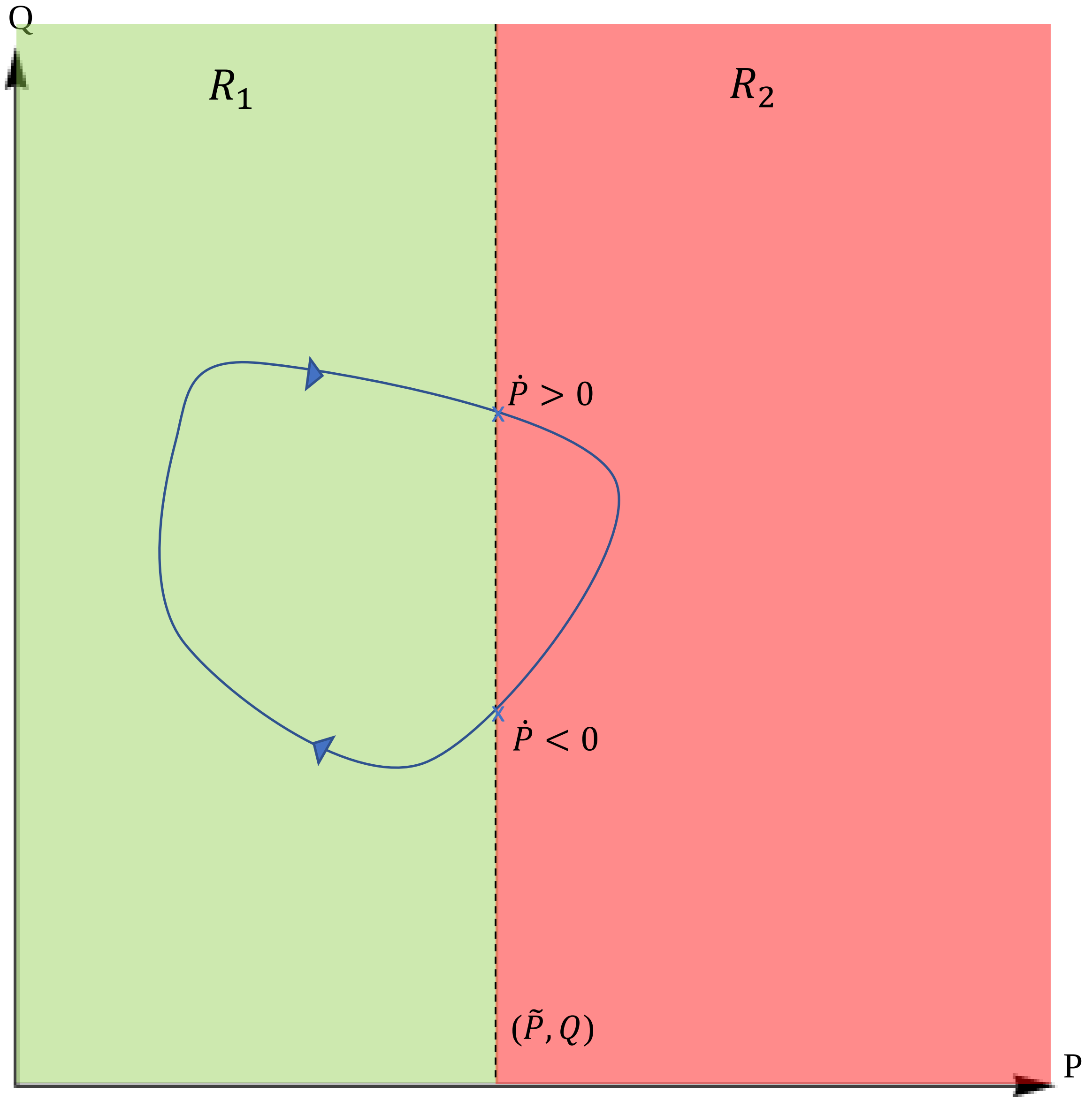
2.1. Modelo sin medicación

$$\frac{\partial \dot{P}}{\partial P} + \frac{\partial \dot{Q}}{\partial Q} = r - b - c - d + (-(1+a)r\left(\frac{P}{K}\right)^a)$$

$$\tilde{P} = K\sqrt[a]{\frac{r-b-c-d}{(1+a)r}}$$

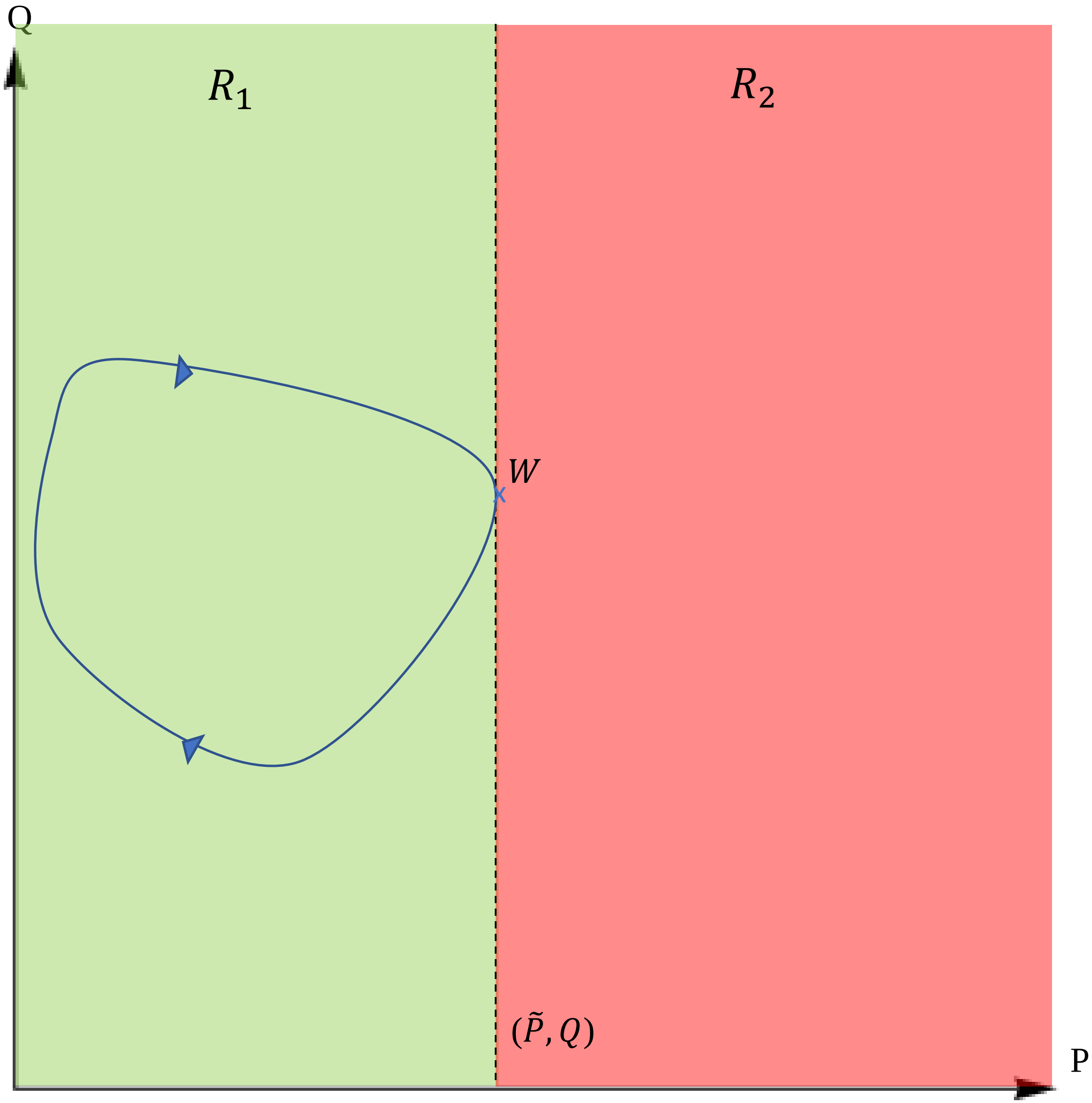


2.1. Modelo sin medicación



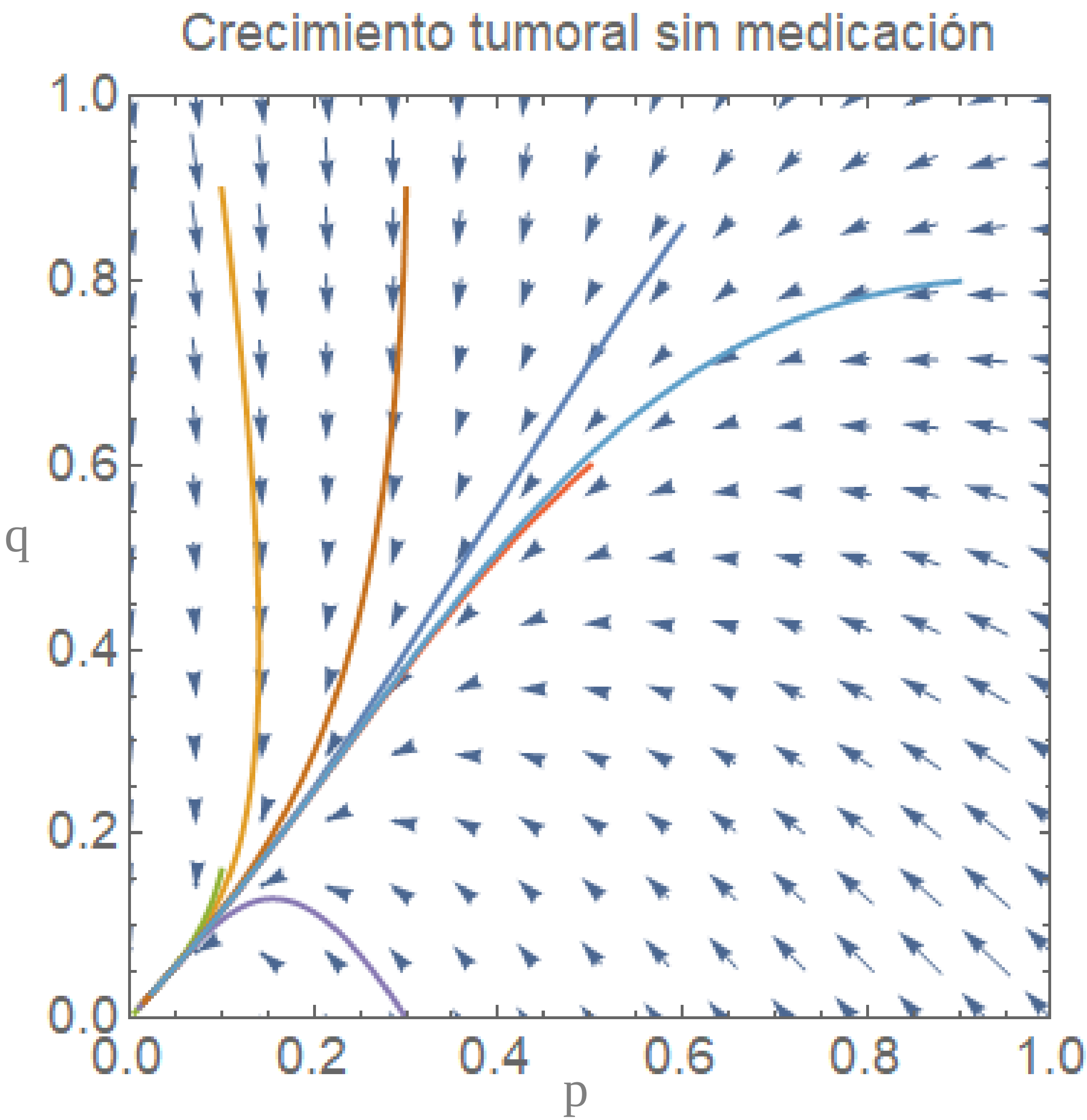
$$r - b - c - d > 0$$

$$\tilde{P} = K \sqrt[a]{\frac{r - b - c - d}{(1 + a)r}}$$



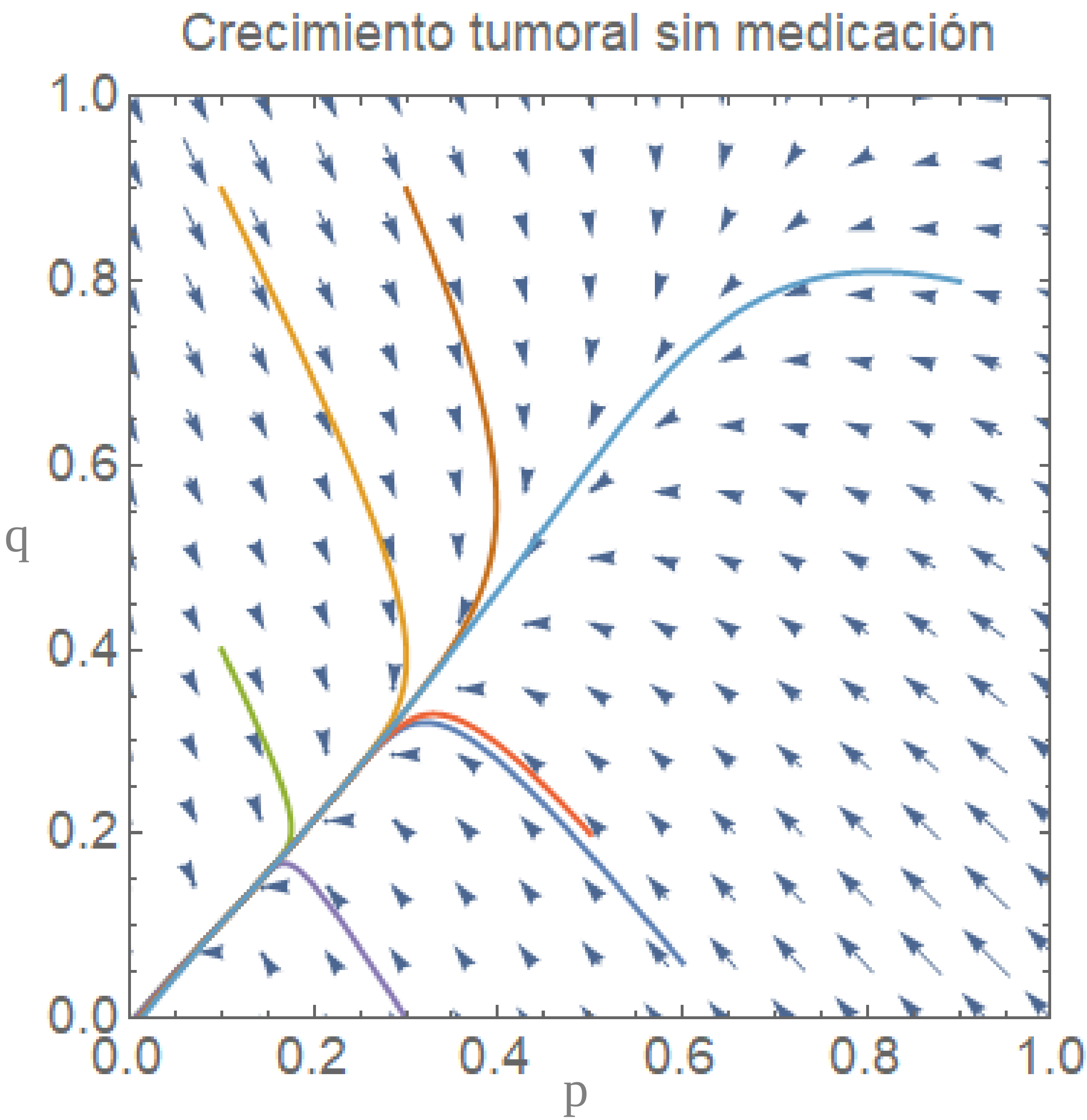
$$R_1' = R_1 \cup W$$

2.1. Modelo sin medicación



Caso $bd > (c + d)r$

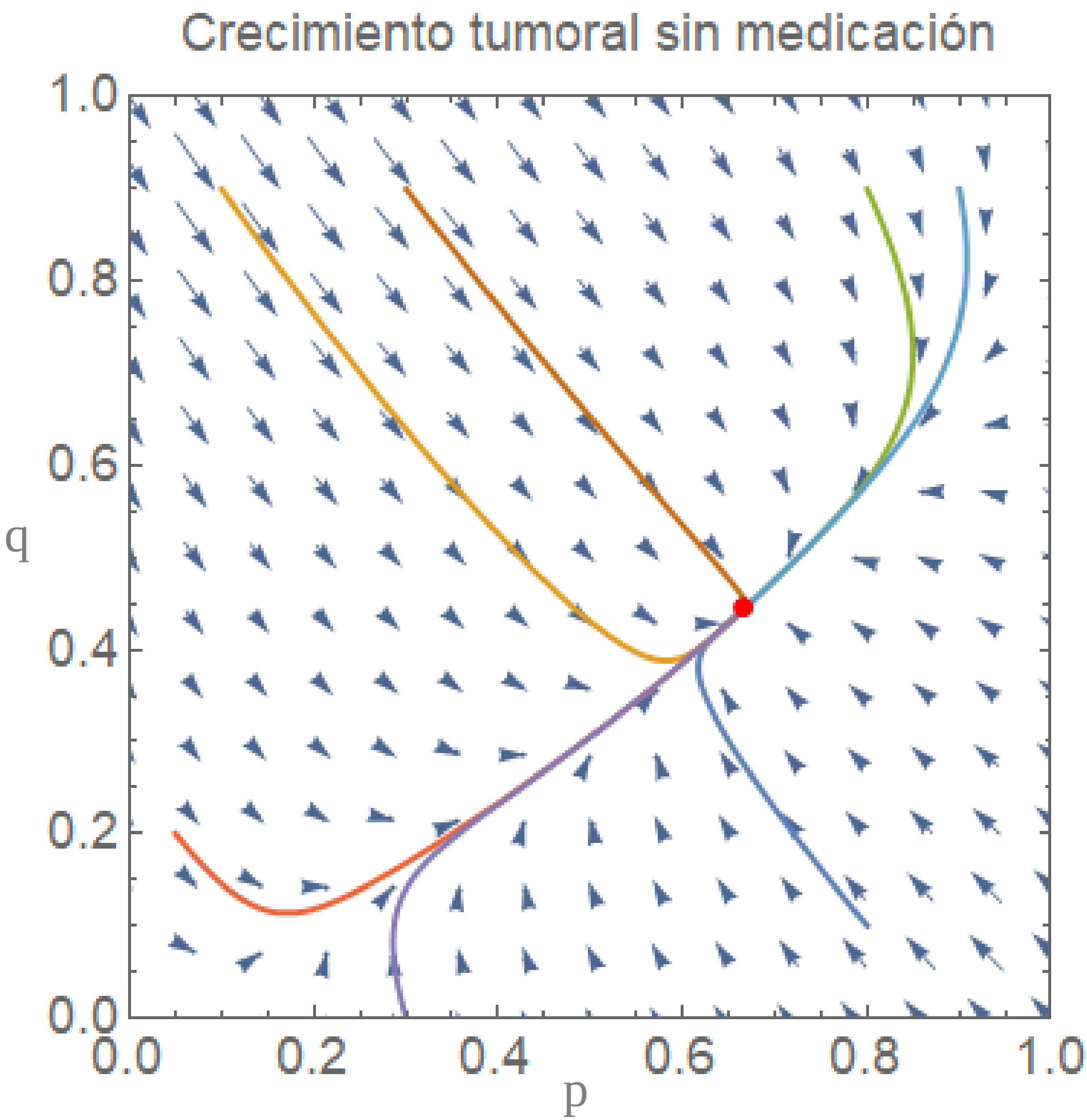
$$\begin{cases} r = 0.5 \\ a = 1 \\ b = 1 \\ c = 0.2 \\ d = 1 \end{cases}$$



Caso $bd = (c + d)r$

$$\begin{cases} r=1 \\ a=1 \\ b=2 \\ c=1 \\ d=1 \end{cases}$$

2.1. Modelo sin medicación



Caso $bd < (c + d)r$

$$\begin{cases} r=1 \\ a=1 \\ b=2 \\ c=1 \\ d=0.5 \end{cases}$$

2.1. Modelo sin medicación

$$(P_1, Q_1) = \left(K\left(1 - \frac{bd}{r(c+d)}\right)^{1/a}, \frac{bK}{c+d}\left(1 - \frac{bd}{r(c+d)}\right)^{1/a}\right)$$

$$P_1 \in (0, K)$$

$$Q_1 \in \left(0, \frac{bK}{c+d}\right)$$

$$N_1 \in \left(0, K\left(1 + \frac{b}{c+d}\right)\right)$$

2.2. Modelo con medicación

*“**CHEMOTHERAPY** destroys and shrinks cancer cells, prevents them from thriving and multiplying. After surgery, chemotherapy may be given to reduce the chances of the cancer coming back. ”*

- Puntos fijos

$$\begin{cases} 0 = rP\left(1 - \left(\frac{P}{K}\right)^a\right) - b_1P + cQ \\ 0 = b_2P - cQ - dQ \end{cases} \rightarrow Q = \frac{b_2P}{c+d}$$

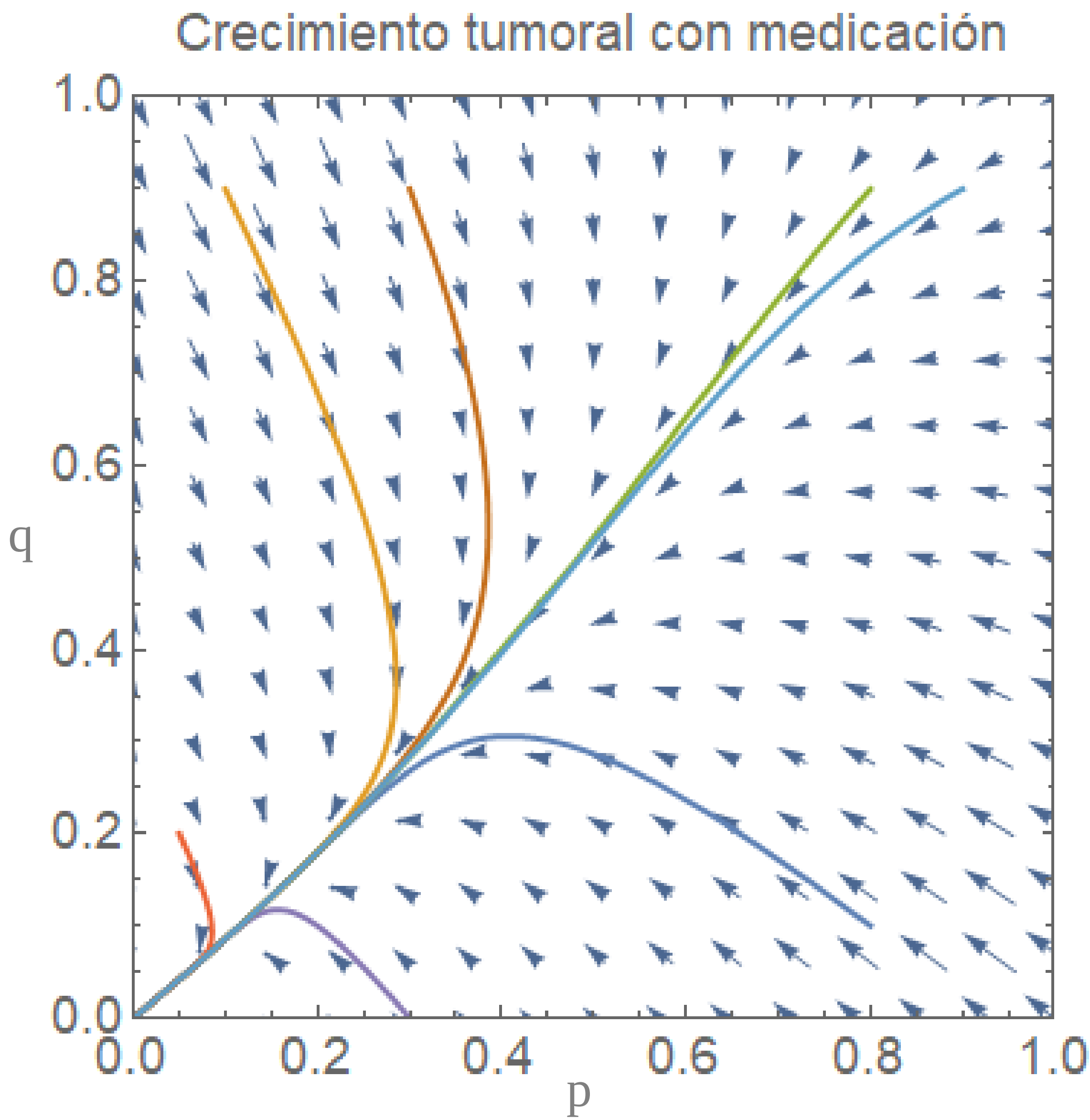
$$(P_0, Q_0) = (0,0)$$

$$(P_1, Q_1) = \left(K\left(1 - \frac{(b + c_{stat} + c_{tox})d + c\ c_{tox}}{r(c+d)}\right)^{1/a}, \frac{(b + c_{stat})}{c+d} P_1\right)$$

- Matriz Jacobiana

$$\mathcal{J} = \begin{pmatrix} r\left(1-\left(\frac{P}{K}\right)^{a}(1+a)\right)-(b+c_{stat}+c_{tox}) & c \\ \mathrm{b}+c_{stat} & -(c+d) \end{pmatrix}$$

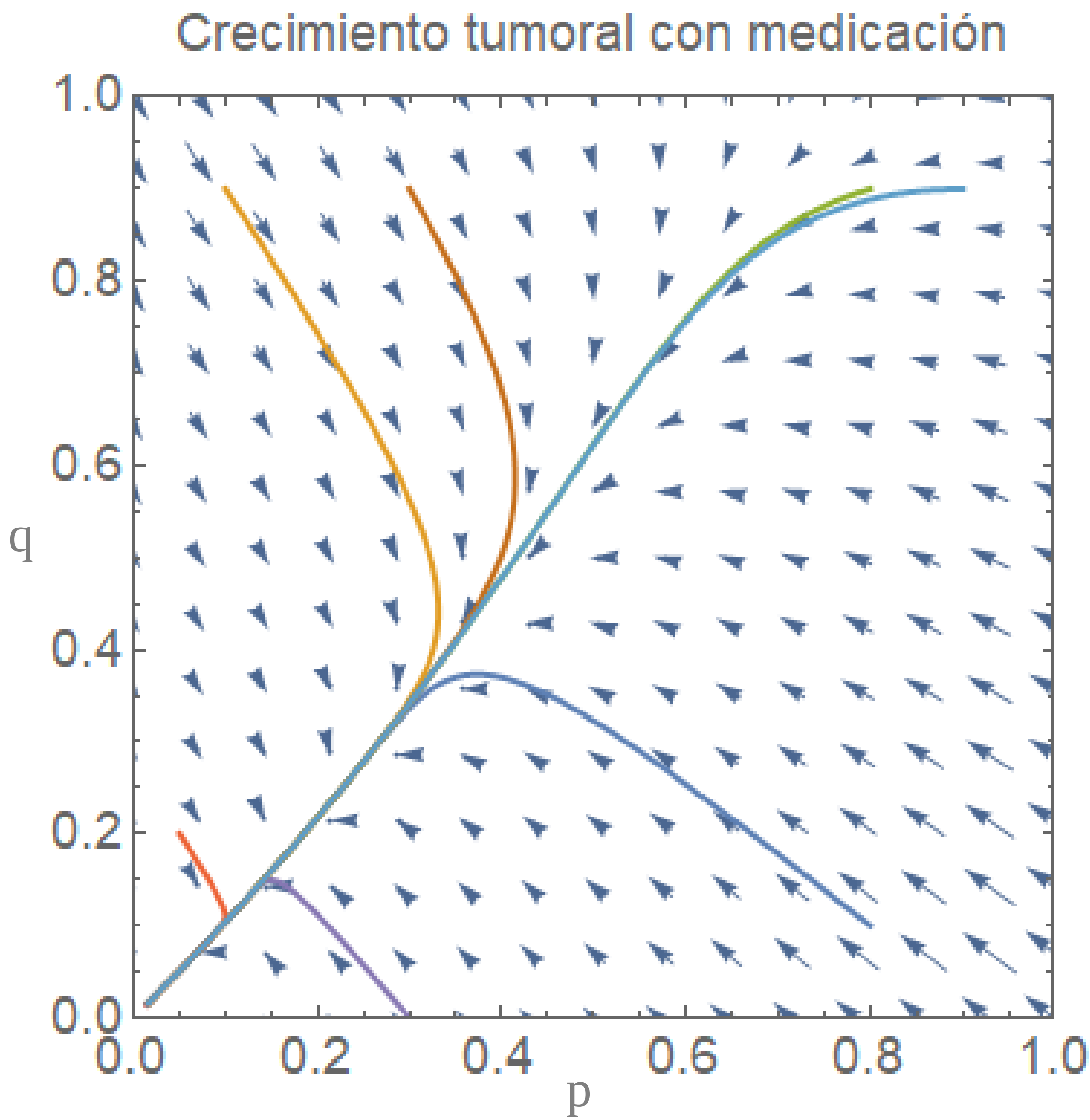
2.2. Modelo con medicación



$(b+c_{stat}+c_{tox})d > (c+d)r - c\,c_{tox}$

$$\begin{cases} r=1 \\ a=1 \\ b=1 \\ c=1 \\ c_{stat}=0.5 \\ c_{tox}=0.5 \\ d=1 \end{cases}$$

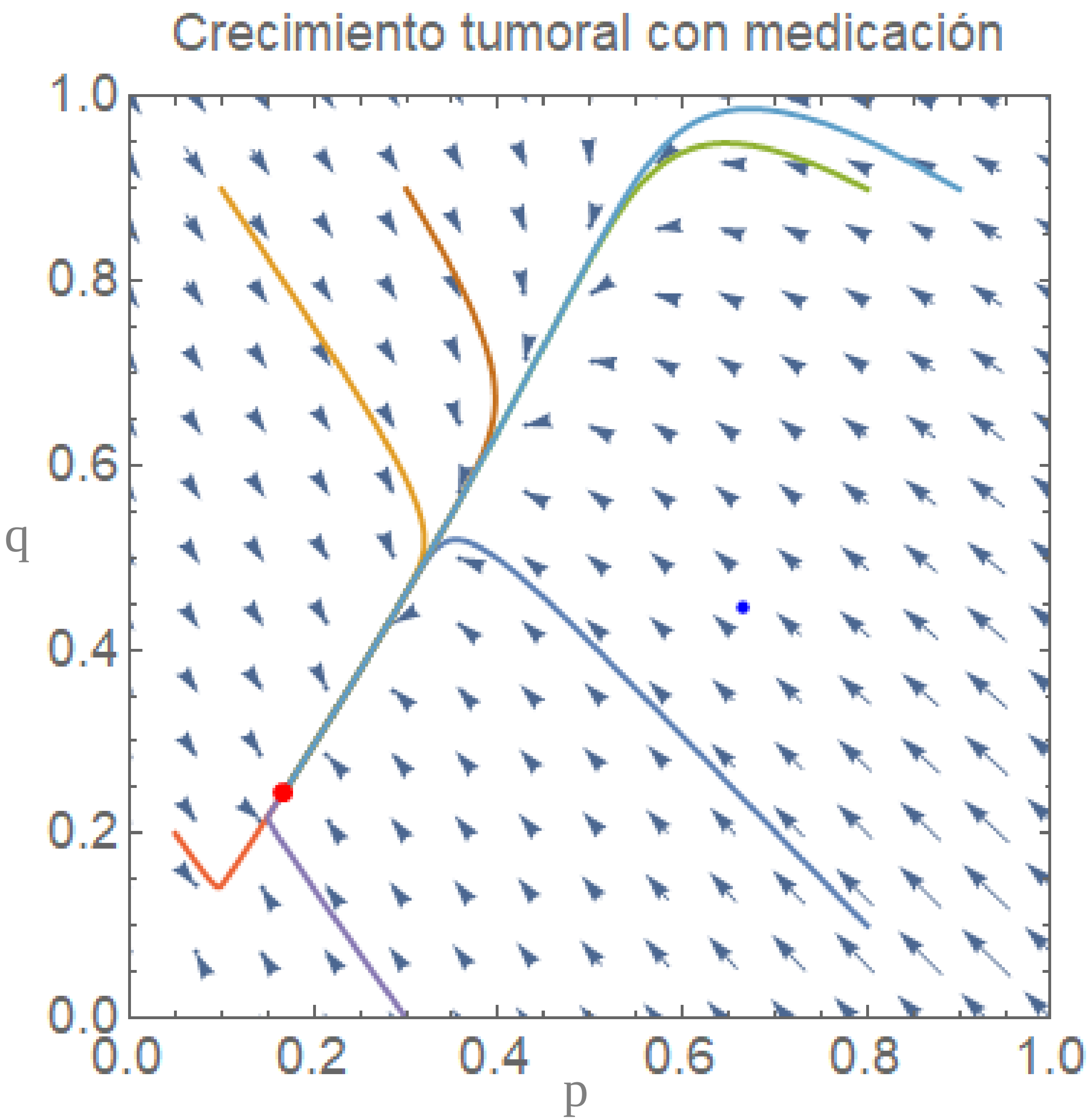
2.2. Modelo con medicación



$(b+c_{stat}+c_{tox})d = (c+d)r - c\, c_{tox}$

$$\begin{cases} r=1 \\ a=1 \\ b=1 \\ c=1 \\ c_{stat}=0.5 \\ c_{tox}=0.5 \\ d=0.5 \end{cases}$$

2.2. Modelo con medicación



$(b+c_{stat}+c_{tox})d < (c+d)r - c\,c_{tox}$

$$\begin{cases} r=1 \\ a=1 \\ b=2 \\ c=1 \\ c_{stat}=0.2 \\ c_{tox}=0.1 \\ d=0.5 \end{cases}$$

2.2. Modelo con medicación

$$(P_1, Q_1) = (K(1 - \frac{(b + c_{stat} + c_{tox})d + c\ c_{tox}}{r(c + d)})^{1/a}, \frac{(b + c_{stat})}{c + d} P_1)$$

$$P_2 \in (0, k)$$

$$Q_2 \in \left(0, \frac{(b + c_{stat})K}{c + d}\right)$$

$$N_2 \in \left(0, K\left(1 + \frac{b + c_{stat}}{c + d}\right)\right)$$

2.2. Modelo con medicación

Sin medicacion

$$bd < (c + d)r$$

$$\bar{P}_1 = K\left(1 - \frac{bd}{r(c+d)}\right)^{1/a}$$

$$\bar{Q}_1 = \frac{bK}{c+d}\bar{P}_1$$

$$N_1 \in \left(0, k\left(1 + \frac{b}{c+d}\right)\right)$$

Con medicación

$$(b + c_{stat} + c_{tox})d < (c + d)r - c\, c_{tox}$$

$$\bar{P}_2 = K(1 - \frac{(b+c_{stat}+c_{tox})d + c\, c_{tox}}{r(c+d)})^{1/a}$$

$$\bar{Q}_2 = \frac{(b + c_{stat})K}{c+d}\bar{P}_2$$

$$N_2 \in \left(0, K\left(1 + \frac{b+c_{stat}}{c+d}\right)\right)$$

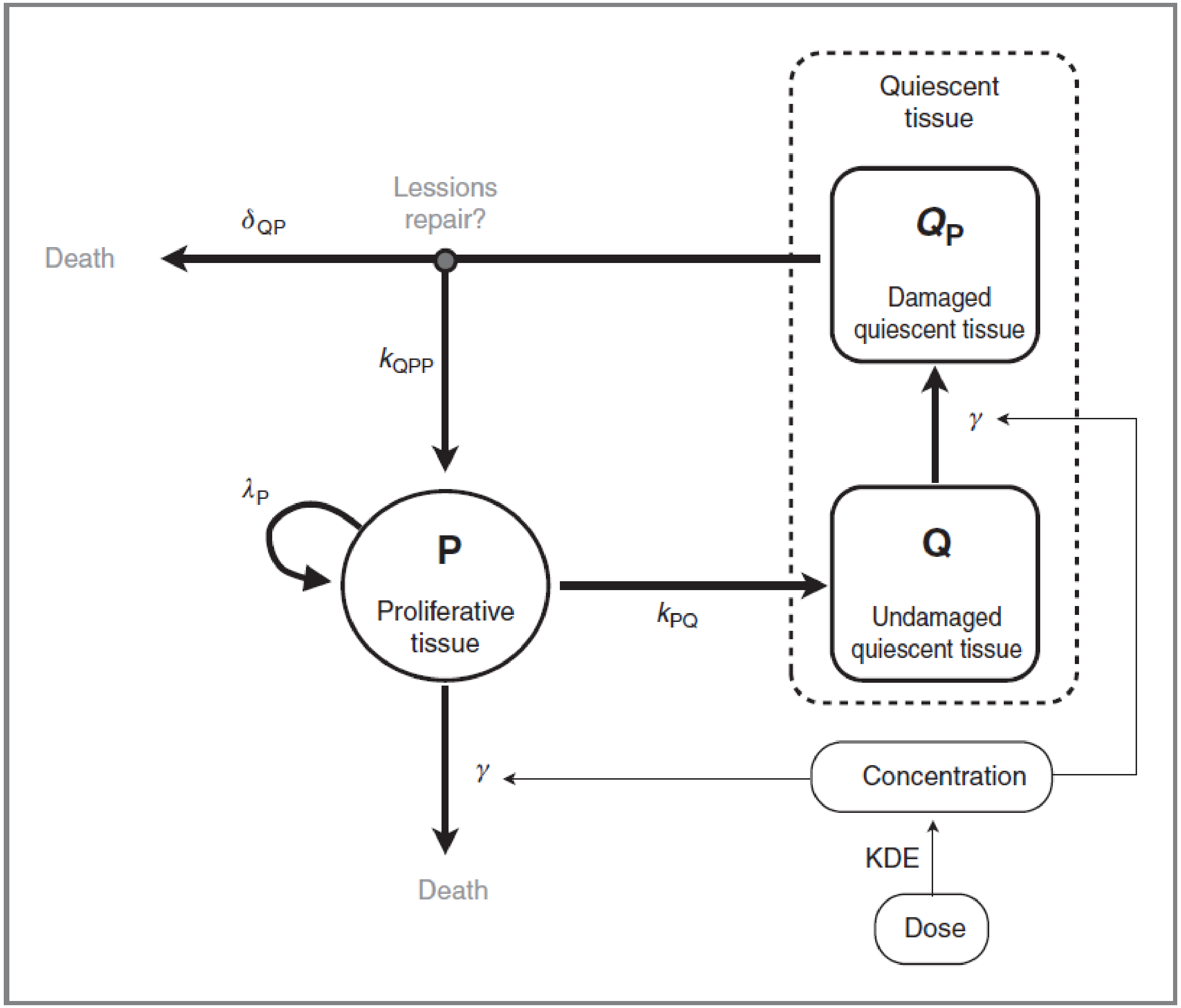


Figure 2. Schematic view of the model. *P* denotes the proliferative tissue and *Q* the nonproliferative or quiescent tissue. Proliferative tissue is assumed to transition to quiescence at a rate constant k_{PQ}. The treatment concentration, calculated from the individual dose through an exponential decay with the rate constant KDE, affects both proliferative and quiescent tissue. The tissue composed of cells in proliferation (*P*) is directly eliminated because of lethal DNA damages induced by the treatment. Nonproliferative tissue (*Q*) is also subject to DNA damages due to the treatment. When re-entering the cell cycle, the DNA-damaged quiescent cells (Q_P) can either repair their DNA damages and return to a proliferative state (*P*) or die because of unrepaired damages.

Fuente: Benjamin Ribba et al. A Tumor Growth Inhibition Model for Low-Grade Glioma Treated with Chemotherapy or Radiotherapy. 2012

2.3. Extra

$$\frac{dC}{dt} = -\text{KDE} \times C$$

$$\frac{dP}{dt} = \lambda_P \times P\left(1 - \frac{P^*}{K}\right) + k_{Q_PP} \times Q_P - k_{PQ} \times P - \gamma_P \times C \times \text{KDE} \times P$$

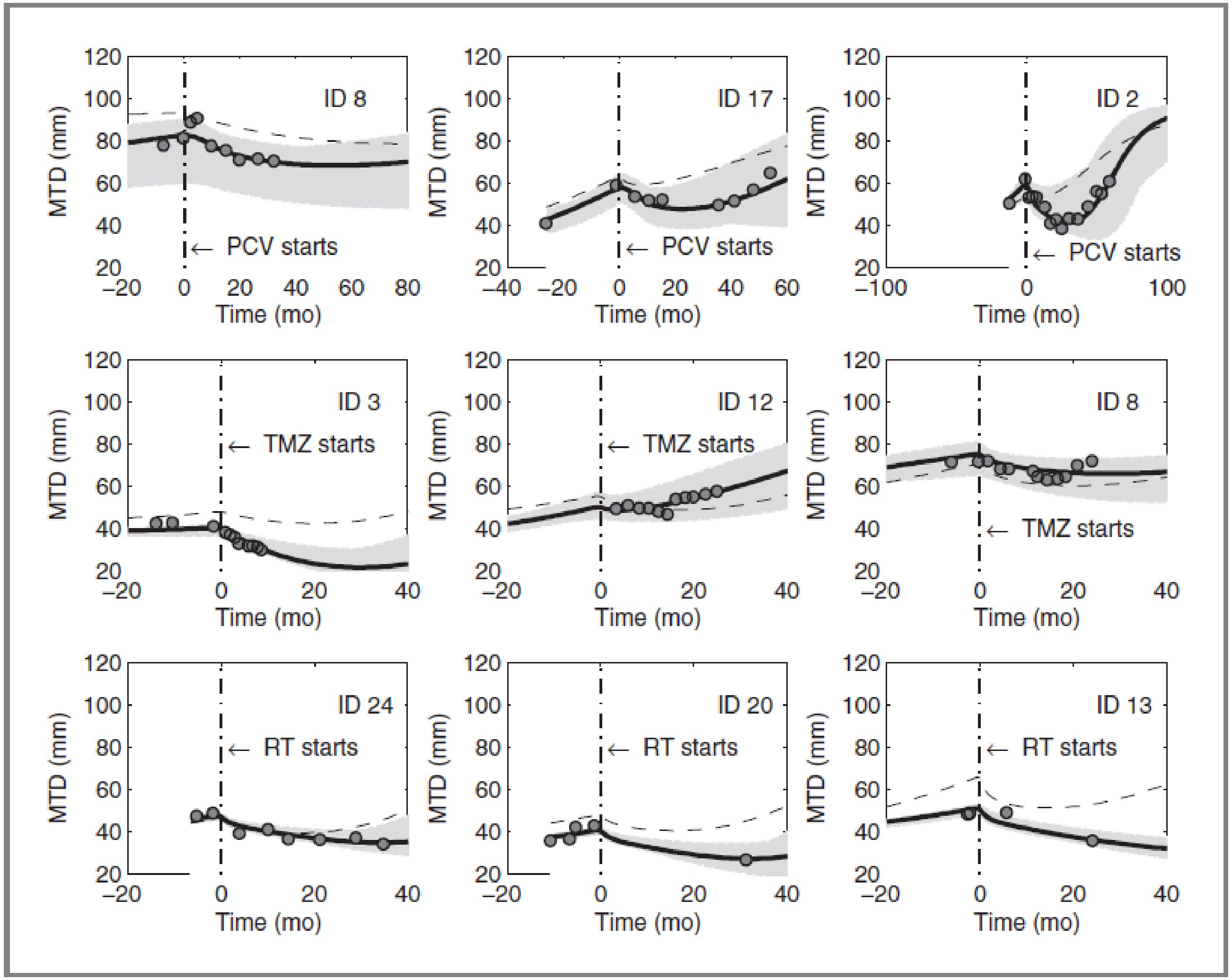
$$\frac{dQ}{dt} = k_{PQ}P - \gamma_Q \times C \times \text{KDE} \times Q$$

$$\frac{dQ_P}{dt} = \gamma_Q \times C \times \text{KDE} \times Q - k_{Q_PP}Q_P - \delta_{QP} \times Q_P$$

$$P^* = P + Q + Q_P$$

Fuente: Benjamin Ribba et al. A Tumor Growth Inhibition Model for Low-Grade Glioma Treated with Chemotherapy or Radiotherapy. 2012

Figure 4. MTD observed (circles), individual predictions (solid line), and population predictions on the basis of mean parameter values (dashed line) for 3 individuals in each study (top, PCV; middle: TMZ; bottom, RT) selected on the basis of their typical residual error magnitude (the individual's average absolute weight residual is at the population median). Included is the 90% confidence interval around the individual predictions obtained by simulation using the SEs of the empirical Bayes estimates.



Fuente: Benjamin Ribba et al. A Tumor Growth Inhibition Model for Low-Grade Glioma Treated with Chemotherapy or Radiotherapy. 2012

Gracias por asistir