HAL open science

Ecole chercheurs Modèles ressources-consommateurs

Bertrand Cloez, Simon Boudsocq, Thomas Koffel, Jérôme Harmand, Claude Lobry, Alain Rapaport, Tewfik Sari, Claude Plassard

To cite this version:

Bertrand Cloez, Simon Boudsocq, Thomas Koffel, Jérôme Harmand, Claude Lobry, et al.. Ecole chercheurs Modèles ressources-consommateurs. École thématique. Modèles Ressources-Consommateurs, Montpellier, France. 2015. cel-01206385v2

HAL Id: cel-01206385

https://inria.hal.science/cel-01206385v2

Submitted on 13 Jan 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Le cas d'une ressource abiotique

Le modèle du chémostat

Ecole-chercheur sur les modèles ressources-consommateurs

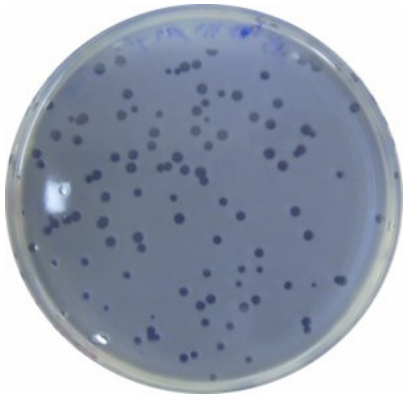
UMR MISTEA et UMR Eco&Sols

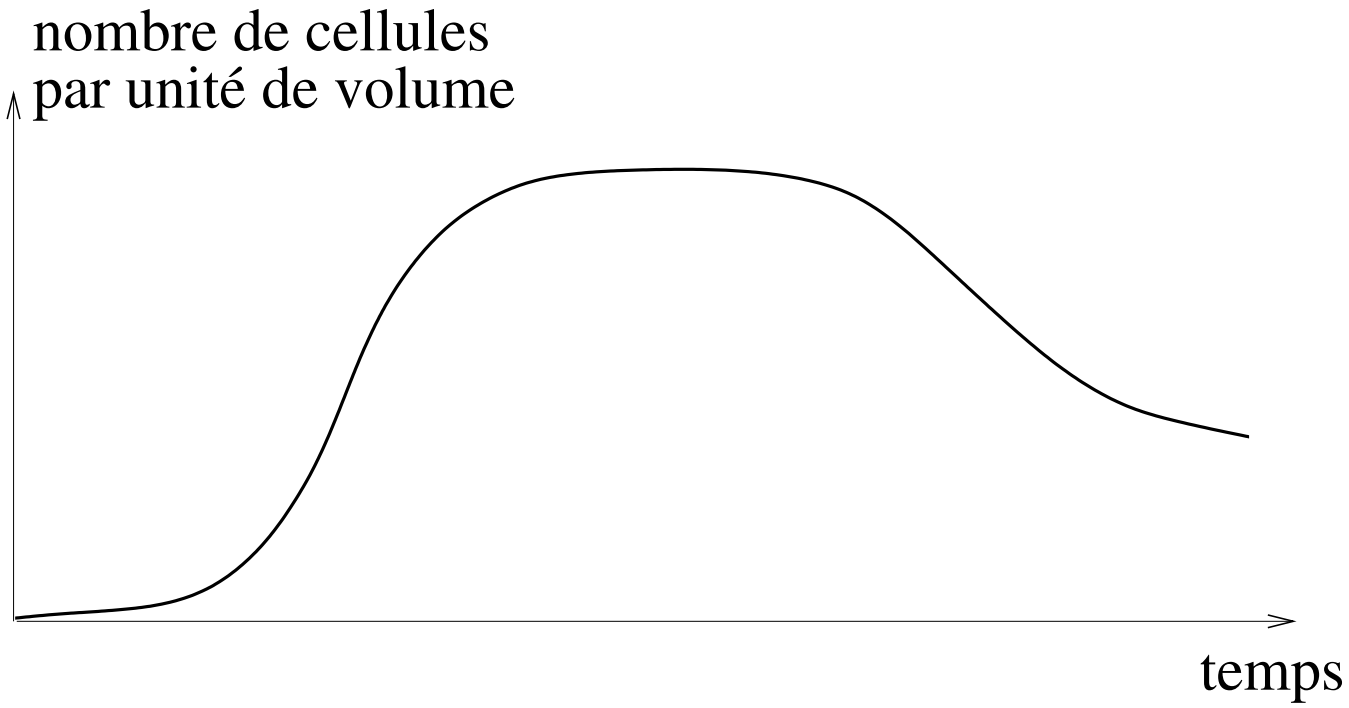
21–25 septembre 2015

Plan du cours

- La croissance bactérienne en bach
- Le dispositif du chémostat
- Le modèle classique du chémostat
- Inhibition dans la croissance bactérienne
- A propos d'identification expérimentale
- Compétition entre souches
- Une application possible : la bio-augmentation

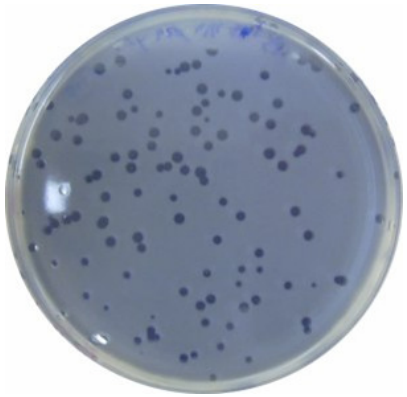
La croissance bactérienne en batch

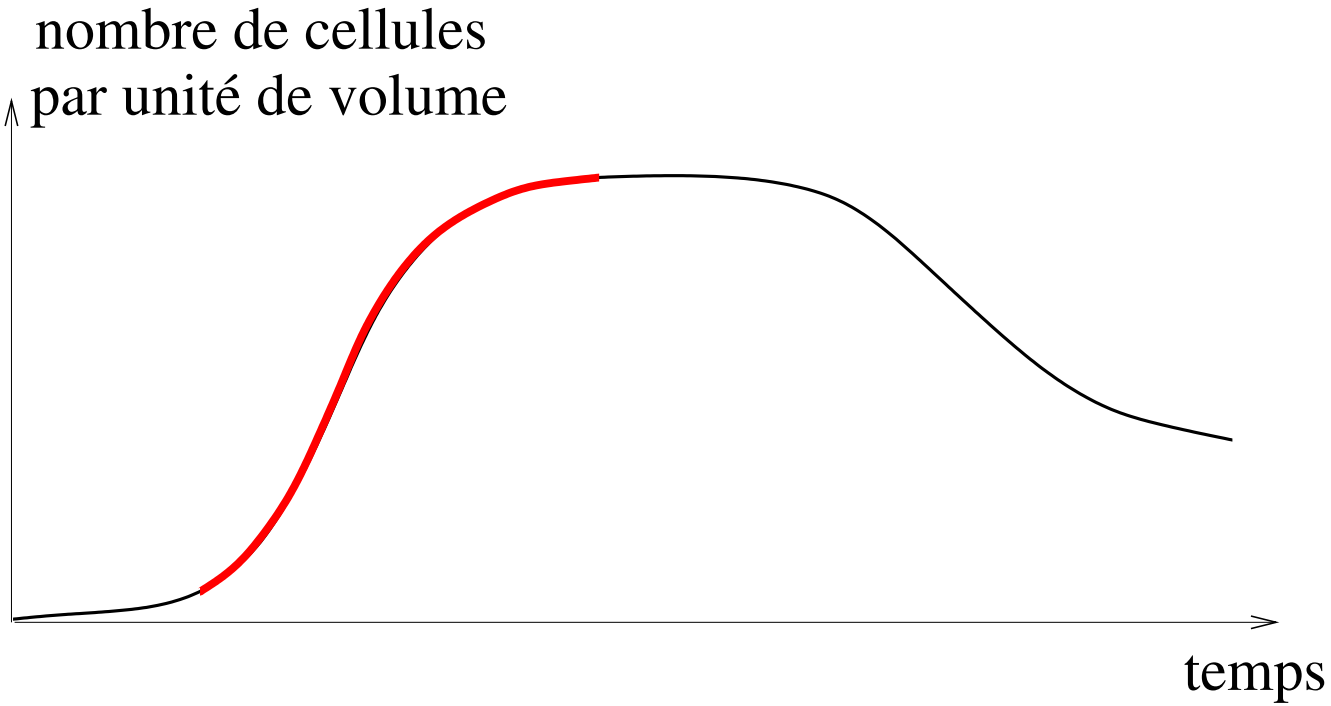




cf *J. Pirt. Principles of microbe and cell cultivation*, Wiley 1975

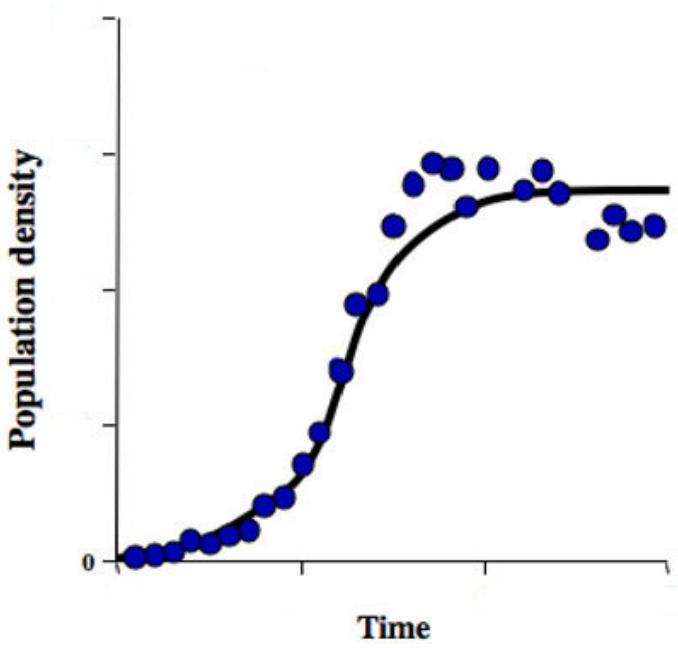
La croissance bactérienne en batch





cf *J. Pirt. Principles of microbe and cell cultivation*, Wiley 1975

La croissance logistique (Verhulst, 1838)

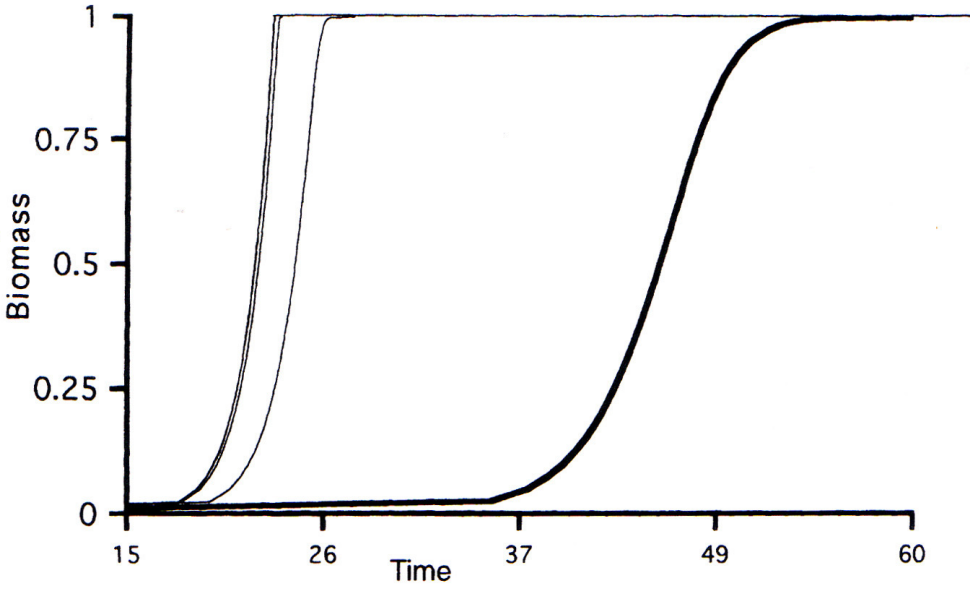


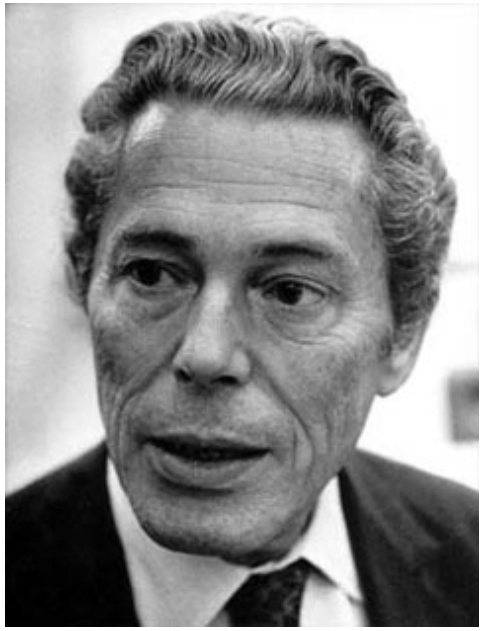
$$\boxed{x(t) = \frac{x_{\max}}{1 + e^{-rt}\left(\frac{x_{\max}}{x_0} - 1\right)}}$$

Autre formulation : $x(\cdot)$ est solution de l'équation différentielle

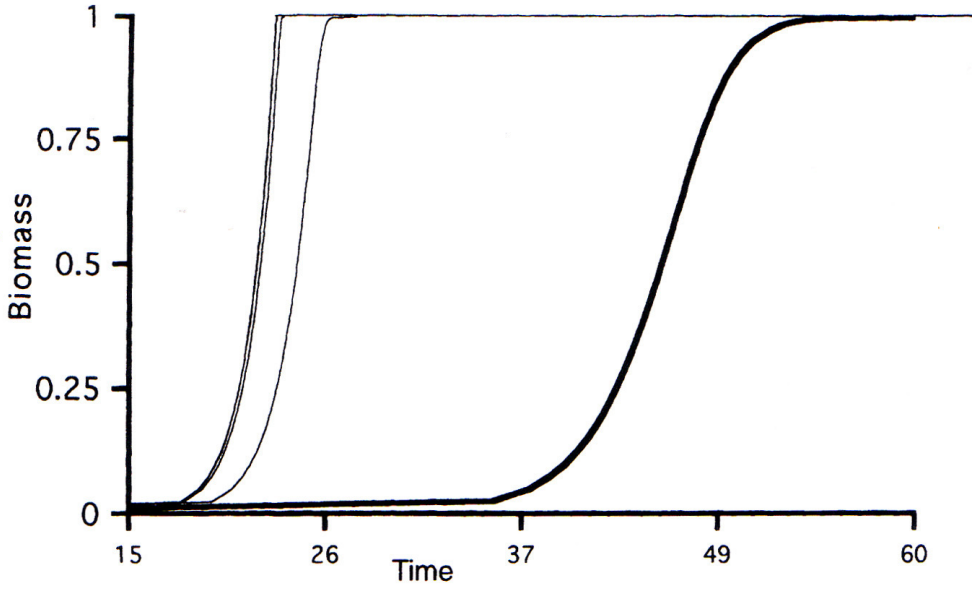
$$\frac{dx}{dt} = rx\left(1 - \frac{x}{x_{\max}}\right)$$

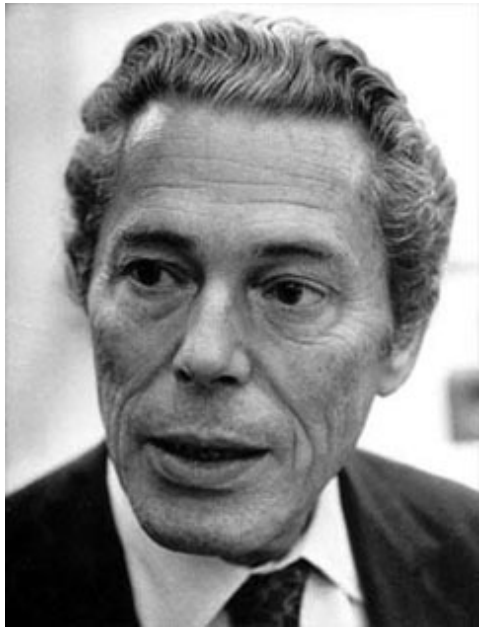
Les expériences des Jacques Monod (1930)





Les expériences des Jacques Monod (1930)





ne s'ajuste pas bien à la croissance logistique...

Modélisation mathématique

Hypothèse H0. Il existe y tel que $x + ys = m = Constante$

Modélisation mathématique

Hypothèse H0. Il existe y tel que $x + ys = m = Constante$

Hypothèse H1a. $\dfrac{dx}{dt} = \mu s x \Rightarrow \dfrac{dx}{dt} = \underbrace{\mu \dfrac{m}{y}}_{r} x \left(1 - \dfrac{x}{m}\right)$

Modélisation mathématique

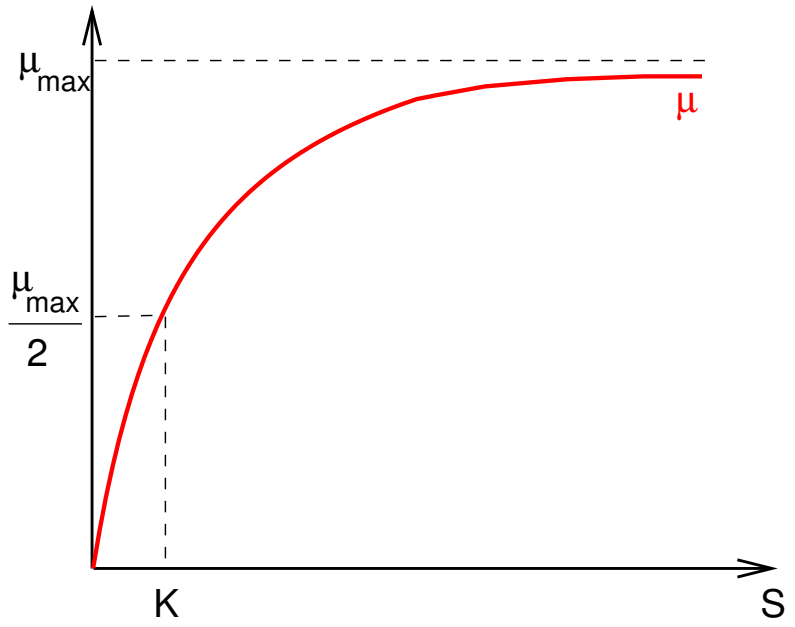
Hypothèse H0. Il existe y tel que $x + ys = m = Constante$

Hypothèse H1a. $\dfrac{dx}{dt} = \mu s x \Rightarrow \dfrac{dx}{dt} = \underbrace{\mu \dfrac{m}{y}}_{r} x \left(1 - \dfrac{x}{m}\right)$

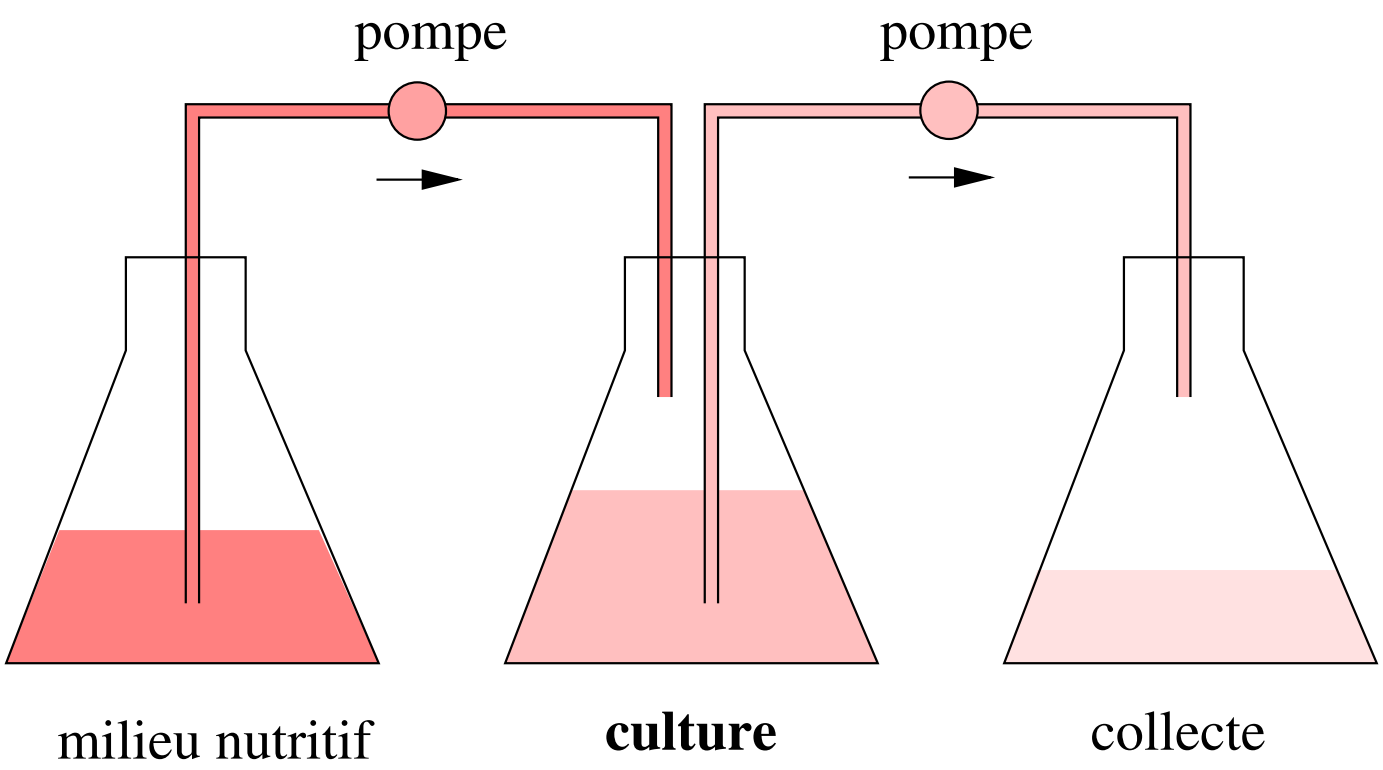
Hypothèse H1b. $\dfrac{dx}{dt} = \mu(s)x$ avec

$$\mu(s) = \frac{\mu_{\max} s}{K + s} :$$

("loi" de Monod)



Le dispositif du chémostat



Monod 1950 – Novick & Szilard 1950

Le modèle mathématique (en concentrations)

$$\begin{bmatrix} \dfrac{dx}{dt} \\ \dfrac{ds}{dt} \end{bmatrix} = \underbrace{\boxed{\begin{matrix} \mu(s)x \\ -\dfrac{\mu(s)}{y}x \end{matrix}}}_{\text{croissance}} + \underbrace{\boxed{\begin{matrix} -\dfrac{Q}{V}x \\ \dfrac{Q}{V}(s_{in} - s) \end{matrix}}}_{\text{dilution}}$$

Le modèle mathématique (en concentrations)

$$\begin{bmatrix} \dfrac{dx}{dt} \\ \dfrac{ds}{dt} \end{bmatrix} = \underbrace{\boxed{\begin{matrix} \mu(s)x \\ -\dfrac{\mu(s)}{y}x \end{matrix}}}_{\text{croissance}} + \underbrace{\boxed{\begin{matrix} -\dfrac{Q}{V}x \\ \dfrac{Q}{V}(s_{in} - s) \end{matrix}}}_{\text{dilution}}$$

Remarque : $Q = 0 \Rightarrow x + ys = constant$

Le modèle mathématique (en concentrations)

$$\begin{bmatrix} \dfrac{dx}{dt} \\ \dfrac{ds}{dt} \end{bmatrix} = \underbrace{\boxed{\begin{matrix} \mu(s)x \\ -\dfrac{\mu(s)}{y}x \end{matrix}}}_{\text{croissance}} + \underbrace{\boxed{\begin{matrix} -\dfrac{Q}{V}x \\ \dfrac{Q}{V}(s_{in} - s) \end{matrix}}}_{\text{dilution}}$$

Remarque : $Q = 0 \Rightarrow x + ys = constant$

Simplification et notations : $y = 1 \quad \dfrac{d}{dt} = \cdot \quad \dfrac{Q}{V} = D$

- $$\boxed{\begin{aligned} \dot{s} &= -\mu(s)x + D(s_{in} - s) \\ \dot{x} &= \mu(s)x - Dx \end{aligned}}$$

Au delà du dispositif expérimental

Ecologie des lacs de montagne

Au delà du dispositif expérimental

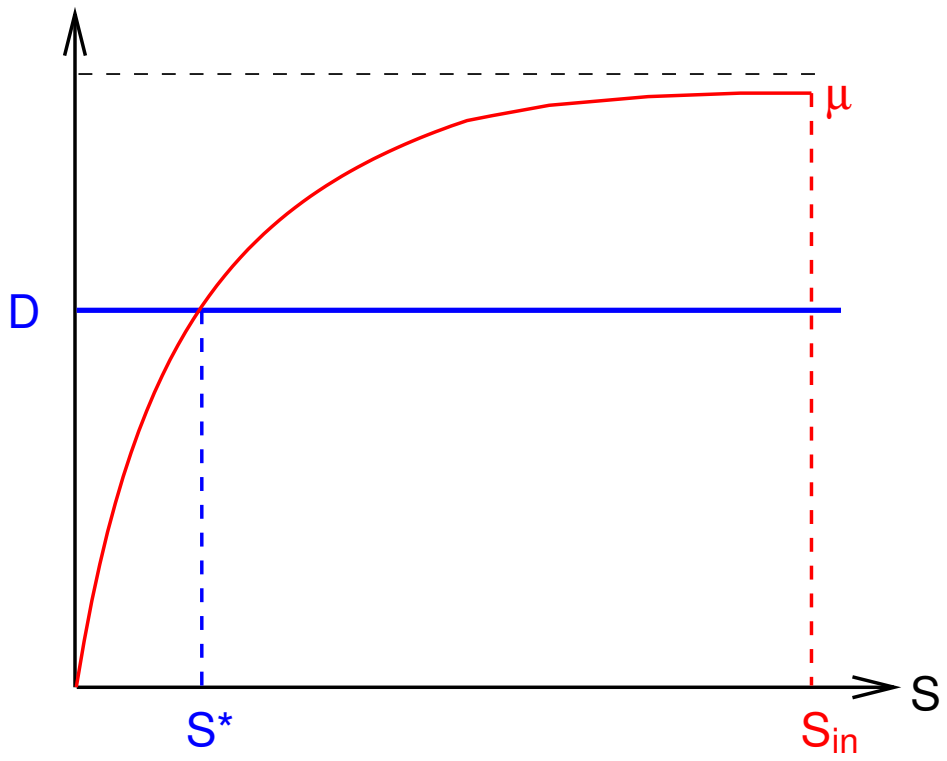
Bioréacteurs industriels

Détermination des équilibres

$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$

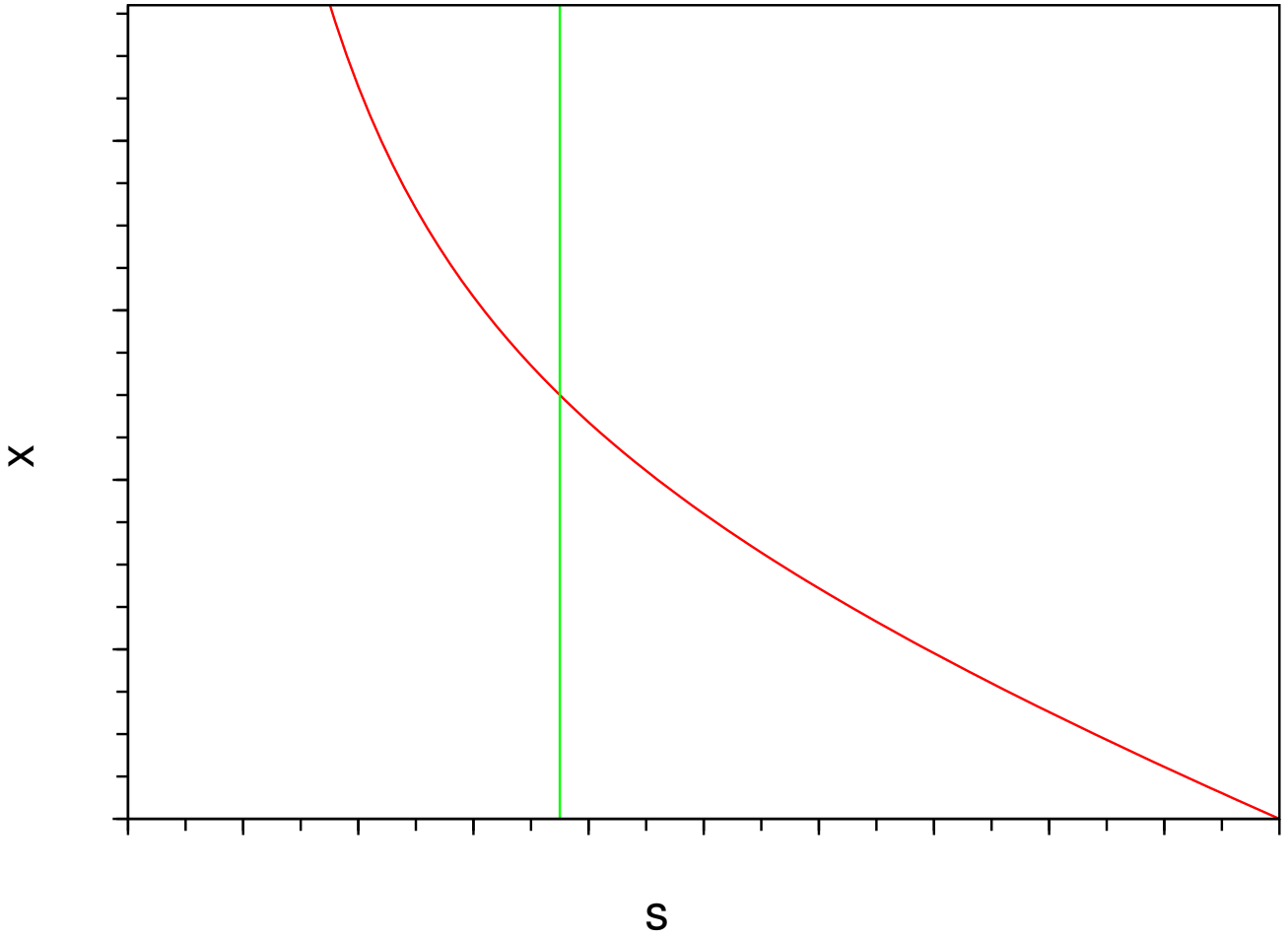
$\Rightarrow$ $\boxed{\begin{array}{c} x^\star = 0 \\ s^\star = s_{in} \end{array}}$ or $\boxed{\begin{array}{c} \mu(s^\star) = D \\ x^\star = s_{in} - s^\star \end{array}}$

lessivage — équilibre positif



Isoclines

$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$

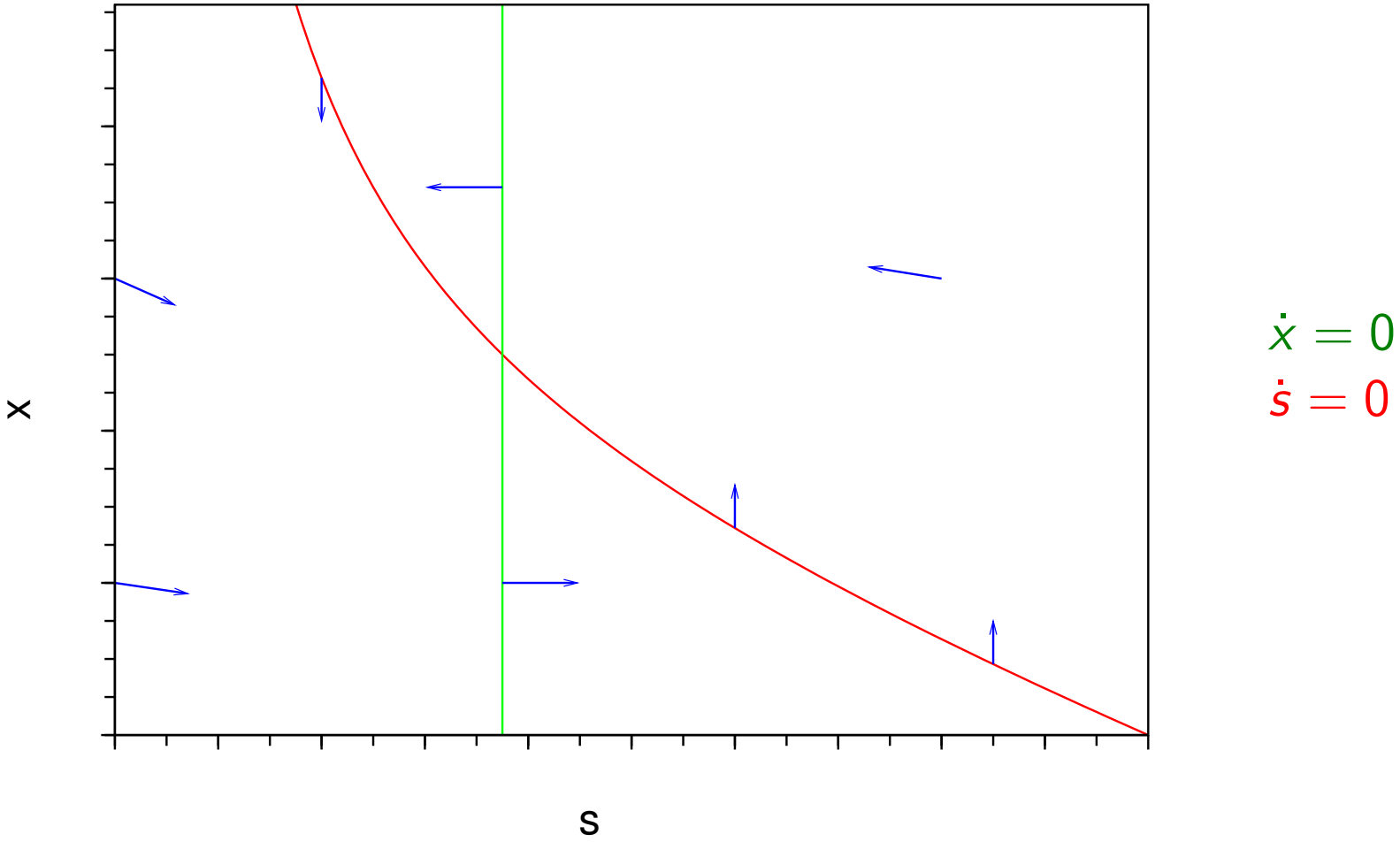


$\dot{x} = 0$

$\dot{s} = 0$

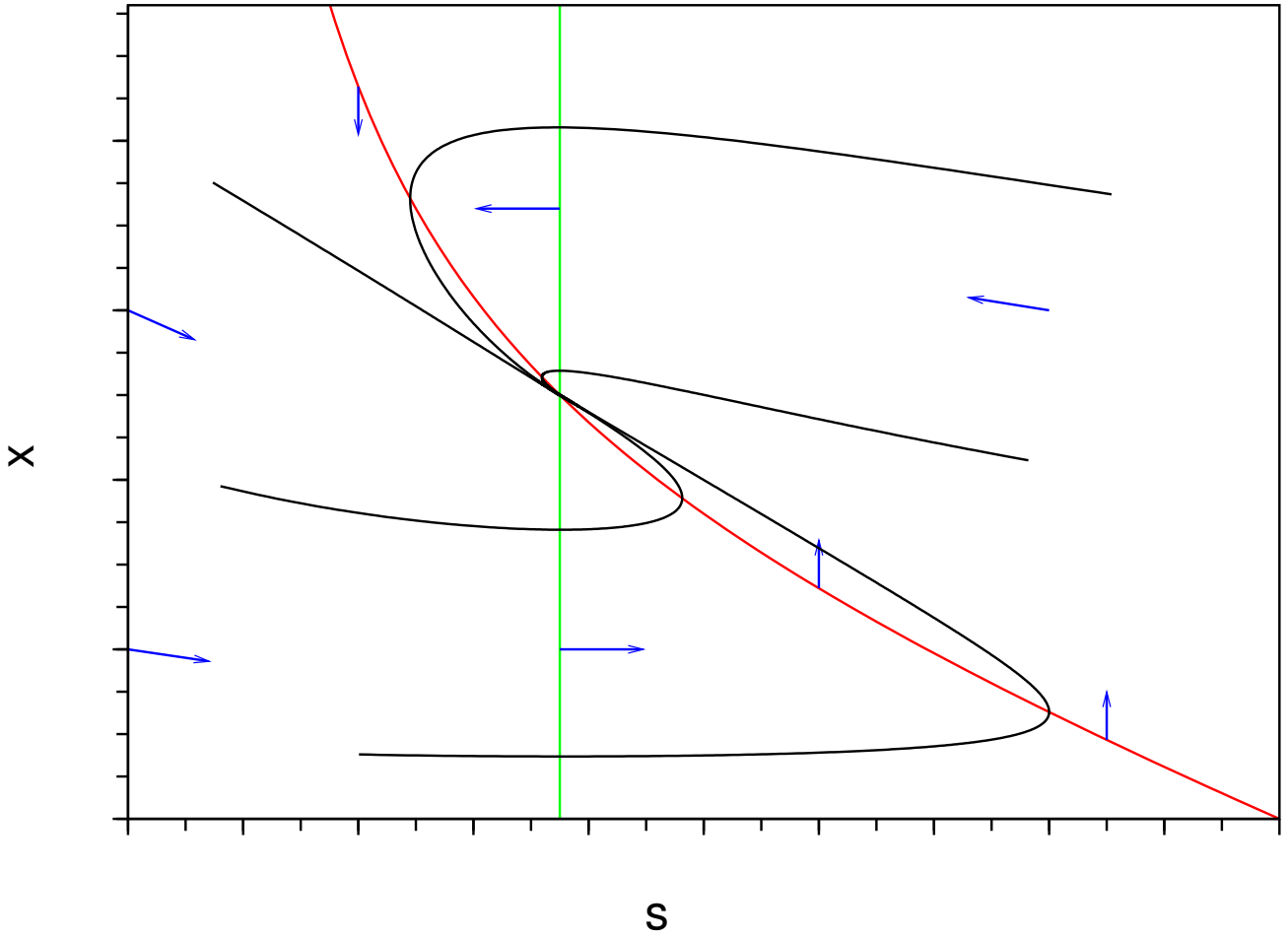
Champ de vecteurs

$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$



Portrait de phase

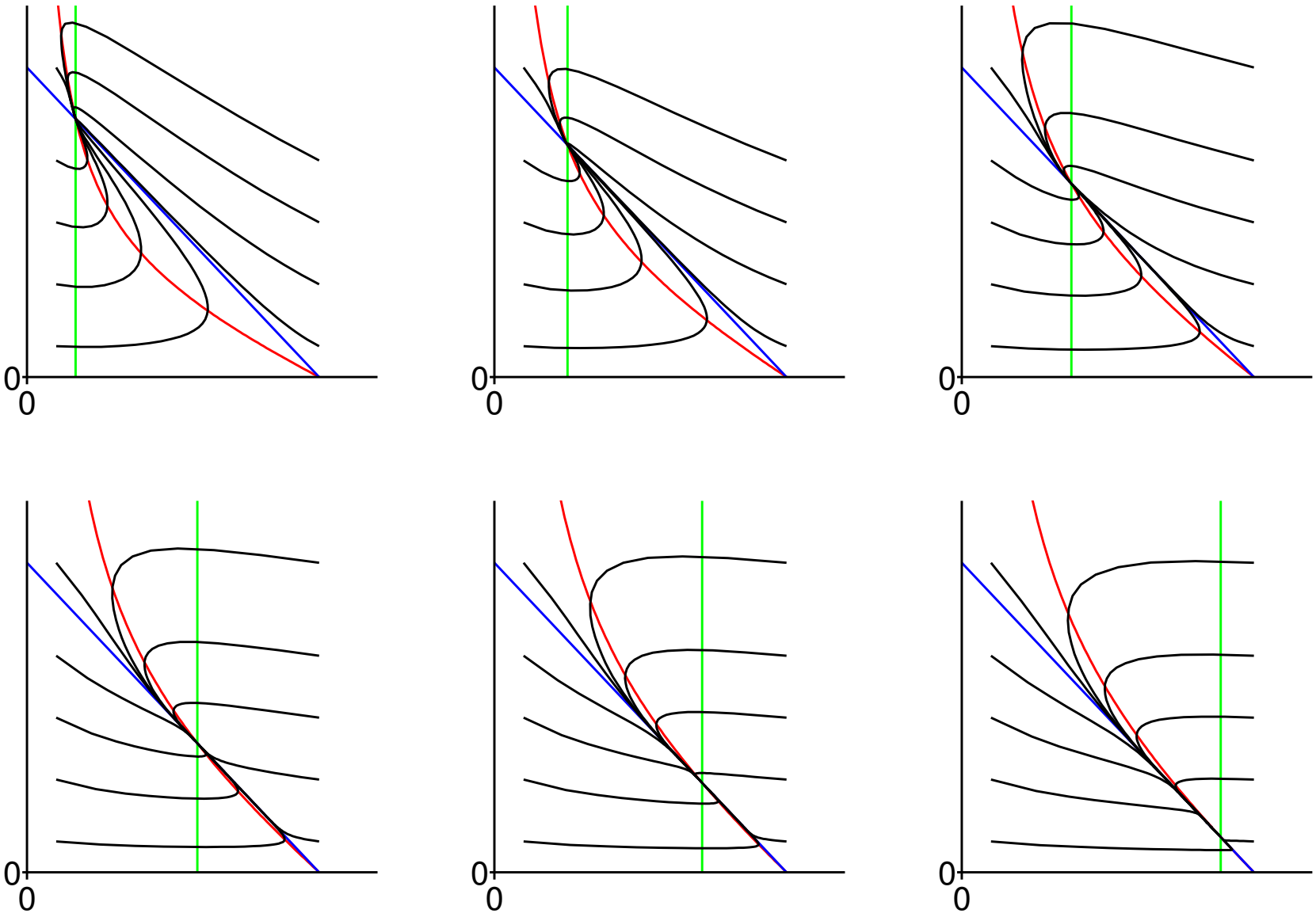
$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$



$\dot{x} = 0$

$\dot{s} = 0$

En augmentant le taux de dilution



En augmentant la concentration en entrée

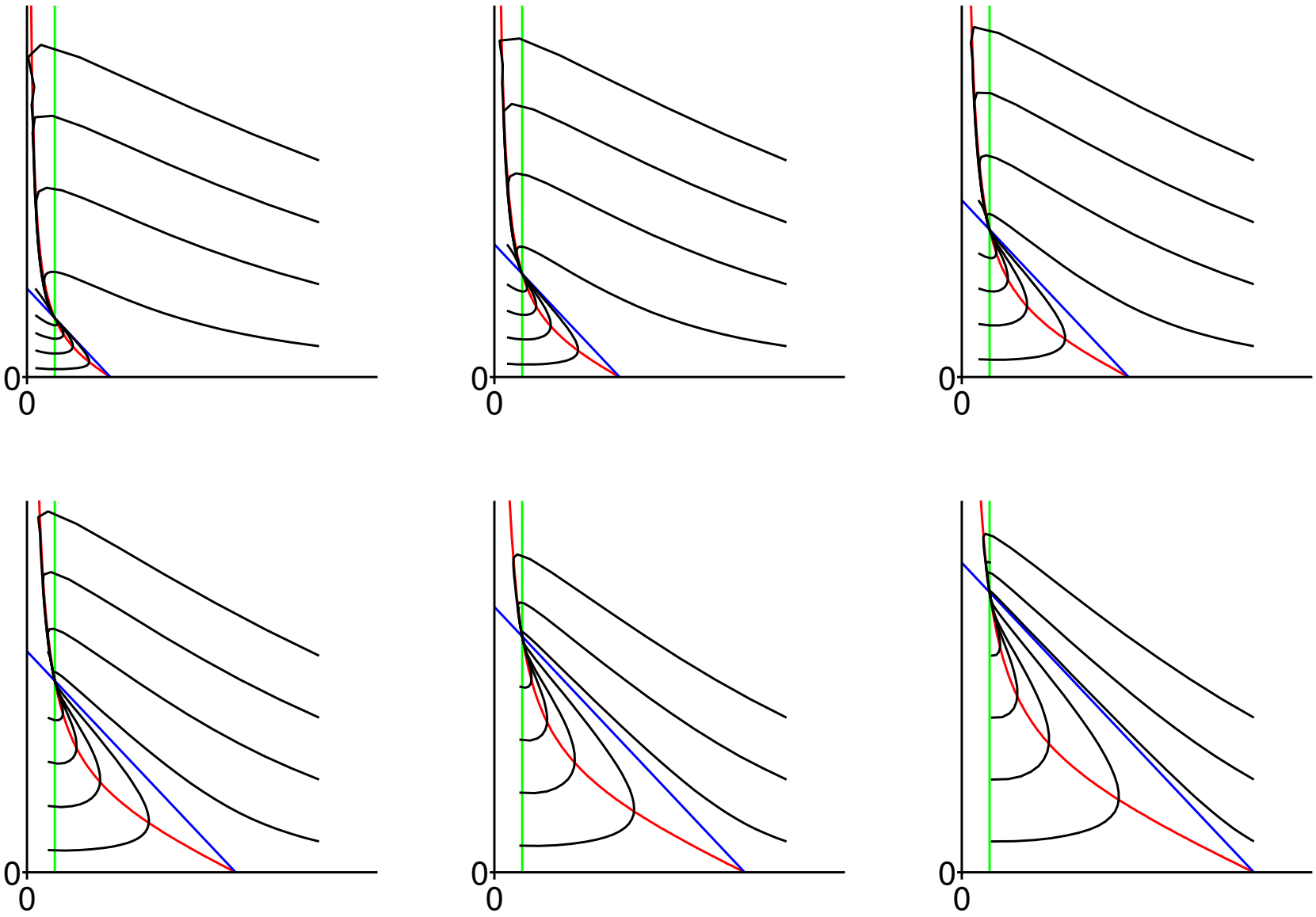
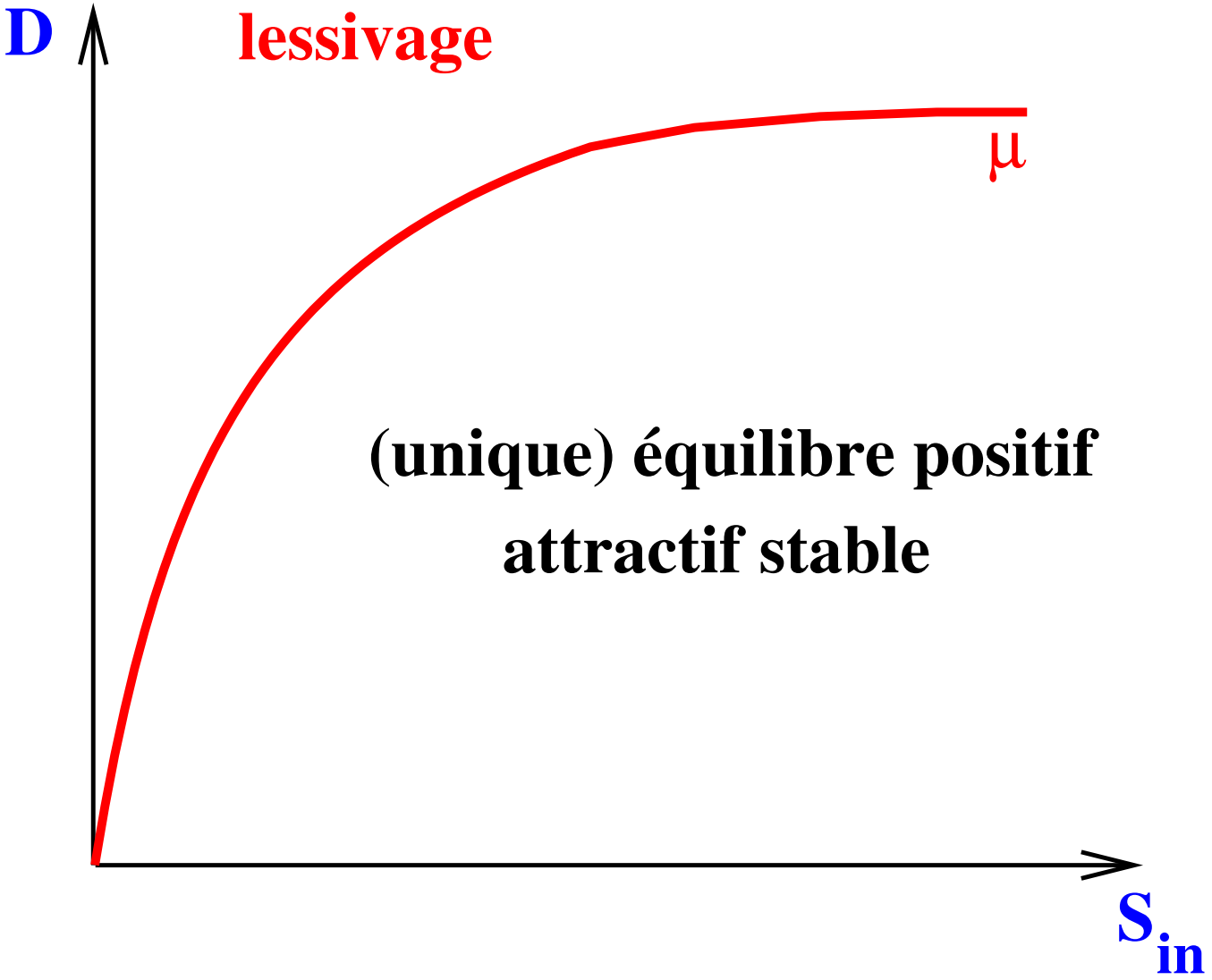


Diagramme opératoire



Critiques du modèle de Monod

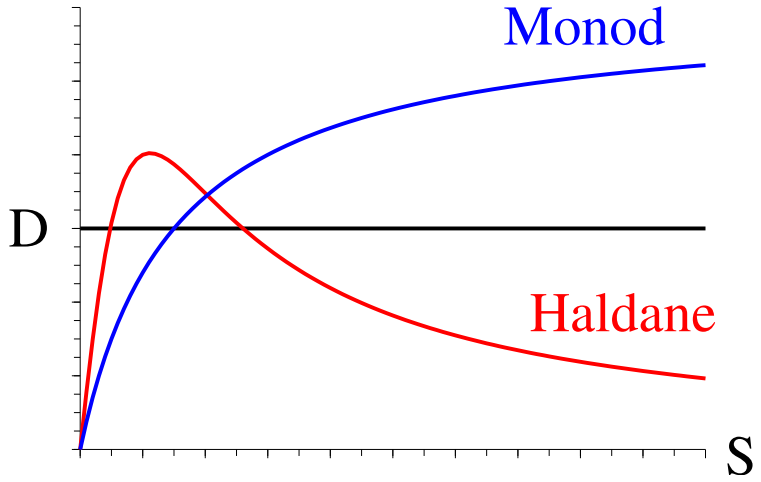
1. La croissance spécifique $\mu(\cdot)$ est impactée par des concentrations en biomasse élévées.
   - Modèle de Contois (1959) : $\boxed{\mu(S, X) = \frac{\mu_{max} S}{K X + S}}$

2. De fortes concentrations en substrat peuvent inhiber la croissance.
   - Equation d'Haldane (1930) : $\boxed{\mu(S) = \frac{\bar{\mu} S}{K + S + S^2/K_i}}$

Le modèle d'Andrews (1968)

À la place de la loi de Monod : $\mu(s) = \dfrac{\mu_{\max} s}{K + s}$,
on considère l'équation d'Haldane :

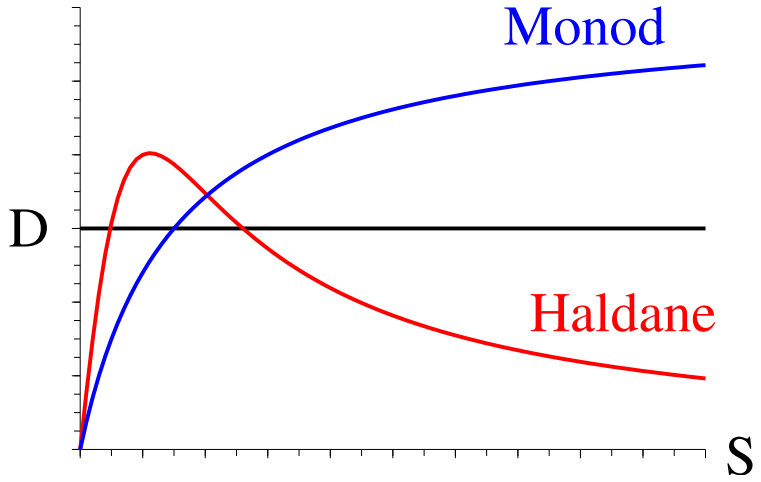
$$\boxed{\mu(s) = \frac{\bar{\mu} s}{K + s + s^2/K_i}}$$



Le modèle d'Andrews (1968)

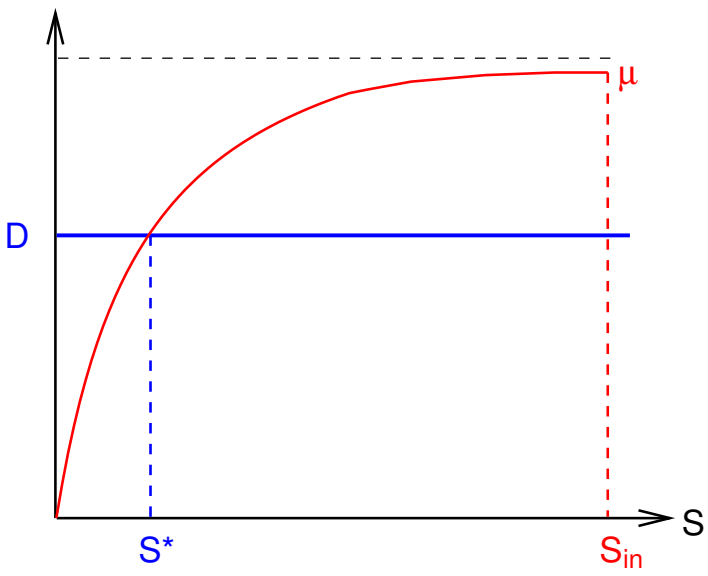
À la place de la loi de Monod : $\mu(s) = \dfrac{\mu_{\max} s}{K + s}$,
on considère l'équation d'Haldane :

$$\boxed{\mu(s) = \frac{\bar{\mu} s}{K + s + s^2/K_i}}$$

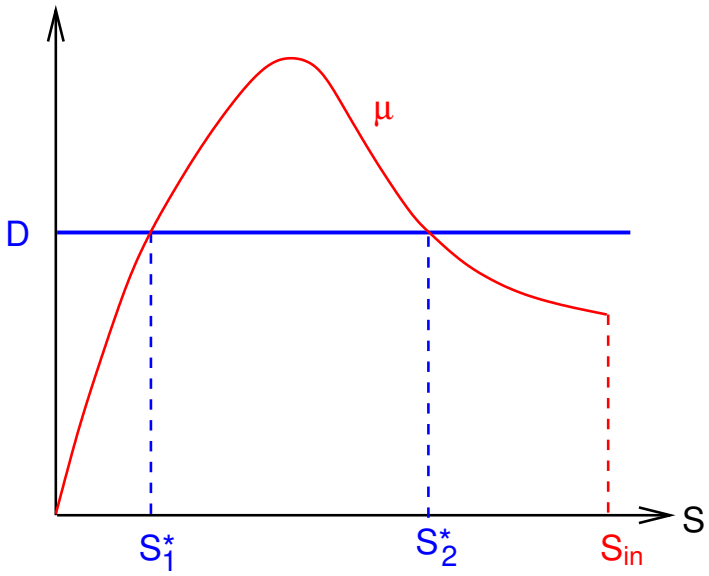


Remarque : $K_i = +\infty$ correspond à la loi de Monod.

Détermination des équilibres



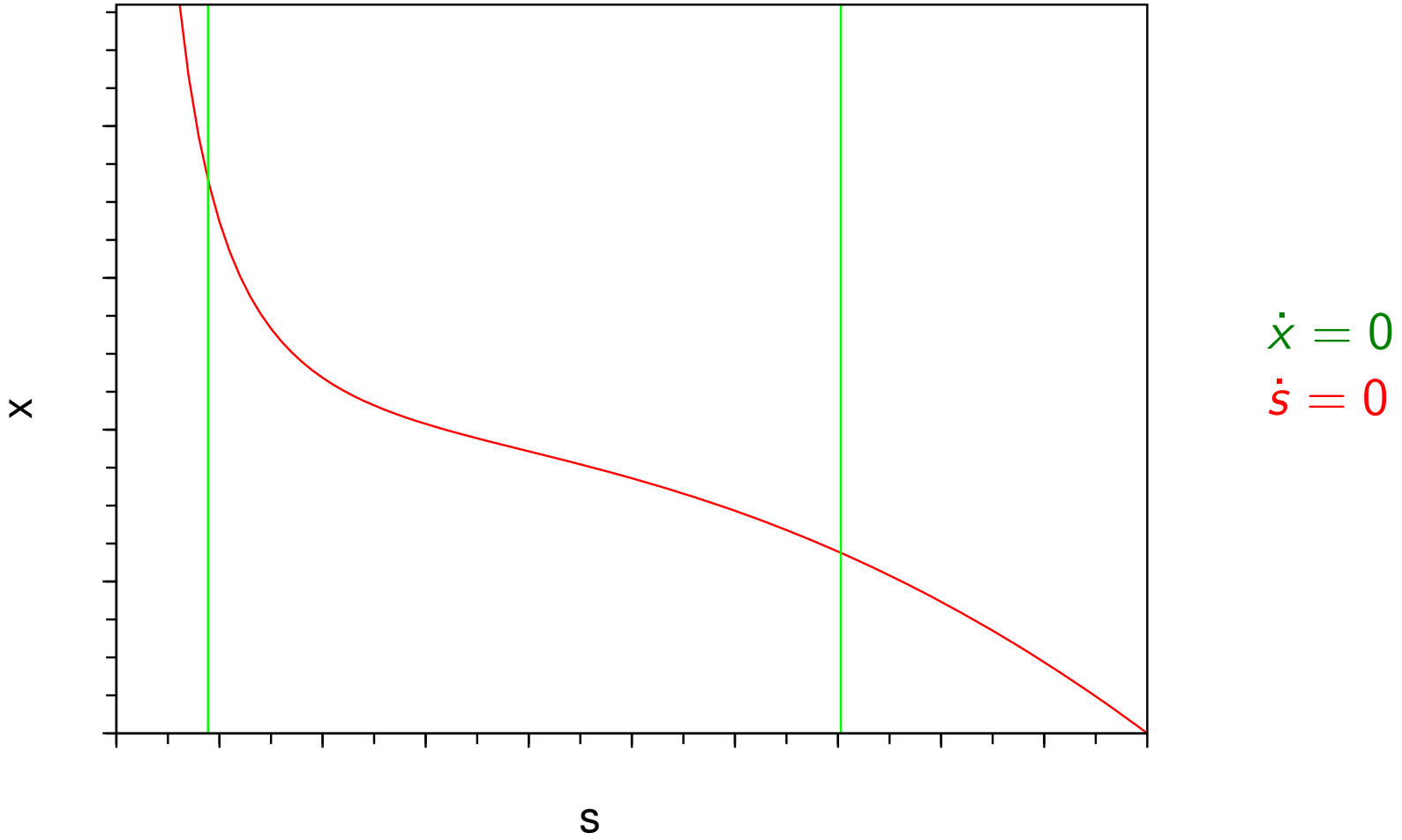
croissance monotone



croissance non monotone

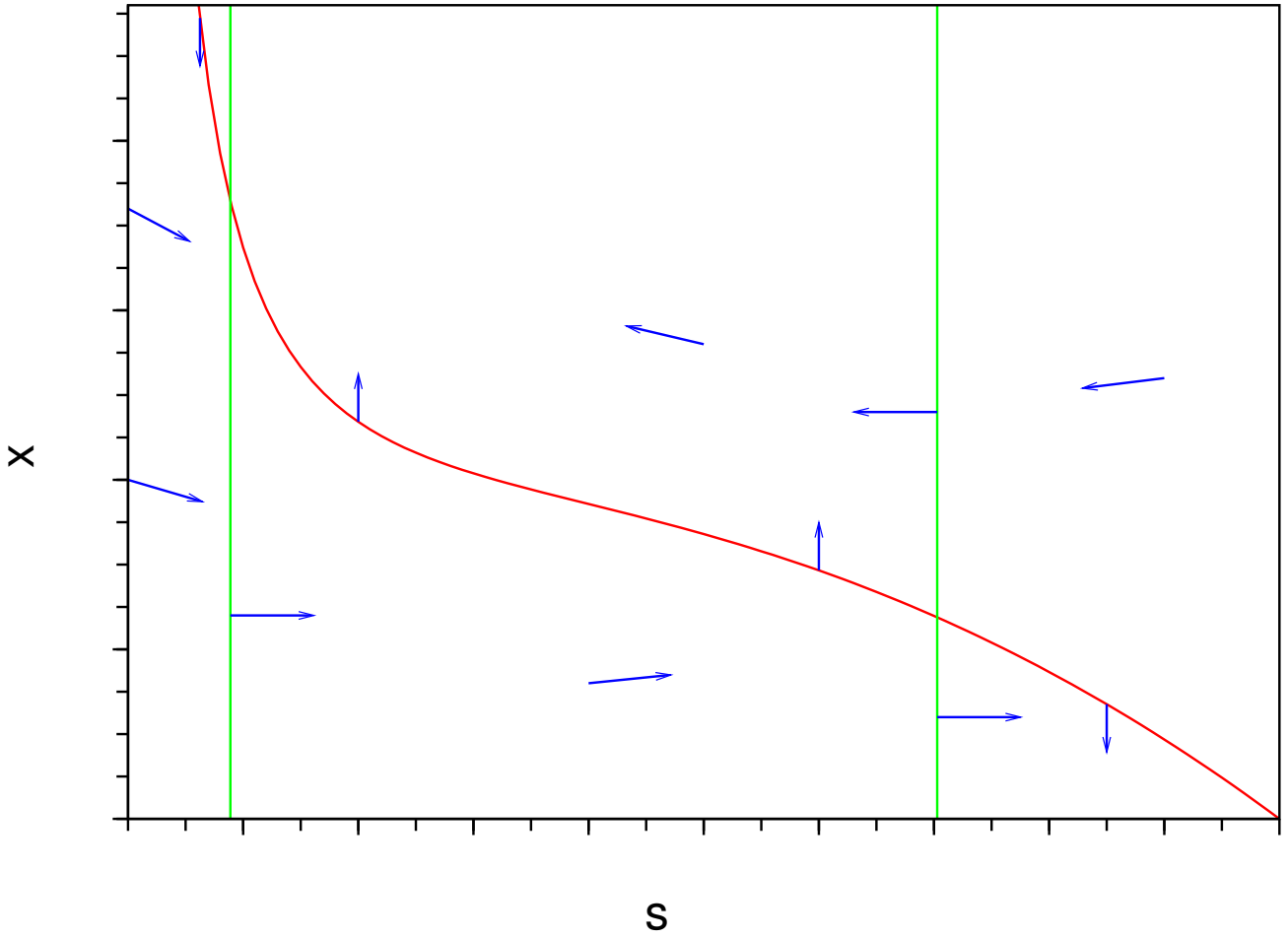
Isoclines

$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$



Champ de vecteurs

$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$

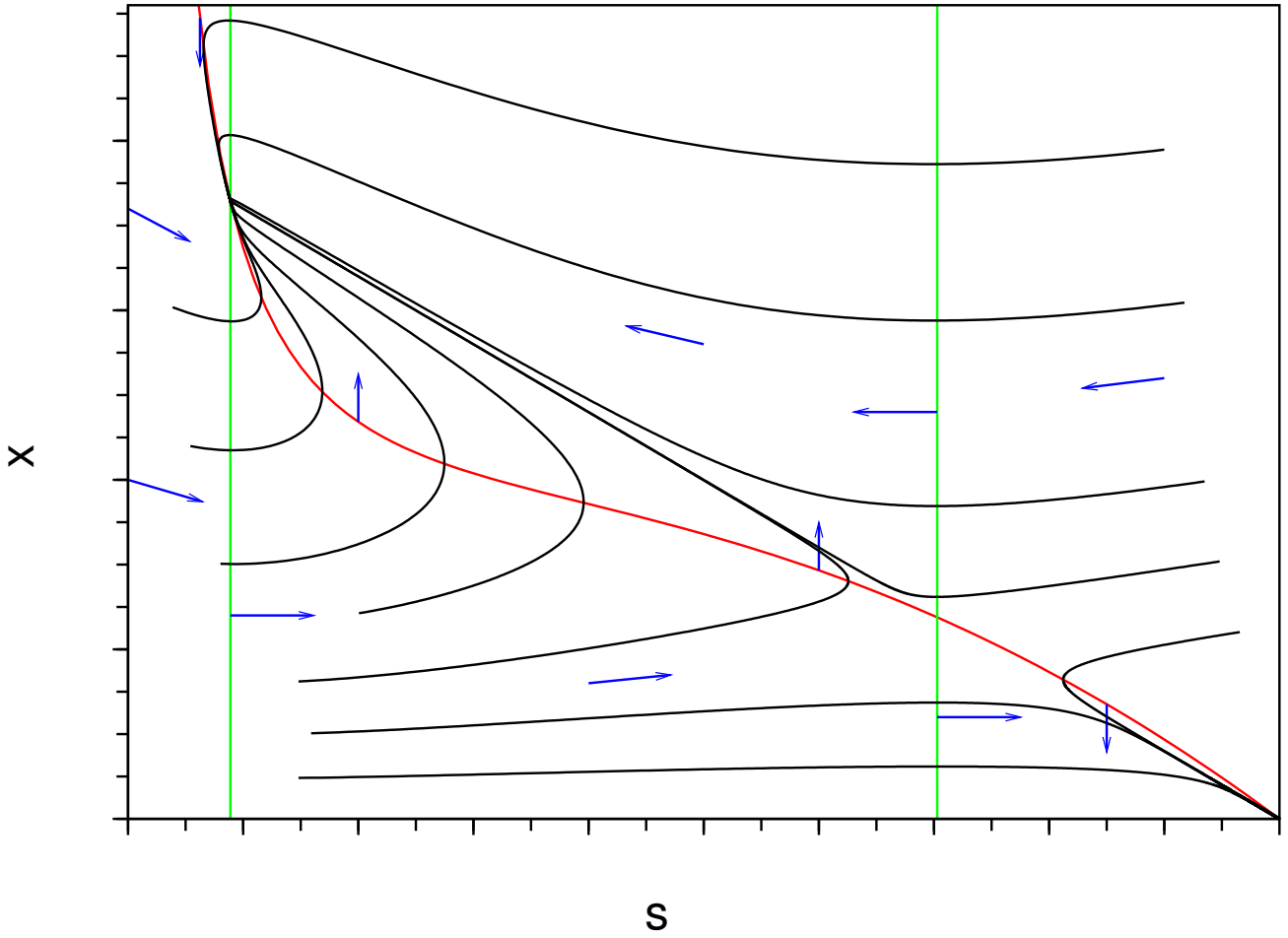


$\dot{x} = 0$

$\dot{s} = 0$

Portrait de phase

$$\dot{s} = -\mu(s)x + D(s_{in} - s)$$
$$\dot{x} = \mu(s)x - Dx$$



$\dot{x} = 0$

$\dot{s} = 0$

Analyse mathématique de la stabilité

$$\begin{aligned} \dot{s} &= -\mu(s)x + D(s_{in} - s) \\ \dot{x} &= \mu(s)x - Dx \end{aligned}$$

$\rightarrow$ on écrit la matrice Jacobienne :

$$J = \begin{bmatrix} -\mu'(s)x - D & -\mu(s) \\ \\ \mu'(s)x & \mu(x) - D \end{bmatrix}$$

Analyse mathématique de la stabilité

- équilibre du lessaivge :

$$J = \begin{bmatrix} -D & -\mu(s_{in}) \\ 0 & \mu(s_{in}) - D \end{bmatrix}$$

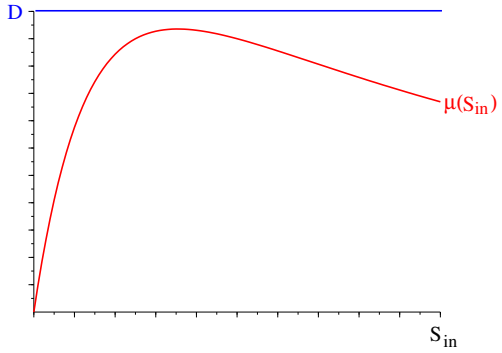
valeurs propres :
$-D$,
$\mu(s_{in}) - D$

- équilibre positif :

$$J = \begin{bmatrix} -\mu'(s^\star)x^\star - D & -D \\ \mu'(s^\star)x^\star & 0 \end{bmatrix}$$

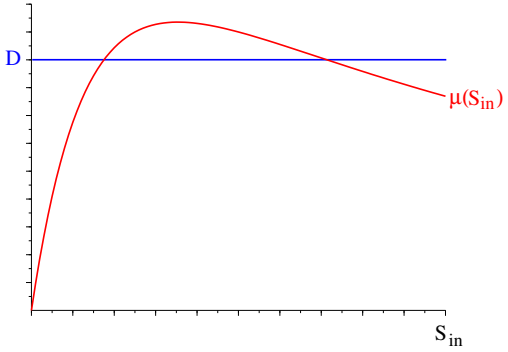
valeurs propres :
$-D$,
$-\mu'(s^\star)x^\star$

Résumé



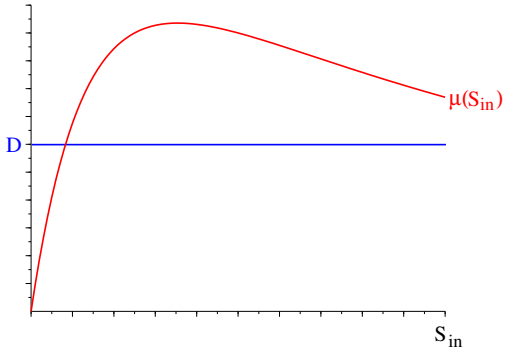
$$D > \max_{s \in [0, S_{in}]} \mu(s)$$

1 équilibre : lessivage



$$\mu(s_{in}) < D < \max_{s \in [0, S_{in}]} \mu(s)$$

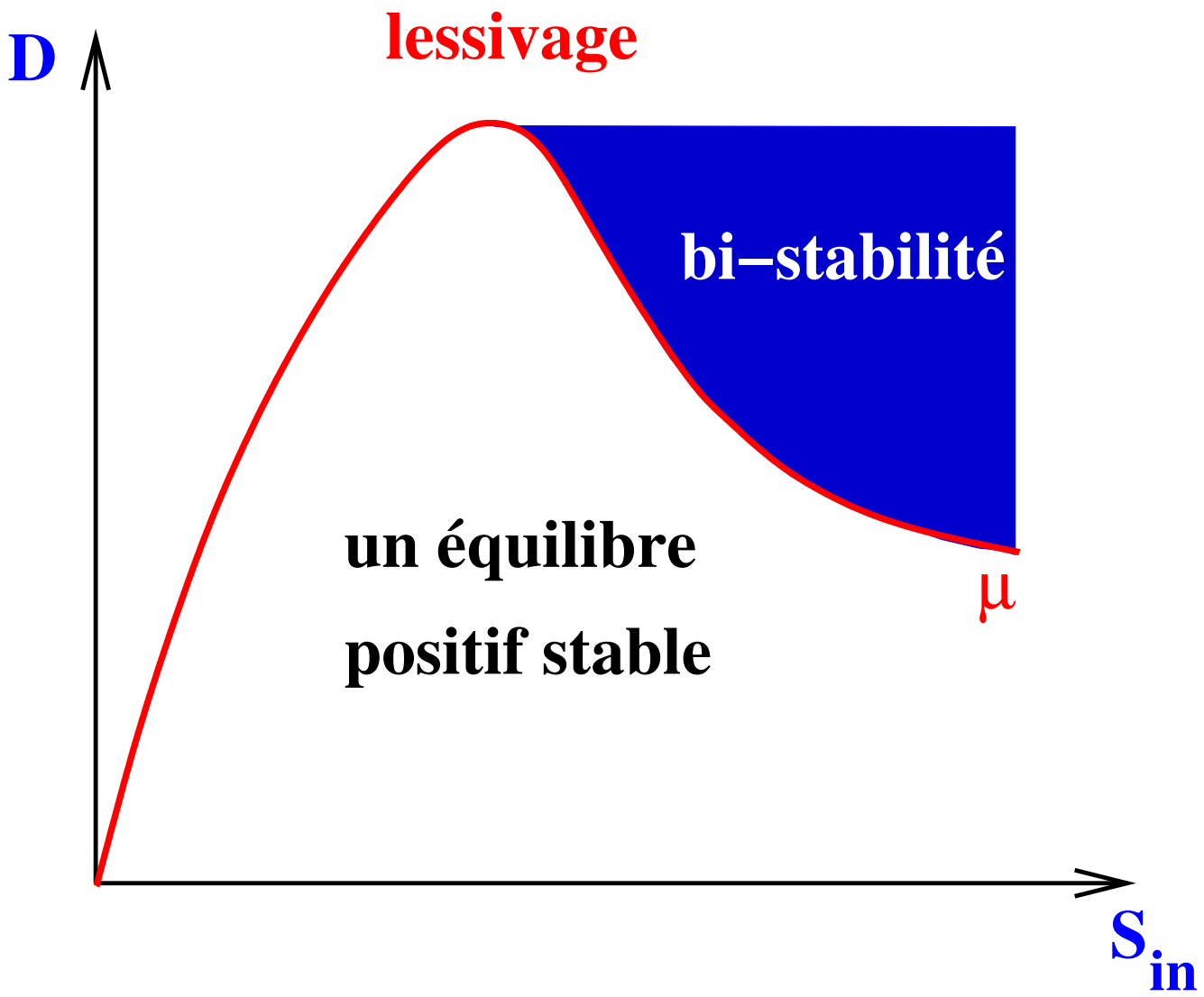
3 équilibres : bi-stabilité



$$D < \mu(s_{in})$$

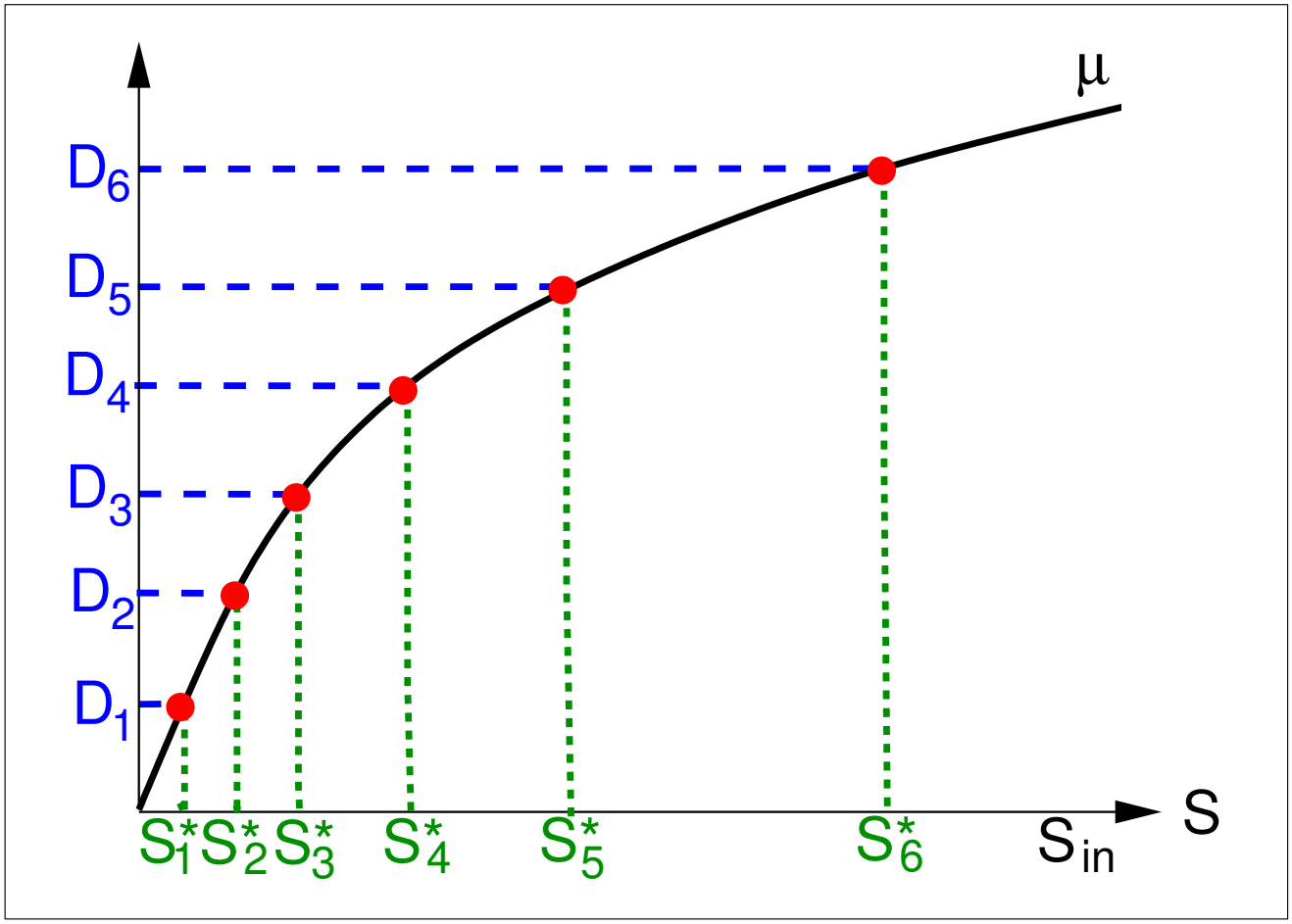
2 équilibres : stabilité

Diagramme opératoire



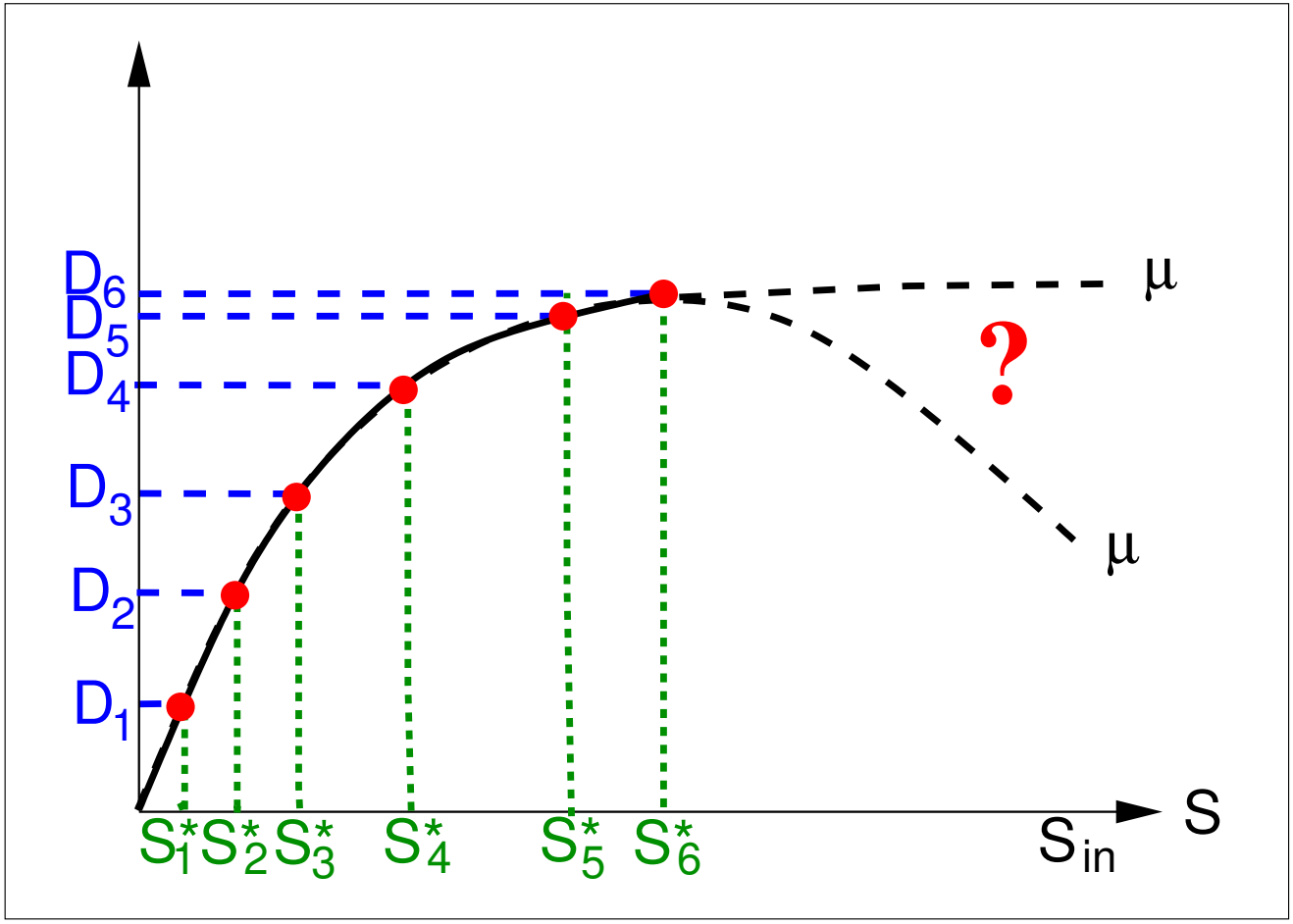
À propos d'identification expérimentale

On choisit un taux de dilution D_i et on "attend" l'équilibre $s_i^\star$:



À propos d'dentification expérimentale

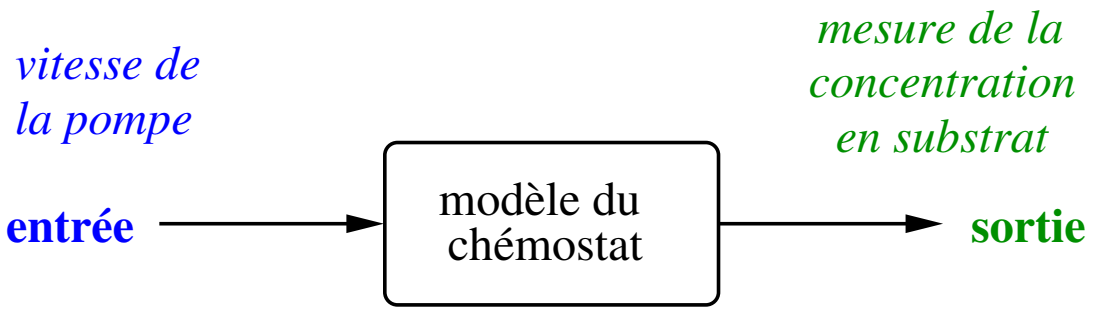
On choisit un taux de dilution D_i et on "attend" l'équilibre $s_i^\star$:



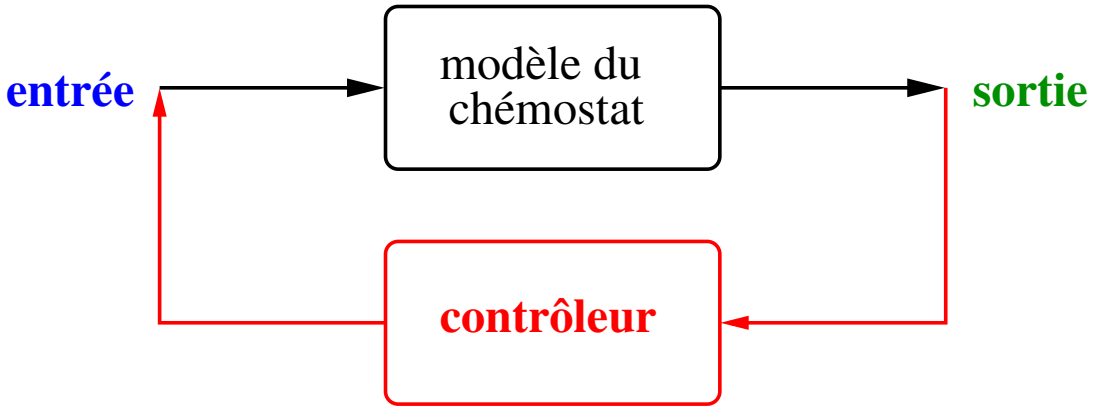
Changement de point de vue

On choisit une valeur de référence $s^\star$ et cherche à **stabiliser** le chémostat en $s = s^\star$ **en ajustant le taux de dilution** D.

boucle ouverte :



boucle fermée :



Contrôleur adaptatif

Soit une valeur $\bar{D}$ de taux de dilution,

- *Etape 1 :* Le contrôleur

$$D(\bar{D}, s) = \bar{D} + K_1(s^\star - s)$$

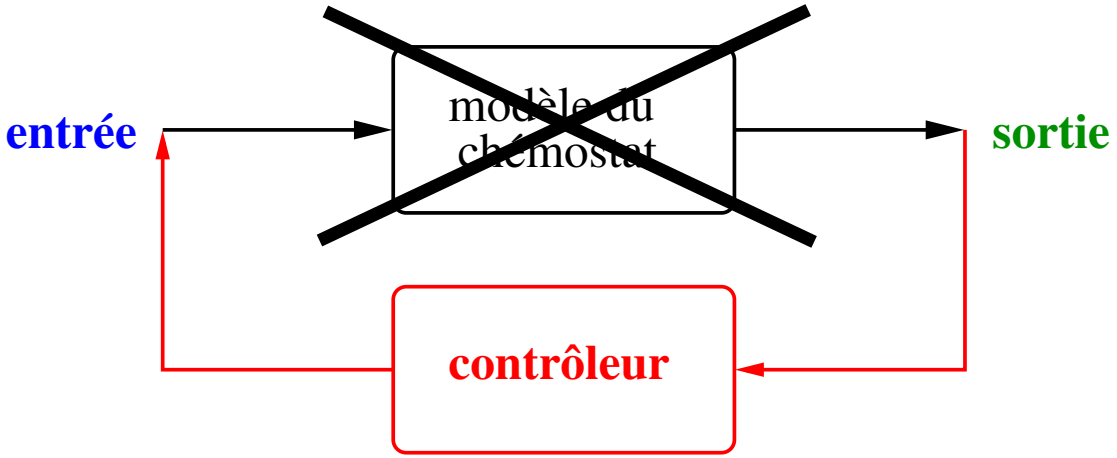
avec $\mathbf{K_1} > \mathbf{0}$ suffisamment grand stabilise le chémostat en $\bar{s}$ tel que $\mu(\bar{s}) = D(\bar{D}, \bar{s})$.

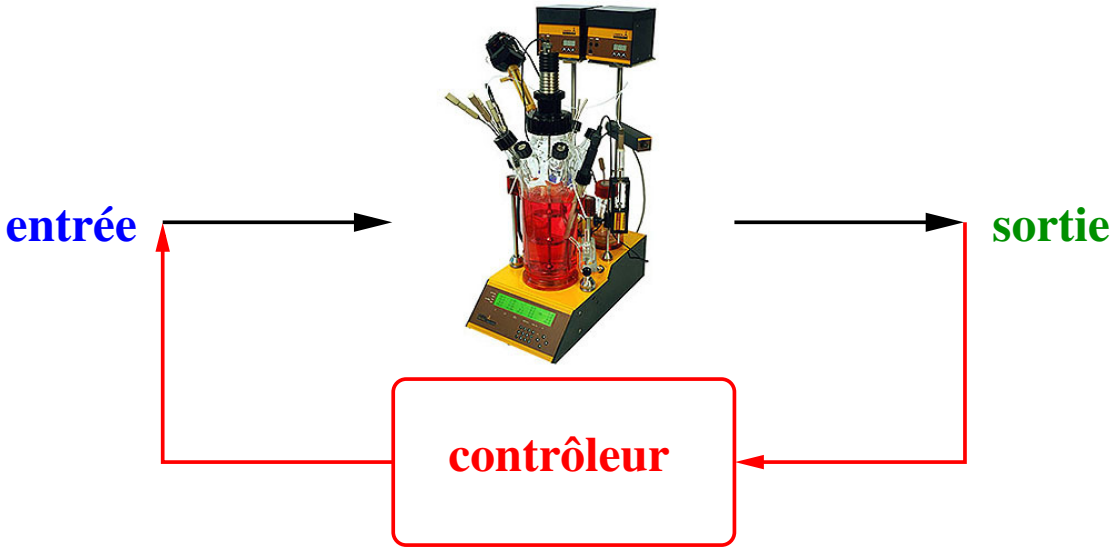
- *Etape 2 :* L'adaptation de la valeur de $\bar{D}$:

$$\frac{d\bar{D}}{dt} = K_2(s^\star - s)$$

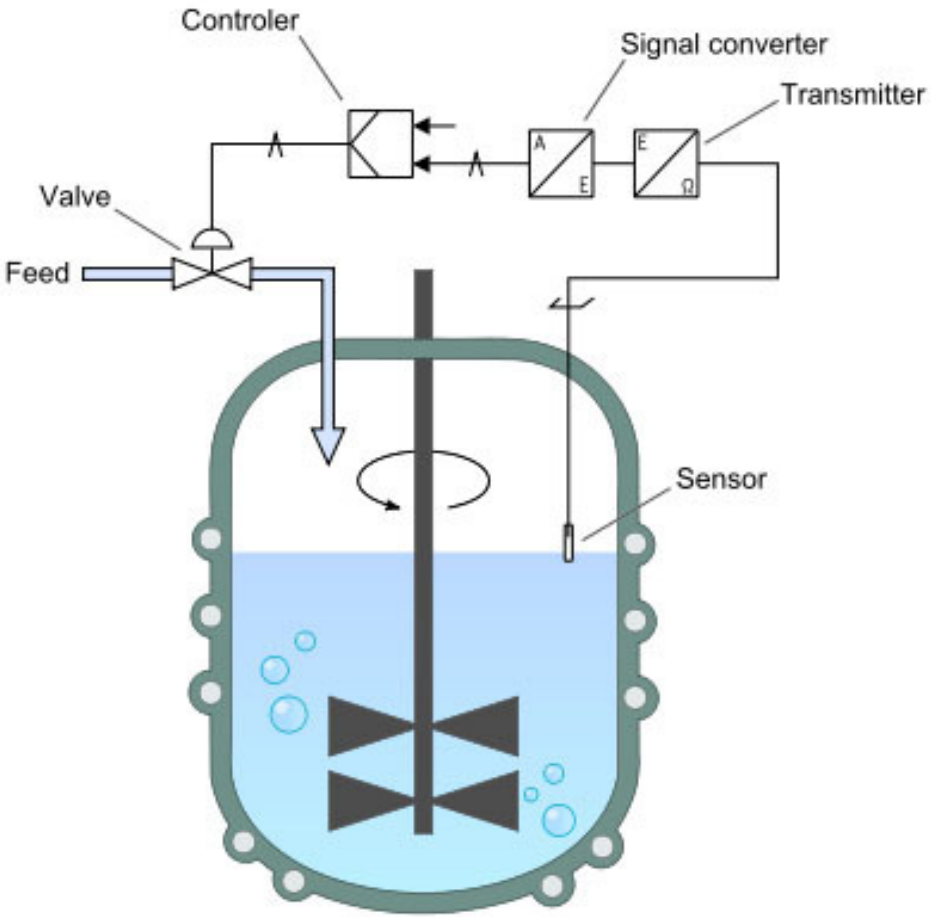
avec $\mathbf{K_2} > \mathbf{0}$ conduit à $\lim_{t \to +\infty} \bar{D}(t) = D^\star = \mu(s^\star)$.

Si tout va bien...



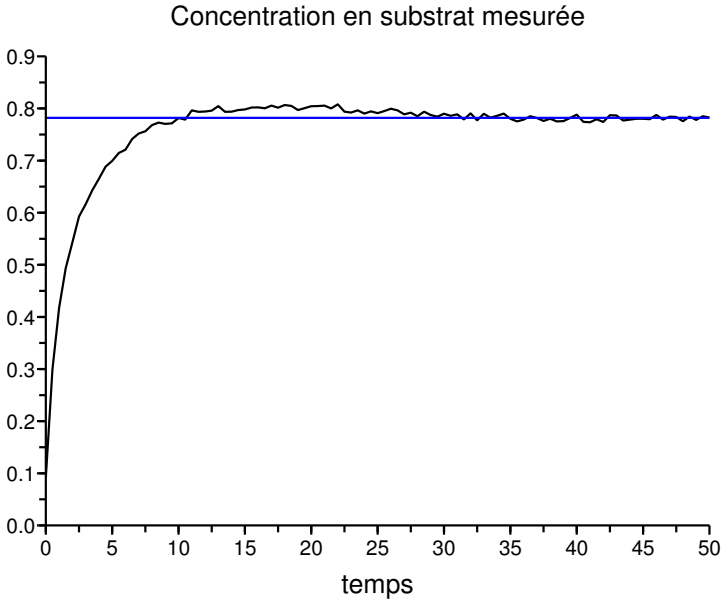


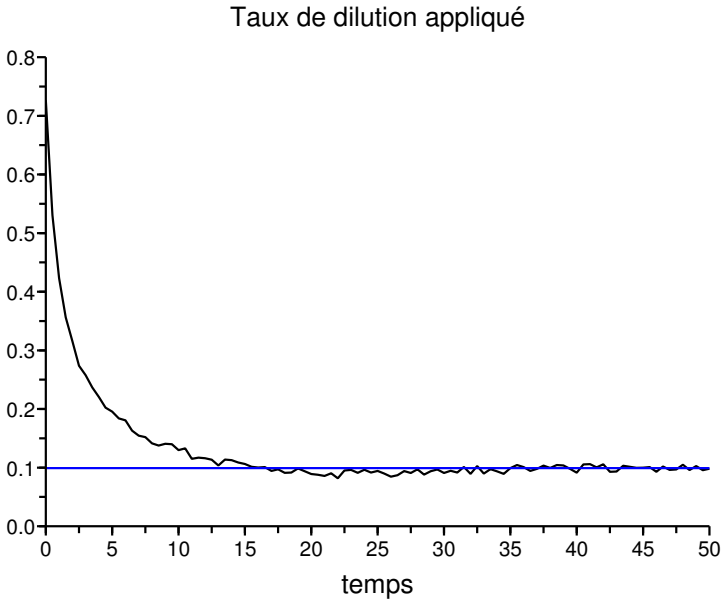
L'auxostat



Exemple : P. Gostomski, M. Muhlemann, Y.H. Lin, R. Mormino and H. Bungay. *Auxostats for continuous culture research.* Journal of Biotechnology 37 (1994), pp. 167-177

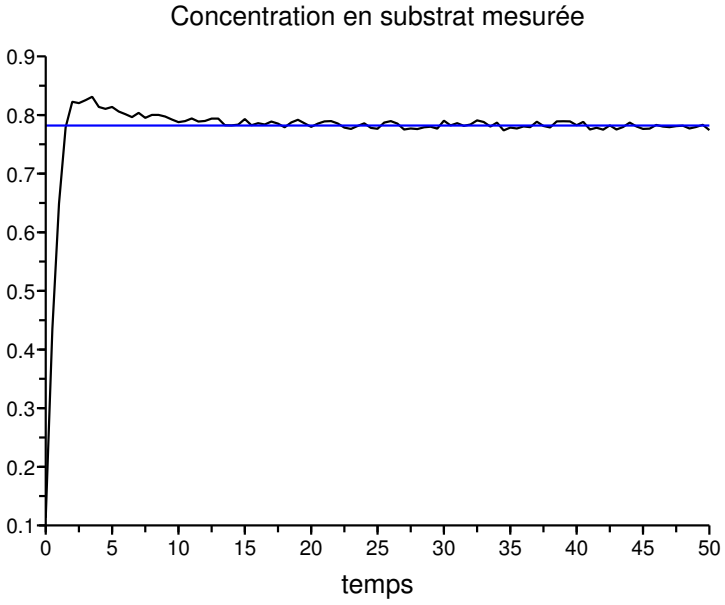
Simulations avec bruit de mesure

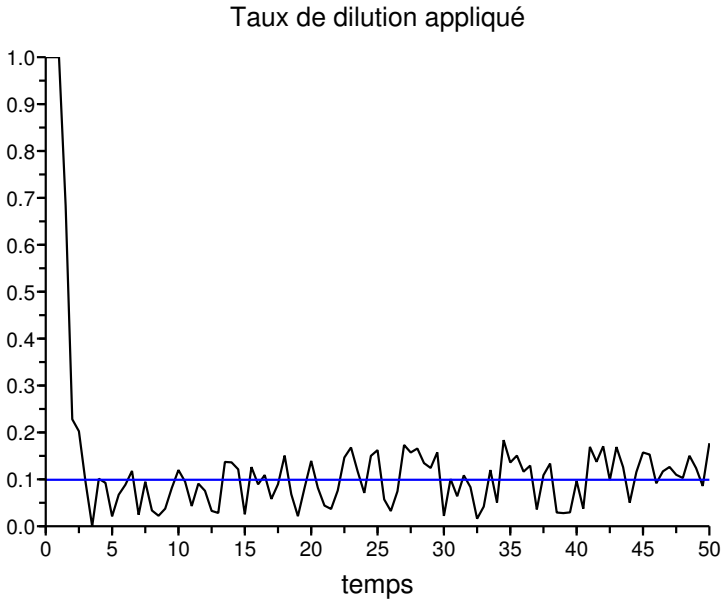




$$K_1 = 1, \; K_2 = 1$$

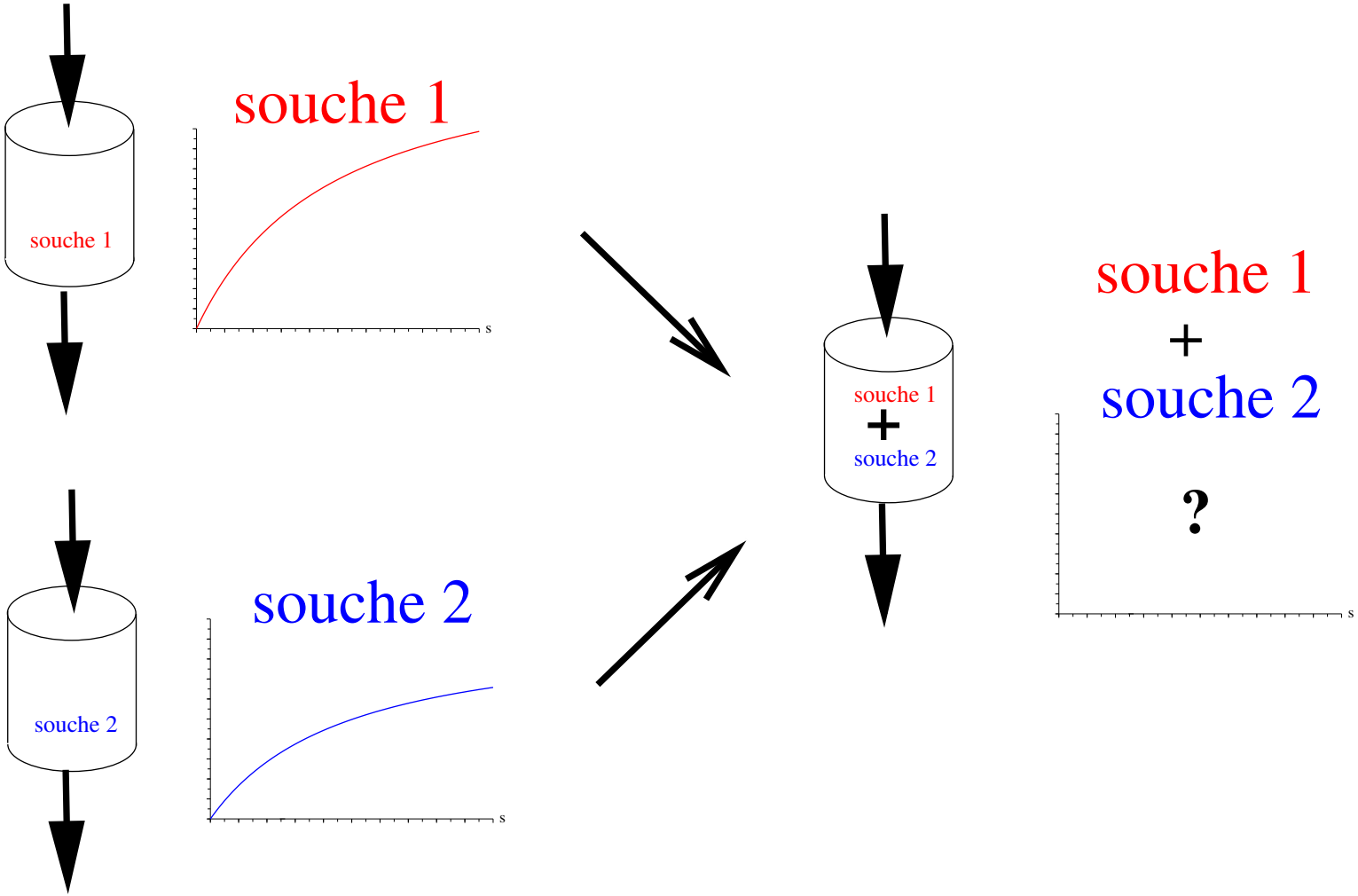
Simulations avec bruit de mesure





$$K_1 = 10, \; K_2 = 10$$

Compétition entre souches



Le modèle du chémostat à deux souches

$$
\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}
$$

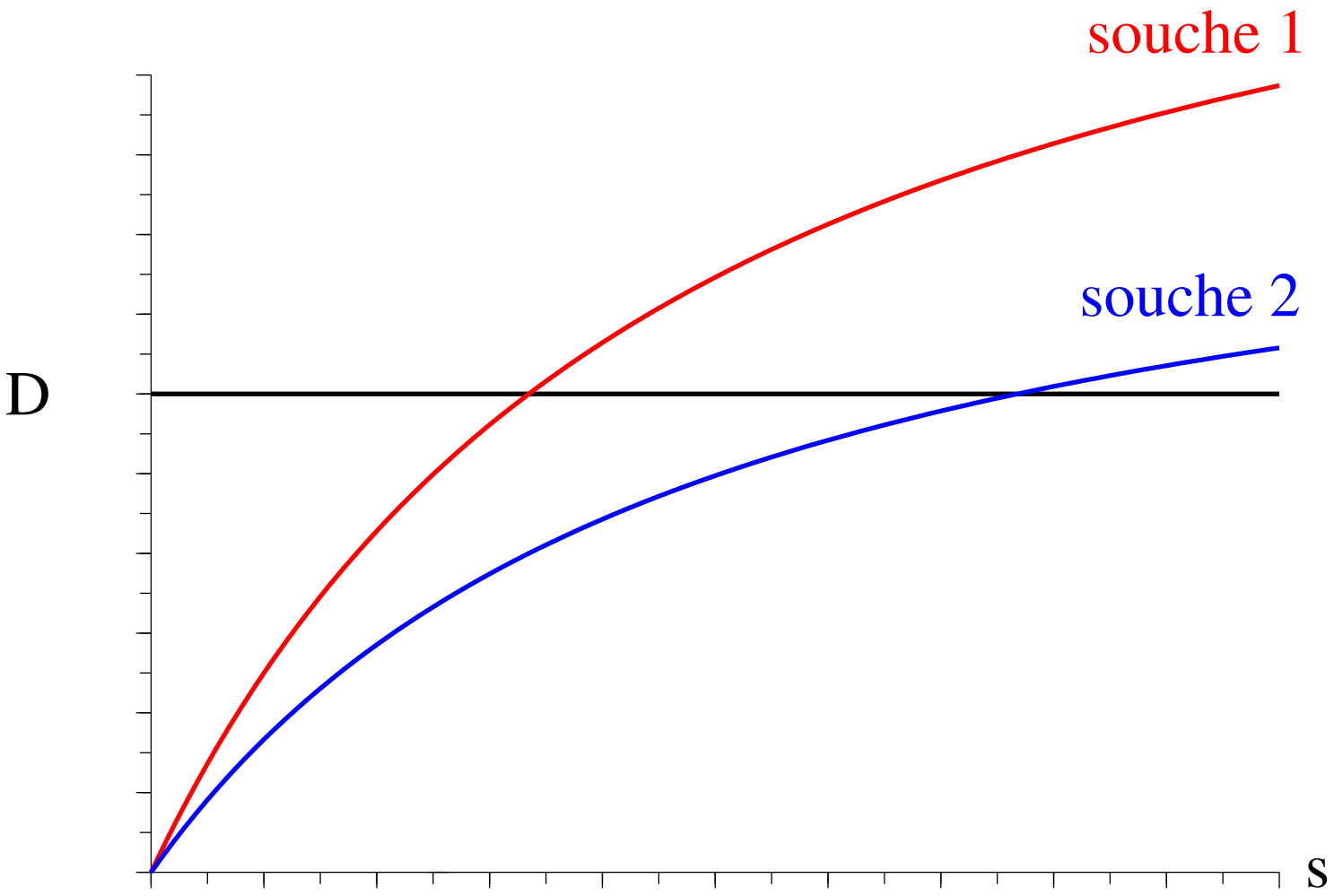
Le modèle du chémostat à deux souches

$$
\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}
$$

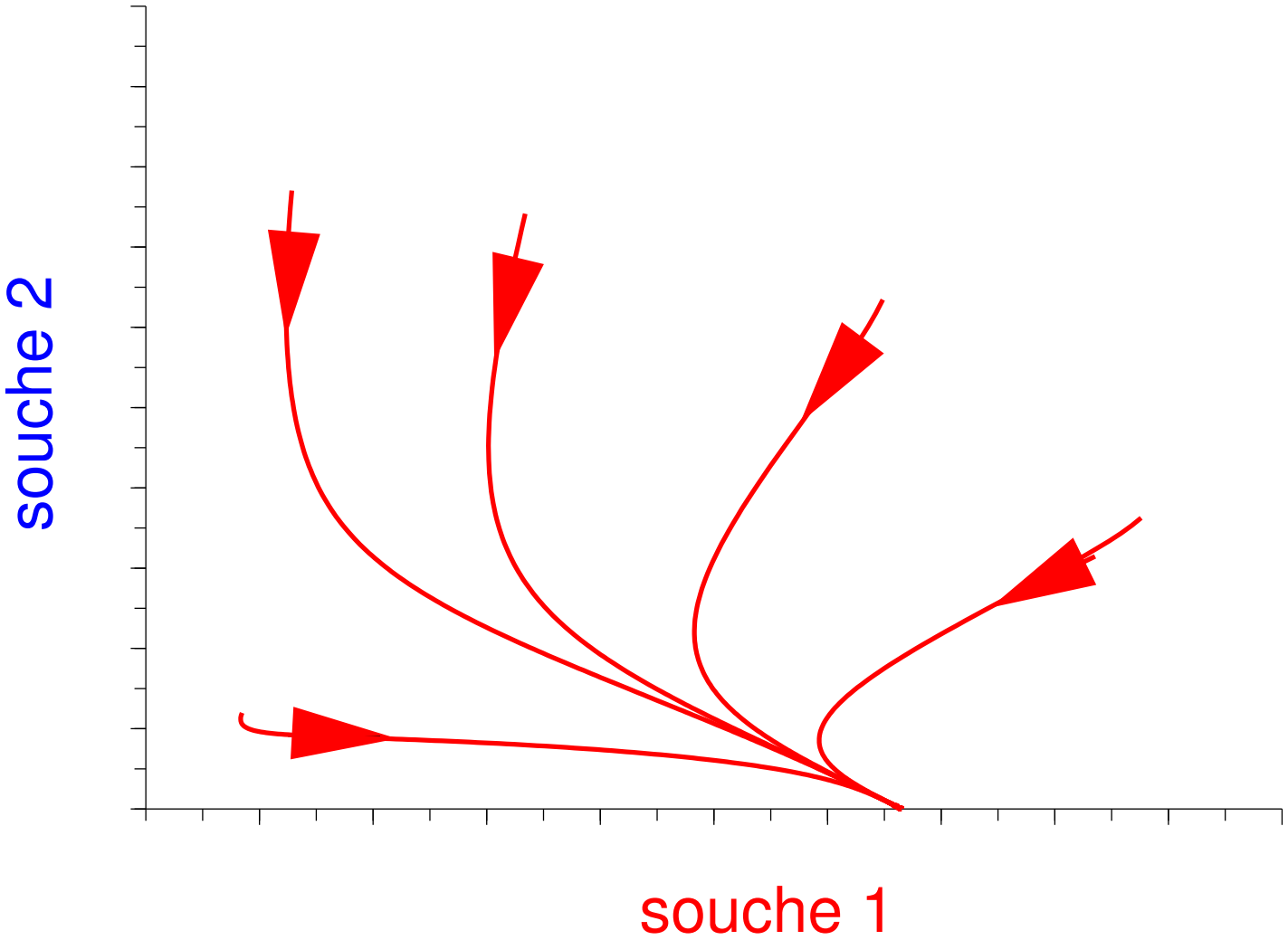
Equilibres :

lessivage	souche 1 seule	souche 2 seule	coexistence
$\begin{bmatrix} s_{in} \\ 0 \\ 0 \end{bmatrix}$	$\begin{bmatrix} s_1^\star \\ s_{in} - s_1^\star \\ 0 \end{bmatrix}$	$\begin{bmatrix} s_2^\star \\ 0 \\ s_{in} - s_2^\star \end{bmatrix}$	implique $\mu_1(s^\star) = \mu_2(s^\star) = D$ condition non générique !

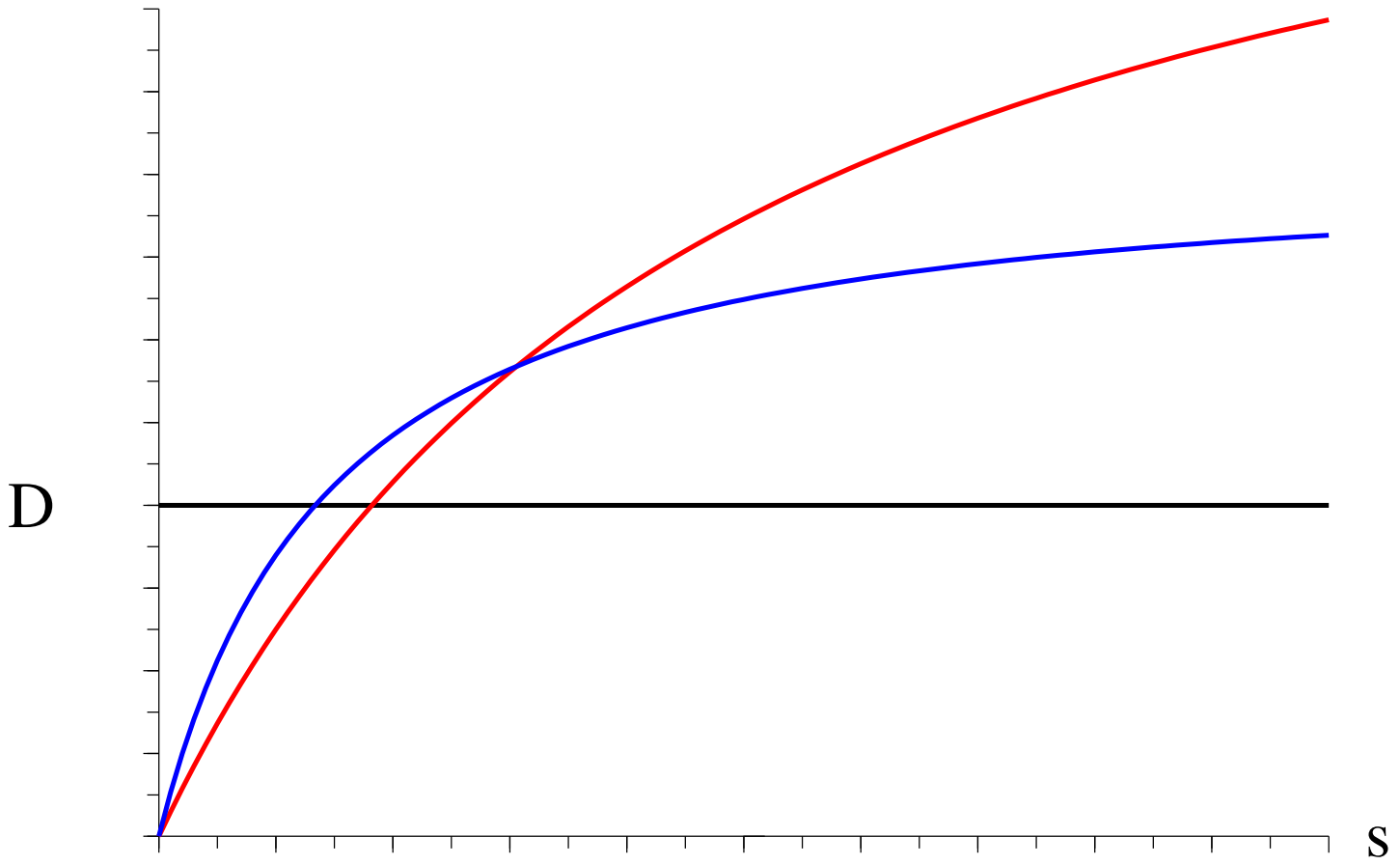
Compétition entre souches



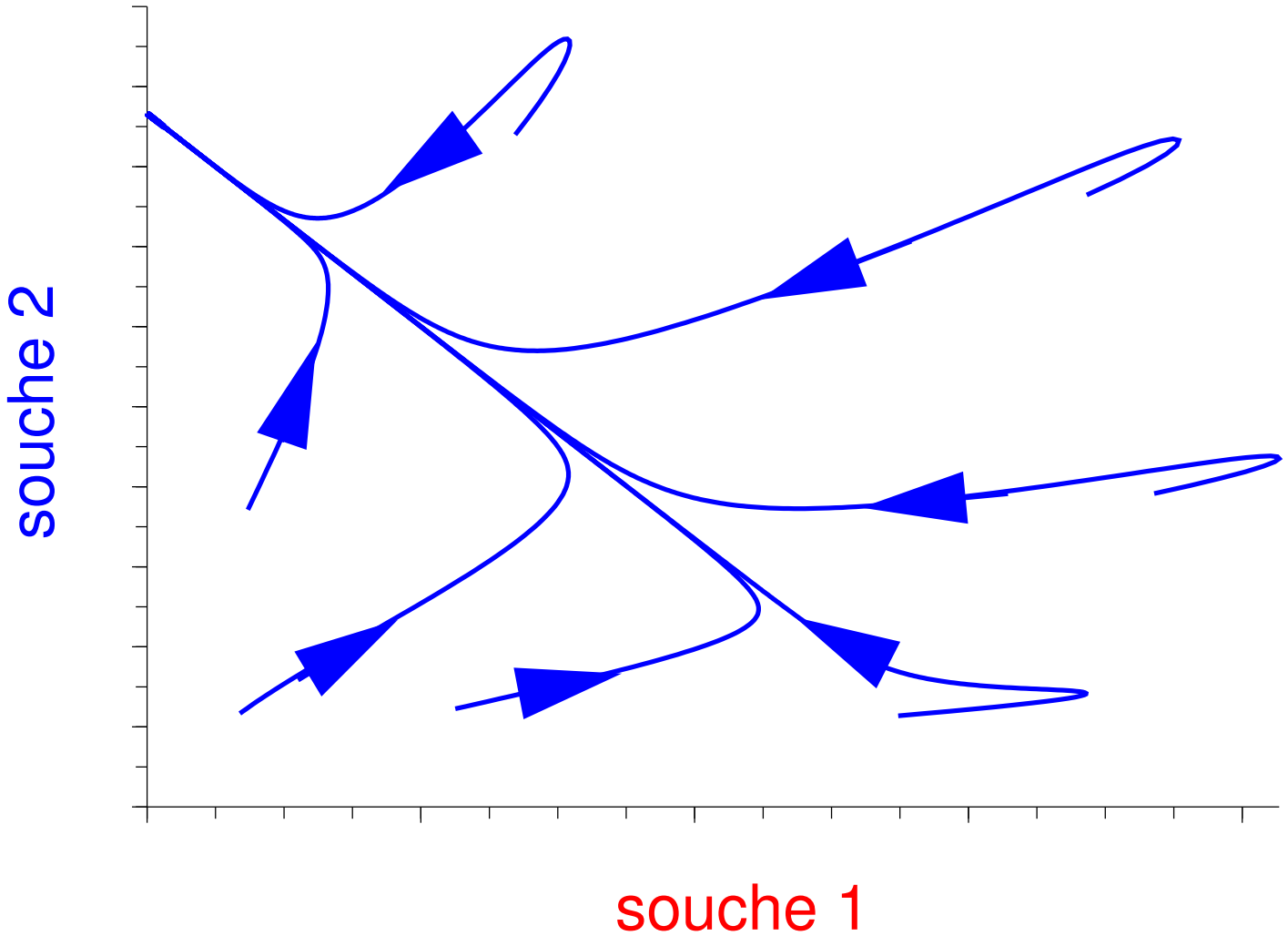
Simulations



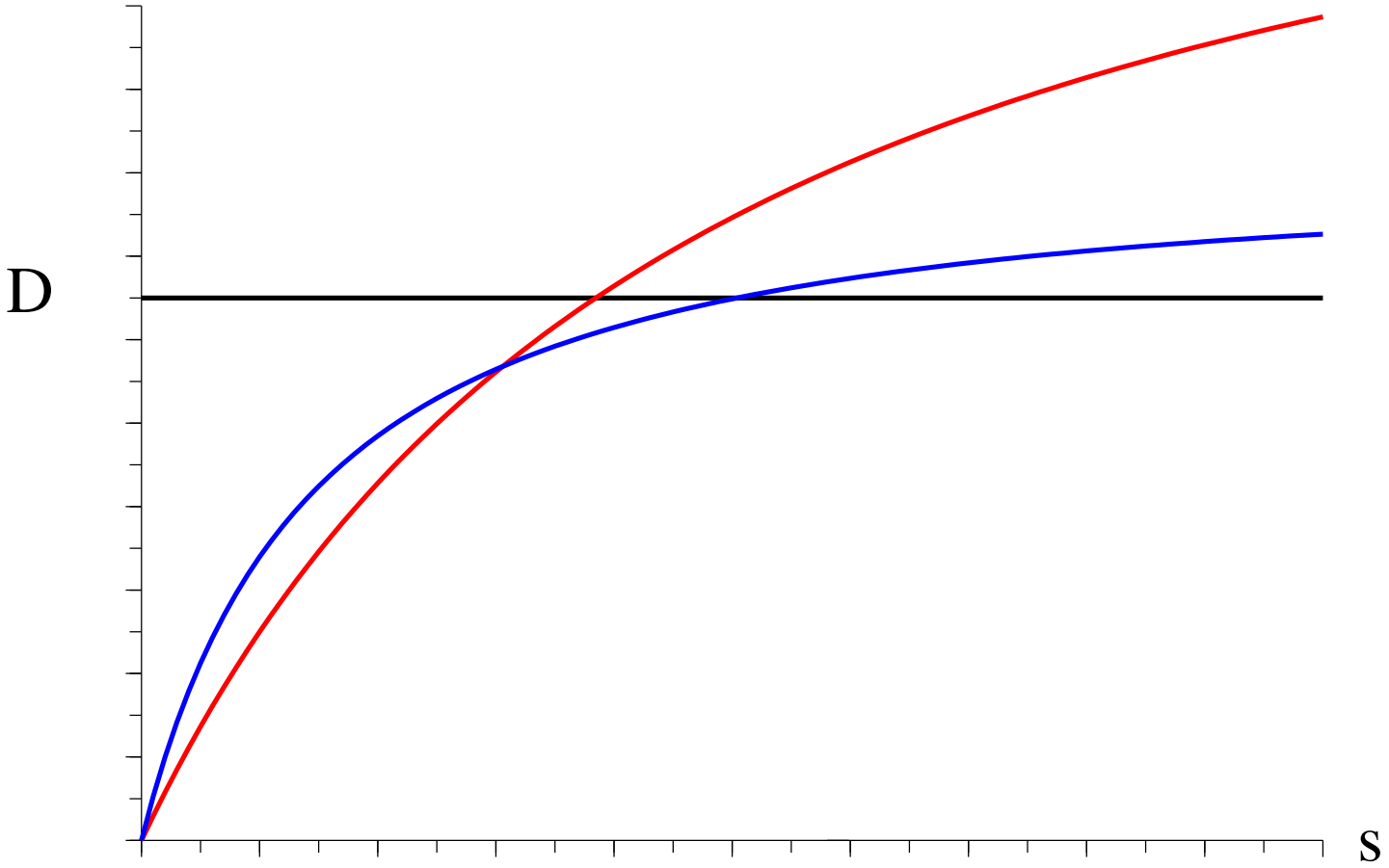
Compétition entre souches



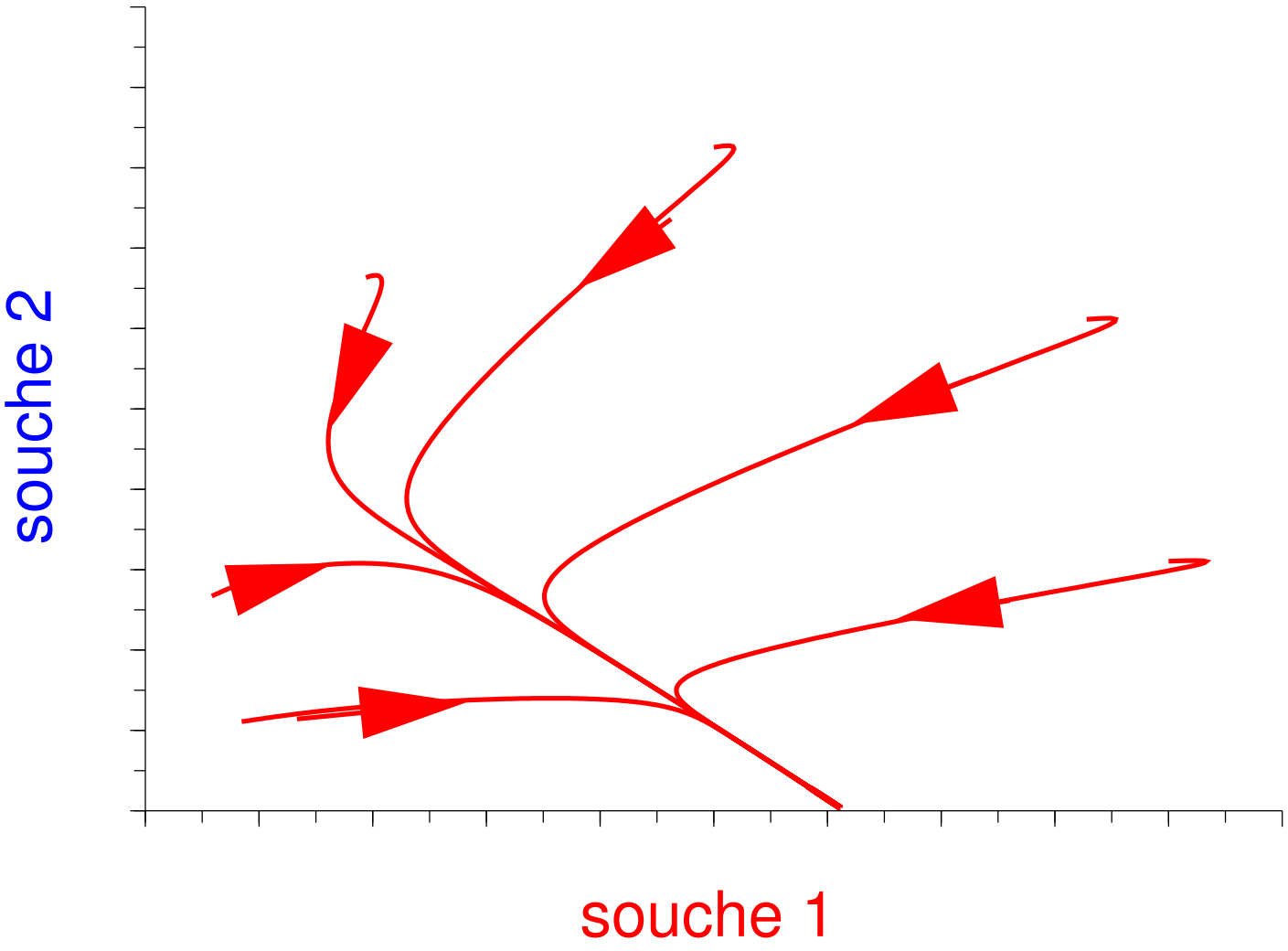
Simulations



Compétition entre souches



Simulations



Analyse mathématique de la stabilité

$$\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}$$

$\rightarrow$ on écrite la matrice Jacobienne :

$$J = \begin{bmatrix} -\mu_1'(s)x_1 - \mu_2'(s)x_2 - D & -\mu_1(s) & -\mu_2(s) \\ \mu_1'(s)x_1 & \mu_1(s) - D & 0 \\ \mu_2'(s)x_2 & 0 & \mu_2(s) - D \end{bmatrix}$$

Analyse mathématique de la stabilité

- lessivage :

$$J = \begin{bmatrix} -D & -\mu_1(s_{in}) & -\mu_2(s_{in}) \\ 0 & \mu_1(s_{in}) - D & 0 \\ 0 & 0 & \mu_2(s_{in}) - D \end{bmatrix}$$

valeurs propres :
$-D$,
$\mu_1(s_{in}) - D$,
$\mu_2(s_{in}) - D$

- souche 1 seule :

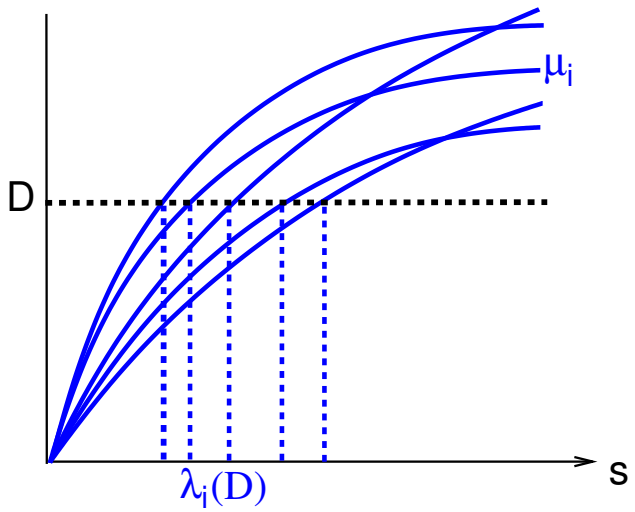
$$J = \begin{bmatrix} -\mu_1'(s_1^\star)x_1^\star - D & -D & -\mu_2(s_1^\star) \\ \mu_1'(s_1^\star)x_1^\star & 0 & 0 \\ 0 & 0 & \mu_2(s_1^\star) - D \end{bmatrix}$$

valeurs propres :
$\mu_2(s_1^\star) - D$,
$-D$,
$-\mu_1'(s_1^\star)x_1^\star$

Le Principe d'Exclusion Compétitive

Supposons les $\mu_i(\cdot)$ croissantes

Soit $\Lambda_i(D) = \{s \geq 0 \,|\, \mu_i(s) > D\}$
et le seuil de rentabilité :
$\lambda_i(D) = \inf \Lambda_i(D)$



Principe.

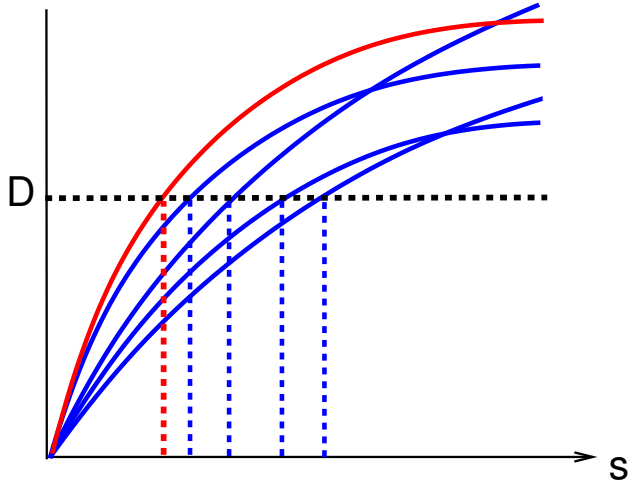
- Génériquement, il y a au plus une souche à l'équilibre.
- L'équilibre (s'il existe) pour lequel la souche possède le *plus petit* seuil de rentabilité et l'unique équilibre attractif.

cf *Hsu, Hubbell & Waltman. A mathematical theory of single-nutrient competition in continuous cultures of micro-organisms.* SIAM J. Appl. Math. 1977.

Le Principe d'Exclusion Compétitive

Supposons les $\mu_i(\cdot)$ croissantes

Soit $\Lambda_i(D) = \{s \geq 0 \,|\, \mu_i(s) > D\}$
et le seuil de rentabilité :
$\lambda_i(D) = \inf \Lambda_i(D)$



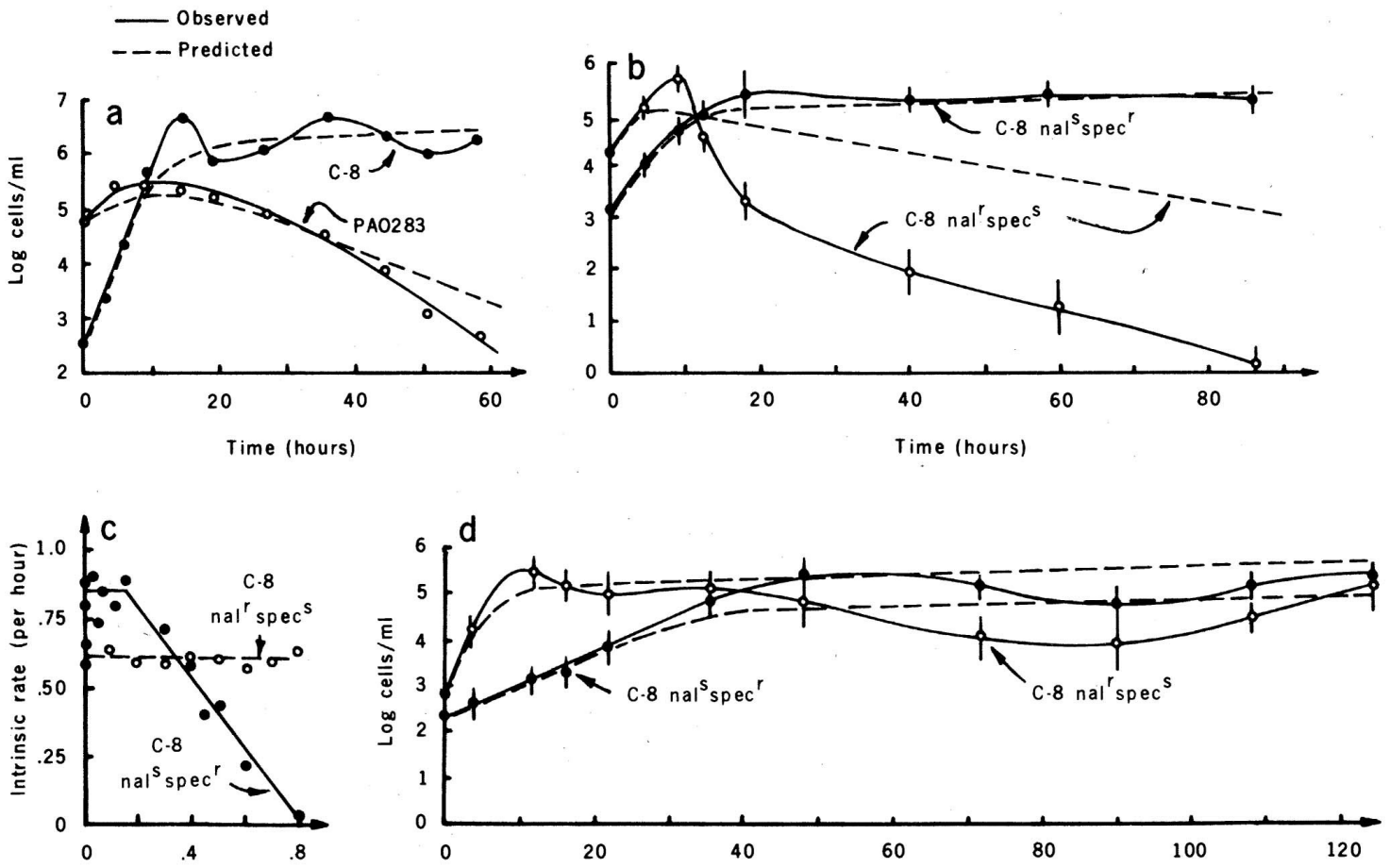
Principe.

- Génériquement, il y a au plus une souche à l'équilibre.
- L'équilibre (s'il existe) pour lequel la souche possède le *plus petit* seuil de rentabilité et l'unique équilibre attractif.

cf *Hsu, Hubbell & Waltman. A mathematical theory of single-nutrient competition in continuous cultures of micro-organisms.* SIAM J. Appl. Math. 1977.

Les expériences de Hansen et Hubbell

Science, 1980 : *"Single-Nutrient Microbial Competition : Qualitative Agreement between Experimental and Theoretically Forecast Outcomes"*



Modèle réduit

$$
\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}
$$

Modèle réduit

$$\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}$$

Soit $m = s + x_1 + x_2$, alors $\boxed{\frac{dm}{dt} = D(s_{in} - m)}$

$$\Rightarrow m(t) = s_{in} + (m(0) - s_{in})e^{-Dt} \underset{t \to +\infty}{\longrightarrow} s_{in}$$

Modèle réduit

$$\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}$$

Soit $m = s + x_1 + x_2$, alors $\boxed{\frac{dm}{dt} = D(s_{in} - m)}$

$$\Rightarrow m(t) = s_{in} + (m(0) - s_{in})e^{-Dt} \underset{t \to +\infty}{\longrightarrow} s_{in}$$

$$\boxed{\textit{modèle asymptotique :} \left\{ \begin{aligned} \dot{x}_1 &= \mu_1(s_{in} - x_1 - x_2)x_1 - Dx_1 \\ \dot{x}_2 &= \mu_2(s_{in} - x_1 - x_2)x_2 - Dx_2 \end{aligned} \right.}$$

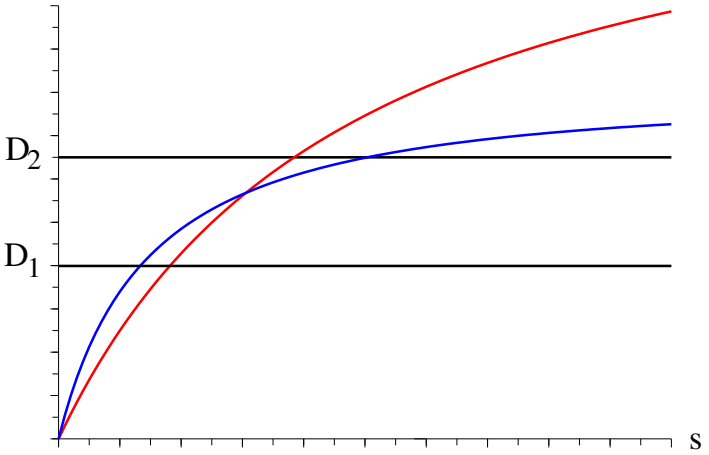
Remarque

- $\mu_i(S) = r_i S$ $(i = 1, 2)$ avec $r_1 \neq r_2$, modèle réduit :

$$\begin{aligned} \dot{x}_1 &= r_1 x_1 \left(S_{in} - \frac{D}{r_1} - x_1 - x_2 \right) \\ \dot{x}_2 &= r_2 x_2 \left(S_{in} - \frac{D}{r_2} - x_1 - x_2 \right) \end{aligned}$$

$=$ **modèle de compétition de Lotka-Volterra sans équilibre de coexistence**

- 2 lois de Monod dont les graphes s'intersectent hors de 0 :

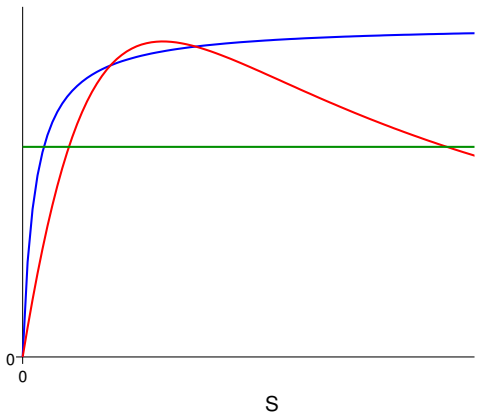


▶

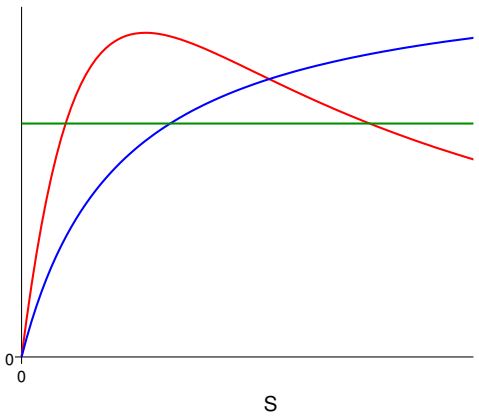
$D = D_1$	$D = D_2$
bleu l'emporte	rouge l'emporte

Effet d'une inhibition

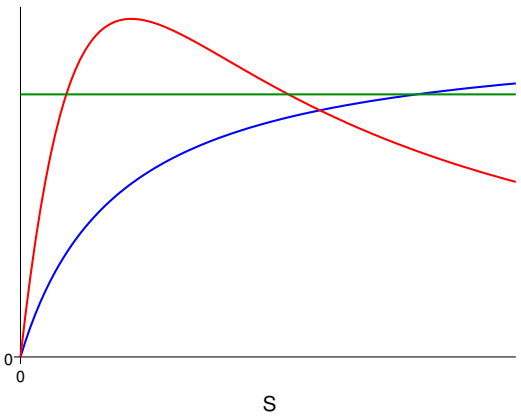
$$
\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 && \textit{de type Haldane} \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2 && \textit{de type Monod}
\end{aligned}
$$



cas 1



cas 2



cas 3

Retour sur l'analyse de stabilité

- équilibre de lessivage :

$$J = \begin{bmatrix} -D & -\mu_1(s_{in}) & -\mu_2(s_{in}) \\ 0 & \mu_1(s_{in}) - D & 0 \\ 0 & 0 & \mu_2(s_{in}) - D \end{bmatrix}$$

valeurs propres :
$-D$,
$\mu_1(s_{in}) - D$,
$\mu_2(s_{in}) - D$

- souche 1 seule :

$$J = \begin{bmatrix} -\mu_1'(s_1^\star)x_1^\star - D & -D & -\mu_2(s_1^\star) \\ \mu_1'(s_1^\star)x_1^\star & 0 & 0 \\ 0 & 0 & \mu_2(s_1^\star) - D \end{bmatrix}$$

valeurs propres :
$\mu_2(s_1^\star) - D$,
$-D$,
$-\mu_1'(s_1^\star)x_1^\star$

Modèle réduit

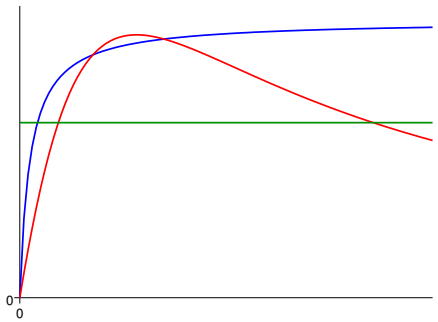
$$\begin{aligned}
\dot{s} &= -\mu_1(s)x_1 - \mu_2(s)x_2 + D(s_{in} - s) \\
\dot{x}_1 &= \mu_1(s)x_1 - Dx_1 \\
\dot{x}_2 &= \mu_2(s)x_2 - Dx_2
\end{aligned}$$

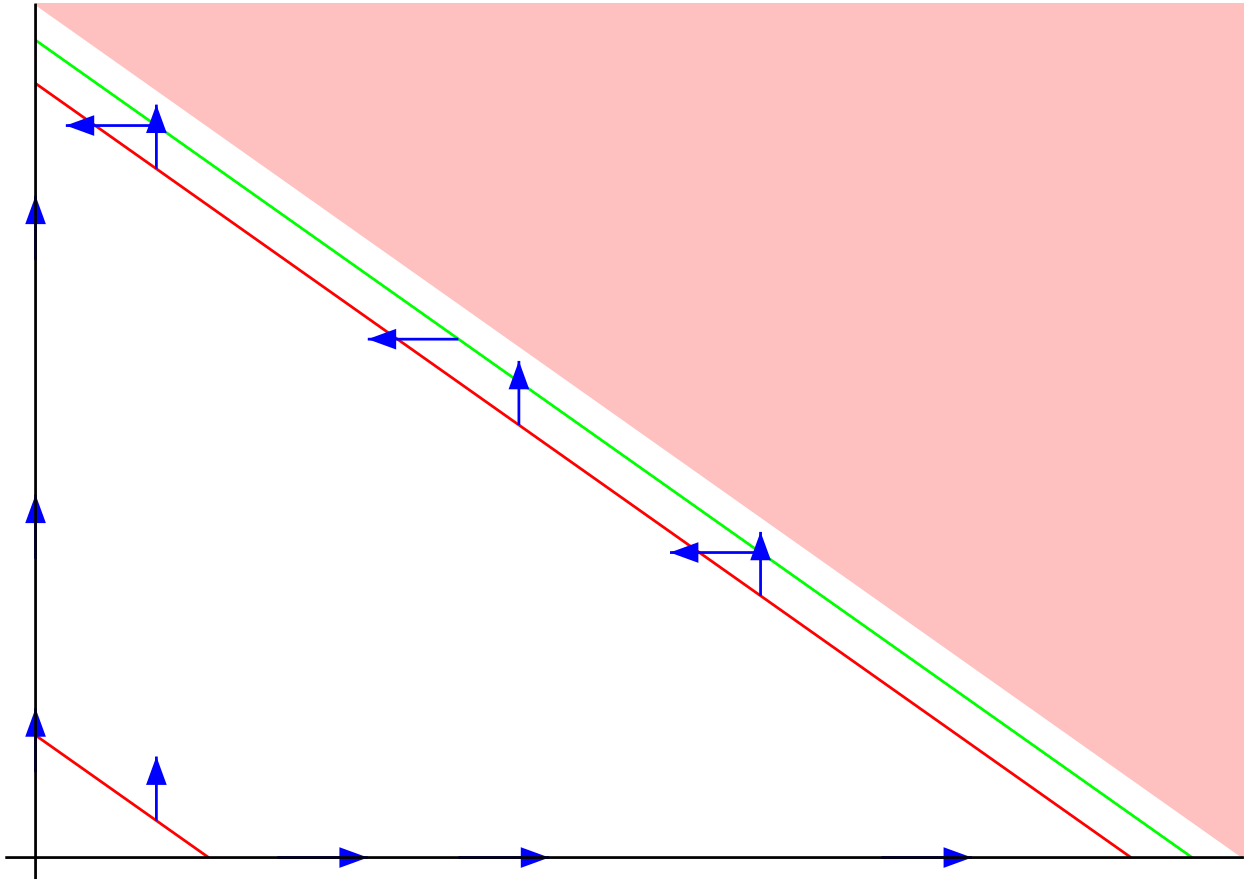
Soit $m = s + x_1 + x_2$, alors $\boxed{\frac{dm}{dt} = D(s_{in} - m)}$

$$\Rightarrow m(t) = s_{in} + (m(0) - s_{in})e^{-Dt} \underset{t \to +\infty}{\longrightarrow} s_{in}$$

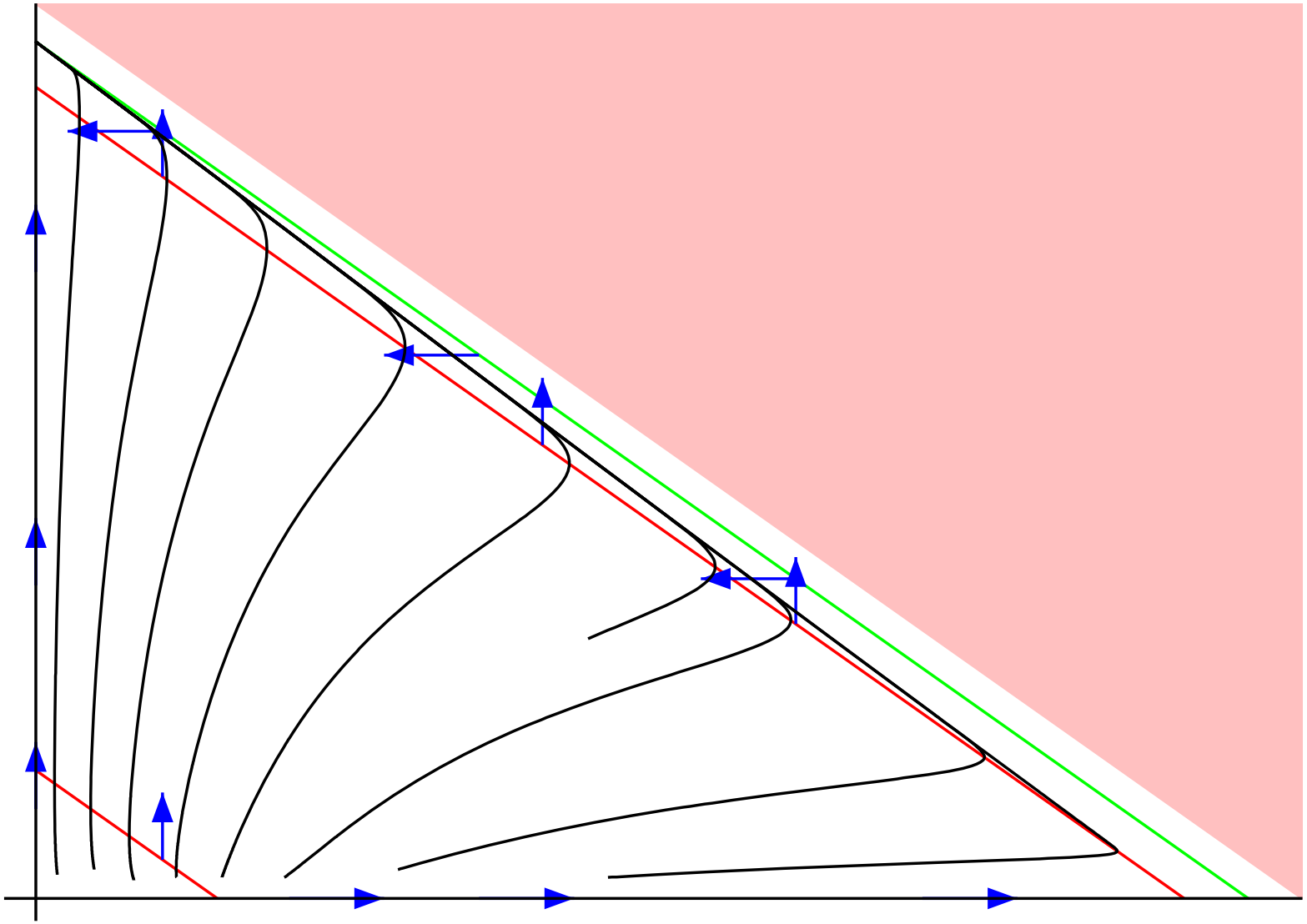
$$\boxed{\textit{modèle asymptotique :} \begin{cases} \dot{x}_1 = \mu_1(s_{in} - x_1 - x_2)x_1 - Dx_1 \\ \dot{x}_2 = \mu_2(s_{in} - x_1 - x_2)x_2 - Dx_2 \end{cases}}$$

Modèle asymptotique - Cas 1

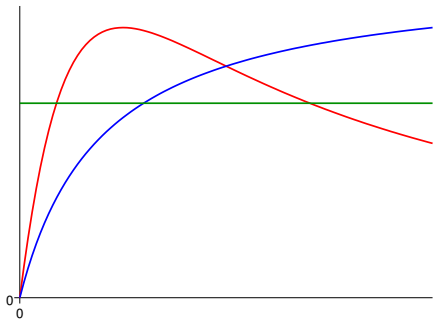


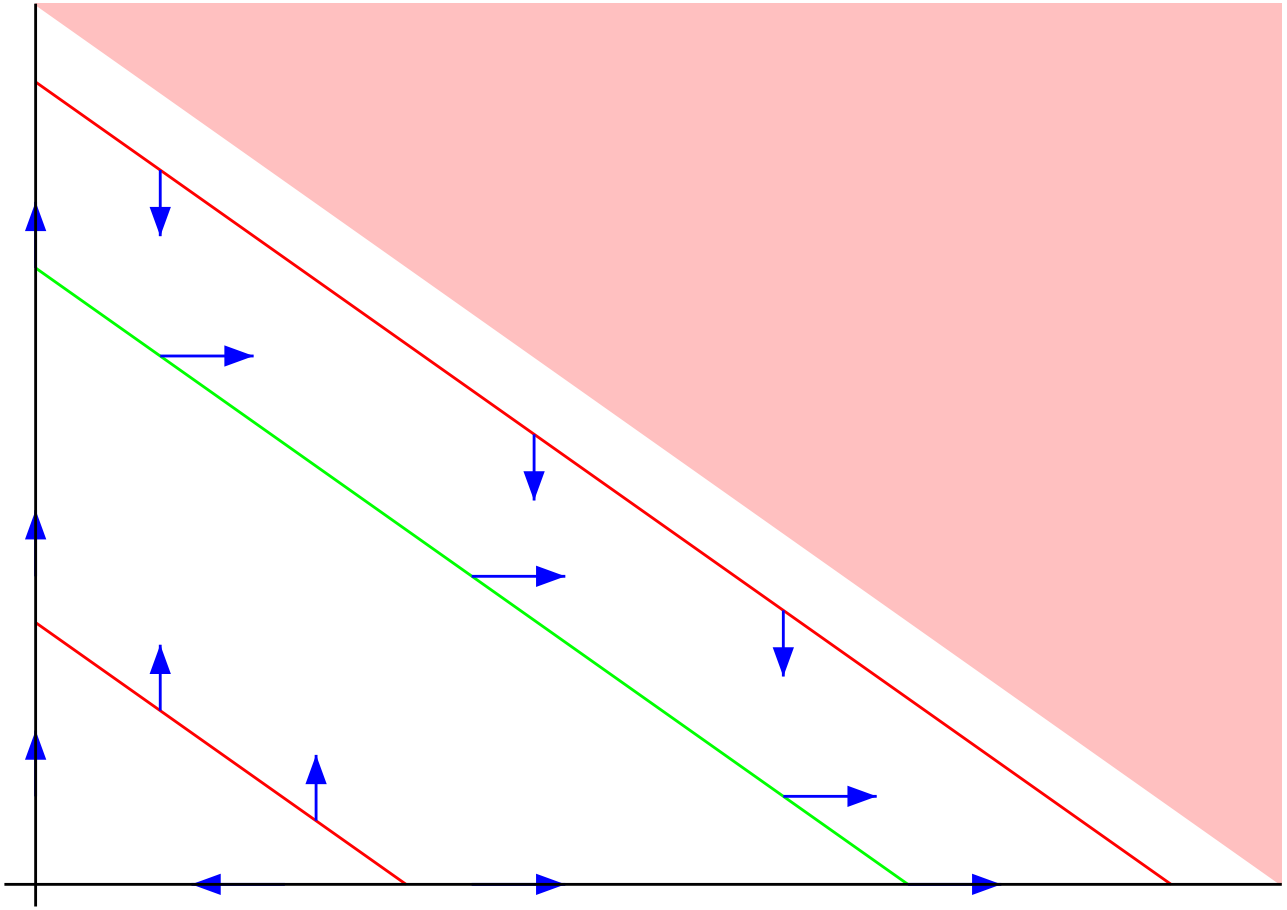


Modèle asymptotique - Cas 1

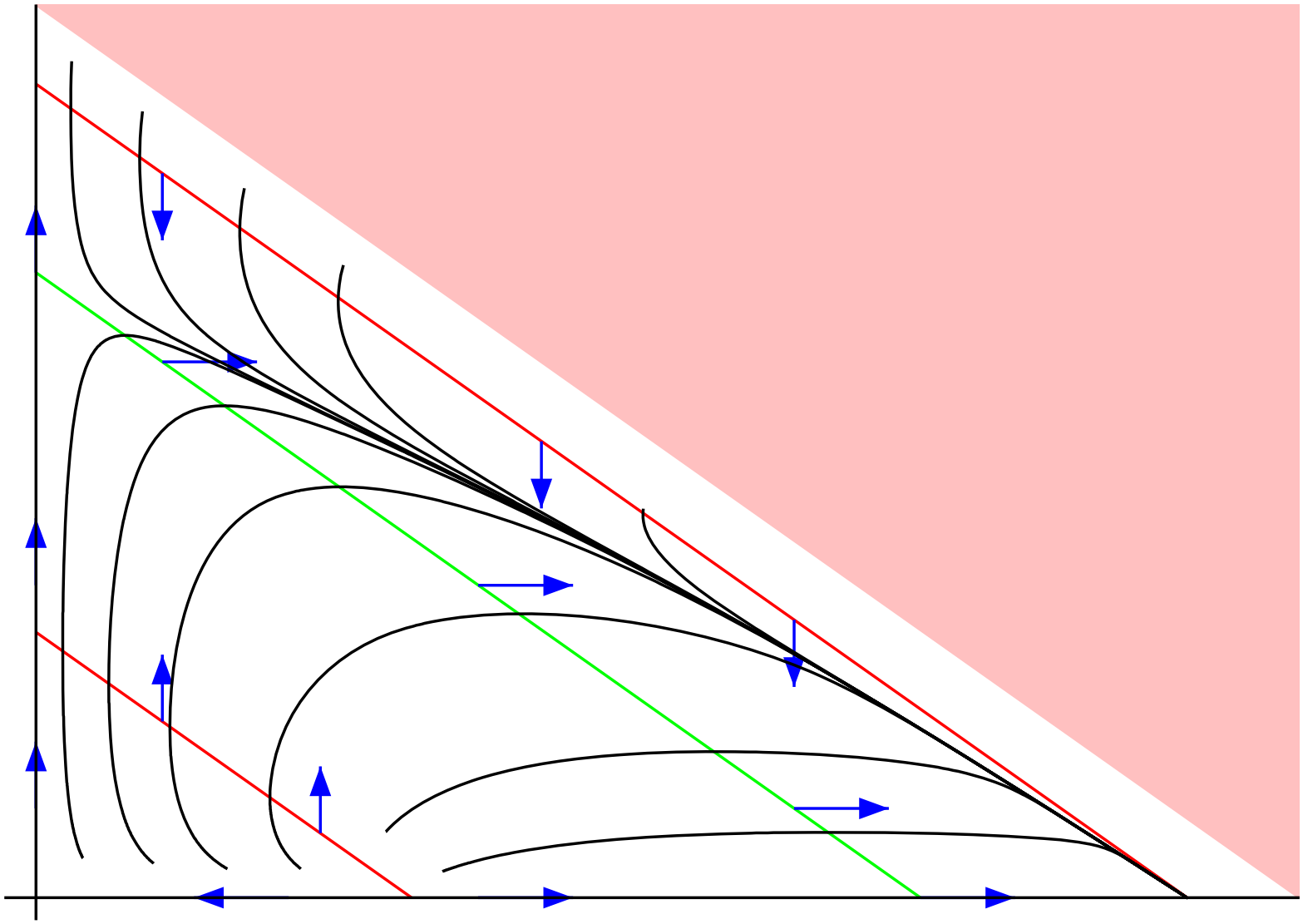


Modèle asymptotique - Cas 2

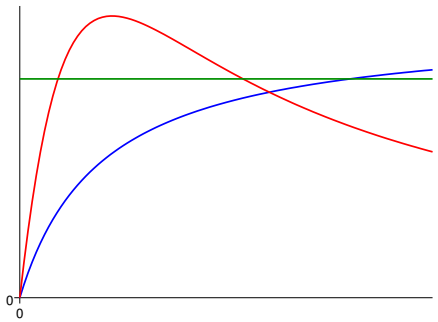


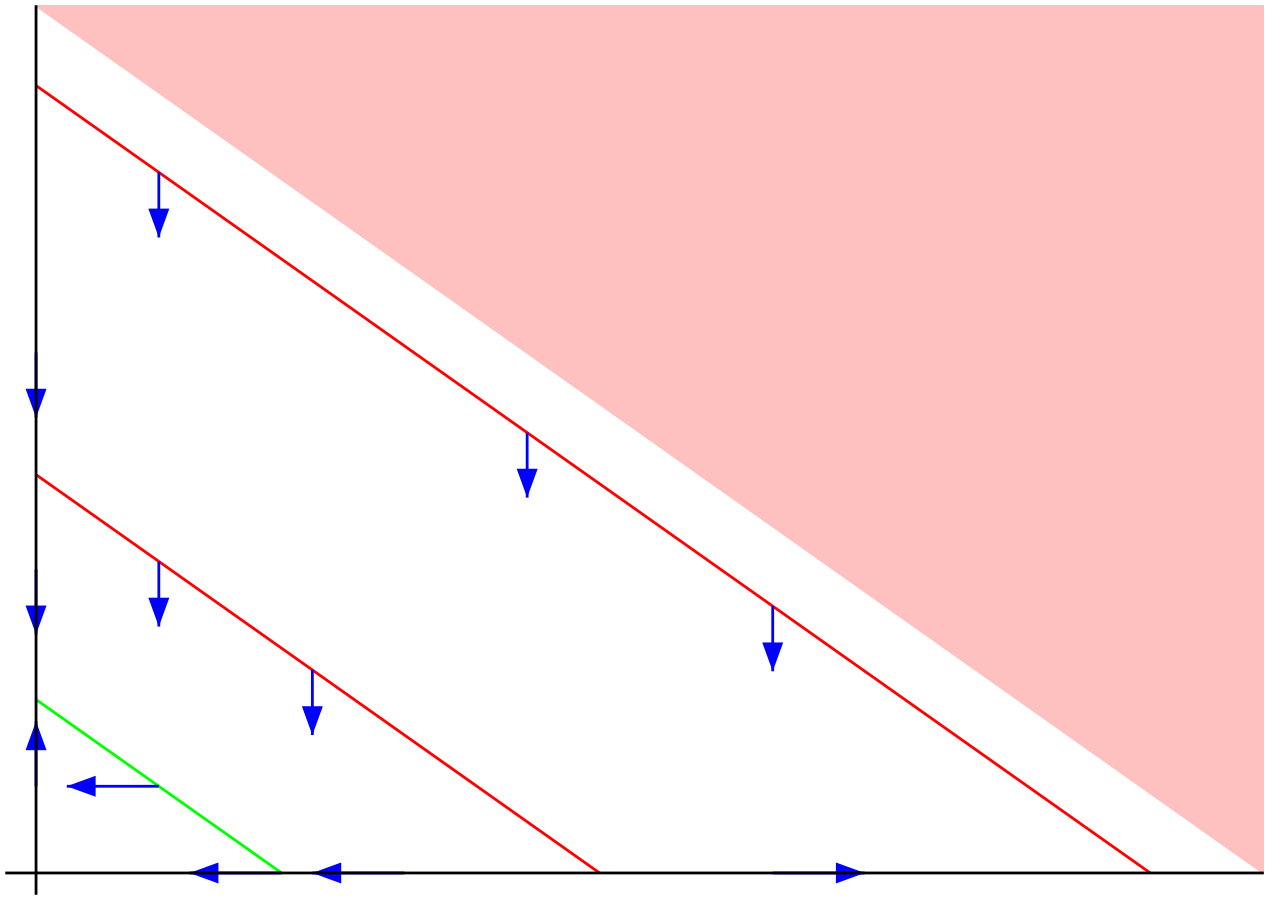


Modèle asymptotique - Cas 2

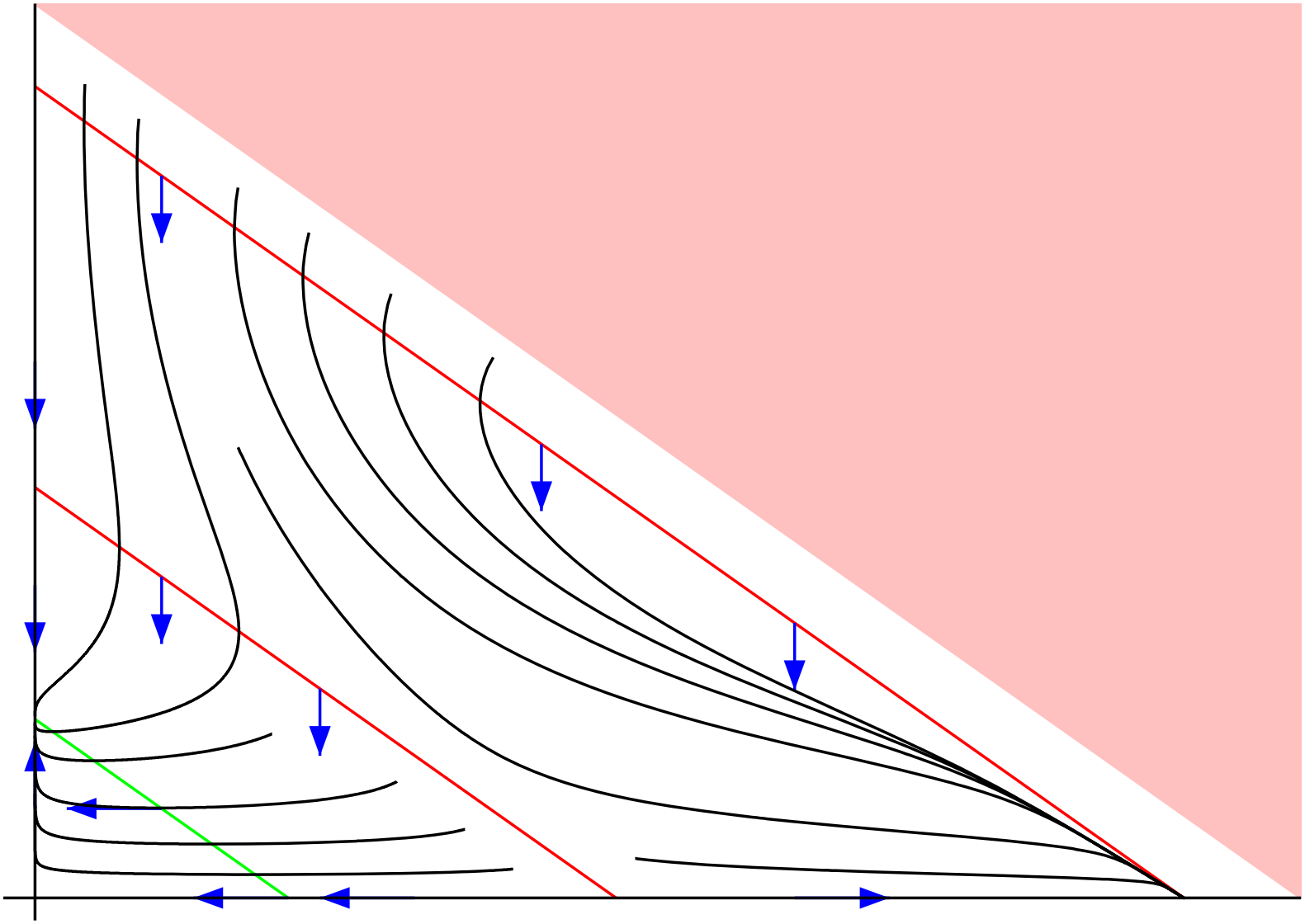


Modèle asymptotique - Cas 3





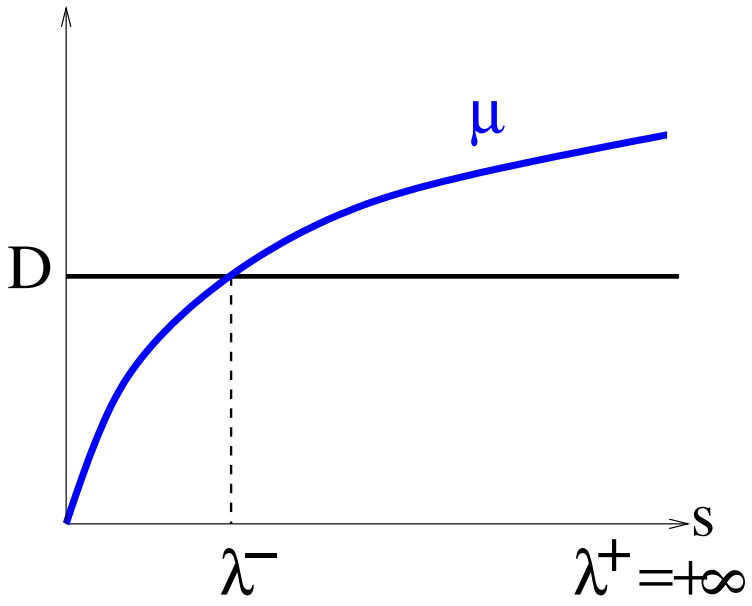
Modèle asymptotique - Cas 3

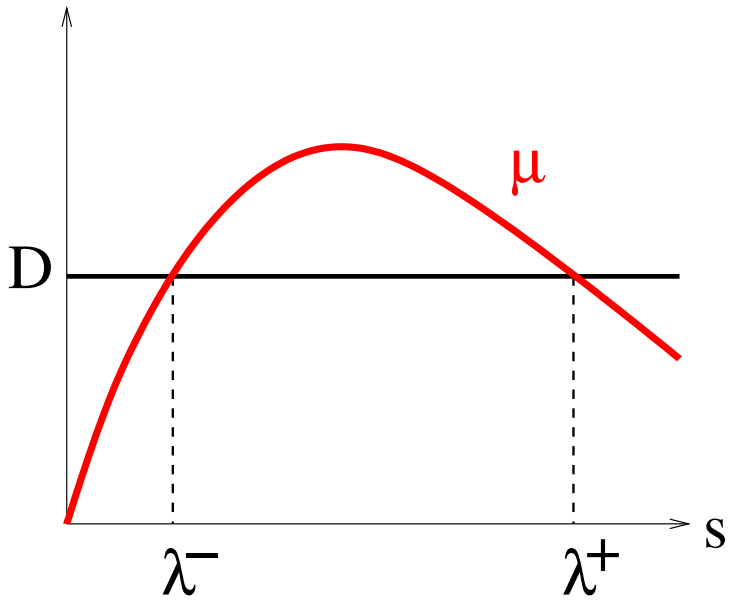


Une généralisation du Principe d'Exclusion

Hypothèse : $E_i(D) = \{s > 0 \,|\, \mu_i(s) > D\}$ est un intervalle

$$(\lambda_i^-(D), \lambda_i^+(D))$$





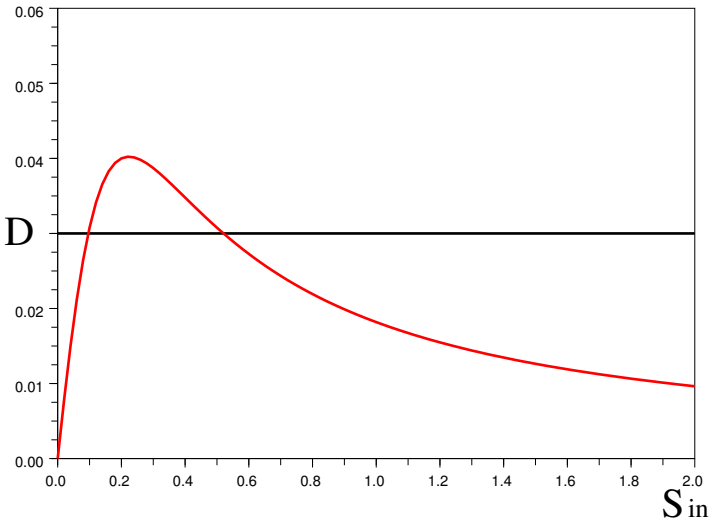
Une généralisation du Principe d'Exclusion

Proposition. Soit $Q(D) = \bigcup_i E_i(D) = \bigcup_i (\lambda_i^-(D), \lambda_i^+(D))$

- Il y génériquement exclusion compétitive.
- Il y a autant de souches qui peuvent emporter la compétition que de composantes connexes de l'ensemble $Q(D)$.

cf *Butler & Wolkowicz. A mathematical model of the chemostat with a general class of functions describing the nutrient uptake.* SIAM J. Appl. Math. 1985.

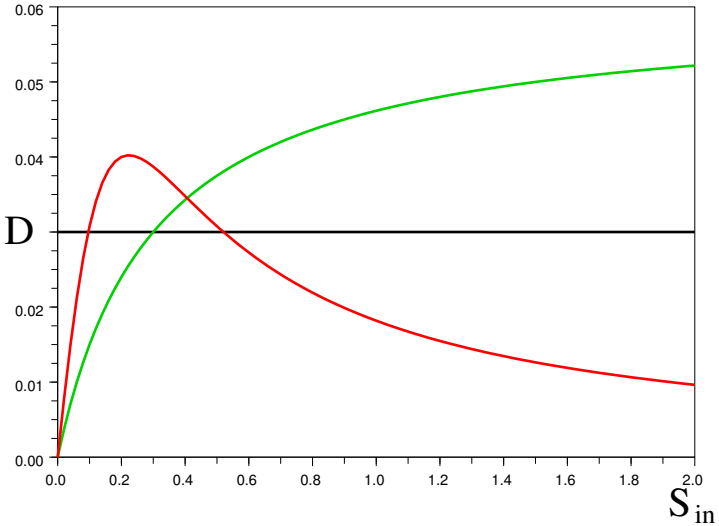
À propos de bio-augmentation

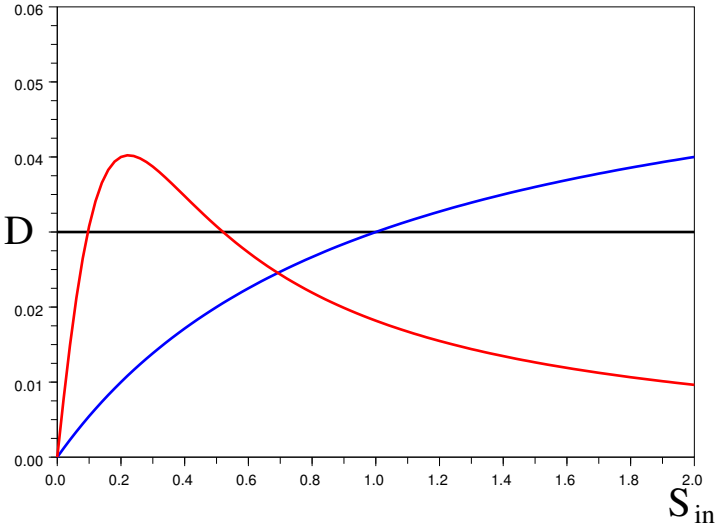


$$\max_{[0,s_{in}]} \mu < \mu(s_{in}) < D$$

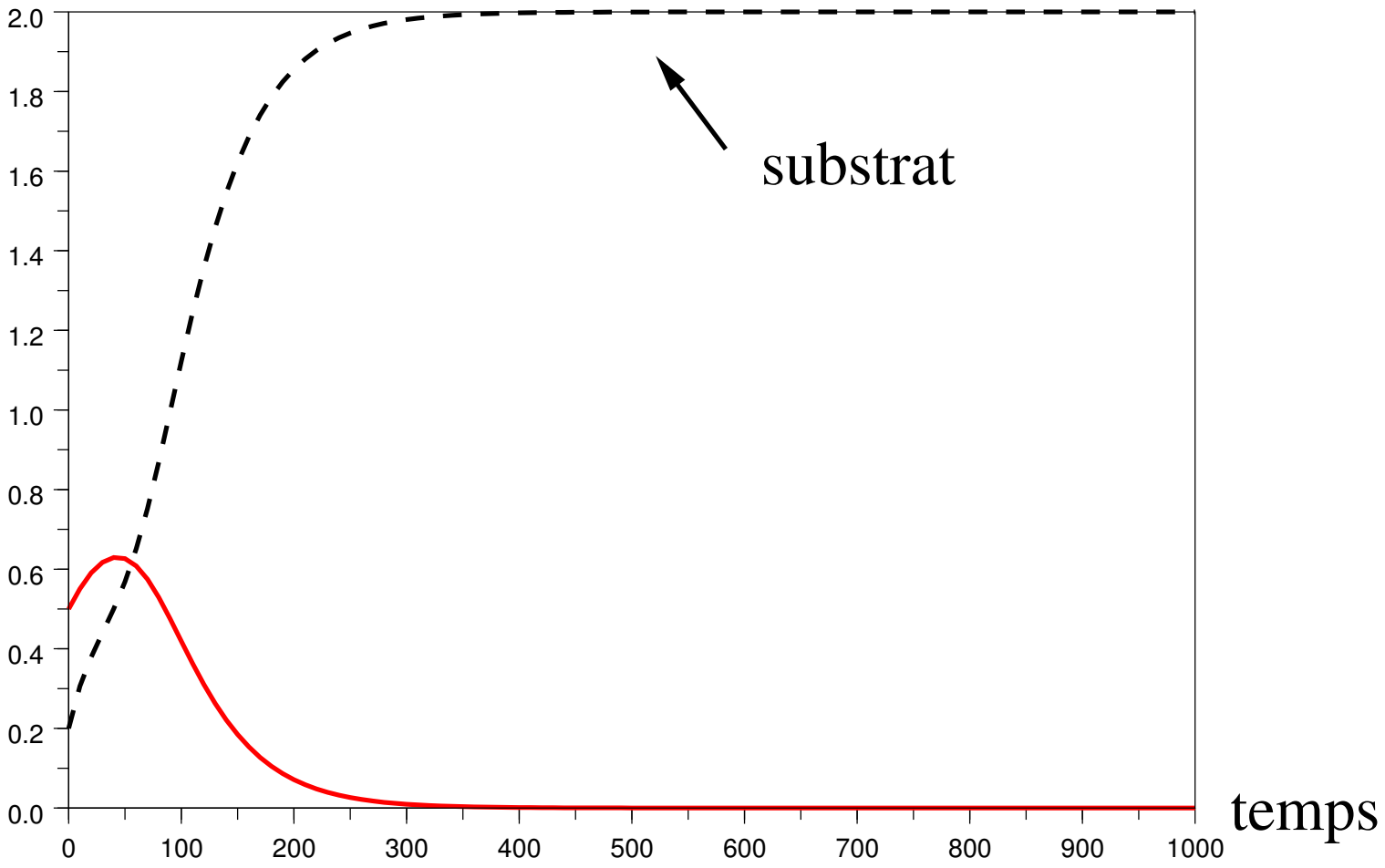
$\Rightarrow$ le lessivage is attractif...

Quel est l'effet d'un ajout d'une souche "bleue" ou d'une souche "verte" (en petite quantité) ?

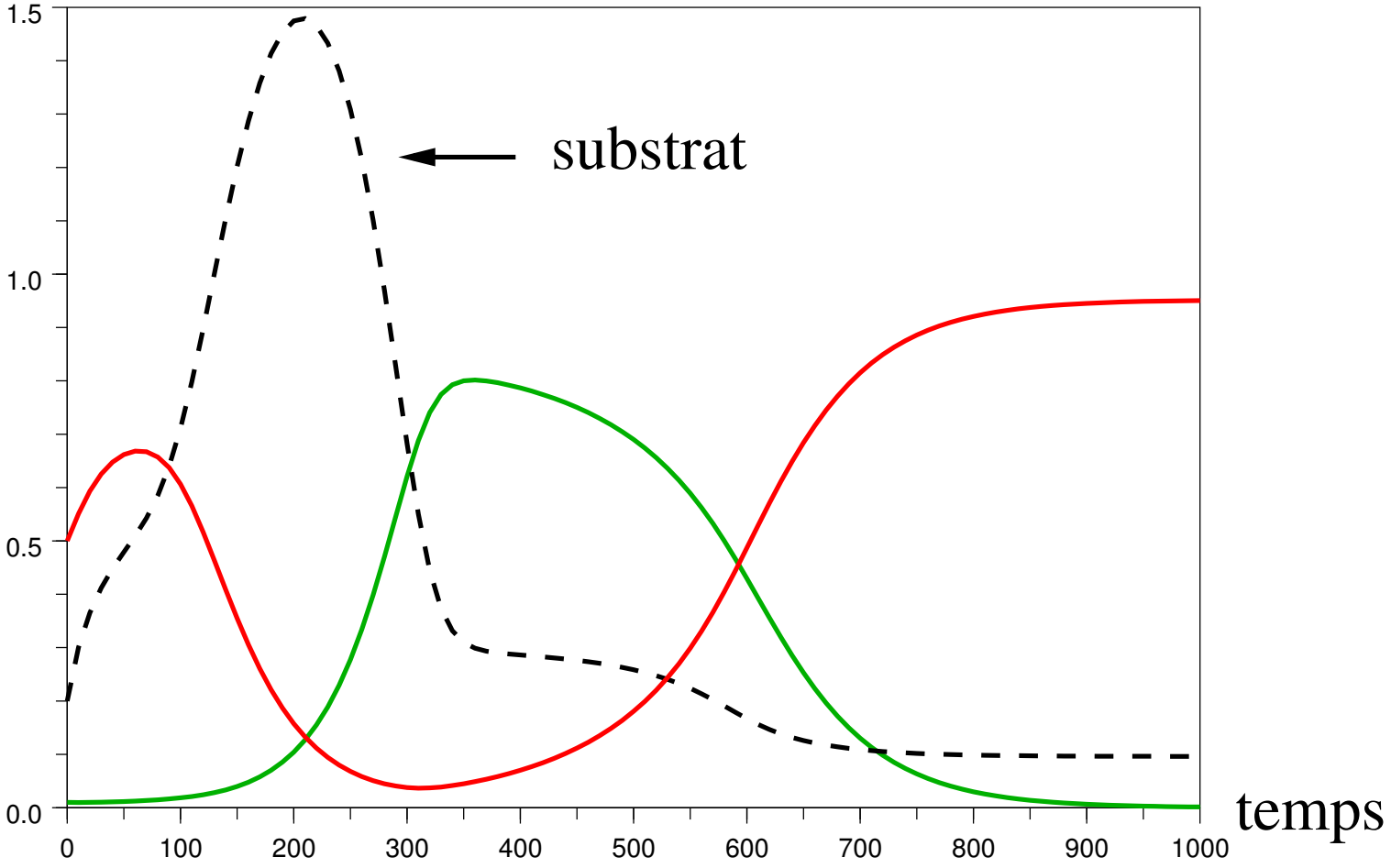




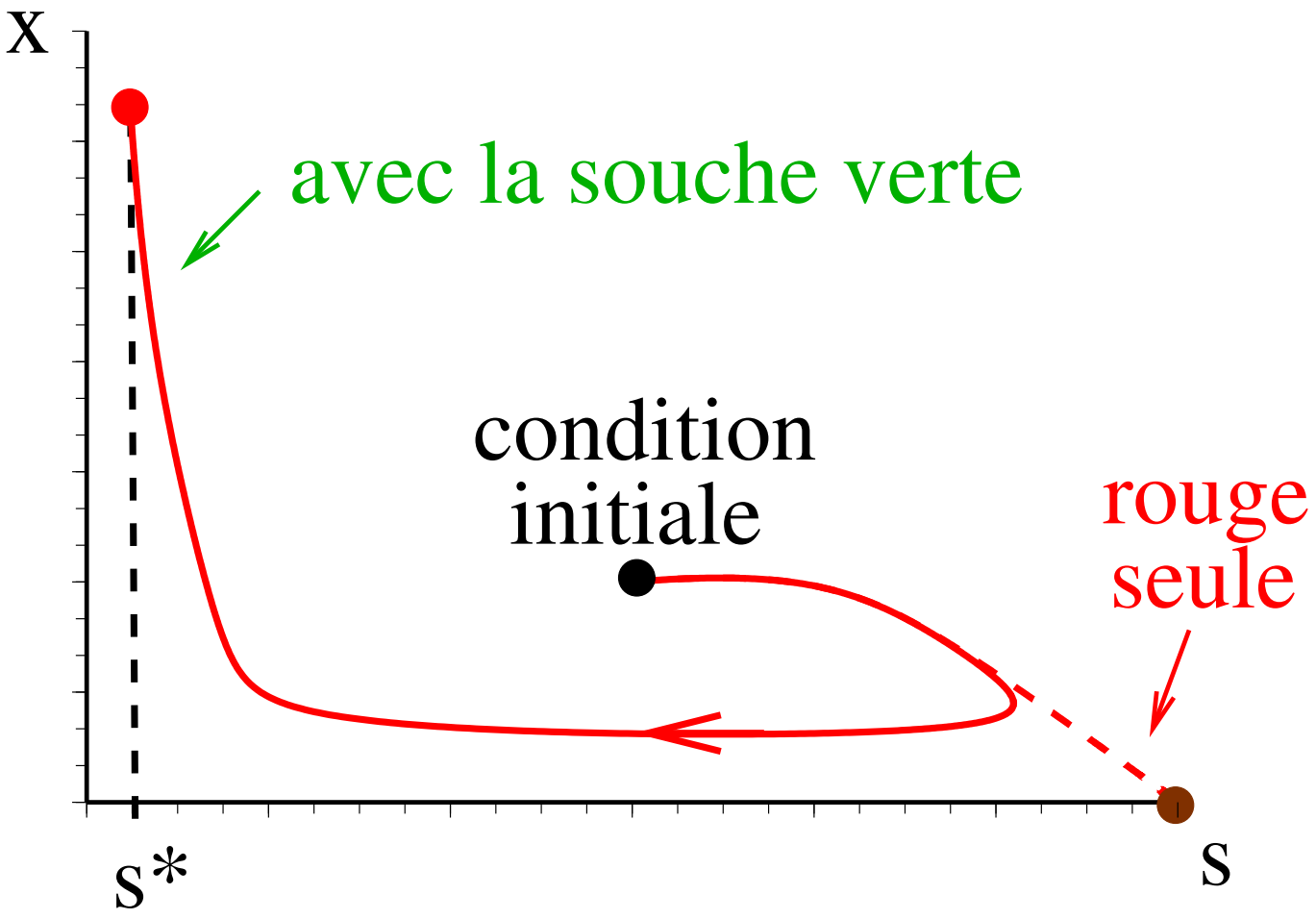
Souche rouge seule



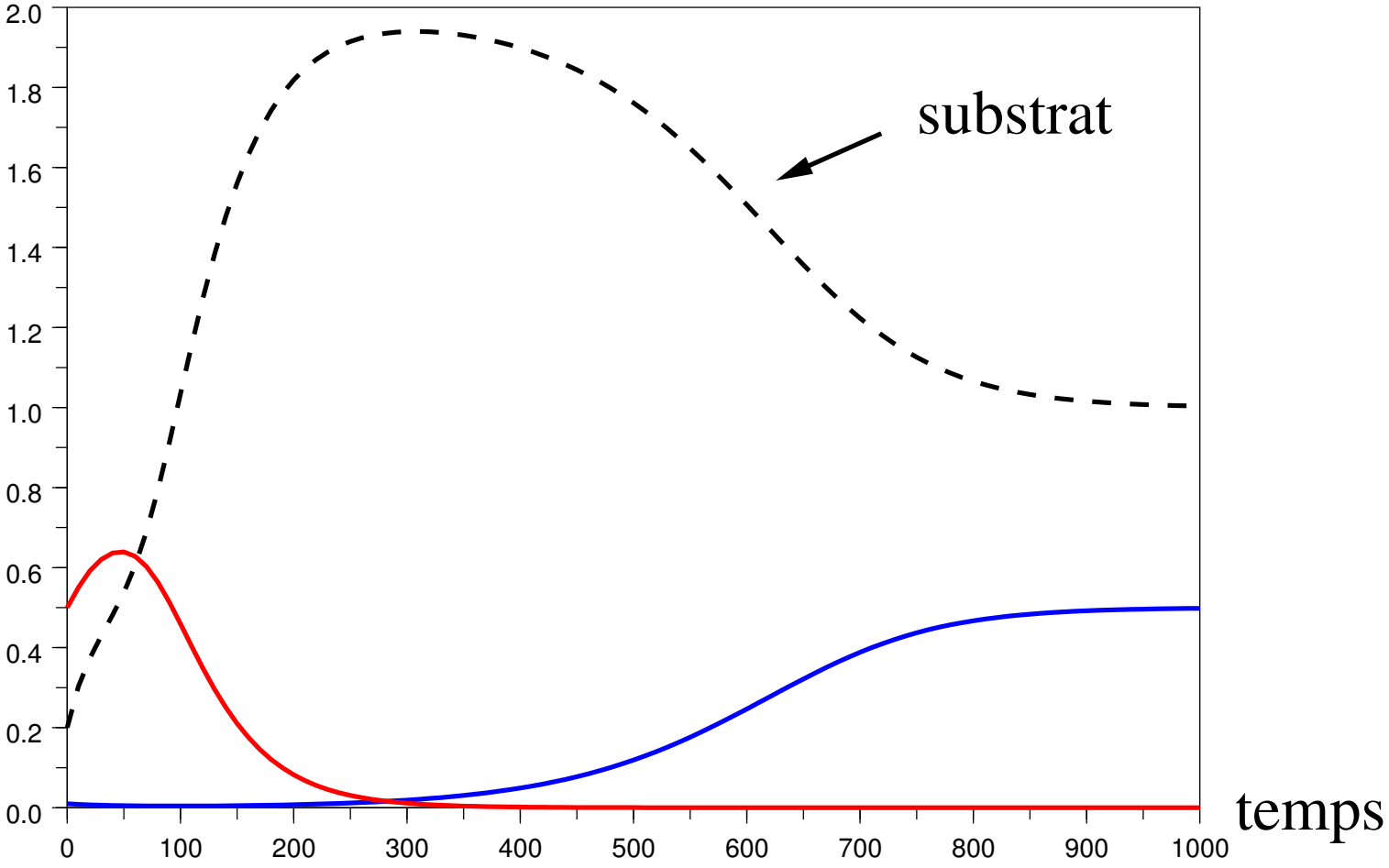
Ajout de la souche verte



Portrait de phase



Ajout de la souche bleue



Résumé : le “contrôle biologique”

Soit $E = (\lambda^-, \lambda^+)$ pour une espèce rouge.
Soit λ le seuil de rentabilité d'une souche additionnelle.

- $\lambda \in E$: stabilisation globale de l'espèce rouge
- $\lambda \notin E$: possibilité d'une invasion

cf *R. & Harmand. Biological control of the chemostat with nonmonotonic response and differnt removal rates.* Math. Bio. Eng. 2008.