Asymptotic stability of a coupled Advection-Diffusion-Reaction system arising in bioreactor processes.

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Abstract

In this work, we perform an asymptotic analysis of a coupled system of two Advection-Diffusion-Reaction equations with Danckwerts boundary conditions, which models the interaction between a microbial population (e.g., bacterias), called biomass, and a diluted organic contaminant (e.g., nitrates), called substrate, in a continuous flow bioreactor. This system exhibits, under suitable conditions, two stable equilibrium states: one steady state in which the biomass becomes extinct and no reaction is produced, called *washout*, and another steady state, which corresponds to the partial elimination of the substrate. We use the method of linearization to give sufficient conditions for the asymptotic stability of the two stable equilibrium configurations. Finally, we compare our asymptotic analysis with the usual asymptotic analysis associated to the continuous bioreactor when it is modeled with ordinary differential equations.

1. Introduction

A bioreactor is a vessel in which a microorganism (e.g., bacteria), called biomass, is used to degrade a considered diluted organic contaminant, called substrate. There exist various modes of operation in chemical reactor execution [5, 10], among which continuous flow bioreactors are commonly used in the bioremediation of water resources (see, for instance, [13, 16, 27]). These biological reactors are filled from a polluted resource with a flow rate Q (m^3/s), and their output returns the treated water with the same flow rate Q, producing a desired quality effluent for a reasonable operating and maintenance cost. A simplified model for this process could be given by the equations [37]

$$\begin{cases} \frac{\mathrm{d}S}{\mathrm{d}t} = -\mu(S)B + \frac{Q(t)}{V}(S_{\mathrm{e}}(t) - S), & t > 0, \\ \frac{\mathrm{d}B}{\mathrm{d}t} = \mu(S)B - \frac{Q(t)}{V}B, & t > 0, \end{cases} \tag{1}$$

where S ($\mathrm{kg/m}^3$) and B ($\mathrm{kg/m}^3$) are the concentrations of substrate and biomass, respectively; $S_{\mathrm{e}}(t)$ ($\mathrm{kg/m}^3$) is the concentration of substrate that enters the reactor at time t; V (m^3) is the reactor volume; $Q(t)$ (m^3/s) is the volumetric flow rate at time t; and $\mu(\cdot)$ (1/s) refers to the growth rate of the biomass in function of the substrate concentration. From a general point of view, due to experimental observations, we consider growth rate functions, that satisfy the following assumptions (see [9, 10, 34]):

Assumption. Function $\mu : [0,+\infty) \to [0,+\infty)$ fulfills $\mu(0) = 0$, $\mu(z) > 0$ for $z > 0$ and one of the following properties:

- μ is increasing and concave. (A1)
- There exists $s > 0$ such that μ is increasing on $(0, s)$ and decreasing on $(s,+\infty)$. (A2)

The Monod function [37], defined by

$$\mu(S) = \mu_{\max}\frac{S}{K_{\mathrm{S}} + S},$$

satisfies (A1), and the Haldane function [1], described by

$$\mu(S) = \mu^{*}\frac{S}{K_{\mathrm{S}} + S + S^2/K_{\mathrm{I}}},$$

satisfies (A2). Both functions are extensively used in the literature.

In the particular case when S_{e} and Q are constant, system (1) can be non-dimensionalized by setting $\hat{S} = \frac{S}{S_{\mathrm{e}}}$, $\hat{B} = \frac{B}{S_{\mathrm{e}}}$, $\hat{\mu}(\hat{S}) = \frac{\mu(S_{\mathrm{e}}\hat{S})}{\|\mu\|_{L^\infty(\Omega)}}$ and $\hat{t} = \|\mu\|_{L^\infty(\mathbb{R})}t$. For simplicity, we drop the ˆ notation, and so S, B, μ and t denote the non-dimensional variables. System (1) in non-dimensional form is therefore given by

$$\begin{cases} \frac{\mathrm{d}S}{\mathrm{d}t} = -\mu(S)B + d(1-S), & t > 0, \\ \frac{\mathrm{d}B}{\mathrm{d}t} = \mu(S)B - dB, & t > 0, \end{cases} \tag{2}$$

where $d = \frac{Q}{\|\mu\|_{L^\infty}V}$ is the dimensionless dilution rate.

If μ fulfills (A1), system (2) has two equilibrium configurations $(S_1^*, B_1^*) = (1, 0)$, usually called *washout*, and $(S_2^*, B_2^*) = (S_2^*, 1 - S_2^*)$, where S_2^* is such that $\mu(S_2^*) = d$ (see [37]). In [14], [33] and [37] the authors conclude that the steady state $(1, 0)$ is asymptotically stable if $d \geq \mu(1)$, while the steady state $(S_2^*, 1 - S_2^*)$ is asymptotically stable if $d < \mu(1)$.

Similarly (see [1]), if μ fulfills (A2), system (2) has three equilibrium configurations $(S_1^*, B_1^*) = (1, 0)$, $(S_2^*, B_2^*) = (S_2^*, 1 - S_2^*)$ and $(S_3^*, B_3^*) = (S_3^*, 1 - S_3^*)$, where $\mu(S_2^*) = \mu(S_3^*) = d$ and $S_2^* < S_3^*$. In [6], [9] and [34], the authors show that the steady state $(1, 0)$ is asymptotically stable if $d > \mu(1)$, the steady state $(S_2^*, 1 - S_2^*)$ is asymptotically stable if $d < 1$ and the steady state $(S_3^*, 1 - S_3^*)$ is unstable. Thereby, if $\mu(1) < 1$, there is bistability when $\mu(1) < d < 1$.

System (2) describes the bioreactor dynamics under the assumption that both substrate and biomass concentrations are spatially uniform through the tank. It is of interest to consider more realistic models, for instance those based on partial differential equations, to study the influence of spatial inhomogeneities in the bioreactor (see the comparison between Ordinary Differential Equation (ODE) and Partial Differential Equation (PDE) bioreactor model approaches performed in [3] and [8]). Particularly, system (2) can be improved by considering a coupled system of spatio-temporal parabolic equations of the form

$$\begin{cases} \frac{\mathrm{d}S}{\mathrm{d}t} = L_{\mathrm{S}}(S) - \mu(S)B & x \in \Omega,\ t > 0, \\ \frac{\mathrm{d}B}{\mathrm{d}t} = L_{\mathrm{B}}(B) + \mu(S)B & x \in \Omega,\ t > 0, \end{cases} \tag{3}$$

where Ω is the bioreactor domain and L_{S}, L_{B} are linear second order elliptic partial differential operators on Ω. The asymptotic analysis of system (3) should provide more accurate results, compared with the asymptotic ones detailed above for system (2), about the behavior of the substances in the bioreactor.

The asymptotic behavior of parabolic equations has received a considerable attention in the literature [15, 35, 20, 22, 24, 25]. Most theoretical studies focusing on bioreactor processes consider the assumption that both L_{S} and L_{B} are diffusion operators (see, e.g. [18, 20, 28, 29]). For instance, in Yosida and Morita [28], the authors show the existence of two different steady states (one constant, and another one spatially distributed) and develop bifurcation diagrams of the equilibrium solutions for specific model parameters. Nevertheless, such diffusion-reaction systems describe the behavior of batch type bioreactors, which are different to continuous flow type bioreactors, for which the addition of an advective term in operators L_{S} and L_{B} is required. Indeed, during batch operation no substrate is added to the initial charge and the product is not removed until the end of the process; whereas in continuous operation the substrate is continually added and the product is continually removed.

The asymptotic behavior and stability analysis of Advection-Diffusion-Reaction systems is mainly devoted to the one-dimensional case [11, 12, 26, 31, 36, 40]. In [11, 12, 26, 40], the authors study system (3) together with Danckwerts boundary conditions (typically used for continuous flows bioreactors) under the assumption that $L_{\mathrm{S}} = L_{\mathrm{B}}$. Presuming that the diffusion rates of both substrate and biomass are the same, the authors discuss the asymptotic stability of the different steady states of the system. The case $L_{\mathrm{S}} \neq L_{\mathrm{B}}$ has been tackled in [31, 36], where the authors consider periodic boundary conditions and analyze the influence of the model parameters on the stability of the different equilibrium configurations of the system.

In this work, we carry out the asymptotic stability of a coupled system of two Advection-Diffusion-Reaction equations completed with boundary conditions of mixed type, which models the interaction between substrate and biomass in a continuous flow bioreactor. We use the method of linearization to give sufficient conditions for the asymptotic stability of the two stable equilibrium configurations that the system may exhibit. In contrast to the works presented in [11, 26, 31, 36, 40], we consider cylindrical reactors with two spatial variables (height and radius), in order to study radial inhomogeneities of concentrations in the tank. We impose Danckwerts boundary conditions and allow the differential operators L_{S} and L_{B} to have different substrate and biomass diffusion rates.

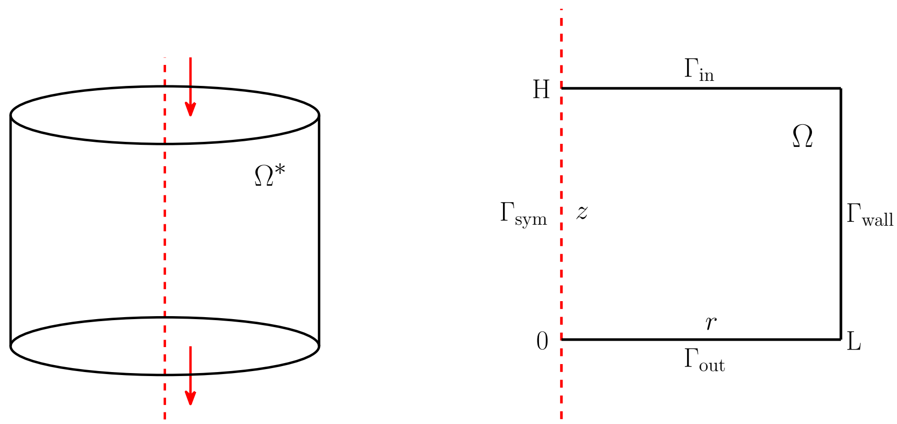
The paper is organized as follows: In Section 2, we introduce a PDE model describing the dynamics of the bioreactor by using a coupled system of parabolic semilinear equations together with Danckwerts boundary conditions. Additionally, we perform its dimensional analysis. In Section 3, we present the steady states of the system and analyze the asymptotic stability using linearization methods. Then, Section 4 presents numerical experiments to analyze the validity and robustness of the stability results obtained in Section 3. Finally, we perform a comparison with the asymptotic results related to system (2).

2. Mathematical Modeling

In this section, we introduce an Advection-Diffusion-Reaction system to model a continuous flow bioreactor and perform a dimensional analysis of this model.

The bioreactor in consideration is a cylinder denoted by Ω^* (see Figure 1-(a)). Since this device's geometry is a solid of revolution, it can be simplified, in cylindrical coordinates, by a rectangular 2D domain, denoted by Ω and represented in Figure 1-(b).

At the beginning of the process, there is an initial concentration of biomass in Ω that is reacting with the polluted water entering the device through the inlet Γ_{in} (i.e., the upper boundary of the rectangle Ω). Treated water leaves the reactor through the outlet Γ_{out} (i.e., the lower boundary of the rectangle Ω). Moreover, $\Gamma_{\mathrm{sym}} = \{0\} \times (0, H)$ is the axis of symmetry and $\Gamma_{\mathrm{wall}} = \delta\Omega \setminus (\Gamma_{\mathrm{in}} \cup \Gamma_{\mathrm{out}} \cup \Gamma_{\mathrm{sym}})$ is the bioreactor wall for which no flux passes through. By using cylindrical coordinates (r, z), where r is the distance to the symmetrical cylinder axis, we consider the following system describing the behavior of the



(a) 3D reactor

(b) 2D simplification

Figure 1: Typical representation of the domain geometry.

continuous bioreactor [7]:

$$
\begin{cases}
\frac{\partial S}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}(rD_{\mathrm{S}}\frac{\partial S}{\partial r}) + \frac{\partial}{\partial z}(D_{\mathrm{S}}\frac{\partial S}{\partial z}) + u\frac{\partial S}{\partial z} - \mu(S)B & \text{in } \Omega \times (0,T), \\
\frac{\partial B}{\partial t} = \frac{1}{r}\frac{\partial}{\partial r}(rD_{\mathrm{B}}\frac{\partial B}{\partial r}) + \frac{\partial}{\partial z}(D_{\mathrm{B}}\frac{\partial B}{\partial z}) + u\frac{\partial B}{\partial z} + \mu(S)B & \text{in } \Omega \times (0,T), \\
D_{\mathrm{S}}\frac{\partial S}{\partial z} + uS = uS_{\mathrm{e}} & \text{in } \Gamma_{\mathrm{in}} \times (0,T), \\
D_{\mathrm{B}}\frac{\partial B}{\partial z} + uB = 0 & \text{in } \Gamma_{\mathrm{in}} \times (0,T), \\
D_{\mathrm{S}}\frac{\partial S}{\partial r} = 0 & \text{in } \left(\Gamma_{\mathrm{wall}} \cup \Gamma_{\mathrm{sym}}\right) \times (0,T), \\
D_{\mathrm{B}}\frac{\partial B}{\partial r} = 0 & \text{in } \left(\Gamma_{\mathrm{wall}} \cup \Gamma_{\mathrm{sym}}\right) \times (0,T), \\
D_{\mathrm{S}}\frac{\partial S}{\partial z} = 0 & \text{in } \Gamma_{\mathrm{out}} \times (0,T), \\
D_{\mathrm{B}}\frac{\partial B}{\partial z} = 0 & \text{in } \Gamma_{\mathrm{out}} \times (0,T), \\
S(r,z,0) = S_0(r,z) & \forall (r,z) \in \Omega, \\
B(r,z,0) = B_0(r,z) & \forall (r,z) \in \Omega,
\end{cases}
\tag{4}
$$

where $T > 0$ (s) is the length of the time interval for which we want to model the process; S (kg/m^3) and B (kg/m^3) are the substrate and biomass concentrations inside the bioreactor, which diffuse throughout the water in the vessel with diffusion coefficients D_{S} (m^2/s) and D_{B} (m^2/s), respectively; the fluid velocity is taken as $\mathbf{u} = (0,0,-u)$, where u (m/s) is the flow speed; S_{e} (kg/m^3) is the concentration of substrate that enters into the bioreactor; S_0 (kg/m^3) and B_0 (kg/m^3) are the initial concentrations of substrate and biomass inside the bioreactor, respectively. Furthermore, as in system (1), we consider a term corresponding to the reaction between biomass and substrate, governed by the growth rate function μ (s^{-1}). According to [7], if $\mu \in L^\infty(\mathbb{R})$ is continuous and Lipschitz, $u \in L^\infty(\bar{\Omega} \times (0,T))$, $S_{\mathrm{e}} \in L^\infty(0,T)$, $S_{\mathrm{e}} \geq 0$ in $(0,T)$, $S_0 \in L^\infty(\Omega)$, $S_0 \geq 0$ in Ω, $B_0 \in L^\infty(\Omega)$ and $B_0 \geq 0$ in Ω, there exists a unique solution $(S,B) \in L^2(0,T,H^1(\Omega))^2 \cap \mathcal{C}(0,T,L^2(\Omega))^2 \cap L^\infty(\Omega \times (0,T))^2$ of system (4).

System (4) is non-dimensionalized by setting:

$$\hat{B} = \frac{B}{b}, \quad \hat{S} = \frac{S}{s}, \quad \hat{t} = \frac{t}{\tau}, \quad \hat{u} = \frac{u}{\gamma}, \quad \hat{S}_{\mathrm{e}} = \frac{S_{\mathrm{e}}}{e}, \quad \hat{\mu}(\hat{S}) = \frac{\mu(s\hat{S})}{\nu}, \quad \hat{z} = \frac{z}{Z} \text{ and } \hat{r} = \frac{r}{R},$$

where b, s, τ, γ, e, ν, Z and R are suitable scales. Thus, for $0 \leq \hat{t} \leq \hat{T} = \frac{T}{\tau}$ and $(\hat{r}, \hat{z}) \in \hat{\Omega}$ (the nondimensional domain obtained from Ω with the change of variables $(\hat{r}, \hat{z}) = (\frac{r}{R}, \frac{z}{Z})$) the first and second equations in system (4) become

$$\frac{\partial \hat{S}}{\partial \hat{t}} = \frac{\tau D_{\mathrm{S}}}{R^2 \hat{r}} \frac{\partial}{\partial \hat{r}}(\hat{r}\frac{\partial \hat{S}}{\partial \hat{r}}) + \frac{\tau D_{\mathrm{S}}}{Z^2}\frac{\partial^2 \hat{S}}{\partial \hat{z}^2} + \frac{\gamma\tau}{Z}\hat{u}\frac{\partial \hat{S}}{\partial \hat{z}} - \frac{b\tau\nu}{s}\hat{\mu}(\hat{S})\hat{B} \tag{5}$$

and

$$\frac{\partial \hat{B}}{\partial \hat{t}} = \frac{\tau D_{\mathrm{B}}}{R^2 \hat{r}} \frac{\partial}{\partial \hat{r}}(\hat{r}\frac{\partial \hat{B}}{\partial \hat{r}}) + \frac{\tau D_{\mathrm{B}}}{Z^2}\frac{\partial^2 \hat{B}}{\partial \hat{z}^2} + \frac{\gamma\tau}{Z}\hat{u}\frac{\partial \hat{B}}{\partial \hat{z}} + \tau\nu\hat{\mu}(\hat{S})\hat{B}. \tag{6}$$

The dimensionless groups of parameters in equations (5) and (6) are

$$\alpha_1 = \frac{\tau D_{\mathrm{S}}}{R^2}, \quad \alpha_2 = \frac{\tau D_{\mathrm{S}}}{Z^2}, \quad \alpha_3 = \frac{\tau D_{\mathrm{B}}}{R^2}, \quad \alpha_4 = \frac{\tau D_{\mathrm{B}}}{Z^2}, \quad \alpha_5 = \frac{\tau\gamma}{Z}, \quad \alpha_6 = \tau\nu \text{ and } \alpha_7 = \frac{\tau\nu b}{s}.$$

The radius and the height scales proposed here come from the dimensions of the bioreactor, giving $R = L$ and $Z = H$. We set $\nu = \|\mu\|_{L^\infty(\mathbb{R})}$ and $\gamma = \|u\|_{L^\infty(\bar{\Omega}\times(0,T))}$ for the reaction and velocity scales, respectively. Finally, for the entering substrate scale we set $e = \|S_{\mathrm{e}}\|_{L^\infty(0,T)}$ and, for the sake of simplicity, we choose $s = b = \|S_{\mathrm{e}}\|_{L^\infty(0,T)}$. The time scale τ is chosen from equations (5) and (6) depending on the process (diffusion, advection or reaction) we want to focus on. In particular, we can choose

$$\tau \in \{\frac{L^2}{D_{\mathrm{S}}}, \frac{L^2}{D_{\mathrm{B}}}, \frac{H^2}{D_{\mathrm{S}}}, \frac{H^2}{D_{\mathrm{B}}}, \frac{H}{\|u\|_{L^\infty(\Omega\times(0,T))}}, \frac{1}{\|\mu\|_{L^\infty(\mathbb{R})}}\},$$

where $\tau = \frac{L^2}{D_{\mathrm{S}}}$ (resp., $\tau = \frac{H^2}{D_{\mathrm{S}}}$) corresponds to the case focusing on the substrate diffusion rate on the horizontal (resp., vertical) axis; $\tau = \frac{L^2}{D_{\mathrm{B}}}$ (resp., $\tau = \frac{H^2}{D_{\mathrm{B}}}$) focuses on the biomass diffusion rate on the horizontal (resp., vertical) axis; $\tau = \frac{H}{\|u\|_{L^\infty(\bar{\Omega}\times(0,T))}}$ focuses on the advection transport rate; and $\tau = \frac{1}{\|\mu\|_{L^\infty(\mathbb{R})}}$ focuses on the reaction rate.

Since in next sections we perform a comparison with system (2), we center our study on the reaction process and take $\tau = \frac{1}{\|\mu\|_{L^\infty(\mathbb{R})}}$. Two well-known dimensionless numbers (see [23]) appear now in the non-dimensional form of system (4):

- Damkhöler Number: $\mathrm{Da} = \frac{\text{reaction rate}}{\text{advective transport rate}} = \frac{\tau_{\mathrm{a}}}{\tau_{\mathrm{r}}}$,
- Thiele Modulus: $\mathrm{Th} = \frac{\text{reaction rate}}{\text{diffusive transport rate}} = \frac{\tau_{\mathrm{d}}}{\tau_{\mathrm{r}}}$,

where τ_{d}, τ_{a} and τ_{r} are diffusion, advection and reaction times scales, respectively. For ease of notation, we drop the $\hat{}$ symbol, and so B, S, t, u, S_{e}, μ, z, r and T denote now the non-dimensional variables.

Particularly, if S_{e} and u are constants, system (4) in its non-dimensional form is given by

$$
\begin{cases}
\frac{\partial S}{\partial t} = \sigma^2(\mathrm{Th_S})^{-1}\frac{1}{r}\frac{\partial}{\partial r}(r\frac{\partial S}{\partial r}) + (\mathrm{Th_S})^{-1}\frac{\partial^2 S}{\partial z^2} + (\mathrm{Da})^{-1}\frac{\partial S}{\partial z} - \mu(S)B & \text{in } \Omega\times(0,T),\\
\frac{\partial B}{\partial t} = \sigma^2(\mathrm{Th_B})^{-1}\frac{1}{r}\frac{\partial}{\partial r}(r\frac{\partial B}{\partial r}) + (\mathrm{Th_B})^{-1}\frac{\partial^2 B}{\partial z^2} + (\mathrm{Da})^{-1}\frac{\partial B}{\partial z} + \mu(S)B & \text{in } \Omega\times(0,T),\\
(\mathrm{Th_S})^{-1}\frac{\partial S}{\partial z} + (\mathrm{Da})^{-1}S = (\mathrm{Da})^{-1} & \text{in } \Gamma_{\mathrm{in}}\times(0,T),\\
(\mathrm{Th_B})^{-1}\frac{\partial B}{\partial z} + (\mathrm{Da})^{-1}B = 0 & \text{in } \Gamma_{\mathrm{in}}\times(0,T),\\
\frac{\partial S}{\partial r} = 0 & \text{in } \left(\Gamma_{\mathrm{wall}}\cup\Gamma_{\mathrm{sym}}\right)\times(0,T),\\
\frac{\partial B}{\partial r} = 0 & \text{in } \left(\Gamma_{\mathrm{wall}}\cup\Gamma_{\mathrm{sym}}\right)\times(0,T),\\
\frac{\partial S}{\partial z} = 0 & \text{in } \Gamma_{\mathrm{out}}\times(0,T),\\
\frac{\partial B}{\partial z} = 0 & \text{in } \Gamma_{\mathrm{out}}\times(0,T),
\end{cases}
\tag{7}
$$

completed by the following initial conditions

$$S(r,z,0) = S_{\mathrm{init}} \quad \text{and} \quad B(r,z,0) = B_{\mathrm{init}} \qquad \forall (r,z)\in\Omega, \tag{8}$$

where $\Omega = (0,1)\times(0,1)$ is the nondimensional domain, $\Gamma_{\mathrm{in}} = (0,1)\times\{1\}$, $\Gamma_{\mathrm{out}} = (0,1)\times\{0\}$, $\Gamma_{\mathrm{wall}} = \{1\}\times(0,1)$ and $\Gamma_{\mathrm{sym}} = \{0\}\times(0,1)$ are the non-dimensional boundary edges. The final dimensionless parameters are

$$\mathrm{Da} = \frac{H\|\mu\|_{L^\infty(\mathbb{R})}}{u},\ \mathrm{Th_S} = \frac{H^2\|\mu\|_{L^\infty(\mathbb{R})}}{D_{\mathrm{S}}},\ \mathrm{Th_B} = \frac{D_{\mathrm{S}}}{D_{\mathrm{B}}}(\mathrm{Th_S}) \text{ and } \sigma = \frac{H}{L},$$

and the dimensionless initial conditions are $S_{\mathrm{init}}(r,z) = \dfrac{S_0(r,z)}{S_{\mathrm{e}}}$ and $B_{\mathrm{init}} = \dfrac{B_0(r,z)}{S_{\mathrm{e}}}$ $\forall (r,z)\in\Omega$.

Remark 2.1. *Since the bioreactor into consideration is a cylinder of height H and radius L, the reactor volume is πHL^2 and the volumetric flow rate in system* (1) *can be written as $Q = \pi L^2 u$, where u (m/s) is the vertical inflow. Thus, the nondimensional dilution rate d in system* (2) *corresponds to the nondimensional flow rate $\frac{1}{\mathrm{Da}}$ in system* (7)*.*

3. Steady states and stability analysis

In this section, we study the asymptotic behavior of system (7)-(8). Firstly, we study the particular case for which diffusion terms in system (7) are neglected. Then, we perform the stability analysis of system (7) for the general case.

The asymptotic stability of an equilibrium solution of system (7) is defined as follows (see [30]).

Definition 3.1 (Asymptotically Stable Equilibrium)**.** *An equilibrium solution (S^*, B^*) of system* (7) *is said to be asymptotically stable if there exists $\delta > 0$ such that*

$$\text{if } \|(S_{\mathrm{init}}, B_{\mathrm{init}}) - (S^*, B^*)\|_{(L^2(\Omega))^2} < \delta, \text{ then } \lim_{t\to\infty} \|(S(t), B(t)) - (S^*, B^*))\|_{(L^2(\Omega))^2} = 0, \tag{9}$$

where (S, B) is the solution of system (7)-(8)*.*

3.1. Case $\frac{1}{\mathrm{Th_S}}$, $\frac{1}{\mathrm{Th_B}}$, $\frac{\sigma^2}{\mathrm{Th_S}}$, $\frac{\sigma^2}{\mathrm{Th_B}} \ll 1$.

We consider the particular case where the nondimensional diffusion coefficients are negligible with respect to the advection and reaction coefficients in system (7). For each fixed value of $r \in (0,1)$, the solution $S(r,\cdot)$, $B(r,\cdot)$ can be approximated by the solution of the following 1-dimensional advection reaction system:

$$\begin{cases} \frac{\partial S}{\partial t} = (\mathrm{Da})^{-1}\frac{\partial S}{\partial z} - \mu(S)B, & \text{in } (0,1)\times(0,T), \\ \frac{\partial B}{\partial t} = (\mathrm{Da})^{-1}\frac{\partial B}{\partial z} + \mu(S)B & \text{in } (0,1)\times(0,T), \\ S(r,1,t) = 1 & \forall t \in (0,T), \\ B(r,1,t) = 0 & \forall t \in (0,T), \\ S(r,z,0) = S_{\mathrm{init}}(r,z) & \forall z \in (0,1), \\ B(r,z,0) = B_{\mathrm{init}}(r,z) & \forall z \in (0,1). \end{cases} \tag{10}$$

Let us prove that $(1,0)$ (which is called the *washout* state), is an asymptotically stable equilibrium. The following theorem shows, in fact, a property for $(1,0)$ stronger than asymptotic stability.

Theorem 3.2. *For any arbitrary initial condition* $(S_{\mathrm{init}}, B_{\mathrm{init}}) \in (L^\infty(\Omega))^2$*, the solution of* (10) *satisfies that* $S(r,z,t)= 1$ *and* $B(r,z,t) = 0$*, for all* $(r,z) \in \Omega$ *and* $t \geq \mathrm{Da}$.

Proof. For any fixed value of $r \in (0,1)$, we apply the Euler-Lagrange transformation from (r,z,t) to $(r,\tilde{z}(t,z),t)$, where $\tilde{z}(t,z) = z - \frac{1}{\mathrm{Da}}t$, so that for every fixed value of $(r,z) \in \Omega$, the second equation of system (10) is rewritten as

$$\frac{\mathrm{d}B}{\mathrm{d}t}(r,\tilde{z}(t,z),t) = \frac{\partial B}{\partial t}(r,\tilde{z}(t,z),t) - \frac{1}{\mathrm{Da}}\frac{\partial B}{\partial \tilde{z}}(r,\tilde{z}(t,z),t) = \mu(S(r,\tilde{z}(t,z),t))B(r,\tilde{z}(t,z),t).$$

Thus, for any $(r,z) \in \Omega$, one has that

$$B(r,\tilde{z}(t,z),t) = B(r,\tilde{z}(0,z),0) + \int_0^t \mu(S(r,\tilde{z}(\tau,z),\tau))B(\tilde{z}(\tau,z),\tau)\mathrm{d}\tau.$$

Particularly, for $z = 1$, we obtain

$$B(r,\tilde{z}(t,1),t) = \int_0^t \mu(S(r,\tilde{z}(\tau,1),\tau))B(r,\tilde{z}(\tau,1),\tau)\mathrm{d}\tau$$

and, by applying the Gronwall's inequality, we have that $B(r,\tilde{z}(t,1),t) = 0$ for all $t > 0$.

Using the same reasoning for the first equation of system (10), it follows that for $z = 1$

$$S(r,\tilde{z}(t,1),t) = 1 + \int_0^t \mu(S(r,\tilde{z}(\tau,1),\tau))B(r,\tilde{z}(\tau,1),\tau)\mathrm{d}\tau.$$

Since $B(r,\tilde{z}(t,1),t) = 0$ for all $t > 0$, we deduce that $S(r,\tilde{z}(t,1),t) = 1$ for all $t > 0$.
Coming back to Eulerian coordinates, one has that

$$B(r,1-\frac{1}{\mathrm{Da}}t,t) = 0 \text{ and } S(r,1-\frac{1}{\mathrm{Da}}t,t) = 1 \text{ for all } t > 0.$$

Consequently, if $t \geq \mathrm{Da}$, $B(r,z,t) = 0$ and $S(r,z,t) = 1$ for all $(r,z) \in \Omega$. □

3.2. General Case

In order to obtain a parallelism with the asymptotic analysis of system (2), shown in Section 1, we assume that μ fulfills properties (A1) or (A2). In both cases, the constant (washout) solution $(S_1^*, B_1^*) = (1, 0)$ is a steady state of system (7). By analogy with system (2), we conjecture, supported by numerical experiments, that system (7) has, under suitable conditions, another asymptotically stable steady state (different from the washout) denoted by (S_2^*, B_2^*). First, we use the method of linearization to give a sufficient condition for the asymptotic stability of the washout equilibrium. Then, we use this result to infer a sufficient condition for the asymptotic stability of the other equilibrium solution.

Remark 3.3. *We did not find any work studying the multiplicity of steady state solutions of a two dimensional coupled system of Advection-Diffusion-Reaction equations together with boundary conditions of mixed type in a domain with Lipschitz boundary, comparable to (7). Similar problems, but with other hypothesis, have been tackled for instance in [2, 22, 26].*

We first define the following functions, which will be used through the rest of the manuscript.

Definition 3.4.

- *In terms of the dimensionless variables appearing in system* (7), *we define* $\beta_1(\mathrm{Da}, \mathrm{Th_B})$ *as the smallest positive solution of the transcendental equation* $\tan(\beta) = \dfrac{\mathrm{Th_B}\beta}{\mathrm{Da}\big(\beta^2 - (\frac{\mathrm{Th_B}}{2\mathrm{Da}})^2\big)}$ *if* $\mathrm{Th_B} \neq \pi\mathrm{Da}$. *If* $\mathrm{Th_B} = \pi\mathrm{Da}$, *we define* $\beta_1(\mathrm{Da}, \mathrm{Th_B}) = \pi/2$.
- *In terms of the variables with dimensions appearing in system* (4), *we define* $\tilde{\beta}_1(H, u, D_\mathrm{B})$ *as the smallest positive solution of the transcendental equation* $\tan(\beta) = \dfrac{Hu\beta}{D_\mathrm{B}\big(\beta^2 - (\frac{Hu}{2D_\mathrm{B}})^2\big)}$ *if* $Hu \neq \pi D_\mathrm{B}$. *If* $Hu = \pi D_\mathrm{B}$ *we define* $\tilde{\beta}_1(H, u, D_\mathrm{B}) = \pi/2$.

Theorem 3.5. *A sufficient condition for* $(S_1^*, B_1^*) = (1, 0)$ *to be an asymptotically stable steady state of system* (7) *is that*

$$\mu(1) < \frac{\mathrm{Th_B}}{(2\mathrm{Da})^2} + \frac{(\beta_1(\mathrm{Da}, \mathrm{Th_B}))^2}{\mathrm{Th_B}}. \tag{11}$$

Remark 3.6. *In terms of the variables with dimensions appearing in system* (4), *the steady state is* $(S_\mathrm{e}, 0)$ *and inequality* (11) *is reformulated as*

$$\mu(S_\mathrm{e}) < \frac{u^2}{4D_\mathrm{B}} + \frac{D_\mathrm{B}}{H^2}(\tilde{\beta}_1(H, u, D_\mathrm{B}))^2.$$

Proof of Theorem 3.5. In order to check the stability of the equilibrium solution $(S_1^*, B_1^*) = (1, 0)$ we choose initial conditions close to it given by $S(r, z, 0) = 1 + \delta S_{\mathrm{init}} \geq 0$, $B(r, z, 0) = \delta B_{\mathrm{init}} \geq 0$, with $\|\delta S_{\mathrm{init}}\|_{L^2(\Omega)} \ll 1$ and $\|\delta B_{\mathrm{init}}\|_{L^2(\Omega)} \ll 1$. Linearizing around $(1, 0)$, we obtain

$$\begin{pmatrix} S(r,z,t) \\ B(r,z,t) \end{pmatrix} \approx \begin{pmatrix} 1 \\ 0 \end{pmatrix} + \begin{pmatrix} \bar{S}(r,z,t) \\ \bar{B}(r,z,t) \end{pmatrix}, \tag{12}$$

with

$$
\begin{cases}
\frac{\mathrm{d}\bar{S}}{\mathrm{d}t} = \sigma^2(\mathrm{Th_S})^{-1}\frac{1}{r}\frac{\mathrm{d}}{\mathrm{d}r}(r\frac{\mathrm{d}\bar{S}}{\mathrm{d}r}) + (\mathrm{Th_S})^{-1}\frac{\mathrm{d}^2\bar{S}}{\mathrm{d}z^2} + (\mathrm{Da})^{-1}\frac{\mathrm{d}\bar{S}}{\mathrm{d}z} - \mu(1)\bar{B} & \text{in } \Omega\times(0,T), \\
\frac{\mathrm{d}\bar{B}}{\mathrm{d}t} = \sigma^2(\mathrm{Th_B})^{-1}\frac{1}{r}\frac{\mathrm{d}}{\mathrm{d}r}(r\frac{\mathrm{d}\bar{B}}{\mathrm{d}r}) + (\mathrm{Th_B})^{-1}\frac{\mathrm{d}^2\bar{B}}{\mathrm{d}z^2} + (\mathrm{Da})^{-1}\frac{\mathrm{d}\bar{B}}{\mathrm{d}z} + \mu(1)\bar{B} & \text{in } \Omega\times(0,T), \\
(\mathrm{Th_S})^{-1}\frac{\mathrm{d}\bar{S}}{\mathrm{d}z} + (\mathrm{Da})^{-1}\bar{S} = 0 & \text{in } \Gamma_{\mathrm{in}}\times(0,T), \\
(\mathrm{Th_B})^{-1}\frac{\mathrm{d}\bar{B}}{\mathrm{d}z} + (\mathrm{Da})^{-1}\bar{B} = 0 & \text{in } \Gamma_{\mathrm{in}}\times(0,T), \\
\frac{\mathrm{d}\bar{S}}{\mathrm{d}r} = 0 & \text{in } \big(\Gamma_{\mathrm{wall}}\cup\Gamma_{\mathrm{sym}}\big)\times(0,T), \\
\frac{\mathrm{d}\bar{B}}{\mathrm{d}r} = 0 & \text{in } \big(\Gamma_{\mathrm{wall}}\cup\Gamma_{\mathrm{sym}}\big)\times(0,T), \\
\frac{\mathrm{d}\bar{S}}{\mathrm{d}z} = 0 & \text{in } \Gamma_{\mathrm{out}}\times(0,T), \\
\frac{\mathrm{d}\bar{B}}{\mathrm{d}z} = 0 & \text{in } \Gamma_{\mathrm{out}}\times(0,T), \\
\bar{S}(r,z,0) = \delta S_{\mathrm{init}}(r,z) & \forall(r,z)\in\Omega, \\
\bar{B}(r,z,0) = \delta B_{\mathrm{init}}(r,z) & \forall(r,z)\in\Omega.
\end{cases}
\tag{13}
$$

We are going to prove that the steady state $(S_1^*, B_1^*) = (1,0)$ is asymptotically stable by showing that (see Definition 3.1)

$$
\|\bar{S}(t)\|_{L^2(\Omega)} \longrightarrow 0 \quad \text{and} \quad \|\bar{B}(t)\|_{L^2(\Omega)} \longrightarrow 0 \text{ as } t\to\infty.
$$

Step 1. Let us prove that $\|\bar{B}(t)\|_{L^2(\Omega)} \longrightarrow 0$ as $t\to\infty$:
Notice that the equations involving the biomass in system (13) are decoupled from those involving the substrate, and may be solved by separation of variables by imposing

$$
\bar{B}(r,z,t) = R(r)Z(z)T(t).
$$

Step 1.1. Separation of variables.
From the second equation in system (13) one has that

$$
\frac{T'(t)}{T(t)} = \frac{\sigma^2}{\mathrm{Th_B}}\Big(\frac{R''(r)}{R(r)} + \frac{1}{r}\frac{R'(r)}{R(r)}\Big) + \frac{1}{\mathrm{Th_B}}\frac{Z''(z)}{Z(z)} + \frac{1}{\mathrm{Da}}\frac{Z'(z)}{Z(z)} + \mu(1).
$$

If we equate this expression to a constant λ, it follows that

$$
T'(t) - \lambda T(t) = 0 \text{ and}
$$

$$
\frac{\sigma^2}{\mathrm{Th_B}}\Big(\frac{R''(r)}{R(r)} + \frac{1}{r}\frac{R'(r)}{R(r)}\Big) = -\frac{1}{\mathrm{Th_B}}\frac{Z''(z)}{Z(z)} - \frac{1}{\mathrm{Da}}\frac{Z'(z)}{Z(z)} + \lambda - \mu(1).
$$

Equating this expression to an arbitrary constant η, one obtains

$$
R''(r) + \tfrac{1}{r}R'(r) - \tfrac{\mathrm{Th_B}}{\sigma^2}\eta R(r) = 0 \text{ and}
$$

$$
\tfrac{1}{\mathrm{Th_B}}Z''(z) + \tfrac{1}{\mathrm{Da}}Z'(z) - \big(\lambda - \mu(1) - \eta\big)Z(z) = 0.
$$

Proceeding as in the proof of Theorem 3 in [7], it is easy to see that

$$
\bar{B}(r,z,t) = |\bar{B}(r,z,t)| \le \|\delta B_{\mathrm{init}}\|_{L^\infty(\Omega)}\mathrm{e}^{\mu(1)t} \qquad \forall(r,z,t)\in\Omega\times(0,T).
$$

Particularly, the function $R : [0,1] \to \mathbb{R}$ must be bounded in $(0,1)$ (this fact will be used in the step 1.2 of this proof).

Step 1.2. Calculation of $R(r)$.
Using the boundary conditions of system (13) on Γ_{wall} and Γ_{sym}, it is clear that $R(r)$ is a solution of system

$$\begin{cases} R''(r) + \frac{1}{r}R'(r) - \frac{\text{Th}_\text{B}}{\sigma^2}\eta R(r) = 0 \quad r \in (0,1), \\ R'(0) = R'(1) = 0. \end{cases} \tag{14}$$

Taking the change of variables $s = ar$, with $a = \sqrt{|\eta|\frac{\text{Th}_\text{B}}{\sigma^2}}$, the differential equation for R can be rewritten in one of the following forms

1. $s^2R''(s) + sR'(s) + s^2R(s) = 0$ if $\eta < 0$,
2. $s^2R''(s) + sR'(s) - s^2R(s) = 0$ if $\eta > 0$,
3. $sR''(s) + R'(s) = 0$ if $\eta = 0$.

- **Case 1:** $\eta < 0$.

In this case the equation for $R(s)$ is known as the *Bessel equation of order zero*, with general solution

$$R(s) = C_1J_0(s) + C_2Y_0(s),$$

where C_1, $C_2 \in \mathbb{R}$ and J_n and Y_n are, respectively, the Bessel functions of first and second kind of order n. Since Y_0 has a singularity at $s = 0$, to ensure that function $R(s)$ is bounded, C_2 must be zero, and consequently, $R(s) = C_1J_0(s)$. It is well known that $J_0'(s) = -J_1(s)$ and $0 \in \{s \in [0,+\infty)\colon J_1(s) = 0\}$, which is a countable set $\{T_n\}_{n\in\mathbb{N}}$ with an infinite number of elements (see, e.g., [4]). Therefore, $R'(0) = 0$ is always satisfied and from the boundary condition at $s = a$ $(r = 1)$, one has that the eigenvalues η are such that $J_0'(\sqrt{\frac{-\eta\text{Th}_\text{B}}{\sigma^2}}) = 0$. Consequently, $\eta \in \{\eta_n\}_{n\in\mathbb{N}}$, with

$$\eta_n = -\frac{(\sigma T_n)^2}{\text{Th}_\text{B}}, \tag{15}$$

and the solution $R(r)$ is given by

$$R(r) = \sum_{n\in\mathbb{N}} C_nJ_0(\frac{\sqrt{-\text{Th}_\text{B}\eta_n}}{\sigma}r).$$

- **Case 2:** $\eta > 0$.

In this case the equation for $R(s)$ is known as the *modified Bessel equation of order zero*, with general solution

$$R(r) = C_1I_0(s) + C_2K_0(s),$$

where C_1, $C_2 \in \mathbb{R}$ and I_n and K_n are, respectively, the modified Bessel functions of first and second kind of order n. Again, since K_n has a singularity at $s = 0$, we have that $R(s) = C_1I_0(s)$. It is well known that $I_0'(s) = I_1(s)$ and the boundary condition at $s = a$ implies that that the eigenvalues η satisfy that

$$C_1I_0'(\sqrt{\frac{\eta\text{Th}_\text{B}}{\sigma^2}}) = 0.$$

Nevertheless, $I_0'(s) = I_1(s) > 0$, so that C_1 must be zero and the corresponding solution $R(s)$ is the trivial one.

- **Case 3:** $\eta = 0$.

Denoting $Q(s) = R'(s)$, the second order differential equation in R can be rewritten as $sQ'(s)+Q(s) = 0$. Easy calculations lead to

$$R(s) = -C_1 e^{-s} + C_2,$$

where C_1 and C_2 are constants to be determined with the boundary conditions. Thus, since $R'(0) = 0$, it follows that $C_1 = 0$ and one concludes that

$$R(s) = C_2.$$

Consequently, one has that the countable set of admissible eigenvalues η is

$$E = \{0\} \cup \{-\frac{(\sigma T_n)^2}{\mathrm{Th_B}}\}_{n\in\mathbb{N}}, \tag{16}$$

where T_n is such that $J_1(T_n) = 0$, J_1 being the Bessel function of first kind and order one. The general solution for the second order differential equation for R is

$$R(r) = C_0 + \sum_{n\in\mathbb{N}} C_n J_0(\frac{\sqrt{-\mathrm{Th_B}\eta_n}}{\sigma} r).$$

<u>Step 1.3.</u> Calculation of $Z(z)$.

Using the boundary conditions of system (13) on Γ_{in} and Γ_{out}, it is clear that function $Z(z)$ is solution of system

$$\begin{cases} (\mathrm{Th_B})^{-1}Z''(z) + (\mathrm{Da})^{-1}Z'(z) - (\lambda - \mu(1) - \eta)Z(z) = 0, \quad z \in (0,1), \\ (\mathrm{Th_B})^{-1}Z'(1) + (\mathrm{Da})^{-1}Z(1) = 0, \\ Z'(0) = 0, \end{cases} \tag{17}$$

which corresponds to a regular Sturm-Liouville eigenvalue problem (see, e.g., Theorem 1.3 in [19]). The corresponding characteristic equation is

$$\frac{1}{\mathrm{Th_B}}\rho^2 + \frac{1}{\mathrm{Da}}\rho - (\lambda - \mu(1) - \eta) = 0,$$

with roots

$$\rho = \frac{-\mathrm{Th_B}}{2\mathrm{Da}} \pm \frac{\mathrm{Th_B}}{2}\sqrt{(\frac{1}{\mathrm{Da}})^2 + \frac{4(\lambda - \mu(1) - \eta)}{\mathrm{Th_B}}}.$$

Now, depending on the value of $\Delta = (\frac{1}{\mathrm{Da}})^2 + \frac{4(\lambda-\mu(1)-\eta)}{\mathrm{Th_B}}$, three possible solutions appear.

- **Case 1:** $\Delta = 0 \Leftrightarrow \lambda = \eta + \mu(1) - \mathrm{Th_B}(\frac{1}{2\mathrm{Da}})^2$**.**

In this case, the solution of system (17) is

$$Z(z) = D_1 e^{\alpha z} + D_2 z e^{\alpha z},$$

where $\alpha = \frac{-\mathrm{Th_B}}{2\mathrm{Da}}$ and D_1, D_2 are constants which are determined by the boundary conditions of the system. Since

$$Z'(z) = \alpha e^{\alpha z}(D_1 + zD_2) + D_2 e^{\alpha z},$$

then $Z'(0) = \alpha D_1 + D_2 = 0$ if and only if $D_2 = -\alpha D_1$. Thus, the solution and its derivative can be rewritten as

$$Z(z) = D_1 e^{\alpha z}\big(1 - \alpha z\big) \qquad \text{and} \qquad Z'(z) = -D_1\alpha^2 z e^{\alpha z}.$$

From the boundary condition at $z = 1$ it follows that

$$D_1 e^{\alpha}\big(\frac{1}{\mathrm{Da}}(1-\alpha) - \frac{\alpha^2}{\mathrm{Th_B}}\big) = 0. \tag{18}$$

By replacing α by its value into equation (18), we conclude that this equation is true either if $\frac{\mathrm{Th_B}}{\mathrm{Da}} = -4$ or if $D_1 = 0$. The first option is not possible since constants Da and $\mathrm{Th_B}$ are assumed strictly positive. Thus, the only solution in this case is $Z(z) = 0$.

- **Case 2:** $\Delta < 0 \Leftrightarrow \lambda < \eta + \mu(1) - \mathrm{Th_B}(\frac{1}{2\mathrm{Da}})^2$**.**

In this case, we have two complex conjugate roots $\rho = \alpha \pm i\beta$, where $\alpha \in (-\infty, 0)$ and $\beta \in (0, +\infty)$. Then, the solution of system (17) is of the form

$$Z(z) = e^{\alpha z}\big(D_1 \cos(\beta z) + D_2 \sin(\beta z)\big),$$

where D_1 and D_2 are constants which will be determined by the boundary conditions.

Since

$$Z'(z) = \alpha Z(z) + \beta e^{\alpha z}\big(-D_1 \sin(\beta z) + D_2 \cos(\beta z)\big),$$

then $Z'(0) = \alpha D_1 + \beta D_2 = 0$ if and only if $D_2 = -\frac{\alpha}{\beta} D_1$.

Thus, the solution and its derivative can be rewritten as

$$Z(z) = D_1 e^{\alpha z}\big(\cos(\beta z) - \frac{\alpha}{\beta}\sin(\beta z)\big) \qquad \text{and} \qquad Z'(z) = -D_1 e^{\alpha z}\sin(\beta z)(\frac{\alpha^2}{\beta} + \beta).$$

From the boundary condition at $z = 1$ it follows that:

$$D_1 e^{\alpha}\Big(\frac{1}{\mathrm{Da}}\cos(\beta) - \sin(\beta)\big(\frac{1}{\mathrm{Da}}\frac{\alpha}{\beta} + \frac{1}{\mathrm{Th_B}}(\frac{\alpha^2}{\beta} + \beta)\big)\Big) = 0,$$

which solutions are $D_1 = 0$ or

$$\tan(\beta) = \frac{\frac{1}{\mathrm{Da}}}{\frac{\alpha}{\beta}\frac{1}{\mathrm{Da}} + (\frac{\alpha^2}{\beta} + \beta)\frac{1}{\mathrm{Th_B}}} = \frac{\beta}{\frac{\mathrm{Da}}{\mathrm{Th_B}}\beta^2 + \frac{\alpha}{2}} = \frac{\beta}{\frac{1}{2}(-\frac{\beta^2}{\alpha} + \alpha)} = \frac{2\alpha\beta}{-\beta^2 + \alpha^2}. \tag{19}$$

As $F(\beta) = \dfrac{2\alpha\beta}{\alpha^2 - \beta^2}$ is a decreasing function and has an asymptote at $\beta = -\alpha$, there exists a countable set $\{\beta_n\}_{n\in\mathbb{N}}$ with $\beta_n \in ((n-1)\pi, n\pi)$ satisfying $F(\beta_n) = \tan(\beta_n)$.

Consequently,

$$Z(z) = \sum_{n\in\mathbb{N}} D_n e^{-\frac{\mathrm{Th_B}}{2\mathrm{Da}}z}\big(\cos(\beta_n z) + \frac{\mathrm{Th_B}}{2\mathrm{Da}\beta_n}\sin(\beta_n z)\big),$$

where $\beta_n \in (0, +\infty)$ fulfills equation (19).

- **Case 3:** $\Delta > 0 \Leftrightarrow \lambda > \eta + \mu(1) - \mathrm{Th_B}(\frac{1}{2\mathrm{Da}})^2$**.**

In this case, we have two different real roots $\rho_{1,2} = \alpha \pm \beta$, with $\alpha = \frac{-\mathrm{Th_B}}{2\mathrm{Da}}$, $\beta = \frac{\mathrm{Th_B}}{2}\sqrt{(\frac{1}{\mathrm{Da}})^2 + \frac{4(\lambda - \mu(1) - \eta)}{\mathrm{Th_B}}}$, and the solution of equation (17) is of the form

$$Z(z) = D_1 e^{(\alpha+\beta)z} + D_2 e^{(\alpha-\beta)z},$$

where D_1 and D_2 are constants which will be determined by the boundary conditions.

Since $Z'(z) = (\alpha+\beta)D_1 e^{(\alpha+\beta)z} + (\alpha-\beta)D_2 e^{(\alpha-\beta)z}$, $\alpha < 0$ and $\beta > 0$, then $Z'(0) = (\alpha+\beta)D_1 + (\alpha - \beta)D_2 = 0$ if and only if $D_2 = -\frac{(\alpha+\beta)}{(\alpha-\beta)}D_1$.

Thus, the solution and its derivative can be rewritten as

$$Z(z) = D_1\big(\mathrm{e}^{(\alpha+\beta)z} - \frac{(\alpha+\beta)}{(\alpha-\beta)}\mathrm{e}^{(\alpha-\beta)z}\big) \qquad \text{and} \qquad Z'(z) = D_1(\alpha+\beta)\big(\mathrm{e}^{(\alpha+\beta)z} - \mathrm{e}^{(\alpha-\beta)z}\big).$$

From the boundary condition at $z = 1$, it follows that:

$$D_1\mathrm{e}^{\alpha}\frac{(\alpha+\beta)}{\mathrm{Th_B}}\big(\mathrm{e}^{\beta} - \mathrm{e}^{-\beta}\big) + D_1\mathrm{e}^{\alpha}\frac{1}{\mathrm{Da}}\big(\mathrm{e}^{\beta} - \frac{(\alpha+\beta)}{(\alpha-\beta)}\mathrm{e}^{-\beta}\big) = 0,$$

which implies $D_1 = 0$ or

$$\mathrm{e}^{\beta}\big(\frac{(\alpha+\beta)}{\mathrm{Th_B}} + \frac{1}{\mathrm{Da}}\big) = \mathrm{e}^{-\beta}\big(\frac{(\alpha+\beta)}{\mathrm{Th_B}} + \frac{(\alpha+\beta)}{(\alpha-\beta)}\frac{1}{\mathrm{Da}}\big) \Leftrightarrow$$

$$\mathrm{e}^{2\beta} = \frac{\frac{(\alpha+\beta)}{\mathrm{Th_B}} + \frac{1}{\mathrm{Da}}\frac{(\alpha+\beta)}{(\alpha-\beta)}}{\frac{(\alpha+\beta)}{\mathrm{Th_B}} + \frac{1}{\mathrm{Da}}} = \frac{(\alpha+\beta)}{(\alpha-\beta)}\big(\frac{(\alpha-\beta)\mathrm{Da} + \mathrm{Th_B}}{(\alpha+\beta)\mathrm{Da} + \mathrm{Th_B}}\big) = \frac{(\alpha+\beta)}{(\alpha-\beta)}\big(\frac{-(\beta+\alpha)\mathrm{Da}}{(\beta-\alpha)\mathrm{Da}}\big) \Leftrightarrow$$

$$\mathrm{e}^{2\beta} = \big(\frac{\alpha+\beta}{\alpha-\beta}\big)^2. \tag{20}$$

Again, as $\beta > 0$ and $\alpha < 0$, then $(\beta+\alpha)^2 < (\alpha-\beta)^2$ and thus $(\frac{\alpha+\beta}{\alpha-\beta})^2 < 1$. This implies that $D_1 = 0$ is the unique admissible solution and $Z(z) = 0$.

Step 1.4. General expression of $\bar{B}(r, z, t)$.
Given $\eta_n \in E$ (see equation (16)), there exists a countable set of admissible eigenvalues λ

$$\Lambda_n = \{\lambda_{nm}\}_{m\in\mathbb{N}} = \{\mu(1) + \eta_n - \frac{1}{(2\mathrm{Da})^2}\mathrm{Th_B} - \frac{\beta_m^2}{\mathrm{Th_B}}\}_{m\in\mathbb{N}}, \tag{21}$$

where β_m fulfills system (19).
Consequently,

$$\bar{B}(r, z, t) = \sum_{n\in\{0\}\cup\mathbb{N}}\sum_{m\in\mathbb{N}} A_{nm}\mathrm{e}^{\lambda_{nm}t}J_0\big(\frac{\sqrt{-\mathrm{Th_B}\eta_n}}{\sigma}r\big)\mathrm{e}^{-\frac{\mathrm{Th_B}}{2\mathrm{Da}}z}\big(\cos(\beta_m z) + \frac{\mathrm{Th_B}}{2\mathrm{Da}\beta_m}\sin(\beta_m z)\big),$$

where $\eta_n \in E$, β_m fulfills (19), $\lambda_{nm} \in \Lambda_n$ and the constants A_{nm} are chosen such that $\bar{B}(r, z, 0) = \delta B_{\mathrm{init}}(r, z)$. Notice that the constants A_{nm} are well defined since the two systems (14) and (17) are regular Sturm-Liouville eigenvalue problems (see, e.g., Theorem 1.3 in [19]).

Using Parseval's equation (see, for instance, [39]) one has that

$$\|\bar{B}(t)\|^2_{L^2(\Omega)} = \sum_{n\in\mathbb{N}\cup\{0\}}\sum_{m\in\mathbb{N}} A_{nm}^2\mathrm{e}^{2\lambda_{nm}t}.$$

Furthermore, it is straightforward to see that

$$\lambda_{nm} \leq \lambda_{01} = \mu(1) - \frac{1}{(2\mathrm{Da})^2}\mathrm{Th_B} - \frac{\beta_1^2}{\mathrm{Th_B}} \qquad \forall\ (n, m) \in (\{0\}\cup\mathbb{N})\times\mathbb{N}.$$

Therefore, if

$$\lambda_{01} = \mu(1) - \big(\frac{1}{2\mathrm{Da}}\big)^2\mathrm{Th_B} - \frac{\beta_1^2}{\mathrm{Th_B}} < 0, \tag{22}$$

(which is the same condition as (11)) it follows that

$$\|\bar{B}(t)\|^2_{L^2(\Omega)} \leq \mathrm{e}^{2\lambda_{01}t} \sum_{n\in\mathbb{N}\cup\{0\}} \sum_{m\in\mathbb{N}} A^2_{nm} = \mathrm{e}^{2\lambda_{01}t}\|\bar{B}(0)\|^2_{L^2(\Omega)} \xrightarrow{t\to\infty} 0.$$

Notice that, if $\lambda_{01} < 0$, one can also deduce inequality (that will be used at the end of this proof)

$$\|\bar{B}(t)\|^2_{L^2(\Omega)} \leq \|\bar{B}(0)\|^2_{L^2(\Omega)} \leq K^2\|\delta B_{\mathrm{init}}\|^2_{L^\infty(\Omega)}, \tag{23}$$

where K is a constant relating the norms $\|\cdot\|_{L^2(\Omega)}$ and $\|\cdot\|_{L^\infty(\Omega)}$.

Step 2. Let us prove that $\|\bar{S}(t)\|_{L^2(\Omega)} \longrightarrow 0$ as $t \to \infty$:
Regarding $\bar{S}$, the main equation involving the substrate in system (13) is an Advection-Diffusion equation with non-homogeneous term $-\mu(1)\bar{B}(r,z,t)$, which makes complex the use of separation of variables. Here, we prove that $\|\bar{S}(\cdot,\cdot,t)\|_{L^2(\Omega)} \xrightarrow{t\to\infty} 0$ by using variational techniques. To this aim, we multiply the first equation in system (13) by $r\bar{S}$ and integrate as follows

$$\begin{aligned}
\int_0^t\int_\Omega r\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}\tau}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau = {} & \tfrac{\sigma^2}{\mathrm{Th_S}}\int_0^t\int_\Omega \tfrac{\mathrm{d}}{\mathrm{d}r}(r\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}r})\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau + \tfrac{1}{\mathrm{Th_S}}\int_0^t\int_\Omega r\tfrac{\mathrm{d}^2\bar{S}}{\mathrm{d}z^2}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
& +\tfrac{1}{\mathrm{Da}}\int_0^t\int_\Omega r\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau - \mu(1)\int_0^t\int_\Omega r\bar{B}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
= {} & \tfrac{\sigma^2}{\mathrm{Th_S}}\int_0^t\int_{\Gamma_{\mathrm{sym}}\cup\Gamma_{\mathrm{wall}}} r\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}r}\bar{S}\mathrm{d}z\mathrm{d}\tau - \tfrac{\sigma^2}{\mathrm{Th_S}}\int_0^t\int_\Omega r(\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}r})^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
& +\int_0^t\int_{\Gamma_{\mathrm{in}}} r\big(\tfrac{1}{\mathrm{Th_S}}\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z} + \tfrac{1}{\mathrm{Da}}\bar{S}\big)\bar{S}\mathrm{d}r\mathrm{d}\tau - \int_0^t\int_{\Gamma_{\mathrm{out}}} r\big(\tfrac{1}{\mathrm{Th_S}}\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z} + \tfrac{1}{\mathrm{Da}}\bar{S}\big)\bar{S}\mathrm{d}r\mathrm{d}\tau \\
& -\tfrac{1}{\mathrm{Th_S}}\int_0^t\int_\Omega r(\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z})^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau - \tfrac{1}{\mathrm{Da}}\int_0^t\int_\Omega r\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
& -\mu(1)\int_0^t\int_\Omega r\bar{B}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
= {} & -\tfrac{\sigma^2}{\mathrm{Th_S}}\int_0^t\int_\Omega r(\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}r})^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau - \tfrac{1}{\mathrm{Th_S}}\int_0^t\int_\Omega r(\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z})^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
& -\tfrac{1}{\mathrm{Da}}\int_0^t\int_{\Gamma_{\mathrm{out}}} r\bar{S}^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \underbrace{-\frac{1}{\mathrm{Da}}\int_0^t\int_\Omega r\frac{\mathrm{d}\bar{S}}{\mathrm{d}z}\bar{S}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau}_{(I)} \\
& -\mu(1)\int_0^t\int_\Omega r\bar{S}\bar{B}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau.
\end{aligned} \tag{24}$$

The integral denoted by (I) in equation (24) can be rewritten as

$$(I) = -\frac{1}{2\mathrm{Da}}\int_0^t\int_\Omega r\frac{\mathrm{d}(\bar{S}^2)}{\mathrm{d}z}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau = -\frac{1}{2\mathrm{Da}}\int_0^t\int_{\Gamma_{\mathrm{in}}} r\bar{S}^2\mathrm{d}r\mathrm{d}\tau + \frac{1}{2\mathrm{Da}}\int_0^t\int_{\Gamma_{\mathrm{out}}} r\bar{S}^2\mathrm{d}r\mathrm{d}\tau.$$

Thus, equation (24) leads to

$$\begin{aligned}
&\tfrac{1}{2}\int_0^t\int_\Omega r\tfrac{\mathrm{d}(\bar{S}^2)}{\mathrm{d}\tau}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau + \tfrac{\sigma^2}{\mathrm{Th_S}}\int_0^t\int_\Omega r(\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}r})^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau + \tfrac{1}{\mathrm{Th_S}}\int_0^t\int_\Omega r(\tfrac{\mathrm{d}\bar{S}}{\mathrm{d}z})^2\mathrm{d}r\mathrm{d}z\mathrm{d}\tau \\
&+\tfrac{1}{2\mathrm{Da}}\int_0^t\int_{\Gamma_{\mathrm{in}}} r\bar{S}^2\mathrm{d}r\mathrm{d}\tau + \tfrac{1}{2\mathrm{Da}}\int_0^t\int_{\Gamma_{\mathrm{out}}} r\bar{S}^2\mathrm{d}r\mathrm{d}\tau = -\mu(1)\int_0^t\int_\Omega r\bar{S}\bar{B}\mathrm{d}r\mathrm{d}z\mathrm{d}\tau.
\end{aligned} \tag{25}$$

By multiplying equation (25) by 2π and applying Young's inequality (with $\epsilon > 0$ to be chosen afterward), we obtain

$$\begin{aligned}
&\tfrac{1}{2}\int_0^t \tfrac{\mathrm{d}}{\mathrm{d}\tau}\big(\|\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\big)\mathrm{d}\tau + \tfrac{\min(1,\sigma^2)}{\mathrm{Th_S}}\int_0^t\|\nabla\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}\tau + \tfrac{1}{2\mathrm{Da}}\int_0^t\|\bar{S}(\tau)\|^2_{L^2(\Gamma^*_{\mathrm{out}})}\mathrm{d}\tau \\
&\leq \epsilon\mu(1)\int_0^t\|\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}\tau + \tfrac{\mu(1)}{4\epsilon}\int_0^t\|\bar{B}(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}\tau.
\end{aligned} \tag{26}$$

Considering $A = \min\{\frac{1}{\mathrm{Th_S}}, \frac{\sigma^2}{\mathrm{Th_S}}, \frac{1}{2\mathrm{Da}}\}$, it follows that

$$\begin{aligned} &\tfrac{1}{2}\int_0^t \tfrac{\mathrm{d}}{\mathrm{d}\tau}\big(\|\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\big)\mathrm{d}\tau + A\int_0^t(\|\nabla\bar{S}(\tau)\|^2_{L^2(\Omega^*)} + \|\bar{S}(\tau)\|^2_{L^2(\Gamma^*_{\mathrm{out}})})\mathrm{d}\tau \\ &\leq \epsilon\mu(1)\int_0^t \|\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}\tau + \tfrac{\mu(1)}{4\epsilon}\|\bar{B}\|^2_{L^2((0,t)\times\Omega^*)}. \end{aligned} \tag{27}$$

Now, applying Friedrich's inequality (see. e.g., Theorem 6.1 in [21]) to inequality (27) with $E = \Gamma^*_{\mathrm{out}}$, there exits a constant C depending on Ω^* and Γ^*_{out} such that

$$\tfrac{1}{2}\int_0^t \tfrac{\mathrm{d}}{\mathrm{d}\tau}\big(\|\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\big)\mathrm{d}\tau \leq \big(\epsilon\mu(1) - \tfrac{A}{C}\big)\int_0^t \|\bar{S}(\tau)\|^2_{L^2(\Omega^*)}\mathrm{d}\tau + \tfrac{\mu(1)}{4\epsilon}\|\bar{B}\|^2_{L^2(\Omega^*\times(0,t))}. \tag{28}$$

Next, applying the Gronwall's inequality in its integral form, it follows that

$$\|\bar{S}(t)\|^2_{L^2(\Omega^*)} \leq \underbrace{\big(\|\delta S_{\mathrm{init}}\|^2_{L^2(\Omega^*)} + \frac{\mu(1)}{2\epsilon}\|\bar{B}\|^2_{L^2(\Omega^*\times(0,t))}\big)}_{(:=m(t))}\,\mathrm{e}^{\overbrace{2(\epsilon\mu(1) - \frac{A}{C})}^{(:=\alpha)}t}.$$

Since $\|\bar{B}(t)\|^2_{L^2(\Omega)} \leq K^2\|\delta B_{\mathrm{init}}\|^2_{L^\infty(\Omega)}$ for all $t > 0$ (see equation (23)), taking $\epsilon < \frac{A}{\mu(1)C}$ it follows that $\alpha < 0$. Thus,

$$\|\bar{S}(t)\|^2_{L^2(\Omega^*)} \leq \big(\|\delta S_{\mathrm{init}}\|^2_{L^2(\Omega^*)} + \frac{\mu(1)}{2\epsilon}tK^2\|\delta B_{\mathrm{init}}\|^2_{L^\infty(\Omega^*)}\big)\mathrm{e}^{\alpha t} \xrightarrow{t\to\infty} 0.$$

□

Taking into account Theorem 3.5, we conjecture (supported by the numerical experiments presented in Section 4) that the following result holds:

Proposition 3.7. *If μ fulfills* (A1) *(respectively,* (A2)*), a sufficient condition for* (S_2^*, B_2^*) *to be an asymptotically stable steady state of system* (7) *is that*

$$\mu(1) > \frac{\mathrm{Th_B}}{(2\mathrm{Da})^2} + \frac{(\beta_1(\mathrm{Da},\mathrm{Th_B}))^2}{\mathrm{Th_B}} \tag{29}$$

(respectively,

$$1 > \frac{\mathrm{Th_B}}{(2\mathrm{Da})^2} + \frac{(\beta_1(\mathrm{Da},\mathrm{Th_B}))^2}{\mathrm{Th_B}}). \tag{30}$$

Remark 3.8. *In terms of the variables with dimensions appearing in system* (4)*, conditions* (29) *and* (30) *are reformulated, respectively, as*

$$\mu(S_{\mathrm{e}}) > \frac{u^2}{4D_{\mathrm{B}}} + \frac{D_{\mathrm{B}}}{H^2}(\tilde{\beta}_1(H,u,D_{\mathrm{B}}))^2,$$

and

$$\|\mu\|_{L^\infty(\mathbb{R})} > \frac{u^2}{4D_{\mathrm{B}}} + \frac{D_{\mathrm{B}}}{H^2}(\tilde{\beta}_1(H,u,D_{\mathrm{B}}))^2.$$

Remark 3.9. *From Theorem 3.5 and Proposition 3.7, it follows that if μ fulfills* (A2) *and $\mu(1) < 1$, there is bistability in system* (7) *when*

$$\mu(1) < \frac{\mathrm{Th_B}}{(2\mathrm{Da})^2} + \frac{(\beta_1(\mathrm{Da},\mathrm{Th_B}))^2}{\mathrm{Th_B}} < 1.$$

3.2.1. Bounds for the flow rate assuring asymptotic stability of the steady states

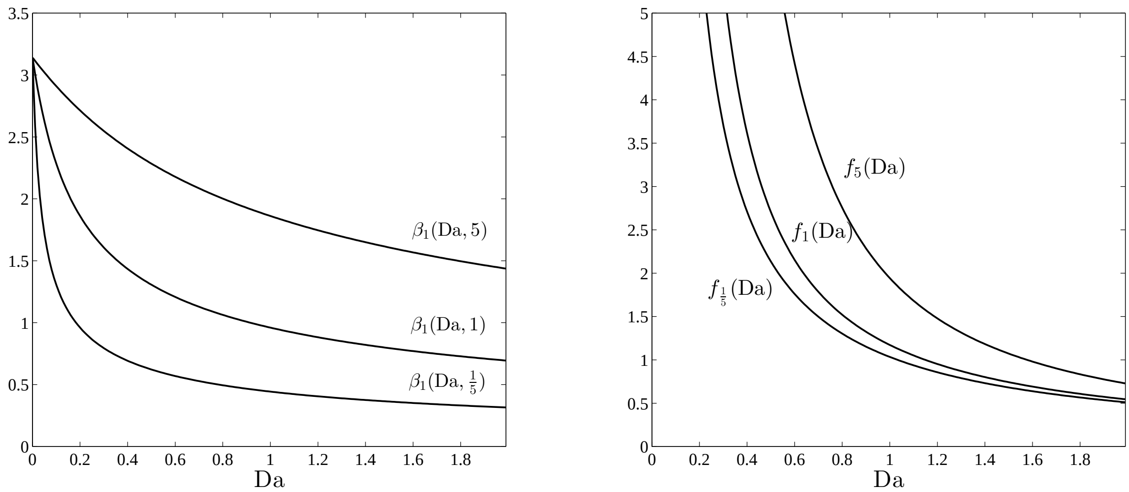
Conditions (11) and (30) include in their analytical expression the model parameters Da, $\mathrm{Th_B}$ and $\mu(1)$, among which the flow rate Da can be seen as a bioreactor control parameter. In this section, we present bounds for the parameter Da assuring the asymptotic stability of the steady states $(1,0)$ and (S_2^*, B_2^*). To do so, we first define the following function.

Definition 3.10. *For a fixed value* $\mathrm{Th_B}$*, one can define the function*

$$f_{\mathrm{Th_B}}: \quad [0,+\infty) \longrightarrow [0,+\infty)$$

$$\mathrm{Da} \quad \rightarrow \quad \frac{\mathrm{Th_B}}{(2\mathrm{Da})^2} + \frac{(\beta_1(\mathrm{Da},\mathrm{Th_B}))^2}{\mathrm{Th_B}}.$$

In Figure 2 we plot the value of functions $\beta_1(\mathrm{Da},\mathrm{Th_B})$ and $f_{\mathrm{Th_B}}(\mathrm{Da})$ for $\mathrm{Th_B} \in \{\frac{1}{5}, 1, 5\}$ and $\mathrm{Da} \in [0,2]$. For a fixed value $\mathrm{Th_B}$, function $\beta_1(\cdot,\mathrm{Th_B})$ is decreasing, bounded by π (see the proof of Theorem 3.5 for a detailed explanation of this feature) and $\beta_1(\mathrm{Da},\mathrm{Th_B}) \xrightarrow{\mathrm{Da}\to+\infty} 0$. One can also conclude that, for a fixed value $\mathrm{Th_B}$, function $f_{\mathrm{Th_B}}$ is decreasing, $f_{\mathrm{Th_B}}(\mathrm{Da}) \xrightarrow{\mathrm{Da}\to 0} +\infty$ and $f_{\mathrm{Th_B}}(\mathrm{Da}) \xrightarrow{\mathrm{Da}\to+\infty} 0$. Taking into account these properties of $f_{\mathrm{Th_B}}$, we define the following variables.



(a) $\beta_1(\mathrm{Da},\mathrm{Th_B})$ (b) $f_{\mathrm{Th_B}}(\mathrm{Da})$

Figure 2: Graphical plots of functions $\beta_1(\mathrm{Da},\mathrm{Th_B})$ and $f_{\mathrm{Th_B}}(\mathrm{Da})$ (described in Definitions 3.4 and 3.10, respectively) for $\mathrm{Th_B} \in \{\frac{1}{5}, 1, 5\}$ and $\mathrm{Da} \in [0,2]$.

Definition 3.11. *We define*

- $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B},\mu(1)) := (f_{\mathrm{Th_B}})^{-1}(\mu(1))$.
- $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A1}),(7)}(\mathrm{Th_B},\mu(1)) := \mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B},\mu(1))$.
- $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B}) := (f_{\mathrm{Th_B}})^{-1}(1)$.

Remark 3.12. *Following Theorem 3.5 and Proposition 3.7, it follows that:*

- *If* $\mathrm{Da} < \mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B},\mu(1))$*, then the equilibrium state* $(1,0)$ *of system* (7) *is asymptotically stable.*

- *If μ fulfills* (A1) *and* $\mathrm{Da} > \mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A1}),(7)}(\mathrm{Th_B}, \mu(1))$*, then the equilibrium state* (S_2^*, B_2^*) *of system* (7) *is asymptotically stable.*

- *If μ fulfills* (A2) *and* $\mathrm{Da} > \mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$*, then the equilibrium state* (S_2^*, B_2^*) *of system* (7) *is asymptotically stable.*

4. Numerical Experiments

In this section, we describe the results of the numerical experiments performed to analyze the validity and robustness of the stability analysis done in Section 3. In Section 4.1, we study the sensitivity of variables $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$, defined in Section 3.2.1, regarding the model parameters. Then, In Section 4.2, we carry out the numerical implementation of system (7)-(8) in order to check the interest of these functions. Finally, in Section 4.3, we compare the results of the stability analysis of systems (2) and (7).

Through this section, the value of functions $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ is approximated numerically using a self-implemented *Dichotomy method* (see, e.g. [17]). Moreover, for each pair $(\mathrm{Th_B}, \mathrm{Da})$, the value of $\beta_1(\mathrm{Th_B}, \mathrm{Da})$ (see Definition 3.4) was computed by using the MATLAB function `vpasolve` (see `www.mathworks.com/help/symbolic/vpasolve.html`).

4.1. Sensitivity to model parameters

In this section, we perform the sensitivity analysis of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ with respect to the nondimensional parameters $\mathrm{Th_B}$ and $\mu(1)$ (the sensitivity analysis of $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ can be obtained with a similar methodology).

4.1.1. Sensitivity with respect to $\mu(1)$

Taking into account that $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1)) = (f_{\mathrm{Th_B}})^{-1}(\mu(1))$ and $f_{\mathrm{Th_B}}$ is decreasing, one concludes that, for any fixed value $\mathrm{Th_B}$, the function $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ decreases as $\mu(1)$ increases. This is physically reasonable since, as parameter $\mu(1)$ increases, the range of flow rates $\frac{1}{\mathrm{Da}}$ suitable to avoid washout also increases (see, e.g, [8, 12, 38]).

4.1.2. Sensitivity with respect to $\mathrm{Th_B}$

In order to easily analyze the sensitivity of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ with respect to $\mathrm{Th_B}$, we aim to approximate $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ by using the following variables:

- $\overline{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1)) := \frac{1}{2}\sqrt{\frac{\mathrm{Th_B}}{\mu(1)}}$. This should be a good approximation of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ assuming that the second term of the right hand side of condition (11) is negligible.

- $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1)) := (g_{\mathrm{Th_B}})^{-1}(\mu(1))$, where

$$g_{\mathrm{Th_B}} : [0, +\infty) \longrightarrow [0, +\infty)$$
$$\mathrm{Da} \to \frac{(\beta_1(\mathrm{Th_B}, \mathrm{Da}))^2}{\mathrm{Th_B}}.$$

  This should be a good approximation of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ assuming that the first term of the right hand side of condition (11) is negligible. Since $\beta_1(\mathrm{Th_B}, \mathrm{Da}) < \pi$ (see the proof of Theorem 3.5 for a detailed explanation of this fact), if $\mathrm{Th_B}\mu(1) > \pi^2$, then the function $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ is not defined. We approximate numerically $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ applying the same methodology that the one used to approximate numerically $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$, described above.

Figure 3 illustrates the difference between the functions $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$, $\overline{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ when $\mu(1) = 0.5$ and $\mathrm{Th_B} \in [5 \cdot 10^{-3}, 5 \cdot 10^{3}]$. We observe that $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ approximates $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ for values smaller than $\log(\mathrm{Th_B}) = -2$ ($\mathrm{Th_B} \approx 0.1$) while $\overline{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ approximates $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ for values larger than $\log(\mathrm{Th_B}) = 6$ ($\mathrm{Th_B} \approx 400$).

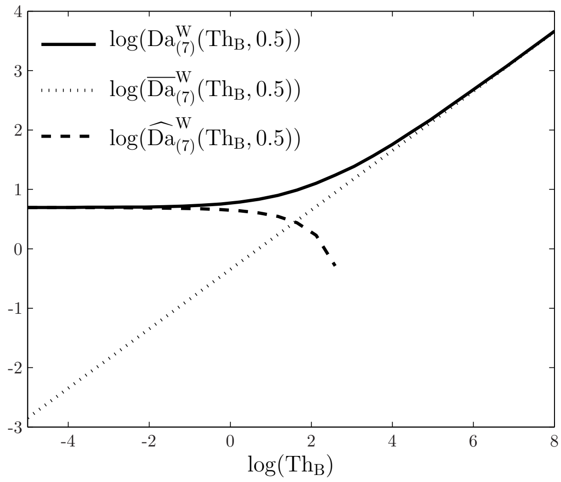


Figure 3: Comparison between the functions $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$, $\overline{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ and $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ (depicted with solid, dotted and dashed lines, respectively), when $\mathrm{Th_B} \in [5 \cdot 10^{-3}, 5 \cdot 10^{3}]$.

The comparison between the functions $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$, $\overline{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(2)}(\mathrm{Th_B}, \mu(1))$, shown in Figure 3 for $\mu(1) = 0.5$, has been reproduced for reaction values $\mu(1) \in \{\frac{i}{20}\}_{i=1}^{20}$ and the results seems to indicate that in general: if $\mathrm{Th_B} \geq 10^4$, the function $\overline{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ can be used as an approximation of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$; and if $\mathrm{Th_B} \leq 10^{-1}$, the function $\widehat{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mu(1))$ can be used as an approximation of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$.

Taking into account the approximations of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ presented above and Figure 3, the sensitivity of $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ with respect to $\mathrm{Th_B}$ reads as follows:

- If $\mathrm{Th_B} \leq 0.1$, the variable $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ is not sensible to parameter $\mathrm{Th_B}$. Indeed, small values of $\mathrm{Th_B}$ correspond, for instance, to high diffusion coefficients implying almost spatial homogeneous biomass concentration. In this case, there would be no differences when considering even higher diffusion coefficients. As we will see in Section 4.3, if $\mathrm{Th_B} \leq 0.1$, the dynamics of the bioreactor can be modeled with ordinary differential equations.

- If $\mathrm{Th_B} > 0.1$, the variable $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ seems to increase with parameter $\mathrm{Th_B}$. This outcome is physically reasonable, since as parameter $\mathrm{Th_B}$ increases (equivalently, the diffusion coefficient decreases) the flow rate $\frac{1}{\mathrm{Da}}$ should be chosen smaller to favor the reaction between the substrate and the biomass (see [8]).

- If $\mathrm{Th_B} \geq 10^4$, the variable $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ is quadratically proportional to $\mathrm{Th_B}$.

4.2. Numerical validation of the results

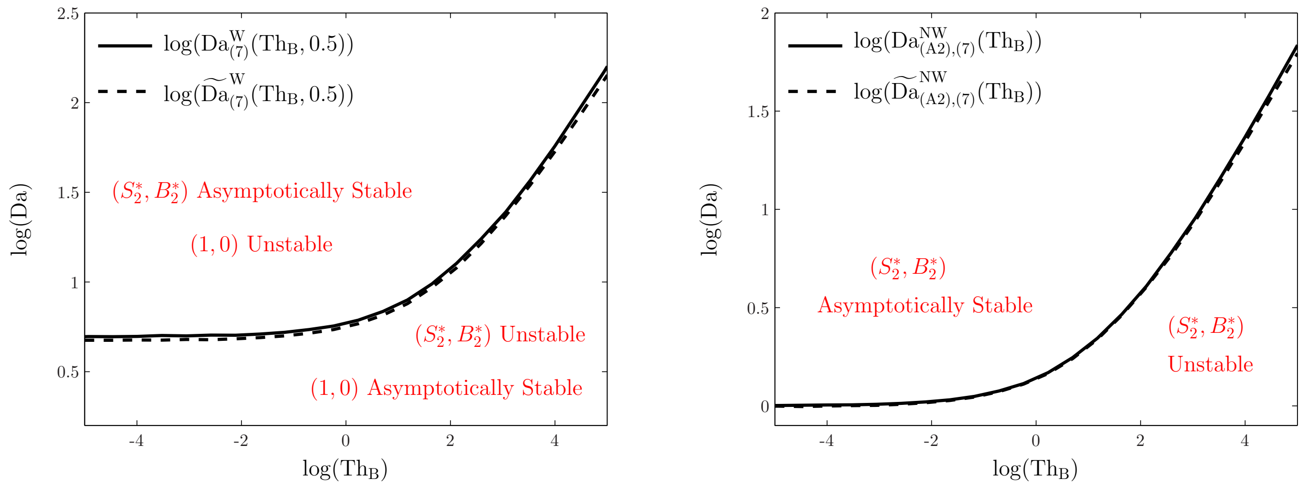
In this section, we check the properties given in Remark 3.12 for the threshold values $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B}, \mu(1))$ by using the numerical solution of system (7)-(8). To do that computation, we use the software COMSOL Multiphysics 5.0 (`www.comsol.com`), based on the Finite Element Method (see [32]). The numerical experiments were carried out in a 2.8Ghz Intel i7-930 64bits computer with 12Gb of RAM. We used a triangular mesh with around 1000 elements and final nondimensional time $T = 300$.

In order to validate the properties of the threshold values $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B}, \mu(1))$, we define the following variables:

- $\widetilde{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1)) := \sup\{\mathrm{Da}$: the numerical solution of system (7)-(8) (with parameters $\mathrm{Th_B}$, Da, $\mathrm{Th_S} = \mathrm{Th_B}$, $\sigma = 1$, μ the nondimensional Monod function with $K_\mathrm{S} = \frac{1-\mu(1)}{\mu(1)}$, $S_\mathrm{init} = 0.1$ and $B_\mathrm{init} = 0.9$) approaches asymptotically the steady state $(1, 0)\}$.

- $\widetilde{\mathrm{Da}}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B}) := \inf\{\mathrm{Da}$: the numerical solution of system (7)-(8) (with parameters $\mathrm{Th_B}$, Da, $\mathrm{Th_S} = \mathrm{Th_B}$, $\sigma = 1$, μ the nondimensional Haldane function with $\frac{\mu^*}{\|\mu\|_{L^\infty}} = 1.7071$, $K_\mathrm{S} = 0.3536$ and $K_\mathrm{I} = 2.8284$) approaches asymptotically a steady state different from $(1, 0)\}$.

We approximate numerically the value of $\widetilde{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\widetilde{\mathrm{Da}}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ by using again a self-implemented *Dichotomy method*. Figure 4-(a) illustrates the difference between $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\widetilde{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ when $\mathrm{Th_B} \in [5 \cdot 10^{-3}, 1.5 \cdot 10^2]$ and $\mu(1) = 0.5$. Similarly, Figure 4-(b) shows the difference between $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ and $\widetilde{\mathrm{Da}}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ when $\mathrm{Th_B} \in [5 \cdot 10^{-3}, 1.5 \cdot 10^2]$. We point out that these comparisons were also performed with $\widetilde{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and $\widetilde{\mathrm{Da}}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ defined using other model parameters σ, $\mathrm{Th_S}$ and μ and similar results were obtained.

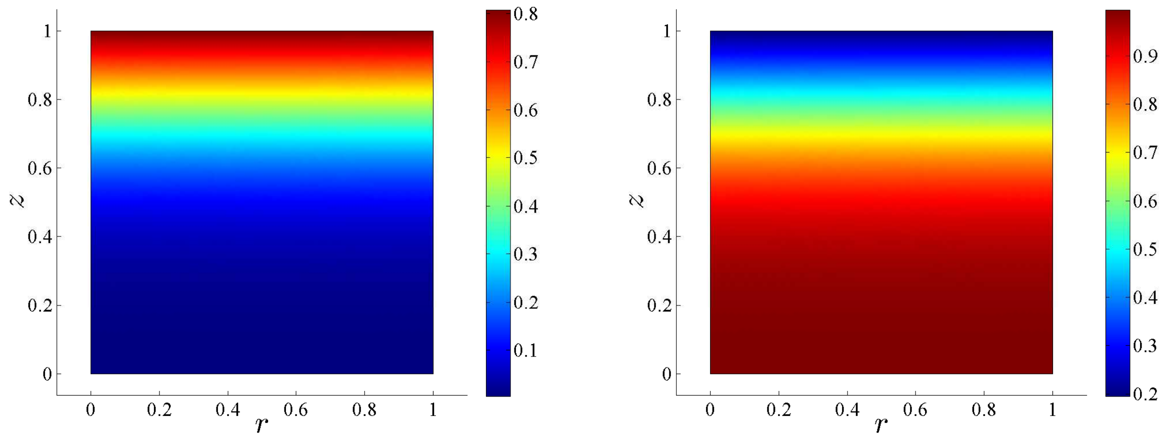


(a) Comparison between $\log(\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5))$ (depicted with solid line) and $\log(\widetilde{\mathrm{Da}}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5))$ (depicted with dashed lines).

(b) Comparison between $\log(\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ (depicted with solid line) and $\log(\widetilde{\mathrm{Da}}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B}))$ (depicted with dashed lines).

Figure 4: Numerical validation of the results.

In Figure 5, we plot the steady-state solution (S_2^*, B_2^*) of system (7), computed numerically when $\mathrm{Th_B} = \mathrm{Th_S} = \mathrm{e}^4$, $\mathrm{Da} = \mathrm{e}^2$, $\sigma = 1$, $S_\mathrm{init} = 0.1$, $B_\mathrm{init} = 0.9$ and μ being the nondimensional Monod function with $K_\mathrm{S} = 1$ (so that $\mu(1) = 0.5$). With these parameters, e.g. when $\log(\mathrm{Th_B}) = 4$ and $\log(\mathrm{Da}) = 2$, the equilibrium solution (S_2^*, B_2^*) is asymptotically stable (see Figure 4-(a)). Notice that the same steady-state solution can be obtained with nonhomogeneous initial conditions (for instance, $S_{\text{init}}(r,z) = rz$ and $B_{\text{init}}(r,z) = r(1-z)$).



(a) $S_2^*(r,z)$

(b) $B_2^*(r,z)$

Figure 5: Representation of the steady-state solution (S_2^*, B_2^*) of system (7) computed numerically when $\mathrm{Th}_{\mathrm{B}} = \mathrm{Th}_{\mathrm{S}} = \mathrm{e}^4$, $\mathrm{Da} = \mathrm{e}^2$, $\sigma = 1$, $S_{\text{init}} = 0.1$, $B_{\text{init}} = 0.9$ and μ being the nondimensional Monod Function with $K_{\mathrm{S}} = 1$ (so that $\mu(1) = 0.5$).

The bistability of system (7), stated in Remark 3.9, is perceivable when numerically solving system (7). For instance, if $\mathrm{Th}_{\mathrm{B}} = 0.01$, $\mathrm{Da} = 1.5$ and $\mu(1) = 0.5$, we observe that the solution of system (7) (computed with parameters $\sigma = 1$, $\mathrm{Th}_{\mathrm{S}} = 0.01$ and μ the nondimensional Haldane function with $\frac{\mu^*}{\|\mu\|_{L^\infty(\mathbb{R})}} = 1.7071$, $K_{\mathrm{S}} = 0.0529$ and $K_{\mathrm{I}} = 0.4235$) approaches $(1,0)$ if we choose $S_{\text{init}} = 0.9$ and $B_{\text{init}} = 0.1$, while it approaches a different equilibrium (similar to the one represented in Figure 5) solution if we set $S_{\text{init}} = 0.1$ and $B_{\text{init}} = 0.9$.

4.3. Comparison with the stability analysis of system (2)

In this section, we compare the stability analysis conditions associated to the ODE and PDE systems (2) and (7), respectively. As done in Section 3.2.1 for system (7), we define the following variables:

Definition 4.1.

- $\mathrm{Da}^{\mathrm{W}}_{(2)}(\mu(1)) := \frac{1}{\mu(1)}$.
- $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A1}),(2)}(\mu(1)) := \mathrm{Da}^{\mathrm{W}}_{(2)}(\mu(1))$.
- $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(2)} := 1$.

Remark 4.2. *According to Remark 2.1 and Definition 4.1, the stability analysis of system* (2) *(shown in Section 1) can be rewritten as*

- *If* $\mathrm{Da} < \mathrm{Da}^{\mathrm{W}}_{(2)}(\mu(1))$*, then the equilibrium solution* $(1,0)$ *of system* (2) *is asymptotically stable.*
- *If* μ *fulfills* (A1) *and* $\mathrm{Da} > \mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A1}),(2)}(\mu(1))$*, then the equilibrium solution* (S_2^*, B_2^*) *of system* (2) *is asymptotically stable.*

- *If μ fulfills* (A2) *and* $\mathrm{Da} > \mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(2)}(1)$*, then the equilibrium solution* (S_2^*, B_2^*) *of system* (2) *is asymptotically stable.*

Figure 6 illustrates the difference between the variable $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ and the constant $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(2)} = 1$ (and the difference, when $\mu(1) = 0.5$, between the variable $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, \mu(1))$ and the constant $\mathrm{Da}^{\mathrm{W}}_{(2)}(\mu(1)) = 2$). In both cases $\mathrm{Th_B} \in [5\cdot 10^{-3}, 1.5\cdot 10^2]$. Notice that the area limited between the curves $\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})$ and $\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)$ is the region of bistability of system (7) (see Remark 3.9).

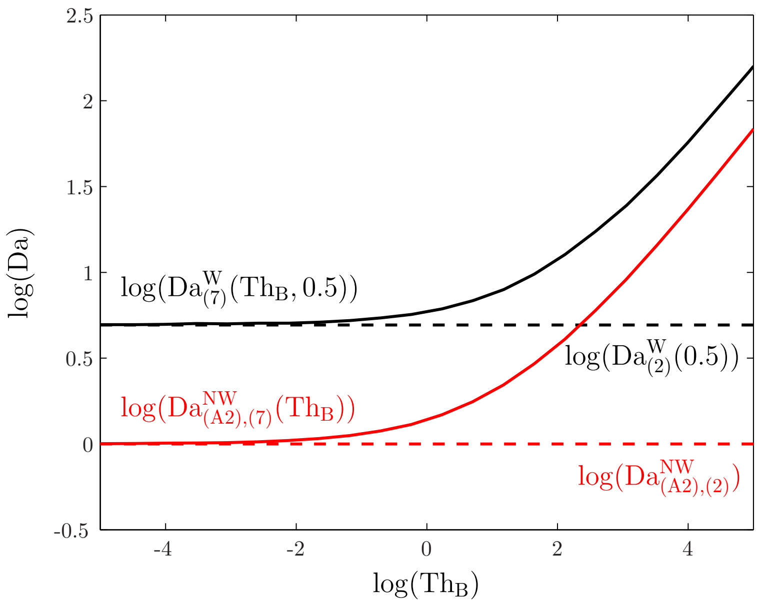


Figure 6: Comparison between $\log(\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5))$, $\log(\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B}))$ (depicted with solid lines) and constant values $\log(\mathrm{Da}^{\mathrm{W}}_{(2)}(0.5)) = \log(2)$, $\log(\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(2)}) = 0$ (depicted with dashed lines) when $\mathrm{Th_B} \in [5 \cdot 10^{-3}, 1.5 \cdot 10^2]$.

We observe that $\log(\mathrm{Da}^{\mathrm{NW}}_{(\mathrm{A2}),(7)}(\mathrm{Th_B})) \approx 0$ for values smaller than $\log(\mathrm{Th_B}) \approx -2$ ($\mathrm{Th_B} \approx 0.1$). Similarly, for the particular case when $\mu(1) = 0.5$, we observe that $\log(\mathrm{Da}^{\mathrm{W}}_{(7)}(\mathrm{Th_B}, 0.5)) \approx \log(2)$ also for values smaller than $\log(\mathrm{Th_B}) \approx -2$ ($\mathrm{Th_B} \approx 0.1$). This comparison, performed with other reaction values $\mu(1) \in \{\frac{i}{20}\}_{i=1}^{20}$, lead to the same conclusion, and consequently, we can deduce that if $\mathrm{Th_B} < 0.1$, the stability results obtained for the ODE and PDE systems (2) and (7) are similar. This result is consistent with the physics of the problem. Indeed, small values of $\mathrm{Th_B}$ correspond, for instance, to high diffusion coefficients implying almost spatial homogeneous biomass concentration. In this case, the dynamics in the reactor can be modeled with an ordinary differential equation cheaper to implement numerically (see [8]).

5. Conclusions

In this work, we have performed an asymptotic analysis of a coupled system of two Advection-Diffusion-Reaction equations with Danckwerts boundary conditions, which models the interaction between a microbial population and a diluted substrate in a continuous flow bioreactor.

First, we have showed that for the particular case where the diffusion coefficients are negligible, after some finite time, the biomass becomes extinct and no reaction is produced (this state is usually called *washout*).

Next, we have studied the case when the diffusion coefficients are not negligible, and in this case the system exhibits, under suitable conditions, two stable equilibrium states: the *washout* state and another steady state, which corresponds to the partial elimination of substrate. We have also taken into account that, depending on the reaction function, the system may exhibit either single stability or bistability. We have used the method of linearization to give a sufficient condition for the asymptotic stability of the washout equilibrium, and used this result, together with numerical experiments, to conjecture a sufficient condition for the asymptotic stability of the other stable equilibrium solution. These conditions were written in terms of nondimensional parameters Da (Damkhöler Number, relating reaction and advective rates), $\mathrm{Th_B}$ (Thiéle Modulus, relating reaction and biomass diffusion rates) and $\mu(1)$ (nondimensional reaction rate).

Finally, our asymptotic stability results have been validated numerically and compared to the stability analysis results associated to the continuous bioreactor when it is modeled with ordinary differential equations. Results seem to indicate that the stability analysis results for the ODE are also valid for values of Thiéle Modulus ($\mathrm{Th_B}$) lower than 0.1, but not valid for values of Thiéle Modulus above this value.

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