Coupling Hyperbolic and Parabolic Equations

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Resumo

Nesta tese estudamos um sistema de equações diferenciais parciais constituído por uma equação hiperbólica e uma equação parabólica que surge, frequentemente, na descrição da libertação controlada de fármacos. Neste contexto, a evolução da concentração é definida por uma equação de difusão-convecção-reação em que a velocidade convectiva é induzida por um campo elétrico.

Apresentamos um estudo qualitativo e quantitativo para o modelo contínuo e para o modelo discreto construído de forma conveniente. Realçamos que, para este último, estabelecemos resultados de convergência que mostram que os métodos numéricos propostos são supraconvergentes.

Palavras Chave: Equação hiperbólica, Equação parabólica, Sistema de libertação de fármacos, Método numérico, Supraconvergência

Abstract

In this work we study a system of two PDEs: a hyperbolic and a parabolic equation. This system arise often in the mathematical modelling of the controlled drug release. In this scope, the time and space evolution of the concentration is described by a convective-diffusion-reaction equation, where the convective velocity is induced by an electric field.

We present a qualitative and quantitative study for the continuous and the proposed discrete models. We remark that in the quantitative analysis we include supraconvergence results.

Keywords: Hyperbolic equation, Parabolic equation, Drug delivery system, Numerical method, Supraconvergence

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Contents

Chapter 1

Introduction

This work aims to study systems of partial differential equations composed by a parabolic equation and a hyperbolic equation, and completed by convenient initial and boundary conditions that arises in the scope of drug delivery.

Systems of partial differential equations that describe different physical processes interacting arise in several applications. For instance, if different species diffuse and react together, then the time and space evolution of the corresponding concentrations are described by a system of diffusion-reaction equations ([27], [28]). In this case, we have the coupling between different parabolic equations. Otherwise, if we would like to describe the stationary state of the previous physical system, then we should consider the corresponding elliptic equations. Moreover, if we consider a diffusion process that is enhanced by the application of an electric field, then the evolution of the drug concentration and the electric field are described by an elliptic equation coupled with a parabolic equation ([5], [15]). It remains to remark that coupling between partial differential equations and ordinary differential equations also arise in the mathematical modeling of drug release, for instance, when the viscoelastic properties of the diffusion medium are taken into account ([1]).

The system of equations that will be studied in this thesis can be considered in drug delivery when the diffusion process is enhanced by an electric field. It should be remarked that different types of enhancers have been used to increase the drug transport (physical and chemical enhancers [10]). Iontophoresis and electroporation belong to the class of physical processes used to increase the drug transport. In this case, an electric field is applied to the diffusion medium that induces a convective transport. These two enhancer processes have been considered in several medical applications: dermatology - transdermal drug delivery ([10]); oncology - cancer treatment ([7]); opthalmology - anterior and posterior segment eye diseases treatment ([39]). While the first enhancer is characterized by long and lower electric pulses, the medical protocols defined by the second one are characterized by short and high electric pulses. We observe that electroporation induces the increasing of pores in the live target tissue, and consequently, a higher transport than the one induced if iontophoresis is applied.

The propagation of the electric potential or electric field is described by the Maxwell's equations. In certain scenarios, these equations can be reduced to wave equations. In the literature, elliptic equations were used to describe the electric properties of the physical system when the two previous enhancers are considered ([5], [30]). Consequently, the drug concentration evolution is described by the Poisson equation that is coupled with a convection-diffusion equation. This last equation is established considering the conservation mass principle and the Nernst-Planck equation for the mass flux. A natural mathematical question is the mathematical study of the coupling between the more general equations - the wave equation, and the diffusion equation for the drug transport. The mathematical support from analytical and numerical point of view are well established for the coupling between parabolic equations, elliptic equations and elliptic-parabolic equations ([6], [21], [22], [29], [31], [32], [33], [34], [41], [43]).

For systems of hyperbolic and parabolic equations, we found in the literature the analytical and numerical study when the spatial domain is split into two domains Ω_1 and Ω_2 and the coupling is made by the interface between both ([9], [11], [37]). However, to the best of our knowledge, the mathematical treatment of systems of second order (in time) hyperbolic equations and diffusion equations was not considered in the literature. In this work we consider a system composed by a telegraph equation and a convection-diffusion-reaction equation, linked by the convective velocity and completed with initial and Dirichlet boundary conditions. Our aim is to establish some energy estimates for the drug concentration depending on energy estimates for the solution of the wave equation. We propose a numerical method for the coupled model that mimics the continuous one. We study the convergence properties of such numerical method. We prove that, although the truncation errors for both discretizations are of first order with respect to the space stepsize, the spatial discretization errors are of second order with respect to convenient discrete H^1 and L^2 norms. Numerical experiments illustrating the theoretical results are included.

This work is organized as follows. In Chapter 2 we present the basis of the motivation of this work - the wave equations for the electric field intensity and for the electric potential established from the Maxwell's equations. Although the electric potential or the electric field intensity have been described by Poisson equation, when iontophoresis and electroporation processes are used to enhance the drug diffusion, a more general scenario requires naturally an evolution equation that have as stationary states the ones used before. Chapter 3 is focused on the study of a telegraph equation: a wave equation with a damping effect. We study some energy estimates for the solution of the initial boundary value problem defined by this equation, and we propose a spatial discretization that induces a semi-discrete solution presenting the qualitative properties of the continuous one. The convergence analysis is also presented in this chapter. The coupling telegraph-diffusion equations is studied in Chapter 4. We start this chapter analysing the stability of the coupled initial boundary value problem. A coupled semi-discrete problem is proposed and its convergence is established. Finally numerical results illustrating the main results are also included. We remark that the existence of the solution of the continuous model is not established in this work and will be addressed in the future.

We would like to highlight Theorem 6 in Chapter 3 and Theorem 9 in Chapter 4 where the convergence properties of the semi-discrete schemes are established. These two results are proved assuming that the solution of both initial boundary value problems are smooth enough. Numerically we observe that the same result of the Theorem 6 is observed for solution without the required smoothness. The convergence analysis for less smooth solutions will be also studied in the near future.

Chapter 2

Maxwell's Telegraph Equations

2.1. Introduction

The first question that we need to clarify is why arises the coupling between a telegraph equation and a diffusion equation in the scope of drug delivery. To answer this question, we start this chapter by highlighting the main difference between iontophoresis and electroporation and how the electric potentials induced by their protocols are described in the literature. A general scenario of application of an electric field or electric potential to enhance a drug diffusion requires a time and space evolution equation for both. These equations will be deduced from the general Maxwell's equations in what follows.

2.2. Iontophoresis and Electroporation

The main objective of iontophoresis and electroporation is the enhancement of polarized drug diffusion. In these two processes, an electrode with the drug charge is placed in the neighbourhood of the polarized drug placed in a target tissue. This electrode exerts a repulsion force on the drug particles and the other electrode, normally placed in the opposite side of the tissue, induces an attraction force on the drug. These two forces create a convective velocity that increases the drug transport. We observe that they could also induce a fluid movement which contributes to the convective transport.

The main difference between the iontophoresis and the electroporation is given by the applied potential protocols ([2]). The iontophoresis is characterized by the use of constants electric pulses of low intensity (less or equal to 10V) during long time periods, while the electroporation consists in the application of several electric pulses of high intensity, but during short periods. Iontophoresis and electroporation protocols can be applied independently or they can be combined.

In the iontophoresis the drug is only transferred by the free spaces of the tissue, this means, we do not have changes in the porosity. When the intensity of the electric current is too high, pores arise in the target tissue. For this reason, in the electroporation, the diffusion of drug molecules with high molecular weight is possible. The formation of pores is not always reversible, it is only possible until a certain value of intensity, so in most situations, the applied electric field should be controlled such that an increasing of the permeability is observed, but without irreversible damage in the tissue ([30]).

Note that the irreversible electroporation is also a promising technique when the applied electric field intends to destroy target tissue like in cancer treatment. In this case, the intensity and the duration of electric pulses should be such that the tissue cannot return to its normal state.

In both processes, the drug transport is determined by the characteristics of the applied current and the properties of the drug and target tissue. If the drug is contained in a reservoir, usually a polymeric reservoir, then its characteristics have an important role in the drug transport.

In the drug transport we identify three main contributions: passive diffusion, convective transport induced by the repulsion and attraction forces, and transport due to fluid movement (the so called electro-osmosis) ([18], [35], [42]). The time and space of the drug evolution is described by the mass conservation law, being c ($kg\, m^{-3}$) the drug concentration,

$$\frac{\partial c}{\partial t} + \nabla \cdot J = 0,$$

where J ($kg\, m^{-2}\, s^{-1}$) denotes the mass flux which is given by the Nernst-Planck equation ([38])

$$J = -D\nabla c - vc,$$

where D ($m^2\, s^{-1}$) is the diffusion coefficient and v ($m\, s^{-1}$) is the convective velocity given by

$$v = -\frac{zDF_c}{RTemp}E,$$

where z is the valence of ionic species, F_c ($9.6485 \times 10^{-4}\, C\, mol^{-1}$) the Faraday's constant, $Temp$ the temperature of the tissue (K), R ($8.314\, J\, K^{-1}\, mol^{-1}$) is the universal gas constant and E ($V\, m^{-1}$) is the electric field intensity. To complete the mathematical description of the diffusion process we need to establish a partial differential equation for the electric field intensity. We observe that in [5], [8], [17], the authors assume a time independent situation, so $E = -\nabla\phi$, where ϕ is the electric potential (V) . In this case the electrical potential is defined by the Laplace equation

$$\nabla(\sigma\nabla\phi) = 0,$$

where σ denotes the electric conductivity ($S\,m^{-1}$).

The time and space evolution of an electric potential or electric field intensity can be deduced from the Maxwell's equations whose stationary states leads to the Poisson equation. However, to obtain an accurate description of the drug evolution in a more general setting, it is necessary to construct an equation for the electric field intensity or for the electric potential. In what follows we deduce such equations from the general Maxwell's equations in a three dimensional setting.

2.3. Maxwell's Equations

The Maxwell equations were presented by Maxwell in 1865 ([30]), being its construction from physical laws that we present in what follows ([45]).

Let S be an arbitrary smooth and bounded oriented 2-manifold in $\mathbb{R}^3$ with boundary ∂S. Let E be the electric field intensity defined on ∂S, and B the magnetic field (T) induced in S. The Faraday's law states that

$$\frac{\partial}{\partial t}\int_S B\ dA + \int_{\partial S} E\ dS = 0. \tag{2.1}$$

Applying the Stokes's Theorem ([23]) we obtain

$$\int_S \left(\frac{\partial B}{\partial t} + \nabla \times E\right)\ dA = 0,$$

and therefore, assuming continuity of the vector function, we conclude

$$\frac{\partial B}{\partial t} + \nabla \times E = 0. \tag{2.2}$$

The Ampére's law allows us to compute the time variation of the electric displacement D_e ($C\,m^{-2}$) on the boundary of a surface S from J_e, the density of the electric current (A), and from a magnetic field H ($A\,m^{-1}$) in S, by

$$\frac{\partial}{\partial t}\int_S D_e\ dA - \int_{\partial S} H\ dS + \int_S J_e\ dA = 0. \tag{2.3}$$

Let V be an arbitrary domain in $\mathbb{R}^3$ with piecewise smooth boundary ∂V. The Gauss's law for the electric field states that

$$\int_{\partial V} D_e\ dA = \int_V \rho\ dV, \tag{2.4}$$

where ρ denotes the total charge density ($C\,m^{-3}$). Moreover, Gauss's law for the magnetic field states that

$$\int_{\partial V} B\; dA = 0. \tag{2.5}$$

Following the establishment of (2.2), using the Stoke's Theorem and the Gauss's Theorem ([23]), it can be easily shown that

$$\frac{\partial D_e}{\partial t} - \nabla \times H + J_e = 0, \tag{2.6}$$

$$\nabla \cdot D_e - \rho = 0 \tag{2.7}$$

and

$$\nabla \cdot B = 0. \tag{2.8}$$

Moreover, from (2.6), (2.7) and the fact that $\nabla \cdot (\nabla \times u) = 0$ for any smooth u, we obtain the continuity equation

$$\nabla \cdot J_e = -\frac{\partial \rho}{\partial t}. \tag{2.9}$$

Furthermore, as for bound surfaces we have $\int_{\partial V} \nabla \times H\; dA = \int_V \nabla \cdot (\nabla \times H)\; dV = 0$, then

$$\frac{\partial}{\partial t}\int_V \rho\; dV = \frac{\partial}{\partial t}\int_{\partial V} D_e\; dA = \int_{\partial V} (\nabla \times H - J_e)\; dA = -\int_V \nabla \cdot J_e\; dV.$$

A compatibility relation between the electric current J_e and the electric field E is given by the Ohm's law. In fact, this law allows us to define J_e in function of E through the relation

$$J_e = \sigma E, \tag{2.10}$$

where σ denotes the electric conductivity.

Considering now the system (2.2), (2.6)-(2.8), we verify that it is not complete, that means that the number of unknowns is different from the number of equations (twelve variables and eight equations). So we need to specify two called constitutive equations, to obtain a complete system. Functional relations relating D_e, E, B and H are usually assumed

$$D_e = \epsilon E, \tag{2.11}$$

$$B = \mu H, \tag{2.12}$$

where ϵ represents the electric permittivity ($F\,m^{-1}$) and μ is the magnetic permeability ($H\,m^{-1}$). However, (2.2), (2.6)-(2.8), (2.11), and (2.12) define a system of fourteen equations for twelve variables. So, now, we need to decrease the number of equations. In the following result we specify two conditions that can be used to reduce the number of equations.

Theorem 1. *Let us assume that* $\nabla \cdot (D_e(x,0)) = \rho(x,0)$ *and* $\nabla \cdot (B(x,0)) = 0$*. Then any solution of the system (2.2), (2.6) and (2.9), verifies* $\nabla \cdot D_e = \rho$ *and* $\nabla \cdot B = 0$ *for* $t > 0$*.*

Proof. As we have $\nabla \cdot (\nabla \times u) = 0$ for any sufficiently smooth function u, we have successively

$$\frac{\partial}{\partial t}(\nabla \cdot B) = \nabla \cdot \frac{\partial B}{\partial t} = -\nabla \cdot (\nabla \times E) = 0$$

and

$$\frac{\partial}{\partial t}(\nabla \cdot D_e - \rho) = \nabla \cdot (\nabla \times H - J_e) - \frac{\partial \rho}{\partial t} = \nabla \cdot (\nabla \times H) = 0.$$

Finally, as consequence of the initial conditions we obtain the desired result. □

Considering (2.11), (2.12), (2.10), we can give to equations (2.2) and (2.6) the followings equivalent form

$$\mu \frac{\partial H}{\partial t} + \nabla \times E = 0, \tag{2.13}$$

$$\epsilon \frac{\partial E}{\partial t} - \nabla \times H + \sigma E = 0. \tag{2.14}$$

In the above equations, ϵ, μ and σ are matrices of order 3, we remark that μ, ϵ, σ and ρ can be position dependents. If the medium is isotropic, that means, it is uniform in all directions, μ, ϵ and σ are reduced to real functions. Furthermore, if the medium is homogeneous which means that its properties do not depend on the position, then, if the medium is isotropic and homogeneous then μ, ϵ and σ are constants.

2.4. Telegraph Equations

In the previous section we established the equations (2.13) and (2.14) as a consistent system of Maxwell's equations. Applying the rotational operator to both members of these equations, and using (2.7), (2.8), and the equality $\nabla \times \nabla \times u = \nabla(\nabla \cdot u) - \Delta u$ that holds for all smooth functions, we obtain the following two telegraph equations for the electric and magnetic fields

$$\mu\epsilon \frac{\partial^2 E}{\partial t^2} + \mu\sigma \frac{\partial E}{\partial t} - \Delta E = -\nabla \left(\rho \epsilon^{-1}\right), \tag{2.15}$$

$$\mu\epsilon \frac{\partial^2 H}{\partial t^2} + \mu\sigma \frac{\partial H}{\partial t} - \Delta H = 0.$$

If the medium is homogeneous and isotropic, (2.15) becomes

$$\frac{\partial^2 E}{\partial t^2} + \frac{\sigma}{\epsilon}\frac{\partial E}{\partial t} - \frac{1}{\epsilon\mu}\Delta E = 0, \tag{2.16}$$

with ϵ, $\mu \neq 0$.

We observe that the telegraph equation (2.16) can be rewritten as an integro-differential equation. In fact, (2.16) is equivalent to

$$\frac{\partial}{\partial t}\left(e^{\frac{\sigma t}{\epsilon}}\frac{\partial E}{\partial t}(x,t) - \frac{1}{\epsilon\mu}\int_0^t e^{\frac{\sigma s}{\epsilon}}\ \Delta E(x,s)ds\right) = 0$$

that implies that

$$\frac{\partial E}{\partial t}(x,t) = \frac{1}{\epsilon\mu}\int_0^t e^{-\frac{\sigma}{\epsilon}(t-s)}\ \Delta E(x,s)ds + f(x)e^{-\frac{\sigma}{\epsilon}t}. \tag{2.17}$$

Finally we remark that (2.17) can be deduced considering the mass conservation law

$$\frac{\partial E}{\partial t} + \nabla \cdot J = fe^{-\frac{\sigma}{\epsilon}t}$$

where the mass flux J is given by

$$J(x,t) = -\frac{1}{\epsilon\mu}\int_0^t e^{-\frac{\sigma}{\epsilon}(t-s)}\nabla E(x,s)\ ds. \tag{2.18}$$

Integro-differential equations of type (2.17) have been considered in the description of diffusion phenomena, where a decay effect defined by the time integral term in (2.18) is introduced ([12]).

In this section we obtain a partial differential equation that describes the behaviour of the electric field. However, in what concerns the application of electric enhancers to the drug delivery, an intuitive approach is defined by the electric potential ϕ. In the next section we establish a telegraph equation for ϕ.

2.5. Electric Potential

We start this section with the following proposition not directly related with the electric potential.

Proposition 1. *For u a sufficiently smooth vector function defined on all of $\mathbb{R}^3$, we have*

1. *If $\nabla \times u = 0$, then there exists a scalar function ϕ such that $u = -\nabla\phi$.*
2. *If $\nabla \cdot u = 0$, then there exists a vector function A such that $u = \nabla \times A$.*

Proof. [25] □

From the equation (2.8), there exists a magnetic vector A called vector potential ($Wb\,s^{-1}$), such that

$$B = \nabla \times A. \tag{2.19}$$

Then from equation (2.2), we obtain

$$\nabla \times \left(\frac{\partial A}{\partial t} + E \right) = 0.$$

Using Proposition 1, we have for the electric field intensity E, vector potential A, and scalar potential ϕ, the following relation

$$E + \frac{\partial A}{\partial t} = -\nabla \phi. \tag{2.20}$$

The relations (2.19) and (2.20) define A and ϕ, however A is not uniquely determined.

Before the establishment of a condition that leads to the uniqueness of A, we deduce mathematical relations between the electric field and the vector potential A that will be useful. The first one comes from (2.20) and (2.7) that lead to

$$-\Delta \phi - \frac{\partial}{\partial t}(\nabla \cdot A) = \rho \epsilon^{-1}. \tag{2.21}$$

Analogously, from (2.14) and (2.19), we have

$$\mu \epsilon \frac{\partial E}{\partial t} = \nabla \times (\nabla \times A) - \mu \sigma E, \tag{2.22}$$

that combined with (2.20), and $\nabla \times \nabla \times u = \nabla(\nabla \cdot u) - \Delta u$ allows us to establish

$$\left(\Delta A - \epsilon \mu \frac{\partial^2 A}{\partial t^2} \right) - \nabla \left(\nabla \cdot A + \epsilon \mu \frac{\partial \phi}{\partial t} \right) = \mu \sigma \left(\nabla \phi + \frac{\partial A}{\partial t} \right). \tag{2.23}$$

Another relation can be obtained using the Ohm's law (2.10) and (2.9). In fact those relations give

$$\nabla \cdot (\sigma \nabla \phi) + \frac{\partial}{\partial t}(\sigma \nabla \cdot A) = \frac{\partial \rho}{\partial t}. \tag{2.24}$$

To complete the specification of A, we need to impose an additional condition on $\nabla \cdot A$. An usual condition used is the so called Coulomb gauge given by ([19])

$$\nabla \cdot A = 0.$$

Then from (2.24) we obtain, for the electric potential, the Poisson equation

$$\nabla \cdot (\sigma \nabla \phi) = \frac{\partial \rho}{\partial t}. \tag{2.25}$$

The same relation is obtained if the vector potential A is time independent. Moreover, in this case the electric potential ϕ satisfies the Laplace equation

$$\nabla \cdot (\sigma \nabla \phi) = 0. \tag{2.26}$$

Another relation can be deduced from (2.21) if the stationary state is considered. In fact in this case we get $-\nabla \cdot (\nabla \phi) = \rho \epsilon^{-1}$. We remark that the common equation used to describe ϕ in iontophoresis and electroporation procedures is the Laplace equation (2.26) which is deduced assuming that A is time independent. Then naturally arises the question: what is the equation for a time dependent A?

Let us suppose that A satisfies the Lorentz gauge ([19])

$$\nabla \cdot A = -\mu\sigma\phi - \mu\epsilon \frac{\partial \phi}{\partial t}.$$

Then, from (2.21) we get

$$\mu\epsilon^2 \frac{\partial^2 \phi}{\partial t^2} + \mu\sigma\epsilon \frac{\partial \phi}{\partial t} - \nabla \cdot (\epsilon \nabla \phi) = \rho,$$

and from (2.23) we obtain

$$\mu\epsilon \frac{\partial^2 A}{\partial t^2} + \mu\sigma \frac{\partial A}{\partial t} - \Delta A = 0.$$

Finally from (2.24) we conclude, for the scalar electric potential, that

$$\mu\epsilon\sigma \frac{\partial^2 \phi}{\partial t^2} + \mu\sigma^2 \frac{\partial \phi}{\partial t} - \nabla \cdot (\sigma \nabla \phi) = -\frac{\partial \rho}{\partial t}. \tag{2.27}$$

Chapter 3

Electric Field-Telegraph Equation

3.1. Introduction

In the previous chapter, telegraph equations for E and ϕ were established from the Maxwell's equations. One of this equations will be coupled with the diffusion equation to describe the drug evolution when the diffusion is enhanced by an applied electric field or electric potential. The analytical and numerical study of the coupled model requires, as a first step, the study of the deduced telegraph equations. In this chapter we consider the telegraph equation (2.16) for the electric field intensity.

In what follows, we consider that the target tissue is an isotropic medium. Let V, represented in Figure 3.1, be a reference element in the target tissue, let E be the electric field intensity and let c be the drug concentration in (x, y, z) at time t. Let $\mathcal{A}$ be a cross section with fixed area A. We suppose that

$$E(x, y, z, t) = E(x, 0, 0, t)$$

$$c(x, y, z, t) = c(x, 0, 0, t)$$

for all $(x, y, z) \in \mathcal{A}$. We represent by $E(x, t)$ the electric field intensity $E(x, 0, 0, t)$, and by $c(x, t)$ the concentration $c(x, 0, 0, t)$. This means that under the previous condition, a three-dimensional problem can be seen as an one-dimensional problem. We also consider that the target tissue is an homogeneous medium, so ϵ, σ, and μ are constants, that we consider positive.

In this chapter we consider the spacial domain $\Omega = (0, 1)$. Equation (2.16) is coupled with initial and boundary conditions that define the following initial boundary value problem (IBVP)

$$\begin{cases} \dfrac{\partial^2 E}{\partial t^2} = \dfrac{1}{\epsilon\mu}\Delta E - \dfrac{\sigma}{\epsilon}\dfrac{\partial E}{\partial t} + F & \text{in } (0,1) \times (0,T], \\ E(0,t) = \phi_0(t),\ E(1,t) = \phi_1(t) & t \in (0,T], \\ E(x,0) = \psi_0(x) & x \in (0,1), \\ \dfrac{\partial E}{\partial t}(x,0) = \psi_1(x) & x \in (0,1), \end{cases} \tag{3.1}$$

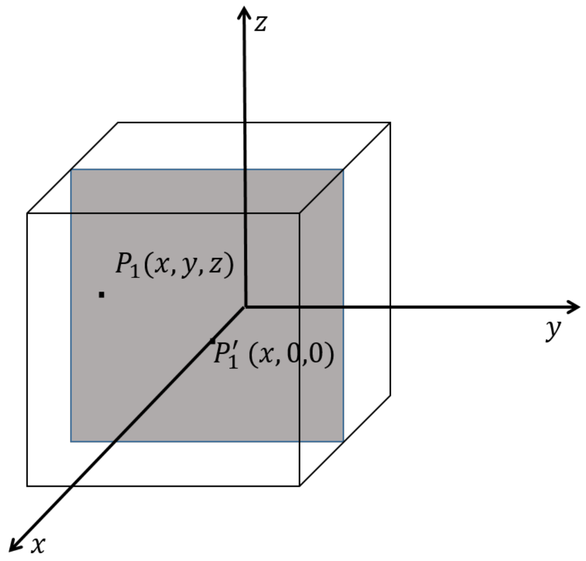


Figure 3.1: Reference element.

where $\phi_0(t)$ and $\phi_1(t)$ are the boundary conditions, $\psi_0(x)$ and $\psi_1(x)$ are the initial conditions, and F defines a reaction term.

This chapter aims to study analytically and numerically the IBVP (3.1). In Section 3.2 we construct the solution of (3.1) using Fourier series, we establish some energy estimates that allow us to conclude the uniqueness of the constructed solution. In Section 3.3 we propose a numerical discretization of the IBVP (3.1) that is obtained considering the Method of Lines Approach: a spatial discretization on nonuniform grid that leads to a semi-discrete approximation (continuous in time) followed by a time integration.

We prove in the main theorem of this chapter - Theorem 6 - that the proposed method leads to a second convergence order approximation in space with respect to a discrete H^1-norm. This result is unexpected because the spacial truncation error is only of first order in the $\|\cdot\|_\infty$ norm. Some numerical experiments are included to illustrate Theorem 6. In the proof of Theorem 6 we assume that E is sufficiently smooth in space, more precisely, we assume that $E(t) \in C^4(\bar{\Omega})$. The numerical simulations allow us to believe that the same result holds for less smooth solutions. This problem will be studied in the near future.

3.2. Existence and Uniqueness of Solution

We observe that the initial conditions ψ_0, ψ_1, and the boundary conditions functions ϕ_0, ϕ_1, should be compatible in the sense that (3.1) has a solution. To compute such solution we use in what follows the method of separation of variables that leads to Fourier series. We start by rewriting (3.1) as an IBVP with homogeneous initial and boundary conditions introducing the following change of variables

$$w(x,t) = (1-x)\phi_0(t)+x\phi_1(t)+\psi_0(x)-(1-x)\phi_0(0)-x\phi_1(0)+t(\psi_1(x)-(1-x)\phi_0'(0)-x\phi_1'(0)). \tag{3.2}$$

Then $\tilde{E} = E - w$ satisfies

$$\begin{cases} \dfrac{\partial^2 \tilde{E}}{\partial t^2} = \dfrac{1}{\epsilon\mu}\Delta \tilde{E} - \dfrac{\sigma}{\epsilon}\dfrac{\partial \tilde{E}}{\partial t} + \tilde{F} & \text{in } (0,1)\times(0,T], \\ \tilde{E}(0,t) = \tilde{E}(1,t) = 0 & t \in (0,T], \\ \tilde{E}(x,0) = 0 & x \in (0,1), \\ \dfrac{\partial \tilde{E}}{\partial t}(x,0) = 0 & x \in (0,1), \end{cases} \tag{3.3}$$

with $\tilde{F} = F + \dfrac{1}{\epsilon\mu}\Delta w - \dfrac{\sigma}{\epsilon}\dfrac{\partial w}{\partial t} - \dfrac{\partial^2 w}{\partial t^2}$.

To simplify the application of Fourier method, we rewrite now (3.3) as an IBVP without the reaction term. Let $\tau > 0$ be a parameter and let $v(\cdot,\cdot;\tau)$ be solution of the IBVP

$$\begin{cases} \dfrac{\partial^2 v}{\partial t^2} = \dfrac{1}{\epsilon\mu}\Delta v - \dfrac{\sigma}{\epsilon}\dfrac{\partial v}{\partial t} & \text{in } (0,1)\times(\tau,T], \\ v(0,t;\tau) = v(1,t;\tau) = 0 & t \in (\tau,T], \\ v(x,\tau;\tau) = 0 & x \in (0,1), \\ \dfrac{\partial v}{\partial t}(x,\tau;\tau) = \tilde{F}(x,\tau) & x \in (0,1). \end{cases} \tag{3.4}$$

Then, if v is sufficiently smooth, we have

$$\tilde{E}(x,t) = \int_0^t v(x,t;\tau)\, d\tau,\ t \in [0,T],\ x \in [0,1].$$

To obtain $\tilde{E}$ we deduce, in what follows, a formal expression for v as a sum of a Fourier series. We prescribe the following expression

$$v(x,t;\tau) = \sum_{j\in\mathbb{N}} c_j(t,\tau)\sin(j\pi x). \tag{3.5}$$

Then, formally v satisfies the partial differential equation of (3.4) if

$$c_j''(t,\tau) + \frac{\sigma}{\epsilon}c_j'(t,\tau) = -\frac{1}{\epsilon\mu}(j\pi)^2 c_j(t,\tau),\ \forall j \in \mathbb{N},\ t > \tau. \tag{3.6}$$

The solution of (3.6) depends on the relations between j and the other constants σ, ϵ, μ and π. So we have to consider three different cases

1. $\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}} \in \mathbb{N}$ and $j = \frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}$;

2. $\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}} \notin \mathbb{N}$ and $j > \frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}$;

3. $\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}} \notin \mathbb{N}$ and $j < \frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}$.

As in general $\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}} \in \mathbb{R}\backslash\mathbb{N}$, we do not consider the first case. For $j \in \mathbb{N}$ satisfying the second case, we obtain for c_j the following expression

$$c_j(x,t;\tau) = e^{-\frac{\sigma}{2\epsilon}(t-\tau)}\Bigg[A_j(\tau)\cos\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right) + B_j(\tau)\sin\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\Bigg],$$

where $A_j(\tau)$ and $B_j(\tau)$ represent appropriate constants that will be specified later. At last, for j in the third case condition, the solution of (3.6) is given by

$$c_j(x,t;\tau) = e^{-\frac{\sigma}{2\epsilon}(t-\tau)}\left[C_j(\tau)e^{\sqrt{\frac{\sigma^2\mu-4(j\pi)^2\epsilon}{4\epsilon^2\mu}}(t-\tau)} + D_j(\tau)e^{-\sqrt{\frac{\sigma^2\mu-4(j\pi)^2\epsilon}{4\epsilon^2\mu}}(t-\tau)}\right],$$

where $C_j(\tau)$ and $D_j(\tau)$ represent constants to be specified.

Then, the solution v introduced in (3.5) can be written as

$$\begin{aligned} v(x,t;\tau) = e^{-\frac{\sigma}{2\epsilon}(t-\tau)}\Bigg[&\sum_{j\in\mathbb{N}:j\leq\left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]}\Bigg(C_j(\tau)e^{\sqrt{\frac{\sigma^2\mu-4(j\pi)^2\epsilon}{4\epsilon^2\mu}}(t-\tau)} \\ &+ D_j(\tau)e^{-\sqrt{\frac{\sigma^2\mu-4(j\pi)^2\epsilon}{4\epsilon^2\mu}}(t-\tau)}\Bigg)\sin(j\pi x)+ \\ &+\sum_{j\in\mathbb{N}:j>\left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]}\Bigg(A_j(\tau)\cos\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right) \\ &+ B_j(\tau)\sin\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\Bigg)\sin(j\pi x)\Bigg]. \end{aligned} \tag{3.7}$$

We need to find now the constants $A_j(\tau)$, $B_j(\tau)$, $C_j(\tau)$ and $D_j(\tau)$ such that v satisfies the initial conditions of (3.4).

If

- $A_j(\tau) = 0$, $j \in \mathbb{N} : j > \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$,
- $C_j(\tau) = -D_j(\tau)$, $j \in \mathbb{N} : j \leq \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$,

then the initial condition in (3.4) is satisfied.

In what follows we use the initial velocity in (3.4) to complete the computation of the previous constants. We consider that

$$\tilde{F}(x,\tau) = \sum_{j\in\mathbb{N}}\tilde{f}_j(\tau)\sin(j\pi x),$$

where $\tilde{f}_j(\tau) = 2\displaystyle\int_0^1 \tilde{F}(x,\tau)\sin(j\pi x)\ dx$. Taking this into account, we easily get

(A) $A_j(\tau) = 0,\ j \in \mathbb{N} : j > \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$,

(B) $B_j(\tau) = \dfrac{\tilde{f}_j(\tau)}{\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}},\ j \in \mathbb{N} : j > \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$,

(C) $C_j(\tau) = \dfrac{\tilde{f}_j(\tau)}{2\sqrt{\frac{\sigma^2\mu - 4(j\pi)^2\epsilon}{4\epsilon^2\mu}}},\ j \in \mathbb{N} : j \leq \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$,

(D) $D_j(\tau) = -\dfrac{\tilde{f}_j(\tau)}{2\sqrt{\frac{\sigma^2\mu - 4(j\pi)^2\epsilon}{4\epsilon^2\mu}}},\ j \in \mathbb{N} : j \leq \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$.

In the following result we specify sufficient conditions on $\tilde{F}$ that allow us to conclude that $v(x,t;\tau)$ is solution of the IBVP (3.4).

Theorem 2. *If*

1. $\dfrac{\partial \tilde{F}}{\partial x}$ *is continuous in* $[0,1]$;
2. $\dfrac{\partial^2 \tilde{F}}{\partial x^2}$ *is piecewise continuous in* $[0,1]$;
3. $\tilde{F}(0,\tau) = \tilde{F}(1,\tau) = 0$;

then

$$\begin{aligned} v(x,t;\tau) = e^{-\frac{\sigma}{2\epsilon}(t-\tau)}\Bigg[\sum_{j\in\mathbb{N}: j\leq\left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]} \Bigg(& C_j(\tau) e^{\sqrt{\frac{\sigma^2\mu-4(j\pi)^2\epsilon}{4\epsilon^2\mu}}(t-\tau)} \\ & + D_j(\tau) e^{-\sqrt{\frac{\sigma^2\mu-4(j\pi)^2\epsilon}{4\epsilon^2\mu}}(t-\tau)} \Bigg) \sin(j\pi x) + \end{aligned} \tag{3.8}$$

$$\begin{aligned} + \sum_{j\in\mathbb{N}: j>\left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]} \Bigg(& A_j(\tau)\cos\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right) \\ & + B_j(\tau)\sin\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\Bigg)\sin(j\pi x)\Bigg], \end{aligned}$$

$x \in [0,1],\ t \in [\tau, T]$ *with* $A_j(\tau),\ B_j(\tau),\ C_j(\tau)$ *and* $D_j(\tau)$ *given by (A), (B), (C) and (D) respectively, is solution of (3.4) in the sense that*

(a) $v \in C^1([\tau,T], C[0,1]) \cap C^2((\tau,T], C(0,1)) \cap C((\tau,T], C^2(0,1))$;

(b) *v verifies the differential equation, the initial conditions and the boundary conditions in (3.4).*

Proof. We start by remarking that the expression v was established using the condition defined in (b).

In what concerns (a), we observe that the finite sum defined for $j \leq \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$ is smooth enough. Next we prove that the sum of the series that arises in (3.8) satisfies the smoothness requirements specified in (a).

The first step shows that the sum of the series in (3.8) defines a continuous function in $[0,1] \times [\tau, T]$. The general term of the series, for $j \in \mathbb{N}, j > \left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]$, satisfies the following inequality

$$\Bigg| e^{-\frac{\sigma(t-\tau)}{2\epsilon}} \left(A_j(\tau) \cos\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau) \right) \right.$$
$$\left. + B_j(\tau) \sin\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau) \right) \right) \sin(j\pi x) \Bigg| \leq |B_j(\tau)|, \text{ for } x \in [0,1],\ t \in [\tau, T].$$

We have

$$\sum_{j\in\mathbb{N}, j>\left[\frac{\sigma}{2\pi}\sqrt{\frac{\mu}{\epsilon}}\right]} |B_j(\tau)| \leq \frac{1}{2} \left(\sum_{j\in\mathbb{N}: j>\left[\frac{\mu\sigma^2}{4\epsilon\pi^2}\right]} \frac{4\epsilon^2\mu}{4(j\pi)^2\epsilon - \sigma^2\mu} \right)^{1/2} \left(\sum_{j\in\mathbb{N}: j>\left[\frac{\mu\sigma^2}{4\epsilon\pi^2}\right]} (\tilde{f}_j(\tau))^2 \right)^{1/2},$$

where by Parseval's identity

$$\left(\sum_{j\in\mathbb{N}: j>\left[\frac{\mu\sigma^2}{4\epsilon\pi^2}\right]} (\tilde{f}_j(\tau))^2 \right)^{1/2} \leq \|\tilde{F}\|_{L^2(-1,1)}.$$

Then, the series with general term $|B_j|$ is convergent, and therefore the series in (3.8) is uniformly convergent. Finally, (3.8) defines a continuous function in $[0,1] \times [\tau, T]$.

Now we want to show that the time derivative of the series in (3.8) exists and is continuous in $[0,1] \times [\tau, T]$. For the series of the time derivatives we have

$$\Bigg| -\frac{\sigma}{2\epsilon} e^{-\frac{\sigma(t-\tau)}{2\epsilon}} \left(A_j(\tau) \cos\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau) \right) \right.$$
$$\left. + B_j(\tau) \sin\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau) \right) \right) \sin(j\pi x)$$
$$+ e^{-\frac{\sigma(t-\tau)}{2\epsilon}} \left(-A_j(\tau) \sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}} \sin\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau) \right) \right.$$
$$\left. + B_j(\tau) \sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}} \cos\left(\sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}(t-\tau) \right) \right) \sin(j\pi x) \Bigg|$$
$$\leq \frac{\sigma}{2\epsilon}|B_j(\tau)| + \sqrt{\frac{4(j\pi)^2\epsilon - \sigma^2\mu}{4\epsilon^2\mu}}|B_j(\tau)|, \tag{3.9}$$

for $[0,1]\times[\tau,T]$, where

$$\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}|B_j(\tau)| \leq |\tilde{f}_j(\tau)|$$

and

$$|\tilde{f}_j(\tau)| = \frac{2}{j\pi}|\tilde{f'}_j(\tau)|,$$

being $\tilde{f'}_j$, $j\in\mathbb{N}$, the Fourier coefficients of $\dfrac{\partial\tilde{F}}{\partial x}$. Using again the Parseval's identity, and considering that $\dfrac{\partial\tilde{F}}{\partial x}\in L^2(0,1)$, we conclude the convergence of the series defined by the left side in (3.9). Therefore, the initial series is uniformly convergent in $[0,1]\times[\tau,T]$ and consequently $\dfrac{\partial v}{\partial t}$ is continuous in $[0,1]\times[\tau,T]$, and this function is the sum of the series of the time derivatives in (3.8).

We need to prove now that $\dfrac{\partial^2 v}{\partial t^2}$ exists and that it is continuous in $(0,1)\times(\tau,T]$. Let $\delta>0$ be such that $\delta+\tau<T$ and $t\in[\tau+\delta,T]$. Considering the finite sum of (3.8), of course its second derivative is continuous. The series of the second order time derivative satisfies the following

$$\begin{aligned}
&\Bigg|\left(\frac{\sigma}{2\epsilon}\right)^2 e^{-\frac{\sigma(t-\tau)}{2\epsilon}}\left(A_j(\tau)\cos\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\right.\\
&\left.+B_j(\tau)\sin\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\right)\sin(j\pi x)\\
&-\frac{\sigma}{\epsilon}e^{-\frac{\sigma(t-\tau)}{2\epsilon}}\left(-A_j(\tau)\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}\sin\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\right.\\
&\left.+B_j(\tau)\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}\cos\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\right)\sin(j\pi x)\\
&+e^{-\frac{\sigma(t-\tau)}{2\epsilon}}\left(-A_j(\tau)\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}\sin\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\right.\\
&\left.-B_j(\tau)\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}\cos\left(\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}(t-\tau)\right)\right)\sin(j\pi x)\Bigg|\\
&\leq\left(\frac{\sigma}{2\epsilon}\right)^2|B_j(\tau)|+\frac{\sigma}{\epsilon}\sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}|B_j(\tau)|+\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}|B_j(\tau)|. \qquad (3.10)
\end{aligned}$$

for $(0,1)\times[\tau+\delta,T]$, where

$$\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}|B_j(\tau)| \leq \sqrt{\frac{4(j\pi)^2\epsilon-\sigma^2\mu}{4\epsilon^2\mu}}|\tilde{f}_j(\tau)|$$

and

$$|\tilde{f}_j(\tau)| = \frac{4}{(j\pi)^2}|\tilde{f''}_j(\tau)|,$$

being $\tilde{f''}_j$, $j\in\mathbb{N}$ the Fourier coefficient of $\dfrac{\partial^2\tilde{F}}{\partial x^2}$. Then, $\dfrac{\partial^2 v}{\partial t^2}$ exists and it is the sum of the series defined by the second order time derivate of each term of the series in

(3.8), being continuous in $(0,1)\times[\tau+\delta,T]$. As $\delta>0$ can be considered arbitrarily small, we conclude our result.

Following the previous analysis, it can be shown that the first and second space derivatives of v exist and are continuous in $(0,1)\times(\tau,T]$. $\square$

Duhamel Principle allows us to conclude that a solution of the IBVP 3.1 is given by

$$E(x,t)=\int_0^t v(x,t;\tau)\,d\tau+w(x,t), \tag{3.11}$$

where w is given by (3.2), $x\in[0,1]$ and $t\in[0,T]$.

Theorem 3. *If*

1. $\phi_0,\ \phi_1\in C^1[0,T]\cap C^2(0,T]$;
2. $\psi_0,\ \psi_1\in C^3[0,1]$;
3. $\psi_0^{(iv)},\ \psi_1^{(iv)}$ *are piecewise continuous in* $[0,1]$;
4. $F\in C((0,T],C^1[0,1])$;
5. $\dfrac{\partial^2 F}{\partial x^2}$ *is piecewise continuous in* $[0,1]$;
6. $F(0,t)=-\dfrac{1}{\epsilon\mu}(\psi_0''(0)+t\psi_1''(0))+\dfrac{\sigma}{\epsilon}(\phi_0'(t)+\psi_1(0)-\phi_0'(0))+\phi_0''(t)$ *for* $t\in(0,T]$;
7. $F(1,t)=-\dfrac{1}{\epsilon\mu}(\psi_0''(1)+t\psi_1''(1))+\dfrac{\sigma}{\epsilon}(\phi_1'(t)+\psi_1(1)-\phi_1'(0))+\phi_1''(t)$ *for* $t\in(0,T]$;

then the IBVP (3.1) has at least one solution E *in the sense that* $E\in C^1([0,T],C[0,1])$ $\cap C^2((0,T],C(0,1))\cap C((0,T],C^2(0,1))$; E *satisfies the telegraph equation in (3.1), and the initial and boundary conditions in (3.1).*

To conclude the uniqueness of the computed solution, we establish, in what follows, energy estimates similar to the ones well known for the wave equation. To do that we reduce the IBVP (3.1) to an IBVP with homogeneous boundary conditions.

Let $h:[0,1]\times[0,T]\to\mathbb{R}$ be given by

$$h(x,t)=(1-x)\phi_0(t)+x\phi_1(t). \tag{3.12}$$

The $\hat{E}=E-h$ is solution of the following IBVP, where $\hat{F},\ \hat{\psi}_0$ and $\hat{\psi}_1$ are appropriate functions.

$$\begin{cases} \dfrac{\partial^2 \hat{E}}{\partial t^2} = \dfrac{1}{\epsilon\mu}\Delta \hat{E} - \dfrac{\sigma}{\epsilon}\dfrac{\partial \hat{E}}{\partial t} + \hat{F} & \text{in } (0,1)\times(0,T], \\ \hat{E}(0,t) = \hat{E}(1,t) = 0 & t \in (0,T], \\ \hat{E}(x,0) = \hat{\psi}_0(x) & x \in (0,1), \\ \dfrac{\partial \hat{E}}{\partial t}(x,0) = \hat{\psi}_1(x) & x \in (0,1). \end{cases} \tag{3.13}$$

In what follows, we use the next notation: if $v : \bar{\Omega}\times[0,T] \to \mathbb{R}$ then $v(t)$ denotes a function defined of $\bar{\Omega}$ in $\mathbb{R}$ defined by $v(t)(x) = v(x,t)$.

Let $(\cdot,\cdot)$ be the usual inner product in $L^2(0,1)$ and $\|\cdot\|$ the corresponding norm. From the telegraph equation of the system (3.13), we get

$$\int_\Omega \frac{d^2\hat{E}}{dt^2}(t)\frac{d\hat{E}}{dt}(t)\,dx = \frac{1}{\epsilon\mu}\int_\Omega \Delta\hat{E}(t)\frac{d\hat{E}}{\partial t}(t)\,dx - \frac{\sigma}{\epsilon}\int_\Omega \left(\frac{d\hat{E}}{dt}(t)\right)^2 dx + \int_\Omega \hat{F}(t)\frac{d\hat{E}}{dt}(t)\,dx.$$

By the Cauchy-Schwartz and the Cauchy with ε inequalities, we obtain, for $\delta > 0$,

$$\frac{1}{2}\frac{d}{dt}\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \frac{1}{2\epsilon\mu}\frac{d}{dt}\left\|\nabla\hat{E}(t)\right\|^2 + \frac{\sigma}{\epsilon}\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 \le \frac{1}{4\delta}\left\|\hat{F}(t)\right\|^2 + \delta\left\|\frac{d\hat{E}}{dt}(t)\right\|^2.$$

Considering now $\delta = \dfrac{\sigma}{2\epsilon}$, we deduce

$$\frac{d}{dt}\left(\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \frac{1}{\epsilon\mu}\left\|\nabla\hat{E}(t)\right\|^2 + \frac{\sigma}{\epsilon}\int_0^t \left\|\frac{d\hat{E}}{dt}(t)\right\|^2 ds\right) \le \frac{\epsilon}{\sigma}\left\|\hat{F}(t)\right\|^2.$$

That allows us to establish

$$\begin{aligned}\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \frac{1}{\epsilon\mu}\left\|\nabla\hat{E}(t)\right\|^2 + \frac{\sigma}{\epsilon}\int_0^t \left\|\frac{d\hat{E}}{dt}(s)\right\|^2 ds \le \frac{\epsilon}{\sigma}\int_0^t \left\|\hat{F}(s)\right\|^2 ds \\ + \left\|\frac{d\hat{E}}{dt}(0)\right\|^2 + \frac{1}{\epsilon\mu}\left\|\nabla\hat{E}(0)\right\|^2.\end{aligned}$$

Taking into account the initial conditions of (3.13), we conclude

$$\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \frac{1}{\epsilon\mu}\left\|\nabla\hat{E}(t)\right\|^2 + \frac{\sigma}{\epsilon}\int_0^t \left\|\frac{d\hat{E}}{dt}(s)\right\|^2 ds \le \frac{\epsilon}{\sigma}\int_0^t \left\|\hat{F}(s)\right\|^2 ds + \left\|\hat{\psi}_1\right\|^2 + \frac{1}{\epsilon\mu}\left\|\hat{\psi}_0'\right\|^2. \tag{3.14}$$

The energy in the context of the wave equation is given by $\left\|\dfrac{d\hat{E}}{dt}(t)\right\|^2 + \dfrac{1}{\epsilon\mu}\left\|\nabla\hat{E}(t)\right\|^2$. The new term $\displaystyle\int_0^t \left\|\frac{d\hat{E}}{dt}(s)\right\|^2 ds$ that arises in (3.14) is induced by the damping term $\dfrac{\sigma}{\epsilon}\dfrac{\partial\hat{E}}{\partial t}$. Moreover, if we do not have a reaction term then holds the following energy conservative law

$$\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \frac{1}{\epsilon\mu}\left\|\nabla\hat{E}(t)\right\|^2 + \frac{2\sigma}{\epsilon}\int_0^t \left\|\frac{d\hat{E}}{dt}(s)\right\|^2 ds = \left\|\hat{\psi}_1\right\|^2 + \frac{1}{\epsilon\mu}\left\|\hat{\psi}_0'\right\|^2,\ t \in [0,T]. \tag{3.15}$$

Considering Poincaré inequality in (3.14) we conclude

$$\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \left\|\hat{E}(t)\right\|_{H_1}^2 \leq C\left(\left\|\hat{\psi}_1\right\|^2 + \left\|\hat{\psi}_0'\right\|^2 + \int_0^t \left\|\hat{F}(s)\right\|^2\, ds\right),\ t\in[0,T], \quad (3.16)$$

where $\|\cdot\|_{H^1}$ represents the usual H^1 norm, and consequently, as $H^1(0,1)$ is embedding in $C[0,1]$ we conclude

$$\left\|\frac{d\hat{E}}{dt}(t)\right\|^2 + \left\|\hat{E}(t)\right\|_{\infty}^2 \leq C\left(\left\|\hat{\psi}_1\right\|^2 + \left\|\hat{\psi}_0'\right\|^2 + \int_0^t \left\|\hat{F}(s)\right\|^2\, ds\right),\ t\in[0,T], \quad (3.17)$$

where C denotes a positive constant depending on the coefficients ϵ, μ and σ. In (3.17) $\|\cdot\|_\infty$ denotes the usual maximum norm.

Theorem 4. *Under the condition of Theorem 3 the IBVP (3.1) has a unique solution.*

Proof. We need only to prove the uniqueness. Since E and E^* are two solutions of (3.1) in the sense specified in Theorem 3, then $E-E^*$ is solution of the correspondent homogeneous telegraph IBVP. The energy conservation equality (3.15) leads to $\left\|\frac{\partial}{\partial t}(E-E^*)\right\|^2 = 0$, $\left\|\frac{\partial}{\partial x}(E-E^*)\right\|^2 = 0$. As E, E^* are smooth enough functions, we conclude that $E=E^*$ in $[0,1]\times[0,T]$. □

3.3. Numerical Analysis of Telegraph IBVP

3.3.1. Introduction

To obtain an accurate numerical description of the hyperbolic-parabolic coupled IBVP we need to propose a numerical discreptization of the hyperbolic IBVP (3.1) that mimics the solution of such system, and that presents a high convergence order.

The method that we propose is obtained considering two steps:

1. Discretization of the spatial derivatives that reduces (3.1) to a second order ordinary differential system;

2. Time integration of the initial value problem obtained in the first step.

The spatial discretization is defined on non uniform spatial grids and the convergence properties of the semi-discrete approximations are studied. Finally in the time integration we consider a standard implicit method. The fully discrete solution is not studied in the present work but will be considered in the near future.

3.3.2. Spatial Discretization

We reduce our study to the homogeneous problem

$$\begin{cases} \dfrac{\partial^2 E}{\partial t^2} = \dfrac{1}{\epsilon\mu}\Delta E - \dfrac{\sigma}{\epsilon}\dfrac{\partial E}{\partial t} + F & \text{in } (0,1)\times(0,T], \\ E(0,t) = E(1,t) = 0 & t \in (0,T], \\ E(x,0) = \psi_0(x) & x \in (0,1), \\ \dfrac{\partial E}{\partial t}(x,0) = \psi_1(x) & x \in (0,1). \end{cases} \tag{3.18}$$

In the spatial domain $\bar{\Omega} = [0,1]$ we introduce the non-uniform mesh $0 = x_0 < x_1 < \cdots < x_{I-1} < x_I = 1$. Let $h = (h_1, h_2, \ldots, h_I)$ be the stepsize vector with $h_i = x_i - x_{i-1}$, $i = 1, \ldots, I$, and let Ω_h be the interior grid points. Let D_2 be the finite difference operator

$$D_2 u_h(x_i) = 2\frac{u_h(x_{i-1})h_{i+1} - u_h(x_i)(h_i + h_{i+1}) + u_h(x_{i+1})h_i}{h_i h_{i+1}(h_i + h_{i+1})},\ i = 1, \ldots, I-1, \tag{3.19}$$

where u_h is a grid function, that will be considered in the discretization of the spatial derivative in the PDE of (3.18). Let $E_h(t)$ be the grid function with entries $E_h(x_i,t)$, $i = 0, \ldots, I$, defined by

$$\begin{cases} \dfrac{d^2 E_h}{dt^2} = \dfrac{1}{\epsilon\mu}D_2 E_h - \dfrac{\sigma}{\epsilon}\dfrac{dE_h}{dt} + F_h & \text{in } \Omega_h \times (0,T], \\ E_h(x_0,t) = E_h(x_I,t) = 0 & t \in (0,T], \\ E_h(x_i,0) = \psi_0(x_i) & i = 1, \ldots, I-1 \\ \dfrac{dE_h}{dt}(x_i,0) = \psi_1(x_i) & i = 1, \ldots, I-1, \end{cases} \tag{3.20}$$

where $F_h(x_i,t)$, is an approximation of the reaction term $F(x_i,t)$, $i = 1, \ldots, I-1$. In what follows we consider $F_h(x_i,t) = F(x_i,t)$ and $E_h(t)$ is called semi-discrete approximation for E.

System (3.20) is an initial boundary problem, so it is important to check if it has solution. Let $Y(t)$ be a vector with entries of $E_h(x_i,t)$ for $i = 1, \ldots, I-1$, that is $E_h(t)$ is a grid function defined in Ω_h. By D_E we denote the diagonal matrix with diagonal entries $\dfrac{\sigma}{\epsilon}$ and B_h the tridiagonal matrix induced by the operator D_2. Then (3.20) becomes

$$\begin{cases} Y'' + D_E Y' = B_h Y + F_h, & t \in (0,T] \\ Y(0) = \psi_0,\ Y'(0) = \psi_1, \end{cases} \tag{3.21}$$

where ψ_0, ψ_1 are the vectors with entries $\psi_0(x_i)$, $\psi_1(x_i)$, respectively.

Let $Z = [Y \; Y']^T$ and $f = [0 \; F_h]^T$, then (3.21) can be written as

$$\begin{cases} Z' = \begin{bmatrix} 0 & Id \\ B_h & -D_E \end{bmatrix} Z + f, \quad t \in (0, T] \\ Z(0) = [\psi_0 \; \psi_1]^T \end{cases} \tag{3.22}$$

where Id denotes the identity matrix with order $I - 1$.

Considering M defined by

$$M = \begin{bmatrix} 0 & Id \\ B_h & -D_E \end{bmatrix},$$

then

$$Z = e^{tM} Z(0) + \int_0^t e^{(t-s)M} f(s) \; ds, \; t \in [0, T].$$

The previous relation gives simultaneously $E_h(t)$ and $E_h'(t)$.

Now, we intend to study the accuracy properties of $E_h(t)$. Let $T_h(t)$ be the truncation error induced by the previous discretization. This error admits the following representation

$$T_h(x_i, t) = \frac{1}{3\epsilon\mu}(h_i - h_{i+1})\frac{\partial^3 E}{\partial x^3} + \mathcal{O}(h_{\max}^2), \; i = 1, \ldots, I-1, \tag{3.23}$$

where $h_{\max} = \max\limits_{i=1,\ldots,I} h_i$, and $\mathcal{O}(h_{\max}^2)$ denotes a quantity that satisfies $|\mathcal{O}(h_{\max}^2)| \leq Ch_{\max}^2$. Notice that the previous relation is verified provided that E admits bounded fourth partial spatial derivative.

From (3.23), the truncation error has first order on non-uniform meshes, so we expect an equal or bigger order of convergence. In particular case for uniform meshes with stepsize h, we have $\|T_h(t)\|_\infty \leq Ch^2$ provided that E has bounded fourth partial spatial derivative. In the main result of this section we establish that $E_h(t)$ has second order of convergence for non-uniform meshes. We introduce now the convenient functional context. Let $V_{h,0}$ be the space of grid functions with value zero in the extreme points of the partition. In $V_{h,0}$ we introduce the inner product

$$(u_h, v_h)_h = \sum_{i=1}^{I-1} \frac{h_i + h_{i+1}}{2} u_h(x_i) v_h(x_i), \; u_h, v_h \in V_{h,0}. \tag{3.24}$$

By $\|\cdot\|_h$ we denote the norm induced by $(\cdot,\cdot)_h$. We use the notation

$$\|D_{-x} u_h\|_{h,+} = \left(\sum_{i=1}^{I} h_i (D_{-x} u_h(x_i))^2 \right)^{\frac{1}{2}}, \tag{3.25}$$

where D_{-x} denotes the backward difference operator defined by

$$D_{-x}u_h(x_i) = \frac{u_h(x_i) - u_h(x_{i-1})}{h_i}.$$

We observe that

$$(D_2 u_h, v_h)_h = -(D_{-x}u_h, D_{-x}v_h)_{h,+},\ u_h, v_h \in V_{h,0},$$

where

$$(D_{-x}u_h, D_{-x}v_h)_{h,+} = \sum_{i=1}^{I} h_i D_{-x}u_h(x_i) D_{-x}v_h(x_i).$$

As for non-uniform meshes the truncation error (3.23) has only first order, the second order of convergence is not immediate. However, we start presenting a stability result for the semi-discrete solution $E_h(t)$ of (3.20), whose proof is similar to the proof of Theorem 6.

Theorem 5. *If the semi-discretized model (3.20) has a solution $E_h(t)$, then*

$$\begin{aligned} &\left\| \frac{dE_h}{dt}(t) \right\|_h^2 + \frac{1}{\epsilon\mu} \|D_{-x}E_h(t)\|_{h,+}^2 + \frac{\sigma}{\epsilon} \int_0^t \left\| \frac{dE_h}{dt}(s) \right\|_h^2 ds \leq \\ &\leq \frac{\epsilon}{\sigma} \int_0^t \|F_h(s)\|_h^2\ ds + \|\psi_1\|_h^2 + \frac{1}{\epsilon\mu} \|D_{-x}\psi_0\|_{h,+}^2 \end{aligned} \tag{3.26}$$

and

$$\frac{1}{\epsilon\mu}\|E_h\|_\infty^2 \leq \frac{\epsilon}{\sigma} \int_0^t \|F_h(s)\|_h^2\ ds + \|\psi_1\|_h^2 + \frac{1}{\epsilon\mu} \|D_{-x}\psi_0\|_{h,+}^2\,, \tag{3.27}$$

for $t \in [0, T]$.

From the previous theorem we conclude the stability of the IBVP (3.20) and the uniqueness of solution for this semi-discretized problem.

By R_h we represent the restriction operator.

Theorem 6. *If the IBVP (3.18) has solution $E \in C^1([0,T], C^4[0,1]) \cap C^2((0,T], C(0,1))$, then there exist positive constants C_1, C_2 such that the error $e_h(t) = R_hE(t) - E_h(t)$ verifies*

$$\begin{aligned} &\left\| \frac{de_h(t)}{dt} \right\|_h^2 + \|D_{-x}e_h(t)\|_{h,+}^2 + \int_0^t \left\| \frac{de_h(s)}{dt} \right\|_h^2 ds \leq \\ &\leq C_1 h_{\max}^4 e^{C_2 t} \left(\int_0^t \|E'(s)\|_{C^4(\bar\Omega)}^2\ ds + \|E(t)\|_{C^4(\bar\Omega)}^2 \right),\ t \in [0, T] \end{aligned} \tag{3.28}$$

where $E_h(t)$ is solution of (3.20) defined on non-uniform mesh.

Proof. The errors $e_h(t)$ and $T_h(t)$ verify

$$\begin{cases} \dfrac{d^2e_h}{dt^2} = \dfrac{1}{\epsilon\mu}D_2e_h - \dfrac{\sigma}{\epsilon}\dfrac{de_h}{dt} + T_h & \text{in } \Omega_h \times (0,T], \\ e_h(x_0,t) = e_h(x_I,t) = 0 & t \in (0,T], \\ e_h(x_i,0) = 0 & i = 1,\dots,I-1, \\ \dfrac{de_h}{dt}(x_i,0) = 0 & i = 1,\dots,I-1. \end{cases} \tag{3.29}$$

From the differential equation of (3.29) we obtain

$$\left(\frac{d^2e_h}{dt^2}(t), \frac{de_h}{dt}(t)\right)_h = \frac{1}{\epsilon\mu}\left(D_2e_h(t), \frac{de_h}{dt}(t)\right)_h - \frac{\sigma}{\epsilon}\left(\frac{de_h}{dt}(t), \frac{de_h}{dt}(t)\right)_h + \left(T_h(t), \frac{de_h}{dt}(t)\right)_h,$$

that is,

$$\frac{1}{2}\frac{d}{dt}\left\|\frac{de_h}{dt}(t)\right\|_h^2 + \frac{1}{2\epsilon\mu}\frac{d}{dt}\left\|D_{-x}e_h(t)\right\|_{h,+}^2 + \frac{\sigma}{\epsilon}\left\|\frac{de_h}{dt}(t)\right\|_h^2 = \left(T_h(t), \frac{de_h}{dt}(t)\right)_h.$$

If we use in the second hand member the Cauchy with ϵ inequality, we get $\|T_h\|_h$ which gives an error estimate of first order. To avoid this result we need to remark that

$$\left(T_h(t), \frac{de_h}{dt}(t)\right)_h = \frac{d}{dt}(T_h(t), e_h(t))_h - \left(\frac{dT_h}{dt}(t), e_h(t)\right)_h.$$

The previous relation enable us to conclude that

$$\frac{1}{2}\frac{d}{dt}\left\|\frac{de_h}{dt}(t)\right\|_h^2 + \frac{1}{2\epsilon\mu}\frac{d}{dt}\left\|D_{-x}e_h(t)\right\|_{h,+}^2 + \frac{\sigma}{\epsilon}\left\|\frac{de_h}{dt}(t)\right\|_h^2 = \frac{d}{dt}(T_h(t), e_h(t))_h - \left(\frac{dT_h}{dt}(t), e_h(t)\right)_h,$$

which is equivalent to

$$\begin{aligned} &\left\|\frac{de_h}{dt}(t)\right\|_h^2 + \frac{1}{\epsilon\mu}\left\|D_{-x}e_h(t)\right\|_{h,+}^2 + \frac{2\sigma}{\epsilon}\int_0^t \left\|\frac{de_h}{dt}(s)\right\|_h^2 ds = \\ &= 2(T_h(t), e_h(t))_h - 2\int_0^t \left(\frac{dT_h}{dt}(s), e_h(s)\right)_h ds. \end{aligned} \tag{3.30}$$

We need now to obtain upper bounds for $\left(\dfrac{dT_h}{dt}(t), e_h(t)\right)_h$ and $(T_h(t), e_h(t))_h$. We remark that $\dfrac{dT_h}{dt}(t)$ admits the representation

$$\begin{aligned} \frac{dT_h}{dt}(x_i,t) = \frac{1}{3\epsilon\mu}(h_i - h_{i+1})\frac{\partial^4 E}{\partial x^3 \partial t}(x_i,t) &+ \frac{h_i^2}{12\epsilon\mu}\left(\frac{h_{i+1}}{h_i + h_{i+1}} - 1\right)\frac{\partial^5 E}{\partial x^4 \partial t}(\xi_1,t) \\ &+ \frac{h_{i+1}^2}{12\epsilon\mu}\left(\frac{h_i}{h_i + h_{i+1}} - 1\right)\frac{\partial^5 E}{\partial x^4 \partial t}(\xi_2,t) \end{aligned}$$

with ξ_1, $\xi_2 \in (0,1)$.

In fact such error satisfies

$$\frac{d^3e_h}{dt^3}(t) = \frac{1}{\epsilon\mu}D_2\frac{de_h}{dt}(t) - \frac{\sigma}{\epsilon}\frac{d^2e_h}{d^2t}(t) + \frac{dT_h}{dt}(t).$$

That is, $\dfrac{dT_h}{dt}$ is the truncation error induced by the discretization of the second order spatial derivative in the equation

$$\frac{\partial^3 E}{\partial t^3} = \frac{1}{\epsilon\mu}\frac{\partial^3 E}{\partial x \partial t} - \frac{\sigma}{\epsilon}\frac{\partial^2 E}{\partial^2 t}.$$

Let be

$$T^{(1)}_{h,d}(t) = \frac{1}{3\epsilon\mu}(h_i - h_{i+1})\frac{\partial^4 E}{\partial x^3 \partial t}(t)$$

and

$$T^{(2)}_{h,d}(t) = \frac{h_i^2}{12\epsilon\mu}\left(\frac{h_{i+1}}{h_i + h_{i+1}} - 1\right)\frac{\partial^5 E}{\partial x^4 \partial t}(\xi_1, t) + \frac{h_{i+1}^2}{12\epsilon\mu}\left(\frac{h_i}{h_i + h_{i+1}} - 1\right)\frac{\partial^5 E}{\partial x^4 \partial t}(\xi_2, t).$$

We have successively

$$\begin{aligned}
-\epsilon\mu\left(T^{(1)}_{h,d}(t), e_h(t)\right)_h &= \sum_{i=1}^{I-1}\frac{h_{i+1}^2 - h_i^2}{6}\frac{\partial^4 E}{\partial x^3 \partial t}(x_i, t)e_h(x_i, t)\\
&= \sum_{i=2}^{I}\frac{h_i^2}{6}\frac{\partial^4 E}{\partial x^3 \partial t}(x_{i-1}, t)e_h(x_{i-1}, t) - \sum_{i=1}^{I-1}\frac{h_i^2}{6}\frac{\partial^4 E}{\partial x^3 \partial t}(x_i, t)e_h(x_i, t) \qquad (3.31)\\
&= -\frac{1}{6}\sum_{i=1}^{I} h_i^2\frac{\partial^4 E}{\partial x^3 \partial t}(x_{i-1}, t)[e_h(x_i, t) - e_h(x_{i-1}, t)] \qquad (3.32)\\
&\quad - \frac{1}{6}\sum_{i=1}^{I} h_i^2\left[\frac{\partial^4 E}{\partial x^3 \partial t}(x_i, t) - \frac{\partial^4 E}{\partial x^3 \partial t}(x_{i-1}, t)\right]e_h(x_i, t)\\
&= -\frac{1}{6}\sum_{i=1}^{I} h_i^3\frac{\partial^4 E}{\partial x^3 \partial t}(x_{i-1}, t)D_{-x}e_h(x_i, t)\\
&\quad - \frac{1}{6}\sum_{i=1}^{I} h_i^2\int_{x_{i-1}}^{x_i}\frac{\partial^5 E}{\partial x^4 \partial t}(s, t)\,ds\; e_h(x_i, t) \qquad (3.33)\\
&\le \frac{h_{\max}^2}{6}\left\|E'(t)\right\|_{C^3(\bar{\Omega})}\|D_{-x}e_h(t)\|_{h,+}\\
&\quad + \frac{\sqrt{2}h_{\max}^2}{6}\left\|E'(t)\right\|_{C^4(\bar{\Omega})}\|e_h(t)\|_h. \qquad (3.34)
\end{aligned}$$

Consequently we get, for $\delta_1, \delta_2 > 0$,

$$\begin{aligned}
\left|\epsilon\mu\left(T^{(1)}_{h,d}(t), e_h(t)\right)_h\right| \le & \frac{\delta_1}{36}h_{\max}^4\left\|E'(t)\right\|^2_{C^3(\bar{\Omega})} + \frac{\delta_2}{18}h_{\max}^4\left\|E'(t)\right\|^2_{C^4(\bar{\Omega})}\\
&+ \frac{1}{4\delta_1}\|D_{-x}e_h(t)\|^2_{h,+} + \frac{1}{4\delta_2}\|e_h(t)\|_h^2.
\end{aligned}$$

For $(T^{(2)}_{h,d}(t), e_h(t))_h$, with $\delta_3 > 0$, we obtain

$$\left|\epsilon\mu\left(T^{(2)}_{h,d}(t), e_h(t)\right)_h\right| \le \frac{\delta_3 h_{\max}^4}{36}\left\|E'(t)\right\|^2_{C^4(\bar{\Omega})} + \frac{1}{4\delta_3}\|e_h(t)\|_h^2.$$

Putting it all together, we have

$$\begin{aligned}\left|\epsilon\mu\left(\frac{dT_h}{dt}(t),e_h(t)\right)_h\right| \leq & Ch_{\max}^4\left(\left\|E'(t)\right\|^2_{C^4(\bar\Omega)}+\left\|E'(t)\right\|^2_{C^3(\bar\Omega)}\right)\\ &+\left(\frac{1}{4\delta_2}+\frac{1}{4\delta_3}\right)\|e_h(t)\|_h^2+\frac{1}{4\delta_1}\|D_{-x}e_h(t)\|^2_{h,+},\end{aligned}$$

where C is a convenient positive constant independent on E, t and h. Considering now the discrete Poincaré-Friedrichs inequality ([40]), we conclude

$$\begin{aligned}\left|\epsilon\mu\left(\frac{dT_h}{dt}(t),e_h(t)\right)_h\right| \leq & Ch_{\max}^4\left(\left\|E'(t)\right\|^2_{C^4(\bar\Omega)}+\left\|E'(t)\right\|^2_{C^3(\bar\Omega)}\right)\\ &+\left(\frac{1}{4\delta_1}+\frac{1}{4\delta_2}+\frac{1}{4\delta_3}\right)\|D_{-x}e_h(t)\|^2_{h,+}.\end{aligned} \tag{3.35}$$

Taking into account that

$$\begin{aligned}T_h(x_i,t)=&\frac{1}{3\epsilon\mu}(h_i-h_{i+1})\frac{\partial^3 E}{\partial x^3}(x_i,t)+\frac{h_i^2}{12\epsilon\mu}\left(\frac{h_{i+1}}{h_i+h_{i+1}}-1\right)\frac{\partial^4 E}{\partial x^4}(\eta_1,t)\\ &+\frac{h_{i+1}^2}{12\epsilon\mu}\left(\frac{h_i}{h_i+h_{i+1}}-1\right)\frac{\partial^4 E}{\partial x^4}(\eta_2,t)\end{aligned}$$

with η_1, $\eta_2\in(0,1)$ and following the construction of the upper bound (3.35), it can be shown that, for $\rho_1,\rho_2,\rho_3>0$, we have

$$\begin{aligned}|\epsilon\mu\,(T_h(t),e_h(t))_h| \leq & Ch_{\max}^4\left(\|E(t)\|^2_{C^4(\bar\Omega)}+\|E(t)\|^2_{C^3(\bar\Omega)}\right)\\ &+\left(\frac{1}{4\rho_1}+\frac{1}{4\rho_2}+\frac{1}{4\rho_3}\right)\|D_{-x}e_h(t)\|^2_{h,+}.\end{aligned} \tag{3.36}$$

Considering the upper bounds (3.35) and (3.36) in (3.30) we conclude

$$\begin{aligned}&\left\|\frac{de_h}{dt}(t)\right\|_h^2+\frac{1}{\epsilon\mu}\|D_{-x}e_h(t)\|^2_{h,+}+\frac{2\sigma}{\epsilon}\int_0^t\left\|\frac{de_h}{dt}(s)\right\|_h^2 ds\\ &\leq\frac{1}{\epsilon\mu}\left(\frac{1}{2\rho_1}+\frac{1}{2\rho_2}+\frac{1}{2\rho_3}\right)\|D_{-x}e_h(t)\|^2_{h,+}\\ &+\frac{1}{\epsilon\mu}\left(\frac{1}{2\delta_1}+\frac{1}{2\delta_2}+\frac{1}{2\delta_3}\right)\int_0^t\|D_{-x}e_h(s)\|^2_{h,+}\,ds\\ &+Ch_{\max}^4\left[\int_0^t\left(\left\|E'(s)\right\|^2_{C^4(\bar\Omega)}+\left\|E'(s)\right\|^2_{C^3(\bar\Omega)}\right)ds\right.\\ &\left.+\left(\|E(t)\|^2_{C^4(\bar\Omega)}+\|E(t)\|^2_{C^3(\bar\Omega)}\right)\right].\end{aligned}$$

Considering $\rho_1=\rho_2=\rho_3=3$ and $\delta_1=\delta_2=\delta_3=\dfrac{3}{2}$, we get

$$\begin{aligned}&\left\|\frac{de_h}{dt}(t)\right\|_h^2+\frac{1}{2\epsilon\mu}\|D_{-x}e_h(t)\|^2_{h,+}+\frac{2\sigma}{\epsilon}\int_0^t\left\|\frac{de_h}{dt}(s)\right\|_h^2 ds\\ &\leq\frac{1}{\epsilon\mu}\int_0^t\|D_{-x}e_h(s)\|^2_{h,+}\,ds\\ &+Ch_{\max}^4\left[\int_0^t\left\|E'(s)\right\|^2_{C^4(\bar\Omega)}ds+\|E(t)\|^2_{C^4(\bar\Omega)}\right].\end{aligned}$$

Finally applying the Gronwall inequality, we conclude (3.28). □

Under the conditions of the Theorem 6 we conclude that

$$\|e_h(t)\|_h^2,\ \|D_{-x}e_h(t)\|_{h,+}^2 \leq C_1 h_{\max}^4 e^{C_2 t}\left(\int_0^t \|E'(s)\|^2_{C^4(\bar{\Omega})}\, ds + \|E(t)\|^2_{C^4(\bar{\Omega})}\right),$$

that is

$$\|e_h(t)\|_{1,h}^2 \leq C_1 h_{\max}^4 e^{C_2 t}\left(\int_0^t \|E'(s)\|^2_{C^4(\bar{\Omega})}\, ds + \|E(t)\|^2_{C^4(\bar{\Omega})}\right),$$

where $\|\cdot\|_{1,h}$ represents the following discrete H^1-norm

$$\|u_h\|_{1,h} = (\|u_h\|_h^2 + \|D_{-x}u_h\|_{h,+}^2)^{1/2},\ u_h \in V_{h,0}.$$

As $\|u_h\|_\infty \leq \|u_h\|_{1,h}$, $u_h \in V_{h,0}$, we obtain for $\|e_h(t)\|_\infty$ the following upper bound

$$\|e_h(t)\|_\infty^2 \leq C_1 h_{\max}^4 e^{C_2 t}\left(\int_0^t \|E'(s)\|^2_{C^4(\bar{\Omega})}\, ds + \|E(t)\|^2_{C^4(\bar{\Omega})}\right).$$

The previous upper bounds were unexpected because $T_h(t)$ is only of first order with respect to the $\|\cdot\|_\infty$ norm. This phenomenon is usually called supraconvergence ([16], [20], [44]), and was firstly studied for elliptic equations ([13], [14]) and parabolic equations ([3], [24]). Here we observe that this phenomenon is also present when hyperbolic equations are considered. It should be pointed out that the upper bounds were obtained assuming that the solution E belongs to $C^1([0,T], C^4[0,1])$.

3.3.3. Numerical Simulation

This section aims to illustrate the main result of this chapter - Theorem 6. As this result is for the semi-discrete approximation $E_h(t)$ defined by (3.20), we need to specify a fully discrete method.

In $[0,T]$ we introduce the time grid $\{t_n,\, n = 0,\ldots,N\}$, with $t_{n+1} - t_n = \Delta t$, and $N\Delta t = T$. Let $D_{2,t}$ be the second order centred operator in time, and D_{-t} the backward finite difference operator in time. Replacing the time derivative in (3.20) by $D_{2,t}$ and D_{-t}, and considering non-homogeneous boundary conditions, we obtain

$$D_{2,t}E_h^n(x_i) + \frac{\sigma}{\epsilon}D_{-t}E_h^{n+1}(x_i) = \frac{1}{\epsilon\mu}D_2E_h^{n+1}(x_i) + F_h^{n+1}(x_i),\ i = 1,\ldots,I-1,$$
$$n = 1,\ldots,N-1 \tag{3.37}$$

with

$$E_h^j(x_0) = \phi_0(t_j),\ E_h^j(x_I) = \phi_1(t_j),\ j = 0,\ldots,N \tag{3.38}$$

and

$$E_h^0(x_i) = \psi_0(x_i) \ i = 1, \ldots, I-1. \tag{3.39}$$

Considering the forward finite difference operator in time D_t to replace the first order time derivative in the initial velocity we get

$$D_t E_h^0(x_i) = \psi_1(x_i), \ i = 1, \ldots, I-1. \tag{3.40}$$

We remark that $E_h^n(x_i) \approx E(x_i, t_n)$, $i = 0, \ldots, I$, $n = 0, \ldots, N$. The stability and convergence properties of the finite difference method (3.37)-(3.40) will be studied in the near future.

Example 1. *Let $E(x,t) = e^{\frac{-\pi}{\sqrt{\epsilon\mu}}t}\cos(\pi x)$, $x \in [0,1]$, $t \in [0,T]$, and let ψ_0, ψ_1, ϕ_0, ϕ_1, and F be such that E is solution of the IBVP (3.1). We also consider ϵ, μ, $\sigma = 1$.*

We introduce in $[0,1]$ a random non-uniform grid $\Omega_h^{(0)}$, being the new grids $\Omega_h^{(l)}$ defined introducing a medium point in each spatial subinterval. Let $h^{(l)}$ be the vector of stepsizes that defines the grid $\Omega_h^{(l)}$. By $E_{h^{(l)}}^n$ we represent the numerical solution defined by the grid $\Omega_h^{(l)}$ at time level t_n and $e_{h^{(l)}}^n$ denotes the correspondent error. Let $e_l = \max_{1 \leq n \leq N} \|e_{h^{(l)}}^n\|_{1,h^{(l)}}$.

The convergence rate r_l is given by

$$r_l = \frac{\log \frac{e_{l-1}}{e_l}}{\log\left(\frac{h_{max}^{(l-1)}}{h_{max}^{(l)}}\right)}, \tag{3.41}$$

and we take $T = 1$ and $N = 90000$, because we intend to illustrate the behaviour of the error induced by the spatial discretization.

In Table 3.1 we present the obtained numerical results for the referenced meshes. In Figure 3.2 we plot the least squares line for the set $(\log(h_{\max}^{(l)}), \log(e_l))$, for seven meshes with $I = 5 \times 2^i$, $i = 0, \ldots, 6$. The obtained angular coefficient illustrates the second order convergence rate.

Example 2. *Let $E(x,t) = e^{-\frac{\pi}{\sqrt{\epsilon\mu}}t}|x - 0.5|^{3,1}$, $x \in [0,1]$, $t \in [0,T]$. This function belongs to $H^3(0,1)$. Let the initial and boundary conditions, and F be such that E is solution of the IBVP (3.1), and take ϵ, μ, σ equal to 1.*

We consider the approach introduced in Example 1 to define the sequence of spacial grids. By $E_h^n(x_i)$, $i = 1, \ldots, I-1$ we denote the numerical solution defined by (3.37)-(3.40) with

$$F_h(x_i,t) = \frac{1}{(h_i + h_{i+1})^{\frac{1}{2}}} \int_{x_{i-\frac{1}{2}}}^{x_{i+\frac{1}{2}}} F(x,t)\, dx, \ i = 1, \ldots, I-1, \tag{3.42}$$

I	h_{max}	e_l	r_l
50	0.0901	0.0124	-
100	0.0450	0.0030	2.0533
200	0.0225	0.0007	2.0130
400	0.0113	0.0002	2.0006

Table 3.1: Numerical results for smooth E.

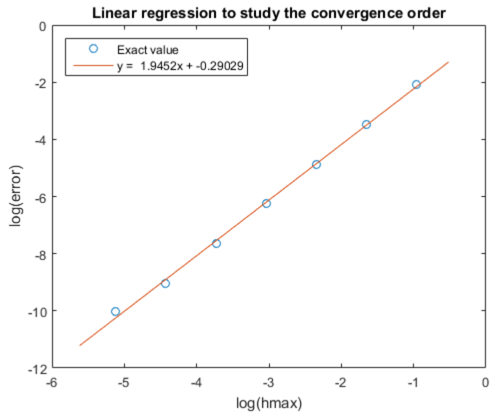


Figure 3.2: Linear regression illustrating the convergence order of the method.

where $x_{i-\frac{1}{2}} = x_i - \frac{h_i}{2}$, $x_{i+\frac{1}{2}} = x_i + \frac{h_{i+1}}{2}$.

We consider $T = 1$ *and* $N = 90000$. *In Table 3.2 we include the numerical results obtained by method (3.37)-(3.40), with* F_h *given by (3.42). We use the notations introduced in Example 1. In Figure 3.3 we plot the least squares line for* $(\log(h_{\max}^{(l)}), \log(e_l))$ *for seven meshes with* $I = 5 \times 2^i$, $i = 0, \ldots, 6$.

Table 3.2 and Figure 3.3 illustrate the second convergence order of the method (3.37)-(3.40) with F_h *given by (3.42) for solutions with lower smoothness* $(E(t) \in H^3(\Omega))$. *The theoretical support for this fact cannot be developed using the approach used in the proof of Theorem 6. The extension of this result for solutions in* $H^3(\Omega)$ *will be consider in the near future.*

I	h_{max}	$\|\|e_l\|\|_{1,h}$	r_l
50	0.0889	0.00076	-
100	0.0445	0.00020	1.9429
200	0.0222	0.00005	1.9947
400	0.0111	0.00001	2.0384

Table 3.2: Numerical results for less smoother E.

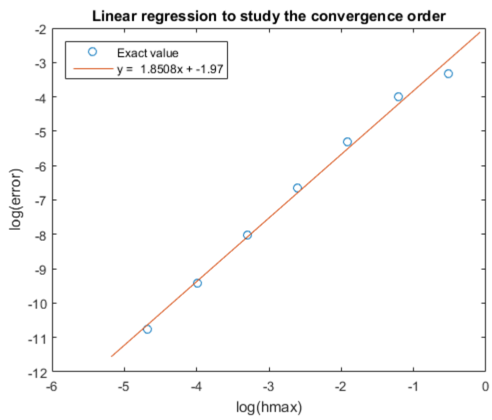


Figure 3.3: Linear regression illustrating the convergence order of the method.

Chapter 4

Hyperbolic-Parabolic Coupled Model

4.1. Introduction

Our goal in this chapter is to study the coupling between the IBVP studied in Chapter 3 with a parabolic IBVP that can be used to describe a diffusion process.

This coupling, as we mentioned before, can be used to study a drug diffusion process in a target tissue when an electric field or a scalar electric potential is generated to enhance the drug diffusion. We recall that a coupling between a diffusion equation and a Poisson equation was considered in this scope when iontophoresis or electroporation protocols are applied ([5], [15]). Such Poisson equation defines the stationary state of the telegraph equation that we studied before, when a electric field or a scalar electric potential is applied to enhance the diffusion of a drug, then in the drug transport were identified three main contributions: passive diffusion, convective transport induced by the electric field or electric potential, and convective transport induced by the fluid flux. The last contribution arises namely when high currents are applied. In what follows we do not consider this last contribution usually called electro-osmosis. Remark that when high electric pulses are applied, the structure of the target tissue changes and its porosity increases. To take into account this property, the diffusion process should be seen in a porous medium. In this case the coupling of the diffusion equation and one of the telegraph equations, introduced in Chapter 2, is not enough to describe all physical problem. We need to introduce another contribution in the drug transport induced by the porosity of the medium, and to consider Darcy's law ([4]).

If we consider only the convective transport induced by the electric field, then the mass flux J is given by the Nernst-Planck equation

$$J = -D\nabla c - vc, \tag{4.1}$$

where c denotes the drug concentration, D the diffusion coefficient and v the convective velocity given by

$$v = -\frac{zDF_c}{RTemp}E. \tag{4.2}$$

If we consider the scalar electric potential ϕ to describe the electric properties generated in the target tissue, then the convective velocity is given by

$$v = \frac{zDF_c}{RTemp}\left(\nabla\phi + \frac{\partial A}{\partial t}\right). \tag{4.3}$$

As the concentration of the drug is described by the mass conservation

$$\frac{\partial c}{\partial t} + \nabla \cdot J = 0 \text{ in } (0,1) \times (0,T], \tag{4.4}$$

then for c we conclude

$$\frac{\partial c}{\partial t} = \nabla \cdot (D\nabla c) + \nabla \cdot (vc). \tag{4.5}$$

Equation (4.5) is coupled with initial and boundary conditions. If, for instance, drug degradation is taken into account, then c is described by the following IBVP

$$\begin{cases} \dfrac{\partial c}{\partial t} = \nabla \cdot (D\nabla c) + \nabla \cdot (vc) + G & \text{in } (0,1) \times (0,T], \\ c(x,0) = c_0(x) & \text{in } (0,1), \\ c(0,t) = c_{ext}(t) & \text{in } (0,T], \\ c(1,t) = 0 & \text{in } (0,T], \end{cases} \tag{4.6}$$

where v is given by (4.2) or (4.3), c_0 describes the initial drug concentration, c_{ext} defines a source at the left size of the domain Ω. We also assume that all drug that attains the right side of the domain is removed. In (4.6) G represents a reaction that we suppose c independent.

In what follows, we study the coupled hyperbolic-parabolic IBVP (3.1) and (4.6). We observe that if the electric potential is considered then the partial differential equation in (3.1) should be replaced by (2.27). This last coupling is not considered in this work because as v depends on $\nabla\phi$ several analytical difficulties need to be solved and we do not have now the right answers.

In Section 4.2 we study the stability of the coupled model (3.1), (4.6). The existence of solution of such problem will be not considered here. However from the stability analysis we conclude that (3.1), (4.6) has at most one solution. In section 4.3 we couple the semi-discrete initial value (3.20) with a semi-discrete approximation of (4.6) and we study the stability and convergence properties of the hyperbolic-parabolic semi-discrete problem. Finally, some numerical experiments illustrating the theoretical results established in this chapter are included in Section 4.4.

4.2. Stability of the Coupled Problem

The IBVP (3.1) has at most one solution. We prove now that (4.6) has also at most one solution. Let us suppose that for E given by (3.1), (4.6) has two solutions c and $\tilde{c}$. Let consider $w = c - \tilde{c}$. It can be shown that w satisfies

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\|w(t)\|^2 &= -D\|\nabla w(t)\|^2 - (vw(t), \nabla w(t)) \\ &\leq -D\|\nabla w(t)\|^2 + \|v\|_\infty \|w(t)\|\|\nabla w(t)\| \\ &\leq -D\|\nabla w(t)\|^2 + \frac{\|v\|_\infty^2}{4\chi_1}\|w(t)\|^2 + \chi_1\|\nabla w(t)\|^2,\ t \geq 0,\end{aligned}$$

where $\chi_1 > 0$ is an arbitrary constant.

For χ_1 such that $D - \chi_1 > 0$ we obtain

$$\frac{d}{dt}\|w(t)\|^2 \leq \frac{1}{2\chi_1}\|v(t)\|_\infty^2\|w(t)\|^2,\ t \geq 0,$$

that leads to

$$\|w(t)\|^2 \leq e^{\frac{1}{2\chi_1}\int_0^t \|v(s)\|_\infty^2\ ds}\|w(0)\|^2,\ t \geq 0. \tag{4.7}$$

As $\|w(0)\| = 0$ we conclude that exists at most one solution $c \in C^1((0,T], C(0,1)) \cap C([0,T], C[0,1]) \cap C((0,T], C^2(0,1))$, with the corresponding partial derivatives in the space of uniformly Hölder continuous functions, defined in Ω with exponent δ, $0 < \delta < 1$.

Theorem 4 and the previous remark allow us to conclude that the hyperbolic-parabolic IBVP (3.1), (4.6) has at most one solution. To conclude the existence of a unique solution we need to establish conditions that enable to guarantee such existence ([26]).

In what follows we consider $c_{ext} = 0$. Similarly to the proof of the inequality (4.7) it can be shown

$$\|c(t)\|^2 \leq \left(\|c(0)\|^2 + 2\xi_2\int_0^t \|G(s)\|^2\,ds\right)e^{\int_0^t\left(\frac{1}{2\xi_1}\|v\|_\infty^2 + \frac{1}{2\xi_2}\right)ds}, \tag{4.8}$$

for $\xi_1,\ \xi_2 > 0$ such that $D - \xi_1 > 0$.

We analyse now the stability of the coupled IBVP (3.1), (4.6).

Theorem 7. *Let $E, \tilde{E}$ be solutions of (3.1) with initial conditions ψ_0, ψ_1, $\tilde{\psi}_0$, $\tilde{\psi}_1$, and c, $\tilde{c}$ be the corresponding solutions of (4.6) with initial conditions c_0, $\tilde{c}_0$. If $c, \tilde{c} \in C^1((0,T], C(0,1)) \cap C([0,T], C[0,1]) \cap C((0,T], C^2(0,1))$, then there exist two* *positive constants* χ_1, χ_2 *such that*

$$\|c(t)-\tilde{c}(t)\|^2+\int_0^t \|\nabla(c-\tilde{c})(t)\|^2 \leq$$
$$\leq c_3\left(\|(c-\tilde{c})(0)\|^2+\frac{zDF_c}{RTemp\chi_2}\int_0^t \|\tilde{c}(s)\|^2\|w_E(s)\|_\infty^2\,ds\right)e^{\frac{c_3}{\chi_1}\int_0^t \|v_E(s)\|_\infty^2\,ds},\ t\in[0,T],$$

for $c_3=\dfrac{1}{\min\{1,2D-\chi_1-\chi_2\}}$, *with* $w_E=E-\tilde{E}$.

Proof. For $w_c=c-\tilde{c}$ we easily deduce

$$\frac{d}{dt}\|w_c(t)\|^2+2D\|\nabla w_c(t)\|^2=-2(v_E(t)w_c(t),\nabla w_c(t))-2(w_v(t)\tilde{c}(t),\nabla w_c(t)),\quad (4.9)$$

where $v_E=\dfrac{zDF_cE}{RTemp}$, $w_v=v_E-v_{\tilde{E}}$. Equality (4.9) leads to

$$\frac{d}{dt}\|w_c(t)\|^2+2D\|\nabla w_c(t)\|^2\leq 2\|v_E(t)\|_\infty\|w_c(t)\|\|\nabla w_c(t)\|+2\|\tilde{c}(t)\|\|w_v(t)\|_\infty\|\nabla w_c(t)\|$$
$$\leq\frac{1}{\chi_1}\|v_E(t)\|_\infty^2\|w_c(t)\|^2+\frac{1}{\chi_2}\|\tilde{c}(t)\|^2\|w_v(t)\|_\infty^2+(\chi_1+\chi_2)\|\nabla w_c(t)\|^2,x$$

where $\chi_i>0$, $i=1,2$, are arbitrary constants. Then

$$\|w_c(t)\|^2+(2D-\chi_1-\chi_2)\int_0^t\|\nabla w_c(t)\|^2\,ds\leq\|w_c(0)\|^2+\frac{1}{\chi_1}\int_0^t\|v_E(s)\|_\infty^2\|w_c(s)\|^2\,ds$$
$$+\frac{1}{\chi_2}\int_0^t\|\tilde{c}(s)\|^2\|w_v(s)\|_\infty^2\,ds,\ t\in[0,T].$$

Fixing χ_1, χ_2 such that $2D-\chi_1-\chi_2>0$, we obtain

$$\|w_c(t)\|^2+\int_0^t\|\nabla w_c(s)\|^2\,ds\leq c_3\left(\|w_c(0)\|^2+\frac{1}{\chi_2}\int_0^t\|\tilde{c}(s)\|^2\|w_v(s)\|_\infty^2\,ds\right)$$
$$+\frac{c_3}{\chi_1}\int_0^t\|v_E(s)\|_\infty^2\|w_c(s)\|^2\,ds,\ t\in[0,T],$$

where $c_3=\dfrac{1}{\min\{1,2D-\chi_1-\chi_2\}}$. Applying Gronwall Lemma we get,

$$\|w_c(t)\|^2+\int_0^t\|\nabla w_c(s)\|^2\,ds\leq$$
$$\leq c_3\left(\|w_c(0)\|^2+\frac{1}{\chi_2}\int_0^t\|\tilde{c}(s)\|^2\|w_v(s)\|_\infty^2\,ds\right)e^{\frac{c_3}{\chi_1}\int_0^t\|v_E(s)\|_\infty^2\,ds},\ t\in[0,T].$$

□

In the conditions of Theorem 7, taking into account (3.17), (3.12) and that from (4.8) we have

$$\|\tilde{c}(t)\|^2\leq\left(\|\tilde{c}_0\|^2+2\xi_2\int_0^t\|G(s)\|^2\,ds\right)e^{\int_0^t\left(\frac{1}{2\xi_1}\|v_{\tilde{E}}\|_\infty^2+\frac{1}{2\xi_2}\right)ds}$$

we conclude the stability of the IBVP (3.1), (4.6). Moreover, under these conditions, we also conclude that exists at most one solution of the coupled problem.

The previous estimates allow us to obtain an upper bound for the drug mass in the system, during drug diffusion processes when an electric field is generated. We define the drug mass in the system, in the instant t by

$$M(t) = \int_0^1 A(x)c(x,t)\,dx,$$

where $A(x)$ is the area of the cross section for the position x. Here, by simplicity, we consider $A(x) = 1$ for all x. So, we have for $\xi_1,\ \xi_2 > 0$

$$M(t) \le \|c(t)\| \le \left(\|c(0)\|^2 + 2\xi_2 \int_0^t \|G(s)\|^2\,ds\right)^{\frac{1}{2}} e^{\int_0^t \left(\frac{1}{4\xi_1}\|v\|_\infty^2 + \frac{1}{4\xi_2}\right) ds},$$

with $\|v(t)\|_\infty \le \frac{zDF_c}{RTemp}(\|\hat{E}(t)\|_\infty + \|h(t)\|_\infty)$ e $\|\hat{E}(t)\|_\infty$ which has (3.17) as an upper bound.

4.3. A Semi-Discrete Approximation

To simulate the behaviour of the solution of the hyperbolic-parabolic IBVP (3.1), (4.6) we use in what follows a method of lines approach. As the spatial discretization has a crucial role in the error of the numerical approximation for the solution of such coupled problem, we should consider an accurate spatial discretization. We remark that the semi-discrete approximation (3.20) for the hyperbolic IBVP (3.1) presents an unexpected convergence rate established in Theorem 6.

Our aim in this section is to propose a spatial discretization for IBVP (4.6) such that the corresponding semi-discrete approximation and the one defined by the differential problem (3.20) for the electric field presents second convergence order.

In $\bar{\Omega} = [0,1]$ we consider the spatial grid defined in Section 3.3.2. Let D_c be the finite difference operator given by

$$D_c u_h(x_i) = \frac{u_h(x_{i+1}) - u_h(x_{i-1})}{h_i + h_{i+1}}.$$

Let $c_h(x_i,t)$ be the approximation for $c(x_i,t)$, $i = 0,\ldots,I$, defined by the ordinary differential system

$$\begin{cases} \dfrac{dc_h}{dt} = DD_2 c_h + D_c(c_h v_h) + G_h & \text{in } \Omega_h \times (0,T], \\ c_h(x_0,t) = c_h(x_I,t) = 0 & t \in (0,T], \\ c_h(x_i,0) = c_0(x_i) & i = 1,\ldots,I-1, \end{cases} \tag{4.10}$$

for $c_{ext} = 0$ where $v_h(t) = -\dfrac{zDF_c}{RTemp}E_h(t)$, $E_h(t)$ is defined by (3.20), $G_h(x_i,t)$ is an approximation for the reaction term $G(x_i,t)$, $i = 1,\ldots,I-1$. In this work we take

$$G_h(x_i,t) = G(x_i,t),\ i = 1,\ldots,I-1.$$

The solution of the IBVP (4.10) admits the representation

$$c_h(t) = e^{tA_h} c_h(0) + \int_0^t e^{(t-s)A_h} G_h(s)\ ds,\ t \geq 0,$$

where A_h is the matrix induced by the operators D_2 and D_c.

This solution is unique. In fact, if $\tilde{c}_h(t)$ is another solution, then $w_h(t) = c_h(t) - \tilde{c}_h(t)$ satisfies (4.10) with $w_h(0) = 0$, $G_h(t) = 0$. As $(D_c(v_h(t)w_h(t)), w_h(t))_h = -(M_h(v_h(t)w_h(t)), D_{-x}w_h(t))_{h,+}$, where

$$M_h u_h(x_i) = \frac{u_h(x_i) + u_h(x_{i-1})}{2},$$

it can be shown that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\|w_h(t)\|_h^2 + D\|D_{-x}w_h(t)\|_{h,+}^2 = -\left(M_h(v_h(t)w_h(t)), D_{-x}w_h(t)\right)_{h,+} \\
&\leq \|v_h(t)\|_\infty \|w_h(t)\|_{h,+} \|D_{-x}w_h(t)\|_{h,+} \\
&\leq \sqrt{2}\|v_h(t)\|_\infty \|w_h(t)\|_h \|D_{-x}w_h(t)\|_{h,+} \\
&\leq \frac{1}{2\chi_1}\|v_h(t)\|_\infty^2 \|w_h(t)\|_h^2 + \chi_1 \|D_{-x}w_h(t)\|_{h,+}^2,
\end{aligned}$$

where $\chi_1 > 0$ is an arbitrary constant. Then, for χ_1 such that $D - \chi_1 > 0$ we get

$$\frac{d}{dt}\|w_h(t)\|_h^2 \leq \frac{1}{2\chi_1}\|v_h(t)\|_\infty^2 \|w_h(t)\|_h^2,\ t \geq 0,$$

and consequently,

$$\|w_h(t)\|_h^2 \leq e^{\frac{1}{2\chi_1}\int_0^t \|v_h(s)\|_\infty^2\ ds} \|w_h(0)\|_h^2,\ t \geq 0.$$

As $w_h(0) = 0$ we conclude $\|w_h(t)\|_h^2 = 0$, $t \geq 0$, that is $c_h(t) = \tilde{c}_h(t)$, $t \geq 0$.

Theorem 8. *Let $E_h(t)$ be defined by (3.20). Then the IBVP (4.10) has a unique solution.*

The last result and Theorem 5 guarantee that the coupled IBVP (3.20), (4.10) has a unique solution.

We study now the convergence properties of the semi-discrete approximation defined by (4.10). Let $e_{c,h}(t) = R_h c(t) - c_h(t)$ and $e_{vc,h}(t) = R_h(vc)(t) - v_h(t)c_h(t)$ be the induced spatial error where $v_h(t) = -\dfrac{zDF_c}{RTemp}E_h(t)$. These errors satisfy

$$\begin{cases}
\dfrac{de_{c,h}}{dt} = DD_2 e_{c,h} + D_c e_{cv,h} + T_h & \text{in } \Omega_h \times (0,T], \\
e_{c,h}(x_0,t) = e_{c,h}(x_I,t) = 0 & t \in (0,T], \\
e_{c,h}(x_i,0) = 0 & i = 1,\dots,I-1,
\end{cases} \tag{4.11}$$

where the truncation error $T_h(t)$ is given by

$$
\begin{aligned}
T_h(x_i,t) = {} & \frac{D}{3}(h_i - h_{i+1})\frac{\partial^3 c}{\partial x^3}(x_i,t) + (h_i - h_{i+1})\frac{\partial^2 (vc)}{\partial x^2}(x_i,t) \\
& + \frac{Dh_i^2}{12}\left(\frac{h_{i+1}}{h_i + h_{i+1}} - 1\right)\frac{\partial^4 c}{\partial x^4}(\eta_1,t) + \frac{Dh_{i+1}^2}{12}\left(\frac{h_i}{h_i + h_{i+1}} - 1\right)\frac{\partial^4 c}{\partial x^4}(\eta_2,t) \\
& + \frac{h_i^2}{6}\left(\frac{h_{i+1}}{h_i + h_{i+1}} - 1\right)\frac{\partial^3 (vc)}{\partial x^3}(\xi_1,t) + \frac{h_{i+1}^2}{6}\left(\frac{h_i}{h_i + h_{i+1}} - 1\right)\frac{\partial^3 (vc)}{\partial x^3}(\xi_2,t),
\end{aligned}
$$

with η_1, η_2, ξ_1, $\xi_2 \in (0,1)$.

From the differential equations of (4.11), it can be shown that

$$
\frac{1}{2}\frac{d}{dt}\|e_{c,h}(t)\|_h^2 = -D\|D_{-x}e_{c,h}(t)\|_{h,+}^2 - (M_h e_{cv,h}(t), D_{-x}e_{c,h}(t))_{h,+} + (T_h(t), e_{c,h}(t))_h\,. \tag{4.12}
$$

Let $k = \dfrac{zDF_c}{RTemp}$, and $e_h(t) = R_h E(t) - E_h(t)$, where $E_h(t)$ is defined by (3.20). We have successively

$$
\begin{aligned}
& \left| - (M_h e_{cv,h}(t), D_{-x}e_{c,h}(t))_{h,+} \right| \\
& \le k\|c(t)\|_\infty \|e_h(t)\|_{h,+}\|D_{-x}e_{c,h}(t)\|_{h,+} + k\|E_h(t)\|_\infty\|D_{-x}e_{c,h}(t)\|_{h,+}\|e_{c,h}(t)\|_{h,+} \\
& \le \frac{k^2}{2\chi_1}\|c(t)\|_\infty^2\|e_h(t)\|_h^2 + (\chi_1+\chi_2)\|D_{-x}e_{c,h}(t)\|_{h,+}^2 + \frac{k^2}{2\chi_2}\|E_h(t)\|_\infty^2\|e_{c,h}(t)\|_h^2.
\end{aligned}
$$

Applying the last upper bound in (4.12) we obtain

$$
\begin{aligned}
& \frac{d}{dt}\|e_{c,h}(t)\|_h^2 + 2(D - \chi_1 - \chi_2)\|D_{-x}e_{c,h}(t)\|_{h,+}^2 \\
& \le \frac{k^2}{\chi_1}\|c(t)\|_\infty^2\|e_h(t)\|_h^2 + \frac{k^2}{\chi_2}\|E_h(t)\|_\infty^2\|e_{c,h}(t)\|_h^2 + 2(T_h(t), e_{c,h}(t))_h,\ t \ge 0.
\end{aligned} \tag{4.13}
$$

Now we need to find an upper bound for $(T_h(t), e_{c,h}(t))_h$. We start by splitting the truncation error $T_h(x_i,t) = T_h^{(1)}(x_i,t) + T_h^{(2)}(x_i,t)$, with

$$
T_h^{(1)}(x_i,t) = \frac{D}{3}(h_i - h_{i+1})\frac{\partial^3 c}{\partial x^3}(x_i,t) + (h_i - h_{i+1})\frac{\partial^2 (vc)}{\partial x^2}(x_i,t)
$$

and

$$
\begin{aligned}
T_h^{(2)}(x_i,t) = {} & \frac{Dh_i^2}{12}\left(\frac{h_{i+1}}{h_i + h_{i+1}} - 1\right)\frac{\partial^4 c}{\partial x^4}(\eta_1,t) + \frac{Dh_{i+1}^2}{12}\left(\frac{h_i}{h_i + h_{i+1}} - 1\right)\frac{\partial^4 c}{\partial x^4}(\eta_2,t) \\
& + \frac{h_i^2}{6}\left(\frac{h_{i+1}}{h_i + h_{i+1}} - 1\right)\frac{\partial^3 (vc)}{\partial x^3}(\xi_1,t) + \frac{h_{i+1}^2}{6}\left(\frac{h_i}{h_i + h_{i+1}} - 1\right)\frac{\partial^3 (vc)}{\partial x^3}(\xi_2,t).
\end{aligned}
$$

As

$$
\left|(T_h^{(1)}(t), e_{c,h}(t))_h\right| \le \frac{\sqrt{2}}{2}h_{\max}^2\left\|\frac{\partial f}{\partial x}(t)\right\|_\infty\|e_{c,h}(t)\|_h + \frac{1}{2}h_{\max}^2\|f(t)\|_\infty\|D_{-x}e_{c,h}(t)\|_{h,+},
$$

for $f(x,t) = \dfrac{D}{3}\dfrac{\partial^3 c}{\partial x^3}(x,t) + \dfrac{\partial^2 (vc)}{\partial x^2}(x,t)$, we conclude

$$\left|T_h^{(1)}(t), e_{c,h}(t))_h\right| \leq \frac{1}{8\delta_1} h_{\max}^4 \left\|\frac{\partial f}{\partial x}(t)\right\|_\infty^2 + \delta_1 \|e_{c,h}(t)\|_h^2 + \frac{1}{16\delta_2} h_{\max}^4 \|f(t)\|_\infty^2 + \delta_2 \|D_{-x} e_{c,h}(t)\|_{h,+}^2, \tag{4.14}$$

where δ_1, $\delta_2 > 0$ are arbitrary constants.

Moreover, as

$$\left|(T_h^{(2)}(t), e_{c,h}(t))_h\right| \leq \max\{1, D\} h_{\max}^2 \left(\frac{1}{6}\left\|\frac{\partial^4 c}{\partial x^4}(t)\right\|_\infty + \frac{1}{3}\left\|\frac{\partial^3 vc}{\partial x^3}(t)\right\|_\infty\right) \|e_{c,h}(t)\|_h,$$

we have

$$\left|(T_h^{(2)}(t), e_{c,h}(t))_h\right| \leq \frac{(\max\{1, D\})^2}{2\delta_3} h_{\max}^4 \left(\frac{1}{36}\left\|\frac{\partial^4 c}{\partial x^4}(t)\right\|_\infty^2 + \frac{1}{9}\left\|\frac{\partial^3 vc}{\partial x^3}(t)\right\|_\infty^2\right) + \delta_3 \|e_{c,h}(t)\|_h^2, \tag{4.15}$$

where $\delta_3 > 0$ is an arbitrary constant.

Taking in (4.13) the upper bounds (4.14), (4.15) we deduce

$$\begin{aligned} &\frac{d}{dt}\|e_{c,h}(t)\|_h^2 + 2(D - \chi_1 - \chi_2 - \delta_2)\|D_{-x} e_{c,h}(t)\|_{h,+}^2 \\ &\leq \frac{k^2}{\chi_1}\|c(t)\|_\infty^2 \|e_h(t)\|_h^2 + \left(\frac{k^2}{\chi_2}\|E_h(t)\|_\infty^2 + 2(\delta_1 + \delta_3)\right)\|e_{c,h}(t)\|_h^2 + h_{\max}^4 g(t), \end{aligned} \tag{4.16}$$

where

$$g(t) = \frac{1}{4\delta_1}\left\|\frac{\partial f}{\partial x}(t)\right\|_\infty^2 + \frac{1}{8\delta_2}\|f(t)\|_\infty^2 + \frac{(\max\{1, D\})^2}{2\delta_3}\left(\frac{1}{18}\left\|\frac{\partial^4 c}{\partial x^4}\right\|_\infty^2 + \frac{2}{9}\left\|\frac{\partial^3 vc}{\partial x^3}(t)\right\|_\infty^2\right).$$

The inequality (4.16) leads to

$$\begin{aligned} &\|e_{c,h}(t)\|_h^2 + 2(D - \chi_1 - \chi_2 - \delta_2)\int_0^t \|D_{-x} e_{c,h}(s)\|_{h,+}^2 \, ds \\ &\leq \|e_{c,h}(0)\|_h^2 + \int_0^t \left(\frac{k^2}{\chi_1}\|c(s)\|_\infty^2 \|e_h(s)\|_h^2 + h_{\max}^4 g(s)\right) ds \\ &+ \int_0^t \left(\frac{k^2}{\chi_2}\|E_h(s)\|_\infty^2 + 2\delta_1 + 2\delta_3\right)\|e_{c,h}(s)\|_h^2 \, ds. \end{aligned} \tag{4.17}$$

For χ_1, χ_2, δ_2 such that $D - \chi_1 - \chi_2 - \delta_2 > 0$ and using the Gronwall Lemma we obtain

$$\begin{aligned} &\|e_{c,h}(t)\|_h^2 + 2(D - \chi_1 - \chi_2 - \delta_2)\int_0^t \|D_{-x} e_{c,h}(s)\|_{h,+}^2 \, ds \\ &\leq \int_0^t \left(\frac{k^2}{\chi_1}\|c(s)\|_\infty^2 \|e_h(s)\|_h^2 + h_{\max}^4 g(s)\right) ds \; e^{\int_0^t \left(\frac{k^2}{\chi_2}\|E_h(s)\|_\infty^2 + 2\delta_1 + 2\delta_3\right) \, ds}. \end{aligned}$$

Finally we obtain the following result.

Theorem 9. *Let E and c be solutions of the coupled hyperbolic-parabolic problem (3.1), (4.6) and let E_h and c_h be the corresponding semi-discrete approximations defined by (3.20) and (4.10). If $E \in C^1([0,T], C^4[0,1]) \cap C^2((0,T], C(0,1))$ and $c \in C((0,T], C^4[0,1]) \cap C([0,T], C[0,1]) \cap C^1((0,T], C(0,1))$, then there are positive constants C_i, $i = 1,2,3$ such that the error $e_{c,h}(t) = R_h c(t) - c_h(t)$ satisfies*

$$\|e_{c,h}(t)\|_h^2 + \int_0^t \|D_{-x} e_{c,h}(s)\|_{h,+}^2 \, ds \leq C_1 h_{\max}^4 e^{C_2 t} \Bigg[\int_0^t \Bigg(\|c(s)\|_{C^3(\bar\Omega)}^2 \|E(s)\|_{C^4(\bar\Omega)}^2 + \|c(s)\|_{C^4(\bar\Omega)}^2 \Bigg) ds + \int_0^t \|E'(s)\|_{C^4(\bar\Omega)}^2 \, ds \int_0^t \|c(s)\|_{C(\bar\Omega)}^2 \, ds \Bigg] e^{C_3 \int_0^t \|E_h(s)\|_\infty^2 \, ds},$$

for $t \in [0,T]$.

We remark that $E_h(t)$ is given by (3.20) and considering the upper bound (3.27) we conclude that $\|E_h(t)\|_\infty$ is uniformly bounded in t and h. This fact enable us to conclude that, under the conditions of Theorem 9 there are positive constants C_1 and C_2 independent of E, C, h and t such that

$$\|e_{c,h}(t)\|_h^2 + \int_0^t \|D_{-x} e_{c,h}(s)\|_{h,+}^2 \, ds \leq C_1 h_{\max}^4 e^{C_2 t} \Bigg[\int_0^t \Bigg(\|c(s)\|_{C^3(\bar\Omega)}^2 \|E(s)\|_{C^4(\bar\Omega)}^2 + \|c(s)\|_{C^4(\bar\Omega)}^2 \Bigg) ds + \int_0^t \|E'(s)\|_{C^4(\bar\Omega)}^2 \, ds \int_0^t \|c(s)\|_{C(\bar\Omega)}^2 \, ds \Bigg],$$

for $t \in [0,T]$.

4.4. Numerical Simulation

To illustrate the behaviour of the solution of the hyperbolic-parabolic IBVP (3.1), (4.6) we propose the fully implicit-explicit discrete finite difference scheme

$$\begin{cases} D_{-t} c_h^{j+1}(x_i) = D D_2 c_h^{j+1}(x_i) + D_c(v_h^{j+1}(x_i) c_h^j(x_i)) + G_h^{j+1}(x_i), i = 1, \ldots, I-1, \\ \hfill j = 1, \ldots, N-1, \\ c_h^j(x_0) = c_{ext}(t_j), j = 1, \ldots, N, \\ c_h^j(x_I) = 0, j = 1, \ldots, N, \\ c_h^0(x_i) = c_0(x_i), i = 1, \ldots, I-1, \end{cases} \tag{4.18}$$

which is coupled with the fully discrete finite difference scheme (3.37)-(3.40) for electric field intensity. In (4.18), $c_h^j(x_i)$ represents the approximation for $c(x_i, t_j)$, $i = 0, \ldots, I$, $j = 0, \ldots, N$.

For the numerical approximation for the electric field intensity E and the numerical approximation for the concentration c, we use the following steps:

1. Solve (3.37)-(3.40);
2. Solve (4.18).

The fully discrete coupled problem (3.37)-(3.40), (4.18) will be studied in the near future. In what follows we present some numerical experiments that allow us to illustrate the main convergence result of this chapter - Theorem 9 - and the qualitative behaviour of the hyperbolic-parabolic IBVP (3.1), (4.6).

Example 3. *Let ψ_0, ψ_1, ϕ_0, ϕ_1, F be such that $E(x,t) = e^{\frac{-\pi}{\sqrt{\epsilon\mu}}t}\cos(\pi x)$, $x \in [0,1]$, $t \in [0,T]$ is solution of (3.1). Let c_0, c_{ext} and G be such that $c(x,t) = e^{-\pi t}\sin(\pi x)$, $x \in [0,1]$, $t \in [0,T]$ is solution of the IBVP (4.6).*

In (3.37)-(3.40) we take $F_h(x_i,t_n) = F(x_i,t_n)$ and in (4.18) $G_h(x_i,t_n) = G(x_i,t_n)$. We consider the sequence of the spatial grids as in Example 1 and we take $T = 1$ and $N = 90000$. For the constants of this processes, we consider ϵ, μ, $\sigma = 1$, $D = 10^{-2}$, $z = 1$ and $Temp = 310$.

Let $e_l = \max\limits_{1\leq n\leq N} \|R_h^{(l)}c(t_n) - c^n_{h^{(l)}}\|_{h^{(l)}}$ and r_l be defined in $h^{(l)}$ as in (3.41). In Table 4.1 we present the obtained numerical results. In Figure 4.1 we plot the least squares line for $(\log(h^{(l)}_{\max}), \log(e_l))$ for seven meshes with $I = 5\times 2^i$, $i = 0,\dots,6$. Such results illustrate the second order convergence rate established in Theorem 9.

I	$h_{\max}$	e_l	r_l
50	0.0882	0.00187	-
100	0.0441	0.00045	2.0656
200	0.0221	0.00011	2.0617
400	0.0110	0.00002	2.0945

Table 4.1: Numerical results for the coupled model.

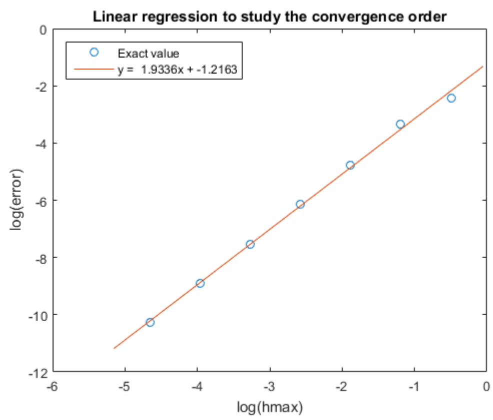


Figure 4.1: Linear regression illustrating the convergence order of the numerical coupled model.

Example 4. *In what follows we illustrate the behaviour of the concentration defined by the coupled problem (3.1), (4.6). We consider our domain a cube of edge 1, so considering that the medium is isotropic, we can simplify our study to $x \in [0,1]$. For the electric field intensity we take $\epsilon = 4\times 10^{-4}$, $\mu = 2$ and $\sigma = 0$. We also consider*

$F = 0$, $\phi_0(t_j) = 0.008$, $\phi_1(t_j) = 0$, $j = 1, \ldots, N$, and $\psi_0(x_i) = 2\cos\left(\frac{\pi}{2}(1 + 2x_i)\right) + 0.008(1 - x_i)$, $\psi_1(x_i) = -\frac{\pi}{\sqrt{\epsilon\mu}}\cos\left(\frac{\pi}{2}(2 + 2x_i)\right)$ with $i = 1 \ldots, I-1$. In what concerns the concentration, we take $z = 1$, $Temp = 310$ and $D = 10^{-2}$. The numerical $E_h(t)$ and $c_h(t)$ are obtained with $T = 100$, $M = 5000$ and $N = 100$.

Let $M_a(t)$ be the drug mass released at $x = 1$, that is given by

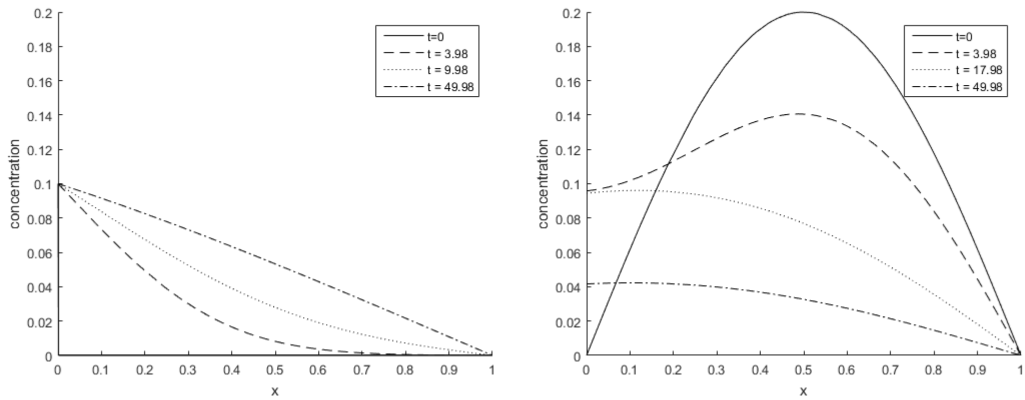
$$M_a(t) = \int_0^t AJ(x_I, s)\ ds,$$

where A is the area of the cross section which is assumed equal to the unity (see Figure 3.1). Its numerical approximation is computed by

$$M_a(t) \simeq \Delta t \sum_{m=0}^{L} \left(-D\frac{c_I^m - c_{I-1}^m}{h} - vc_I^m\right),$$

where $L\Delta t = t$. As $c(x_I, t_j) = 0$ for all j, then

$$M_a(t) \simeq \Delta t \sum_{m=0}^{L} D\frac{c_{I-1}^m}{h}.$$



(a) $c_{ext}(t) = 0.1$ for $t \in (0, T]$; $c_0(0) = 0.1, c_0(x) = 0$ for $x \in (0, 1)$.

(b) $c_{ext}(t) = 0$ for $t \in (0, T]$; $c_0(x) = 0.2\sin(\pi x)$ for $x \in [0, 1)$.

Figure 4.2: Drug concentration in the domain for several time instants.

In Figure 4.2a we plot the drug concentration obtained with $c_{ext}(t) = 0.1$, for $t \in (0, T]$, and $c_0(x) = 0$, $x \in (0, 1)$, for different time levels. The results plotted in Figure 4.2b were obtained assuming that the target tissue has an isolated left hand side and the drug is removed at the right hand side. In this case the diffusion equation (4.5) is complemented with the boundary conditions

$$J(0, t) = 0,\ \ c(x_I, t) = 0,\ \ t \in (0, 1],$$

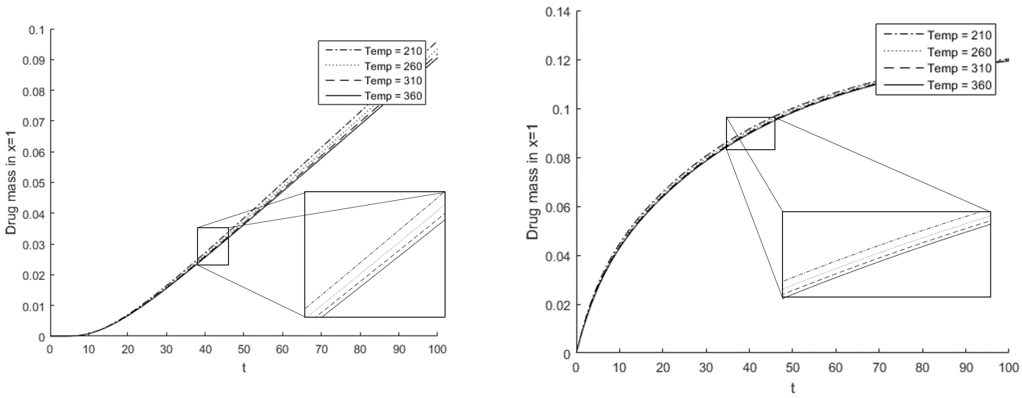
where $J(x, t) = -D\nabla c(x, t) - v(x, t)c(x, t)$.

The discretization of this problem is made considering an additional grid point $x_{-1} = -h_1$*, considering* $v(x_{-1}, t) = v(x_0, t)$*, for* $t \in (0, 1]$*, and using the following discretization*

$$DD_c c_h^j(x_0) + v_h^j(x_0) c_h^j(x_0) = 0.$$

We also consider that we do not have reaction.

The effect of the temperature in the released mass for different initial conditions is illustrated in Figure 4.3. In Figure 4.3a we plot the released mass for different temperatures when at the left hand side of the spatial domain we have the source used before in the scenario illustrated in Figure 4.2a. When the temperature increases, a decreasing of the released mass is observed. The behaviour of the concentration for different temperatures, where the diffusion process is enhanced by an applied electric field is illustrated in Figure 4.3b. From these results, we conclude that an increase of the temperatures leads to a decrease of the released mass.

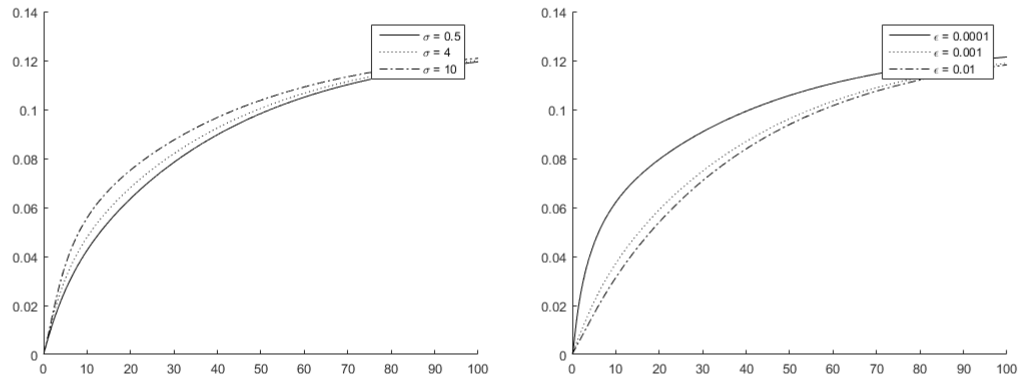


(a) $c_{ext}(t) = 0.1$ for $t \in (0, T]$;
$c_0(0) = 0.1, c_0(x) = 0$ for $x \in (0, 1)$.

(b) $c_{ext}(t) = 0$ for $t \in (0, T]$;
$c_0(x) = 0.2 \sin(\pi x)$ for $x \in [0, 1)$.

Figure 4.3: Released drug mass at $x = 1$ for different temperatures.

Figure 4.4 illustrates the behaviour of the drug diffusion for different electric conductivities and different electric permittivities of the target tissue. The results in Figure 4.4a show that the convective transport is higher for higher electric conductivities. In Figure 4.4b we observe an opposite behaviour, that is, an increase of the electric permittivity induces a decrease of the electric transport. These results were obtained using a pulse initial condition.



(a) Variation of σ.

(b) Variation of ϵ.

Figure 4.4: Released drug mass at $x = 1$ where $c_{ext}(t) = 0$ for $t \in (0, T]$ and $c_0(x) = 0.2\sin(\pi x)$ for $x \in [0, 1)$.

Chapter 5

Conclusions

In this work we studied a coupled initial boundary value problem (3.1), (4.6) that describes the time and space evolution of the electric field E and the concentration c. As we mentioned before, this system is a natural extension of the coupling between Laplace equation for the electric potential and equation (4.5) for the concentration. We believe that the coupling hyperbolic-parabolic problem can be used to study the drug absorption enhanced by a physical enhancer like electric currents, as considered in the references included in this work, or light ([36]).

Theorems 6 and 9 are the main results of this work. In the first result we establish that the error for the semi-discrete approximation $E_h(t)$, defined by (3.20), for the electric field $E(t)$, defined by (3.18), presents second convergence order with respect to the H^1 discrete norm $\|\cdot\|_{1,h}$. Using this result, we prove in the second result that the error for semi-discrete approximation $c_h(t)$, defined by (4.10), for the concentration c, defined by (4.6) with homogeneous boundary conditions, presents second convergence order but with respect to the L^2 discrete norm $\|\cdot\|_h$. These results are unexpected because the truncation errors induced by the considered spatial discretizations have only first order with respect to the norm $\|\cdot\|_\infty$.

Numerical results illustrating these results are also presented. We remark that these results require smoothness for the electric field and for the concentration. Numerical simulation for weaker smooth solutions is also included.

The qualitative behaviour of the coupled model (3.1), (4.6) is illustrated considering the fully discrete coupled method (3.37)-(3.40), (4.18). This scheme was constructed using the method of lines approach: the time integration of the semi-discrete coupled problem (3.20), (4.10) using Euler method.

As this work is the first study in the analysis from analytical and numerical point of view of the IBVPs (3.1), (4.6), several questions are still without an answer. Firstly, from the numerical simulation of the method (3.1), when the electric field $E(t)$ is in $H^3(0,1)$, we think that Theorem 6 remains true when lower smoothness assumptions are imposed. The stability and convergence analysis of the fully discrete schemes (3.37)-(3.40), (4.18) under the smoothness assumptions considered in this work or under weaker assumptions will be studied in a near future. The electric field $E(t)$ (equation (2.16)) was used in the Nernst-Planck relation (4.1) to define the convective velocity for the drug concentration. Let us consider now that the convective velocity is induced by the gradient of the electric potential ϕ defined by the equation (2.27). The study of results similar to Theorems 6 and 9 need to be consider for this last scenario. High dimensions for the space variable will be also considered.

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