MATHEMATICAL MODEL OF SIGNAL PROPAGATION IN EXCITABLE MEDIA

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Abstract. This article deals with a model of signal propagation in excitable media based on a system of reaction-diffusion equations. Such media have the ability to exhibit a large response in reaction to a small deviation from the rest state. An example of such media is the nerve tissue or the heart tissue. The first part of the article briefly describes the origin and the propagation of the cardiac action potential in the heart. In the second part, the mathematical properties of the model are discussed. Next, the numerical algorithm based on the finite difference method is used to obtain computational studies in both a homogeneous and heterogeneous medium with an emphasis on interactions of the propagating signals with obstacles in the medium.

1. Introduction and model description. This article deals with the mathematical modelling of a signal propagation in excitable media. Such a medium possesses the property of excitability – it responds to a small deviation (over a certain threshold) from a fixed point with a large reaction. Examples of the excitable media are the cardiac and the nerve tissue. While the nerve tissue is studied e.g. in [8], [19] and [29], we will focus on the cardiac tissue.

By the signal propagation in the heart we mean the spreading of a wave of contractions of the cardiomyocytes (the heart muscle cells), which is driven by an electrical excitement called the cardiac action potential (CAP). The CAP describes the change of the membrane potential from the resting state of $-90\text{mV}$ to $20\text{mV}$ and back. For more information see e.g. [21], [3], [31] or [32].

In physiological context the signal originates in the sinoatrial (SA) node located at the top of the heart. This signal then spreads through atria, causing their contraction, to atrioventricular (AV) node. After a slight delay, which is needed for passing the blood from atria to ventricles, the signal continues to the rest of the heart causing the contraction of the ventricles and expulsion of the blood out of the heart (see [10], [30]).

In pathological cases, however, this regular spreading of signal can be disturbed and dangerous medical conditions – such as a ventricular tachycardia and ventricular fibrillation – can develop. The study of such phenomena is therefore worthwhile

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and is one of the main motivations of this article. As shown in [26] a mathematical modelling of the heart is a realistic goal.

We can find many papers devoted to the study of the signal propagation in excitable media in general. Classical results about aggregation waves were presented in [7]. More recent results include the study of vibrational resonance (see [28]), fast inhibitor diffusion (see [34]) and spiral wave initiation (see [33]). Inhomogeneous excitable media (see [35]) and media with randomly distributed obstacles (see [27]) are also studied. Among papers more closely focused on the cardiac tissue we can include: [1], which discusses the wave propagation in such a tissue, [5], which is devoted to the study of the wave reentry in a chick embryo, and [15], which studies the influence of electromagnetic waves on the propagation of the signal in the heart.

The currently used model for simulations involving pathologies in the heart is called a bidomain model. It treats the healthy and damaged tissue as two separated regions with a shared border (see [4]). However, due to the computational complexity of this model, simplified models can be used in some cases (see [3]). The purpose of this article is to present such a simplified model still capturing heterogeneity of the excitable medium reflecting the above mentioned pathological cases and to study the interaction of the solution with strong and time dependent spatial heterogeneities of the medium.

The model of signal propagation in homogeneous excitable media by a system of reaction-diffusion equations is originally suggested by Chen, Ninomiya and Taguchi in [2]. This model was derived from the FitzHugh-Nagumo model (see [9], [17] and [18]). In this article, we newly suggest that the diffusion coefficients may depend on space and time as $D_i = D_i(t,x)$ for $i = 1, 2$, reflecting heterogeneity of the medium.

We then study the following problem

$$\partial_t u_1 = \nabla \cdot (D_1 \nabla u_1) + \frac{1}{\varepsilon^2} (f_\varepsilon(u_1) - \varepsilon \beta u_2), \quad \text{in } (0,T) \times \Omega,$$

$$\partial_t u_2 = \nabla \cdot (D_2 \nabla u_2) + g_0(u_1, u_2), \quad \text{in } (0,T) \times \Omega,$$

where the right hand side non-linear functions take form

$$f_\varepsilon(u_1) = u_1 \left( u_1 - \frac{1}{2} + \varepsilon \alpha \right) (1 - u_1),$$

$$g_0(u_1, u_2) = g_1 u_1 - g_2 u_2 + g_3.$$

This system is subject to the initial conditions

$$u_1|_{t=0} = u_{ini,1}, \quad u_2|_{t=0} = u_{ini,2} \quad \text{in } \Omega,$$

and the boundary conditions

$$u_1|_{\partial \Omega} = \gamma_1, \quad u_2|_{\partial \Omega} = \gamma_2 \quad \text{on } \partial \Omega.$$

Here $D_i = D_i(t,x), 0 < d_0 \leq D_i(t,x) \leq D_0$, are continuously differentiable for $i = 1, 2$ where $d_0, D_0$ are constants, $\varepsilon > 0$ and $\alpha, \beta, g_1, g_2$ and $g_3$ are real constants. $\Omega \subset \mathbb{R}^n, n \in \mathbb{N}$, is a domain with the Lipschitz boundary $\partial \Omega$. The functions $u_{ini,i}$ for $i = 1, 2$ are defined in $\Omega$, and $\gamma_i$ for $i = 1, 2$ on $\partial \Omega, T > 0$. The boundary conditions of the Dirichlet type have been chosen for simplicity as the solution behaviour is mainly studied in the interior of $\Omega$. The Neumann boundary conditions can be considered alternatively.

The paper is organized as follows. First, model (1)-(3) is justified by proving the existence and uniqueness of the weak solution where the standard tools as the Fiedo-Galerkin approximation and the compactness method together with the
invariant regions were used. Main contribution of this article can be seen in studying the signal propagation in a heterogeneous medium with obstacles leading to an oscillatory behaviour. This is observed in computational studies performed by the numerical solution based on the finite-difference method. The obtained results were verified by evaluating their numerical convergence.

2. Notation. We rewrite system (1)-(3) into the form
\[ \partial_t u = Au + F(u) \quad \text{in } (0, T) \times \Omega, \]
\[ u|_{t=0} = u_{ini} \quad \text{in } \Omega, \]
\[ u|_{\partial \Omega} = \gamma \quad \text{on } (0, T) \times \partial \Omega, \]
where \( u = (u_1, u_2)^T \) and \( u_i = u_i(t, x) \) for \( i = 1, 2, t \in (0, T) \) and \( x = (x_1, x_2)^T \in \Omega \subset \mathbb{R}^2 \), where \( \Omega \) is a bounded domain with a Lipschitz boundary. \( A \) is a linear second-order differential operator in the form \( Au = (\nabla(D_1 \nabla u_1), \nabla(D_2 \nabla u_2))^T \). \( F(u) \) is given in the form \( F(u) = (f_1(u), f_2(u))^T \) where \( f_1(u) = \frac{1}{2\varepsilon}(f_2(u_1) - \varepsilon \beta u_2) \) and \( f_2(u) = g_0(u_1, u_2) \) as follows from (1)-(3). Finally, \( u_{ini} = (u_{ini,1}, u_{ini,2})^T \), where for \( i = 1, 2 : u_{ini,i} = u_{ini,i}(x) \) are the initial conditions for \( x \in \Omega \) and \( \gamma = (\gamma_1, \gamma_2)^T \), where for \( i = 1, 2 : \gamma_i = \gamma_i(t, x) \) are the boundary conditions for \( t \in (0, T), x \in \partial \Omega \).

Remark 1. In the existence analysis below, we assume that \( F(u) \) is bounded and Lipschitz-continuous. For \( F(u) \) given by (1)-(3) such a property can be obtained by using the concept of invariant regions (e.g., see [23], [24]) which will be discussed in Section 5. For example, we can use the following sufficient conditions to find an invariant region for problem (4)

1. Let \( D \) be a diagonal matrix. Then any region of the form
\[ \Sigma = \{ u \in \mathbb{R}^2 | a_x \leq u_1 \leq b_x, a_y \leq u_2 \leq b_y \}, \]
where \( a_x, b_x, a_y, b_y \) are constants, is an invariant region for problem (4), if \( F \) points strictly into domain \( \Sigma \) on its boundary \( \partial \Sigma \).

2. If \( D \) is an arbitrary \( \varepsilon \)-multiple of the identity matrix for some \( \varepsilon > 0 \), then every convex domain \( \Sigma \) for which \( F \) points strictly into \( \Sigma \) on \( \partial \Sigma \) is an invariant region for (4).

We then proceed by considering the weak solution of (4) and showing its existence.

3. Weak solution. We introduce the following expressions
\[ (u, v) = \sum_{i=1}^{2} \int_{\Omega} u_i(x)v_i(x) \, dx, \]
\[ ((u, v)) = \sum_{i=1}^{2} \int_{\Omega} \nabla u_i(x) \cdot \nabla v_i(x) \, dx, \]
\[ a(u, v) = \sum_{i=1}^{2} (D_i \nabla u_i, \nabla v_i) \]
for the functions \( u, v \in W^{(1)}_2(\Omega; \mathbb{R}^2) \), where \( \cdot \) denotes the scalar product in \( \mathbb{R}^2 \), and the norm
\[ ||u|| = \sqrt{(u, u)}. \]
Furthermore, for $u, v \in W_2^1(\Omega; \mathbb{R}^2)$ we define the scalar product and the norm as follows
\[
(u, v)_{W_2^1} = (u, v) + ((u, v)),
\]
\[
\|u\|_{W_2^1} = \sqrt{(u, u)_{W_2^1}}.
\] (9)

The weak solution will be searched in the Bochner spaces
\[
L_p(0, T; L^2(\Omega; \mathbb{R}^2))\) and $L_p(0, T; W_2^1(\Omega; \mathbb{R}^2))$ for $p \geq 1$.

We can now proceed to the derivation of a weak identity. Let $u = u(t, x)$ be a classical solution of (4), let $v = (v_1(x), v_2(x))^T, v \in C_0^\infty(\Omega; \mathbb{R}^2)$ and $\varphi = \varphi(t), \varphi \in C^1([0, T])$ and $\varphi(T) = 0$. Using the Green formula and the integration [... over the domain $\Omega$ and over $(0, T)$ and summing over $i = 1, 2$ yields
\[
\int_0^T dt \varphi(t)(\partial_t u(t, \cdot), v) = \int_0^T dt \varphi(t)(A u(t, \cdot), v) + \int_0^T dt \varphi(t)(F(u(t, \cdot)), v),
\]
from which we derive the weak identity using the Green formula and the integration by parts
\[
-\varphi(0)(u_{ini}, v) - \int_0^T dt \varphi(t)(u(t, \cdot), v) = -\int_0^T dt \varphi(t)a(u(t, \cdot), v)
\]
\[
+ \int_0^T dt \varphi(t)(F(u(t, \cdot)), v).
\] (10)

Remark 2. The mapping $u: (0, T) \to W_2^1(\Omega; \mathbb{R}^2)$ is the weak solution of (4) if a function $w \in W_2^1(\Omega; \mathbb{R}^2)$ exists such that $w|_{\partial \Omega} = \gamma$ and $u - w: (0, T) \to W_2^1(\Omega; \mathbb{R}^2)$ and (10) is satisfied for all $v \in W_2^1(\Omega; \mathbb{R}^2)$ and for all $\varphi \in C^1([0, T])$ satisfying $\varphi(T) = 0$.

Remark 3. In this article system (4) with homogeneous boundary conditions is considered. This describes $\partial \Omega$ as a non-excitable boundary. The use of other boundary conditions is possible while adjusting weak identity (10) correspondingly.

4. Existence and uniqueness of solution. In this section, model (4) is justified by verifying the existence and uniqueness of the weak solution on a global interval. This is obtained by exploring standard tools (summarized in, e.g. [25], [23], also in [12], [13]), such as the Faedo-Galerkin method and the compactness method. The non-linear reaction terms are treated by means of the invariant regions (as in [23], [24]). Particular form of the invariant region is provided for the given system of equations. Such a result justifies further use of (4) in numerical studies presented later in the text.

Exploring the assumptions on the right hand side functions of the studied model, we are able to pass to the limit and obtain the weak solution on any bounded time interval $(0, T)$.

Let $v \in \dot{W}_2^1(\Omega; \mathbb{R}^2)$ and let $\varphi \in C_0^\infty((0, T))$ be an arbitrary test function. Then, we can rewrite (10) as
\[
\frac{d}{dt}(u(t, \cdot), v) + a(u(t, \cdot), v) = (F(u(t, \cdot)), v) \quad \text{in } \mathcal{D}'((0, T)),
\]
\[
u|_{t=0} = u_{ini},
\] (11)
where the assumptions on \( u_{\text{ini}} \) will be specified below. Let \( u \in \tilde{W}_{2}^{1}(\Omega; \mathbb{R}^2) \) and let \((v_{1}^{(1)}, v_{2}^{(1)}, \ldots, v_{m}^{(1)}, v_{m}^{(2)}, \ldots)\) be an orthogonal basis of \( \tilde{W}_{2}^{1}(\Omega; \mathbb{R}^2) \). For the first \( 2m \) vectors we denote the Faedo-Galerkin approximation as

\[
 u_m(t, x) = \sum_{i=1}^{m} \sum_{l=1}^{2} \alpha_{i}^{(l)}(t) v_{i}^{(l)}(x).
\]

Inserting (12) to equation (11) we obtain the following set of 2m ordinary differential equations

\[
 \frac{d}{dt}(u_m(t, \cdot), v_j^{(l)}) + a(u_m(t, \cdot), v_j^{(l)}) = (F(u_m(t, \cdot)), v_j^{(l)}) \quad \forall j \in \{1, \ldots, m\}, \, l \in \{1, 2\},
\]

for the unknowns \( \alpha_{i}^{(l)} \). System (13) has a unique solution on \([0,T_m]\), where \( T_m \) generally depends on \( m \in \mathbb{N} \), due to the Picard theorem [22]. We use following two propositions to remove the dependency on \( m \).

**Proposition 1. A Priori Estimate (i)** Let \( u_m \) be the Faedo-Galerkin approximation (12) satisfying (13). Let the right hand side functions \( F \) of problem (4) be bounded and Lipschitz-continuous. Let \( u_{\text{ini}} \in L_2(\Omega; \mathbb{R}^2) \). Then a constant \( K > 0 \) exists such that, for all \( m \in \mathbb{N} \), \( u_m \) satisfies

\[
 ||u_m||^2(t) \leq ||u_m||^2(0) e^t + K^2(e^t - 1).
\]

**Proof.** We substitute for \( u_m \) in (13) with (12) and then multiply the resulting equation by \( \alpha_{j}^{(l)} \), sum over \( j \) from 1 to \( m \) and over \( l = 1, 2 \) and get

\[
 \sum_{j=1}^{m} \sum_{l=1}^{2} \alpha_{j}^{(l)} \sum_{k=1}^{m} \sum_{p=1}^{2} \alpha_{k}^{(p)} (v_{k}^{(p)}, v_{j}^{(l)}) + \sum_{j=1}^{m} \sum_{l=1}^{2} \alpha_{j}^{(l)} \sum_{k=1}^{m} \sum_{p=1}^{2} \alpha_{k}^{(p)} (D_p \nabla v_{k}^{(p)}, \nabla v_{j}^{(l)})
\]

\[
 = \sum_{j=1}^{m} \sum_{l=1}^{2} \alpha_{j}^{(l)} (F(u_m), v_{j}^{(l)}).
\]

Using orthogonality and the form of \( u_m \), we obtain the energy equality

\[
 \frac{1}{2} \frac{d}{dt} ||u_m||^2 + a(u_m, u_m) = (F(u_m), u_m).
\]

(16)

Pointwise boundedness of \( F \) gives a constant \( K > 0 \) such that \( ||F(u_m)|| \leq K \).

Neglecting the second term on the left hand side of (16), using the Schwarz inequality and the estimate for \( F \), we obtain

\[
 \frac{1}{2} \frac{d}{dt} ||u_m||^2 \leq (F(u_m), u_m) \leq K \cdot ||u_m||
\]

Then, by the Young inequality,

\[
 \frac{d}{dt} ||u_m||^2 \leq K^2 + ||u_m||^2.
\]

(17)

The Grönwall argument yields the estimate (14).

**Proposition 2. A Priori Estimate (ii)** Let consider the assumptions as in Proposition 1 and \( u_{\text{ini}} \in W_{2}^{1}(\Omega; \mathbb{R}^2) \). Then a constant \( K > 0 \) exists such that, for all \( m \in \mathbb{N} \), \( u_m \) satisfies

\[
 a(u_m, u_m)(t) \leq a(u_m, u_m)(0) + K^2 t.
\]

(18)
Proof. We multiply (13) by $\alpha_j^{(l)}$, sum over $j$ from 1 to $m$ and over $l = 1, 2$ and use the orthogonality of the basis. We obtain

$$
\sum_{j=1}^{m} \sum_{l=1}^{2} (\alpha_j^{(l)})^2 (v_j^{(l)}, v_j^{(l)}) + \sum_{j=1}^{m} \sum_{l=1}^{2} \frac{1}{2} \frac{d}{dt} (\alpha_j^{(l)}) (D_l \nabla v_j^{(l)}, \nabla v_j^{(l)})
= \sum_{j=1}^{m} \sum_{l=1}^{2} \alpha_j^{(l)} (F(u_m), v_j^{(l)}).
$$

(19)

Then we get the energy equality

$$
||\partial_t u_m||^2 + \frac{1}{2} \frac{d}{dt} a(u_m, u_m) = (F(u_m), \partial_t u_m).
$$

(20)

The Schwarz and the Young inequalities and the upper bound $K$ for $F$ yield

$$(F(u_m), \partial_t u_m) \leq \frac{1}{2} K^2 + \frac{1}{2} ||\partial_t u_m||^2.
$$

(21)

Combining (20) and (21), we have

$$
||\partial_t u_m||^2 + \frac{d}{dt} a(u_m, u_m) \leq K^2.
$$

(22)

Since the first term on the left hand side of the expression above is non-negative, we obtain

$$
\frac{d}{dt} a(u_m, u_m) \leq K^2.
$$

(23)

and integrating over $(0, t)$ we conclude the proof.

The properties of the diffusion terms $D_i(t, x)$ lead to inequalities

$$
d_0(\langle u_m, u_m \rangle) \leq a(u_m, u_m) \leq D_0(\langle u_m, u_m \rangle).
$$

(24)

Proposition 2 and (24) give the estimate $d_0(\langle u_m, u_m \rangle(t)) \leq D_0(\langle u_m, u_m \rangle(0)) + K^2 T$. Since $u_{mi} \in W^{1,2}_2(\Omega; \mathbb{R}^2)$, we have

- $(u_m)_{m=1}^{+\infty}$ uniformly bounded in $L_{\infty} \left(0, T; W^{1,2}_2(\Omega; \mathbb{R}^2)\right)$,
- $(\partial_t u_m)_{m=1}^{+\infty}$ uniformly bounded in $L_2 \left(0, T; L_2(\Omega; \mathbb{R}^2)\right)$.

Then $T_m > T$ for any fixed $T > 0$. Therefore, a subsequence $(u_{m'})_{m'=1}^{+\infty}$ exists such that it converges weakly in $L_2 \left(0, T; W^{1,2}_2(\Omega; \mathbb{R}^2)\right)$ to some $\hat{u} \in L_2 \left(0, T; W^{1,2}_2(\Omega; \mathbb{R}^2)\right)$ for $m' \to +\infty$. We denote this fact as $u_{m'} \rightharpoonup \hat{u}$.

Furthermore, we can prove that $u_{m'}$ converges to $\hat{u}$ strongly in $L_2 \left(0, T; L_2(\Omega; \mathbb{R}^2)\right)$. Using the uniform boundedness of $(u_m)_{m=1}^{+\infty}$ in $L_2 \left(0, T; W^{1,2}_2(\Omega; \mathbb{R}^2)\right)$ and $(\partial_t u_m)_{m=1}^{+\infty}$ in $L_2 \left(0, T; L_2(\Omega; \mathbb{R}^2)\right)$ and the Theorem on Compact Embedding (see, e.g., [25], [14]) which states that

$$
L_2 \left(0, T; W^{1,2}_2(\Omega)\right) \supset \subset \supset L_2(0, T; L_2(\Omega)),
$$

we can conclude that $(u_{m'})_{m'=1}^{+\infty}$ converges strongly in $L_2(0, T; L_2(\Omega))$. 
The existence of the weak limit allows us to pass to the limit
\[
\int_0^T dt \varphi(t)(u_m', v) + \int_0^T dt \varphi(t)((u_m', v)) \quad \downarrow \quad \text{for } m \to \infty
\]
\[
\int_0^T dt \varphi(t)(\hat{u}, v) + \int_0^T dt \varphi(t)((\hat{u}, v)).
\]  

We use this weak convergence in the weak identity (10) and we perform the passage to the limit in (10) which gives us
\[
(u_{ini}, v)\varphi(0) - \int_0^T dt \varphi(t)(u_m', v) + \int_0^T dt \varphi(t)a(u_m', v) = \int_0^T dt \varphi(t) (F(u_m'), v)
\]
\[
\downarrow 
\int_0^T dt \varphi(t)(\hat{u}, v) + \int_0^T dt \varphi(t)a(\hat{u}, v) = \int_0^T dt \varphi(t) (G, v),
\]
\[
(25)
\]
for some element \(G\). We prove that \(G\) is equal to \(F(\hat{u})\). As assumed above, \(F\) is Lipschitz-continuous with constant \(L > 0\). Then
\[
\left| \int_0^T dt \varphi(t)[(F(u_m', t, \cdot), v) - (F(\hat{u}(t, \cdot)), v)] \right| \leq L \left( \int_0^T dt \|u_m' - \hat{u}\|^2 \right)^{\frac{1}{2}} \cdot \left( \int_0^T dt \|\varphi(t)\|^2 \|v\|^2 \right)^{\frac{1}{2}},
\]
\[
(27)
\]
and using the above proven strong convergence we see that the limit vector function \(G\) is equal to \(F(\hat{u})\).

**Proposition 3.** The solution of problem (4) is unique.

**Proof.** Let \(u\) and \(w\) be two weak solutions of problem (10) and let us denote \(z = u - w\). By subtracting equalities (10) for \(u, w\) and multiplying by \(\alpha_j^{(l)}\), summing over \(j, l\) we have
\[
\frac{1}{2} \frac{d}{dt} ||z||^2 + a(z, z) = (F(u) - F(w), z).
\]
\[
(29)
\]
Since \(F\) is Lipschitz-continuous, there exists \(L > 0\) such that
\[
(F(u) - F(w), z) \leq ||F(u) - F(w)|| \|z\| \leq L ||u - w|| \|z\| \leq L ||z||^2,
\]
and therefore we have the estimate
\[
\frac{1}{2} \frac{d}{dt} ||z||^2 \leq L ||z||^2.
\]
\[
(30)
\]
The Grönwall argument gives
\[
||z||^2(t) \leq ||z||^2(0)e^{2Lt},
\]
\[
(31)
\]
for \(t \in (0, T)\). As \(z|_{t=0} = 0\) we have \(z = 0\) in \((0, T) \times \Omega\). \(\square\)
The above shown steps lead to the following theorem:

**Theorem 4.1. (Theorem on existence)** Let the non-linear term \( F = F(u) \) be bounded and Lipschitz-continuous, \( \gamma \equiv c \) and \( u_{\text{ini}} \in W^{(1)}(\Omega; \mathbb{R}^2) \). Then the problem (4) formulated in the form of weak identity (10) has a unique weak solution.

5. **Invariant region.** In this section, we demonstrate how to find an invariant region compliant with the specific conditions of Remark 1 (see [23], Corollary 14.8).

The orientation of the vector field created by the right hand side functions at any given point is determined by the relative position of that point to the nullclines – graphs of functions in \((u_1, u_2)\) phase space obtained when the right hand side functions are set equal to zero. Let us denote these functions \( v_1 = v_1(u_1) \) and \( v_2 = v_2(u_1) \) for the cubic and linear functions expressed from the right hand side functions, respectively. An example of nullclines for the values of the parameters \( \varepsilon = 0.008, \alpha = 0.139, \beta = 2.54, g_1 = 20, g_2 = 1.5, \) and \( g_3 = -5.5 \) can be seen in Figure 1.

It can easily be seen that in a rectangle on whose boundary the vector field has an inward direction the graph of function \( v_1 \) has to have one intersection with upper boundary and one with lower boundary while the graph of function \( v_2 \) has to intersect the left and right boundary\(^1\).

To verify the existence of such a rectangle for problem (1)-(3), we denote \( \frac{du_i}{du_1} = v'_i(u_1) \) for \( i = 1, 2 \). It follows that

\[
    v'_1(u_1) = \frac{1}{\varepsilon \beta} \left( -3u_1^2 + (3 - 2\varepsilon \alpha)u_1 - \frac{1}{2} + \varepsilon \alpha \right), \quad (32)
\]

\[
    v'_2(u_1) = \frac{g_1}{g_2}. \quad (33)
\]

\(^1\)Where the directions correspond with those in Figure 1.

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**Figure 1.** An example of nullclines for problem (1). The green curve represents cubic function \( v_1 \) and the dashed red line is the graph of the linear function \( v_2 \). The values of the parameters are \( \varepsilon = 0.008, \alpha = 0.139, \beta = 2.54, g_1 = 20, g_2 = 1.5, \) and \( g_3 = -5.5 \).
We can see that the derivative of \( v_1 \) is quadratic in \( u_1 \) while the derivative of \( v_2 \) is constant. We can select a fixed ratio between the lengths of the sides of the rectangle such that the linear \( v_2 \) function passes through the left and right boundary\(^2\). Additionally, we can find a size of the rectangle such that both local extremes of the \( v_1 \) function are located inside the rectangle. Then the part of the graph of \( v_1 \) located outside of the rectangle is always descending or ascending.

We can now enlarge the rectangle until the only intersections of \( v_1 \) and the rectangle are on the upper and lower boundary. This situation has to occur since the ratio of the rectangle is fixed but the value of \( |v'_1| \) grows towards \( +\infty \) for \( u_1 \) going to \( \pm\infty \), which supports the property of the invariant region.

6. Numerical approximation. In this section, we derive the numerical approximation of problem (1)-(3) in domain \( \Omega = (a_x, b_x) \times (a_y, b_y) \) for time \( t \in (0, T) \), where \( a_x < b_x, a_y < b_y \) and \( T > 0 \) by the finite difference method. On \( \Omega_h \), a two-dimensional equidistant numerical mesh

\[
\omega_h = \{(i h_x, j h_y)|i = 1, \ldots, N_x - 1, j = 1, \ldots, N_y - 1\};
\]

\[
\bar{\omega}_h = \{(i h_x, j h_y)|i = 0, \ldots, N_x, j = 0, \ldots, N_y\},
\]

\[
\partial \omega_h = \bar{\omega}_h \setminus \omega_h,
\]

is used for the spatial discretization, where \( N_x, N_y \in \mathbb{N} \) are the numbers of meshes in \( x \) and \( y \) direction, respectively, and \( h_x = \frac{b_x - a_x}{N_x} \) and \( h_y = \frac{b_y - a_y}{N_y} \) are the mesh sizes. The coordinates of the \((i, j)\)-th point can be obtained as \( x_i = a_x + i h_x \) and \( y_j = a_y + j h_y \). For the discretization in time, we use a time step \( \tau > 0 \) and the initial time level \( t_0 = 0 \). The \( k \)-th level is then the \( t_k = k \tau \).

For the discretization of problem (1)-(3) the finite difference method (FDM) was selected due to its suitability for solving the reaction-diffusion equations. As shown in [11], [16] and [20] the FDM performs better than e.g. the general Galerkin method or the finite-element method in its standard form. A comparison of such methods is presented in [16].

For the spatial coordinates \( x_i = a_x + i h_x, y_j = a_y + j h_y \) and time level \( t_k = k \tau \) we denote the corresponding values of \( u_1, u_2, D_1 \) and \( D_2 \) as

\[
u_1(t_k, x_i, y_j) = u^{k}_{1,1,i,j}, \quad u_2(t_k, x_i, y_j) = u^{k}_{2,1,i,j}
\]

and

\[
D_1(t_k, x_i, y_j) = D^{k}_{1,1,i,j}, \quad D_2(t_k, x_i, y_j) = D^{k}_{2,1,i,j}.
\]

Using the finite differences in problem (1)-(3) we obtain the explicit scheme:

\[
\frac{u^{k+1}_{1,1,i,j} - u^{k}_{1,1,i,j}}{\tau} = \frac{1}{h_x^2}(D^{k}_{1,1,i+1,j}(u^{k}_{1,1,i+1,j} - u^{k}_{1,1,i,j}) - D^{k}_{1,1,i,j}(u^{k}_{1,1,i,j} - u^{k}_{1,1,i-1,j})),
\]

\[
+ \frac{1}{h_y^2}(D^{k}_{1,1,i+1,j}(u^{k}_{1,1,i+1,j} - u^{k}_{1,1,i,j}) - D^{k}_{1,1,i,j}(u^{k}_{1,1,i,j} - u^{k}_{1,1,i,j-1})) + f_1(u^{k}_{1,1,i,j}, u^{k}_{2,1,i,j}),
\]

\(^2\)This is equivalent to selection of a linear function \( v_3 \) such that it is on the diagonal of the rectangle and its derivative satisfies \( |v'_3| > |v'_2| \).
\[ u_{2,i,j}^{k+1} - u_{2,i,j}^k \frac{1}{\tau} = \frac{1}{h_x^2} (D_{2,i+1,j}^k (u_{2,i+1,j}^k - u_{2,i,j}^k) - D_{2,i,j}^{k-1} (u_{2,i,j}^k - u_{2,i-1,j}^k)) + \frac{1}{h_y^2} (D_{2,i,j+1}^k (u_{2,i,j+1}^k - u_{2,i,j}^k) - D_{2,i,j}^{k-1} (u_{2,i,j}^k - u_{2,i,j-1}^k)) \]
\[ + f(u_{1,i,j}^k, u_{2,i,j}^k) \]
for \( i = 1, \ldots, N_x, j = 1, \ldots, N_y - 1 \) and \( k = 0, 1, \ldots \), with the order of convergence\(^3 \) \( O(\tau) \) and \( O(h_x + h_y) \) in time and space, respectively.

In the case of homogeneous diffusion the explicit scheme can be simplified and has higher order of convergence in space – namely \( O(h_x^2 + h_y^2) \).

The boundary values, that cannot be calculated using scheme (37), are copied from the closest inner node value.

7. Computational examples. In this section we first conduct the quantitative study of used numerical scheme (37) by evaluating the experimental orders of convergence (EOCs, see, e.g., [6]) for different settings. Then we present the qualitative study in the form of several computational examples demonstrating the behaviour of solutions of problem (1)-(3).

Let us denote \( z = (z_1, z_2)^T \) the benchmark solution of problem (1)-(3) and let \( z_h^k = (z_{h,1}^k, z_{h,2}^k)^T \) be the numerical solution of the problem obtained on the mesh \( \omega_h \) with the spatial step \( h = h_x = h_y \) and the time step \( \tau \). Furthermore let us suppose that \( z \) and \( z_h^k \) satisfy
\[ ||z_i - z_h^k|| = K_i h^{\delta_i} \quad \text{for } i = 1, 2, \quad (38) \]
where \( K_i \) and \( \delta_i \) are constant and \( || \cdot || \) is a suitable norm. For the solution on two different meshes \( h_1, h_2 \), and their respective \( \tau_1 \) and \( \tau_2 \), we obtain the following relation
\[ \frac{||z_i - z_{h_1}^{\tau_1}||}{||z_i - z_{h_2}^{\tau_2}||} = \left( \frac{h_1}{h_2} \right)^{\delta_i} \quad \text{for } i = 1, 2, \quad (39) \]
The coefficient \( \delta_i \) for \( i = 1, 2 \) expressed from the above equations is known as the experimental order of convergence.

In the following qualitative computations, we consider \( n \in \mathbb{N} \) different mesh spatial steps \( h_i \), whose lengths decrease with increasing \( i \) for all \( i = 1, 2, \ldots, n \), and appropriate time steps \( \tau_i \). We denote \( M_i = (\omega_i, \tau_i) \). Furthermore, we denote the value of the function \( u \) at node \((p, q)\) at time level \( t_k \), for \( i = 1, \ldots, n, p = 0, \ldots, N_x, q = 0, \ldots, N_y \) and \( k = 0, 1, \ldots \) as \( u(M_i)^k_{p,q} \). Additionally, we compute the solution on a very dense mesh \( M = (\omega_h, \tau) \). Then we select \( m \in \mathbb{N} \) time levels such that for all \( i = 1, \ldots, m \) there exists \( l^i_k \in \mathbb{N} \) satisfying \( t_k = l^i_k \tau_i \) for all \( k = 1, \ldots, m \). At these \( m \) time levels we project solutions of meshes \( M_i \) and \( M \) onto an even denser mesh \( \hat{M}^4 \) using the linear interpolation. We denote these projections \( \hat{M}_i^4 \) and \( \hat{M}^4 \) and the values of \( u \) at node \((p, q)\) at time \( t_k \) as \( u(M_i^4)^{k}_{p,q} \).
and \( u(\hat{M}^k)_{p,q} \). Subsequently, we calculate the following norms\(^5\)

\[
E_{1,i} = \max_{k \in \{1,\ldots,m\}} E_{1,i}^k = \max_{k \in \{1,\ldots,m\}} \sum_{p,q=0}^{\tilde{N}_x,\tilde{N}_y} \left| u(\hat{M}^k)_{p,q} - u(\hat{M}^k)_{p,q} \right|, \tag{40}
\]

\[
E_{2,i} = \max_{k \in \{1,\ldots,m\}} E_{2,i}^k = \max_{k \in \{1,\ldots,m\}} \left( \sum_{p,q=0}^{\tilde{N}_x,\tilde{N}_y} \left| u(\hat{M}^k)_{p,q} - u(\hat{M}^k)_{p,q} \right|^2 \right)^{1/2}, \tag{41}
\]

\[
E_{\infty,i} = \max_{k \in \{1,\ldots,m\}} E_{\infty,i}^k = \max_{k \in \{1,\ldots,m\}} \max_{q=0,\ldots,\tilde{N}_y} \left| \sum_{p=0}^{\tilde{N}_x} u(\hat{M}^k)_{p,q} - u(\hat{M}^k)_{p,q} \right|, \tag{42}
\]

where \( i = 1,\ldots,n \), \( \tilde{N}_x = \frac{b_x - a_x}{h} \) and \( \tilde{N}_y = \frac{b_y - a_y}{h} \) are the numbers of spatial steps in each axis and \( p, q \) go through all nodes onto which the solutions are projected. Finally, the EOC is calculated from the maximal errors on two consecutive meshes as

\[
EOC_{p,i} = \log \left( \frac{E_{p,i}}{E_{p+1,i}} \right), \tag{43}
\]

where \( p = 1, 2, \infty \) and \( i = 1,\ldots,n-1 \).

We have computed several scenarios validating the numerical scheme (37) for the excitation in a heterogeneous medium. The set-up, initial state and boundary conditions are given in Table 3 with \( \Omega_0 = \Omega = (0,1) \times (0,1) \) and with \( \Omega_{obs} \) given by the first row of Table 4. The time span was \( T = 4.75 \) with the internal time step \( \tau_i = h_i^2 \). Number of output time levels for EOC was \( m = 20 \) with the time step between these levels \( \Delta t = 0.25 \). The reference mesh and the mesh for interpolation had spacial step \( h = 1.95 \cdot 10^{-3} \) and \( \tilde{h} = 4.9 \cdot 10^{-4} \), respectively.

The resulting \( L_p \) errors for \( p \in \{1, 2, \infty \} \) and the EOCs can be found in Tables 1 and 2, respectively. We can notice that for the mesh dense enough the EOCs reach the expected value of two given by the order of approximation of the differential operator.

| Mesh | time step \( \tau \) | \( L_1 \) error of \( u \) | \( L_1 \) error of \( v \) | \( L_2 \) error of \( u \) | \( L_2 \) error of \( v \) | \( L_{\infty} \) error of \( u \) | \( L_{\infty} \) error of \( v \) |
|------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 0.0625 | 0.001953 | 0.056240 | 0.161228 | 0.108336 | 0.265209 | 0.363029 | 0.779687 |
| 0.0313 | 0.000488 | 0.021852 | 0.049984 | 0.043336 | 0.094244 | 0.235573 | 0.651494 |
| 0.0156 | 0.000122 | 0.004384 | 0.008584 | 0.008694 | 0.014913 | 0.053264 | 0.107053 |
| 0.0078 | 0.000031 | 0.000884 | 0.001813 | 0.001997 | 0.002953 | 0.013961 | 0.021748 |
| 0.0039 | 0.000008 | 0.000217 | 0.000472 | 0.000505 | 0.000698 | 0.003454 | 0.004255 |

Table 1. Table of the numerical parameters and the maximal \( L_1, L_2 \) and \( L_{\infty} \) errors at 20 time levels for an excitation in a medium with heterogeneous diffusion. Measured against the reference mesh with spatial step \( h = 1.95 \cdot 10^{-3} \).

After the functionality of the numerical scheme has been validated, we present several qualitative examples showing the properties of the solution.

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\(^5\)which we denote \( L_1, L_2 \) and \( L_{\infty} \), respectively
Table 2. Table of the EOC coefficients for an excitation in a medium with the heterogeneous diffusion.

| Mesh | Mesh | EOC u | EOC v | EOC u | EOC v | EOC u | EOC v |
|------|------|-------|-------|-------|-------|-------|-------|
| $h_1$ | $h_2$ | $L_1$ | $L_1$ | $L_2$ | $L_2$ | $L_\infty$ | $L_\infty$ |
| 0.0625 | 0.0313 | 1.363831 | 1.689564 | 1.321875 | 1.492657 | 0.623411 | 0.259143 |
| 0.0313 | 0.0156 | 2.317446 | 2.541744 | 2.317474 | 2.659830 | 2.144942 | 2.605427 |
| 0.0156 | 0.0078 | 2.310130 | 2.243271 | 2.317474 | 2.659830 | 2.144942 | 2.605427 |
| 0.0078 | 0.0039 | 2.026351 | 1.941520 | 1.983479 | 2.080882 | 2.015062 | 2.353652 |

Table 3. The common parameters for all Examples.

| Example | $\Omega_{\text{obs}}$ | $\Omega_0$ |
|---------|-----------------------|-------------|
| 1       | no obstacle           | (0.02, 0.12) $\times$ (0.02, 0.92) |
| 2       | triangle obstacle in orange in Figure 3 | (0.1, 0.3) $\times$ (0.3, 0.5) |
| 3       | triangle obstacle in orange in Figure 4 | (0.1, 0.3) $\times$ (0.3, 0.5) |

Table 4. Table of parameter values in which the Examples differ.

Example 1. In the first example we simulate a functional reentry known in the biomechanical context (see [3]). A functional reentry emerges in excitable media when a signal is spreading through the domain, followed by a second “wave” of cells
MATHEMATICAL MODEL OF SIGNAL PROPAGATION IN EXCITABLE MEDIA

Initial state of the second wave at time $t = 3$

| Initial state | Definition          | Domain | Parameters and Values |
|---------------|---------------------|--------|-----------------------|
| $u_{ini,1}$   | $u_1^0 + \sin\left(\frac{\pi(x-a_x^1)}{b_x^1-a_x^1}\right)\sin\left(\frac{\pi(y-a_y^1)}{b_y^1-a_y^1}\right)$ | $\Omega_2$ | $a_x^1, b_x^1 = (0.3, 0.4) \times (0.4, 0.6)$ |
| $u_{ini,2}$   | $u_2^0$             | $\Omega_2$ |                         |

Table 5. The parameters for the second wave in Example 1 – the functional reentry.

Example 2. In the second example we simulate an anatomical reentry. Similarly as in Example 1 the key property of the reentry is the emergence of a circular motion that excites itself indefinitely. The difference is in the way how the circular wave emerges. Instead of interaction between two waves, the signal interacts with an obstacle. By the obstacle we mean a subdomain of domain $\Omega$ with zero diffusion coefficients. In such a subdomain the signal cannot spread in space and diminishes on its boundary.

If the obstacle is smaller than the signal wave, the signal turns on the boundary of the obstacle, staying perpendicular to it. When the obstacle does not change during the time the wave is passing it, any circular motion cannot emerge since either the wave diminishes on the other side of the obstacle\(^6\) or the wave which was separated into two by the obstacle\(^7\) reconnects again on the other side of the obstacle and continues as a single wave again.

The first way how to let the circular wave emerge by an obstacle is by the removal of the obstacle after the wave starts turning on it. In this example, the obstacle divides the wave into two parts on its tip. These two waves then start to turn on the other two tips of the obstacle. At that time we remove the obstacle from the domain, which frees space for the two waves to turn into. When they collide they stop each other except for a narrow half-circle-shaped wave. This wave than starts excite itself indefinitely. This can be seen in Figure 3. The parameter values can be found in Tables 3 and 4.

Example 3. The last example shows that an anatomical reentry can be achieved not only by a removal of the obstacle, but also by a moving obstacle. The settings for this example are the same as in Example 2, but the triangular obstacle now moves across the domain from the lower boundary to the upper one. This motion is set such that the obstacle reaches the location of the one from Example 2 approximately in the time when the wave reaches the obstacle. The movement is fast enough so that by the time the two separated waves reach the tips of the obstacle and start turning, the obstacle frees space for them to turn into. This induces a circular movement.

\(^6\)if the obstacle is connected to the boundary of the domain  
\(^7\)if the obstacle is not connected to the boundary of the domain
Figure 2. The time evolution of the component $u_1$ of the solution for the set parameter values and the initial conditions for Example 1. Each subfigure represents one selected time level $t$.

Figure 3. The time evolution of the component $u_1$ of the solution for the set parameter values and the initial conditions for Example 2. Each subfigure represents one selected time level $t$. The obstacle is marked in orange in Figures 3a and 3b.
Figure 4. The time evolution of the component $u_1$ of the solution for the set parameter values and the initial conditions for Experiment 3. Each subfigure represents one selected time level $t$. The obstacle is marked in orange.

similar to the one from Example 2. The time evolution of the solution is in Figure 4 and parameter values can again be found in Tables 3 and 4.

8. Conclusions. In this article we presented a spatially heterogeneous reaction-diffusion FitzHugh-Nagumo model of an excitable media. We have verified its basic mathematical properties and presented an example of the invariant region. As a numerical approximation a finite-difference scheme was proposed. The experimental order of convergence was evaluated. Several computational examples of signal wave propagation and emergence of self-inducing waves in heterogeneous media were presented.

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REFERENCES
[1] O. Bernus and E. Vigmond, Asymptotic wave propagation in excitable media, Phys. Rev. E, 92 (2015), 010901.
[2] Y.-Y. Chen, H. Ninomiya and R. Taguchi, Travelling spots in multidimensional excitable media, Journal of Elliptic and Parabolic Equations, 1 (2015), 281–305.
[3] P. Colli Franzone, L. F. Pavarino and S. Scacchi, Mathematical Cardiac Electrophysiology, MS&A. Modeling, Simulation and Applications, 13. Springer, Cham, 2014.
[4] P. Colli-Franzone, V. Gionti, S. Scacchi and C. Storti, Role of infarct scar dimensions, border zone repolarization properties and anisotropy in the origin and maintenance of cardiac reentry, Mathematical Biosciences, 315 (2019), 108–128.
[33] V. S. Zykov, Spiral wave initiation in excitable media, Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences, 376 (2018).

[34] V. S. Zykov, A. S. Mikhailov and S. C. Müller, Wave propagation in excitable media with fast inhibitor diffusion, Lecture Notes in Physics, 532 (2007), 308–325.

[35] V. S. Zykov and E. Bodenschatz, Wave propagation in inhomogeneous excitable media, Annual Review of Condensed Matter Physics, 9 (2018), 435–461.

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