COUPLED BULK-SURFACE FREE BOUNDARY PROBLEMS ARISING FROM A MATHEMATICAL MODEL OF RECEPTOR-LIGAND DYNAMICS

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ABSTRACT. We consider a coupled bulk-surface system of partial differential equations with nonlinear coupling modelling receptor-ligand dynamics. The model arises as a simplification of a mathematical model for the reaction between cell surface resident receptors and ligands present in the extra-cellular medium. We prove the existence and uniqueness of solutions. We also consider a number of biologically relevant asymptotic limits of the model. We prove convergence to limiting problems which take the form of free boundary problems posed on the cell surface. We also report on numerical simulations illustrating convergence to one of the limiting problems as well as the spatio-temporal distributions of the receptors and ligands in a realistic geometry.

1. INTRODUCTION

We start by outlining the mathematical model for receptor-ligand dynamics whose analysis and asymptotic limits will be the main focus of this work. Let Γ be a smooth, compact closed n-dimensional hypersurface contained in a domain $D \subset \mathbb{R}^{n+1}$, $n = 1, 2$. The surface Γ separates the domain D into an interior domain I and an exterior domain Ω. We will denote by $\partial_0\Omega$ the outer boundary of Ω, i.e. the boundary ∂D (c.f., Fig. 1). We will assume that this boundary is Lipschitz. We consider the following problem: Find $u\colon \bar{\Omega} \times [0,T] \to \mathbb{R}^+$ and $w\colon \Gamma \times [0,T] \to \mathbb{R}^+$ such that

$$\delta_\Omega \partial_t u - \Delta u = 0 \quad \text{in } \Omega \tag{1.1a}$$

$$\nabla u \cdot \boldsymbol{\nu} = -\frac{1}{\delta_k} uw \quad \text{on } \Gamma \tag{1.1b}$$

$$u = u_D \text{ or } \nabla u \cdot \boldsymbol{\nu}_\Omega = 0 \quad \text{on } \partial_0\Omega \tag{1.1c}$$

$$\partial_t w - \delta_\Gamma \Delta_\Gamma w = \nabla u \cdot \boldsymbol{\nu} \quad \text{on } \Gamma \tag{1.1d}$$

$$u(\cdot, 0) = u^0(\cdot) \quad \text{in } \Omega \tag{1.1e}$$

$$w(\cdot, 0) = w^0(\cdot) \quad \text{on } \Gamma, \tag{1.1f}$$

where $\delta_\Omega, \delta_\Gamma, \delta_k > 0$ are given model parameters and the initial data are bounded, non-negative functions, i.e., $u^0 \in L^\infty(\Omega)$, $w^0 \in L^\infty(\Gamma)$ and $u^0, w^0 \geq 0$. In the above Δ_Γ denotes the Laplace-Beltrami operator on the surface Γ and Δ the usual Cartesian Laplacian in $\mathbb{R}^{n+1}$. We will use either Dirichlet or Neumann boundary conditions on $\partial_0\Omega$. For the Dirichlet case, we assume that the Dirichlet boundary data u_D is a positive scalar constant. Our analysis remains valid if we consider bounded positive functions for the Dirichlet boundary data, we restrict the discussion to positive scalar boundary data for the sake of simplicity. The restriction to non-negative solutions is made since we are interested in biological problems where u and w represent chemical concentrations and hence are non-negative.

Problem (1.1) may be regarded as a basic model for receptor-ligand dynamics in cell biology, modelling the dynamics of mobile cell surface receptors reacting with a mobile bulk ligand, which is a reduction of the model (2.1) presented in §2.

Receptor-ligand interactions and the associated cascades of activation of signalling molecules, so called signalling cascades, are the primary mechanism by which cells sense and respond to their environment. Such processes therefore constitute a fundamental part of many basic phenomena in cell biology such as proliferation, motility, the maintenance of structure or form, adhesion, cellular signalling, etc. [Bongrand, 1999; Hynes, 1992; Locksley et al., 2001]. Due to the complexity of the biochemistry involved in signalling networks, an integrated approach combining theoretical studies with experimental

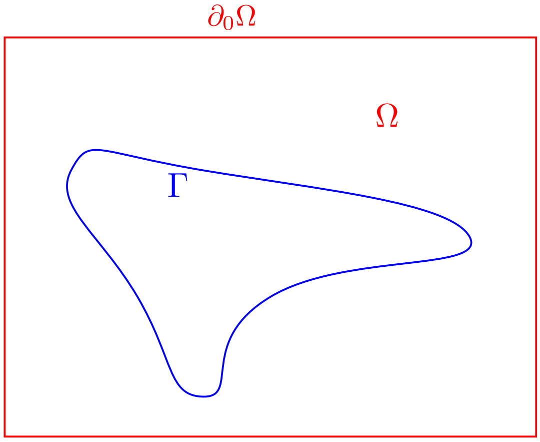


FIGURE 1. A sketch of the cell membrane Γ and the extra-cellular medium Ω.

and modelling efforts appears necessary. Motivated by this need, in this work we focus on understanding a mathematical reduction of theoretical models for receptor-ligand dynamics in cell biology consisting of a coupled system of bulk-surface partial differential equations (PDEs).

A number of recent theoretical and computational studies of receptor-ligand interactions, [e.g., García-Peñarrubia et al., 2013], employ models which are similar in structure to those considered in this work. Models with similar features arise in the modelling of signalling networks coupling the dynamics of ligands within the cell (e.g., G-proteins) with those on the cell surface [Bao et al., 2014; Jilkine et al., 2007; Levine and Rappel, 2005; Madzvamuse et al., 2015; Mori et al., 2008; Rätz and Röger, 2012, 2014]. The ability of cells to create their own chemotactic gradients, i.e., to influence the bulk ligand field, has been conjectured to play a crucial role in collective directed migration for example during neural crest formation [McLennan et al., 2012, 2015a,b] and hence understanding such models is of much biological importance.

Through proving well-posedness results, this work gives a mathematically sound foundation for the use and simulation of coupled bulk-surface models for receptor-ligand dynamics. Moreover, we justify the consideration of various small parameter asymptotic limits of such models, through non-dimensionalisation using experimentally measured parameter values. We provide a rigorous derivation of the limiting problems and discuss their well-posedness. We also discuss the numerical solution of the original and limiting problems illustrating the asymptotic convergence together with robust and efficient methods for their approximation. This work suggests that models for receptor-ligand dynamics featuring fast reaction kinetics can be derived using classical elements of free boundary methodology as components of the modelling.

Whilst our focus is on receptor-ligand dynamics, problems of a similar structure arise in fields such as ecology where one considers populations consisting of two or more competing species [Holmes et al., 1994]. Such a scenario can be modelled by so-called spatial segregation models and the corresponding asymptotic limits have been the subject of much mathematical study, [e.g., Conti et al., 2005; Crooks et al., 2004; Dancer et al., 1999]. Further details on the cell-biological motivation for studying (1.1), together with the limits $\delta_\Omega, \delta_\Gamma, \delta_k \to 0$, is given in §2.

The main focus of this work is to show the system of partial differential equations (1.1) is well posed and so is meaningful from the mathematical perspective. Furthermore, to obtain reduced models as limits of this system as we send the parameters $\delta_\Omega, \delta_\Gamma$ and δ_k to zero. Specifically, we establish existence and uniqueness of a solution to (1.1) and show that in the limits $\delta_k \to 0$, $\delta_\Omega, \delta_\Gamma > 0$ fixed, $\delta_\Gamma = \delta_k \to 0$, $\delta_\Omega > 0$ fixed, $\delta_\Omega = \delta_\Gamma = \delta_k \to 0$, this solution to (1.1) converges to a solution of suitably defined limit problems. Furthermore, in the latter two cases, $\delta_\Gamma = \delta_k \to 0$ and $\delta_\Omega = \delta_\Gamma = \delta_k \to 0$, the uniqueness of the solution to the limit problems, respectively constrained parabolic and elliptic problems with dynamic boundary conditions, is also shown. We then show that the limit problems with dynamic boundary conditions may be reformulated as variational inequalities and briefly explore some connections with classical free boundary problems. These reduced models in the form of free boundary problems may be considered as models in their own right and offer simplifications with respect to numerical computation.

That the fast reaction limit ($\delta_k \to 0$) leads to interesting free boundary problems is because of the complementarity nature of the resulting limit

$$u \geq 0, \qquad w \geq 0, \qquad uw = 0 \qquad \text{on } \Gamma.$$

Such limits have been considered for coupled systems of parabolic equations (posed in the same domain) in a number of previous works [e.g., Bothe, 2001; Bothe and Pierre, 2012; Evans, 1980] with the limiting problem corresponding to a Stefan problem [Hilhorst et al., 1996, 2001, 2003]. Here in this paper the main complication in the analysis is that the species reside in different domains and the coupling is on the boundary of the bulk domain which results in added technical complications in passing to the limit.

For the limit problems $\delta_\Gamma = \delta_k = 0$ and $\delta_\Gamma = \delta_k = \delta_\Omega = 0$ with dynamic boundary conditions, we obtain Stefan and Hele-Shaw type problems on the hypersurface Γ with a differential operator, which may be interpreted as a non-local fractional differential operator, obtained by using the Dirichlet to Neumann map for the bulk parabolic and elliptic operators. This leads to an interesting variational inequality reformulation in the case of the limit bulk elliptic equation consisting of a boundary obstacle problem that is satisfied by the integral in time of the solution. The approach follows that employed for the reformulation of the one-phase Stefan problem and the Hele-Shaw problem for which the transformed variable (integral in time of the solution) satisfies a parabolic [Duvaut, 1973] or elliptic [Elliott, 1980; Elliott and Janovskỳ, 1981] variational inequality respectively.

Problems related to those considered in this work have been the focus of recent studies. For example, Schimperna et al. [2013] consider the well posedness of singular heat equation with dynamic boundary conditions of reactive-diffusive type (i.e., including the Laplace-Beltrami of the trace of the solution on the boundary). Bao et al. [2014] consider a reaction-diffusion equation in a bulk domain coupled to a reaction-diffusion equation posed on the boundary. They prove existence and uniqueness of a weak solution to the problem and establish exponential convergence to equilibrium. Vázquez and Vitillaro [2008, 2009, 2011] study the well posedness of the Laplace and heat equations with dynamic boundary conditions of reactive- and reactive-diffusive type. The heat equation with nonlinear dynamic Neumann boundary conditions which arises in problems of boundary heat control is considered by Athanasopoulos and Caffarelli [2010]. The authors prove continuity of the solution and furthermore, they extend their results to the case where the heat operator in the interior is replaced with a fractional diffusion operator. Existence and uniqueness of weak solutions to Hele-Shaw problems which are Stefan-type free boundary problems with vanishing specific heat are considered by Crowley [1979]. Elliptic equations with non-smooth nonlinear dynamic boundary conditions have been studied in a number of applications. Aitchison et al. [1984] propose a simplified model for an electropaint process that consists of an elliptic equation with nonlinear dynamic boundary conditions involving the normal derivative. The authors formally derive the steady state stationary problem which consists of a Signorini problem similar to the elliptic variational inequality we derive in §9. This problem is studied by Caffarelli and Friedman [1985] where the authors prove that the steady state solution ($t \to \infty$) of an implicit time discretisation solves the Signorini problem proposed as the formal limit by Aitchison et al. [1984]. A similar problem, which models percolation in gently sloping beaches, that consists of an elliptic variational inequality with dynamic boundary conditions involving the normal derivative is proposed and analysed by Aitchison et al. [1983]; Colli and Kenmochi [1987]; Elliott and Friedman [1985]. Perthame et al. [2014] derive Hele-Shaw type free boundary problems as limits of models for tumour growth. Finally we mention the work of Nochetto et al. [2015] who consider the numerical approximation of obstacle problems, in particular, they prove optimal convergence rates for the thin obstacle (Signorini) problem and prove quasi-optimal convergence rates for the approximation of the obstacle problem for the fractional Laplacian.

Our main results are stated in Theorems 4.2, 5.3, 6.3 and 7.3.

- In Theorem 4.2 we establish the existence of a unique, bounded solution to (1.1).
- In Theorem 5.3 we present a rigorous derivation that in the limit $\delta_k \to 0$, $\delta_\Omega, \delta_\Gamma > 0$ fixed, the solution to (1.1) converges to a solution of a system of constrained coupled bulk-surface parabolic equations (c.f., (5.1)).
- In Theorem 6.3 we present a rigorous derivation that in the limit $\delta_\Gamma = \delta_k \to 0$, with $\delta_\Omega > 0$ fixed, the solution to (1.1) converges to the unique solution of constrained parabolic problem with dynamic boundary condition (c.f., (6.1)).
- In Theorem 7.3 we present a rigorous derivation that in the limit $\delta_\Omega = \delta_\Gamma = \delta_k \to 0$, the solution to (1.1) converges to the unique solution of constrained elliptic problem with dynamic boundary condition (c.f., (7.1)).

We conclude the paper by providing some numerical experiments employing a coupled bulk-surface finite element method where we support numerically the theoretical convergence results to a limiting problem and investigate the resulting free boundary problem on a surface.

2. Biological motivation

We now present a model for receptor-ligand dynamics and justify, through non-dimensionalisation of the model using parameter values previously measured in experimental studies, the simplifications and limiting problems considered in this work.

The reaction under consideration is between mobile receptors that reside on the cell surface with ligands present in the extra-cellular medium (the bulk region surrounding the cell). We assume a single species of mobile surface (cell membrane) resident receptor whose concentration (surface density) is denoted by c_r and a single species of bulk resident diffusible ligand whose concentration (bulk concentration) is denoted by c_L. The receptor and ligand react reversibly on the surface to form a (surface resident, mobile) receptor-ligand complex, whose concentration is denoted by c_{rl}. The kinetic constants k_{on} and k_{off} represent the forward and reverse reaction rates. Denoting by Γ the cell surface and by Ω the extra-cellular medium with outer boundary $\partial_0\Omega$ (c.f., Fig. 1), we have in mind models of the following form,

$$\partial_t c_L - D_L \Delta c_L = 0 \qquad \text{in } \Omega \times (0,T] \tag{2.1a}$$

$$D_L \nabla c_L \cdot \boldsymbol{\nu} = -k_{\text{on}} c_L c_r + k_{\text{off}} c_{rl} \qquad \text{on } \Gamma \times (0,T] \tag{2.1b}$$

$$c_L = c_D \text{ or } D_L \nabla c_L \cdot \boldsymbol{\nu}_\Omega = 0 \qquad \text{on } \partial_0\Omega \times (0,T] \tag{2.1c}$$

$$\partial_t c_r - D_r \Delta_\Gamma c_r = -k_{\text{on}} c_L c_r + k_{\text{off}} c_{rl} \qquad \text{on } \Gamma \times (0,T] \tag{2.1d}$$

$$\partial_t c_{rl} - D_{rl} \Delta_\Gamma c_{rl} = k_{\text{on}} c_L c_r - k_{\text{off}} c_{rl} \qquad \text{on } \Gamma \times (0,T]. \tag{2.1e}$$

The model is closed by suitable (bounded, non-negative) initial conditions. For the outer boundary condition we take either a Dirichlet or a Neumann boundary condition. The Dirichlet boundary condition, with $c_D > 0$ a positive constant, arises due under the modelling assumption that the background concentration of ligands sufficiently far away from the cell is uniform. Alternatively, the Neumann boundary condition arises from assuming zero flux across $\partial_0\Omega$.

A number of experimental studies have measure the so called "affinity constant" $k_{\text{on}}/k_{\text{off}}$ with estimates ranging form $10^4 - 10^9$ moles/litre [Bongrand, 1999; Friguet et al., 1985; Glynn and Steward, 1977]. This motivates us, in this primarily theoretical work, to consider a further reduction of (2.1) in which we neglect completely the receptor-ligand complexes and simply consider a system of coupled bulk-surface equations where a single PDE in the bulk for the bulk ligand concentration is coupled to a single PDE on the surface for the surface receptor density with a large reaction rate, i.e., $k_{\text{on}} \gg 1$.

2.1. **Non-dimensionalisation and limit problems.** We are interested in different limit problems arising from model (2.1) for ligand-receptor binding. We neglect the reverse reaction where a ligand-receptor complex separates into its two constituent parts. To simplify notation, we write the unknowns as $u = c_L$ and $w = c_r$ the parameters $D_\Omega = D_L$, $D_\Gamma = D_r$ and $k = k_{\text{on}}$.

The first problem we consider is to find $u\colon \Omega \times [0,T) \to \mathbb{R}$ and $w\colon \Gamma \times [0,T) \to \mathbb{R}$ such that

(2.2a) $$\partial_t u - D_\Omega \Delta u = 0 \qquad \text{in } \Omega \times (0,T)$$

(2.2b) $$D_\Omega \nabla u \cdot \boldsymbol{\nu} = -kuw \qquad \text{on } \Gamma \times (0,T)$$

(2.2c) $$u = u_D \text{ or } D_\Omega \nabla u \cdot \boldsymbol{\nu}_\Omega = 0 \qquad \text{on } \partial_0\Omega \times (0,T)$$

(2.2d) $$\partial_t w - D_\Gamma \Delta_\Gamma w = D_\Omega \nabla u \cdot \boldsymbol{\nu} \qquad \text{on } \Gamma \times (0,T).$$

In order to determine the sizes of each coefficient, we take the following rescaling. We set

$$\tilde{x} = x/L, \quad \tilde{t} = t/S, \quad \tilde{u} = u/U, \quad \tilde{w} = w/W,$$

where L is a length scale, S is a time scale, U is a typical concentration value for u and W is a typical concentration value for w.

Applying the chain rule, this leads to

(2.3a) $$\delta_\Omega \partial_{\tilde{t}} \tilde{u} - \Delta \tilde{u} = 0 \qquad \text{in } \tilde{\Omega} \times (0,\tilde{T})$$

(2.3b) $$\nabla \tilde{u} \cdot \boldsymbol{\nu} = -\frac{1}{\delta_k} \tilde{u}\tilde{w} \qquad \text{on } \tilde{\Gamma} \times (0,\tilde{T})$$

(2.3c) $$\tilde{u} = \tilde{u}_D \text{ or } \nabla \tilde{u} \cdot \boldsymbol{\nu}_{\tilde{\Omega}} = 0 \qquad \text{on } \partial_0\tilde{\Omega} \times (0,\tilde{T})$$

(2.3d) $$\partial_{\tilde{t}} \tilde{w} - \delta_\Gamma \Delta_{\tilde{\Gamma}} \tilde{w} = \mu \nabla \tilde{u} \cdot \boldsymbol{\nu} \qquad \text{on } \tilde{\Gamma} \times (0,\tilde{T}),$$

where we have four non-dimensional coefficients

$$\delta_\Omega = \frac{L^2}{SD_\Omega}, \qquad \delta_k = \frac{D_\Omega}{kWL}, \qquad \delta_\Gamma = \frac{D_\Gamma S}{L^2}, \qquad \mu = \frac{1}{\delta_\Omega}\frac{UL}{W}.$$

We take the following values of these parameters [García-Peñarrubia et al., 2013, and references therein]:

$$\begin{aligned} U &= 10^{-4}\,\mathrm{mol\,m^{-3}} & D_\Omega &= 10^{-12}\,\mathrm{m^2\,s^{-1}} \\ W &= 2.3 \cdot 10^{-9}\,\mathrm{mol\,m^{-2}} & D_\Gamma &= 2 \cdot 10^{-15}\,\mathrm{m^2\,s^{-1}} \\ L &= 7.5 \cdot 10^{-6}\,\mathrm{m} & k &= 10^3\,\mathrm{m^3\,mol^{-1}\,s^{-1}}. \end{aligned}$$

Thus, we infer that

$$\delta_\Omega = \frac{1}{S} 56\,\mathrm{s}, \quad \delta_k = 2.0 \cdot 10^{-2}, \quad \delta_\Gamma = S \cdot 3.6 \cdot 10^{-5}\,\mathrm{s^{-1}}, \quad \mu = S \cdot 5.7 \cdot 10^{-3}\,\mathrm{s^{-1}}.$$

We see that $\delta_k \ll 1$. Reverting to the original variables, we consider the limit problem: Find $u\colon \Omega \times [0,T] \to \mathbb{R}$ and $w\colon \Gamma \times [0,T] \to \mathbb{R}$ such that

(2.4a) $$\partial_t u - \delta_\Omega^{-1} \Delta u = 0 \qquad \text{in } \Omega$$

(2.4b) $$uw = 0 \qquad \text{on } \Gamma$$

(2.4c) $$u = u_D \text{ or } \nabla u \cdot \boldsymbol{\nu}_\Omega = 0 \qquad \text{on } \partial_0\Omega$$

(2.4d) $$\partial_t w - \delta_\Gamma \Delta_\Gamma w = \mu \nabla u \cdot \boldsymbol{\nu} \qquad \text{on } \Gamma,$$

where $\delta_\Omega, \delta_\Gamma$ and μ are positive parameters. We consider this problem as a large ligand–receptor binding rate limit of (2.2). We consider the well posedness of the problem and the justification of the limit in Section 5.

We can consider different problems by choosing different time scales S. We can achieve two different problems by resolving the timescale of the volumetric diffusion ($\delta_\Omega \approx 1$) or the timescale of the surface adsorption flux ($\mu \approx 1$).

For $S = L^2/D_\Omega = 56\,\mathrm{s}$, we have

$$\delta_\Omega = 1, \qquad \delta_\Gamma = 2.0 \cdot 10^{-3} \ll 1, \qquad \mu = 3.2 \cdot 10^{-1} \approx 1.$$

This leads to parabolic limit problem with dynamic boundary condition: Find $u \colon \Omega \times [0,T) \to \mathbb{R}$ and $w \colon \Gamma \times [0,T) \to \mathbb{R}$ such that

$$\partial_t u - \delta_\Omega^{-1} \Delta u = 0 \qquad \text{in } \Omega \tag{2.5a}$$
$$uw = 0 \qquad \text{on } \Gamma \tag{2.5b}$$
$$u = u_D \qquad \text{on } \partial_0\Omega \tag{2.5c}$$
$$\partial_t w = \nabla u \cdot \boldsymbol{\nu} \qquad \text{on } \Gamma, \tag{2.5d}$$

In this case, we have resolved the timescale of the diffusion of ligand, but the effect of the diffusion of surface bound receptor is lost. We consider the well posedness of this problem and the justification of the limit in Section 6.

Alternatively, taking $S = 10^3\,\mathrm{s}$, we have

$$\delta_\Omega = 5.6 \cdot 10^{-2} \ll 1, \qquad \delta_\Gamma = 3.6 \cdot 10^{-2} \ll 1, \qquad \mu = 5.7 \approx 1.$$

This leads to an elliptic problem with dynamic boundary condition: Find $u \colon \Omega \times [0,T) \to \mathbb{R}$ and $w \colon \Gamma \times [0,T) \to \mathbb{R}$ such that

$$-\Delta u = 0 \qquad \text{in } \Omega \tag{2.6a}$$
$$uw = 0 \qquad \text{on } \Gamma \tag{2.6b}$$
$$u = u_D \qquad \text{on } \partial_0\Omega \tag{2.6c}$$
$$\partial_t w = \nabla u \cdot \boldsymbol{\nu} \qquad \text{on } \Gamma. \tag{2.6d}$$

In this regime, we chosen a time scale so that the diffusion of ligand has no memory of its previous value, except via the boundary condition. This means this problem no longer requires an initial condition for u to be a closed system. We do not consider the exterior Neumann boundary condition in this case, since we arrive at a trivial problem where the solution is $u = 0$ and $w = w_0$. The well posedness of this problem and a rigorous justification of limit is given in Section 7. We also show in Section 9 that we can reformulate problems (2.5) and (2.6) by integrating forwards in time to derive variational inequalities.

3. Preliminaries

In this section, we collect some technical results that will be used in the subsequent sections. We also prove some compact embedding results in Lemmas 3.8, 3.9 and 3.10 that are used to deduce strong convergence from weak convergence in suitable spaces.

3.1. Surface fractional Sobolev spaces and trace inequalities.

Along with the surface function spaces $L^2(\Gamma)$ and $H^1(\Gamma)$. We will use the space $H^{1/2}(\Gamma)$ and $H^{-1/2}(\Gamma)$.

Definition 3.2. *The space $H^{1/2}(\Gamma)$ is defined by*

$$H^{1/2}(\Gamma) := \left\{ \xi \in L^2(\Gamma) : \|\xi\|_{H^{1/2}(\Gamma)} < +\infty \right\}, \tag{3.1}$$

where

$$\|\xi\|_{H^{1/2}(\Gamma)} := \left(\int_\Gamma \xi^2 \,\mathrm{d}\sigma + \int_\Gamma \int_\Gamma \frac{|\xi(x) - \xi(y)|^2}{|x-y|^n} \,\mathrm{d}\sigma(x)\,\mathrm{d}\sigma(y) \right)^{\frac{1}{2}}. \tag{3.2}$$

The space can be characterised via the following result.

Proposition 3.3 (Trace Theorem)**.** *The trace operator from $H^1(\Omega)$ to $H^{1/2}(\Gamma)$ is bounded and surjective.*

Proof. The result can be found in [Grisvard, 2011, Thm 1.5.1.3]. □

We recall the following interpolated trace inequality.

Proposition 3.4 (Interpolated trace theorem)**.** *For all $\phi \in H^1(\Omega)$ and for any $\delta > 0$*

$$\|\phi\|^2_{L^2(\Gamma)} \leq \delta \|\nabla\phi\|^2_{L^2(\Omega)} + c_\delta \|\phi\|^2_{L^2(\Omega)}. \tag{3.3}$$

Proof. See e.g. [Grisvard, 2011, Thm 1.5.1.10]. □

We define the space $H^{-1/2}(\Gamma)$ to be the dual space to $H^{1/2}(\Gamma)$. Note that for $\xi, \rho \in L^2(\Gamma)$ the duality pairing is equal to $L^2(\Gamma)$ inner-product:

$$_{H^{-1/2}(\Gamma)}\langle \xi, \rho \rangle_{H^{1/2}(\Gamma)} = \int_\Gamma \xi\rho \ \mathrm{d}\sigma \tag{3.4}$$

3.5. **Compact embeddings.** Since we are dealing with nonlinear problems, we will need to use some compact embeddings of Bochner spaces.

We recall that if $\{f_k\}$ is a sequence of bounded functions in $L^p(0,T;B)$, with B a Banach space, for $1 \leq p < \infty$, then there exists a subsequence $\{f_{k_j}\} \subset \{f_k\}$ and $f \in L^p(0,T;B)$ such that

$$f_{k_j} \rightharpoonup f \qquad \text{in } L^p(0,T;B). \tag{3.5}$$

Here we are interested to show under what conditions we may assert the existence of a strongly convergent subsequence. The basic results we require are summarised by Simon [1986].

Lemma 3.6 (Aubin-Lions-Simons compactness theory)**.** *Let $\{f_k\}$ be a bounded sequence of functions in $L^p(0,T;B)$ where B is a Banach space and $1 \leq p \leq \infty$. If*

(1) the sequence of functions $\{f_k\}$ is bounded in $L^p(0,T;X)$ where X is compactly embedded in B;
(2) either
  (a) the derivatives $\{\partial_t f_k\}$ are bounded in the space $L^p(0,T;Y)$ where $B \subset Y$; or
  (b) for each k, the time translates of $\{f_k\}$ are such that

$$\int_0^{T-\tau} \left\|f_k(t+\tau) - f_k(t)\right\|^p_B \ \mathrm{d}t \to 0 \quad \text{as} \quad \tau \to 0. \tag{3.6}$$

Then there exists a subsequence $\{f_{k_j}\} \subset \{f_k\}$ and $f \in L^p(0,T;X)$ such that

$$\begin{aligned} f_{k_j} &\rightharpoonup f \quad \text{in } L^p(0,T;X) \\ f_{k_j} &\to f \quad \text{in } L^p(0,T;B). \end{aligned} \tag{3.7}$$

Remark 3.7. *Using the criterion 2(a), we see that if $\{\eta_k\} \subset L^2(0,T;L^2(\Omega))$ with a constant $C > 0$ such that*

$$\|\eta_k\|_{L^2(0,T;H^1(\Omega))} + \|\partial_t\eta_k\|_{L^2(0,T;H^{-1}(\Omega))} \leq C \qquad \text{for all } k,$$

then, there exists a subsequence, for which will use the same subscript $\{\eta_k\}$, and $\eta \in L^2(0,T;H^1(\Omega))$ such that

$$\begin{aligned} \eta_k &\rightharpoonup \eta \quad \text{in } L^2(0,T;H^1(\Omega)) \\ \eta_k &\to \eta \quad \text{in } L^2(0,T;L^2(\Omega)). \end{aligned} \tag{3.8}$$

This follows from the compact embedding of $H^1(\Omega)$ in $L^2(\Omega)$.

However, we wish to recover strong convergence of a subsequence with less control over the time derivatives. The generality of criterion 2(b) allows a more general weak in time notion of solution to be used.

We will want to apply this result for sequences to derive strongly convergent subsequences in $L^2(0,T;H^{-1/2}(\Gamma))$.

Lemma 3.8. *Let $\{\xi_k\}$ be a bounded sequence in $H^{1/2}(\Gamma)$. Then there exists a subsequence $\{\xi_{k_j}\} \subset \{\xi_k\}$ and $\xi \in H^{1/2}(\Gamma)$ such that*

$$\begin{aligned} &\xi_{k_j} \rightharpoonup \xi \quad \text{in } H^{1/2}(\Gamma) \\ &\xi_{k_j} \to \xi \quad \text{in } L^2(\Gamma). \end{aligned} \tag{3.9}$$

Proof. For any $\rho \in H^{1/2}(\Gamma)$, we define an extension to Ω, written $E\rho \in H^1(\Omega)$, as the unique solution of:

$$\begin{aligned} -\Delta(E\rho) &= 0 && \text{in } \Omega \\ E\rho &= 0 && \text{on } \partial_0\Omega \\ E\rho &= \rho && \text{on } \Gamma. \end{aligned}$$

We note that for a constant independent of ρ, we have

$$\|E\rho\|_{H^1(\Omega)} \leq c\|\rho\|_{H^{1/2}(\Gamma)} .$$

This implies we have a sequence $\{E\xi_k\}$ which is uniformly bounded in $H^1(\Omega)$: There exists $C_0 > 0$ such that

$$\|E\xi_k\|_{H^1(\Omega)} \leq C_0.$$

From the compact embedding of $H^1(\Omega)$ into $L^2(\Omega)$, we know that there exists a subsequence $\{\xi_{k_j}\} \subset \{\xi_k\}$, and $\eta \in H^1(\Omega)$ such that

$$E\xi_{k_j} \to E\xi \qquad \text{in } L^2(\Omega),$$

where $\xi = \eta|_\Gamma$.

Fix $\varepsilon > 0$ and choose $\delta \leq \varepsilon/(2C_0)$. From the strong convergence of $\{E\xi_{k_j}\}$, we know there exists K such that for $j \geq K$,

$$\left\|E\xi_{k_j} - E\xi\right\|_{L^2(\Omega)} \leq \frac{\varepsilon}{2c_\delta},$$

where c_δ is from Proposition 3.4. It follows that for $j \geq K$, we can infer by applying the interpolated trace inequality (Proposition 3.4), with δ as above, that

$$\begin{aligned} \left\|\xi_{k_j} - \xi\right\|_{L^2(\Gamma)} &\leq \delta\left\|E\xi_{k_j} - E\xi\right\|_{H^1(\Omega)} + c_\delta\left\|E\xi_{k_j} - E\xi\right\|_{L^2(\Omega)} \\ &\leq \delta C_0 + \frac{\varepsilon}{2} \leq \varepsilon. \end{aligned}$$

Thus, we have shown the strong convergence of ξ_k to ξ in $L^2(\Gamma)$. □

Lemma 3.9. *Let $\{\xi_k\}$ be a bounded sequence in $L^2(\Gamma)$. Then there exists a subsequence $\{\xi_{k_j}\} \subset \{\xi_k\}$ and $\xi \in L^2(\Gamma)$ such that*

$$\begin{aligned} &\xi_{k_j} \rightharpoonup \xi \quad \text{in } L^2(\Gamma) \\ &\xi_{k_j} \to \xi \quad \text{in } H^{-1/2}(\Gamma). \end{aligned} \tag{3.10}$$

Proof. Since $\{\xi_k\}$ is uniformly bounded in $L^2(\Gamma)$, we know that is has a subsequence $\{\xi_{k_j}\}$ which weakly converges to some $\xi \in L^2(\Gamma)$. We suppose, for contradiction, that there exists no subsequence of $\{\xi_{k_j}\}$ that strongly converges to ξ in $H^{-1/2}(\Gamma)$. This implies that there exists $\delta > 0$ such that

$$\left\|\xi_{k_j} - \xi\right\|_{H^{-1/2}(\Gamma)} \geq \delta.$$

Using the definition of $H^{-1/2}(\Gamma)$ as the dual space to $H^{1/2}(\Gamma)$, this implies there exists a sequence $\{\rho_j\} \subset H^{1/2}(\Gamma)$, with $\left\|\rho_j\right\|_{H^{1/2}(\Gamma)} = 1$, such that

$${}_{H^{-1/2}(\Gamma)}\langle \xi_{k_j} - \xi, \rho_j \rangle_{H^{1/2}(\Gamma)} = \int_\Gamma (\xi_{k_j} - \xi)\rho_j \, \mathrm{d}\sigma \geq \delta.$$

From Lemma 3.8, we know that a subsequence $\{\rho_{j_l}\} \subset \{\rho_j\}$ converges strongly to $\rho \in H^{1/2}(\Gamma)$ in $L^2(\Gamma)$. Hence, we can infer

$$\int_\Gamma (\xi_{k_j} - \xi)\rho \ \mathrm{d}\sigma \geq \delta.$$

However, this contradicts the supposition that ξ_{k_j} converges weakly to ξ in $L^2(\Gamma)$. □

We conclude this section with a result which is similar in nature to the previous results.

Lemma 3.10. *Let $\{\eta_k\}$ be a bounded sequence in $L^2(0,T;H^1(\Omega))$ and $\eta \in L^2(0,T;H^1(\Omega))$ such that*

$$\eta_k \to \eta \qquad \text{in } L^2(0,T;L^2(\Omega)). \tag{3.11}$$

Then the trace sequence converges to the trace of the limit:

$$\eta_k|_\Gamma \to \eta|_\Gamma \qquad \text{in } L^2(0,T;L^2(\Gamma)). \tag{3.12}$$

Proof. Denote by $C_0 > 0$ the upper bound of $\{\eta_k\}$ and η in $L^2(0,T;H^1(\Omega))$:

$$\|\eta_k\|_{L^2(0,T;H^1(\Omega))} + \|\eta\|_{L^2(0,T;H^1(\Omega))} \leq C_0.$$

Fix $\varepsilon > 0$ and choose $\delta \leq \varepsilon/(2C_0)$. Then from the convergence of $\{\eta_k\}$ in $L^2(0,T;L^2(\Omega))$, there exists K such that for $k \geq K$,

$$\|\eta_k - \eta\|_{L^2(0,T;L^2(\Omega))} \leq \frac{\varepsilon}{2c_\delta},$$

where c_δ is from Proposition 3.4. It follows that for $k \geq K$, we can infer by applying the interpolated trace inequality (Proposition 3.4), with δ as above, that

$$\begin{aligned}\|\eta_k - \eta\|_{L^2(0,T;L^2(\Gamma))} &\leq \delta\|\eta_k - \eta\|_{L^2(0,T;H^1(\Omega))} + c_\delta\|\eta_k - \eta\|_{L^2(0,T;L^2(\Omega))} \\ &\leq \delta C_0 + \frac{\varepsilon}{2} \leq \varepsilon.\end{aligned}$$

Thus, we have shown the strong convergence of η_k to η in $L^2(0,T;L^2(\Gamma))$. □

4. LIGAND-RECEPTOR MODEL

In this section, we establish an existence and uniqueness theory for (1.1). As described in §2.1, (1.1) arises from (2.1) if one neglects the receptor-ligand complexes, non-dimensionalises as in (2.3) and (for simplicity) sets the surface interchange flux $\mu = 1$.

In order to introduce the concept of a weak solution to (1.1), for $\gamma \in \mathbb{R}$, we introduce the Sobolev space

$$H^1_{e_\gamma}(\Omega) := \{v \in H^1(\Omega) | v = \gamma \text{ on } \partial_0\Omega\},$$

where the boundary values are understood in the sense of traces and we adopt the notation, that we maintain throughout the manuscript, of using the same symbol for a function and its trace. We now introduce our concept of a weak solution to (1.1).

Definition 4.1 (Weak solution of (1.1))**.** *For the Dirichlet boundary data case, we say that a pair $(u,w) \in L^2((0,T);H^1_{e_{u_D}}(\Omega)) \times L^2((0,T);H^1(\Gamma))$ with $u, w \geq 0$ and with $(\partial_t u, \partial_t w) \in L^2((0,T);H^{-1}_{e_{u_D}}(\Omega)) \times L^2((0,T);H^{-1}(\Gamma))$ is a weak solution of (1.1) if for all $(\eta,\rho) \in H^1_{e_0}(\Omega) \times H^1(\Gamma)$*

$$\delta_\Omega \int_\Omega \partial_t u \eta \ \mathrm{d}x + \int_\Omega \nabla u \cdot \nabla \eta \ \mathrm{d}x = -\frac{1}{\delta_k}\int_\Gamma uw\eta \ \mathrm{d}\sigma \tag{4.1a}$$

$$\int_\Gamma \partial_t w \rho \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma \nabla_\Gamma w \cdot \nabla_\Gamma \rho \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma uw\rho \ \mathrm{d}\sigma. \tag{4.1b}$$

In the case of Neumann boundary data, we say that a pair $(u,w) \in L^2((0,T);H^1(\Omega))\times L^2((0,T);H^1(\Gamma))$ *with* $u,w \geq 0$ *and with* $(\partial_t u, \partial_t w) \in L^2((0,T),H^{-1}(\Omega)) \times L^2((0,T);H^{-1}(\Gamma))$ *is a weak solution of (1.1) if for all* $(\eta,\rho) \in H^1(\Omega)\times H^1(\Gamma)$

$$\delta_\Omega \int_\Omega \partial_t u \eta \ \mathrm{d}x + \int_\Omega \nabla u \cdot \nabla \eta \ \mathrm{d}x = -\frac{1}{\delta_k}\int_\Gamma uw\eta \ \mathrm{d}\sigma \tag{4.2a}$$

$$\int_\Gamma \partial_t w \rho \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma \nabla_\Gamma w \cdot \nabla_\Gamma \rho \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma uw\rho \ \mathrm{d}\sigma, \tag{4.2b}$$

We note that if $u \in L^2((0,T);H^1(\Omega))$ then by the trace theorem $u \in L^2((0,T);H^{1/2}(\Gamma))$. We now show the well posedness of problem (1.1) in the sense of the following Theorem.

Theorem 4.2 (Existence and uniqueness of a bounded solution pair to (1.1))**.** *Given bounded, positive initial data* u_0 *and* w_0*, there exists a unique solution pair* (u,w) *to (1.1). Furthermore, we have that in the case of Dirichlet data*

$$\begin{aligned} &0 \leq u(x,t) \leq \max(\|u_0\|_{L^\infty(\Omega)}, u_D) && \text{for a.e. } (x,t) \in \Omega\times(0,T) \\ &0 \leq w(x,t) \leq \|w_0\|_{L^\infty(\Gamma)} && \text{for a.e. } (x,t) \in \Gamma\times(0,T), \end{aligned} \tag{4.3}$$

or in the case of Neumann data

$$\begin{aligned} &0 \leq u(x,t) \leq \|u_0\|_{L^\infty(\Omega)} && \text{for a.e. } (x,t) \in \Omega\times(0,T) \\ &0 \leq w(x,t) \leq \|w_0\|_{L^\infty(\Gamma)} && \text{for a.e. } (x,t) \in \Gamma\times(0,T). \end{aligned} \tag{4.4}$$

Proof. In the interests of brevity we give the full details of the proof only in the Dirichlet case. An analogous argument holds for the case of Neumann boundary conditions.

We start by replacing w by $M(w)$ in the nonlinear coupling terms, where $M\colon \mathbb{R}\to\mathbb{R}^+$ is the cut off function

$$M(r) = \begin{cases} 0 & r < 0 \\ r & 0 \leq r \leq M \\ M & r > M, \end{cases} \tag{4.5}$$

with $M \geq \|w_0\|_{L^\infty(\Gamma)}$. This leads us to consider the following problem. Find (u,w), in the same spaces as Definition 4.1, that satisfy for all $(\eta,\rho) \in H^1_{e_0}(\Omega)\times H^1(\Gamma)$

$$\delta_\Omega \int_\Omega \partial_t u \eta \ \mathrm{d}x + \int_\Omega \nabla u \cdot \nabla \eta \ \mathrm{d}x = -\frac{1}{\delta_k}\int_\Gamma uM(w)\eta \ \mathrm{d}\sigma \tag{4.6}$$

$$\int_\Gamma \partial_t w \rho \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma \nabla_\Gamma w \cdot \nabla_\Gamma \rho \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma uM(w)\rho \ \mathrm{d}\sigma. \tag{4.7}$$

As M is bounded, existence for this problem with the cutoff nonlinearity can be shown via a Galerkin method and standard energy arguments. We now show positivity of the solutions to (4.6), (4.7): $u,w \geq 0$ almost everywhere in their domains and that the trace of $u \geq 0$. Testing (4.6) with $u_- = \min(u,0)$ and using the fact that $M(w) \geq 0$, we have

$$\frac{\delta_\Omega}{2}\frac{d}{dt}\int_\Omega (u_-)^2 \ \mathrm{d}x + \int_\Omega |\nabla(u_-)|^2 \ \mathrm{d}x = -\frac{1}{\delta_k}\int_\Gamma (u_-)^2 M(w) \ \mathrm{d}\sigma \leq 0.$$

Since $u_0 \geq 0$, we have $u \geq 0$ almost everywhere in $\Omega\times(0,T)$. Moreover, by the trace inequality we have that the trace of u is positive. We next test (4.7) with $w_- = \min(w,0)$ to get

$$\frac{1}{2}\frac{d}{dt}\int_\Gamma (w_-)^2 \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma |\nabla_\Gamma(w_-)|^2 \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma uM(w)w_- \ \mathrm{d}\sigma = 0,$$

as $M(w)w_- = 0$ from the definition of $M(\cdot)$ (4.5). Since $w_0 \geq 0$, we see that $w \geq 0$ almost everywhere in $\Gamma \times (0,T)$. We now show the pointwise bounds of Theorem 4.2. Let (u,w) be solutions of (4.6) and (4.7) and set $\theta^w = (w - \|w_0\|_{L^\infty(\Gamma)})$. The variable θ^w satisfies

$$\int_\Gamma \partial_t \theta^w \rho \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma \nabla_\Gamma \theta^w \cdot \nabla_\Gamma \rho \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma uw\rho \ \mathrm{d}\sigma.$$

We test with $\rho = (\theta^w)_+ \geq 0$ and recall that $u, w \geq 0$ then

$$\frac{1}{2}\frac{d}{dt}\int_\Gamma (\theta^w_+)^2 \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma |\nabla \theta^w_+|^2 \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma uw\theta^w_+ \ \mathrm{d}\sigma \leq 0.$$

This implies that $\theta^w_+ = 0$ and hence $w \leq \|w_0\|_{L^\infty(\Gamma)}$. The same argument for u with $\theta^u = (u - \max(u_D, \|u\|_{L^\infty(\Omega)})$ so that $\theta^u_+ \in H^1_{e_0}$, gives $u \leq \max(u_D, \|u\|_{L^\infty(\Omega)})$. As M was chosen such that $M \geq \|w_0\|_{L^\infty(\Gamma)}$ and $w \geq 0$, we have that $M(w) = w$, hence we have constructed a solution to (4.1) which satisfies

$$0 \leq u \leq \max(\|u_0\|_\infty, u_D) \quad \text{and } 0 \leq w \leq \|w_0\|_\infty. \tag{4.8}$$

It remains to show that the solution is unique. To do this, we argue as follows. Let (u_1, w_1) and (u_2, w_2) be two (weak) solutions of (1.1). Defining $e^u := u_1 - u_2$ and $e^w := w_1 - w_2$ we have that e^u, e^w satisfy for all $(\eta, \rho) \in H^1_{e_0}(\Omega) \times H^1(\Gamma)$

$$\int_\Omega \delta_\Omega \partial_t e^u \eta \mathrm{d}x + \int_\Omega \nabla e^u \cdot \nabla \eta \ \mathrm{d}x = -\frac{1}{\delta_k}\int_\Gamma (u_1w_1 - u_2w_2)\eta \ \mathrm{d}\sigma \tag{4.9a}$$

$$\int_\Gamma \partial_t e^w \rho \ \mathrm{d}\sigma + \int_\Gamma \delta_\Gamma \nabla_\Gamma e^w \cdot \nabla_\Gamma \rho \ \mathrm{d}\sigma = -\frac{1}{\delta_k}\int_\Gamma (u_1w_1 - u_2w_2)\rho \ \mathrm{d}\sigma \tag{4.9b}$$

Let $\beta : \mathbb{R} \to \mathbb{R}$ be a smooth convex function satisfying $\beta(0) = \beta'(0) = 0$. Setting $\eta = \beta'(e^u)$ and $\rho = \beta'(e^w)$ in (4.9) and combining the equations gives

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\left(\int_\Omega \delta_\Omega \beta(e^u) \ \mathrm{d}x + \int_\Gamma \beta(e^w) \ \mathrm{d}\sigma\right) + \int_\Omega \beta''(e^u)\left|\nabla e^u\right|^2 \ \mathrm{d}x + \int_\Gamma \delta_\Gamma \beta''(e^w)\left|\nabla_\Gamma e^w\right|^2 \ \mathrm{d}\sigma \\ = -\frac{1}{\delta_k}\int_\Gamma (u_1w_1 - u_2w_2)\left(\beta'(e^u) + \beta'(e^w)\right) \ \mathrm{d}\sigma.\end{aligned} \tag{4.10}$$

Hence as β is convex we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\int_\Omega \delta_\Omega \beta(e^u) \ \mathrm{d}x + \int_\Gamma \beta(e^w) \ \mathrm{d}\sigma\right) \leq -\frac{1}{\delta_k}\int_\Gamma (u_1w_1 - u_2w_2)\left(\beta'(e^u) + \beta'(e^w)\right) \ \mathrm{d}\sigma. \tag{4.11}$$

Integration in time gives

$$\int_\Omega \delta_\Omega \beta(e^u(\cdot,t)) \ \mathrm{d}x + \int_\Gamma \beta(e^w(\cdot,t)) \ \mathrm{d}\sigma \leq -\frac{1}{\delta_k}\int_0^t \int_\Gamma (u_1w_1 - u_2w_2)\left(\beta'(e^u) + \beta'(e^w)\right) \ \mathrm{d}\sigma \ \mathrm{d}t, \tag{4.12}$$

as $e^u(\cdot, 0) = 0$ and $e^w(\cdot, 0) = 0$ and we have chosen β such that $\beta(0) = 0$. Next we replace β by a sequence β_n such that

$$\beta_n(x) \to |x|, \quad \beta_n'(x) \to \mathrm{sgn}(x), \quad x \in \mathbb{R},$$

and pass to the limit, which yields

$$\int_\Omega \delta_\Omega \left|e^u(\cdot,t)\right| \ \mathrm{d}x + \int_\Gamma \left|e^w(\cdot,t)\right| \ \mathrm{d}\sigma \leq -\frac{1}{\delta_k}\int_0^t \int_\Gamma (u_1w_1 - u_2w_2)\left(\mathrm{sgn}(e^u) + \mathrm{sgn}(e^w)\right) \ \mathrm{d}\sigma \ \mathrm{d}t. \tag{4.13}$$

We now show that the right hand side of (4.13) is non-positive. The result is trivial if e^u and e^w have different signs since then $\operatorname{sgn}(e^u) + \operatorname{sgn}(e^w) = 0$. As

$$-\frac{1}{\delta_k}(u_1 w_1 - u_2 w_2)\left(\operatorname{sgn}(e^u) + \operatorname{sgn}(e^w)\right) = -\frac{1}{\delta_k}(u_1 e^w + w_2 e^u)\left(\operatorname{sgn}(e^u) + \operatorname{sgn}(e^w)\right),$$

we have that if $e^u = 0$

$$-\frac{1}{\delta_k}(u_1 w_1 - u_2 w_2)\left(\operatorname{sgn}(e^u) + \operatorname{sgn}(e^w)\right) = -\frac{1}{\delta_k} u_1 \left|e^w\right| \le 0$$

as we have assumed positivity of the solutions. A similar argument applies if $e^w = 0$. If $e^u, e^w > 0$ we have

$$-\frac{1}{\delta_k}(u_1 w_1 - u_2 w_2)\left(\operatorname{sgn}(e^u) + \operatorname{sgn}(e^w)\right) = -\frac{2}{\delta_k}(u_1 e^w + w_2 e^u) \le 0$$

once again due to the assumption of positivity of the solutions. If $e^u, e^w < 0$ we have

$$-\frac{1}{\delta_k}(u_1 w_1 - u_2 w_2)\left(\operatorname{sgn}(e^u) + \operatorname{sgn}(e^w)\right) = \frac{2}{\delta_k}(u_1 e^w + w_2 e^u) \le 0$$

due to the positivity of solutions to (1.1). Hence the right hand side of (4.13) is negative. Thus

$$\sup_{t \in [0,T]} \left(\int_\Omega \delta_\Omega \left|e^u\right| \,\mathrm{d}x + \int_\Gamma \left|e^w\right| \,\mathrm{d}\sigma \right) = 0,$$

which completes the proof of uniqueness and hence the proof of the theorem. □

In the subsequent sections we will consider the limit problems obtained on sending $\delta_\Omega, \delta_\Gamma$ and δ_k to zero in (1.1). To this end we derive some estimates on the solution pair (u, w) of (1.1), which we will use in the subsequent sections to deduce the existence of convergent subsequences which converge to solutions of the limit problems. We note that the bounds hold for constants which are independent of δ_k, δ_Γ and δ_Ω.

Lemma 4.3 (Estimates for the solution of (1.1))**.** *The solution pair (u, w) to (1.1) satisfy the following estimates,*

$$\begin{aligned} \delta_\Omega \|u\|^2_{L^\infty((0,T);L^2(\Omega))} + \|\nabla u\|^2_{L^2((0,T);L^2(\Omega))} &\le \delta_\Omega \int_\Omega u_0^2 \,\mathrm{d}x + C_D \\ \|w\|^2_{L^\infty((0,T);L^2(\Gamma))} + \delta_\Gamma \|\nabla_\Gamma w\|^2_{L^2((0,T);L^2(\Gamma))} &\le \int_\Gamma w_0^2 \,\mathrm{d}\sigma, \end{aligned} \tag{4.14}$$

where $C_D \in \mathbb{R}^+$ depends only on the Dirichlet boundary data u_D and $C_D = 0$ in the case of Neumann boundary data. Furthermore, we have an estimate on the nonlinearity:

$$\frac{1}{\delta_k} \|uw\|_{L^1((0,T)\times(\Gamma))} \le \|w_0\|_{L^1(\Gamma)}. \tag{4.15}$$

The following estimate on time translates of u and w along with Lemma 3.6 will be used to deduce the necessary compactness

(4.16)
$$\delta_\Omega \int_0^{T-\tau} \int_\Omega \left(u(\cdot, t+\tau) - u(\cdot, t)\right)^2 \,\mathrm{d}x \,\mathrm{d}t + \int_0^{T-\tau} \int_\Gamma \left(w(\cdot, t+\tau) - w(\cdot, t)\right)^2 \,\mathrm{d}\sigma \,\mathrm{d}t \le C\tau,$$

where the constant C is independent of $\tau, \delta_\Omega, \delta_\Gamma$ and δ_k.

Proof. The first estimate (4.14) follows from a straightforward energy argument due to the non negativity of u and w. Specifically, test with $(u - \mathbb{D}u, w)$ where $\mathbb{D}u$ satisfies $\Delta \mathbb{D}u = 0$ in Ω, $\mathbb{D}u = 0$ on Γ and $\mathbb{D}u = u_D$ on $\partial_0\Omega$ in the Dirichlet case (4.1) or simply with (u, w) in the Neumann case (4.2).

For the estimate (4.15) we have using the positivity of u, w

$$\begin{aligned}\frac{1}{\delta_k}\|uw\|_{L^1((0,T)\times(\Gamma))} &= \frac{1}{\delta_k}\int_0^T\int_\Gamma wu \; \mathrm{d}\sigma \; \mathrm{d}t\\ &= \int_0^T\int_\Gamma -\partial_t w \; \mathrm{d}\sigma \; \mathrm{d}t\\ &= \int_\Gamma -w(\cdot,T)+w^0(\cdot) \; \mathrm{d}\sigma\\ &\le \left\|w^0\right\|_{L^1(\Gamma)},\end{aligned}$$

where we have used the positivity of w and the bound (4.8) in the last step.

For the estimate (4.16) we argue as follows. For a fixed $\tau \in (0,T)$ and for $t \in [0, T-\tau]$ introducing the notation $\bar{\partial}_\tau f(t) := f(t+\tau) - f(t)$ we have using (4.1)

$$\begin{aligned}&\int_\Gamma \big(w(\cdot,t+\tau)-w(\cdot,t)\big)^2 \; \mathrm{d}\sigma = \int_0^\tau\int_\Gamma \partial_t w(\cdot,t+s)\bar{\partial}_\tau w(\cdot,t) \; \mathrm{d}\sigma \; \mathrm{d}s\\ &\quad = \int_0^\tau\int_\Gamma -\delta_\Gamma\nabla_\Gamma w(\cdot,t+s)\cdot\nabla_\Gamma\bar{\partial}_\tau w(\cdot,t) - \frac{1}{\delta_k}[uw](\cdot,t+s)\bar{\partial}_\tau w(\cdot,t) \; \mathrm{d}\sigma \; \mathrm{d}s.\end{aligned}$$

Integrating in time gives

$$\begin{aligned}&\int_0^{T-\tau}\int_\Gamma \big(w(\cdot,t+\tau)-w(\cdot,t)\big)^2 \; \mathrm{d}\sigma \; \mathrm{d}t \qquad (4.17)\\ &= \int_0^\tau\int_0^{T-\tau}\int_\Gamma -\delta_\Gamma\nabla_\Gamma w(\cdot,t+s)\cdot\nabla_\Gamma\bar{\partial}_\tau w(\cdot,t) - \frac{1}{\delta_k}[uw](\cdot,t+s)\bar{\partial}_\tau w(\cdot,t) \; \mathrm{d}\sigma \; \mathrm{d}t \; \mathrm{d}s\\ &\le \int_0^\tau \frac{3}{2}\delta_\Gamma\|\nabla_\Gamma w\|^2_{L^2((0,T)\times(\Gamma))} + \left\|\bar{\partial}_\tau w\right\|_{L^\infty((0,T)\times(\Gamma))}\frac{1}{\delta_k}\|uw\|_{L^1((0,T)\times(\Gamma))} \; \mathrm{d}s,\end{aligned}$$

where we have used Young's inequality in the last step. Applying the estimates (4.8), (4.14) and (4.15) in (4.17) yields the desired estimate for the second term in (4.16). For the bound on the first term in (4.16), we note that as $\bar{\partial}_\tau u \in H^1_{e_0}(\Omega)$

$$\begin{aligned}&\delta_\Omega\int_\Omega \bar{\partial}_\tau u(\cdot,t)^2 \; \mathrm{d}x\\ &\qquad = \int_0^\tau\int_\Omega -\nabla u(\cdot,t+s)\cdot\nabla\bar{\partial}_\tau u(\cdot,t) - \frac{1}{\delta_k}[uw](\cdot,t+s)\bar{\partial}_\tau u(\cdot,t) \; \mathrm{d}\sigma \; \mathrm{d}s,\end{aligned}$$

from which the desired bound follows from an analogous calculation to (4.17) together with the estimates (4.8), (4.14) and (4.15). □

5. Fast reaction limit problem ($\delta_k = 0$)

We now show that for fixed $\delta_\Omega, \delta_\Gamma > 0$ as $\delta_k \to 0$ the solution to (1.1) converges to a (weak) solution to the following constrained parabolic limit problem. For convenience we work with $v = -w$ and set $v^0 = -w^0$.

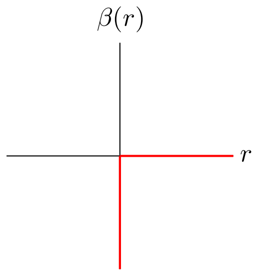


FIGURE 2. Sketch of the function β c.f., (5.2)

Problem 5.1 (Problem for instantaneous reaction rate)**.** *Find* $\bar{u}\colon \Omega \times (0,T) \to \mathbb{R}^+$, $\bar{v}\colon \Gamma \times (0,T) \to \mathbb{R}^-$ *such that*

$$\delta_\Omega \partial_t \bar{u} - \Delta \bar{u} = 0 \qquad \text{in } \Omega \times (0,T) \tag{5.1a}$$

$$\nabla \bar{u} \cdot \boldsymbol{\nu} + \partial_t \bar{v} - \delta_\Gamma \Delta_\Gamma \bar{v} = 0 \quad \text{and} \quad \bar{v} \in \beta(\bar{u}) \qquad \text{on } \Gamma \times (0,T) \tag{5.1b}$$

$$\bar{u} = u_D \quad \text{or} \quad \nabla \bar{u} \cdot \boldsymbol{\nu}_\Omega = 0 \qquad \text{on } \partial_0 \Omega \times (0,T) \tag{5.1c}$$

$$\bar{u}(\cdot,0) = u^0(\cdot) \geq 0 \qquad \text{in } \Omega \tag{5.1d}$$

$$\bar{v}(\cdot,0) = v^0(\cdot) \leq 0 \qquad \text{on } \Gamma. \tag{5.1e}$$

Here $\beta\colon \mathbb{R} \to \{0,1\}^{\mathbb{R}}$ *is the set valued function (c.f., Figure 2)*

$$\beta(r) = \begin{cases} \emptyset & \text{if } r < 0 \\ [-\infty, 0] & \text{if } r = 0 \\ \{0\} & \text{if } r > 0. \end{cases} \tag{5.2}$$

We consider (5.1) as a parabolic equation with dynamic boundary conditions interpreted a differential inclusion.

In order to define a weak solution to (5.1) we define the Sobolev space

$$\mathcal{V}_{e_0}(\Omega,\Gamma) := \Big\{ v \in H^1_{e_0}(\Omega \times (0,T)) : v \in H^1(\Gamma \times (0,T)) \Big\}.$$

Definition 5.2 (Weak solution of Problem 5.1)**.** *We say that a pair* $(\bar{u},\bar{v})$ *with* $u \in L^2((0,T);H^1_{e_{u_D}}(\Omega)) \cap L^\infty((0,T);L^2(\Omega))$ *and* $\bar{v} \in L^2((0,T);H^1(\Gamma)) \cap L^\infty((0,T);L^2(\Gamma))$ *is a weak solution of Problem 5.1 if for all* $\eta \in \mathcal{V}_{e_0}(\Omega,\Gamma)$ *with* $\eta(\cdot,T) = 0$*, we have*

$$\int_0^T \left(\int_\Omega -\delta_\Omega \bar{u} \partial_t \eta + \nabla \bar{u} \cdot \nabla \eta \,\,\mathrm{d}x + \int_\Gamma -\bar{v} \partial_t \eta + \delta_\Gamma \nabla_\Gamma \bar{v} \cdot \nabla_\Gamma \eta \,\,\mathrm{d}\sigma \right) \,\mathrm{d}t = \int_\Omega \delta_\Omega u^0 \eta(\cdot,0) \,\,\mathrm{d}x + \int_\Gamma v^0 \eta(\cdot,0) \,\,\mathrm{d}\sigma \tag{5.3}$$

and

$$\bar{v} \in \beta(\bar{u}) \quad \text{a.e. on } \Gamma \times (0,T]. \tag{5.4}$$

We make the corresponding modifications to the function spaces for the Neumann boundary condition.

Theorem 5.3 (Convergence of the solution of (1.1) to a solution of (5.1))**.** *As $\delta_k \to 0$ the solution pair (u, w) to (1.1) converge (up to a subsequence) to a pair $(\bar{u}, \bar{w})$ in the following topologies*

$$u \rightharpoonup \bar{u} \quad \text{in } L^2(0,T; H^1_{e_{u_D}}(\Omega)) \tag{5.5}$$

$$(u \rightharpoonup \bar{u} \quad \text{in } L^2(0,T; H^1(\Omega)), \quad \text{in the Neumann case})$$

$$w \rightharpoonup \bar{w} \quad \text{in } L^2(0,T; H^1(\Gamma)), \tag{5.6}$$

$$u \to \bar{u} \quad \text{in } L^2(\Omega \times (0,T]), \tag{5.7}$$

$$w \to \bar{w} \quad \text{in } L^2(\Gamma \times (0,T]). \tag{5.8}$$

Moreover, the pair $(\bar{u}, \bar{v})$, with $\bar{v} = -\bar{w}$ are a weak solution to Problem 5.1.

Proof. In the interests of brevity we give the details for the Dirichlet boundary condition case. The Neumann case is handled similarly. From standard weak compactness arguments (3.5) together with the estimate (4.14), we can extract a subsequence which we will still denote (u, w) such that

$$u \rightharpoonup \bar{u} \quad \text{in } L^2(0,T; H^1_{e_{u_D}}(\Omega)),$$
$$w \rightharpoonup \bar{w} \quad \text{in } L^2(0,T; H^1(\Gamma)).$$

From the Aubin-Lions-Simon compactness theory (Lemma 3.6), the estimate on time translates (4.16) means we can extract a subsequence which we will still denote (u, w) such that

$$u \to \bar{u} \quad \text{in } L^2(\Omega \times (0,T]),$$
$$w \to \bar{w} \quad \text{in } L^2(\Gamma \times (0,T]).$$

We now show the pair $(\bar{u}, \bar{v})$, with $\bar{v} = -\bar{w}$, are a weak solution to Problem 5.1. We start by noting that for all $\eta \in C^\infty(\Omega \times (0,T))$ with $\eta = 0$ on $\partial_0\Omega \times (0,T)$ and $\eta(\cdot, T) = 0$, we have

$$\int_0^T \int_\Omega -\delta_\Omega u \partial_t \eta + \nabla u \cdot \nabla \eta \ \mathrm{d}x \ \mathrm{d}t - \int_\Omega u^0 \eta(\cdot, 0) \ \mathrm{d}x$$
$$= \int_0^T \int_\Gamma \boldsymbol{\nu} \cdot \nabla u \eta \ \mathrm{d}\sigma \ \mathrm{d}t = \int_0^T \int_\Gamma -\frac{1}{\delta_k} u w \eta \ \mathrm{d}\sigma \ \mathrm{d}t$$
$$= \int_0^T \int_\Gamma -w \partial_t \eta + \delta_\Gamma \nabla_\Gamma w \cdot \nabla_\Gamma \eta \ \mathrm{d}\sigma \ \mathrm{d}t - \int_\Gamma w^0 \eta(\cdot, 0) \ \mathrm{d}\sigma.$$

Letting $\delta_k \to 0$ the convergence results (5.5)—(5.8) give

$$\int_0^T \left(\delta_\Omega \int_\Omega -\bar{u} \partial_t \eta \ \mathrm{d}x + \int_\Omega \nabla \bar{u} \cdot \nabla \eta \ \mathrm{d}x \right) \mathrm{d}t - \int_\Omega u^0 \eta(\cdot, 0) \ \mathrm{d}x$$
$$= \int_0^T \left(\int_\Gamma -\bar{w} \partial_t \eta \ \mathrm{d}\sigma + \delta_\Gamma \int_\Gamma \nabla_\Gamma \bar{w} \cdot \nabla_\Gamma \eta \ \mathrm{d}\sigma \right) \mathrm{d}t - \int_\Gamma w^0 \eta(\cdot, 0) \ \mathrm{d}\sigma,$$

and hence with $\bar{v} = -\bar{w}$

$$\int_0^T \left(\int_\Omega -\delta_\Omega \bar{u} \partial_t \eta + \nabla \bar{u} \cdot \nabla \eta \ \mathrm{d}x + \int_\Gamma -\bar{v} \partial_t \eta + \delta_\Gamma \nabla_\Gamma \bar{v} \cdot \nabla_\Gamma \eta \ \mathrm{d}\sigma \right) \mathrm{d}t = \int_\Omega u^0 \eta(\cdot, 0) \ \mathrm{d}x + \int_\Gamma v^0 \eta(\cdot, 0) \ \mathrm{d}\sigma. \tag{5.9}$$

A density argument yields that the above holds for all $\eta \in \mathcal{V}_{e_0}(\Omega, \Gamma)$.

It remains to show that $\bar v \in \beta(\bar u)$. As $u, w \geq 0$ for all δ_k, we have $\bar u \geq 0$ and $\bar v = -\bar w \leq 0$. Moreover from (4.15) we have

$$\int_0^T \int_\Gamma uw \leq \delta_k \left\| w_0 \right\|_{L^1(\Gamma)},$$

and hence the strong convergence results (5.7) and (5.8) imply

$$\bar u \bar v = -\bar u \bar w = 0 \quad \text{a.e. in } \Gamma \times (0,T].$$

Thus the limit pair $(\bar u, \bar v)$ are a weak solution to Problem 5.1 in the sense of Definition 5.2. □

6. Parabolic limit problem with dynamic boundary condition ($\delta_k = \delta_\Gamma = 0$)

We now present a rigorous derivation of the parabolic problem with dynamic boundary conditions presented in §2.1 as a limit of (1.1). Specifically we show that for fixed $\delta_\Omega > 0$, in the limit $\delta_k = \delta_\Gamma \to 0$ the unique solution of the problem (1.1) converges to the unique solution of the following problem.

Problem 6.1. *Find $\tilde u \colon \Omega \times (0,T) \to \mathbb{R}^+$ and $\tilde v \colon \Gamma \times (0,T) \to \mathbb{R}^-$ such that*

(6.1a) $\delta_\Omega \partial_t \tilde u - \Delta \tilde u = 0$ *in* $\Omega \times (0,T)$

(6.1b) $\nabla \tilde u \cdot \boldsymbol{\nu} + \partial_t \tilde v = 0$ *on* $\Gamma \times (0,T)$

(6.1c) $\tilde v \in \beta(\tilde u)$ *on* $\Gamma \times (0,T)$

(6.1d) $\tilde u = u_D$ *or* $\nabla \tilde u \cdot \boldsymbol{\nu} = 0$ *on* $\partial_0 \Omega \times (0,T)$

(6.1e) $\tilde u(\cdot, 0) = u_0(\cdot) \geq 0$ *on* Ω

(6.1f) $\tilde v(\cdot, 0) = v_0(\cdot) \leq 0$ *on* Γ,

where $\beta \colon \mathbb{R} \to \{0,1\}^{\mathbb{R}}$ is the set valued function defined in (5.2).

Definition 6.2 (Weak solution of (6.1))**.** *We say a function pair $(\tilde u, \tilde v)$ with $\tilde u \in L^2(0,T; H^1_{e_{u_D}}(\Omega)) \cap L^\infty((0,T); L^2(\Omega))$ and $\tilde v \in L^\infty(0,T; L^2(\Gamma))$ is a weak solution of* (6.1)*, if for all $\eta \in L^2\left((0,T); H^1_{e_0}(\Omega)\right)$ with $\partial_t \eta \in L^2\left((0,T) \times \Omega\right) \cap L^2\left((0,T) \times \Gamma\right)$ with $\eta(\cdot, T) = 0$, we have*

(6.2)
$$\int_0^T \left(\int_\Omega -\delta_\Omega \tilde u \partial_t \eta + \nabla \tilde u \cdot \nabla \eta \, \mathrm{d}x + \int_\Gamma -\tilde v \partial_t \eta \, \mathrm{d}\sigma \right) \mathrm{d}t = \int_\Omega u^0 \eta(\cdot, 0) \, \mathrm{d}x + \int_\Gamma v^0 \eta(\cdot, 0) \, \mathrm{d}\sigma$$

and $\tilde v \in \beta(\tilde u)$ *a.e. in* $\Gamma \times (0,T)$.

We make the obvious modifications for the Neumann case.

Theorem 6.3 (Convergence of the solution of (1.1) to a solution of (6.1))**.** *As $\delta_k = \delta_\Gamma \to 0$ the solution pair (u, w) to (1.1) converge to a pair $(\tilde u, \tilde w)$ in the following topologies*

(6.3) $u \rightharpoonup \tilde u$ *in* $L^2(0,T; H^1_{e_{u_D}}(\Omega))$

($u \rightharpoonup \tilde u$ *in* $L^2(0,T; H^1(\Omega))$ *in the Neumann case*)

(6.4) $w \rightharpoonup \tilde w$ *in* $L^2(0,T; L^2(\Gamma))$,

(6.5) $u \to \tilde u$ *in* $L^2(\Omega \times (0,T])$,

(6.6) $u|_\Gamma \to \tilde u|_\Gamma$ *in* $L^2(\Gamma \times (0,T])$.

Moreover, the pair $\tilde u, \tilde v$, with $\tilde v = -\tilde w$ are the unique weak solution to (6.1) *in the sense of Definition (6.2). The fact that the full sequence and not a subsequence converges is a consequence of the uniqueness of the solution to (6.1).*

Proof. As in the proof of Theorem 5.3, the uniform estimates of Lemma 4.3 together with the compactness results of Lemma 3.6 and Lemma 3.10 imply the weak and strong convergence results given in the theorem.

We now show that the limit pair $(\tilde{u}, \tilde{v})$, with $\tilde{v} = -\tilde{w}$ are a weak solution of (6.1). We start by noting that for all $\eta \in C^\infty(\Omega \times (0,T))$ with $\eta = 0$ on $\partial_0\Omega \times (0,T)$ and $\eta(\cdot, T) = 0$, we have

$$\begin{aligned}
&\int_0^T \int_\Omega -\delta_\Omega u \partial_t \eta + \nabla u \cdot \nabla \eta \ \mathrm{d}x \ \mathrm{d}t - \int_\Omega u^0 \eta(\cdot, 0) \ \mathrm{d}x \\
&= \int_0^T \int_\Gamma \boldsymbol{\nu} \cdot \nabla u \eta \ \mathrm{d}\sigma \ \mathrm{d}t = \int_0^T \int_\Gamma -\frac{1}{\delta_k} u w \eta \ \mathrm{d}\sigma \ \mathrm{d}t \\
&= \int_0^T \int_\Gamma -w \partial_t \eta + \delta_\Gamma \nabla_\Gamma w \cdot \nabla_\Gamma \eta \ \mathrm{d}\sigma \ \mathrm{d}t - \int_\Gamma w^0 \eta(\cdot, 0) \ \mathrm{d}\sigma \\
&= \int_0^T \int_\Gamma -w \partial_t \eta - \delta_\Gamma w \Delta_\Gamma \eta \ \mathrm{d}\sigma \ \mathrm{d}t - \int_\Gamma w^0 \eta(\cdot, 0) \ \mathrm{d}\sigma
\end{aligned}$$

Letting $\delta_k = \delta_\Gamma \to 0$, the convergence results (6.3)—(6.5) give

$$\int_0^T \int_\Omega -\delta_\Omega \tilde{u} \partial_t \eta + \nabla \tilde{u} \cdot \nabla \eta \ \mathrm{d}x \ \mathrm{d}t - \int_\Omega u^0 \eta(\cdot, 0) \ \mathrm{d}x = \int_0^T \int_\Gamma -\tilde{w} \partial_t \eta \ \mathrm{d}\sigma \ \mathrm{d}t - \int_\Gamma w^0 \eta(\cdot, 0) \ \mathrm{d}\sigma,$$

and hence with $\bar{v} = -\bar{w}$, we infer that

(6.7)
$$\int_0^T \int_\Omega -\delta_\Omega \tilde{u} \partial_t \eta + \nabla \tilde{u} \cdot \nabla \eta \ \mathrm{d}x \ \mathrm{d}t - \int_\Omega u^0 \eta(\cdot, 0) \ \mathrm{d}x - \int_0^T \int_\Gamma \tilde{v} \partial_t \eta \ \mathrm{d}\sigma \ \mathrm{d}t - \int_\Gamma v^0 \eta(\cdot, 0) \ \mathrm{d}\sigma = 0.$$

A density argument yields that the above holds for all test functions η in the spaces of Definition 6.2. As $u, w \geq 0$ we have $\tilde{u} \geq 0, \tilde{v} = -\tilde{w} \leq 0$. To check $\tilde{v} \in \beta(\tilde{u})$ it remains to show that $\int_\Gamma \tilde{u}\tilde{v} = 0$. This follows since

$$\begin{aligned}
\int_0^T \int_\Gamma \tilde{u}\tilde{v} \ \mathrm{d}\sigma \ \mathrm{d}t &= \int_0^T \int_\Gamma -\tilde{u}\tilde{w} \ \mathrm{d}\sigma \ \mathrm{d}t \\
&= -\lim_{\delta_k, \delta_\Gamma \to 0} \int_0^T \int_\Gamma (\tilde{u} - u)\tilde{w} + u(\tilde{w} - w) + uw \ \mathrm{d}\sigma \ \mathrm{d}t = 0,
\end{aligned}$$

where we have used that the first term on the right hand side is zero since $\tilde{u} \to u$ and $\tilde{w}$ is bounded in $L^2(0,T; L^2(\Gamma))$ (6.6), (4.14), the second term is zero since $\tilde{w} \rightharpoonup w$ and u is bounded in $L^2(0,T; L^2(\Gamma))$ (6.4) and the final term is zero from the estimate (4.15).

To prove that the solution is unique we argue as follows. Let $(\tilde{u}_1, \tilde{v}_1)$ and $(\tilde{u}_2, \tilde{v}_2)$ be solutions of (6.1) in the sense of Definition 6.2. We define $\theta^{\tilde{u}}(\cdot, t) := (\tilde{u}_1(\cdot, t) - \tilde{u}_2(\cdot, t)), \theta^{\tilde{v}}(\cdot, t) := (\tilde{v}_1(\cdot, t) - \tilde{v}_2(\cdot, t))$. The pair $(\theta^{\tilde{u}}, \theta^{\tilde{v}})$ satisfy

$$\int_0^T \int_\Omega -\delta_\Omega \theta^{\tilde{u}} \partial_t \eta + \nabla \theta^{\tilde{u}} \cdot \nabla \eta \ \mathrm{d}x \ \mathrm{d}t - \int_0^T \int_\Gamma \theta^{\tilde{v}} \partial_t \eta \ \mathrm{d}\sigma \ \mathrm{d}t = 0, \tag{6.8}$$

for all $\eta \in L^2\left((0,T); H^1_0(\Omega)\right)$ with $\partial_t \eta \in L^2\left((0,T) \times \Omega\right) \cap L^2\left((0,T) \times \Gamma\right)$ with $\eta(\cdot, T) = 0$. For $t \in [0,T]$ we define $\theta^{\tilde{z}}(\cdot, t) = \int_t^T \theta^{\tilde{u}}(\cdot, s) \ \mathrm{d}s$. Noting that $\theta^{\tilde{z}}$ is an admissible test function, we set $\eta = \theta^{\tilde{z}}$ in (6.8) which gives

$$\delta_\Omega \int_0^T \int_\Omega (\theta^{\tilde{u}})^2 \ \mathrm{d}x \ \mathrm{d}t - \int_0^T \frac{1}{2} \frac{\mathrm{d}}{\mathrm{d}t} \int_\Omega \left| \nabla \theta^{\tilde{z}} \right|^2 \ \mathrm{d}x \ \mathrm{d}t + \int_0^T \int_\Gamma \theta^{\tilde{v}} \theta^{\tilde{u}} \ \mathrm{d}\sigma \ \mathrm{d}t = 0.$$

As $\theta^{\tilde{z}}(\cdot,T)=0$ and recalling that $\tilde{v}_i \in \beta(\tilde{u}_i), i=1,2$ we have

$$\delta_\Omega \int_0^T \int_\Omega (\theta^{\tilde{u}})^2 \, \mathrm{d}x \, \mathrm{d}t + \frac{1}{2}\int_0^T \int_\Omega \left|\nabla \theta^{\tilde{u}}\right|^2 \, \mathrm{d}x \, \mathrm{d}t + \int_0^T \int_\Gamma \big(\beta(\tilde{u}_1)-\beta(\tilde{u}_2)\big)\left(\tilde{u}_1-\tilde{u}_2\right) \, \mathrm{d}\sigma \, \mathrm{d}t = 0.$$

The monotonicity of β gives

$$\left\|\theta^{\tilde{u}}\right\|^2_{L^2((0,T);H^1(\Omega))} = 0.$$

Finally, (6.8) and the above bound yield

$$\int_0^T \int_\Gamma \theta^{\tilde{v}} \partial_t \eta \, \mathrm{d}\sigma \, \mathrm{d}t = 0$$

for all η that are admissible test functions in the sense of Definition 6.2. For any $\phi \in L^2((0,T);H^{1/2}(\Gamma))$ we define $P^0\phi$ such that $P^0\phi=\phi$ on Γ, $\Delta P^0\phi = 0$ in Ω and $P^0\phi=0$ on $\partial_0\Omega$. Then we make take $\eta(\cdot,t)=\int_t^T P^0\phi(\cdot,s) \, \mathrm{d}s$ as a test function in the above which gives

$$\int_0^T \int_\Gamma \theta^{\tilde{v}} \phi \, \mathrm{d}\sigma \, \mathrm{d}t = 0,$$

for all $\phi \in L^2((0,T);H^{1/2}(\Gamma))$. Hence

$$\left\|\theta^{\tilde{v}}\right\|_{L^2((0,T);H^{-1/2}(\Gamma))} = 0,$$

which completes the proof of the theorem. □

7. Elliptic limit problem with dynamic boundary condition ($\delta_\Omega = \delta_\Gamma = \delta_k = 0$)

We now present a rigorous derivation of the elliptic problem with dynamic boundary conditions presented in §2.1 as a limit of (1.1). As mentioned in §2.1 we will only consider the case of Dirichlet boundary data. Specifically we show that as $\delta_\Omega = \delta_\Gamma = \delta_k \to 0$ the unique solution to (1.1) with Dirichlet boundary data, converges to the unique solution of the following problem.

Problem 7.1. *Find $\hat{u}\colon \Omega \times (0,T) \to \mathbb{R}^+$ and $\hat{v}\colon \Gamma \times (0,T) \to \mathbb{R}^-$ such that*

(7.1a)	$-\Delta \hat{u} = 0$	*in* $\Omega \times (0,T)$
(7.1b)	$\nabla \hat{u} \cdot \boldsymbol{\nu} + \partial_t \hat{v} = 0$	*on* $\Gamma \times (0,T)$
(7.1c)	$\hat{v} \in \beta(\hat{u})$	*on* $\Gamma \times (0,T)$
(7.1d)	$\hat{u} = u_D$	*on* $\partial_0\Omega \times (0,T)$
(7.1e)	$\hat{u}(\cdot,0) = u^0(\cdot) \geq 0$	*on* Ω
(7.1f)	$\hat{v}(\cdot,0) = v^0(\cdot) \leq 0$	*on* Γ,

where $\beta\colon \mathbb{R} \to \{0,1\}^{\mathbb{R}}$ is the set valued function defined in (5.2).

Definition 7.2 (Weak solution of (7.1))**.** *We say a function pair $(\hat{u},\hat{v})$ with $\hat{u} \in L^2(0,T;H^1_{e_{u_D}}(\Omega))$ and $\hat{v} \in L^\infty(0,T;L^2(\Gamma))$ is a weak solution of* (7.1)*, if for all $\eta \in L^2\left((0,T);H^1_0(\Omega)\right)$ with $\partial_t\eta \in L^2\left((0,T)\times\Gamma\right)$ with $\eta(\cdot,T)=0$ on Γ, we have*

$$\int_0^T \left(\int_\Omega \nabla \hat{u} \cdot \nabla \eta \, \mathrm{d}x - \int_\Gamma \hat{v} \partial_t \eta \, \mathrm{d}\sigma \right) \mathrm{d}t - \int_\Gamma v^0 \eta(\cdot,0) \, \mathrm{d}\sigma = 0, \tag{7.2}$$
$$\text{and} \quad \hat{v} \in \beta(\hat{u}) \text{ a.e. in } \Gamma \times (0,T).$$

The strategy of passing to the limit follows that of §6.

Theorem 7.3 (Convergence of the solution of (1.1) to a solution of (7.1))**.** *As* $\delta_\Omega = \delta_\Gamma = \delta_k \to 0$ *the solution pair* (u, w) *to (1.1) converge to a pair* $(\hat{u}, \hat{w})$ *in the following topologies*

$$u \rightharpoonup \hat{u} \quad \text{in } L^2(0,T;H^1_{e_{u_D}}(\Omega)) \tag{7.3}$$

$$w \rightharpoonup \hat{w} \quad \text{in } L^2(0,T;L^2(\Gamma)), \tag{7.4}$$

$$w \to \hat{w} \quad \text{in } L^2(0,T;H^{-1/2}(\Gamma)), \tag{7.5}$$

Moreover, the pair $\hat{u}, \hat{v}$*, with* $\hat{v} = -\hat{w}$ *are the unique solution to Problem (7.1) in the sense of Definition (7.2). The fact that the full sequence and not a subsequence converges is a consequence of the uniqueness of the solution to (7.1).*

Proof. As in the proof of Theorems 5.3 and 6.3, the estimates of Lemma 4.3, specifically (4.14) together with the compactness results recalled in (3.5) imply the convergence results (7.3) and (7.4). The strong convergence result (7.5) follows due to the Lions-Aubin-Simon compactness theory (Lemma 3.6) together with the estimate on the time translates of w (4.16) and the compact embedding of $L^2(\Gamma)$ into $H^{-1/2}(\Gamma)$ shown in Lemma 3.9.

The fact that the limits $\hat{u}, \hat{v} = -\hat{w}$ satisfy

$$\int_0^T \left(\int_\Omega \nabla \hat{u} \cdot \nabla \eta \, \mathrm{d}x - \int_\Gamma \hat{v} \partial_t \eta \, \mathrm{d}\sigma \right) \mathrm{d}t - \int_\Gamma v^0 \eta(\cdot, 0) \, \mathrm{d}\sigma = 0,$$

for all η as in Definition 7.2, follows from the weak convergence results (7.3) and (7.4) together with an analogous density argument to that used in the proof of Theorem 6.3. It remains to check $\hat{v} \in \beta(\hat{u})$. As previously we have $\hat{u} \geq 0$ and $\hat{v} \leq 0$. The fact that $\hat{u}, \hat{v} \in L^2((0,T) \times \Gamma)$, the strong convergence result (7.5), the weak convergence result (7.3) which implies weak convergence of the trace of u in $L^2(0,T;H^{1/2}(\Gamma))$ and the estimate (4.15) imply

$$\int_0^T \int_\Gamma \hat{u}\hat{v} \, \mathrm{d}\sigma \, \mathrm{d}t = {}_{L^2(0,T;H^{1/2}(\Gamma))}\langle \hat{u}, \hat{v} \rangle_{L^2(0,T;H^{-1/2}(\Gamma))} = 0,$$

and hence $\hat{v} \in \beta(\hat{u})$.

Similarly the uniqueness argument mirrors that used in the proof of Theorem 6.3. Letting $(\hat{u}_1, \hat{v}_1)$ and $(\hat{u}_2, \hat{v}_2)$ be two solutions of (7.1) in the sense of Definition 7.2 and setting $\theta^{\hat{u}}(\cdot, t) := (\hat{u}_1(\cdot, t) - \hat{u}_2(\cdot, t)), \theta^{\hat{v}}(\cdot, t) := (\hat{v}_1(\cdot, t) - \hat{v}_2(\cdot, t))$. The pair $(\theta^{\hat{u}}, \theta^{\hat{v}})$ satisfy

$$\int_0^T \int_\Omega \nabla \theta^{\hat{u}} \cdot \nabla \eta \, \mathrm{d}x \, \mathrm{d}t - \int_0^T \int_\Gamma \theta^{\hat{v}} \partial_t \eta \, \mathrm{d}\sigma \, \mathrm{d}t = 0, \tag{7.6}$$

for all $\eta \in L^2\left((0,T); H^1_0(\Omega)\right)$ with $\partial_t \eta \in L^2\left((0,T) \times (\Gamma)\right)$ with $\eta(\cdot, T) = 0$ on Γ. For $t \in [0,T]$ we define $\theta^{\hat{z}}(\cdot, t) = \int_t^T \theta^{\hat{u}}(\cdot, s) \, \mathrm{d}s$. Noting $\theta^{\hat{z}}$ is an admissible test function, we set $\eta = \theta^{\hat{z}}$ in (7.6) which gives using, as previously that $\theta^{\tilde{z}}(\cdot, T) = 0$ and recalling $\tilde{v}_i \in \beta(\tilde{u}_i), i = 1, 2$,

$$\frac{1}{2} \int_0^T \int_\Omega \left| \nabla \theta^{\hat{u}} \right|^2 \mathrm{d}x \, \mathrm{d}t + \int_0^T \int_\Gamma \left(\beta(\hat{u}_1) - \beta(\hat{u}_2) \right) (\hat{u}_1 - \hat{u}_2) \, \mathrm{d}\sigma \, \mathrm{d}t = 0.$$

The monotonicity of β, together with the Poincare inequality as $\theta^{\hat{z}} \in H^1_{e_0}(\Omega)$ gives

$$\left\| \theta^{\tilde{u}} \right\|^2_{L^2((0,T);H^1(\Omega))} = 0.$$

Finally, via the same argument used in the proof of Theorem 6.3, (7.6) and the above bound yield

$$\left\| \theta^{\hat{v}} \right\|_{L^2((0,T);H^{-1/2}(\Gamma))} = 0,$$

which completes the Proof of the Theorem. □

8. DEGENERATE PARABOLIC EQUATIONS

The structure of the equations is revealed by writing them as abstract degenerate parabolic equations holding on the surface Γ. First, we define a parabolic extension operator

$$P^{\delta_\Omega}\colon L^2(0,T;H^{1/2}(\Gamma)) \to L^2(0,T;H^1_{e_0}(\Omega)),$$

or

$$P^{\delta_\Omega}\colon L^2(0,T;H^{1/2}(\Gamma)) \to L^2(0,T;H^1(\Omega))$$

in the Neumann case. We fix $\tilde\eta \in L^2(\Omega)$ and for $\eta \in L^2(0,T;H^{1/2}(\Gamma))$ we define $P^{\delta_\Omega}\eta$ to be the unique solution of

$$\begin{aligned} \delta_\Omega \partial_t (P^{\delta_\Omega}\eta) - \Delta(P^{\delta_\Omega}\eta) &= 0 && \text{in } \Omega \times (0,T) \\ P^{\delta_\Omega}\eta &= \eta && \text{on } \Gamma \times (0,T) \\ P^{\delta_\Omega}\eta = 0 \text{ or } \nabla(P^{\delta_\Omega}\eta)\cdot \boldsymbol{\nu}_\Omega &= 0 && \text{on } \partial_0\Omega \times (0,T) \\ (P^{\delta_\Omega}\eta)(\cdot,0) &= 0 && \text{in } \Omega. \end{aligned} \tag{8.1}$$

This allows us to define a parabolic Dirichlet to Neumann (DtN) map $\mathcal{A}^{\delta_\Omega}\colon L^2(0,T;H^{1/2}(\Gamma)) \to L^2((0,T);H^{-1/2}(\Gamma))$ by

$$\mathcal{A}^{\delta_\Omega}\eta := \nabla(P^{\delta_\Omega}\eta)\cdot\boldsymbol{\nu} \qquad \text{for } \eta \in L^2(0,T;H^{1/2}(\Gamma)). \tag{8.2}$$

Next, we define a new elliptic extension operator $P^0\colon L^2(0,T;H^{1/2}(\Gamma)) \to L^2(0,T;H^1_{e_0}(\Omega))$, which formally is a limit of P^{δ_Γ} from (8.1). For $\eta \in L^2(0,T;H^{1/2}(\Gamma))$ we define $P^0\eta$ to be the unique solution of

$$\begin{aligned} -\Delta(P^0\eta) &= 0 && \text{in } \Omega\times(0,T) \\ P^0\eta &= \eta && \text{on } \Gamma\times(0,T) \\ P^0\eta &= 0 && \text{on } \partial_0\Omega\times(0,T). \end{aligned} \tag{8.3}$$

This allows us to define the elliptic DtN map $\mathcal{A}^0\colon L^2(0,T;H^{1/2}(\Gamma)) \to L^2((0,T);H^{-1/2}(\Gamma))$ by

$$\mathcal{A}^0\eta := \nabla(P^0\eta)\cdot\boldsymbol{\nu} \qquad \text{for } \eta \in L^2(0,T;H^{1/2}(\Gamma)). \tag{8.4}$$

We note that the operator $\mathcal{A}^0$ may also be viewed as the half-Laplacian $(-\Delta_\Gamma)^{1/2}$ for functions on Γ [Caffarelli and Silvestre, 2007].

It is also convenient to introduce extensions of the data. First we introduce $U_D^{\delta_\Omega}$ as the solution of the parabolic problem

$$\begin{aligned} \delta_\Omega\partial_t U_D^{\delta_\Omega} - \Delta U_D^{\delta_\Omega} &= 0 && \text{in } \Omega\times(0,T) \\ U_D^{\delta_\Omega} &= 0 && \text{on } \Gamma\times(0,T) \\ U_D^{\delta_\Omega} = u_D \text{ or } \nabla(U_D^{\delta_\Omega})\cdot\boldsymbol{\nu}_\Omega &= 0 && \text{on } \partial_0\Omega\times(0,T) \\ U_D^{\delta_\Omega}(\cdot,0) &= 0 && \text{in } \Omega. \end{aligned} \tag{8.5}$$

Second we have U_D as the solution of an elliptic problem

$$\begin{aligned} -\Delta U_D &= 0 && \text{in } \Omega \\ U_D &= 0 && \text{on } \Gamma \\ U_D &= u_D \quad \text{or } \nabla U_D\cdot\boldsymbol{\nu}_\Omega = 0 && \text{on } \partial_0\Omega. \end{aligned} \tag{8.6}$$

In the Neumann case we have $U_D^{\delta_\Omega} = U_D = 0$.

Third, we introduce $U_I^{\delta_\Omega}$ as the solution of the parabolic problem

$$
\begin{aligned}
\delta_\Omega \partial_t U_I^{\delta_\Omega} - \Delta U_I^{\delta_\Omega} &= 0 && \text{in } \Omega \times (0,T) \\
U_I^{\delta_\Omega} &= 0 && \text{on } \Gamma \times (0,T) \\
U_I^{\delta_\Omega} = 0 \text{ or } \nabla(U_I^{\delta_\Omega}) \cdot \boldsymbol{\nu}_\Omega &= 0 && \text{on } \partial_0\Omega \times (0,T) \\
U_I^{\delta_\Omega}(\cdot,0) &= u_0 && \text{in } \Omega.
\end{aligned} \tag{8.7}
$$

Note that as $\delta_\Omega \to 0$ that $U_I^{\delta_\Omega} \to 0$ and $U_D^{\delta_\Omega} \to U_D$ in $L^2(0,T;H^1(\Omega))$. Finally, we write L for $-\Delta_\Gamma$ as an operator $L^2(0,T;H^1(\Gamma)) \to L^2(0,T;H^{-1}(\Gamma))$.

Problem 8.1 (Fast reaction limit, $\delta_k = 0$)**.** *Find* $\bar{u} \in L^2(0,T;H^{1/2}(\Gamma))$ *and* $\bar{v} \in L^2(0,T;H^1(\Gamma))$ *with* $\partial_t \bar{v} \in L^2(0,T;H^{-1}(\Gamma))$ *such that*

$$
\begin{aligned}
\partial_t \bar{v} + \delta_\Gamma L \bar{v} + \mathcal{A}^{\delta_\Omega} \bar{u} + \nabla(U_D^{\delta_\Omega} + U_I^{\delta_\Omega}) \cdot \nu &= 0 && \textit{in } L^2(0,T;H^{-1}(\Gamma)) \\
\bar{v} &\in \beta(\bar{u}) && \textit{on } \Gamma \times (0,T) \\
\bar{v}(\cdot,0) &= v^0 && \textit{in } \Omega.
\end{aligned} \tag{8.8}
$$

Problem 8.2 (Bulk parabolic limit equation with dynamic boundary condition, $\delta_k = \delta_\Gamma = 0$)**.** *Find* $\tilde{u} \in L^2(0,T;H^{1/2}(\Gamma))$ *and* $\tilde{v} \in L^2(0,T;L^2(\Gamma))$ *with* $\partial_t \tilde{v} \in L^2(0,T;H^{-1/2}(\Gamma))$ *such that*

$$
\begin{aligned}
\partial_t \tilde{v} + \mathcal{A}^{\delta_\Omega} \tilde{u} + \nabla(U_D^{\delta_\Omega} + U_I^{\delta_\Omega}) \cdot \nu &= 0 && \textit{in } L^2(0,T;H^{-1/2}(\Gamma)) \\
\tilde{v} &\in \beta(\tilde{u}) && \textit{on } \Gamma \times (0,T) \\
\tilde{v}(\cdot,0) &= v^0 && \textit{in } \Omega.
\end{aligned} \tag{8.9}
$$

Problem 8.3 (Elliptic equation with dynamic boundary condition, $\delta_k = \delta_\Gamma = \delta_\Omega = 0$)**.** *Find* $\hat{u} \in L^2(0,T;H^{1/2}(\Gamma))$ *and* $\hat{v} \in L^2(0,T;L^2(\Gamma))$ *with* $\partial_t \hat{v} \in L^2(0,T;H^{-1/2}(\Gamma))$ *such that*

$$
\begin{aligned}
\partial_t \hat{v} + \mathcal{A}^0 \hat{u} + \nabla U_D \cdot \nu &= 0 && \textit{in } L^2(0,T;H^{-1/2}(\Gamma)) \\
\hat{v} &\in \beta(\hat{u}) && \textit{on } \Gamma \times (0,T) \\
\hat{v}(\cdot,0) &= v^0 && \textit{in } \Omega.
\end{aligned} \tag{8.10}
$$

9. Variational inequality formulation

The degenerate parabolic equations as written in Problem 8.2 and Problem 8.3 are the analogues of the Hele-Shaw and steady one phase Stefan problems with the operator $\boldsymbol{\mathcal{A}}^0$ (here thought of as the half-Laplacian) replacing the usual Laplacian $(-\Delta)$. See [Crowley, 1979; Elliott and Ockendon, 1982] and [Duvaut, 1973; Elliott, 1980; Elliott and Janovskỳ, 1981; Rodrigues, 1987] for a reformulation as variational inequalities via an integration in time. Our systems (6.1) and (7.1) and respectively Problems 8.2 and 8.3 may be reformulated, respectively, as parabolic and elliptic variational inequalities of obstacle type. The obstacle problem lies on the surface Γ and is a consequence of the complementarity which is maintained after an integration with respect to time and noting that this integration commutes with the operators $\mathcal{A}^{\delta_\Omega}$ and $\mathcal{A}^0$. We set

$$
z(\cdot,t) = \int_0^t \hat{u}(\cdot,s) \, \mathrm{d}s, \tag{9.1}
$$

where $\hat{u}$ satisfies (6.1) or (7.1). We find it convenient to introduce $Z_D^{\delta_\Omega}$ as

$$
Z_D^{\delta_\Omega}(\cdot,t) = tU_D. \tag{9.2}
$$

Proceeding formally, we claim that if the pair $(\hat{u},\hat{v})$ satisfy (6.1) (or (7.1) with $\delta_\Omega = 0$) then the pair $(z,\hat{v})$ satisfy the following problem

Problem 9.1. *For each $t \in (0,T)$, find $z(t)$ and $\hat{v}(t)$ such that*

$$\delta_\Omega \partial_t z - \delta_\Omega u_0 - \Delta z = 0 \quad \text{in } \Omega \tag{9.3a}$$

$$\nabla z \cdot \boldsymbol{\nu} + \hat{v} = v^0 = 0 \quad \text{on } \Gamma \tag{9.3b}$$

$$\hat{v} \in \beta(z) \quad \text{on } \Gamma \tag{9.3c}$$

$$z = Z_D \quad \text{on } \partial_0\Omega. \tag{9.3d}$$

We check the condition $\hat{v} \in \beta(z)$ on $\Gamma \times (0,T)$. The remaining conditions follow formally from integration in time of (7.1). Let χ_B denote the characteristic function of the set B, then we have

$$\int_\Gamma \hat{v}\chi_{z>0} \, \mathrm{d}\sigma = \int_\Gamma \hat{v}(\chi_{z>0} - \chi_{\hat{u}>0}) \, \mathrm{d}\sigma + \int_\Gamma \hat{v}\chi_{\hat{u}>0} \, \mathrm{d}\sigma.$$

Noting that $\chi_{z>0} \geq \chi_{\hat{u}>0}$ as $\hat{u} \geq 0$ and recalling $\hat{v} \leq 0$ we have

$$\int_\Gamma v\chi_{z>0} \, \mathrm{d}\sigma \geq \int_\Gamma \hat{v}\chi_{\hat{u}>0} \, \mathrm{d}\sigma = 0.$$

as $\hat{v} \in \beta(\hat{u})$. Finally as $\hat{v} \leq 0$ and $z \geq 0$ this yields $\hat{v} \in \beta(z)$.

We now show that (9.3), in the case $\delta_\Omega = 0$, may be formulated as an elliptic variational inequality. For all $\eta \in H^1_{e_0}(\Omega)$

$$0 = \int_\Omega -\Delta z \eta \, \mathrm{d}x = \int_\Omega \nabla z \cdot \nabla \eta \, \mathrm{d}x - \int_\Gamma \nabla z \cdot \boldsymbol{\nu} \eta \, \mathrm{d}\sigma. \tag{9.4}$$

Thus defining the convex set

$$K_t := \{\eta \in H^1_{eZ_D}(\Omega) |\, \eta \geq 0 \text{ on } \Gamma\}.$$

We see that for any $\eta \in K_t$ we have

$$\begin{aligned} \int_\Omega \nabla z \cdot \nabla(\eta - z) \, \mathrm{d}x &= \int_\Gamma \nabla z \cdot \boldsymbol{\nu}(\eta - z) \, \mathrm{d}\sigma \\ &= \int_\Gamma (v^0 - v)(\eta - z) \, \mathrm{d}\sigma. \end{aligned} \tag{9.5}$$

Now since $z \geq 0, v \leq 0$ and $zv = 0$ we arrive at the following elliptic variational inequality where time enters as a parameter, find $z \in K_t$ such that

$$\int_\Omega \nabla z \cdot \nabla(\eta - z) \, \mathrm{d}x \geq \int_\Gamma v^0(\eta - z) \, \mathrm{d}\sigma \quad \text{for all } \eta \in K_t. \tag{9.6}$$

The same argument outlined above yields that if z is defined by (9.1) with $\hat{u}$ replaced by $\tilde{u}$, the unique solution to the parabolic problem (6.1) then z satisfies the parabolic variational inequality, find $z \in K_t$ such that

$$\int_\Omega \delta_\Omega \partial_t z \eta + \nabla z \cdot \nabla(\eta - z) \, \mathrm{d}x \geq \int_\Omega \delta_\Omega u^0(\eta - z) \, \mathrm{d}x + \int_\Gamma v^0(\eta - z) \, \mathrm{d}\sigma \quad \text{for all } \eta \in K_t. \tag{9.7}$$

We may also integrate the appropriate degenerate parabolic problems in time yielding for example in the case $\delta_\Omega = 0$

$$\begin{aligned} \mathcal{A}^0 z + \nabla Z_D \cdot \nu - v^0 = -\hat{v} \quad & \text{on } \Gamma \\ \hat{v} \leq 0, \;\; z \geq 0, \;\; z\hat{v} = 0 \quad & \text{on } \Gamma \end{aligned} \tag{9.8}$$

and obtain the elliptic variational inequality from this calculation.

10. Numerical experiments

We now present some numerical simulations that support the theoretical results of the previous sections and illustrate a robust numerical method for the simulation of coupled bulk-surface systems of equations. We employ a piecewise linear coupled bulk surface finite element method for the approximation. The method is based on the coupled bulk-surface finite element method proposed and analysed (for linear elliptic systems) by Elliott and Ranner [2013].

10.1. **Coupled bulk-surface finite element method.** We define computational domains Ω_h and Γ_h by requiring that Ω_h is a polyhedral approximation to Ω and we set $\Gamma_h = \partial\Omega_h \setminus \partial_0\Omega_h$, i.e., Γ_h is the interior boundary of the polyhedral domain Ω_h. We assume that Ω_h is the union of $n+1$ dimensional simplices (triangles for $n = 1$ and tetrahedra for $n = 2$) and hence the faces of Γ_h are n dimensional simplices.

We define $\mathcal{T}_h$ to be a triangulation of Ω_h consisting of closed simplices. Furthermore, we assume the triangulation is such that for every $k \in \mathcal{T}_h$, $k \cap \Gamma_h$ consists of at most one face of k. We define the bulk and surface finite element spaces $\mathbb{V}_h^\gamma, \gamma \in \mathbb{R}$ and $\mathbb{S}_h$ respectively by

$$\mathbb{V}_h^\gamma = \left\{\Phi \in C(\hat{\Omega}) : \Phi = \gamma \text{ on } \partial_0\Omega_h \text{ and } \Phi|_k \in \mathbb{P}^1(k), \quad \text{for all } k \in \mathcal{T}_h\right\},$$

and

$$\mathbb{S}_h = \left\{\Psi \in C(\Gamma_h) : \Psi|_s \in \mathbb{P}^1(s), \quad \text{for all } k \in \mathcal{T}_h \text{ with } s = k \cap \Gamma_h \neq \emptyset\right\}.$$

10.2. **Numerical schemes.** In the interests of brevity we only present numerical schemes for the approximation of (4.1) and (9.6), i.e., the original problem with Dirichlet boundary conditions and the elliptic variational inequality respectively. For simplicity we take $u_D = 1$. The modifications for the Neumann case and the parabolic variational inequality are standard. We divide the time interval $[0, T]$ into N subintervals $0 = t_0 < t_1 < \cdots < t_{M-1} < t_M = 1$ and denote by $\tau := t_m - t_{m-1}$ the time step, which for simplicity is taken to be uniform. For a time discrete sequence, we introduce the shorthand $f^m := f(t_m)$.

For the time discretisation of (4.1) we employ an IMEX method where the diffusion terms are treated implicitly whilst the reaction terms are treated explicitly [Lakkis et al., 2013] which leads to two decoupled parabolic systems. The fully discrete scheme for the approximation of (4.1) reads as follows, for $m = 1, \ldots, M$ find $(U^m, W^m) \in (\mathbb{V}_h^{u_D} \times \mathbb{S}_h)$ such that for all $(\Phi, \Psi) \in (\mathbb{V}_h^0 \times \mathbb{S}_h)$

(10.1)

$$\int_{\Omega_h} \delta_\Omega \frac{1}{\tau}\left(U^m - U^{m-1}\right)\Phi \;\mathrm{d}x + \int_{\Omega_h} \nabla U^{m+1} \cdot \nabla\Phi \;\mathrm{d}x = -\frac{1}{\varepsilon}\int_{\Gamma_h} \Lambda^h\left[U^{m-1}W^{m-1}\right]\Phi \;\mathrm{d}\sigma_h$$

$$\int_{\Gamma_h} \frac{1}{\tau}\left(W^m - W^{m-1}\right)\Psi \;\mathrm{d}\sigma_h + \int_{\Gamma_h} \delta_\Gamma \nabla_{\Gamma_h} W^{m+1} \cdot \nabla_{\Gamma_h}\Psi \;\mathrm{d}\sigma_h = -\frac{1}{\varepsilon}\int_{\Gamma_h} \Lambda^h\left[U^{m-1}W^{m-1}\right]\Psi \;\mathrm{d}\sigma_h$$

$$U^0 = \mathcal{I}^h u^0 \quad \text{and} \quad W^0 = \Lambda^h w^0,$$

where $\mathcal{I}^h : C(\Omega_h) \to \mathbb{V}_h^{u_D}$ and $\Lambda^h : C(\Gamma_h) \to \mathbb{S}_h$ denote the Lagrange interpolants into the bulk and surface finite element spaces respectively.

For the approximation of (9.6), we note that at each time step a single elliptic variational inequality must be solved who's solution may be obtained independently of the values at other times. Introducing the bulk finite element space

$$\mathbb{K}_h^t = \left\{\Phi \in C(\Omega_h) : \Phi \geq 0, \Phi = t \text{ on } \partial_0\Omega_h \text{ and } \Phi|_k \in \mathbb{P}^1(k), \quad \text{for all } k \in \mathcal{T}_h\right\},$$

the fully discrete scheme for the approximation of (9.6) reads, for $m = 1, \ldots, N$, find $Z^m \in \mathbb{K}_h^t$ such that for all $\Phi \in \mathbb{K}_h^t$

$$\int_{\Omega_h} \nabla Z^m \cdot \nabla(\Phi - Z^m) \;\mathrm{d}x \geq \int_{\Gamma_h} v^0(\Phi - Z^m) \;\mathrm{d}\sigma_h. \tag{10.2}$$

For a discussion of the analysis of discretisation of this problem we refer to Nochetto et al. [2015].

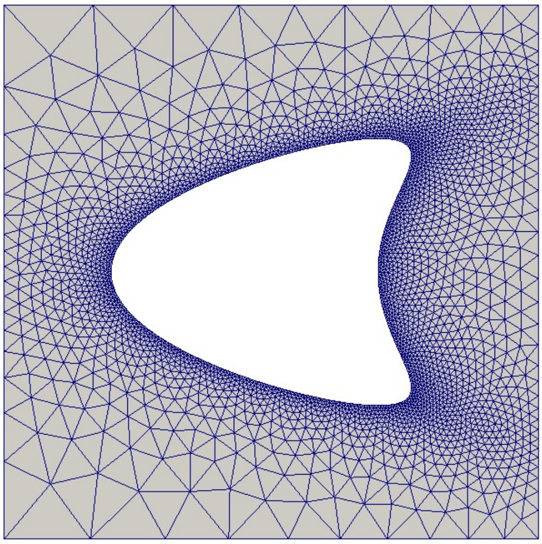


FIGURE 3. The computational domain for the simulations in $2d$ of §10.3, generated using DistMesh [Persson and Strang, 2004].

10.3. **2D simulations.** For all the simulations we use of the finite element toolbox ALBERTA [Schmidt and Siebert, 2005]. For the visualisation we use PARAVIEW [Henderson et al., 2004]. We start with the case where Ω is two dimensional, i.e., the surface Γ is a curve. We set $\partial_0\Omega$ to be the boundary of the square of length four centred at the origin and define the surface of the cell Γ by the level set function $\Gamma = \{\boldsymbol{x} \in \mathbb{R}^2 | (x_1 + 0.2 - x_2^2)^2 + x_2^2 - 1 = 0\}$. We generated a bulk triangulation of the domain Ω_h and the corresponding induced surface triangulation of Γ_h using DistMesh [Persson and Strang, 2004]. We used a graded mesh-size with small elements near Γ, the bulk mesh had 2973 DOFs (degrees of freedom) and the induced surface triangulation had 341 DOFs. Figure 3 shows the mesh used for all the 2D simulations.

In light of the theoretical results of the previous sections, we consider (4.1) with $\varepsilon = \delta_\Omega = \delta_\Gamma = 10^{-1}, 10^{-2}$ and 10^{-3} respectively and compare the simulation results with the results of simulations of (9.6). For the problem data for (4.1), we took the end time $T = 0.7$ and $u_D = 1$. For the initial data for (4.1) we took $w^0 = \max(0, \cos(\pi x_2) + \sin(\pi x_1))$, $\boldsymbol{x} \in \Gamma$ and $u^0 = u_D = 1$ and for (9.6) we took $v^0 = -w^0$. For each of the simulations of (4.1) we used same uniform time step, $\tau = 10^{-8}$. In order to compare the solutions of (4.1) with those of (9.6), we solve (9.6) at a series of distinct times and post-process the solution to obtain $u = \partial_t z$ and $w = \nabla z \cdot \boldsymbol{\nu} + w^0$.

Snapshots of the solution Z to (9.6) at a series of distinct times is shown in Figure 4. We note that to post-process $U^{t_m} := (Z^{t_m} - Z^{t_m - \tau})/\tau$ we solve (9.6) at t_m and $t_m - \tau$ fixing $\tau = 10^{-2}$. We stress that as time simply enters as a parameter in (9.6) its solution may be approximated independently at any given time, it is simply for the recovery of U for which we require values of Z at a previous time.

Figure 5 shows snapshots of the simulated U and W. Initially we observe depletion of the bulk ligand concentration U in each case near regions where the initial data for the surface receptors w^0 is large. As time progresses we observe a decay in W with larger decreases in W observed for smaller values of ε. Similarly the speed at which the system approaches the steady state corresponding to constant solutions $u = 1$ and $w = 0$ appears to be an increasing function of ε. The post-processed U and W obtained from the solution to (9.6) show qualitatively similar behaviour with faster dynamics towards the steady state which is attained by the end time $t = 0.7$, with none of the simulations with $\varepsilon > 0$ attaining this steady state by $t = 0.7$. In order to illustrate more clearly the formation of the free boundary as $\varepsilon \to 0$, in Figure 6 we show plots of W and the trace of U over the surface Γ_h. We observe that $\varepsilon \to 0$ the supports of the trace of U and W become disjoint and their profiles approach that obtained on post-processing the solution of (9.6).

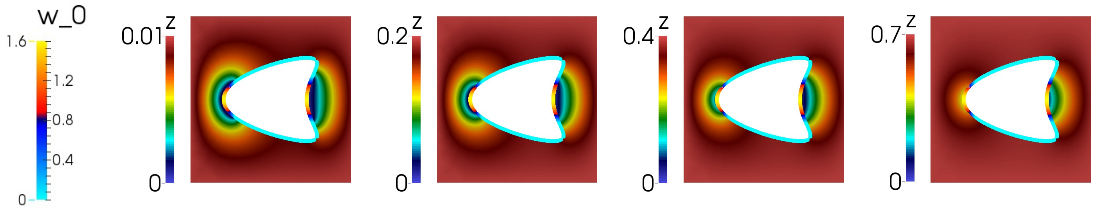


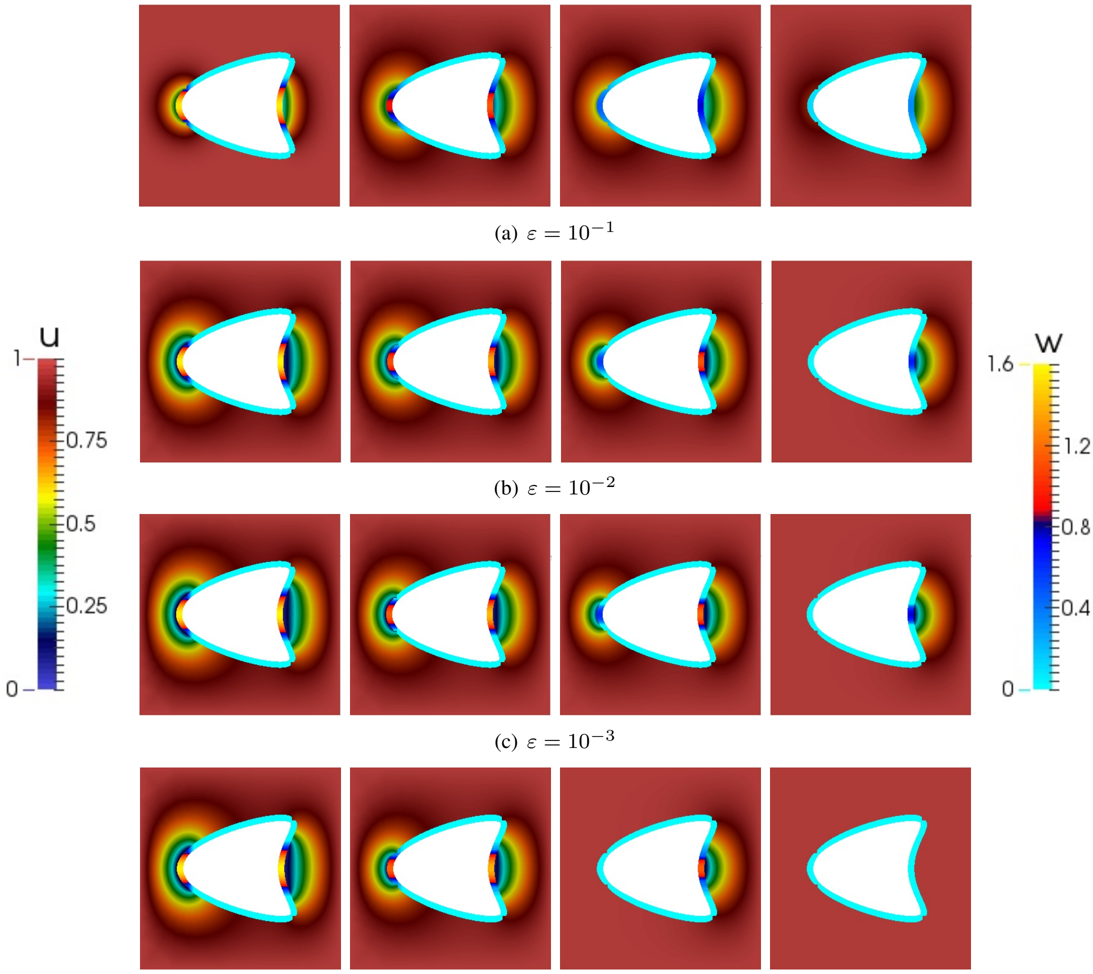
FIGURE 4. Simulation results of §10.3. Snapshots of the computed solution Z together with the initial data W^0 of the elliptic variational inequality (9.6) at times $0.01, 0.2, 0.4$ and 0.7 reading from left to right. The colour scale for W^0 is fixed in every figure.

10.4. **3D simulations.** We conclude this section with some 3D simulations. We set $\partial_0\Omega = \{\boldsymbol{x} \in \mathbb{R}^3 | \, |\boldsymbol{x}| = 2\}$, i.e., the surface of the sphere of radius two centred at the origin and define the surface of the cell Γ by the level set function $\Gamma = \{\boldsymbol{x} \in \mathbb{R}^3 | (x_1 + 0.2 - x_2^2)^2 + 4x_3^2 + x_2^2 - 1 = 0\}$. We generated a triangulation of the bulk domain (and the corresponding induced surface triangulation) using CGAL [Rineau and Yvinec, 2013]. We used a bulk mesh with 11167 DOFs and the induced surface triangulation had 2449 DOFs for the simulation of (4.1) whilst for the simulation of (9.6) we used a finer mesh with 60583 bulk DOFs and 15169 surface DOFs. Figure 7 shows the computational domain used for all the simulation of (4.1).

We report on the results of two simulations. We consider the approximation of (4.1) with $\varepsilon = \delta_\Omega = \delta_\Gamma = 1 \times 10^{-2}$ and for the problem data we set $T = 0.6$, $u_D = u^0 = 1$ and $w^0 = \max(\cos(\pi x_2) + \sin(\pi x_1), 0)$, $\boldsymbol{x} \in \Gamma$ and similarly to §10.3 we compare these results with those obtained from post-processing the solution to the elliptic variational inequality (9.6) with $v^0 = -w^0$. For the simulation of (4.1) we used a fixed uniform time step of 1×10^{-6}. Snapshots of the solution Z to (9.6) at a series of distinct times is shown in Figure 8. As previously, to post-process $U^{t_m} := (Z^{t_m} - Z^{t_m - \tau})/\tau$ we solve (9.6) at t_m and $t_m - \tau$ fixing $\tau = 0.01$. Figure 9 shows snapshots of the simulated U and W. Analogous behaviour to the 2D case of §10.3 is observed. We note that the solution of Z shown in Figure 8 appears quite smooth and the rough nature of the post-processed U and W may be an artefact of the post-processing together with the slice through the bulk triangulation taken for visualisation purposes. As noted in Section 9, the elliptic variational inequality is a reformulation of the Hele-Shaw free boundary problem on the surface Γ with the differential operator now the half-Laplacian rather than the usual Laplacian (Laplace-Beltrami). We therefore conclude the numerical results section with Figure 10 which shows the evolution of the approximated free boundary on the surface Γ_h. We approximate the position of the free boundary by plotting the level curve of the set where the trace of $Z = 5 \times 10^{-3}$ at a series of times.

11. CONCLUSION

In this work we developed a well-posedness theory for a system of coupled bulk-surface PDEs with nonlinear coupling. The system under consideration arises naturally as a simplification of models for receptor-ligand dynamics in cell biology and hence developing a rigorous mathematical framework for the treatment of such systems is an important task due to their widespread use in modelling and computational studies, e.g., [Bao et al., 2014; García-Peñarrubia et al., 2013; Levine and Rappel, 2005; Madzvamuse et al., 2015]. Whilst the model we consider (1.1) is a simplified model problem, the nonlinear coupling



(a) $\varepsilon = 10^{-1}$

(b) $\varepsilon = 10^{-2}$

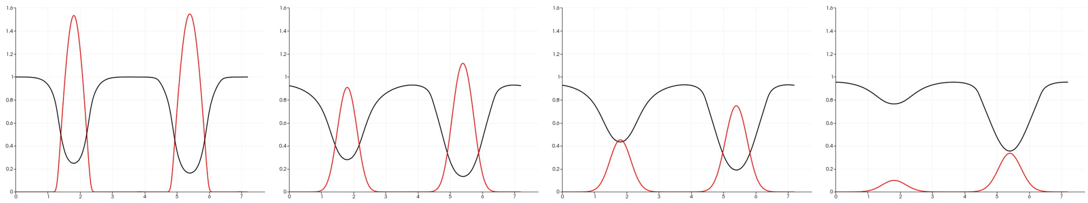
(c) $\varepsilon = 10^{-3}$

(d) $u^n = (z^{t_n} - z^{t_n - 0.01})/0.01, \quad w^n = w^0 + \nabla z^n \cdot \boldsymbol{\nu}$

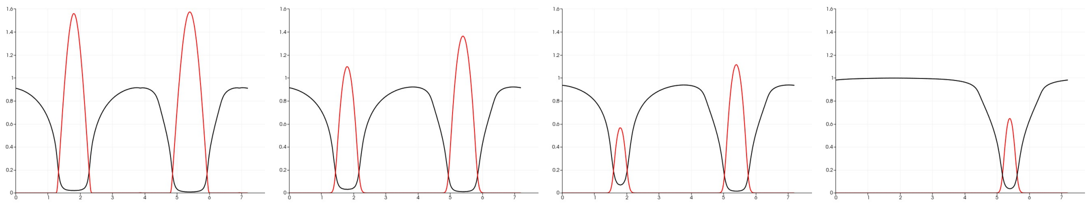
FIGURE 5. Simulation results of §10.3. (First three rows) Snapshots of the computed solutions U and W of (4.1) in 2D at times $0.01, 0.2, 0.4$ and 0.7 (reading from left to right) for different values of $\varepsilon = \delta_\Omega = \delta_\Gamma$. The fourth row shows the computed solutions U and $W = -V$ post-processed from solving the elliptic variational inequality (9.6) at times $0.01, 0.2, 0.4$ and 0.7 reading from left to right.

between the bulk and surface species is preserved and this is expected to be the main difficulty in the mathematical understanding of more biologically complex models of receptor-ligand interactions. Thus our techniques should be applicable to many of the models derived and simulated in the literature.

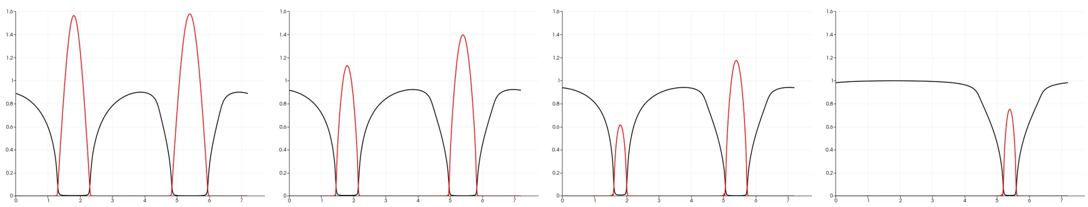
On non-dimensionalisation of the model using experimentally estimated parameter values, we identified three biologically meaningful asymptotic (small-parameter) limits of the model. We present a rigorous derivation of the limiting problems which correspond to free boundary problems on the surface of the cell and we demonstrated the well-posedness of the free boundary problems. Moreover, we discussed connections between the different free boundary problems and classical free boundary problems, namely the one-phase Stefan problem and the Hele-Shaw problem. This perspective gives rise to the possibility of using these ideas when constructing receptor-ligand models with other mechanisms.



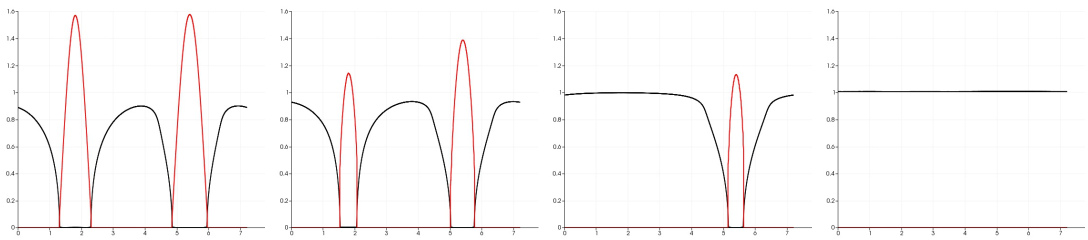
(a) $\varepsilon = 10^{-1}$



(b) $\varepsilon = 10^{-2}$



(c) $\varepsilon = 10^{-3}$



(d) $u^n = (z^{t_n} - z^{t_n - 0.01})/0.01, \quad w^n = w^0 + \nabla z^n \cdot \boldsymbol{\nu}$

FIGURE 6. Simulation results of §10.3. (First three rows) Plots of the trace of U (black) and W (red) of (4.1) over Γ_h at times $0.01, 0.2, 0.4$ and 0.7 (reading from left to right) for different values of $\varepsilon = \delta_\Omega = \delta_\Gamma$. The fourth row shows plots of the trace of U (black) and $W = -V$ (red) post-processed from solving the elliptic variational inequality (9.6) at times $0.01, 0.2, 0.4$ and 0.7 reading from left to right.

Finally, we reported on numerical simulations of the original problem (1.1) and a suitable reformulation of the elliptic limiting problem obtained when one considers fast reaction, slow surface diffusion and fast bulk diffusion. The simulation results illustrated the convergence towards the limiting problem thereby supporting our theoretical findings. We note that the reformulated problem is considerably cheaper to solve computationally. Hence in a biological setting where one is in a parameter regime in which the limiting problem provides a good approximation to the original problem it may be preferable to solve the limiting free boundary problem rather than the original coupled system of parabolic equations.

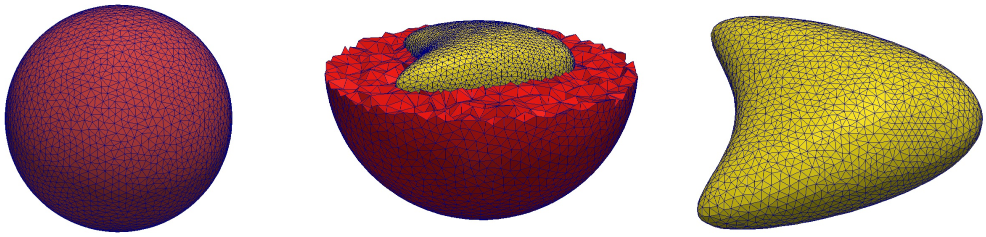


FIGURE 7. The coarser computational domain used for the simulations in $3d$ of §10.4, generated using CGAL [Rineau and Yvinec, 2013]. The left figure shows the outer boundary of the bulk triangulation, the middle figure shows a the bulk triangulation with elements with their barycenters in the top half ($x_3 > 0$) removed together with the surface triangulation of the interior surface Γ_h and the right figure shows the triangulation of the surface Γ_h.

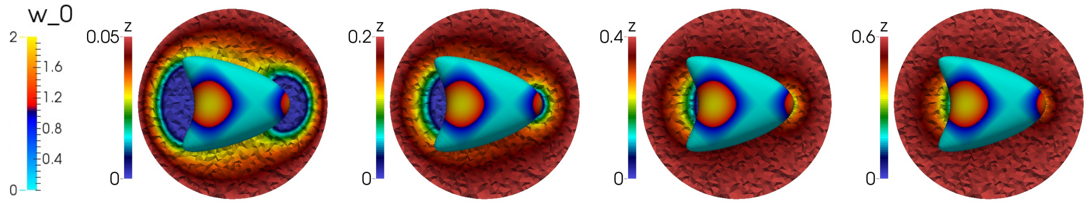


FIGURE 8. Simulation results of §10.4. Snapshots of the computed solution Z together with the initial data W^0 of the elliptic variational inequality (9.6) at times $0.05, 0.2, 0.4$ and 0.6 reading from left to right. The colour scale for W^0 is fixed in every figure. For visualisation, we have hidden elements of the bulk with barycenters with $x_3 > 0$.

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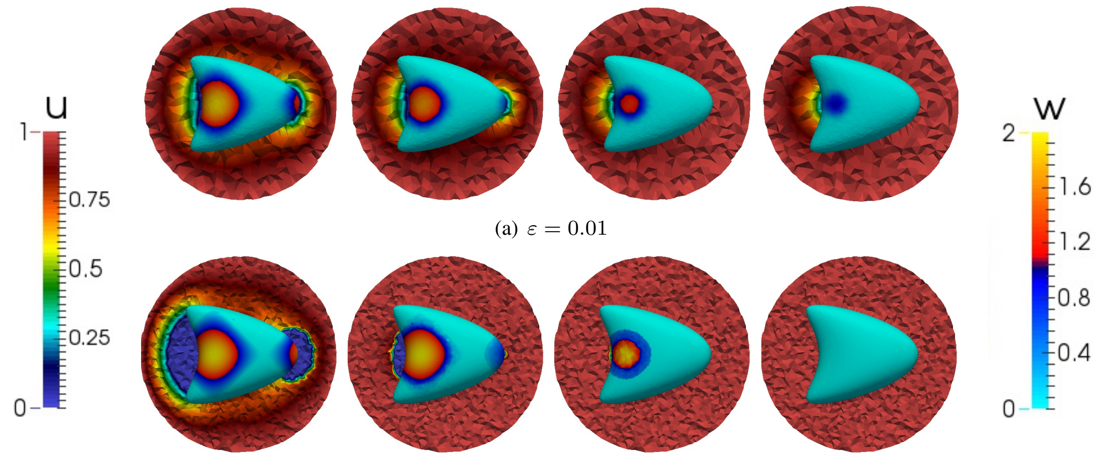

(a) $\varepsilon = 0.01$

(b) $u^m = (z^{t_m} - z^{t_m - 0.01})/0.01, \quad w^m = w^0 + \nabla z^m \cdot \boldsymbol{\nu}$

FIGURE 9. Simulation results of §10.4. Top row, snapshots of the computed solutions U and W of (4.1) in 3D at times $0.05, 0.2, 0.4$ and 0.6 (reading from left to right) for $\varepsilon = \delta_\Omega = \delta_\Gamma = 0.01$ on a coarser mesh. Bottom row, the computed solutions U and $W = -V$ post-processed from solving the elliptic variational inequality (9.6) at times $0.05, 0.2, 0.4$ and 0.6 reading from left to right on a finer mesh. For visualisation, we have hidden elements of the bulk with barycenters with $x_3 > 0$.

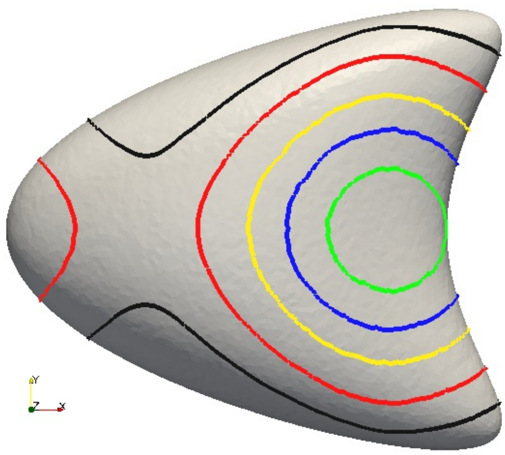

FIGURE 10. Simulation results of §10.4. Snapshots of the level curve on which the trace of $Z = 5 \times 10^{-3}$ that approximates the free boundary in the elliptic variational inequality (9.6) and thus the surface Hele-Shaw problem (9.8) at times 0.05 (black), 0.15 (red), 0.25 (yellow), 0.35 (blue) and 0.45 (green).

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