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Biochemical and mechanical processes in synovial fluid – modeling, analysis and computational simulations

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UNIVERZITA KARLOVA V PRAZE
Matematicko–Fyzikální fakulta

HEIDELBERG UNIVERSITY
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Název práce: Biochemické a mechanické procesy v synoviálních tekutinách – modelování, analýza, počítačové simulace

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Abstrakt: Synoviální tekutina je polymerní roztok, který se obecně chová jako viskoelastická tekutina, a to především díky obsaženým makromolekulám hyaluronanu. V této práci se zabýváme biologickými a biochemickými vlastnostmi synoviálních tekutin, dále jejich komplexní reologií a jejich interakcí se synoviálními membránami během filtrace. Z matema- tického hlediska modelujeme synoviální tekutiny jako vazké nestlačitelné tekutiny, pro něž jsme vyvinuli nový zobecněný model mocninného typu, jehož exponent závisí na koncentraci výše zmíněného hyaluronanu. Takový popis je adekvátní, pokud synoviální tekutina nepodléhá vysokým zátěžovým testům. Dále se zabýváme popisem lineárních viskoelastických odezev synoviálních tekutin z dostupných experimentálních dat, opět hledáme příslušné parametry modelů jako funkce koncentrace. Pro popis proudění používáme zobecněné Navierovy–Stokesovy rovnice svázané s podmínkou nestlačitelnosti a rovnice pro konvekci–difúzi koncentrace hyaluronanu. V části práce zabývající se matematickou analýzou formulujeme stacionární úlohu a dokážeme existenci odpovídajícího slabého řešení. Důkaz existence je založen na metodě monotónních operátorů, kde klíčovou roli hraje důkaz Hölderovské spojitosti koncentrace. V numerické části teze se zabýváme výběrem a implementací vhodných stabilizačních metod pro numerické řešení problému s dominantní konvekcí, jak je charakteristické pro synoviální tekutiny. Numericky pak řešíme pro různé modely zobecněné vazkosti a různé stabilizační metody systém řídících rovnic v obdélníkové oblasti, jakožto testovací domény, která naznačuje případné rozšíření modelu pro realistickou geometrii. Jako poslední se zabýváme problémem filtrace. Zde formulujeme podmínky na hranici membrány pro proudění a tok koncentrace, které formálně popisují částečnou polopropustnost membrány, hromadění koncentrace před membránou (v případě jednosměrného toku) a vliv osmotického tlaku.

Klíčová slova: Synoviální tekutina, zobecněná viskozita, lineární viskoelasticita, Navierovy– Stokesovy rovnice, zobecněné Sobolevovy prostory, $C^{0,\alpha}$–regularita, stabilizované metody konečných prvků, transport přes membránu.

Titel: Biochemische und Mechanische Prozesse von synovialen Fluiden – Modellierung, mathematische Analysis und Computersimulationen

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Kurzfassung: Ein synoviales Fluid ist eine polymerische Flüssigkeit, die sich im Allgemeinen wie eine viskoelastische Flüssigkeit verhält. Dieses Verhalten ist auf die Wirkung enthaltender Polysaccharide, sogenannte Hyaluronen, zurückzuführen. In dieser Arbeit werden biologische und biochemische Eigenschaften von synovialen Flüssigkeiten untersucht, sowie deren komplexe Rheologie und die Interaktion mit synovialen Membranen bei Filterprozessen. Vom mathematischen Standpunkt aus modellieren wir das synoviale Fluid als ein viskoses, inkompressibles Fluid, für welches wir ein neues Potenzgesetz–Modell entwickeln, wobei der Exponent im Potenzgesetz von der Konzentration der Hyaluronen abhängt. Ein solches Modell ist dazu geeignet, um ein synoviales Fluid zu beschreiben, solange es zu keinen plötzlichen Impulsen kommt. Des Weiteren beschreiben wir geeignete lineare viskoelastische Modelle, welche das viskoelastische Verhalten der synovialen Fluide bei kleinen Deformationen als eine Funktion der Konzentration beschreiben. In weiterer Folge werden die zugehörigen Modellgleichungen betrachtet, und zwar die Inkompressibilitätsbedingung, das Momentengleichgewicht – die verallgemeinerten Navier–Stokes Gleichungen und die Konvektionsdiffusionsgleichung für die Konzentration des Hyaluron. Das Kapitel zur mathematischen Analysis konzentriert sich im Wesentlichen auf die Formulierung des stationären Problems im schwachen Sinne und den Beweis der Existenz einer zugehörigen schwachen Lösung für den Fall einer verallgemeinerten Viskosität mit einer vom Potenzgesetzexponenten abhängenden Konzentration. Dazu verwenden wir die Methode der monotonen Operatoren, wobei der Beweis der Hölder–Stetigkeit der Konzentration den Hauptteil darstellt. Im Kapitel zur Numerik werden verschiedene stabilisierte Finite Elemente Methoden für Probleme mit dominierender Konvektion betrachtet, welche typisch für synoviale Fluide sind. Numerische Beispiele werden für rechteckige Gebiete präsentiert, um eine Einsicht in das Verhalten des Fluids zu bekommen und um es zukünftig in realistischeren Gebieten lösen zu können. Des Weiteren werden die Lösungen der verschiedenen Viskositätsmodelle für die einzelnen stabilisierten Finite Elemente Methoden miteinander verglichen. Im letzten Kapitel wird ein mathematisches Modell für die Strömung und den Transport einer verdünnten Lösung betrachtet, welches anschließend auf das synoviale Fluid übertragen wird. Dabei sind die Gebiete durch eine semipermeable Membran getrennt. Wir formulieren Transmissionsbedingungen für die Strömung und die Konzentration der Lösung auf der Membran. Dabei kommt es zu einem teilweisen Rückgang der Konzentration, welcher auf die Eigenschaften der Membran zurückzuführen ist. Die Ablagerung der Lösung an der Membran und der Einfluss der Konzentration der Lösung auf die Strömung ist als osmotischer Effekt bekannt.

Schlüsselwörter: Synoviale Flüssigkeiten, verallgemeinerte Viskosität, lineare Viskoelastizität, Navier–Stokes Gleichungen, verallgemeinerte Sobolev Räume, $C^{0,\alpha}$ –Regularität, Stabilisierte Finite Elemente Methoden, Membrantransport.

Title: Biochemical and mechanical processes in synovial fluid – modeling, mathematical analysis and computational simulations

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Abstract: Synovial fluid is a polymeric liquid which generally behaves as a viscoelastic fluid due to the presence of polysaccharide molecules called hyaluronan. In this thesis, we study the biological and biochemical properties of synovial fluid, its complex rheology and interaction with synovial membrane during filtration process. From the mathematical point of view, we model the synovial fluid as a viscous incompressible fluid for which we develop a novel generalized power–law fluid model wherein the power–law exponent depends on the concentration of the hyaluronan. Such a model is adequate to describe the flows of synovial fluid as long as it is not subjected to instantaneous stimuli. Moreover, we try to find a suitable linear viscoelastic model which can describe the viscoelastic responses of synovial fluid during small deformation experiments, as, again, a function of concentration. Then, we consider the governing equations, namely the constraint of incompressibility, the balance of linear momentum – generalized Navier–Stokes equations and the convection–diffusion equation for the concentration of hyaluronan. The part of mathematical analysis is focused on the formulation of the stationary problem in the weak sense and the proof of the existence of the corresponding weak solution, for the case of a generalized viscous problem with concentration dependent power–law exponent. For that, we use the method of monotone operators, where the essential role plays the proof of Hölder continuity of the concentration. In the numerical part of the thesis, we consider different numerical stabilization methods which ensure better numerical solvability of the system with dominant convection, as is typical for synovial fluid flow. By their implementation into already existing code, we numerically solve for the flow of the synovial fluid in a rectangular cavity, in order to gain some insight into the response of such a fluid so that we can solve in the future the flows in more realistic geometries. We also compare the solutions obtained with different models of generalized viscosities and different stabilization techniques. As last, we propose a mathematical model for flow and transport processes of diluted solutions, and afterwards of synovial fluid, in domains separated by a leaky semipermeable membrane. We formulate transmission conditions for the flow and the solute concentration across the membrane which take into account the property of the membrane to partly reject the solute, the accumulation of rejected solute at the membrane, and the influence of the solute concentration on the volume flow, known as the osmotic effect.

Keywords: Synovial fluid, generalized viscosity, linear viscoelasticity, Navier–Stokes equations, generalized Sobolev space, $C^{0,\alpha}$–regularity, stabilized finite element methods, membrane transport.

1 Introduction

1.1 Why is the mathematical modeling of synovial fluid important?

Mathematical studies of mechanical and rheological behavior of systems close or directly connected with human physiology play an important role in several areas of bio–engineering and medicine. One of the best examples is the mathematical modeling and consecutive computational simulations which can predict important features of particular organs, tissues or whole systems, otherwise difficult or even impossible to determine *in vivo*. Of course, one needs to have by hand reasonable mathematical models, suitable (experimental) data, fast reliable numerical methods, software and hardware, and experts who are able to interact with the models and interpret the results. For example, the modeling of cardiovascular systems, especially of the vessel parts and their interaction with blood, modeling of the heart muscle or evolution of the aneurysms, or modeling in the field of neurology, becomes a standard part of modern medical investigations. For these reasons, the fundamental research on biological systems plays a crucial role for the future medical treatments or bio–engineering development.

In our case, we are focused on the understanding of the physiology and mechanisms concerning human movable joints, more precisely, the mathematical description of the synovial fluid rheology. To this date, there have not been fully understood the conditions and origins of some pathological diseases, the mechanics of human joint lubrication or shock load absorbing, for which the synovial fluid[1] is an essential medium. These features could be, nevertheless, a great enhancement in the engineering of designing the life–long functional joint prostheses or in the disease treatment.

1.2 State of the art and main aims of the thesis

Mathematical modeling. To our knowledge, there are several models describing the synovial fluid, see for example Rudraiah et al. (1991), Lai et al. (1978), Morris et al. (1981). Nevertheless, they are great simplifications of the otherwise complex rheology of synovial fluid, usually based on the simple experiments adapted for the linear theories, both viscoelastic and viscous. In this we see the main obstacle in development of reliable models capturing the most important non–Newtonian features of synovial fluid. To be more specific, the synovial fluid has been modeled as either viscous shear–thinning fluid or linear viscoelastic fluid–like material. The importance of the concentration of the molecules of hyaluronan, which determines its non–linear character, was often undermined or completely neglected. **The aim**: Our aim is to study such rheological behavior of synovial fluid, based on the existing experimental literature, and create novel viscous and viscoelastic models, describing the influence of concentration. Mainly, we focus on the description of viscous responses of synovial fluid, as a fluid thinning the shear. Moreover, we intend to study the filtration process of the synovial fluid through the synovial membrane and, on that basis, to create a reasonable, nevertheless phenomenological, model for the synovial membrane transport.

Mathematical analysis. The existence theory of incompressible Navier–Stokes equations with the viscosity of power–law type has been studied for more than 40 years, see for example Ladyzhenskaya (1967), Málek et al. (1993), Frehse et al. (2000), Diening et al. (2010). On the other hand, the study of non–trivial coupling of the Navier–Stokes equations with another governing equation, for example for temperature or electric field, through the power–law index has been introduced in the recent decade. For instance in Růžička (2004), the variable index is considered as a function of the electric field, in simplification of the space variable, or in Antontsev and Rodrigues (2006), the variable index is temperature dependent. The latter system is the closest to ours, nevertheless the proof is not constructive, based on the use of the fixed point theory. Moreover, the diffusion of the temperature is considered to be linear, and thus the standard Laplacian theory can be used to obtain necessary Hölder continuity of the temperature and consequently of the variable power–law index. To the best of our knowledge, the theory is not known for the case of the non–linear diffusion.

The aim: Since we model the flow of synovial fluid by the incompressible Navier–Stokes equations coupled with the convection–diffusion equation for the concentration, and, the viscosity

[1] Here, of course, other parts of synovial joints, like cartilage and tendons, are essential and their mathematical modeling as well as the understanding of their mutual interaction is necessary.

of synovial fluid by a power–law type model with the shear–thinning exponent dependent of the concentration, the mathematical approach introduced by Růžička (2004) needs to be adopted for our case as well. The aim is then to prove the existence of the weak solution for the stationary problem with Dirichlet boundary conditions for both the velocity and the concentration in the framework of the generalized Sobolev spaces.

Numerical methods. In the case of dominated convection of the concentration, as is the case of hyaluronan in synovial fluid, the numerical method needs to be adapted by an introduction of suitable numerical stabilization. To this date, there are several stabilized finite element methods, nevertheless, their application needs to be considered with respect to several aspects. Since the objective of our study is a physical variable, the positiveness of the scheme plays a crucial role. On the other hand, one needs to consider the convergence rate and, particularly, the requirements for implementation and following numerical computations. For these reasons, the streamline upwind Petrov–Galerkin method (Johnson (1982), Hughes and Franca (1989)), continuous interior penalty method (Douglas and Dupont (1976), Turek and Ouazzi (2007)) and Galerkin least squares method (Jiang (1998), Bochev and Gunzburger (2009)) seems suitable for our case.

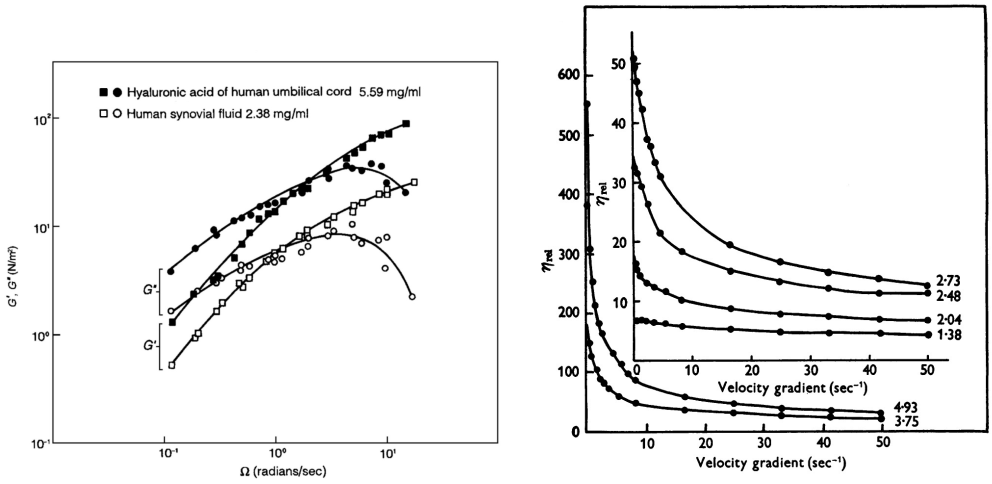
The aim: We intend to implement different stabilizations into existing finite element code and study their characters in connection with the problem of the flow of the synovial fluid. Then, we intend to compute and compare the numerical solutions for different viscosity models and different stabilized finite elements. As last, we aim to simulate the transport of the synovial fluid through the synovial membrane.

2 Rheology of synovial fluid

First intensive scientific investigations of composition and properties of synovial fluid date back to the late thirties of the last century (Meyer et al. (1939), Ropes et al. (1940), Davies (1946)), which were shortly followed by deeper study of the special rheological properties of synovial fluid attributed to the main chemical constituent of synovial fluid, hyaluronan, (Ogston and Stanier (1953), Sunblad (1953)). For this reason, it is necessary to understand the physico–chemical properties of hyaluronan molecules in liquid solutions, on which we can build phenomenologically justified mathematical model describing synovial fluid mechanical responses.

2.1 Viscoelastic properties

Physiological hyaluronate solutions at neutral pH, like in synovial fluid, feature an extraordinary viscoelastic characteristic. Typical and widely used experimental test measuring viscoelastic responses of synovial fluid is the (small amplitude) oscillatory measurement for wide range of frequencies. The response, see Fig. 1(a), is presented in terms of G' and G'', where G' is associated with elastic phenomena and thus called storage modulus, while G'' is associated with viscous dissipation of energy, and it is, therefore, called the loss modulus, for definition see Chapter 3 of the thesis. At low frequencies of oscillation, loss modulus G'' is evidently greater than the store modulus G', in other words viscous responses are dominant to elastic responses, which is the consequence of the fact that at lower frequencies of oscillations the molecular network is transient, or in other words, the period of oscillations is long relative to the lifetime of hyaluronan chain–to–chain interactions and thus the rearrangement of the molecules occurs. Hence the characteristic viscous flow. On the other hand, at higher frequencies elastic responses are predominant which is the consequence of the storing energy in elastic short–time network deformation. The magnitude of the moduli (both G' and G'') is increasing with the concentration which is correlated with the “density” of hyaluronan mesh in the solution. The characteristic crossover of G' and G'' is strongly influenced by the pH, enzymatic activity, protein or cell concentration, and by the concentration and length/molecular weight of hyaluronan molecules. While elastic part in synovial fluid response is important for joint stabilization during the joint loading and high oscillatory shearing (like during running), the viscous part of the response is crucial for joint lubrication at lower rates of the movement. Even though, it is quite tempting to distinguish the elastic responses from viscous ones, it is not possible to separate them, and thus one has to keep in mind that terms “viscous–like” and “elastic–like” are meant in the sense of predominance.



(a) (b)

Figure 1: (a) Small deformation experiment of hyaluronan solution. Dynamic storage moduli G' and dynamic loss moduli G'' plotted against frequency of oscillation in logarithmic scale. Experiment was done in Weissenberg Rheogoniometer. From Balazs and Gibbs (1970). (b) Shear–thinning experiment on synovial fluid over a wide range of physiological concentration of hyaluronan. Relative viscosity η_{rel} against velocity gradient. Viscosity was measured in the Couette viscosimeter. From Ogston and Stanier (1953).

2.2 Bulk flow properties

During unloaded non–oscillating simple shear flows synovial fluid exhibit characteristic viscous behavior. Typical experimental setting for viscosity measurement is then the flow in the Couette viscosimeter, see the example of the experimental result in Fig. 1(b). As one can see, synovial fluid viscosity is not constant as in the case of Newtonian fluid but it exhibits strong shear–thinning, peculiar to polymeric solutions. The difference is, that in the case of hyaluronan solution, this phenomena is observed already at very low concentration due to the extraordinar molecule length. The apparent viscosity of hyaluronan solution is increasing with decreasing rate of shear while at higher rates of movement the viscosity drops. This entails that the joint is "dynamically" stabilized and well lubricated during slower motions but at higher rates of movement the drag of the bones faced against each other in synovial joint is significantly reduced. Here, again, the concentration of hyaluronan in synovial fluid significantly influences the behavior of the mechanical response, as expressed in Fig. 1(b). It is observed that for concentration of hyaluronan close to 1mg/ml, by which the hyaluronan chains are more or less separated, the apparent viscosity becomes almost Newtonian and the shear–thinning vanishes.

The shear thinning of synovial fluid is the well–known phenomena but also other non–Newtonian effects at transient flow were described in relation to synovial fluid. Davies and Palfrey (1968) and King (1966) reported the normal stress differences, one of the physical consequence of non-zero normal stress differences is the effect "die swell". The stress relaxation from modeling point of view was studied for example by Mow and Lai (1979). We, nevertheless shall not describe such responses.

3 Modeling of viscous responses

In this section, we present a new phenomenological model for the generalized viscosity of normal[2] synovial fluid which captures the shear–thinning effect. The rheological model of generalized viscosity shall be also, besides the shear rate, dependent of concentration of hyaluronic acid which

[2]By normal synovial fluid we mean the synovial fluid with rheological responses and biochemical composition as that of a healthy young individual.

plays an important role in mechanical responses of synovial fluid. These rheological properties of synovial fluid were closely described in Chapter 4 of the thesis.

3.1 Constitutive equation

Even though synovial fluid is a complex biological material, a mixture of ultrafiltrated blood plasma and hyaluronan molecules, under normal conditions, it can be approximated as an isotropic incompressible homogeneous single constituent fluid.

Since the response of the fluid depends on the nature of the flow, the model for synovial fluid must depend on the "dynamics" of the flow. Higher shear rates imply higher alignment of the chains and thus a decrease in the viscosity. On the other hand, the influence of concentration works contrariwise because higher concentration of hyaluronan implies higher enlacement of the chains, which increases the viscosity. The restriction of the current models to constant concentration is not appropriate for modeling the synovial fluid behavior under physiological conditions since, in real joints, the concentration of hyaluronan varies. For example, it has been shown (see Coleman et al. (1999)) that hyaluronan creates some kind of a boundary layer near the synovium with concentration five times higher than in the central parts of the synovial joint cavity (this is the consequence of the varying hyaluronan production in the synovium combined with the flow conditions). Thus, we assume that the viscosity μ of the synovial fluid is a function of concentration and shear rate and propose the constitutive equation for synovial fluid when it flows:

$$\boldsymbol{T} = -p\boldsymbol{I} + 2\mu(c, |\boldsymbol{D}|^2), \tag{1}$$

where $\boldsymbol{T}$ is the stress tensor, $\boldsymbol{D}$ is the symmetric part of velocity gradient, $\boldsymbol{I}$ is the identity tensor, p is the hydrodynamic pressure and c is the concentration.

3.2 Model for viscosity

Due to the shear–thinning effect of synovial fluid, we consider only models for the viscosity μ that belong to the power–law class. We compare the model introduced in the literature (for instance Lai et al. (1978); Laurent et al. (1995)), where the varying concentration plays the role only as a "scaling factor" of the shear rate response

$$\mu = \mu_0 e^{\alpha c} \left(1 + \gamma|\boldsymbol{D}|^2\right)^n, \tag{Model 1}$$

with our new model that takes into account the concentration influence on the shear–thinning effect itself, specifically the shear–thinning index of the considered power–law model

$$\mu = \mu_0 \left(\beta + \gamma|\boldsymbol{D}|^2\right)^{n(c)}. \tag{Model 2}$$

In both models, the parameters α, β, γ and n are unknown and they have to be determined by comparison with experiment. Since the synovial fluid with zero concentration of hyaluronan is basically blood plasma, the parameter μ_0 should represent the plasma viscosity. Here, as one can see, the Model 1 exhibit wrong characteristic for this limiting case. When the concentration tends to zero, the fluid should stop to feature any non–Newtonian effects any more and the viscosity should become constant with the value of the plasma. In contrast to the Model 2, the Model 1 captures the shear–thinning effects always.

We decided to use the exponential behavior with one free parameter

$$n(c) = \frac{1}{2}\left(e^{-\alpha c} - 1\right), \tag{Model 2a}$$

and a simple rational function with two free parameters

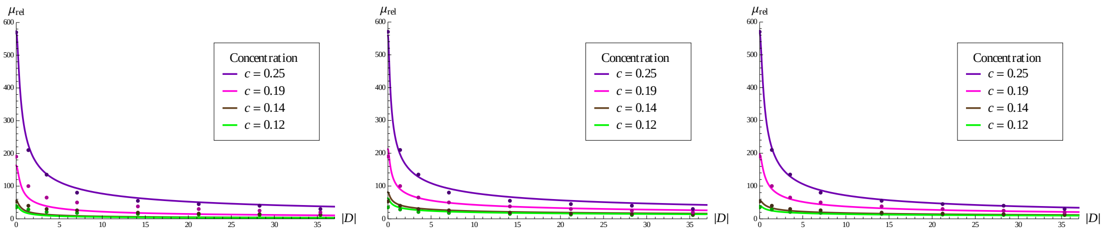
$$n(c) = \omega\left(\frac{1}{\alpha c^2 + 1} - 1\right), \tag{Model 2b}$$

which both satisfy the required conditions, and, mainly, the fitting procedures lead to better results than for any other "simple" function with only one or two free parameters.

3.3 Identification of the model parameters – fitting procedure

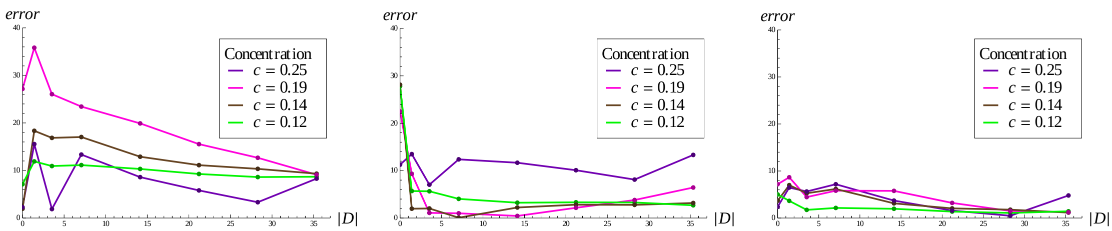
Each of the models introduced above contains some unknown parameters. For Model 1 and Model 2a they are three, α, γ, n and α, β, γ, respectively, and in Model 2b we have four unknown parameters α, β, γ, ω. We find the values of these parameters by a fitting technique applied on the experimental data from Ogston and Stanier (1953). Specifically, we use the least square method.

We present the final fits in Fig. 2. From the fitting procedure, we also present closer diagnostic of the fit departure in each experimental measurement point, in Fig. 3.



(a) $\mu_0\, e^{\alpha c}(1+\gamma\,|\boldsymbol{D}|^2)^n$ (b) $\mu_0\,(\beta+\gamma\,|\boldsymbol{D}|^2)^{\frac{1}{2}(e^{-\alpha c}-1)}$ (c) $\mu_0\,(\beta+\gamma\,|\boldsymbol{D}|^2)^{(\omega\,(1/(\alpha c^2+1)-1))}$

Figure 2: Relative viscosity against shear rate for different physiological concentrations. Graphs of the relative viscosity of all the models show the fitted curves and the experimental data (points) which were taken for the fitting procedure. Here we use the notation from Ogston and Stanier (1953) for $\mu_{\rm rel} = \mu/\mu_{\rm ref}$, where $\mu_{\rm ref}$ refers to the viscosity of the glycerol solution.



(a) Model 1 (b) Model 2a (c) Model 2b

Figure 3: Departures of considered models from experimental data displayed as function of shear rate for different concentrations.

The computed error indicates that the best fit of the experimental data is the Model 2b. As we can see, error of Model 2a is accumulated at the very small shear rates while the rest of the fit is comparable with the fit of Model 2b. Still, from all mentioned above, the Model 1 can fit the data reasonably well for some specific applications in the range of the concentrations in which it was fitted, this means in the range of $0.14 - 0.25$. Moreover, even though the models of class 2 extrapolate the viscosity values for higher concentrations accurately, their reasoning can be validated only by experiments for extended range of concentrations.

4 Modeling of viscoelastic responses

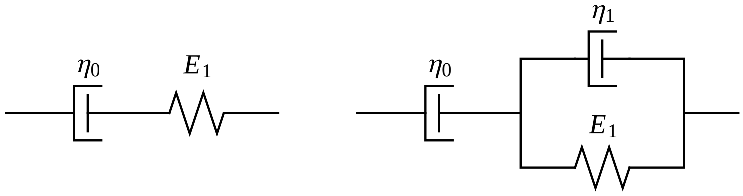
Fitting fully non–linear viscoelastic model to experimental data we have at hand would be at this point useless with respect to their linear character. Thus, we lay stress on the famous Oldroyd–B model in comparison to the model of Maxwell.

Let us present the explicit functions for dynamic moduli G' and G'' for small amplitude oscillatory test in the case of Maxwell and Oldroyd–B models. The (one–dimensional) deformation during such test with frequency of oscillations ω is given by sinusoidal shear strain γ and we call $\dot{\gamma}$ the shear rate. Then the shear stress τ of the Cauchy stress tensor is decomposable into the sines and cosines, as can be expressed as

$$\tau = \gamma_0\{G'(\omega)\cos(\omega t) + G''(\omega)\sin(\omega t)\}. \tag{2}$$

4.1 Mechanical analogues of Maxwell and Oldroyd–B models

Let us introduce the representation of 1–dimensional Maxwell and Oldroyd models by mechanical analogues.



(a) Maxwell (b) Oldroyd–B

Figure 4: (a) Spring–dashpot analogue for the Maxwell fluid. Parameters η_0 and E_1 are the dashpot and spring constants, respectively. (b) Spring–dashpot analogue for the Oldroyd fluid model. Parameters η_0, η_1 and E_1 are the dashpots and spring constants, respectively.

Maxwell

Even though Maxwell himself did not mention dashpot/spring in his famous work (Maxwell (1867)), his model is based on superposition of viscous and elastic forces, which refers to connection of one spring and one dashpot in series, see Fig. 4(a). If we balance the total force with the total displacement of such assemblage, we obtain the (one–dimensional) formula of the Maxwell fluid. After the generalization of the model to three dimensions and following calculations, we obtain dynamic moduli for Maxwell model in terms of "viscosity" η_0 and "elasticity" E_1 as

$$G' = \frac{E_1 \eta_0^2 \omega^2}{E_1^2 + \eta_0^2 \omega^2}, \quad G'' = \frac{E_1^2 \eta_0 \omega}{E_1^2 + \eta_0^2 \omega^2}. \tag{3}$$

Oldroyd

Similar analogue can be constructed for the Oldroyd fluid. Since the model has to have three parameters and it should describe the fluid–like material, the composition of dashpots/spring is unique, as depicted in Fig. 4(b). Again, we express G' and G'' in terms of η_0, η_1 and E_1

$$G' = \frac{E_1 \eta_0^2 \omega^2}{E_1^2 + (\eta_0 + \eta_1)^2 \omega^2}, \quad G'' = \frac{\eta_0 \omega \left(E_1^2 + \eta_1(\eta_0 + \eta_1)\omega^2\right)}{E_1^2 + (\eta_0 + \eta_1)^2 \omega^2}. \tag{4}$$

4.2 Finding fits to data

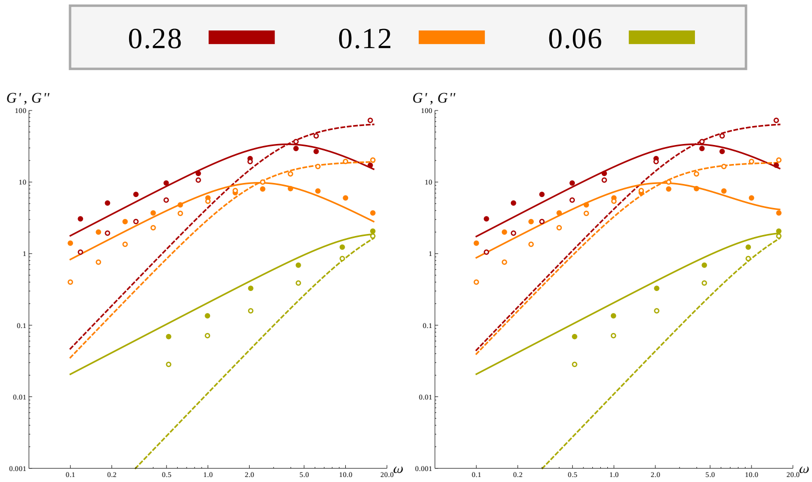
Our goal was to find the best possible fit to available experimental data by the use of the least squares method. We are considering only linear viscoelastic models of Maxwell and Oldroyd–B.

We have fitted the formulas of G' and G'' of both models, (3) and (4), to the experimental data for separate concentrations but simultaneously for both moduli. The results are shown in the following Fig. 5

As we can see, the fits for Maxwell and Oldroyd–B do not differ almost at all. This is caused by the smallness of the third parameter η_1 in Oldroyd–B model, fitted as numerical zero for two cases from three, which represent with respect to the Maxwell fluid the additional dashpot. This suggests, that in the range of linear viscoelasticity of synovial fluid the Maxwell model could be sufficient. Thus, in what follows, we shall assume the Maxwell model, only.

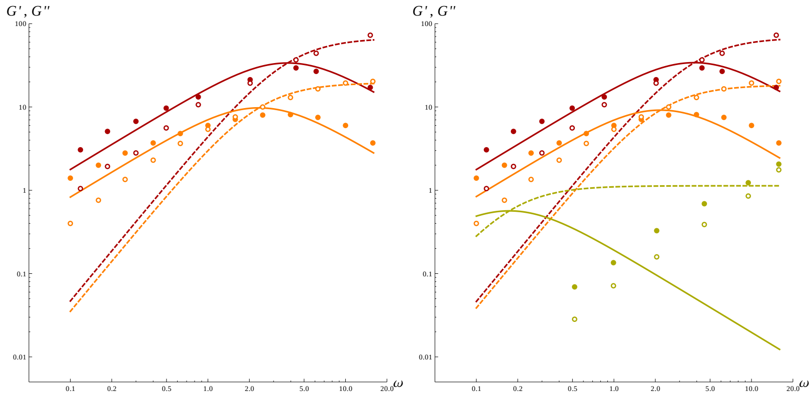
Based on the results of the separate fits, we have suggested a possible phenomenological dependence of the material parameters on the concentration, $E_1 = a_1 c + b_1$, $\eta_0 = b_2 e^{a_2 c}$, and after we fitted the models again, similtaniously to all concentration data, see results in Fig. 6.

For the experiment of small deformations, e. g. amplitudes and frequencies of oscillations are small enough, the models were able to fit the data only approximately. This suggest, that even for small deformations the fluid exhibit some non–linear characteristic. Since we have no more



(a) Maxwell – logarithmic scale (b) Oldroyd–B – logarithmic scale

Figure 5: Fitted curves of dynamic moduli for three different concentrations. The fits are performed separately. Experimental data are represented by points, solid points are data of dynamic loss modulus G'', circles represent dynamic storage modulus G'. Solid lines are calculated curves of dynamic loss modulus and dashed lines are calculated curves of dynamic modulus.



(a) 2data sets – log scale (b) 3data sets – log scale

Figure 6: Resulting curves of fitted dynamic moduli to two (left) and three (right) sets of experimental data corresponding to the concentrations of $\{0.12, 0.28\}$ and $\{0.06, 0.12, 0.23\}$, respectively. Dynamic loss modulus – solid lines, dynamic storage modulus – dashed lines; solid points – dynamic loss modulus experimental data, circles – dynamic storage modulus experimental data.

information about the concentration/frequency dependencies, we can not point out other aspects influencing the dynamic moduli, and thus improve the considered phenomenological model.

5 Problem formulation: governing equations and mathematical analysis

5.1 Governing equations

We describe the flow of synovial fluid in the terms of the velocity field $\boldsymbol{v}$ and the pressure field p which are governed by the *generalized Navier–Stokes equations* and the constrain of *incompressibility*. The concentration distribution, the scalar field c, which influences the flow only through the material parameter(s) in constitutive equation(s) is described by the *convection–diffusion equation*. The system of non–dimensionalized governing equations takes the form

$$\operatorname{div} \boldsymbol{v} = 0, \tag{5}$$

$$\operatorname{div}(\boldsymbol{v} \otimes \boldsymbol{v}) - \operatorname{div} \boldsymbol{S}(c, \boldsymbol{D}(\boldsymbol{v})) = -\nabla p + \boldsymbol{f}, \tag{6}$$

$$\operatorname{div}(\boldsymbol{v}c) - \operatorname{div} \boldsymbol{q}_c(c, \nabla c, \boldsymbol{D}(\boldsymbol{v})) = 0. \tag{7}$$

with the extra stress tensor $\boldsymbol{S}$ and concentration flux vector $\boldsymbol{q}_c$ given by

$$\boldsymbol{S}(c, \boldsymbol{D}(\boldsymbol{v})) = \frac{2}{\mathrm{Re}} \left(\kappa_1 + \kappa_2 \, |\boldsymbol{D}(\boldsymbol{v})|^2\right)^{\frac{p(c)-2}{2}} \boldsymbol{D}(\boldsymbol{v}), \tag{8}$$

$$\boldsymbol{q}_c(c, \nabla c, \boldsymbol{D}(\boldsymbol{v})) = \frac{1}{\mathrm{Pe}} \boldsymbol{K}(c, \boldsymbol{D}(\boldsymbol{v})) \nabla c, \tag{9}$$

where $\boldsymbol{f}$ represents the specific external body force field, $\boldsymbol{K}$ is the diffusivity, the characteristic of solute with respect to the solvent, and, Re, Pe are the reduced Reynolds and Péclet numbers, respectively, κ_1, κ_2 are constants. Moreover, the power–law index, as used before, is expressed as $n(c) = \frac{p(c)-2}{2}$.

5.2 Survey of previous results

The models with non–constant power–law index, developed for electrorheological fluids, are studied for instance in Růžička (2000), Růžička (2004). For this kind of fluids the extra stress tensor is (non–trivially) dependent of electric field $\boldsymbol{E}$ and thus the Navier–Stokes equation has to be solved with the (quasi-static) Maxwell's equations. Nevertheless, the governing equations are essentially uncoupled thus the Maxwell's equations can be solved first. The solution of electric field can be then considered as a known function, resulting that the problem reduces to the problem of incompressible Navier–Stokes problem with extra stress tensor having the growth property of $|\boldsymbol{S}| \leqslant C(1 + |\boldsymbol{D}(\boldsymbol{v})|^2)^{\frac{p(x)-2}{2}}$, where $p(x) := p(|\boldsymbol{E}(x)|^2)$ is given variable function (under some assumption of Hölder continuity), satisfying $1 < p^- < p(x) < p^+ < \infty$. Using the theory of monotone operators, the author was able to prove the existence of a weak solution for lower bound $p^- \geqslant \frac{9}{5}$, and in the case of stationary problem the existence result was extended to $p^- \geqslant \frac{6}{5}$ by Diening et al. (2008), by the means of the method of Lipschitz approximations.

The closest system to ours, (5)–(7), is studied in Antontsev and Rodrigues (2006). The authors consider the stationary system of Navier–Stokes equations coupled with equation for thermal diffusion obtained as Oberbeck–Boussinesq approximation of Fourier equation for the temperature, under the consideration that the power–law index of the generalized viscosity is dependent of temperature θ. For Dirichlet boundary conditions, for both velocity and temperature, they prove the existence of the global weak solution for the case of $\frac{9}{5} \leqslant p_\star < p(\theta) < \infty$ for large and sufficiently smooth data. There, the important assumption simplifying the proof is the assumption of the constant diffusion tensor $\boldsymbol{D}_\theta$, which ensures the Hölder continuity of the temperature.

5.3 Formulation of stationary problem

For definitions of the spaces and corresponding norms, as well as generalization of standard theorems of fluid dynamics analysis, see Chapter 7 of the thesis.

Let us consider the stationary problem (5)–(7) being defined on an open bounded set $\Omega \subset \mathbb{R}^d$, $d \geqslant 3$, with Lipschitz boundary $\partial\Omega$, and Dirichlet boundary conditions for both velocity and concentration

$$\boldsymbol{v}(x) = \boldsymbol{0}, \quad \text{and} \quad c(x) = c_d \quad \text{on } \partial\Omega. \tag{10}$$

We assume that $\boldsymbol{S} : \mathbb{R}_0^+ \times \mathbb{R}^{d\times d}_{sym} \to \mathbb{R}^{d\times d}_{sym}$ fulfills following growth, strict monotonicity and coercivity conditions for all $c \in \langle \min_{x\in\partial\Omega} c_d, \max_{x\in\partial\Omega} c_d\rangle$ and $\boldsymbol{D}$, $\boldsymbol{D}_1$, $\boldsymbol{D}_2 \in \mathbb{R}^{d\times d}_{sym}$

$$|\boldsymbol{S}(c, \boldsymbol{D})| \leqslant C_1(|\boldsymbol{D}|^{p(c)-1} + 1), \tag{11}$$

$$(\boldsymbol{S}(c, \boldsymbol{D}_1) - \boldsymbol{S}(c, \boldsymbol{D}_2)) \cdot (\boldsymbol{D}_1 - \boldsymbol{D}_2) > 0 \quad \boldsymbol{D}_1 \neq \boldsymbol{D}_2, \tag{12}$$

$$\boldsymbol{S}(c, \boldsymbol{D}) \cdot \boldsymbol{D} \geqslant C_2(|\boldsymbol{D}|^{p(c)} + |\boldsymbol{S}(c, \boldsymbol{D})|^{p'(c)} - 1), \tag{13}$$

where $p(\cdot)$ is Hölder continuous function such that $1 < p^- < p(\cdot) < p^+ < \infty$, and the concentration flux vector $\boldsymbol{q}_c$ satisfies the (9), where $\boldsymbol{K}(c, |\boldsymbol{D}(\boldsymbol{v})|) : \mathbb{R}_0^+ \times \mathbb{R}_0^+ \to \mathbb{R}^{d\times d}$ is continuous mapping with $K_{i,j} \in L^\infty(\Omega)$ such that the flux vector fulfills following conditions

$$|\boldsymbol{q}_c(c, \xi, \boldsymbol{D})| \leqslant K_1 |\xi|, \tag{14}$$

$$\boldsymbol{q}_c(c, \xi, \boldsymbol{D}) \cdot \xi \geqslant K_2 |\xi|^2 . \tag{15}$$

Above, $C_1, C_2, K_1, K_2 \in (0, \infty)$ are constants and $\boldsymbol{A} \cdot \boldsymbol{B}$ is notation for the scalar product between two tensors. Moreover, we require that there exists a function

$$\tilde{c}_d \in C^{0,\beta} \cap W^{1,2}(\Omega),\ \beta > 0,\ \text{such that } tr(\tilde{c}_d) = c_d \text{ on } \partial\Omega. \tag{16}$$

For the problem (5)–(7), (10) we proved the following existence theorem.

Theorem 5.1. *Let $\Omega \subset \mathbb{R}^d$ be a bounded domain with Lipschitz boundary $\partial\Omega$ and let $p(\cdot)$ be a Hölder continuous variable exponent such that $p^- \leqslant p(\cdot) \leqslant p^+ < \infty$, where $p^- \geqslant \frac{3d}{d+2}$ and $p^- > \frac{d}{2}$. If $\boldsymbol{f} \in W^{-1,p^{-\prime}}(\Omega)$, $\boldsymbol{S}$ and $\boldsymbol{q}_c$ satisfy conditions* (11)–(15) *and there exists a function $\tilde{c}_d$ such that* (16) *holds and*

$$\exists \beta > 0 :\ \forall x_0 \in \Omega\ \forall R > 0 : \int_{B_R(x_0)\cap\Omega} \frac{|\nabla \tilde{c}_d|^2}{R^{d-2+2\beta}} \leqslant C_3, \quad C_3 \in (0,\infty) \textit{ is a constant,}$$

then there exists a weak solution $(\boldsymbol{v}, c)$ of the problem (5)–(7) *satisfying the boundary conditions* (10) *such that*

$$\boldsymbol{v} \in W^{1,1}_{0,\mathrm{div}}(\Omega), \quad \boldsymbol{D}(\boldsymbol{v}) \in L^{p(c)}(\Omega),$$
$$(c - \tilde{c}_d) \in C^{0,\alpha}(\Omega) \cap W^{1,2}_0,$$

for some $0 < \alpha \leqslant \beta$, α being function of Ω, K_1, K_2, and $(\boldsymbol{v}, c)$ fulfills the following weak formulation of the problem

$$-\int_\Omega \boldsymbol{v} \otimes \boldsymbol{v} \cdot \nabla \boldsymbol{\psi}\, dx + \int_\Omega \boldsymbol{S}(c, \boldsymbol{D}(\boldsymbol{v})) \cdot \boldsymbol{D}(\boldsymbol{\psi})\, dx = \langle \boldsymbol{f}, \boldsymbol{\psi} \rangle \qquad \forall \boldsymbol{\psi} \in W^{1,p(c)}_{0,\mathrm{div}}(\Omega),$$
$$-\int_\Omega \boldsymbol{v} c \cdot \nabla \varphi\, dx + \int_\Omega \boldsymbol{q}_c(c, \nabla c, \boldsymbol{D}(\boldsymbol{v})) \cdot \nabla \varphi\, dx = 0 \qquad \forall \varphi \in W^{1,2}_0(\Omega).$$

To the best of our knowledge, this is the first result concerning the existence of the system (5)–(7), (10) where the variable exponent is concentration dependent. Since the spaces where we look for the weak solution are "dependent" on the solution itself, we a priory do not know them, and thus, a more general concept of function spaces with variable exponent $p(\cdot)$, the so–called generalized Sobolev Spaces, needs to be involved. Nevertheless, certain restriction on $p(\cdot)$ is required, namely its Hölder continuity, a crucial assumption for the density of smooth functions in generalized Sobolev spaces, embedding theorems and Korn's inequality.

In the case, that the diffusivity matrix in the equation for the concentration is constant, or only concentration dependent, the use of standard theory for Laplace operator, see Ladyzhenskaya and Ural'tseva (1968), ensures the Hölder continuity of the concentration, and thus of the variable exponent. In contrast to Antontsev and Rodrigues (2006), where authors assumed the constant diffusivity matrix for similar equation of thermal diffusion, we assume the diffusivity to be non–constant, and thus, we a priori do not know if the concentration satisfies the Hölder continuity. Nevertheless, this we prove for certain, but not restrictive, assumptions by the introduction of Green test functions in the weak formulation for convection–diffusion equation. The proof of Hölder continuity of concentration is based on the results of de Giorgi (1957) and Nash (1958), and application of the Morrey's lemma.

In such setting, we can use the theory of monotone operators to prove the desired existence. Nevertheless, this is restricted to the assumption of $p^- \geqslant \frac{3d}{d+2}$, in 3D setting $p^- \geqslant \frac{9}{5}$, which is required for the convective term $(\boldsymbol{v} \otimes \boldsymbol{v})$ being well defined for the test functions from $W^{1,p(c)}_{0,\mathrm{div}}$. Eventual relaxation of the lower bound of p would require to generalize the approach of Diening et al. (2008), the Lipschitz truncation method.

The second restriction on the minimal value of p in Theorem 5.1, explicitly $p^- > \frac{d}{2}$, comes from the requirement of c being Hölder continuous. The prove of the Hölder continuity is based on de Giorgi result for elliptic equation with measurable coefficients and the right hand side in some $W^{-1,q'}$ space with $q > d$. In our setting this means that we require $\mathrm{div}(c\boldsymbol{v}) \in W^{1,q'}$, which results, using boundedness of c, in $v \in L^q$ for $q > d$, and thus, using the embedding theorem, in the second restriction on p^-.

6 Numerical methods

In the thesis, we focus on the description of the numerical discretization of the system of equations which we use in the next chapters for computational simulations. Then, close description of convection dominated problem typical for synovial fluid and introduction of three different stabilization method for equation of concentration is presented. Here, nevertheless, we shall present the methods very briefly.

The system of governing equations is given by (5)–(7), and the domain of consideration Ω is bounded with Lipschitz boundary $\partial\Omega$. We prescribe Dirichlet and Neumann boundary conditions for velocity on parts of boundary Γ^v_{D} and Γ^v_{N}, respectively. It is assumed, that $\partial\Omega = \overline{\Gamma^v_{\mathrm{D}} \bigcup \Gamma^v_{\mathrm{N}}}$ and $\Gamma^v_{\mathrm{D}} \bigcap \Gamma^v_{\mathrm{N}} = \emptyset$. We can make such boundary decomposition for concentration as well, it means $\partial\Omega = \overline{\Gamma^c_{\mathrm{D}} \bigcup \Gamma^c_{\mathrm{N}}}$ and $\Gamma^c_{\mathrm{D}} \bigcap \Gamma^c_{\mathrm{N}} = \emptyset$, where the Dirichlet and Neumann boundary conditions for the concentration are prescribed. Explicitly, we consider

$$\begin{aligned} (\boldsymbol{v}(t,x)\cdot\boldsymbol{n})\boldsymbol{n} &= \boldsymbol{v}_1(t,x) \quad \text{on } \Gamma^v_{\mathrm{D}}, \qquad & c(t,x) &= c_D(t,x) \quad \text{on } \Gamma^c_{\mathrm{D}}, \\ \boldsymbol{v}_\tau(t,x) &= \boldsymbol{v}_2(t,x) \quad \text{on } \Gamma^v_{\mathrm{D}}, \end{aligned} \tag{17}$$

$$[\boldsymbol{T}(t,x)]\boldsymbol{n} = \boldsymbol{g}^v(t,x) \quad \text{on } \Gamma^v_N, \qquad \boldsymbol{q}_c(t,x)\cdot\boldsymbol{n} = g^c(t,x) \quad \text{on } \Gamma^c_N, \tag{18}$$

where $\boldsymbol{n}$ is the unit outward normal to the boundary and $\boldsymbol{v}_\tau = \boldsymbol{v} - (\boldsymbol{v}\cdot\boldsymbol{n})\boldsymbol{n}$.

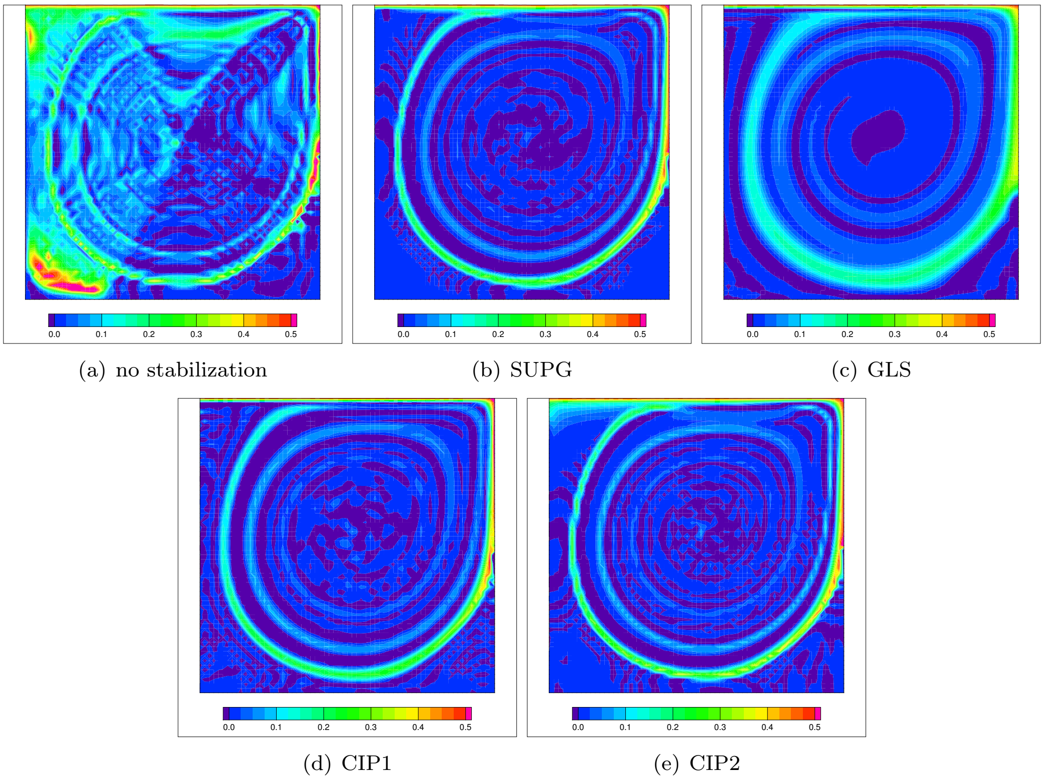
6.1 Discretization, convection–dominated problem

We discretize the system in time by a θ–scheme, and then, after obtaining the stationary set of equations for each time step, we use the finite element method for discretizing the space.

A straightforward numerical discretization works well for moderate values of Reynolds and Péclet numbers. In the case of synovial fluid, the Reynolds number is small due to small velocities and relatively high viscosity. On the other hand, the diffusivity of hyaluronan in synovial fluid is extremely small, and thus very high Péclet numbers are typical for the considered convection–diffusion equation. Due to these reasons, the discretization of equation for velocity behaves as expected, while the algebraic system corresponding to concentration does not meet desired matrix properties and thus the numerical solution exhibits non–physical effects.

It is obvious, that for problems of dominated convection, like in the case of synovial fluid with physical diffusivity of hyaluronan in order of $10^{-7}\mathrm{cm}^2/\mathrm{s}$, one has to stabilize the whole system by suitable tools which should eliminate the spurious oscillations but should not significantly change the character of resulting solution. A number of stabilization methods for finite element method has been developed to overcome these typical numerical problems. Today, the most frequently used stabilization methods are the stream–line diffusion method introduced by Hughes and Brooks in 1979, also called streamline upwind Petrov–Galerkin (SUPG), and the Galerkin least squares (GLS) method. We shall, besides these two, introduce another alternative, two versions of the continuous interior penalty (CIP1, CIP2) method.

From the obtained results, we observe that CIP1 scheme and GLS are the most diffusive. This results that in the CIP1 case the concentration values on the specific cuts does not become negative but, on the other hand, the localized concentrations spiral layers are not well preserved. The sharp layers are conserved mostly by the GLS method. While the SUPG and CIP2 methods are most oscillatory from all the considered stabilizations, for our computations they are least diffusive.



(a) no stabilization (b) SUPG (c) GLS

(d) CIP1 (e) CIP2

Figure 7: Computational results of concentration distribution for driven cavity problem, $\mathrm{Pe} = 10^6$, plotted at time $t = 50$.

7 Computational simulations

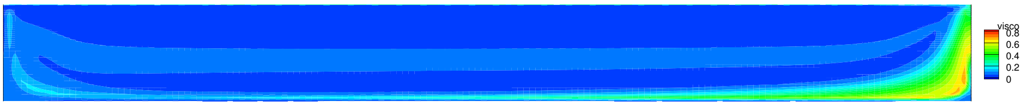
In all cases we assume the fully coupled system of governing equations (5)–(7) with non–constant viscosity and constant diffusivity with the Péclet number of order 10^7. We consider the computational setting of driven cavity on a rectangular domain with the aspect ratio $10 : 1$. We resolve the evolutionary problem with initial conditions of $\boldsymbol{v}(0, x) = 0,\ c(0, x) = 0.1$. We discretize the domain Ω by a quadrilateral mesh, quadratically refined in the vertical direction. By this we meet the higher computational requirements of the boundary condition settings.

For this case we study the influence of two different, having the least diffusive properties, stabilization techniques on the numerical solutions, explicitly the SUPG – streamline upwind Petrov–Galerkin method and the CIP2 – continuous interior penalty method with the weights, from now on called CIP. The comparison is present in see Fig. 7 and 11. And, we present the flow properties of fluid described by the proposed non–linear viscous models for synovial fluid, see comparison of the velocity and viscosity profiles in Fig. 8 and S:sim10modmu.

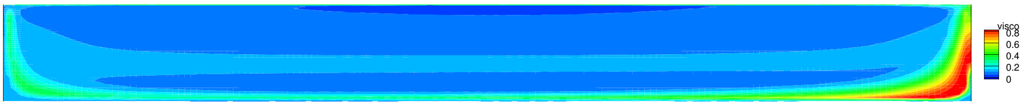
8 Synovial membranes modeling

For our application, we propose a new mathematical model for flow and transport processes in domains separated by a zero–thickness interface representing leaky semipermeable membrane, described by the reflexivity σ. The model of the processes in the bulk domains consists of the the Navier–Stokes equations describing the flow of diluted solution, together with the convection–diffusion equation modeling the solute transport, as introduced above. This system of non–dimensionalized governing equations takes the form of (5)–(7) and has to be complemented with initial conditions, boundary conditions at the outer boundaries, and, mainly, by transmission conditions at the separating membrane. These transmission conditions shall create the membrane model, formulated on the macroscopic scale, assuming the membrane to be fixed and rigid interface, separating the flow domains. Thus, the processes inside the membrane are not resolved, however,

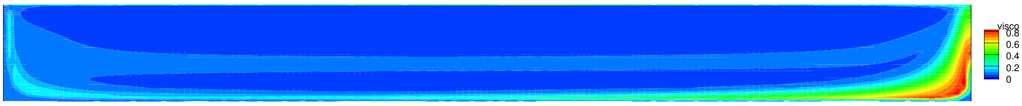
(a) N–S



(b) Model 1



(c) Model 2a



(d) Model 2b

Figure 8: Viscosity distribution for different models.

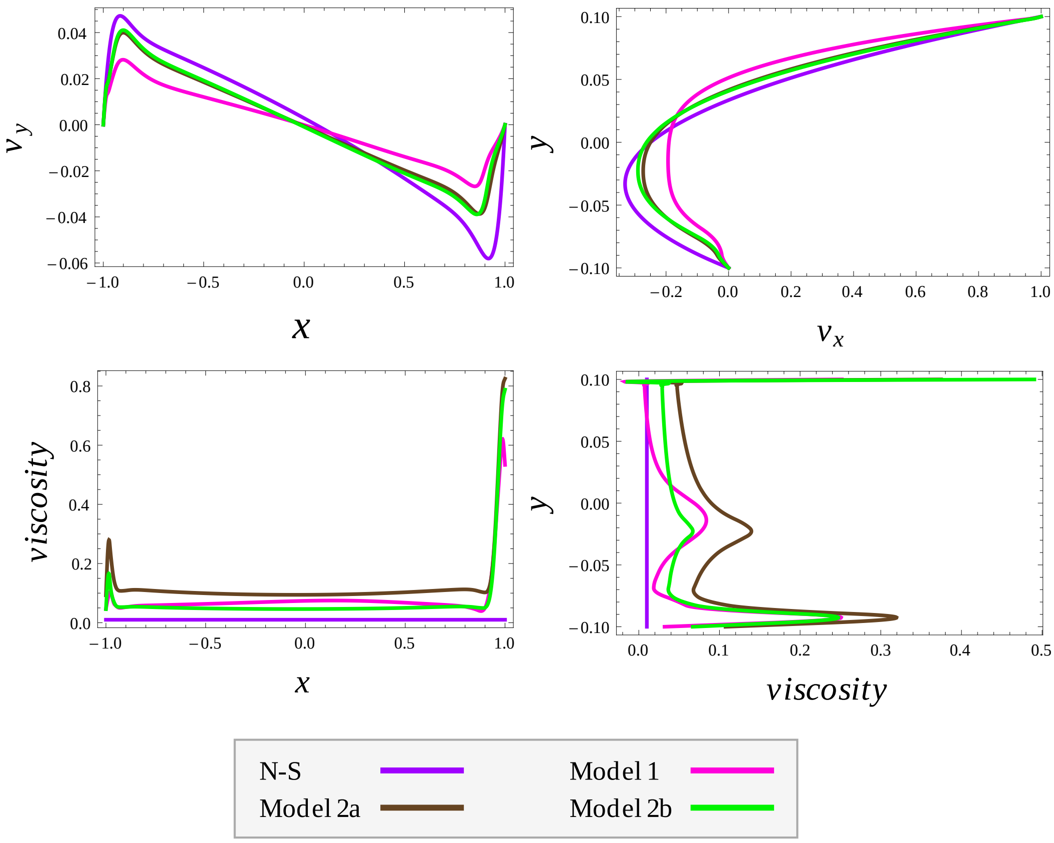


Figure 9: Top: Velocity profiles on vertical and horizontal cuts of the computational domain. Left: v_y velocity component profile on horizontal cut, right: profile of v_x component of velocity on vertical cut.; Bottom: Viscosity profiles on vertical and horizontal cuts of the computational domain.

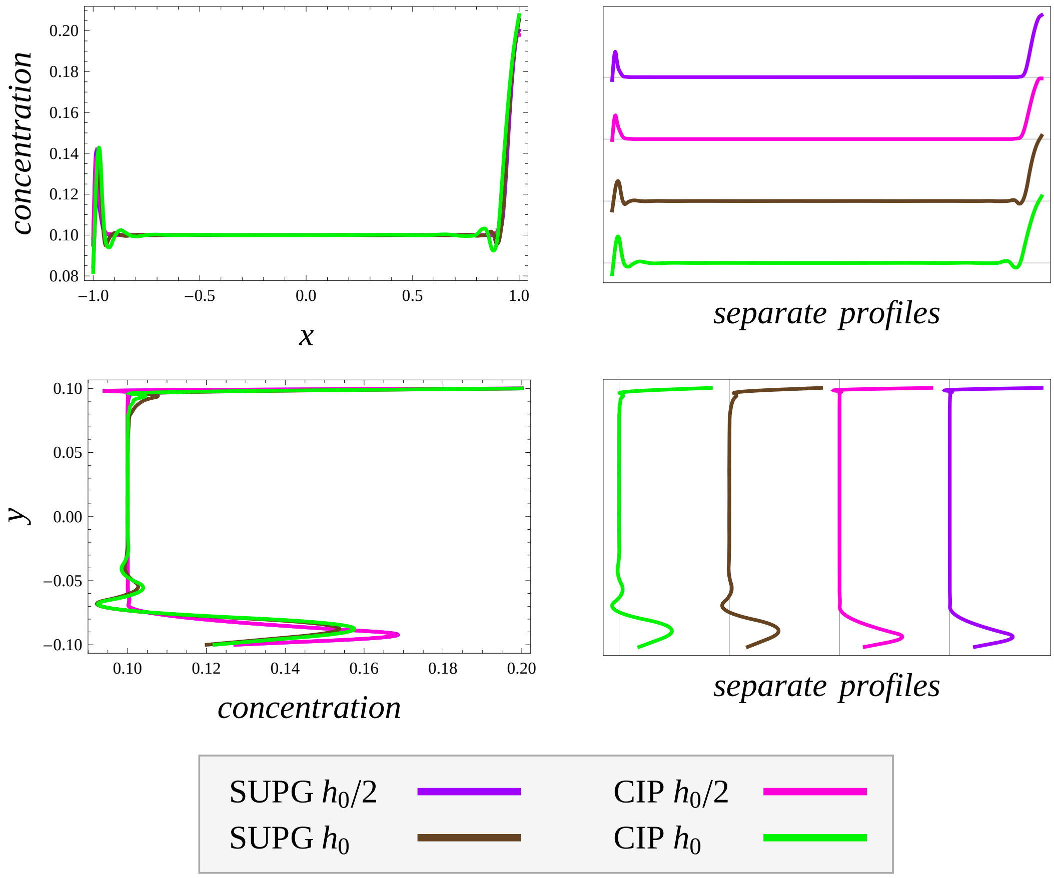


Figure 10: Concentration profiles on the domain cuts for comparison of both stabilizations and two different refinements of the mesh, h_0 and $h_0/2$.

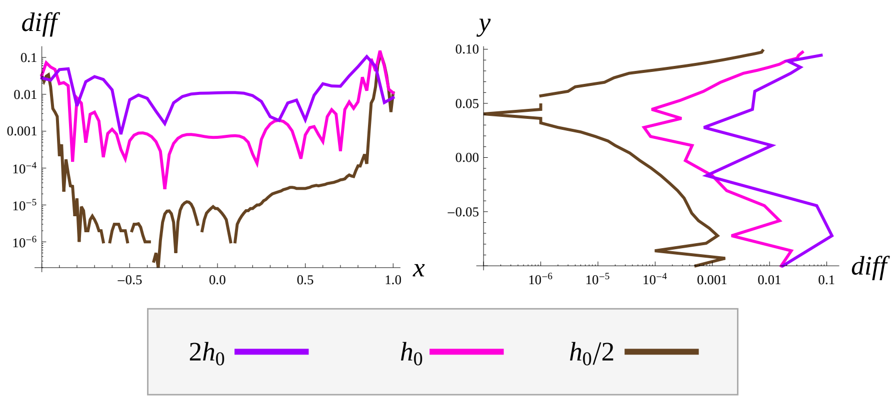


Figure 11: Relative differences between numerical solutions obtained by the use of SUPG and CIP stabilizations: $|c_{\mathrm{SUPG}} - c_{\mathrm{CIP}}|/c_{\mathrm{CIP}}$ for three different refinements of the mesh.

their effective contributions are included phenomenologically in the transmission conditions. We consider the membrane to be symmetric, i.e. the transmission properties of the membrane from both sides are the same, without the influence of its possible curvature on the flow of the solvent, which is however up to now an open question.

In the formulation of the transmission conditions across the membrane, the following aspects are taken into account: first, the separating properties of the membrane with respect to the solvent, which lead to the buffering of solute concentration at the membrane and second, connected with the first aspect, the influence of the concentration accumulation on the volume flow, known as osmotic effect. Such transmission model has similar features with other models existing in the literature, see e.g. Kedem and Katchalsky (1958). However, the important difference is that we shall not formulate equations only for the total volume fluxes across the membrane, as it is done in the existing literature, but we give transmission conditions which can be used to describe the influence of the membrane on the processes in the bulk regions.

The transmission conditions for the solvent flow at the membrane consist of the continuity of the normal component and no–slip condition in the tangential direction with the respect to the membrane interface for the velocity and of the continuity of normal stresses, and due to the physical reasons, we include the osmotic pressure $\pi(c)$ into our model via the the normal stress of the fluid at the membrane. In that case, the transmission conditions for the flow are of the following form

$$\boldsymbol{v_\tau}^+ = \boldsymbol{v_\tau}^- = \boldsymbol{0}, \quad \boldsymbol{v}^+ \cdot \boldsymbol{n}^+ = -\boldsymbol{v}^- \cdot \boldsymbol{n}^- = \boldsymbol{v} \cdot \boldsymbol{n}^+, \tag{19}$$

$$[-(p^- - p^+)\boldsymbol{I} + 2\frac{1}{\mathrm{Re}}(\boldsymbol{D}^- - \boldsymbol{D}^+)]\boldsymbol{n}^- = -(\pi(c^-) - \pi(c^+))\boldsymbol{n}^-. \tag{20}$$

where $\boldsymbol{n}^+, \boldsymbol{n}^-$ are the outer unit normal vectors on Γ_m – the membrane interface in considered domain Ω (divided by the membrane to subdomains Ω^+, Ω^-), with respect to the domains Ω^+, Ω^- and vectors $\boldsymbol{v_\tau}^{+/-}$ represent the tangential components of velocity defined as $\boldsymbol{v_\tau}^{+/-} = \boldsymbol{v}^{+/-} - (\boldsymbol{v}^{+/-} \cdot \boldsymbol{n}^{+/-})\boldsymbol{n}^{+/-}$.

Concerning the transmission conditions for the solute concentration, we require the continuity of the normal fluxes across the membrane, and the condition modeling the partial rejection of the solute by the membrane by the parameter σ. If we assume that the velocity $\boldsymbol{v}$ has the property $\boldsymbol{v} \cdot \boldsymbol{n}^- \geq 0$, then these conditions have the form

$$\begin{aligned} -\frac{1}{\mathrm{Pe}} \operatorname{grad} c^- \cdot \boldsymbol{n}^- + \sigma c^- \boldsymbol{v} \cdot \boldsymbol{n}^- &= 0, \\ -\frac{1}{\mathrm{Pe}} \operatorname{grad} c^+ \cdot \boldsymbol{n}^+ + c^+ \boldsymbol{v} \cdot \boldsymbol{n}^+ &= -(1-\sigma) c^- \boldsymbol{v} \cdot \boldsymbol{n}^-. \end{aligned} \tag{21}$$

The main disadvantage of this formulation is the directional dependence of the conditions for the concentration. Since the buffering occurs in the case of outflow while in the case of inflow the washout of concentration from the membrane is observed, we have to explicitly know the flow direction. One of the possible generalization of the transmission conditions for the concentration (21), assuming symmetric properties of the membrane from both sides, is

$$\begin{aligned} \frac{1}{\mathrm{Pe}} \operatorname{grad} c^- \cdot \boldsymbol{n}^- &= (\sigma c^-) \boldsymbol{v} \cdot \boldsymbol{n}^- + (1-\sigma)(c^- - c^+) \min(0, \boldsymbol{v} \cdot \boldsymbol{n}^-), \\ \frac{1}{\mathrm{Pe}} \operatorname{grad} c^+ \cdot \boldsymbol{n}^+ &= (\sigma c^+) \boldsymbol{v} \cdot \boldsymbol{n}^+ + (1-\sigma)(c^+ - c^-) \min(0, \boldsymbol{v} \cdot \boldsymbol{n}^+). \end{aligned} \tag{22}$$

It is easy to see that (22) reduces to (21) if $\boldsymbol{v} \cdot \boldsymbol{n}^- \geq 0$, and on the other hand, for the case $\boldsymbol{v} \cdot \boldsymbol{n}^- \leq 0$ we obtain analogous condition for outflow in opposite direction.

For the numerical simulations, we use the following computational setting. We consider the rectangular domain with the fixed and rigid membrane Γ_m. The domain Ω^- on the left from membrane is prolonged since there the most interesting accumulation of concentration occurs. We assume the pressure driven flow, for which the fluid of a given concentration enters the channel on left vertical boundary Γ_4, and the filtrate leaves the channel on right vertical boundary Γ_2. The walls of the channel Γ_1 and Γ_3 are impermeable for both, the concentration and velocity. The form of the boundary conditions on the outer boundaries is

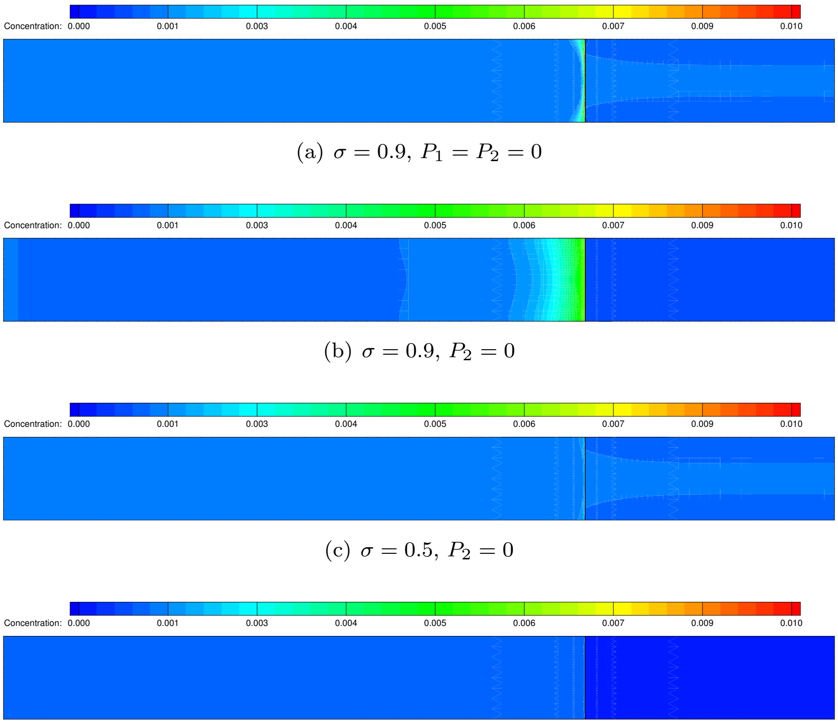
$$\Gamma_4: \quad [-p\boldsymbol{I} + 2\frac{1}{\mathrm{Re}}\boldsymbol{D}]\boldsymbol{n} = -p_{in}\boldsymbol{n}, \qquad c = c_{in}, \tag{23}$$

$$\Gamma_1, \Gamma_3: \quad \boldsymbol{v} = \boldsymbol{0}, \qquad \left(\frac{1}{\mathrm{Pe}} \operatorname{grad} c + c\boldsymbol{v}\right) \cdot \boldsymbol{n} = 0, \tag{24}$$

$$\Gamma_2: \quad [-p\boldsymbol{I} + 2\frac{1}{\mathrm{Re}}\boldsymbol{D}]\boldsymbol{n} = 0\boldsymbol{n}, \qquad \frac{1}{\mathrm{Pe}} \operatorname{grad} c \cdot \boldsymbol{n} = 0, \tag{25}$$

where c_{in} is a constant inlet concentration and p_{in} is a constant pressure inlet. Since we solve the time–dependent problem, we set the initial conditions as a rest state ($\boldsymbol{v} = 0$ and $c = 0$).

First, we present the general computations for the Newtonian fluid with Reynolds number $\mathrm{Re} = 1$ and Péclet number $\mathrm{Pe} = 100$. The computational results are shown in Fig. 12–13.



(a) $\sigma = 0.9$, $P_1 = P_2 = 0$

(b) $\sigma = 0.9$, $P_2 = 0$

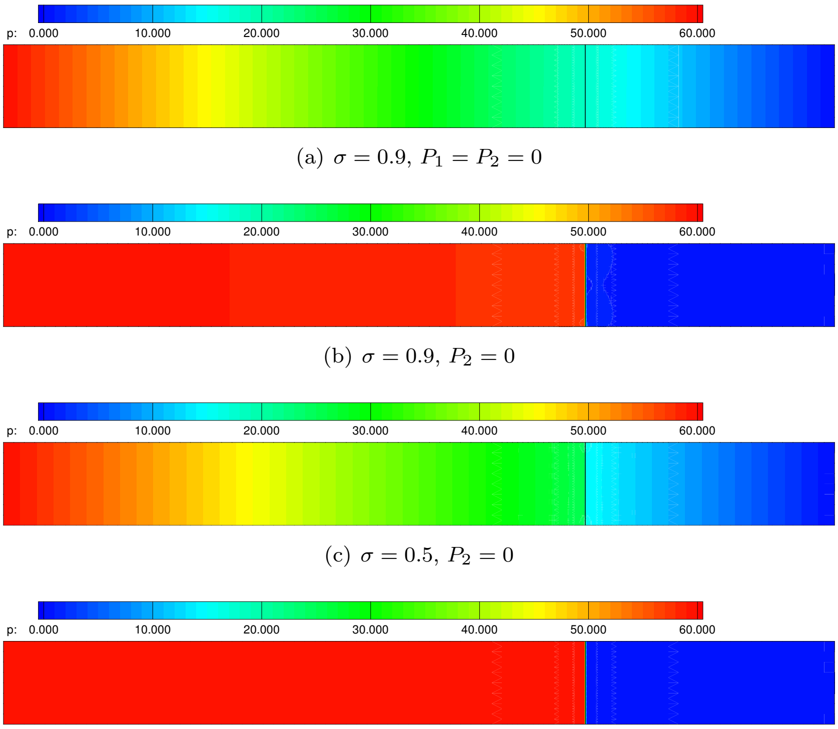
(c) $\sigma = 0.5$, $P_2 = 0$

(d) $\sigma = 0.9$, $P_2 = 5 \cdot P_1$

Figure 12: Concentration distribution at steady state. Four plots for different parameter setting; without osmotic pressure: (a) $\sigma = 0.9\,, P_1 = P_2 = 0$; with osmotic pressure: (b) $\sigma = 0.9\,, P_2 = 0$, (c) $\sigma = 0.5\,, P_2 = 0$, (d) $\sigma = 0.9\,, P_2 = 5 \cdot P_1$.

Fig. 12 present the steady state of the concentration distribution in the whole domain. As we can see, the shape of the concentration layer strongly differs. In the case of simulation without inclusion of osmotic pressure (case (a)), the concentration at the membrane is higher towards the walls than in the middle part. This is caused by the non–decelerated parabolic velocity profile. The velocity is higher in the middle part than close to the walls thus it carries away more of the concentration. This phenomena is not observed for the cases where the velocity at the membrane rapidly drops like in the settings of (b) and (d). For the setting (c) and (d) with low reflection coefficient and quadratic osmotic pressure dependence, a small concentration layer is created compared to the setting with higher σ and linear dependence of osmotic pressure, setting (a) and (b).

Profiles of hydrodynamical pressure are presented in Fig. 13. In the case of computational setting without osmosis, the equations for velocity and concentration are not fully coupled and thus the hydrodynamical pressure is a solution of the classical Navier–Stokes equations, and thus, it has a linear profile. For the settings including osmosis the jumps in the pressure occur. In the case of small σ, the concentration layer at the membrane is not so significant, and thus it does not evoke high difference in the osmotic pressures which could act against the fluid pressure. In the case of the quadratic osmotic pressure dependence on the concentration, the compensation of the pressures occurs even though the drop in concentration was not so high as for the case of (b). It is obvious that for small pressure differences across the membrane, the outflow of the solute is high, and thus high drainage of the solution is observed. In the case of the synovial fluid, that is unwanted feature.



(a) $\sigma = 0.9$, $P_1 = P_2 = 0$

(b) $\sigma = 0.9$, $P_2 = 0$

(c) $\sigma = 0.5$, $P_2 = 0$

(d) $\sigma = 0.9$, $P_2 = 5 \cdot P_1$

Figure 13: Hydrodynamic pressure distribution at steady state. Four plots for different parameter setting; without osmotic pressure: (a) $\sigma = 0.9\,, P_1 = P_2 = 0$; with osmotic pressure: (b) $\sigma = 0.9\,, P_2 = 0$, (c) $\sigma = 0.5\,, P_2 = 0$, (d) $\sigma = 0.9\,, P_2 = 5 \cdot P_1$.

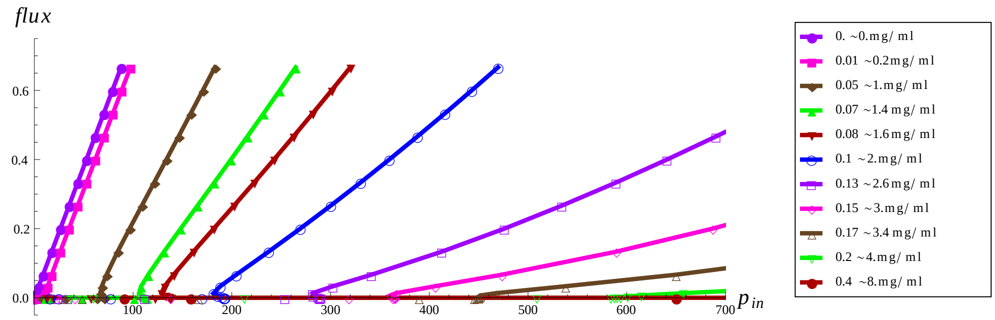
8.1 Application of the transmission model to synovial membranes and synovial fluid

As it has been introduced in chapter of biology of joints in the thesis, the hyaluronan outflow buffering is important for the balance of joint fluid volume and composition of the fluid, which is, generally, important for the whole stability of synovial joint system. For these reasons, it is important to study the filtration processes of synovial fluid through the synovial membrane in relation to the hyaluronan concentration, which can vary with different physiological conditions of the joint. This motivates us to apply our membrane transmission model (developed for diluted polymeric solutions) to synovial fluid drainage.

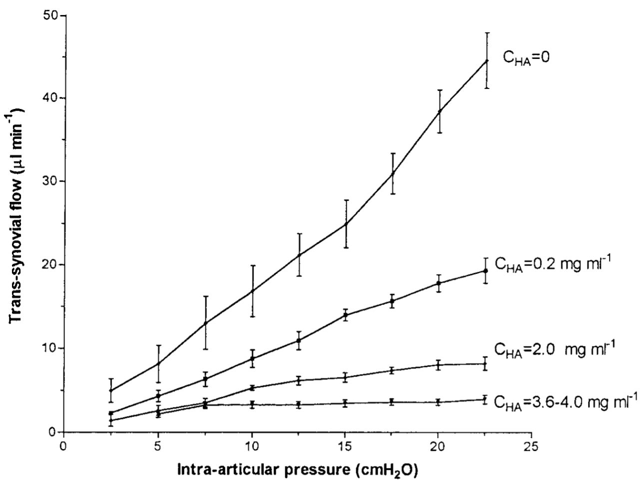
There can be many mechanisms playing a role during the synovial fluid drainage, for example the increase of intramembrane viscosity, the influence of molecular chain length on the critical concentration of molecular overlapping, the influence of inhibitors of chain–chain interactions, etc. We shall nevertheless focus on the concentration polarization due to the reflexivity of the synovial membrane, and newly, we include to the model the resistivity of the membrane to the bulk flow. In the previous subsection, we assumed such membrane properties that the zero reflexivity, $\sigma = 0$, led to a membrane–free model. This means that the flow through the membrane would not be slowed down, or in other words, the fluid would not “feel” the membrane presence, which is physically non–realistic. From the experiment of Scott, see Fig. 14 (a), it is visible that the relation between outflow and imposed intraarticular pressure exhibit linear relation for zero concentration solution of hyaluronan. This can be considered as a specification of the membrane resistivity to the bulk flow of the Newtonian fluid “background”. We therefore, as the membrane is considered as zero–thickness interface, prescribe the resistance R through the normal stress as

$$[-(p^- - p^+)\boldsymbol{I} + 2\frac{1}{\mathrm{Re}}(\boldsymbol{D}^- - \boldsymbol{D}^+)]\boldsymbol{n}^- = -(\pi(c^-) - \pi(c^+))\boldsymbol{n}^- - R(v_n)\boldsymbol{n}^-. \tag{26}$$

For the experiment reproduction, we consider the same two–dimensional test geometry as above



(a) trans–synovial flow – numerical result



(b) trans–synovial flow – experimental result

Figure 14: Qualitative comparison of numerical results of pressure driven flow through the membrane (a), with the experimental results of Scott et al. (2000), (b).

with fixed and rigid interface Γ_m representing the membrane. Moreover, since we assume diffusivity of order 10^{-6}, we solve the problem by the use of the numerical stabilization method, particularly by the continuous interior penalty (CIP) method. As in the experiment, we assume the pressure driven flow, for which the fluid of a given concentration enters the channel and the filtrate leaves the channel on opposite boundary. Here, we record the total flux of the fluid as a function of an imposed pressure on the inflow boundary and qualitatively compare it with the volume outflow relation from the experiment.

The numerical results of the simulations are presented in the Fig. 14. As it is well distinctive, the model is able to capture the main outflow vs. imposed pressure characteristics which are their linear relationship and the rapid decrease of the outflow for the concentration around $0.13 \approx 2$mg/ml and higher. Even though we consider the phenomenologically derived model, under the considered limitations it gives reasonable resulting properties of the filtration process.

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List of Publications

J. Hron, M. Neuss–Radu, and P. Pustějovská. Mathematical modeling and simulation of flow in domains separated by leaky semipermeable membrane including osmotic effect. Applications of Mathematics, 56(1):51–68, 2011.

J. Hron, J. Málek, P. Pustějovská and K. R. Rajagopal. On the Modeling of the Synovial Fluid. Advances in Tribology, 2010(Art. No. 104957), 2010.

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