Comparison of numerical approaches for inverse Laplace transform by the example of intraocular pressure determination

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Abstract

The modification of existing human eye models and the creation of new ones, which take into account an increasing number of sclera parameters, allow ophthalmologists to correct disorders of the eye created by trauma, disease, or aging more rationally and qualitatively. The viscosity of the sclera is ignored in most existing models. The reason is that direct measurements of the sclera viscosity cause technical problems. However, the sclera has viscoelastic properties [1]. This paper investigates a method for determining the shear viscosity of the sclera based on a comparison of results from mathematical modeling with experimental data from discrete measurements of the IntraOcular Pressure (IOP) during several minutes after intravitreal injection (injection into the eyeball aqueous humor) [2]. We propose to find the time-dependent IOP by applying Laplace transforms. In the present case a numerical inverse Laplace transform is required. Several approximation criteria can be applied based on the numerical approach [3], [4], [5]. The main idea of this paper is to present a comparison of numerical approaches based on three different sets of nodes and weights for a quadrature formula for the inverse Laplace transform by the example of IOP determination.

1 Introduction

Healthy human eyes are roughly spherical, filled with a transparent gel-like substance called the aqueous or vitreous humor. The eyeball consists of three concentric layers: A fibrous tunic, including the opaque part called sclera behind and the transparent part called cornea in front; a vascular pigmented tunic called choroid and a nervous tunic called retina [6] (see Fig. ??). The fibrous tunic performs a protection function and determines the eyeball shape. The sclera occupies 93% of the eyeball layers [7].

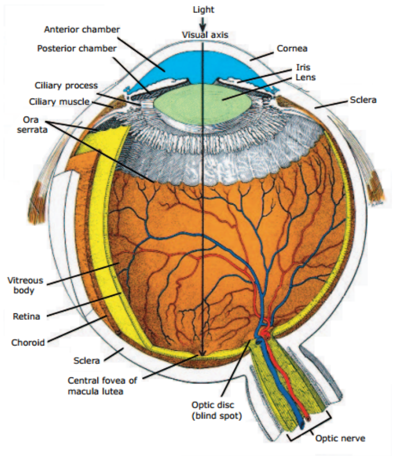

Figure 1: Schematic diagram of the human eye.

The biomechanical properties of the sclera play the leading role when determining the eyeball shape or the volume under IntraOcular Pressure (IOP). Therefore we will consider only the sclera during modeling of the eye behavior after intravitreal injection (injection into the eye, namely into the vitreous humor, near the retina at the back of the eye).

Experimental curves based on IOP measurements for several minutes after intravitreal injection show an increase of the IOP in form of a jump immediately after injection followed by steady decrease. Intraocular fluid outflow can be a reason for the reducing IOP. However, experience indicates that the sclera is a viscoelastic material [1]. Therefore one can explain a time-dependent IOP behavior also by an existing viscosity of the sclera. Direct measurements of sclera viscosity cause technical problems and so the viscosity of the sclera is ignored in most existing models. This paper presents a method for determining the shear viscosity of the sclera based on a comparison between results from mathematical modeling and experimental data of discrete IOP measurements during several minutes after intravitreal injection [2]. Moreover, this work investigates the underlying system of equations with two types of boundary conditions. In the first case we suppose that the eyeball volume does not change during the time of experiment. Therefore we explain the IOP reduction only by the viscous properties of the sclera. In the second case we take intraocular fluid outflow into account. Thus we explain the reducing IOP by both facts, the existing sclera viscosity and the existing intraocular fluid outflow.
The considered solution is based on the Laplace transform approach. We have to apply an inverse Laplace transform in order to determine the sclera displacement and the IOP. Because the mathematical expressions are complicated we apply a numerical approach. Several approximation criteria can be applied as a basis of the numerical inverse Laplace transform. Of particular interest is a comparison of results based on the well-known Zakian's technique [3], [4] and on a numerical approach offered by Jeffreson and Chow [5].

2 Problem statement and governing equations

The experiment we are going to describe is based on discrete measurements of the IOP for several minutes after an intravitreal injection equal to 0.05 ml. The IOP is defined as the difference between the pressure inside the eye and the atmospheric pressure. The experimental curve showing the IOP dependence on time is shown in Fig. 2 (obtained by Kotlyar, Bauer, and Plange [2]). Points on the graph correspond to average IOP values (n =34 patients took part in the experiment). The red line shows the average IOP of vaccinated eyes, the green line corresponds to an IOP control based on measurements of IOP of the second eye in a pair, which was not vaccinated. So far as we are going to use the Pascal (Pa) unit to express the IOP in the framework of this paper we would like to note that 1 mm Hg=133.322 Pa.

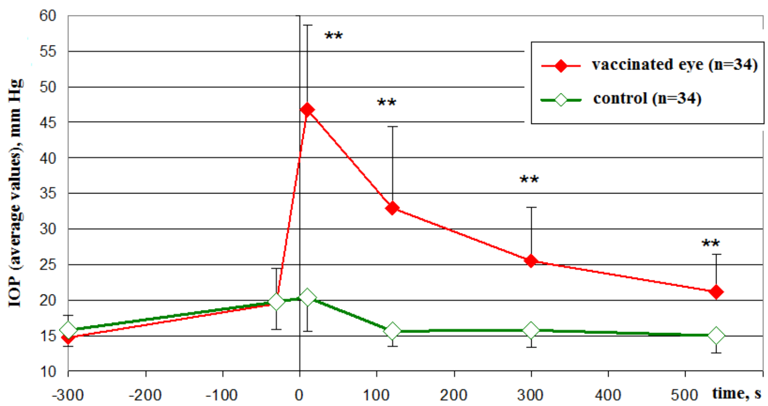

Figure 2: Time dependence of IOP: experimental curve.

In order to model the observed IOP reduction we consider a viscoelastic spherical layer of inner radius R_{i} and outer radius R_{o} under a centrally symmetric load: an external pressure is absent, the displacement of the inner boundary is specified and takes the intravitreal injection volume into account. We suppose the material of human sclera to be linear transversally isotropic (the axis of symmetry coincides with the radial direction). The problem will be considered within the framework of 3D-dimensional linear viscoelastic theory. The equation of motion reduces to the following equilibrium equation in so far as we consider a quasi-static problem:

$$\nabla \cdot \boldsymbol{\sigma} = 0, \qquad (1)$$

where $\boldsymbol{\sigma}$ is the stress tensor.
Linear viscoelastic theory allows us to consider the elastic and the viscous behavior of the sclera separately. We use a Kelvin-Voigt rheological model, which means that we add elastic and viscous stresses. Moreover, in order to find the solution, we restrict ourselves to only one unknown viscous parameter, the shear viscosity of the sclera, η, and ignore volume viscosity. The constitutive equations in this case read:

$$\boldsymbol{\sigma} = {}^4\boldsymbol{C} : \boldsymbol{\varepsilon} + 2\eta\dot{\boldsymbol{e}}, \qquad (2)$$

where $\boldsymbol{C}$ is the fourth-order stiffness tensor [8], $\boldsymbol{\varepsilon}$ is the linear strain tensor, and $\boldsymbol{e}$ is the strain tensor deviator. To rewrite the stiffness tensor by using elastic modules we use the ratios between coefficients of the stiffness tensor and technical constants named elastic modules which are shown in [9], p.79.
Due to the inherent radial symmetry only the radial component of displacement in spherical coordinates is different from zero. Shear strains and stresses are absent. All components of vectors and tensors depend only on the radial coordinate. In this

case we have only one equilibrium equation in coordinate form:

$$\frac{\partial \sigma_{rr}}{\partial r} + 2\frac{\sigma_{rr} - \sigma_{\varphi\varphi}}{r} = 0. \tag{3}$$

The nonzero components of the strain tensor read:

$$\varepsilon_{rr} = \frac{du_r}{dr}\ ,\ \ \varepsilon_{\varphi\varphi} = \varepsilon_{\theta\theta} = \frac{u_r}{r}. \tag{4}$$

We define dimensionless quantities for (radial) position, $\beta = R_{\mathrm{i}}/R_{\mathrm{o}} \leq x = r/R_{\mathrm{o}} \leq 1$, displacement, $u = u_r/R_{\mathrm{o}}$, stress components, $\sigma_{ij\,\mathrm{dim}} = \sigma_{ij}/E_{\theta\theta}$ (where σ_{ij},$E_{\theta\theta}$ are given in Pa unit), time, $\tau = E_{\theta\theta}t/\eta$ and Young's modulus, $\xi = E_{rr}/E_{\theta\theta}$, where E_{rr} is Young's modulus in radial direction, and $E_{\theta\theta}$ is Young's modulus for the isotropic plane. The equilibrium equation (3) can be rewritten by applying Eqns. (2), (4). In this case we obtain the following differential equation for the radial displacement:

$$\frac{\xi^2(1-\nu_{\theta\varphi})}{\xi(1-\nu_{\theta\varphi}) - 2\nu_{r\theta}^2}\left[\frac{\partial^2 u}{\partial x^2} + \frac{2}{x}\frac{\partial u}{\partial x} - \frac{2(1-\nu_{r\theta})}{\xi(1-\nu_{\theta\varphi})}\frac{u}{x^2}\right] + \frac{4}{3}\left[\frac{\partial^2 \dot{u}}{\partial x^2} + \frac{2}{x}\frac{\partial \dot{u}}{\partial x} - 2\frac{\dot{u}}{x^2}\right] = 0, \tag{5}$$

where ν_{ij} refers to Poisson's ratios. Here the indices i and j represent the longitudinal and the transverse direction, respectively.
The IOP is the negative radial stress at the inside of the sclera: The outward normal of the inner boundary of a spherical layer is directed inside the body. The IOP tends to inflate the body. Therefore the dimensionless IOP reads: $IOP_{\mathrm{dim}}(\tau) = -\sigma_{xx}(\tau)|_{x=\beta}$. By applying Eqns. (2), (4) we determine the dimensionless radial stress $\sigma_{xx}(\tau) = \sigma_{rr\,\mathrm{dim}}(\tau)$ as a function of displacement (6):

$$\sigma_{xx}(\tau) = \frac{2\nu_{r\theta}\xi}{\xi(1-\nu_{\theta\varphi}) - 2\nu_{r\theta}^2}\frac{u}{x} + \frac{(1-\nu_{\theta\varphi})\xi^2}{\xi(1-\nu_{\theta\varphi}) - 2\nu_{r\theta}^2}\frac{\partial u}{\partial x} + \frac{4}{3}\left[\frac{\partial \dot{u}}{\partial x} - \frac{\dot{u}}{x}\right]. \tag{6}$$

Two types of boundary condition for the inner radius displacement are considered. In the first case we suppose that the eye volume, which consists of the intravitreal injection volume, ΔV, which is added inside the eye ($r < R_{\mathrm{i}}$), and of the eyeball volume before loading, V_0^{eye}, is constant during the time of the experiment. Hence, the displacement of the inner boundary depends on the intravitreal injection volume as follows:

$$\sigma_{xx}(\tau)\,|_{x=1} = 0\ ,\ \ u(\tau)\,|_{x=\beta} = u_0 H(\tau), \tag{7}$$

where $u_0 \approx \Delta V/(4\pi R_{\mathrm{o}} R_{\mathrm{i}}^2)$, $H(\tau)$ is the Heaviside unit step function.
In the second case the displacement of the inner boundary is caused by the intraocular fluid hydrodynamics. In order to estimate the eyeball volume change based on intraocular fluid in- and outflow we apply the tonography method [10], [11] which uses the velocity associated with the volume change of the eyeball. The current eyeball volume is:

$$V(t) = V(0) + \int\limits_{\tilde{t}=0}^{\tilde{t}=t} \dot{V}(\tilde{t})d\tilde{t} = V_0^{eye} + \Delta V + \int\limits_{\tilde{t}=0}^{\tilde{t}=t} \dot{V}(\tilde{t})d\tilde{t}. \tag{8}$$

The change of the eyeball volume due to the intraocular fluid hydrodynamics is: $V(t) - V(0) = V(t) - V_0^{eye} - \Delta V = 4\pi R_{inj}^2 u_r(t)$, where $R_{inj} \approx \sqrt[3]{R_{\mathrm{i}}^3 + 3\Delta V/(4\pi)}$. The boundary conditions in this case are:

$$\sigma_{xx}\left|_{x=1} = 0, u\left(t\right)\right|_{x=\beta} = u_0 + \frac{\int\limits_{\tilde{t}=0}^{\tilde{t}=t} \dot{V}\left(\tilde{t}\right) d\tilde{t}}{4\pi R_2 R_{inj}^2}. \tag{9}$$

Further use of the dimensionless time in the equation system in combination with the second type of BC becomes difficult because of the time occurs in the integral as well.

In order to estimate $\int_{\tilde{t}=0}^{\tilde{t}=t} \dot{V}(\tilde{t})d\tilde{t}$ we turn to the tonography method consisting in IOP measurement during the time when the cornea is loaded by a known weight [10], [11]. In the framework of this method it is assumed that the velocity of the eyeball volume change depends on the intraocular fluid hydrodynamics (intraocular fluid in- and outflow). Based on the method proposed by Lyubimov and colleagues [11] we estimate the integral in the BC for the inner radius by the following expression:

$$\int\limits_{\tilde{t}=0}^{\tilde{t}=t} \dot{V}(\tilde{t})d\tilde{t} = \int\limits_{\tilde{t}=0}^{\tilde{t}=t} C(P_0 - P_{e0} - P(\tilde{t}) + P_e)d\tilde{t}, \tag{10}$$

where C is a parameter characterizing the ease of intraocular fluid outflow, P_e is an intraepiscleral veins pressure, the index "0" corresponds to the values characterizing the eye condition before the weight is applied. To obtain the function $P(t)$ authors of [11] took the entire time dependence of the IOP into account and applied an exponential approximation. They obtained that $P(t) = P_{st} + (P(0) - P_{st})\exp(-t/\hat{\tau})$, where P_{st} is an intraocular pressure which would take place if the cornea is loaded during the infinite time, $P(0)$ is an initial intraocular pressure, $\hat{\tau}$ is a characteristic time of an intraocular pressure change. We use the following average values for the corresponding values for 10 patients given in [11]: $P_0 = 13.8$ mm Hg, $P_{e0} = 8$ mm Hg, $P_e = 9.25$ mm Hg, $P_{st} = 15.0$ mm Hg, $P(0) = 27.0$ mm Hg, $\hat{\tau} = 2.8$ min. We also calculated that $C = 0.0087$ mm^3/(mm Hg $\cdot$ s) due to the value of $\hat{\tau}$ obtained by Ljubimov and colleagues and formulas describing the dependence between C and $\hat{\tau}$, which are given in [10].

3 Laplace transform approach and numerical approaches for inverse Laplace transform

We obtain expressions for the time-dependent displacement and the radial stress by applying its Laplace transform, which, in general, is defined by:

$$\bar{f}(x,s) = \int\limits_0^{\infty} \exp(-s\tau) f(x,\tau)d\tau, \tag{11}$$

where s is a complex variable, $s = c + i\omega, c > s_0$

The advantage of this method is that differentiation is replaced by multiplication by the operator variable s: $\dot{f}(x,\tau) \to \int\limits_0^\infty e^{-s\tau}\dot{f}(x,\tau)d\tau = s\bar{f}(x,s) - f(x,0)$. The partial differential equation in space-time turns into an ordinary differential equation in space-Laplace-time. As initial condition for displacement we cannot use corresponding experimental data because they are not known (due to measurement problems). Therefore, we assume that at the initial moment the displacement depends linearly on the radial coordinate. Consequently, the partial differential equations (5), (6) become ordinary differential equations with derivatives with respect to the coordinate:

$$\left[\frac{\xi^2(1-\nu_{\theta\varphi})}{\xi(1-\nu_{\theta\varphi})-2\nu_{r\theta}^2}+\frac{4}{3}s\right]\left(\frac{\partial^2\bar{u}}{\partial x^2}+\frac{2}{x}\frac{\partial\bar{u}}{\partial x}-2\frac{\bar{u}}{x^2}\right)-\frac{2\xi[1-\nu_{r\theta}-\xi(1-\nu_{\theta\varphi})]}{\xi(1-\nu_{\theta\varphi})-2\nu_{r\theta}^2}\frac{\bar{u}}{x^2}=0.$$

$$\overline{\sigma_{xx}}=\left[\frac{2\nu_{r\theta}\xi}{\xi(1-\nu_{\theta\varphi})-2\nu_{r\theta}^2}-\frac{4}{3}s\right]\frac{\bar{u}}{x}+\left[\frac{(1-\nu_{\theta\varphi})\xi^2}{\xi(1-\nu_{\theta\varphi})-2\nu_{r\theta}^2}+\frac{4}{3}s\right]\frac{d\bar{u}}{dx}. \tag{12}$$

In order to solve these equations we use BCs that are converted according to the Laplace transform. The solution technique is based on applying of **DSolve** and **Solve** commands from the computer algebra system **WolframMathematica**. As a result we obtain the displacement and the stress in Laplace time space.
The inverse Laplace transform is given by the following complex integral, which is known as the Bromwich inversion integral:

$$f(x,\tau)=\frac{1}{2\pi i}\int\limits_C \bar{f}(x,s)\exp(s\tau)ds, \tau>0, \tag{13}$$

where C is a contour extending from $c - i\infty$ to $c + i\infty$, falling to the right of all singularities of $\bar{f}$ [12].
In order to find the true time-dependent displacement and radial stress we apply the inverse Laplace transform to $\overline{\sigma_{xx}}(s)$ and $\overline{u}(s)$. Due to the complex structures of these functions we use a numerical solution method instead of an analytical solution based on Eqn. (13), which is likely not to exist. We solve the numerical problem by applying a quadrature formula which approximates an unknown function by a finite linear combination of transform values [13]:

$$f(x,\tau)\approx f_n(x,\tau)\equiv f_{n,a,K}(x,\tau)=\frac{1}{\tau}\sum_{j=1}^{n}K_j\bar{f}(x,\frac{a_j}{\tau}), \tag{14}$$

where $\mathbf{a}$, $\mathbf{K}$ are vectors, called nodes and weights, respectively. Eqn. (13) turns into Eqn. (14) after using a MacLaurin series for the exponential function $\exp(z)$, where $z = s\tau$, and an additional Padé approximation [14].
We would like to note that Zakian obtained Eqn. (14) alternatively by approximating a delta function by a finite linear combination of exponential functions. He showed [3] that the coefficients a_j, K_j have to be determined such that they provide a good approximation to the scaled Dirac delta function $\delta(\tilde{\tau}-1), \tilde{\tau}\in[0,\infty)$:

$$\delta(\tilde{\tau}-1)\approx\delta_n(\tilde{\tau}-1)=\sum_{j=1}^{n}K_j\exp(-a_j\tilde{\tau}), \tag{15}$$

where a_j, K_j are complex numbers of vectors $\mathbf{a}, \mathbf{K}$ respectively. As Zakian observed [4], the possibility of good approximations is evident if we take the Laplace transform of the scaled delta function: $\delta(\tilde{\tau}-1) \to \tilde{\tau}\exp(-\tilde{\tau}s)$. The nodes and weights obtained by Zakian are shown in Table 1. He also showed that if one uses these nodes and weights it is necessary to write $f_{n,a,K}^{Zakian}(x, \tilde{\tilde{\tau}}) = 2f_{n,a,K}(x, \tilde{\tilde{\tau}})$ instead of Eqn. (14).

Table 1: Nodes and weights obtained by Zakian

$\mathbf{a_j}$	$\mathbf{K_j}$
$1.283767675E+01+1.666063445iE+00$	$-3.690208210E+04+1.969904257E+05i$
$1.222613209E+01+5.012718792iE+00$	$6.127702524E+04-9.540862551E+04i$
$1.093430308E+01+8.409673116iE+00$	$-2.891656288E+04+1.816918531E+01i$
$8.776434715E+00+1.192185389iE+01$	$4.655361138E+03-1.901528642E+00i$
$5.225453361E+00+1.572952905iE+01$	$-1.187414011E+02-1.413036911E+02i$

Jeffreson and Chow offer different least-square (LS) sets of nodes and weights [5]. Their solution is based on the method of LS approximation by exponential functions as proposed by Miller [15]. They apply the LS approximation to match the function $\delta(\tilde{\tau}-1)$ by $\delta_n(\tilde{\tau}-1)$. In order to derive a set of LS coefficients Jeffreson and Chow minimize the following function:

$$E(a, A) = \int_0^\infty \{f(\tilde{\tau}) - \sum_{j=1}^n A_j \exp(-a_j\tilde{\tau})\}^2 \, d\tilde{\tau}., \tag{16}$$

where $A_j = K_j/a_j$. They consider the square pulse function:

$$f(\tilde{\tau}) = m(\tilde{\tau}-1) = 1 - \int_0^{\tilde{\tau}} \delta(\theta-1)d\theta = \begin{cases} 1, \tilde{\tau} \in [0, 1] \\ 0, \tilde{\tau} \in (1, \infty) \end{cases}, \tag{17}$$

which gives a finite integral in Eqn. (16). The values of the LS coefficients for $n = 10$ and $n = 15$ obtained by Jeffreson and Chow are shown in Table 2.
Stress and displacement are real-valued functions, so we approximate them by the real part of Eqn. (14). Then we obtain true time-dependent displacement and radial stress.

4 Results and conclusions

We obtained expressions for the displacement and radial stress in real time by applying the numerical approaches for the inverse Laplace transform. Consequently, we obtained different functions by using the sets of notes and weights for a quadrature formula for the inverse Laplace transform (Eqn. 14) obtained by Zakian, Jeffreson and Chow for $n = 10$ and $n = 15$. The shear viscosity of the sclera has been determined for two types of BC for the inner radius. During the numerical calculations

Table 2: Nodes and weights obtained by Jeffreson and Chow

$\mathbf{a_j}$	$\mathbf{K_j}$	*
$n = 10$		
$1.1230093058E + 01 - 2.352672861E + 01i$	$4.860502512E - 01 + 2.422640698E + 00i$	(2)
$1.948441344E + 00 - 1.838606040E + 01i$	$5.552772067E + 00 + 2.015535066E + 00i$	(2)
$2.486321472E + 00 - 1.294069981E + 01i$	$9.328911705E + 00 - 4.782670037E + 00i$	(2)
$3.049851019E + 00 - 7.477695691E + 00i$	$4.688193150E + 00 - 1.756397771E + 01i$	(2)
$3.662673996E + 00 - 2.340402588E + 00i$	$-2.290775011E + 01 - 1.934430556E + 01i$	(2)
$n = 15$		
$1.20190013E + 001 - 3.839128154E + 01i$	$+1.454512148E + 00 - 1.896165496E + 00i$	(2)
$1.862570769E + 00 - 3.320749609E + 01i$	$-1.715333565E + 00 - 5.172539073E + 00i$	(2)
$2.292993575E + 00 - 2.766209815E + 01i$	$-7.541523912E + 00 - 4.523961971E + 00i$	(2)
$2.661840425E + 00 - 2.198372929E + 01i$	$-1.295649648E + 01 + 7.506458220E - 01i$	(2)
$3.035577722E + 00 - 1.625582381E + 01i$	$-1.547416249E + 01 + 1.099375660E + 01i$	(2)
$3.470465540E + 00 - 1.055035834E + 01i$	$-1.018991823E + 01 + 2.717989379E + 01i$	(2)
$4.014204990E + 00 - 5.028754130E + 00i$	$+1.938392606E + 01 + 4.294784889E + 01i$	(2)
$4.382910986E + 00$	$6.166590165E + 01$	(1)

(*) means that the complex conjugate pair is also available.

we used the following values: $R_{\mathrm{i}} = 11.75$ mm, $R_{\mathrm{o}} = 12.25$ mm, $E_{22} = 14.3$ MPa, $E_{11} = 0.01E_{22}$, $\nu_{12} = 0.01$, $\nu_{23} = 0.45$ [16].

We start with a discussion of results obtained under the assumption that the eyeball volume does not change during the time of the experiment. In this case we describe everything in dimensionless coordinates as listed in the second chapter of this paper, including dimensionless time. As it has already been discussed, $IOP_{\mathrm{dim}}(\tau) = -\sigma_{xx}(\tau)|_{x=\beta}$. Note that the dimensionless radial stress is explicitly independent on the shear viscosity of the sclera. It depends on dimensionless time, which depends on the shear viscosity of sclera. This coefficient is not used in the equation system and is not specified as a known parameter. In order to estimate the value of the shear viscosity of the sclera we use the expression linking dimensionless and dimensional time. Consequently we write:

$$\eta = E_{\theta\theta} t/\tau. \tag{18}$$

Let us consider four experimental values of the IOP for fixed values of time measured by K. Kotlyar [2] (see Fig. 2): $IOP = 6266$ Pa $(IOP_{\mathrm{dim}} \cdot 10^{-6} = 438.2), t = 10$ s; $IOP = 4533$ Pa $(IOP_{\mathrm{dim}} \cdot 10^{-6} = 317.0), t = 120$ s; $IOP = 3466$ Pa $(IOP_{\mathrm{dim}} \cdot 10^{-6} = 242.4), t = 300$ s; $IOP = 2800$ Pa $(IOP_{\mathrm{dim}} \cdot 10^{-6} = 195.8), t = 500$ s. We use the theoretical function $\sigma_{xx}(\tau)$ which we have already obtained in order to determine τ, when the module of $\sigma_{xx}(\tau)$ is equal to the experimental data. The range of numerical IOP values obtained by simulation is less than the range of experimental values of IOP measured by Kotlyar. Indeed, $IOP_{\mathrm{dim}} \cdot 10^{-6} \in 195.8 - 438.2$ for experimental data and $IOP_{\mathrm{dim}} \cdot 10^{-6} \in 285 - 430$ for numerical simulation. Therefore we are able to use only the experimental value of IOP measured when the time is 120 s. Then we estimate the value of dimensionless time corresponding to this value of IOP and obtain the shear viscosity of the sclera by applying Eqn. (18). When using Zakian's set of nodes and weights and Jeffreson's and Chow's set of nodes and weights for $n = 10$ we obtain $\eta = 12.8$ MPa $\cdot$ s. By using Jeffreson's and Chow's set of nodes and weights for $n = 15$ we arrive at $\eta = 12.9$ MPa $\cdot$ s. The time dependence of the IOP is shown in Fig. 3a. The graph is based on three different numerical approaches for the inverse Laplace transform considered in this paper coinciding for such an IOP scale.

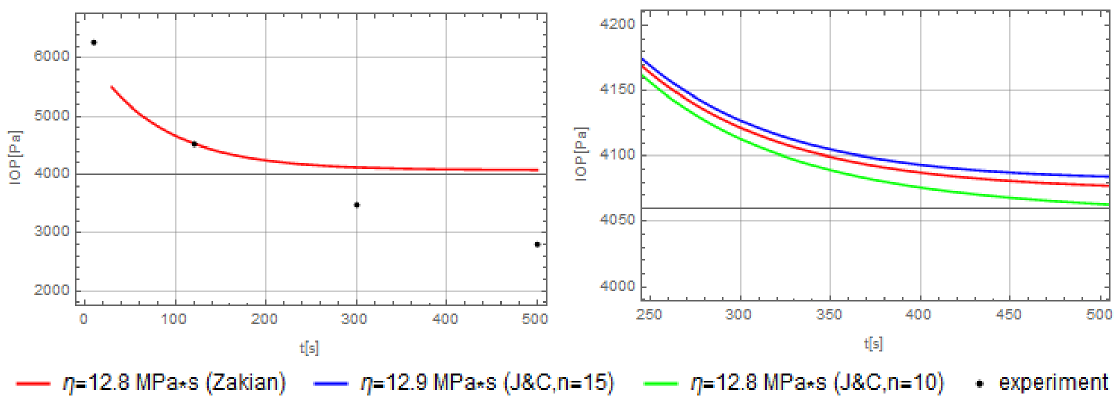

Figure 3: Time dependence of IOP.

A noticeable difference between the three considered approaches is observed only for the second half of the experimental time (see Fig. 3b). As we can use only the second point of the experimental curve corresponding to $IOP = 4533$ Pa we cannot really determine which numerical approach is the most acceptable on the whole, but we may say that all of these three approaches are good enough for application in the framework of the problem of IOP determination. However, Jeffreson's and Chow's approaches are more complicated due to a higher number of coefficients in Eqn. (14). As we can see from Fig. 3a stress relaxation cannot be explained only by an existing sclera viscosity. The match between the theoretical results and experimental data is not good enough since theoretical curves have another character of the decline.

We now discuss the results obtained under the assumption that an intraocular fluid outflow exists. In this case we used a dimensional time (in seconds). The shear viscosity of the sclera is explicitly included in the system of equations. Since we use a numerical solution a starting value must be specified before simulation. The shear viscosity determination was based on the bisection-root-finding method which repeatedly bisects an interval and then selects a subinterval in which the root must be located for further processing. This method is based on Bolzano's Theorem: $\Phi(\eta) \in C[\eta_a, \eta_b], \Phi(\eta_a) \cdot \Phi(\eta_b) < 0 \Rightarrow \exists \eta_c \in [\eta_a, \eta_b] : \Phi(\eta_c) = 0$ [17]. As function $\Phi(\eta)$ we use the function $\Phi(\eta) = (IOP_{experiment(\text{dim})} - (-\sigma_{xx}|_{x=\beta}))\,\big|_{t=t_{\text{experiment}}}$. This method allows us to find roots for all experimental values of IOP from Fig. 2 apart from the first value characterizing the IOP jump immediately after the intravitreal injection. As an initial range we used $\eta \in 0 - 200$ MPa. The reason of this choice is that it is a really wide range. We obtained values of the function $\Phi(\eta)$ when $\eta = 0$ MPa and $\eta = 200$ MPa and made sure that they have different signs. The shear viscosity obtained by applying Zakian's, Jeffreson's and Chow's $(n = 10)$, $(n = 15)$

vectors of nodes and weights are shown in Table 3. Coefficients are presented with one decimal of accuracy. The time dependence of the IOP is shown in Fig. 4.

Table 3: Values of shear viscosity obtained by applying different numerical approaches

Experimantal point	Zakian, MPa · s	J&C, n=10, MPa · s	J&C, n=15, MPa · s
IOP = 4533 Pa, time = 120 s	57.1	57.1	57.1
IOP = 3466 Pa, time = 300 s	58.6	59.1	58.3
IOP = 2800 Pa, time = 500 s	33.8	35.3	33.0

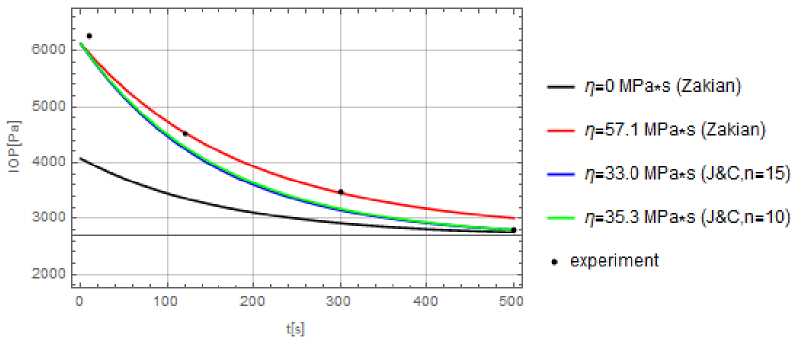

Figure 4: Time dependence of IOP.

The graphs based on three different numerical approaches for inverse Laplace transform considering in this paper coincide on the IOP scale. We also observe coinciding graphs for η obtained for the two middle points from the experimental curve (see Fig. 2). A minor difference can be observed for the last point. The decrease of the curve depends on the shear viscosity coefficient. The more the value of this coefficient the longer the relaxation time and the less abrupt the IOP will reduce. If $\eta = 0$ (this means that the sclera shows no viscosity) the match between the theoretical results and experimental data is not good enough. Hence, stress relaxation cannot be explained only by the existing intraocular fluid outflow. As we can see by comparison of Fig. 3a and Fig. 4 it is necessary to take both into account, the existing sclera viscosity and the existing intraocular fluid outflow, leading to the best agreement between theoretical results and experimental data.

In order to compare the time dependence of the IOP based on the different numerical approaches discussed in this paper we use average values of the IOP for the two middle points and for the three last points of the experimental curve (see Fig. 2). From the average values for the two middle points we find for the viscosity by applying Zakian's and Jeffreson's and Chow's approach for $n = 10$ and for $n = 15$, respectively: $\eta = 57.8$ MPa · s, $\eta = 58.1$ MPa · s, $\eta = 57.7$ MPa · s. The average values for three last points lead to $\eta = 49.8$ MPa · s, $\eta = 50.5$ MPa · s, $\eta = 49.5$ MPa · s, respectively for the listed approaches. A comparison of these approaches by using the average values for two middle points for the second point, the third point, and for the last point is shown in Fig. 5a, Fig. 5b, Fig. 5c respectively.

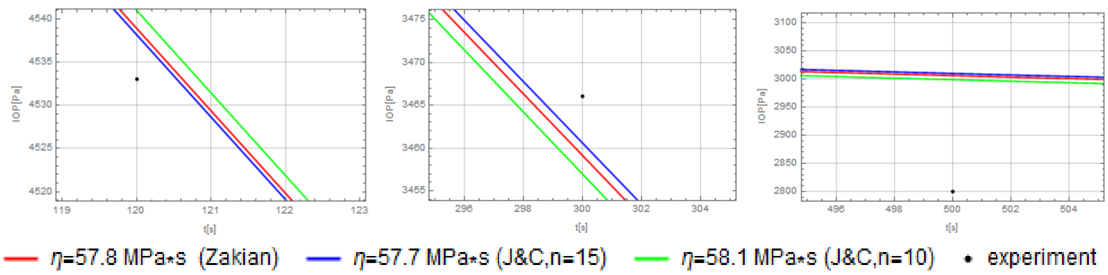

Figure 5: Time dependence of IOP: comparison of numerical approaches.

A comparison of these approaches by using the average values for three last points for the second point, the third point, and for the last point is shown in Fig. 6a, Fig. 6b, Fig. 6c, respectively.

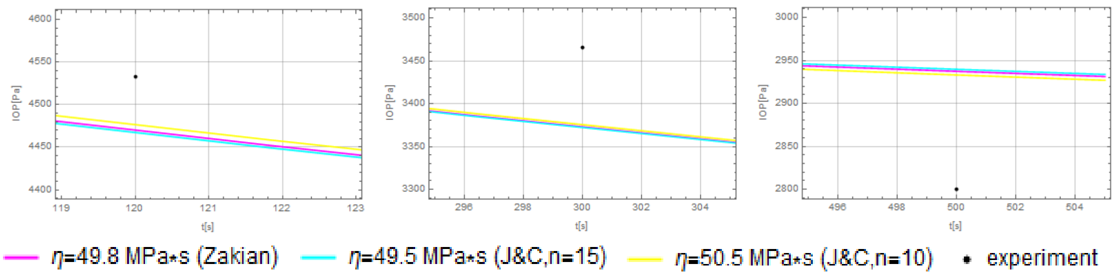

Figure 6: Time dependence of IOP: comparison of numerical approaches.

By comparing the results based on two different types of boundary condition for the inner radius displacement considering in this paper we can conclude that the value of the shear viscosity of the sclera is less if we suppose that the eye volume is constant during the time of the experiment. The possible reason of such a result is that by applying this type of BC we don't have a possibility to take into account all points from the experimental curve (see Fig. 3). We also can see by comparing Fig. 3 and Fig. 4 that we should take into account both facts: the existing sclera viscosity and the existing intraocular fluid outflow, - to have the best coincidence between the experimental data and theoretical results. We conclude that all approaches discussed in this paper are good enough for application in the framework of the problem of IOP determination. Hence, applying any of these approaches is reasonable. We should also note that Zakian's approach is the least complicated due to the least number of coefficients in Eqn. (14).

Consequently, a method for determination the shear viscosity of the sclera based on a comparison of results of mathematical modeling in the framework of 3D-dimensional linear viscoelastic theory and experimental data of IOP discrete measurements during several minutes after the intravitreal injection has been established. A comparison of numerical approaches based on three different sets of nodes and weights for a quadrature formula for the inverse Laplace transform has been performed.

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