Myocardial Material Parameter Estimation — A comparative study for simple shear

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Abstract

The study of ventricular mechanics - analysing the distribution of strain and stress in myocardium throughout the cardiac cycle - is crucially dependent on the accuracy of the constitutive law chosen to represent the highly nonlinear and anisotropic properties of passive cardiac muscle. A number of such laws have been proposed and fitted to experimental measurements of stress-strain behaviour. Here we examine five of these laws and compare them on the basis of (i) "goodness of fit": how well they fit a set of six shear deformation tests, (ii) "determinability": how well determined the objective function is at the optimal parameter fit and (iii) "variability": how well determined the material parameters are over the range of experiments. These criteria are utilised to discuss the advantages and disadvantages of the constitutive laws.

Keywords: parameter estimation, myocardium, orthotropic
Introduction

Knowledge of the mechanical behaviour of myocardium is crucial to understanding mechanisms of defect in regions of the heart, caused by abnormality such as ischaemia, hypertrophy or remodelling of the collagen microstructure.

Cardiac mechanics have been modelled over the last 30 years with different material law (ML) concepts, (elastic $\leftrightarrow$ viscoelastic, phenomenological $\leftrightarrow$ microstructurally based). We will give a brief summary of the attempts to model the passive elastic behaviour of myocardium.

Guccione et al. [1] modelled the equatorial region of the canine left ventricle as a thick-walled cylinder consisting of an incompressible Fung-type hyperelastic material with homogeneous properties incorporating five material parameters. The tissue was assumed to be locally transversely isotropic with respect to the fiber axis. They utilized simultaneous inflation, extension and torsion tests that were measured in the potassium-arrested dog heart to estimate material parameters.

LeGrice et al. [2] then performed histological measurements showing that the microstructure is a composite of discrete layers of myocardial fibres, usually four to six cells thick, which suggested an orthotropic material behaviour. This discovery was taken up by Costa et al. [3] by extending the transversely isotropic exponential Fung-type material law [4], [5] of Guccione into an orthotropic formulation with seven material parameters. The experimental protocol used therein consisted of multiaxial measurements of the canine left ventricle.

Nash & Hunter [6] proposed a “pole–zero” formulation of the strain energy function with 18 material parameters describing uniaxial and shear behaviour with respect to the three orthogonal structural axes. One difficulty with structurally based constitutive laws is the large number of parameters; therefore a number of these parameters were crosslinked by theoretical consideration of similar microstructural components being loaded.

Due to the high nonlinearity of the material parameters within each constitutive law and the high correlation between parameters, robust material parameter estimation is a challenging task [7]. The quality of a certain material law cannot simply be measured by one number; rather there are several aspects that play a role in comparing various material laws with each other and it is usually the
case that these aspects carry relatively different importance.

Here we propose three major criteria which can be used to contrast the behaviour in a parameter estimation process. “Goodness of fit” is the ability of a material law to minimize a given objective function. This comparison is realized by comparing the relative error of the estimate and secondly by the Akaike information criteria (AIC), see [8], which aims to penalize the number of material parameters in a model comparison. Secondly, “determinability”: how well the objective function is determined at the optimal parameter fit by means of the optimality criteria, see [9]. Thirdly we consider the “variability” of the parameters over the range of experiments for a given material law.

In this study, we compare five constitutive laws:

1. Costa law (CL)
2. Separate Fung-type law (SFL)
3. Pole-zero law (PZL)
4. Tangent law (TL)
5. Langevin Eight-chain law (LECL).

The details of these material laws will be presented in the next section. SFL & TL were chosen to have similar features to CL & PZL, respectively, and were chosen to investigate whether any improvement is obtained. Although the theoretically desirable polyconvexity [10, 11, 12] cannot be established under large strain conditions for these constitutive relations, they do prove in practice to provide very useful parametrisation of experimental data and the material properties.

Clearly these studies must be applied to a set of experimental tests. Various studies have proven the importance of shear deformation in myocardial mechanics, [13, 14]. We therefore chose the shear tests performed by Dokos et. al. [15] on small myocardial cubes aligned with the underlying microstructure as a basis for our study.

One aspect of material constitutive properties not taken into account in this study is the viscoelasticity of myocardial tissue since we feel that at present there are insufficient data on the passive viscoelastic properties of ventricular
myocardium at the physiological strain rates occurring in vivo, particularly in shear modes of deformation (relative to the laminar architecture). We therefore decided to limit our analysis to the hyperelastic properties only, with particular regard to shear properties, which remain poorly characterized to date. The Dokos data are a valuable resource in this regard.

We will start with presenting the necessary theoretical background for the material parameter estimation process, i.e. the five material laws in detail and their similarities, the experimental background, the model assumptions and lastly the objective function. This is followed by a theoretical summary of the three measures taken to compare the material laws, the results of the numerical study, and the subsequent statistical analysis including a comparison of the Akaike information criteria.
Methods

We first briefly summarise the fundamentals of continuum mechanics. The deformation is described by the deformation gradient tensor $F$, which connects the reference configuration with the deformed configuration. The strain is usually quantified using the Green strain tensor $E = \frac{1}{2}(F^T F - I)$. The balance of linear momentum states that the body must be in equilibrium with the external forces. This can be expressed using Eq. (1), where $\mathbf{S}$ is the second Piola–Kirchhoff stress tensor, [16].

$$\text{Div}(\mathbf{FS}) = 0$$ (1)

The remaining relationship between the stress $\mathbf{S}$ and the strain $\mathbf{E}$ is then specified by a function, the strain energy density $\Psi = \Psi(\mathbf{E})$. This differs depending on the material symmetry, and must obey the principle of material frame indifference (material objectivity). Strain energy density functions can be formulated in terms of the underlying strain invariants as proposed by [17], or they can be expressed as functions of the individual strain components where an additional condition must be satisfied, namely $\Psi(\mathbf{E}) = \Psi(\mathbf{E}^T)$. Given the stress–strain relationship $\mathbf{S} = \frac{\partial \Psi}{\partial \mathbf{E}}$, the balance equations can be solved.

Tissue Experiments

We base our modelling investigations on experimental data taken from Dokos et al. [15]. Here we give a short summary of the experiments performed and the results of this study.

Passive shear properties of six pig hearts were examined. Samples ($\sim 3 \times 3 \times 3$ mm) were cut from adjacent regions of the lateral left ventricular midwall, with sides aligned with the principal material axes ($f$, $n$, $s$: fiber, normal, sheet). Cycles of sinusoidal shear (shear displacement range [-50%, 50%]) were applied separately to each specimen in two orthogonal directions. Three specimens from each heart were tested in two directions, giving all six possible modes of shear as illustrated in Fig. (1). Data for the fitting of material properties were taken from cycles after strain softening had diminished. Displacements were prescribed to be half of the height of the cube, therefore ensuring that all strain tensors had the same magnitudes. The forces on the top
face of the cube were measured and taken as the data for the material parameter optimization, which is described below.

Constitutive Laws

We have developed a biomechanical simplified model, which assumes the deformation to be homogeneous, as shown in Fig. (1). Here we consider the stress strain relationship in further detail. The myocardium is typically modelled to be incompressible. However, since we assume known homogeneous simple shear deformations, we are guaranteed that the deformation will be isochoric, or in other words that no volume change will occur. The hydrostatic pressure is therefore not needed to enforce the material constraint of incompressibility.

Costa et al., [3], published the following strain energy density function.

$$\Psi_1(E_{ff}, E_{fn}, E_{fn}, E_{nm}, E_{mn}, E_{nf}, E_{mf}, E_{nn}) = \frac{1}{2}a(e^Q - 1)$$

where

$$Q = b_{ff}E_{ff}^2 + 2b_{fn}(\frac{1}{2}(E_{fn} + E_{nf}))^2 + 2b_{nm}(\frac{1}{2}(E_{mn} + E_{nm}))^2 + b_{mn}E_{mn}^2 + 2\varphi_1(\frac{1}{2}(E_{fn} + E_{nf}))^2 + b_{nm}E_{mn}^2$$

(2)

Note that the functional form was adapted such that the shear terms are now formulated as the symmetric part of the strain tensor rather than utilizing a product between shear strain terms as proposed by Costa et al. The meaning of the off-diagonal material parameters, however, remains unchanged.

The material law is based on a general exponential Fung type law, the details
of which can be found in [5]. The 1 in the term \((e^Q - 1)\) is subtracted to ensure that the strain energy density function is zero in the reference configuration, where \(Q = 0\).

We also investigated the following functional form:

\[
\Psi_2(E_{ff}, E_{fn}, E_{fs}, E_{nf}, E_{nm}, E_{rm}, E_{df}, E_{dm}, E_{em}) = \\
\frac{1}{2} a_{ff}(e^{b_{ff} E_{ff}} - 1) + \frac{1}{2} a_{fn}(e^{b_{fn}(\frac{1}{2}(E_{fn} + E_{nf}))^2} - 1) + \frac{1}{2} a_{rm}(e^{b_{rm}(\frac{1}{2}(E_{rm} + E_{sn}))^2} - 1) \\
+ \frac{1}{2} a_{dm}(e^{b_{dm}(\frac{1}{2}(E_{dm} + E_{sn}))^2} - 1) \\
+ \frac{1}{2} a_{em}(e^{b_{em}(\frac{1}{2}(E_{em} + E_{sn}))^2} - 1) - 1
\]

(3)

This “separated Fung-type law” (SFL) was motivated by the desire to decouple the material parameters from the single exponential in the CL.

A rather different form was proposed by Nash & Hunter [6], called the Pole-zero law (PZL), which is based on the idea that the tissue has a strain limit in each direction \(a_{ij}\), a strength \(k_{ij}\) and parameter \(b_{ij}\) that accounts for the nonlinearity of the stress-strain curve. The parameters \(b_{ij}\) were all set to 2, since this ensures a stable optimization:

\[
\Psi_3(E_{ff}, E_{fn}, E_{fs}, E_{nf}, E_{nm}, E_{rm}, E_{df}, E_{dm}, E_{em}) = \\
\frac{k_{ff} E_{ff}^2}{\left| a_{ff} - \left| E_{ff} \right| \right|^2} + \frac{k_{fn}(\frac{1}{2}(E_{fn} + E_{nf}))^2}{\left| a_{fn} - \frac{1}{2}(E_{fn} + E_{nf}) \right|^2} + \frac{k_{rm}(\frac{1}{2}(E_{rm} + E_{sn}))^2}{\left| a_{rm} - \frac{1}{2}(E_{rm} + E_{sn}) \right|^2} + \frac{k_{dm}(\frac{1}{2}(E_{dm} + E_{sn}))^2}{\left| a_{dm} - \frac{1}{2}(E_{dm} + E_{sn}) \right|^2}
\]

(4)

The PZL, however, has an infinite slope at the pole \(a_{ij}\), which is disadvantageous for numerical implementations. We therefore adapted the idea of the pole and modelled it with a Taylor series expansion of the \(IntTan(x)\) function (TL), where \(IntTan(x)\) is the indefinite integral of \(Tan(x)\), and truncated after the fifth term. This had the effect of removing the infinite slope at the pole – instead the curve monotonically increases. The \(IntTan(x)\) was chosen to comply to the convexity requirements of \(\Psi\). The functional form then reads:

\[
\Psi_4(E_{ff}, E_{fn}, E_{fs}, E_{nf}, E_{nm}, E_{rm}, E_{df}, E_{dm}, E_{em}) = \\
\frac{1}{2} a_{ff} IntTan(b_{ff} E_{ff}^2) + \frac{1}{2} a_{fn} IntTan(b_{fn}(\frac{1}{2}(E_{fn} + E_{nf}))^2) \\
+ \frac{1}{2} a_{rm} IntTan(b_{rm}(\frac{1}{2}(E_{rm} + E_{sn}))^2) + \frac{1}{2} a_{dm} IntTan(b_{dm} E_{dm}^2) \\
+ \frac{1}{2} a_{em} IntTan(b_{em}(\frac{1}{2}(E_{em} + E_{sn}))^2) \\
+ \frac{1}{2} a_{em} IntTan(b_{em} E_{em}^2)
\]

(5)

Another law was proposed by Bischoff and coworkers [18]. This constitutive law differs from the four before mentioned in that it is based on micro-structural
modelling of macromolecules. Although the macro–molecular model underlying this approach may not reflect the myocardial micro-structure, it may describe orthotropic mechanical behaviour on a macroscopic level.

For the derivation of the material law please refer to the original paper. Here, we simply restate the major quantities of the law and the strain energy density function. \( a_f, a_n, a_s \) are the dimensions of the orthotropic unit cell in the fiber, normal and sheet direction, \( a_f, a_n, a_s \) are the unit vectors in the direction of the unit cell axes and \( n \) is the density of chain molecules. \( k \) is the Boltzman constant, \( \theta \) the absolute temperature, \( N \) number of freely jointed links of length \( l \) in the macromolecule and \( \Psi_0 \) is a constant to ensure zero strain energy at zero strain. The four vectors \( \mathbf{P}^{(1)}, \mathbf{P}^{(2)}, \mathbf{P}^{(3)}, \mathbf{P}^{(4)} \) are defined as follows and represent the direction of the start to end point vectors of the macromolecules:

\[
\begin{align*}
\mathbf{P}^{(1)} &= \frac{a_f}{2} a_f + \frac{a_n}{2} a_n + \frac{a_s}{2} a_s \\
\mathbf{P}^{(2)} &= \frac{a_f}{2} a_f + \frac{a_n}{2} a_n - \frac{a_s}{2} a_s \\
\mathbf{P}^{(3)} &= \frac{a_f}{2} a_f - \frac{a_n}{2} a_n + \frac{a_s}{2} a_s \\
\mathbf{P}^{(4)} &= \frac{a_f}{2} a_f - \frac{a_n}{2} a_n - \frac{a_s}{2} a_s.
\end{align*}
\]

The deformed length of the individual chains are:

\[
\rho^{(i)} = \sqrt{\mathbf{P}^{(i)} \cdot \mathbb{C} \cdot \mathbf{P}^{(i)}},
\]

where \( \mathbb{C} = 2 \mathbb{E} + \mathbb{I} \) is the right Cauchy–Green stretch tensor and \( \mathbb{E} \) is the Green strain. \( \beta^{(i)}_p = \mathcal{L}^{-1}(\rho^{(i)} / N) \) is the normalised deformed chain length, \( P = \frac{1}{2} \sqrt{a_f^2 + a_n^2 + a_s^2} \) is the normalised undeformed chain length, \( \beta_p = \mathcal{L}^{-1}(P / N) \) and \( \mathcal{L}(x) = \coth(x) - 1 / x \) is the so-called Langevin function. Finally the strain energy density reads like:

\[
\Psi_5(E_{ff}, E_{fn}, E_{fs}, E_{nn}, E_{nm}, E_{mm}) = \Psi_0 + \frac{n k \theta}{4} \left( N \sum_{i=1}^{4} \left[ \frac{\rho^{(i)}_p}{N \beta^{(i)}_p} + \ln \frac{\beta^{(i)}_p}{\sinh \beta^{(i)}_p} \right] - \frac{\beta_p}{\sqrt{N}} \ln \left[ \lambda_a^2 \lambda_b^2 \lambda_c^2 \right] \right) + \frac{B}{\alpha^2} (\cosh[\alpha(J - 1)] - 1).
\]

The inverse Langevin function is used during the computation of the stress strain relationship. Since no closed form of the inverse function exists we utilise the so–called Padé approximant function, see [19]:

\[
\mathcal{L}^{-1}(x) = x \frac{3 - x^2}{1 - x^2} + O(x^6).
\]
The symbol \( O(x^6) \) is the Landau symbol, indicating that the error is restricted in the following way: \( 0 < \limsup_{x \to a} \left| \frac{\mathcal{L}^{-1}(x)}{x^6} \right| < \infty \).

**Objective Function**

Given the constitutive relations and the homogeneous model assumptions, we derived the top face force in an analytical form for any given displacement. We will present this for one material law (CL) and one shear deformation mode (NS-model) as an example. We also introduce a global coordinate system \((x, y, z)\) where the direction of shear is aligned with the \(x\)-axis and the normal of the top face with the \(z\)-axis. This serves to obtain an easier expression for the objective function.

Assuming material dimensions \(\alpha, \beta, \gamma\) in the \(x, y, z\)-directions or \(f, n, s\)-directions, respectively, we have the following deformation gradient tensor:

\[
F = \begin{pmatrix}
1 & 0 & k \\
0 & 1 & 0 \\
0 & 0 & 1 \\
\end{pmatrix}_{(x, y, z)} = \begin{pmatrix}
1 & 0 & 0 \\
0 & 1 & 0 \\
0 & k & 1 \\
\end{pmatrix}_{(f, n, s)},
\]

where \(k\) ranges between \(-\frac{1}{2}\gamma\) and \(\frac{1}{2}\gamma\). From this we can derive the Green strain tensor in both coordinate systems:

\[
E = \frac{1}{2} \begin{pmatrix}
0 & 0 & k \\
0 & 0 & 0 \\
k & 0 & k^2 \\
\end{pmatrix}_{(x, y, z)} = \frac{1}{2} \begin{pmatrix}
0 & 0 & 0 \\
0 & k^2 & k \\
k & 0 & 0 \\
\end{pmatrix}_{(f, n, s)}.
\]

With the stress strain relationship, \(\mathbf{S} = \frac{\partial \Psi}{\partial \varepsilon}\), we finally obtain the second Piola-Kirchhoff stress tensor:

\[
\mathbf{S} = \begin{pmatrix}
0 & 0 & \frac{1}{2}a_1 b_{mn} k e^{\frac{1}{2}k} + \frac{1}{2}b_{mn} k^2 \\
0 & 0 & 0 \\
\frac{1}{2}a_1 b_{mn} k e^{\frac{1}{2}k} + \frac{1}{2}b_{mn} k^2 & 0 & \frac{1}{2}a_1 b_{mn} k^2 e^{\frac{1}{2}k} + \frac{1}{2}b_{mn} k^2 \\
\end{pmatrix}_{(x, y, z)}
\]

\[
= \begin{pmatrix}
0 & 0 & \frac{1}{2}a_1 b_{mn} k^2 e^{\frac{1}{2}k} + \frac{1}{2}b_{mn} k^2 \\
0 & \frac{1}{2}a_1 b_{mn} k^2 e^{\frac{1}{2}k} + \frac{1}{2}b_{mn} k^2 & 0 \\
0 & \frac{1}{2}a_1 b_{mn} k e^{\frac{1}{2}k} + \frac{1}{2}b_{mn} k^2 & 0 \\
\end{pmatrix}_{(f, n, s)}.
\]
From this we can derive the analytic force on the top face by means of Nanson’s formula:

\[
t_{\text{ana}} = F S \cdot N = \begin{pmatrix}
\frac{1}{2} \alpha \beta a_1 \left( b_{\text{reff}} k e \left( 4 b - k^2 + \frac{4 b}{5} - k^3 \right) \right) \\
0 \\
\frac{1}{2} \alpha \beta a_1 \left( b_{\text{rmm}} k^2 e \left( 4 b - k^2 + \frac{4 b}{5} - k^3 \right) \right)
\end{pmatrix}
\]

where \( N = (0, 0, \alpha \beta)_{(x, y, z)} = (0, \alpha \beta, 0)_{(f, n, s)} \) is the normal vector in the reference configuration multiplied with the area of the top face.

From the experiments we have an analogue of \( t_{\text{ana}} \), i.e. \( t_{\text{exp}} \), the measured force on the top face from the experiment. The experiment equips us with approximately 250 data points over the range of deformations from \(-\frac{1}{2} \gamma\) to \(\frac{1}{2} \gamma\) for each mode.

The usual approach of a least squares objective function is adopted, but modified to account for the expensive numerical computations that arise in inverse finite element parameter estimations.

The conventional least squares objective function would sum over all six modes, all three directions of the top face force and all data points of each mode and force direction, resulting in approximately \( 6 \times 3 \times 250 = 4500 \) data points:

\[
\Omega(\theta) = \frac{1}{2} \sum_{\text{nodes}} \sum_{x, y, z} \sum_{\text{data points}} (t_{\text{ana}}(\theta) - t_{\text{exp}})^2,
\]

where \( \theta \) is the vector of all material parameters. By adding a “weight” to each addend, namely the width \( \Delta z \) of each interval of two successive data points, the objective function approximates the following integral, assuming that the data
points imply a piecewise linear function.

$$
\Omega(\theta) = \frac{1}{2} \sum_{\text{nodes}} \sum_{x,y,z=\text{data points}} \sum_{\text{force}} (t_{\text{ana}}(\theta) - t_{\text{exp}})^2 \Delta x
$$

$$
\approx \frac{1}{2} \sum_{\text{nodes}} \sum_{x,y,z=\text{force}} \int \left( t_{\text{ana}}(\theta, x) - t_{\text{exp}}(x) \right)^2 dx
$$

(15)

This weighting was chosen because the integral forms a $L^2$--norm in the functional space of squared integrable functions, and can therefore serve as a measure of the length of the error. The same holds for the piecewise linear approximating functions and this measure can be interpreted as a “pseudo--energy content” (pseudo, because the dimensions of the integrals are $J^2/m$) and serves as a reference for the minimized objective function to obtain a relative error.

The above formulation suggests that it would be numerically more efficient to approximate the integral using a Gaussian quadrature integration method, see for example [20]. This would then read:

$$
\int_{-\gamma_i}^{\gamma_i} \left( t_{\text{ana}}(\theta, x) - t_{\text{exp}}(x) \right)^2 dx \approx \sum_{j=1}^{M} \omega^j \left( t_{\text{ana}}(\theta, x^j) - t_{\text{exp}}(x^j) \right)^2,
$$

(16)

where $M$ is the number of Gauss quadrature points for each of the twelve displacement-force curves. The objective function then reads:

$$
\Omega(\theta) = \frac{1}{2} \sum_{\text{nodes}} \sum_{x,y,z=\text{force}} \sum_{j=1}^{M} \omega^j \left( t_{\text{ana}}(\theta, x^j) - t_{\text{exp}}(x^j) \right)^2
$$

(17)

The question arises whether this modified least square method converges to Eq.(15). We have previously shown, [21], that 12 Gauss points suffice to approximate the full data set with an error of less than 0.01% and the computational time was reduced by 98%. The total number of data points ($N$) then needed was reduced to 144 compared to $\sim 4500$ for the full model.

Note the significant change in meaning by altering the weighted least square approach, i.e. we now also have a means to obtain some kind of physically meaningful objective measure for each experiment. To be more precise, if $t^j_{\text{ana}}(\theta, x) = 0$ in (17) one obtains the “energy content (EC)”, $\Omega_{\text{EC}}^{\text{Exp}^0}$ of each
experiment (ExpNo). The same of course holds for each individual mode and it is therefore also possible to compare the quality of fitting certain modes for certain material laws. More importantly this can be used as a way to scale the value of the objective function at the optimal solution \( \Omega(\vartheta_0)/\Omega_{\text{ExpNo}} \), which then serves as a relative measure to compare amongst experiments rather than amongst material laws.

**Optimization kernel**

With this objective function, we are now ready to perform the constitutive parameter optimization. Since this is a nonlinear problem, we chose to use the Levenberg–Marquardt method, see [22] for details. Here we just summarize the main idea.

To find the minimum of \( \Omega \) we have to find a sequence of steps \( \varepsilon_k \) in the parameter space which successively decreases \( \Omega \):

\[
\Omega(\vartheta_{k+1}) < \Omega(\vartheta_k) \quad \text{with} \quad \vartheta_{k+1} = \vartheta_k + \varepsilon_k.
\]  

(18)

It can be shown that this is guaranteed if \( \varepsilon_k \) is chosen to be:

\[
\varepsilon_k = -R \nabla_{\vartheta} \Omega,
\]  

(19)

where \( \nabla_{\vartheta} \Omega \) is the gradient of \( \Omega \) and if \( R \) is a positive definite matrix.

If the valley was parabolic, a natural choice of \( R \) would be the inverse of the Hessian of \( \Omega \). However, in practical applications this cannot be assumed to be true, especially since the initial guess may lie far outside a convex region. Therefore the Hessian may not be positive definite. This also highlights the need to find good initial guesses with our method for further FEM inverse estimations.

Levenberg [23] proposed to utilize a modified \( R \), namely \( R = (H + \lambda I)^{-1} \), which allows you to adapt \( \lambda \) in a way such that \( R \) becomes positive definite. In particular, if \( \lambda = 0 \), it is the Newton–Raphson method and if \( \lambda = \infty \), it is the steepest descent method.

As stopping criteria we chose the difference of two successive steps for the objective function \( |\Delta \Omega| \) and of the length of the material parameter vector \( |\Delta \vartheta| \) to both be smaller than \( 10^{-5} \).
Comparison amongst material laws

In this section, we investigate methods to compare the four material laws against each other and amongst experiments. We measure how well they fit to the data for different experimental sets (goodness of fit) and how well they are defined for a given set of experimental data in terms of numerical determinability. We describe these measures further below.

Goodness of fit

The first measure is the objective function value at the optimum $\Omega(\hat{\theta}_0)$. We utilize the energy content to normalize this value to form a “relative objective function value” $\Omega_{rel} = \Omega(\theta_0)/\Omega^{Exp}_{EC}$. We can then calculate the mean $\mu$ and standard deviation $\sigma$ of $\Omega_{rel}$ over all experiments for each material law and we can thus form the coefficient of variation $\text{CoV} = \frac{\sigma}{\mu}$.

Akaike Information Criterion (AIC)

The relative objective function has limited use as a “goodness of fit” criterion to compare the five models, since it does not take into account the number of parameters of each model. This challenge is usually overcome by introducing an information criterion that reflects both the objective function value and the model complexity via a common measure.

The idea of an information criterion was derived from a similar question. The challenge was to select an approximating model from a set of models. This was overcome by defining a “distance” between two models (similar to the distance between to functions over a given interval), the so-called Kullback-Leibler “distance”. In the mid-1970s Akaike introduced his “entropy maximisation principle” in a series of papers [24, 25, 26] as a theoretical basis for model selection. This principle is a simple relationship between the Kullback-Leibler distance and Fisher’s maximised log-likelihood function. From this Akaike derived an information criterion (AIC) which is named after him:

$$\text{AIC} = N \ln \left( \frac{1}{N} \Omega(\theta) \right) + 2K. \quad (20)$$

The “best” model is defined as the model with the lowest information criterion.

By taking into account the model complexity $K$ in (20) the variance part of the
error will be considered.

Starting from different statistical assumptions, a number of proposals for the complexity have been made. All of them monotonically increase with the number of parameters in the model. Since it is not clear which information criterion is the best, we chose the Akaike information criterion (AIC) as suggested by Burnham et al. [8]. The information criterion yields a relative measure and can therefore only act to select the best model within a set of models. However, if all the models were very poor, both criteria would still select the one with the best estimate, but that model may be poor in an absolute sense. This is why we also utilize the goodness of fit criteria.

Determinability

The above criteria form a basis for comparing the goodness of fit for the material laws, but it is also important to ask the question whether the material parameters are sensitive to disturbances in the data values, or in other words, how the objective function varies in the neighbourhood of the optimum. For a detailed and thorough discussion of this issue see [9, 27, 28]. Here we briefly describe the basic ideas.

Given the optimal point in the parameter space \( \mathbf{\theta}_0 \), we can form the various criteria to measure different aspects of the behaviour of the material in consideration. If we consider a small deviation \( \delta \mathbf{\theta} \) around the optimum \( \mathbf{\theta}_0 \) then the following equation:

\[
\delta \mathbf{\theta}^T \mathbf{H}_0 \delta \mathbf{\theta} \leq 2 \epsilon
\]

implies an \( Q \)-dimensional hyperellipsoid, where \( Q \) is the number of material parameters for the material law in consideration and \( \mathbf{H}_0 \) is the Hessian at the optimum. This region is sometimes also called the “\( \epsilon \)-indifference region”. The determinant \( \det(\mathbf{H}_0) \) at the optimal point represents the volume of the indifference region and is also referred to as the D–optimality criterion. The higher this number, the least variance the material parameters exhibit.

The condition number of the Hessian at the optimum, \( \text{cond}(\mathbf{H}_0) \), describes the ratio between the highest and the lowest eigenvalue of \( \mathbf{H}_0 \) and can be shown to be the square of the eccentricity of the hyperellipsoid.
The so-called $M$-optimality criterion relates the interaction between material parameters. It is defined as:

$$\det(H_0) \quad \text{where} \quad \tilde{H}_{ij} = \frac{H_{ij}}{H_{ii} H_{jj}} \quad \text{(no sum)}, \quad (22)$$

and describes the alignment of the hyperellipsoid with the material parameter axes. ($\tilde{H}_{ij} = \delta_{ij}$ for perfect alignment, corresponding to no correlation between the material parameters.)

**Variability**

The statistical analysis of the objective function gives insight into the overall ability of the material law to fit a certain set of experimental data. It is, however, also important to consider the variability of each individual parameter as well as the overall variability. We therefore calculated the mean $\mu$ and standard deviation $\sigma$ of each individual parameter over all experiments for each material law and we can thus form the coefficient of variation $\text{CoV} = \frac{\sigma}{\mu}$. Furthermore we calculated the mean of all coefficients of variation for each material law, which gives an indication of the overall variability of the constitutive relation.
Results

The detailed numerical results are given in Tables (1–6). We list all material parameter values and for each of these entries we present the mean, standard deviation and coefficient of variation (CoV = $\frac{\sigma}{\mu}$) across the experiments. We also list the total pseudo energy content ($\Omega_T$) for each experiment in the last column of Table (1).

Comparing the mean of the relative goodness of fit amongst all four material laws, the CL obtained the best relative goodness of fit (2.50%), whereas the coefficient of variation was 54.9%. Comparing the $AIC$ confirms this result. However, it is noteworthy that when comparing the experiments individually that the CL had the best goodness of fit for experiments 2, 3, 6 whereas the PZL had the best goodness of fit for experiments 1, 4, 5.

The condition number for all material laws show that the PZL had the highest eccentricity with $1.9 \cdot 10^{17}$ (please note that this is mainly due to an outlier in experiment 4) whereas LECL was lowest $5.3 \cdot 10^{3}$. Considering the correlation or M-optimality, the CL was best with $2.8 \cdot 10^{-3}$. In contrast the result for the TL was dramatically distorted by experiment 2 where for the computation for the M-optimality the programme suggested that significant numerical errors might occur due to a bad condition number. Comparing the variability in terms of the coefficients of variation for each material law over all material parameters shows that LECL has the lowest $CoV_{Max}$ (40.0%) and TL has the highest (327%). The same holds for the $\mu_{CoV}$ where LECL has the lowest (19.4%) and SFL the highest (79.0%).

It is important to note here that experiment 2 yielded comparably poor results for all material laws. Leaving out experiment 2 would therefore yield a much closer material parameter set for all material laws. These poor results are most likely due to the fact that the micro-structural fiber orientation was not modelled. Inverse finite element studies that include this aspect may shed some more light on the possible reasons.

From these results we can see that the CL had the both the best fit properties and the best determinability properties of the five laws tested in simple shear, whereas the LECL exhibits the least variance while having worse fitting properties.
Table 1: Comparison of material parameter estimates for CL for all experiments

| Exp  | C1   | C1(%) | AIC   | Rank | dCV     | cv(M)  | mcv(M) | tva(M) | s   | blland | bland | bemp | bemp | bemp | bemp | bemp | bemp | bemp | bemp | bemp | bemp |
|------|------|-------|-------|------|---------|--------|--------|--------|-----|--------|--------|------|------|------|------|------|------|------|------|------|------|------|
| Exp 1 | 10.00 | 10.00 | 14.0 | 1 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 | 0.012 |
| Exp 3 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 | 18.0 |
| Exp 4 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 | 22.0 |
| Exp 5 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 | 26.0 |

Table 2: Comparison of material parameter estimates for SFL for all experiments

<table>
<thead>
<tr>
<th>Exp 1</th>
<th>C1</th>
<th>C1(%)</th>
<th>AIC</th>
<th>Rank</th>
<th>dCV</th>
<th>cv(M)</th>
<th>mcv(M)</th>
<th>tva(M)</th>
<th>s</th>
<th>blland</th>
<th>bland</th>
<th>bemp</th>
<th>bemp</th>
<th>bemp</th>
<th>bemp</th>
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<td>10.00</td>
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<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
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<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
<td>0.012</td>
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</tr>
<tr>
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<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
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<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
<td>18.0</td>
</tr>
<tr>
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<td>22.0</td>
<td>22.0</td>
<td>22.0</td>
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<td>22.0</td>
<td>22.0</td>
<td>22.0</td>
<td>22.0</td>
<td>22.0</td>
</tr>
<tr>
<td>Exp 6</td>
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<td>26.0</td>
<td>26.0</td>
<td>26.0</td>
<td>26.0</td>
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<td>26.0</td>
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<td>26.0</td>
<td>26.0</td>
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</tr>
</tbody>
</table>

17
| PZL | C | DBk | ΛE | Rank | det(Δ) | r cof (Δ) | det (Δ) | det (Δ) | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. | s refl. |
|-----|----|-----|-----|------|--------|-----------|---------|---------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| E s 1 | 0.44 | 3.98 | 141.1 | 1.1 | 2.16 | 3.82 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 | 0.26 |
| E s 2 | 1.52 | 3.96 | 171.6 | 2.2 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 |
| E s 3 | 1.43 | 0.95 | 32.3 | 4.2 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 | 0.08 |
| E s 4 | 3.85 | 0.39 | 32.3 | 3.3 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 | 0.05 |
| E s 5 | 0.56 | 2.25 | 101.6 | 2.3 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 | 0.04 |
| E s 6 | 269 | 2.96 | 114.5 | 2.4 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 | 0.28 |
| a | 1.42 | 2.04 | 1.65 | 1.1 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 | 0.09 |
| C s V | 0.96 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 | 90.9 |

Table 3: Comparison of material parameter estimates for PZL for all experiments.

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<tr>
<th>TL</th>
<th>C</th>
<th>DBk</th>
<th>ΛE</th>
<th>Rank</th>
<th>det(Δ)</th>
<th>r cof (Δ)</th>
<th>det (Δ)</th>
<th>det (Δ)</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
<th>s refl.</th>
</tr>
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<tr>
<td>E s 1</td>
<td>0.38</td>
<td>4.12</td>
<td>107.1</td>
<td>1.1</td>
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<td>E s 2</td>
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<td>0.28</td>
<td>0.28</td>
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<td>0.05</td>
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<td>E s 4</td>
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<td>0.08</td>
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<td>0.08</td>
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<tr>
<td>E s 5</td>
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<td>a</td>
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Table 4: Comparison of material parameter estimates for TL for all experiments.
<table>
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<tr>
<th>LECL</th>
<th>G</th>
<th>$t_{20^o C}$</th>
<th>$A C^c$</th>
<th>Shank</th>
<th>$d_{el}$ (in)</th>
<th>$d_{em}$ (in)</th>
<th>$d_{el}$ (in)</th>
<th>$n_f$</th>
<th>$n_m$</th>
<th>$n_d$</th>
<th>$n$</th>
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<tbody>
<tr>
<td>HAG-1</td>
<td>3657</td>
<td>4.05</td>
<td>1690</td>
<td>5</td>
<td>5.0E+18</td>
<td>5.2E+03</td>
<td>5.0E+03</td>
<td>1,288</td>
<td>1,760</td>
<td>1,142</td>
<td>2,24E+10</td>
</tr>
<tr>
<td>HAG-2</td>
<td>53890</td>
<td>14.7%</td>
<td>169</td>
<td>5</td>
<td>5.0E+18</td>
<td>5.2E+03</td>
<td>5.0E+03</td>
<td>1,288</td>
<td>1,760</td>
<td>1,142</td>
<td>2,24E+10</td>
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<td>HAG-3</td>
<td>5055</td>
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<td>169</td>
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<td>5.2E+03</td>
<td>5.0E+03</td>
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<td>1,760</td>
<td>1,142</td>
<td>2,24E+10</td>
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<tr>
<td>HAG-4</td>
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<td>6.0%</td>
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<td>1,760</td>
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Table 5: Comparison of material parameter estimates for LECL for all experiments

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<th>$d_{el}$ (in)</th>
<th>$d_{em}$ (in)</th>
<th>$d_{em}$ (in)</th>
<th>$C_v$</th>
<th>$V_{Elastic}$</th>
<th>$H_C \psi V$</th>
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<td>414%</td>
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<tr>
<td>SFL</td>
<td>2.7%</td>
<td>5.0E+18</td>
<td>5.2E+03</td>
<td>5.0E+03</td>
<td>414%</td>
<td></td>
</tr>
<tr>
<td>PFL</td>
<td>2.5%</td>
<td>5.0E+18</td>
<td>5.2E+03</td>
<td>5.0E+03</td>
<td>414%</td>
<td></td>
</tr>
<tr>
<td>TL</td>
<td>2.6%</td>
<td>1.0E+18</td>
<td>5.0E+03</td>
<td>414%</td>
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<tr>
<td>LECL</td>
<td>0.40%</td>
<td>5.0E+18</td>
<td>5.2E+03</td>
<td>414%</td>
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Table 6: Comparison of all material laws
Figure 2 shows all twelve force displacement curves for the Costa law for experiment 3. The graphs show excellent agreement of the analytical curves (solid) with the experimental data (dotted). Similar results were obtained for all other material laws including LECL which exhibited the highest relative error, figure 3.

Figure 2: The table depicts the experimental (dotted) and fitted force–displacement curves (solid) of the Costa law for all six modes for experiment 3. It is grouped according to Fig.1, whereas groups of two pictures show the x- and z-force, respectively. The overall error is 1.59%. Note the different scales on each graph. The abscissa shows the displacement in mm, whereas the ordinate shows the top face force in mN, where e.g. \( F_{NS_x} \) indicates the x-force for the NS-mode.
Figure 3: The table depicts the experimental (dotted) and fitted force–displacement curves (solid) of the Langevin Eight–Chain law for all six modes for experiment 3. It is grouped according to Fig.1, whereas groups of two pictures show the x- and z-force, respectively. The overall error is 3.88%. Note the different scales on each graph. The abscissa shows the displacement in mm, whereas the ordinate shows the top face force in mN, where e.g. $F_{NS_z}$ indicates the x-force for the NS-mode.
Discussion

In this paper we have examined five alternative forms of constitutive laws for representing the stress-strain behaviour of myocardial tissue. In order to examine the effectiveness of these laws we examined their application to six experimental shear tests on a small block of tissue cut such that the faces aligned with the material axes (fibre, normal and sheet) of the tissue. The tissue blocks were loaded in simple shear spanning each of the six modes Fig. (1) For each mode the applied shear stress loaded the tissue close to the elastic limit (and gave the highly nonlinear J-shaped stress-strain curve characteristic of soft biological tissues). An objective function was defined that summed the squared differences between the observed force and the force predicted by the constitutive model across a range of strains for each mode and summed over the six modes. This sum was replaced by a continuous integral over the strain in which a smooth curve was fitted to the force-displacement relation and Gaussian quadrature was used to calculate the integral. The calculation converged with 12 Gauss points making it much more efficient (for comparable error) than the discrete sum over all data points. Material parameters in the constitutive law were then optimised using a Levenberg-Marquardt method. Three measures were used to assess the four constitutive laws. The first (goodness-of-fit) was a measure of how well each optimised constitutive law fitted the experimental data from the six tests, and the second (determinability) measured how sensitive the optimal fit was to small errors in the data and the third (variability) measured the variance of the material parameters over the range of experiments.

Our results give a very clear outcome regarding the comparative study, i.e. the CL is the most suitable law to capture the mechanical response of myocardium for homogeneous simple shear. However, we need to address some subtleties which may affect this result for a different experimental setup.

The CL exhibits a cross-coupling of strain terms for each stress component, whereas that is not the case for the other three laws. Due to the assumption of a homogeneous deformation (and therefore a sparsely populated strain tensor), this cross-coupling does not occur in the analytic expression of the top face force. This might therefore differentiate the CL from the other three laws when using FEM inverse parameter estimations, especially with more complex deformation
modes. One would also need to consider adding cross-coupling terms for the other three laws. Further studies are needed to investigate this effect.

Preliminary FEM studies with equivalent boundary conditions for the CL showed that some of the shear parameters tended to reach the strain limit imposed by the optimization package. Similar studies with the PZL exhibited problems in determining the material parameters which is why we fixed the values $b_{ij}$ to 2. Additionally we developed the SFL and the TL to address potential disadvantages in the CL and PZL, respectively. The SFL was designed to account for the cross-coupling, which was believed to be too restrictive. The TL was designed to address the infinite slope at the pole which was believed to complicate the parameter estimation. As is clear from Tables (1–4), the SFL did improve the goodness of fit when compared with the CL for experiments 1&3. The TL did not enhance the behaviour of the PZL.

Another issue that is worth noting is that the number of addends after which the TL is truncated only plays a minor role. We performed the material parameter estimation for various numbers of addends ranging from 3–20 and they altered the objective function value by less than 0.01%.

Additionally it is important to point out that all laws still serve to solve forward solutions in FEM calculations. As Criscione points out, certain laws are useful for forward solutions, but may be suboptimally conceived for parameter estimations, see [29].

In further studies we will apply this method using the FEM and we will develop new material parameter estimation techniques based on multi-scale models for the mechanical behaviour of myocardial micro-structure.
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