

An inverse method for non-invasive viscosity measurements

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Abstract. A procedure is presented which allows to compute in a non-invasive manner, blood viscosity through flow measurements obtained at a fixed vessel cross-section. The data set is made of measurements (artery radius and spatially discrete velocity profiles) performed at given time intervals for which the signal to noise ratio is typical of U.S. Doppler velocimetry in clinical situation. This identification approach is based on the minimization, through a backpropagation algorithm, of a cost function quantifying the distance between numerical data obtained through Navier-Stokes simulations and experimental measurements. Since this cost function implicitly depends on the value of viscosity used in numerical simulations, its minimization determines an effective viscosity which is shown to be robust to measurement errors and sampling time. Such an approach is shown to work in an in vitro experiment, and seems to be suitable for in vivo measurements of viscosity by the atraumatic techniques of Doppler echography.

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1 Introduction

Various haemodynamics parameters do vary with pathology which explains their significant clinical interest. Since the work by Womersley [1], many studies [2–5] have been devoted to blood flow properties inside physiological vessels. Three points appear to be predominant in haemodynamics: the vessel system topology, the wall mechanical properties and the blood rheological behavior. For instance, the topology of the circle of Willis is central for the cerebral circulation [6,7]. Similarly wall viscoelasticity, transmural pressure-vessel area relationship play a major role when considering propagative phenomena for the arterial system [8,9] or blood filling in the venous system, respectively. However one of the most basic characteristics governing haemodynamics in the arterial and venous systems is blood viscosity since it modifies peripheral resistance, shape of local velocity profiles and wall shear stress.

The morphology of the arterial system can be easily obtained in an atraumatic way by means of various angiography methods; the wall arterial elasticity is currently roughly evaluated in clinical research by measuring the pulse wave velocity. On the contrary, there is presently only one clinical method to determine blood viscosity. It requires taking a blood sample with a needle and thereafter measuring viscosity in vitro using a viscometer. An efficient real time atraumatic monitoring of viscosity is

hence highly desirable for clinical applications in particular for cardiovascular surgery or disease prevention. The method presented below is robust and requires only in vivo atraumatic measurements: it is consequently a good candidate for such a clinical purpose.

All the presently available procedures which are proposed to determine viscosity, are theoretically based on the dependence with respect to the viscosity value, of unsteady velocity profiles when both inertial and viscous effects are present. Some of them [10] cannot be used in vivo. Various methods have already tried to solve this inverse problem: either the inversion of an over-determined linear system [11] or the comparison of a pre-computed experimental abacus (for periodic signals) [12,13], or an integral method based on the knowledge of instantaneous velocity profiles [14,15]. Except for specific conditions, such approaches are highly noise sensitive. Other difficulties arise when looking for clinical applications. On the theoretical side, the model is necessarily simplified since the true blood flow is an unsteady 3D motion of a non-homogeneous non-Newtonian fluid confined by time-dependent boundaries. As far as laboratory experiments are concerned, the set-up and measurement techniques must recreate a situation as close as possible to the true physiological context. The present work proposes a procedure based on velocity profiles obtained by ultrasonic Doppler velocimetry which is a standard tool in arterial haemodynamics investigations and the only atraumatic one if one excepts the MNR method which have still to be

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improved in this context. Our approach combines direct numerical flow simulation and an inverse technique based on an optimization method. As a first step of the general inverse problem, a fully-developed flow of a Newtonian fluid is considered in a rigid pipe. Clearly the hypothesis of Newtonian behavior is well accepted in large arteries. This is related to the fact that the blood is a red blood cell (RBC) suspension. Its viscosity is mainly dependent on the aggregation state of the RBC. At rest the aggregation induces an increase of the viscosity. Conversely the viscosity decreases when the blood is sheared since the blood is disaggregated. In that case, it behaves like a Newtonian fluid. In human large arteries, the blood has been subjected to high shear rate when passing through the heart. Taking into account arterial mean blood velocity, the RBC have not enough time in the main large arteries to aggregate and the blood behaves like a Newtonian fluid.

Our procedure works for *any* applied unsteady pressure gradient and does not assume a priori the shape of velocity profiles. Theoretically, these latter quantities are only constrained to satisfy the Navier-Stokes equation. Experimentally they are only measured at a unique vessel cross section. The inverse method which evaluates viscosity from velocity profiles, is derived from the optimization of a cost function quantifying the difference between experimental data and equivalent quantities obtained through Navier-Stokes numerical simulations. It is based on an extension of the classical Lagrange multipliers method in which the multipliers become space and time functions satisfying an additional adjoint partial differential equation. This approach is close to the backpropagation procedure used in neuronal nets [16], and has already been used in a geophysical context [17] or else in hydrodynamical problems such as a coupled wakes experiment [18]. In biomechanical studies, an analogous method has been previously introduced to identify the artery wall elasticity [19]. However, this latter work only considered numerical simulated quantities and never experimental data.

The hydrodynamic model is introduced in Section 2.1 and the general principle of the inverse method is given in Section 2.2 while the optimization procedure and its Lagrangian formulation are described in Section 2.3. Details for the implementation of the time discretized model are provided in Appendix A. Section 3 describes the test which were performed to ascertain the precision and robustness of the proposed algorithm in particular with respect to noise and sampling time. Finally, Section 4 describes an experimental set-up on which provided an experimental data set. This set was used as a practical test of our method. Perspectives are given in conclusion.

2 Model and methods

Let us introduce the numerical model as well as the inverse technique based on numerical simulations of this model, which evaluates fluid viscosity using experimental data. For in vivo applications, the mostly used atraumatic way of measuring velocities is the pulsed Doppler ultrasound

technique. This method allows to get instantaneous velocity profiles by determining the frequency shift induced, in a moving fluid, by a Doppler effect. More precisely, the data set obtained in typical echography measurements, consists of an artery radius R_{meas} and longitudinal velocities v_{meas}^{jk} , measured at a unique vessel section for $n_s + 1$ discrete radial locations $r = a_j \equiv j\Delta_{\text{exp}}$, $j = 0, \dots, n_s$, Δ_{exp} being the apparatus spatial resolution. Such measurements are only performed at $n_t + 1$ discrete times $t = S_k \equiv kS$, $k = 0, \dots, n_t$ where S is the sampling time interval. Note that measured velocities profiles v_{meas}^{jk} as well as artery radius R_{meas} are affected by measurement errors.

2.1 Model

Let us consider the laminar axisymmetric fully-developed flow of a Newtonian incompressible fluid when it is confined in a vessel of radius R and generated by a given time-dependent pressure gradient. Moreover as generally assumed in the hemodynamics of large arteries, the fluid density ρ and the kinematic viscosity ν are assumed to be constant. This ideal situation, which can be assumed in arterial blood flow, allows to get rid of entrance effects a few diameters downstream of an arterial bifurcation. In large arteries, as generally well admitted, blood viscosity can be considered as constant since blood disaggregates after passing through the heart and the aggregation process has not enough time to occur. Indeed an order of magnitude of the aggregation characteristic time is about 10 s for standard physiological conditions. The above situation is governed by the axisymmetric Navier-Stokes equations together with boundary conditions. In the following, the radial velocity can be neglected since the variation of vessel radius $\delta R(t, z)$ is assumed to be much smaller than the average radius. In addition, the longitudinal velocity $v(r, z, t)$ is almost independent on the z space variable, the pulse wavelength being much larger than the radius R . Within this approximation, the pipe may be viewed as rigid, the pressure gradient $\partial P/\partial z$ becomes a pure time dependent function and the non linear term in the Navier-Stokes equation vanishes. As a consequence the laminar flow is entirely described by the longitudinal velocity $v(r, t)$ governed by Stokes equation

$$\frac{\partial v}{\partial t} = -\frac{1}{\rho} \frac{\partial P}{\partial z} + \nu \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v}{\partial r} \right). \quad (1)$$

Clearly $\partial P/\partial z$ is a quantity containing a lot of informations about the global problem. By imposing equation (1) at $r = 0$, one gets a relation for the velocity $v_c(t)$ at the center of a cross-section

$$\frac{dv_c}{dt} = -\frac{1}{\rho} \frac{\partial P}{\partial z} + 2\nu \frac{\partial^2 v}{\partial r^2} (r = 0). \quad (2)$$

Eliminating the pressure gradient $\partial P/\partial z$ between equations (1) and (2) one then obtains

$$\frac{\partial v}{\partial t} = \frac{dv_c}{dt} - 2\nu \frac{\partial^2 v}{\partial r^2} (r = 0) + \nu \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v}{\partial r} \right). \quad (3)$$

This latter equation is useful since it allows a numerical resolution leading to the knowledge of the velocity profile which only uses $v_c(t)$ at $r = 0$ as an input. Moreover this quantity can be measured atraumatically. An alternative model may be written using the mass flux $Q(t)$, instead of the centreline velocity. For the sake of simplicity, the presentation below will be entirely based on the first model.

From now on (including the appendix), the model (3) is put in dimensionless form and all quantities are meant to be dimensionless except those written with a superscript $*$ which are left dimensional. Echography measurements provide a characteristic velocity V_{char}^* , a time scale T_{char}^* (for periodic flow the time period is adequate). By contrast, the characteristic length R_{char}^* is chosen to be the *true* artery radius R^* . Its value is close but differs from the measured one R_{meas}^* because of measurement errors. The model is governed by a dimensionless equation

$$\frac{\partial v}{\partial t} = \frac{dv_c}{dt} - \frac{4\pi}{\alpha^2} \frac{\partial^2 v}{\partial r^2}(r=0) + \frac{2\pi}{\alpha^2} \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v}{\partial r} \right) \quad (4)$$

with $v(r=1, t) = 0$ and $\frac{\partial v}{\partial r}(r=0, t) = 0$ which depends on the centreline velocity $v_c(t)$ and on the Womersley number

$$\alpha = R_{\text{char}}^* \sqrt{\frac{\omega_{\text{char}}^*}{\nu^*}} \quad \text{where} \quad \omega_{\text{char}}^* = \frac{2\pi}{T_{\text{char}}^*}. \quad (5)$$

Experimentally, longitudinal velocities v_{meas}^{jk} are measured at well known dimensional radial location a_j^* . However the associated dimensionless radial locations a_j^*/R^* are not precisely known: a_j^*/R_{meas}^* is actually known but R_{meas}^*/R^* is not precisely determined because of the presence of unknown true radius R^* . The simulation of model (4) generates dimensionless profiles $v(r, t)$ which provide the equivalent numerical velocities $v(a_j^*/R^*, S_k)$. Since quantity β

$$\beta = \frac{R_{\text{meas}}^* - R^*}{R^*} \quad (6)$$

is small the true radius R^* being close to the measured one R_{meas}^* , quantity $v(a_j^*/R^*, S_k)$ can be expanded as follows

$$v\left(\frac{a_j^*}{R^*}, S_k\right) = v\left(\frac{a_j^*}{R_{\text{meas}}^*}(1 + \beta), S_k\right) \sim v_{\text{sim}}^{jk}; \quad (7)$$

where

$$v_{\text{sim}}^{jk} \equiv v\left(\frac{a_j^*}{R_{\text{meas}}^*}, S_k\right) + \frac{a_j^* \beta}{R_{\text{meas}}^*} \frac{\partial v}{\partial r}\left(\frac{a_j^*}{R_{\text{meas}}^*}, S_k\right).$$

Moreover, in order to separate the contributions of viscosity and artery radius, equation (4) now reads

$$\begin{aligned} \frac{\partial v}{\partial t} = \frac{dv_c}{dt} - 2\tilde{\nu}(1 + \beta)^2 \frac{\partial^2 v}{\partial r^2}(r=0) \\ + \tilde{\nu}(1 + \beta)^2 \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v}{\partial r} \right) \end{aligned} \quad (8)$$

$$\text{where} \quad \tilde{\nu} = \frac{\nu^* T_{\text{char}}^*}{R_{\text{meas}}^{*2}}. \quad (9)$$

Equation (8) expresses the contribution of viscosity through dimensionless viscosity $\tilde{\nu}$ and the contribution of artery radius through relative error β .

2.2 The inverse method

The proposed inverse method estimates the effective values of parameters $\tilde{\nu}$, β and consequently an effective blood kinematic viscosity ν_{opt}^* and an effective artery radius R_{opt}^* . This is possible since viscosity, vessel boundaries and inertial effects directly govern the haemodynamics. Note that the hematocrit or the blood density which are surely important factors for haemodynamics, only change indirectly the flow by affecting blood kinematic viscosity ν^* . In order to evaluate these parameters, such a dependency should be modelled by phenomenological laws. We will not consider such a problem here.

The identification is performed by determining the values of $\tilde{\nu}$ and β that optimally fit the experimental measurements. This amounts at minimizing a function $\mathcal{F}$ which quantifies the distance between experimentally measured v_{meas}^{jk} and numerically simulated v_{sim}^{jk} longitudinal velocities. In inverse problems, the choice of the cost function is quite important and depends on the experimental data available and also on parameters to be identified. A cost function which is quite sensitive to these parameter values, is clearly the most appropriate. Previous works [13,14] have shown that the identification of viscosity using an inverse method is very much dependent on (i) the value of the Womersley number (5); (ii) the radial position; (iii) the time range at which data have been collected [15]. A priori, this remark is still valid for the present method. In addition, this procedure appears from numerical tests, to be less noise dependent than the methods described in [14,15] and can be even used to clean the data set (see below). In addition, note that, in medium or large arteries, the Womersley number α ranges from 4 to 13 for normal physiological conditions [9]. This interval prevents the flow to exhibit an almost Poiseuille $\alpha \ll 1$ or plug like shape $\alpha \gg 1$ for which the present procedure cannot be used since the associated velocity shapes are not dependent on viscosity. In the present work, the cost function $\mathcal{F}$ used is built on the dimensionless local errors $v_{\text{sim}}^{jk} - v_{\text{meas}}^{jk}$

$$\mathcal{F} = \sum_{j=0}^{n_s} \sum_{k=1}^{n_t} H_j \left(v_{\text{sim}}^{jk} - v_{\text{meas}}^{jk} \right)^2 \quad (10)$$

where H_j varies from 1 near the center of the artery to 0 in the vicinity of the wall. This function is used in order not to sum beyond the true radius R^* and to eliminate measurements near the artery wall where signal to noise ratio and convolution effects are maximal. Practically, we choose $H_j = 1$ for $0 \leq j \leq n_r$, with n_r typically 80% or 90% of n_s , and $H_j = 0$ elsewhere.

This least square expression is chosen for several reasons: it is the most classical cost function, and it is differentiable with respect to v^{jk} . This function depends through v_{sim}^{jk} on several model inputs: two parameters $\tilde{\nu}$, β and the centreline velocity $v_c(t)$. This latter velocity is practically measured at sampling times S_k . This experimental velocity is denoted by v_{meas}^{0k} . As a consequence, velocity $v_c(t)$ is parameterized through the following piecewise linear interpolation

$$v_c(t) = v_c^k + (v_c^{k+1} - v_c^k) \frac{t - S_k}{S} \quad (11)$$

with $S_k < t < S_{k+1}$, where the n_t parameters $v_c^1, \dots, v_c^{n_t}$ are close to the experimental $v_{\text{meas}}^{01}, \dots, v_{\text{meas}}^{0n_t}$. This interpolation is part of the model on which the identification technique is built. A better e.g. spline approximation could be easily introduced but we will not further analyze this point. Note that the initial centreline velocity v_c^0 is left equal to v_{meas}^{00} . Finally the model and cost function $\mathcal{F}(\tilde{\nu}, \beta; v_c^1, \dots, v_c^{n_t})$ depend on parameters $\tilde{\nu}$, β and n_t centreline velocities v_c^k : the optimization of $\mathcal{F}$ is thus performed on $n_t + 2$ quantities. The procedure below implies that $\mathcal{F}$ is also differentiable with respect to these $n_t + 2$ quantities.

Since the first two parameters $\tilde{\nu}$ and β possess quite a different status compared with the centreline velocities v_c^k , we proceed by an iterative procedure in which each iteration is divided in two elementary steps: first (step (i)), the minimum of $\mathcal{F}(\tilde{\nu}, \beta; v_c^1, \dots, v_c^{n_t})$ is found with respect to $\tilde{\nu}$ and β at fixed v_c^k values. Second (step (ii)), the minimum of $\mathcal{F}(\tilde{\nu}, \beta; v_c^1, \dots, v_c^{n_t})$ is found with respect to the n_t values v_c^k at fixed $\tilde{\nu}$ and β values equal to those found in step (i).

This overall iterative procedure is started by the following inputs: $\beta = 0$ i.e. $R^* = R_{\text{meas}}^*$, $v_c^k = v_{\text{meas}}^{0k}$ and a typical value for ν^* e.g. $\nu^* = 5 \times 10^{-6} \text{ m}^2/\text{s}$. After few iterations (actually two are generally sufficient), the algorithm has converged leading to effective values for $\tilde{\nu}$ and β i.e. viscosity ν_{opt}^* , artery radius R_{opt}^* as well as a better evaluation of the centreline velocity signal. In addition, the reconstructed velocity profile is obtained by numerical simulation of the model with the optimal parameters. During the elementary step (i) (resp.(ii)) of each iteration, the minimum of $\mathcal{F}$ with respect to $\tilde{\nu}$ and β (resp. n_t parameters v_c^k) is always found by a conjugate gradient algorithm [20]. The main problem is thus reduced to obtaining the gradient of $\mathcal{F}$ with respect to parameters $\tilde{\nu}$, β and $v_c^1, \dots, v_c^{n_t}$. This task is not straightforward since function $\mathcal{F}$ implicitly depends on these $n_t + 2$ parameters via the simulated velocity profiles v_{sim}^{jk} . The so-called backpropagation algorithm which is introduced in Section 2.3, determines the gradient by solving a dual model. Figure 1 presents the most general procedure to get ν_{opt}^* , R_{opt}^* and $v_{\text{c opt}}^1, \dots, v_{\text{c opt}}^{n_t}$.

The present method is valuable for two main reasons. First, it works with no substantial cost with many parameters. By contrast, a direct approach which could be attempted by using several numerical solutions for various viscosity, radii and centreline velocities and approximating the gradient by finite differences, would not be robust

and its efficiency would deteriorate with the number of parameters. Second, it will be checked in the subsequent analyses that the optimal parameters are not too much sensitive to measurement errors. If inverse methods are to be applied on real data, this is crucial since real experimental data show not a fairly good signal to noise ratio.

2.3 Cost function gradient computation by a backpropagation technique

Since the numerical model must be discretized in space and time, one must consider a discretized version of equation (8) in addition to the already discrete cost function (10). Appendix A is precisely devoted to this intricate case which is actually implemented in Sections 3 and 4. In order to convey the principle of the method, we present here below an easier version implemented on a continuous system and a continuous cost function. One assumes, for simplicity reasons, that time and spatial measurements are continuous. Moreover, $v_c^1, \dots, v_c^{n_t}$ are supposed fixed. However, one can easily assume $v_c^1, \dots, v_c^{n_t}$ to be free parameters within a straightforward generalization.

Velocity is zero at the wall $v(r = 1, t) = 0$ and the centreline velocity $v_c(t)$ is assumed known from equation (11) and parameters $v_c^1, \dots, v_c^{n_t}$. The initial conditions $v(r, t = 0)$ are assumed to be known as well. Equation (8) is equivalent to

$$\forall r \in [0, 1], \forall t \in [0, S_{n_t}], \quad \frac{\partial v}{\partial t} - G(\tilde{\nu}, \beta; v(r, t)) = 0 \quad (12)$$

where

$$G(\tilde{\nu}, \beta; v) = \left[\frac{dv_c}{dt} - 2\tilde{\nu}(1 + \beta)^2 \frac{\partial^2 v}{\partial r^2}(0, t) \right] + \tilde{\nu}(1 + \beta)^2 \frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial v}{\partial r} \right).$$

With continuous time and space measurements, the cost function reads

$$\mathcal{F}(\tilde{\nu}, \beta) = \int_0^1 \int_0^{S_{n_t}} H(r) \left(\underbrace{v(r, t) + \beta r \frac{\partial v}{\partial r}(r, t)}_{v_{\text{sim}}(r, t)} - v_{\text{meas}}(r, t) \right)^2 dr dt \quad (13)$$

where the smooth function $H(r)$ plays the same role as H_j in equation (10).

The main problem now is to compute the variation $\delta \mathcal{F}$ of the cost function with respect to $\delta \tilde{\nu}$ and $\delta \beta$. However, variations of $\tilde{\nu}$ and β appear in $\mathcal{F}$ through the following constraint: velocity field $v(r, t)$ satisfies the dynamics (12)

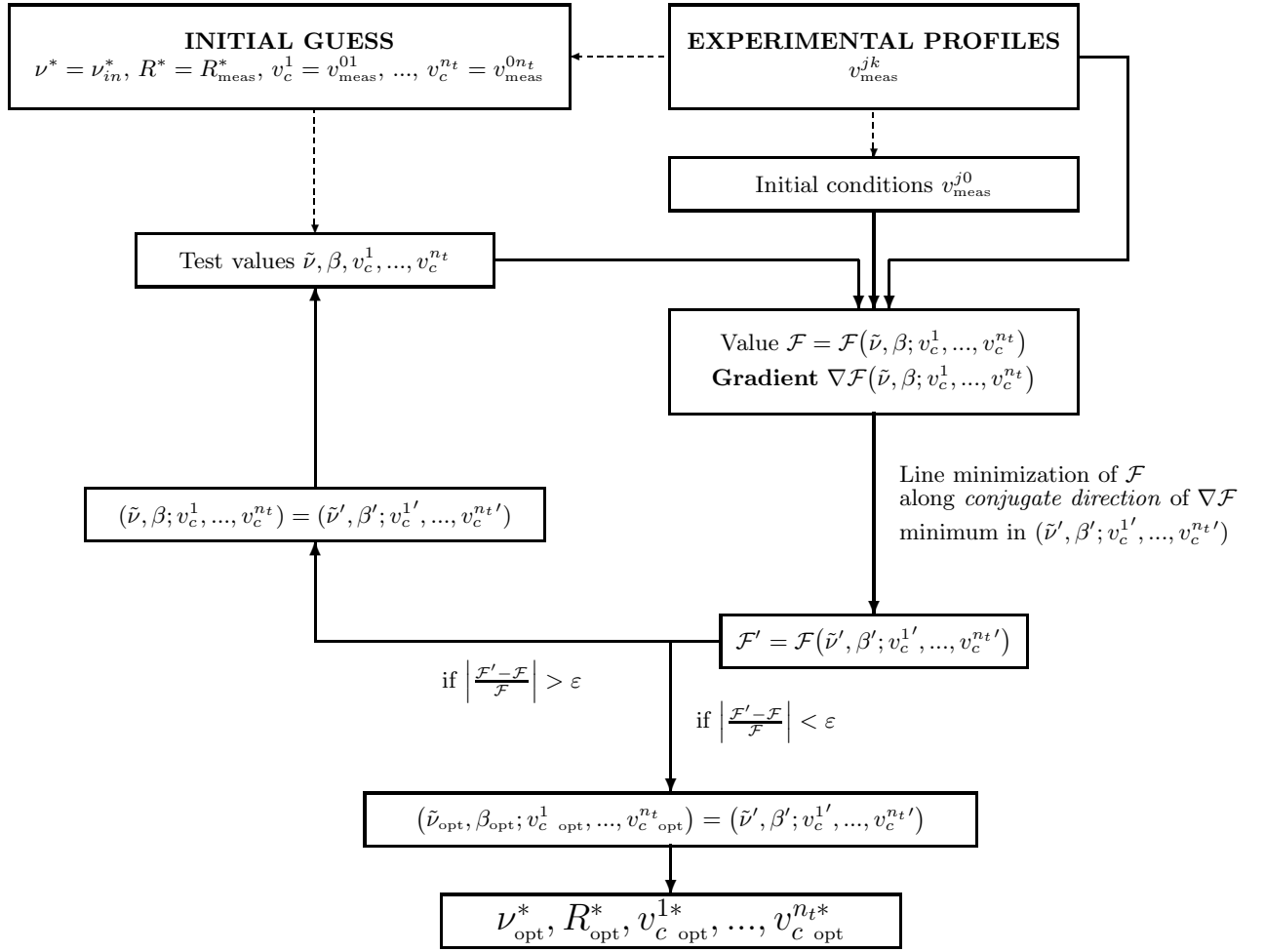


Fig. 1. Simplified synoptic representation of the algorithm employed to compute from experimental data and cost function $\mathcal{F}$, dimensionless viscosity and radius $\tilde{\nu}$ and β and centreline velocities $v_c^1, \dots, v_c^{n_t}$. Dashed arrows are only used for the first time step. Quantity ε is a threshold amplitude which can be tuned to increase the precision.

during the full time interval $[0, S_{n_t}]$. In order to get around this problem, one uses a generalized Lagrange multipliers approach which introduces the following Lagrangian function

$$\mathcal{L} = \mathcal{F} + \int_0^1 \int_0^{S_{n_t}} \left(\frac{\partial v}{\partial t} - G \right) \varphi(r, t) \, dr \, dt \quad (14)$$

where quantities $\varphi(r, t)$ correspond to Lagrange multipliers. If equation (12) is satisfied, one gets $\mathcal{L} = \mathcal{F}$ whatever the value of $\varphi(r, t)$. As a consequence, $\delta \mathcal{L} = \delta \mathcal{F}$ whatever the value of $\varphi(r, t)$. This freedom in the choice of the Lagrange multipliers can be exploited to compute $\delta \mathcal{L}$ – hence $\delta \mathcal{F}$ – as a function of $\delta \tilde{\nu}$ and $\delta \beta$. In the most general way, $\delta \mathcal{L}$ can be expressed as a function of $\delta \tilde{\nu}$, $\delta \beta$, $\delta v(r, t)$ and $\delta \varphi(r, t)$:

$$\delta \mathcal{L} = \delta \mathcal{F}_1 + \delta \mathcal{F}_2 + \delta \mathcal{F}_3 + \delta \mathcal{L}_1 + \delta \mathcal{L}_2 + \delta \mathcal{L}_3 + \delta \mathcal{L}_4$$

where

$$\begin{aligned} \delta \mathcal{F}_1 &= \int_0^1 \int_0^{S_{n_t}} 2 H(r) (v_{\text{sim}} - v_{\text{meas}}) \delta v \, dr \, dt, \\ \delta \mathcal{F}_2 &= \delta \beta \int_0^1 \int_0^{S_{n_t}} 2 H(r) (v_{\text{sim}} - v_{\text{meas}}) r \frac{\partial v}{\partial r} \, dr \, dt, \\ \delta \mathcal{F}_3 &= \int_0^1 \int_0^{S_{n_t}} 2 H(r) (v_{\text{sim}} - v_{\text{meas}}) \beta r \frac{\partial \delta v}{\partial r} \, dr \, dt, \\ \delta \mathcal{L}_1 &= \int_0^1 \int_0^{S_{n_t}} \left(\frac{\partial v}{\partial t} - G \right) \delta \varphi \, dr \, dt, \\ \delta \mathcal{L}_2 &= \int_0^1 \int_0^{S_{n_t}} \left(\frac{\partial \delta v}{\partial t} - \frac{\partial G}{\partial v} \delta v \right) \varphi \, dr \, dt, \\ \delta \mathcal{L}_3 &= -\delta \tilde{\nu} \int_0^1 \int_0^{S_{n_t}} \frac{\partial G}{\partial \tilde{\nu}} \varphi \, dr \, dt, \\ \delta \mathcal{L}_4 &= -\delta \beta \int_0^1 \int_0^{S_{n_t}} \frac{\partial G}{\partial \beta} \varphi \, dr \, dt. \end{aligned}$$

Since quantities $v(r, t)$ satisfy the dynamics (12), one gets $\delta \mathcal{L}_1 = 0$ for any arbitrary $\varphi(r, t)$. In order to explicitly

determine the $\delta v(r, t)$ dependence, one integrates by parts the time derivative in $\delta \mathcal{L}_2$ and the space derivative in $\delta \mathcal{F}_3$. By assuming the initial conditions to be fixed i.e. $\delta v(r, t = 0) = 0$, a new expression is obtained for $\delta \mathcal{L}_2$.

$$\delta \mathcal{L}_2 = \int_0^1 \varphi(r, S_{n_t}) \delta v(r, S_{n_t}) dr - \int_0^1 \int_0^{S_{n_t}} \left(\frac{\partial \varphi}{\partial t} + \frac{\partial G}{\partial v} \varphi \right) \delta v dr dt \quad (15)$$

and for $\delta \mathcal{F}_3$ as well

$$\delta \mathcal{F}_3 = - \int_0^1 \int_0^{S_{n_t}} 2\beta \frac{\partial}{\partial r} \left(r H(r) (v_{\text{sim}} - v_{\text{meas}}) \right) \delta v dr dt.$$

At this point, Lagrange multipliers $\varphi(r, t)$ can be prescribed in such a way that $\delta \mathcal{F}_1 + \delta \mathcal{F}_3 + \delta \mathcal{L}_2 = 0$ for any $\delta v(r, t)$. This prescription allows to suppress the terms $\delta v(r, t)$ in $\delta \mathcal{L}$: it is then unnecessary to compute explicitly these variations $\delta v(r, t)$ in terms of $\delta \tilde{v}$ and $\delta \beta$. Looking at the above expressions for $\delta \mathcal{F}$ and $\delta \mathcal{L}_2$, the above choice implies that $\varphi(r, t)$ satisfy the following dynamical system

$$2H(r) \left(v_{\text{sim}} - v_{\text{meas}} \right) - 2\beta \frac{\partial}{\partial r} \left(r H(r) (v_{\text{sim}} - v_{\text{meas}}) \right) - \frac{\partial \varphi}{\partial t} - \frac{\partial G}{\partial v} \varphi = 0. \quad (16)$$

This system must be integrated backwards in time from $t = S_{n_t}$ to $t = 0$ with the prescribed condition $\varphi(r, S_{n_t}) = 0$ at $t = S_{n_t}$ in order to suppress the first term of $\delta \mathcal{L}_2$ in equation (15). The gradient of the cost function $\mathcal{F}$ now simply reads

$$\begin{aligned} \frac{\partial \mathcal{F}}{\partial \tilde{v}} &= \frac{\delta \mathcal{L}_3}{\delta \tilde{v}} = - \int_0^1 \int_0^{S_{n_t}} \frac{\partial G}{\partial \tilde{v}} \varphi dr dt \\ \frac{\partial \mathcal{F}}{\partial \beta} &= \frac{\delta \mathcal{F}_2}{\delta \beta} + \frac{\delta \mathcal{L}_4}{\delta \beta} = \int_0^1 \int_0^{S_{n_t}} 2 H(r) (v_{\text{sim}} - v_{\text{meas}}) r \frac{\partial v}{\partial r} dr dt \\ &\quad - \int_0^1 \int_0^{S_{n_t}} \frac{\partial G}{\partial \beta} \varphi dr dt. \end{aligned} \quad (17)$$

The exact gradient is hence determined using only two simulations: one of the direct model (12) and one of its backpropagated companion (16).

3 Testing the reconstruction algorithm

The purpose of this section is to test and to understand the advantages, limits and application range of our inverse technique. The efficiency of an identification algorithm naturally depends on the capability of the physical model on which it is based, to incorporate in a sufficiently precise way the physics governing the measured quantities. In addition, its efficiency also relies on the sensitivity of the algorithm to the data set and on other technical issues: precision and stability of the numerical model discretization, precision and stability of the backpropagation

method. All these features are crucial since inverse problems are generally ill-conditioned: small variations on data sets may give large variation on identified parameters. The general consequence is a lack or not of the robustness for the algorithm.

Let us emphasize that all results are here obtained using the complete inverse method presented in Appendix A.

3.1 Testing the accuracy of the backpropagation calculation

Practically, the minimum of cost function $\mathcal{F}$ is hardly reached by the conjugate gradient descent algorithm if the gradient computed by the variational approach differs from the exact gradient $(\partial \mathcal{F} / \partial \tilde{v}, \partial \mathcal{F} / \partial \beta)$. In such a case, a badly estimated set of parameters $(\tilde{v}_{\text{opt}}, \beta_{\text{opt}})$ will be provided by the identification method. The precision attained when evaluating the cost function gradient is hence an important issue. The gradient of the cost function $\mathcal{F}$ (function here defined in Eq. (28)), was computed using the variational approach and its value was compared to the same quantity evaluated by a finite differences scheme

$$\frac{\mathcal{F}(\tilde{v} + \delta \tilde{v}) - \mathcal{F}(\tilde{v} - \delta \tilde{v})}{2\delta \tilde{v}} \quad \text{and} \quad \frac{\mathcal{F}(\beta + \delta \beta) - \mathcal{F}(\beta - \delta \beta)}{2\delta \beta} \quad (18)$$

as $\delta \tilde{v} \rightarrow 0$ and $\delta \beta \rightarrow 0$. The relative errors between both quantities were less than a percent when $\delta \tilde{v} \leq 10^{-2}$ and $\delta \beta \leq 10^{-3}$. Such values were computed based on the synthetic data produced by equation (3) or more precisely by its discretized version (22) with a dynamic viscosity $\mu = 4 \text{ mPa.s}$. As a conclusion, equations (32, 34) correctly and accurately estimate the gradient of $\mathcal{F}$. Note that the component of the gradient with respect to centreline velocities are not presented here for the sake of simplicity.

3.2 The synthetic data set

The identification algorithm is tested on a *synthetic* data set v_{meas}^{jk} . This set is built in a two step process (see Fig. 2 top): a direct numerical simulation of system (22) generates a time signal Y^{jk} followed by an addition of noise to this signal

$$v_{\text{meas}}^{jk} = Y^{jk} + B_{\text{noise}} * \mathcal{N}(j, k). \quad (19)$$

The random variable $\mathcal{N}$ is characterized by a uniform probability distribution function over the interval $[-1, 1]$ and B_{noise} quantifies the ratio between the noise amplitude and the maximum centreline velocity value. The addition of noise to the clean signal Y^{jk} for all times S_k and space locations a_j mimics the effect of measurements errors in true experimental conditions. One thus generates an emulated experimental signal v_{meas}^{jk} .

The numerical simulation to compute Y^{jk} was performed for given parameters $\tilde{v}$ and β (here $\tilde{v} = 0.49$ and $\beta = 0.05$ obtained from the dimensional quantities $\nu^* = 4 \times 10^{-6} \text{ m}^2 \text{ s}^{-1}$, $R^* = 2.85 \text{ mm}$ and $R_{\text{meas}}^* = 3 \text{ mm}$)

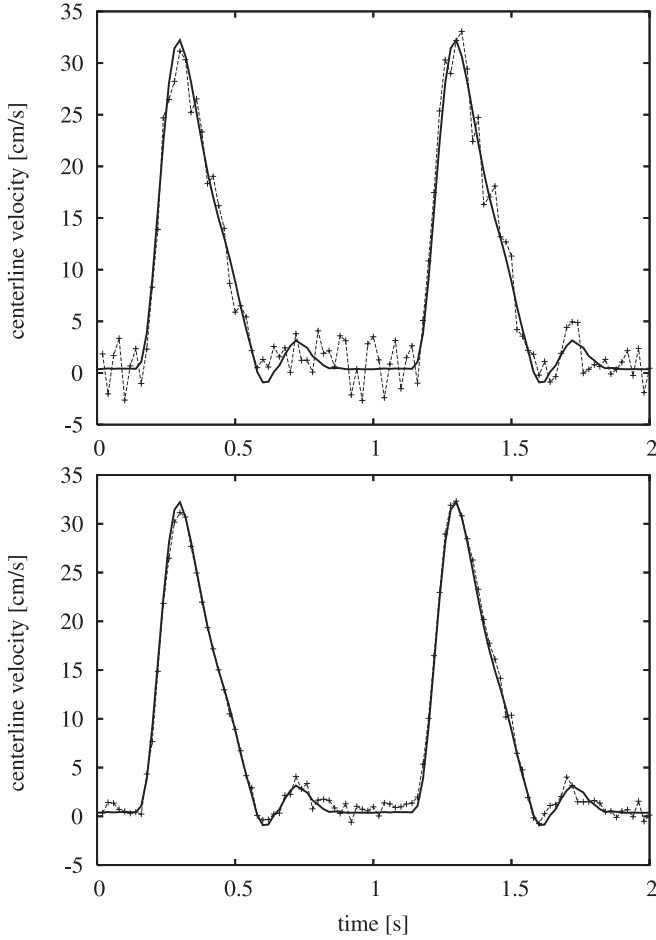


Fig. 2. (Top) Reference centreline velocity used for the synthetic data here represented for two periods (continuous line before noise addition, dotted after noise addition). The noise amplitude is equal to 10% of velocity amplitude. The period of the signal is 1 s (Bottom) Reference centreline velocity as the result of the minimization of $\mathcal{F}$ (dashed) and reference centreline velocity before noise addition (continuous line).

as well as an initial profile and centreline velocity. The centreline velocity was chosen to be equal to a true experimental value (see Fig. 2 top) and the initial conditions to be a Poiseuille like profile. The sampling time S^* and numerical time step Δt were fixed at $S^* = 0.02$ s and $\Delta t = \frac{S}{200}$. The time step Δt was chosen very small in this sub-section to ensure the convergence of the algorithm. It was checked however that a larger value such as $\Delta t = \frac{S}{40}$ is also valid. This latter value will be used in Section 4. Finally, the Womersley number (5), associated to the fundamental frequency of the signal, was set to values close to true experimental situations. A reference data set will be often used which corresponds to a period of 1 s (i.e. a Womersley $\alpha = 3.57$).

By generating such a synthetic data, one is able to test the algorithm itself since (i) the values of ν^* and R^* are known a priori in this case, and (ii) noise amplitude or sampling time can be varied at will. In addition, various independent such time series can be generated using dif-

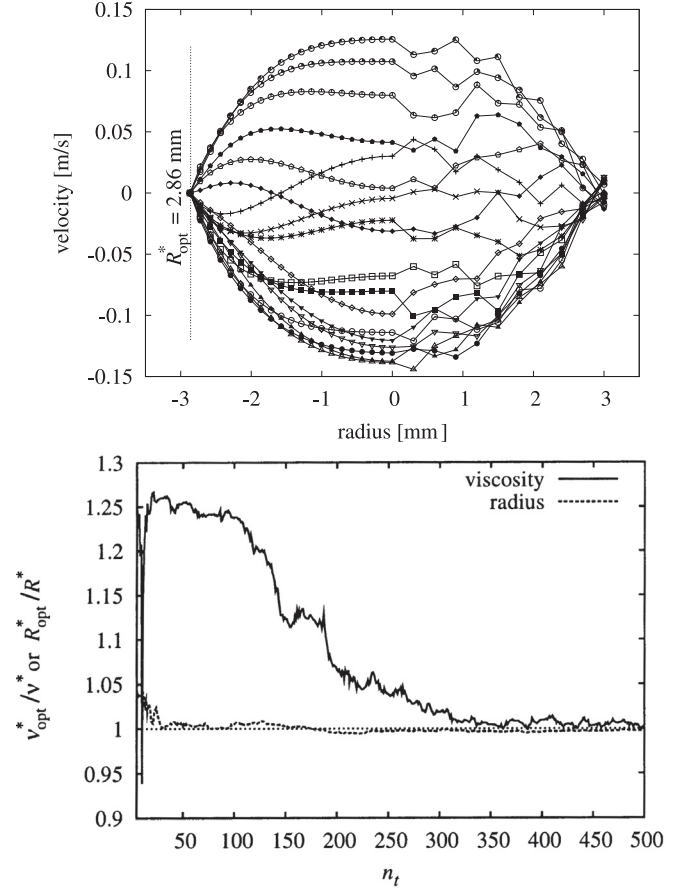


Fig. 3. (Top) Temporal evolution of synthetic data (right side of the profile) for a noise level of 10% and $\alpha = 3.57$. The value of the artery radius used for the simulation is taken to be $R^* = 2.85$ mm and the equivalent measured radius $R_{\text{meas}}^* = 3$ mm. The reconstructed data is depicted on the left side of the profile. Note that the reconstructed radius value is equal to $R_{\text{opt}}^* = 2.86$ mm (see vertical line in the figure). Each curve corresponds to different measurement time S_k^* . (Bottom) Normalized optimal viscosity ν_{opt}^* and radius R_{opt}^* as function of number of measured profiles n_t for a relative noise level of 10%. There are 50 such profiles for a single period.

ferent realizations of the random variable $\mathcal{N}$. The inverse procedure could then be repeated with any given realizations of v_{meas}^{jk} . This provides a value ν_{opt}^* and R_{opt}^* for each realization and consequently an average value and an associated root mean square for ν_{opt}^* or R_{opt}^* .

3.3 Testing the robustness of the reconstruction algorithm

Let us now test the robustness of the algorithm with respect to several features: (i) number of experimental profiles n_t , (ii) noise amplitude B_{noise} , (iii) sampling time S , (iv) Womersley number (5). Note that measurement errors may perturb the quality of parameter identification in two different ways. First, the value of the cost function (28) is directly affected by measurements of the experimental

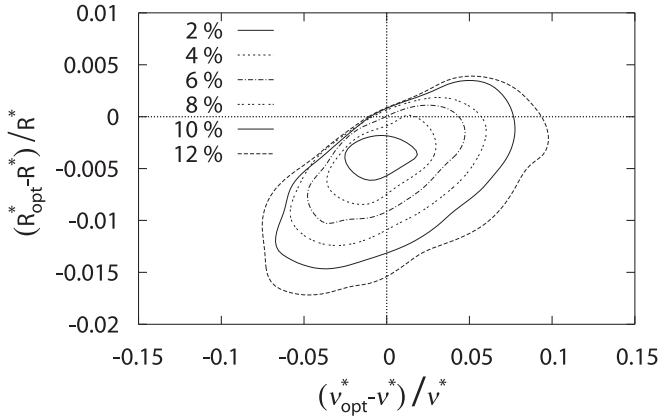


Fig. 4. Influence of noise level on the dispersion of optimal values $(\nu_{\text{opt}}^*, R_{\text{opt}}^*)$. Each curve corresponds to a certain noise level ranging from 2% (inner curve) to 12% (outer curve). It displays the mid-height contour of the probability distribution function which is the result of 20 000 noise realizations. This computation has been performed using the reference data set ($\alpha = 3.57$ for the fundamental frequency).

data set. Second, the centreline velocity $v_c(t)$ explicitly appears in the algorithm through condition (27): a measurement error on this specific quantity modifies the model prediction as well.

Figure 3 (top) displays for a unique noise realization, the result of the identification procedure for velocity profiles with $\alpha = 3.57$: even though the synthetic v_{meas}^{jk} (right hand side of profile) is very much affected by a noise amplitude of 10%, the algorithm is capable to get the reconstructed velocity field (the left hand side of profile) and reconstructs as well the centreline velocity (see Fig. 2 bottom).

For a given sampling time S^* , the optimal value ν_{opt}^* depends on the number of experimental profiles n_t as well as on the noise amplitude B_{noise} . Figure 3 (bottom) illustrates the evolution of ν_{opt}^* and R_{opt}^* as a function of n_t for a given realization, a noise level of 10% and $\alpha = 3.57$. For this specific case, the optimal value converges after $n_t \sim 250$. In the experiment presented below, this means that one must wait 250 consecutive measurements i.e. $250/50 = 5$ s, hence 5 cycles of the experimental signal, to converge towards a value which causes less than 5% relative error. Extensive computational investigations were performed which confirmed the convergence for other realizations of noise. A similar behavior was also found for all noise levels.

The influence of noise amplitude B_{noise} on the optimal values $(\nu_{\text{opt}}^*, R_{\text{opt}}^*)$ can be studied in a more precise manner by considering the dispersion of such optimal values. Figure 4 demonstrates that our approach is quite robust with respect to this parameter since optimal viscosity and radius are found close to the expected value with a high degree of precision even for significant B_{noise} values.

The success of classical identification approaches such as the basic least squares method depends on and is very

Table 1. Average and rms fluctuation of the optimal dynamic viscosity $\mu_{\text{opt}}^* \equiv \nu_{\text{opt}}^* \rho^*$ as a function of sampling time S^* . The total time span $n_t S^*$ is fixed and equivalent to 5 periods and 20 realizations were used to compute averages and rms fluctuations. The true values were chosen to correspond to the reference data set $\mu^* = 4$ cP and $R^* = 2.85$ mm.

S^* (ms)	points per period	viscosity (cP)	radius (mm)
20	50	3.99 ± 0.13	2.84 ± 0.01
40	25	4.07 ± 0.15	2.84 ± 0.01
80	12	4.05 ± 0.31	2.81 ± 0.03
160	6	3.65 ± 0.27	2.73 ± 0.03

much constrained by the value of sampling time S^* characterizing the experimental data. For instance, the classical least squares approach is based on the hypothesis that the time derivatives can be discretized in such a way that

$$\frac{dv}{dt}(S_k) = \frac{v(S_{k+1}) - v(S_k)}{S} \quad (20)$$

and imposes that sampling time S and numerical time step Δt are identical. In this case, the optimal value $\nu_{\text{opt}}^*(S)$ will fit to the true viscosity only for a clean data series ($B_{\text{noise}} = 0$) and a small experimental sampling time S . In the opposite case ($B_{\text{noise}} \neq 0$ or S too large), the dispersion of results becomes significant. Moreover condition $\Delta t = S$ imposes that the Euler scheme falls into an a priori numerically unstable region. In the algorithm here proposed, sampling time S and numerical time step Δt are independent: our procedure still works with S fixed and Δt very small. Some numerical comparisons between a one time step method and ours as well as a complete investigation of parameters dispersion can be found for an hydrodynamical case in [21]. Table 1 displays the average value of ν_{opt}^* (computed using 20 realizations) versus sampling time S^* . Even the last case with 6 points per period gives an acceptable value for viscosity.

Note that we made no hypothesis on the periodic or aperiodic behaviour of the wave or on the absence of multiple reflections. Such situations are implicitly handled by our inverse method. Let us assume that S^* is here fixed so that the temporal frequency acquisition is equal to 50 Hz (hence 50 measurements for the reference data set per period). The influence of the *pulse rate* or else the Womersley number α is displayed in Figure 5 which characterizes the dispersion of optimal values $(\nu_{\text{opt}}^*, R_{\text{opt}}^*)$ for a given noise level (10%). For low Womersley numbers ($\alpha \leq 2$), axial velocities almost follow a Poiseuille profile and are thus independent on viscosity which explains why $\mathcal{F}$ does not possess a clear cut minimum in that case and the method diverges. For greater values of α typically ranging from 4 to 10, relative errors on ν_{opt}^* and R_{opt}^* are less than 10% and 2% respectively. Note that the inverse method tends to slightly underevaluate these parameters. At last, large values of α are unsatisfying since the resulting viscosity is strikingly underestimated (30%). This is a consequence of a bad temporal and spatial sampling of the signal. For high values of α , the shape of profiles hardly depends on α except in the thin boundary layer. If one bears in mind that,

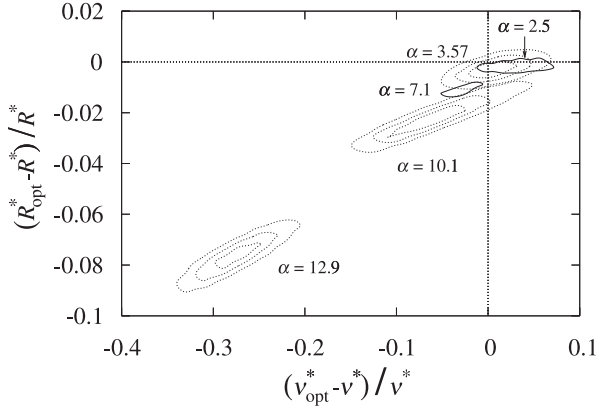


Fig. 5. Contours of probability distribution functions for $(v_{\text{opt}}^*, R_{\text{opt}}^*)$ for various Womersley parameters α ($\alpha = 12.9, 10.1, 3.57$). Each curve corresponds to 25%, 50% and 75% of the peak value of the probability distribution functions. Parameter α is changed by modifying the flow frequency all other parameters, in particular sampling time S^* and noise level being fixed. Each probability distribution function is the result of 20 000 noise realizations. For Womersley parameters $\alpha = 7.1, 2.5$ only the curve corresponding to 75% of the peak value of the probability distribution functions is shown here for the sake of clarity.

when α increases, the boundary layer size decreases and noise mainly affects this boundary layer region. In such a case, an even more plug like flow than the true one, may be used to fit the experimental profile. This reconstructed profile can be naturally associated either to smaller viscosities or smaller radii. Finally, when the width of the boundary layer becomes of the order of Δ_{exp} , information on the viscosity vanishes and the identification method fails. Moreover, α increases with ω^* so that bad results for high α flows may be also the consequence of a bad temporal sampling. Applicability of the method to a complex (non-sinusoidal) signal depends whether the α value of first harmonics are within the above interval. In most of physiological instances, this is the case.

The applicability of the inverse technique to determine blood viscosity and vessel diameter depends on other assumptions: we suppose that measurements are made a few diameters away from any vessel bifurcation in order to make the fully-developed flow approximation. Similarly the radius of curvature of the vessel is assumed to be much larger than the tube radius. Finally, the blood is supposed to behave like a Newtonian fluid. In order to remove such assumptions, it is necessary to modify or to extend the present algorithm. For instance, an extension to non-Newtonian fluids is presently in progress.

4 Experimental setup and results

A validation of our method is also based on true experimental data. We emulated flow conditions close to clinical ones using an experimental set-up depicted in Figure 6.

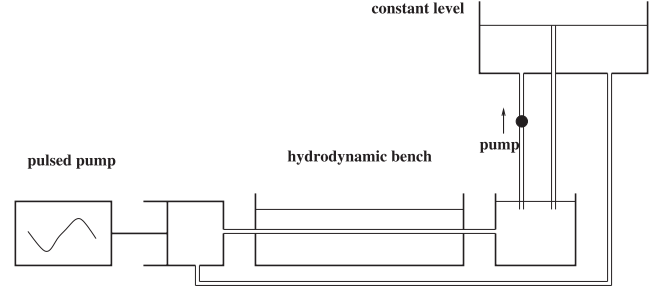


Fig. 6. Schematic diagram of the experimental set-up. The constant level tank ensures a given mean pressure gradient.

Four experiments were performed corresponding to periodic flux rates with positive average value. The radius of the tube was known so that only identification of viscosity was performed in that case.

The hydrodynamic bench is composed of a rigid tube immersed in water to ensure a good US wave propagation. An electromagnetically driven pump associated with a constant level tank ensures a pulsating flow rate of any given shape. Here a purely sinusoidal flow rate superimposed to a mean flow, was generated. The periodic pressure waves were in the 0–100 Hz frequency range. The situation is close to a clinical case when considering the Womersley number and the Reynolds number based on the mean flux rate. A complete description of the experimental setup can be found in [14,22]. The fluid US echogenicity was monitored by adding small latex particles. Its viscosity was adjusted by introducing glycerol and periodically controlled using a Contraves low shear 40 viscometer: the dynamic viscosity μ^* of the fluid was constant and equal to 10 cP with an error bar of 1 cP. Its kinematic viscosity ν^* was hence equal to $\nu^* = 10^{-5}$ in SI units. Since the frequency was fixed to be 0.5 Hz, the corresponding Womersley number (5) equals $\alpha = 4.5$ which is usual in clinical situations. Velocity profiles were measured by an ultrasonic velocimeter (DOP 1000 Signal Processing Ultrasound velocimeter). The tube diameter (1.6 cm) was chosen to allow a good quality of measurements, when considering convolution effects. The deep sample measurement was about 0.3 mm in length (about 2% of the diameter) and convolution effects were negligible. The Doppler characteristics (pulse repetition frequency, P.R.F. = 15.62 kHz, ultrasound frequency = 10 MHz, burst length = 8 cycles, number of emissions/profile = 441) allowed a large enough depth of the investigated zone without significant attenuation of the US waves. Figure 7 displays a typical instantaneous velocity profile. Such profiles were measured every 40 milliseconds. Note the asymmetry between the right and left halves of the velocity profile. This difference is due to echography interference. This effect can also be observed in vivo since the US reflective properties of the blood is different from that of the soft tissues. Once it reaches the proximal wall, the US beam is reflected and propagates into the external soft tissues which are at rest and possess a low reflective power. As a consequence this reflected beam does not alter the

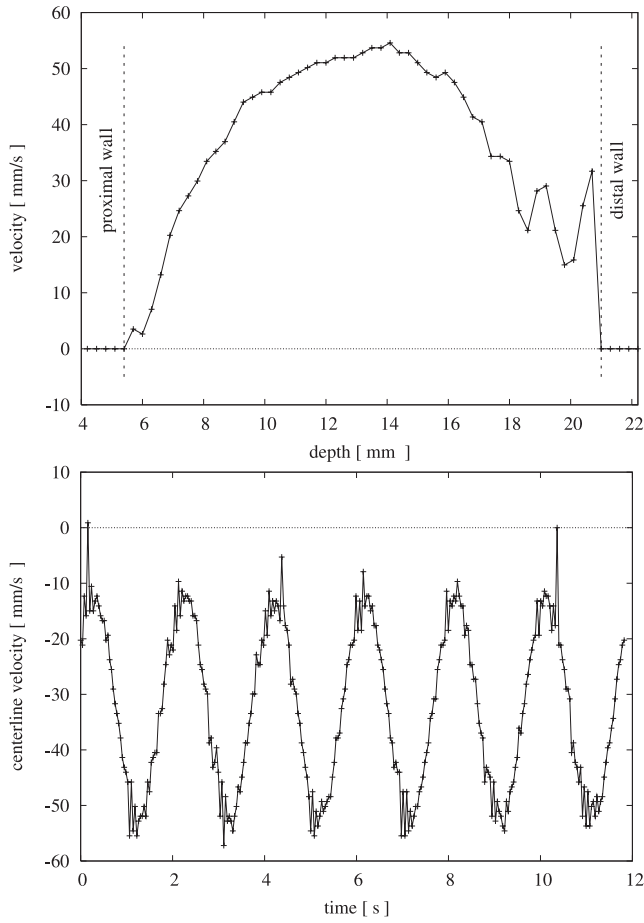


Fig. 7. (Top) An instantaneous velocity profile $U(x)$ as measured by the ultrasonic velocimeter along the radial coordinate x varying from the proximal to the distal walls. Note the anomalous shape near the distal wall due to echography interference problems (see text). (Bottom) Centreline velocity as measured in the experimental set-up.

Doppler signal near the proximal wall. On the contrary, the beam which is reflected on the distal wall propagates in the blood, which is reflective with a non zero velocity, inducing a “mirror” velocity profile which is at the origin of the observed artifact. Only the left half of profiles was used in our method to evaluate viscosity. Note that this configuration is less favorable than the one encountered in vivo.

The optimal viscosity ν_{opt}^* was computed using a low cost personal computer. The experimental data was collected every sampling time $S^* = 0.04$ s and the numerical time step $\Delta t = S/q_t$ was chosen such that $q_t \sim 100$ which ensured numerical convergence. The CPU time necessary to compute the optimal dynamical viscosity $\mu_{\text{opt}}^* = \nu_{\text{opt}}^* \rho^*$ was then similar to the true physical time: *real* time numerical computations could then be performed! For this particular case, we have only one realization for a given experiment. Table 2 shows that the algorithm is performing in a good manner.

Table 2. Optimal dynamical viscosity μ_{opt}^* computed based on the four experimental data sets. The true dynamic viscosity was measured to be 10 cP with a standard viscosimeter.

	viscosity
series 1	9.82 cP
series 2	10.35 cP
series 3	9.48 cP
series 4	9.51 cP

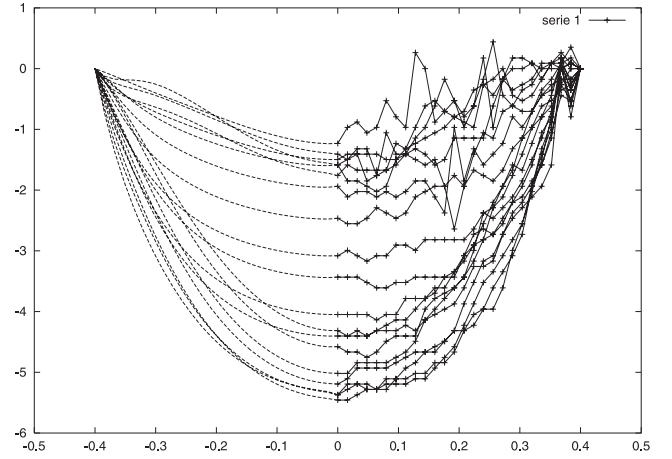


Fig. 8. Temporal evolution of experimental data (right side of the profile) and the reconstructed counterpart (left side of the profile) for series 1.

Experimental data and the reconstructed velocity field are displayed in Figure 8. The experimental data of ultrasonic Doppler velocimetry are clearly affected by measurement noise. Near the vessel wall, at the reversing zone, the signal-to-noise ratio is very low: classical methods will fail under such experimental conditions. Since we have in this experimental situation a very high reproducibility conditions of the periodic imposed flux, we could improve these results by profile averaging. One could build a less noisy signal by averaging over the different periods. However we did not attempt to perform this signal processing since, in clinical situations, this cannot be applied due to the non rigorous periodic character of the signal. In addition, even in ideal conditions, the optimal values given by the classical approaches are worse. Error peaks or rare events (see Fig. 8) appear on experimental data. Because classical algorithms use local approximations for derivatives such as equation (20), these isolated peaks may dominate the overall result. On the contrary, our variational approach uses the complete integration time to compute the gradient function. Solitary peaks thus play a much reduced role which explains the robustness of the method with respect to noise.

5 Conclusion

A method has been presented which directly identifies the fluid viscosity ν^* from atraumatic US velocimetry experimental data. This procedure is capable to handle even

large sampling times S^* and is robust with respect to measurement noise. When applied on experimental data, this approach is shown to provide a high and reproducible precision for viscosity. This method applies within the assumptions of axisymmetry and fully-developed Newtonian flow. The flow is assumed to be laminar which imposes sufficiently low instantaneous Reynolds number. In addition, the Womersley number α should be in the medium range to prevent an almost Poiseuille or plug like shape. The ability of the present technique was demonstrated on periodic flows but it can be used on any time dependent flow in particular with multiple harmonics. For instance it works for starting flow conditions as soon as the viscous boundary layer is large enough to be detected by experimental US devices (spatial discretization) and small enough to prevent a fully developed Poiseuille flow. In other words, the time measurement range must be neither too small nor too large compared to the characteristic time for vorticity diffusion. This work has been limited to in vitro experiments with Newtonian fluid. It leads to improved results when compared to previous methods [13,14]. Note that the latter ones are in agreement with results of in vivo studies. In a future work, we shall extensively apply this procedure to clinical in vivo situations. For clinical purposes, this approach because of its rapidity may be used on real time to detect anomalous behaviors of pathological origin. Because of its precision and flexibility, several extensions can be performed with this computational method. For instance, one possible extension is related to the systematic error produced by the usual convolution problem.

One may also envisage to introduce fluid non-Newtonian rheological laws (ν as function of the shear flow) which are more pertinent in the peripheral arterial system, or to extend of this identification procedure to different physiological parameters such as wall elasticity, arterial shear wall which are fundamental to detect atherosclerosis lesions, stenosis and aneurysms on vessels.

Appendix A: The Algorithm for the discretized model and measurements

Because experimental data and numerical model are discrete in time as well as in space, this section is devoted to a discrete formulation of the Lagrangian approach which is the one actually implemented. The numerical space step Δr (resp. numerical time step Δt) is chosen so that the spatial resolution Δ_{exp} (resp. the sampling time S) is a multiple of Δr (resp. Δt): $\Delta_{\text{exp}} = q_s \Delta r$ (resp. $S = q_t \Delta t$). Practically, q_s is taken to be 3 and q_t of order 100. As a consequence, model (8) is numerically discretized using a classical Euler integration scheme on a space-time grid with $N_t + 1 = q_t n_t + 1$ times and $N_s + 1 = q_s n_s + 1$ space locations

$$t_k = k \Delta t, \quad k = 0, \dots, N_t; \quad r_j = j \Delta r, \quad j = 0, \dots, N_s. \quad (21)$$

For clarity reasons, one introduces the two quantities $\gamma = \partial v / \partial r$ and $\sigma = \tilde{\nu}(1 + \beta)^2 \gamma$ so that equation (8) is

equivalent to

$$\frac{\partial v}{\partial t} = \frac{dv_c}{dt} - 2 \frac{\partial \sigma}{\partial r}(r=0) + \frac{1}{r} \frac{\partial(r\sigma)}{\partial r}.$$

The corresponding discrete equation reads:

$$\frac{v^{j,k+1} - v^{j,k}}{\Delta t} = \frac{v^{0,k+1} - v^{0,k}}{\Delta t} + \frac{\sigma^{2,k} - 4\sigma^{1,k}}{\Delta r} + \frac{(j+1)\sigma^{j+1,k} - (j-1)\sigma^{j-1,k}}{2j\Delta r} \equiv G(\tilde{\nu}, \beta; v^{lm}, \sigma^{pq}) \quad (22)$$

with

$$\sigma^{jk} = \tilde{\nu} \left(1 + \beta\right)^2 \gamma^{jk} \quad (23)$$

and

$$\gamma^{jk} = \frac{v^{j+1,k} - v^{j-1,k}}{2\Delta r}, \quad j = 0, \dots, N_s - 1 \quad (24)$$

and

$$\gamma^{N_s,k} = \frac{v^{N_s-2,k} - 4v^{N_s-1,k}}{2\Delta r}. \quad (25)$$

Note that since $\sigma^{0,k} = 0$ by symmetry, the discrete derivative $\partial \sigma / \partial r$ in $r = 0$ is not centered to ensure the second order precision in Δr . In addition, the value $\gamma^{N_s,k}$ is written in such a way to take into account the no-slip condition $v^{N_s,k} = 0$ at the artery wall. Finally, the centreline velocity $v^{0,k}$ is assumed known from interpolation (11) or rather its discretized counterpart

$$v^{0,k} = v_c^m + \left(v_c^{m+1} - v_c^m\right) \frac{t_k - S_m}{S} \quad (26)$$

with

$$m q_t \leq k \leq (m+1) q_t \quad (27)$$

in which the initial centreline velocity v_c^0 is left equal to $v_{\text{meas}}^{0,0}$ but the other n_t quantities $v_c^1, \dots, v_c^{n_t}$ are assumed to be free parameters which are close to the experimental $v_{\text{meas}}^{01}, \dots, v_{\text{meas}}^{0n_t}$. This interpolation is part of the model on which the identification technique is built. A better e.g. spline approximation could be easily introduced but we won't further analyze this point. We also use an interpolation of $v_{\text{meas}}^{j,0}$ as initial conditions. Finally the cost function $\mathcal{F}(\tilde{\nu}, \beta; v_c^1, \dots, v_c^{n_t})$ depend on parameters $\tilde{\nu}, \beta$ and n_t centreline velocities v_c^k . As a consequence, the optimization of cost function $\mathcal{F}$ is performed on $n_t + 2$ quantities.

Iterating equations (22–23) from $k = 0$ to $k = N_t - 1$ leads to the numerical velocities v^{jk} which is then used in evaluating $\mathcal{F}$. In the discretized case, it is easy to verify that this function reads as follows

$$\mathcal{F} = \sum_{j=0}^{N_s} \sum_{k=1}^{N_t} h_{jk} (w^{jk})^2 \quad (28)$$

where the filter h_{jk} introduces (i) the constraints that experimental measurements are only performed for time t_k

(or space location r_j) coinciding with a sampling time S_m where or a measured location a_m ; and (ii) the constraints of function H_j in equation (10). Consequently, $h_{jk} = 0$ except if (i) j and k are respectively multiple of q_s and q_t and (ii) $j < q_s \cdot n_r$. In that case $h_{jk} = 1$. The value of quantity w^{jk} only matters when $h_{jk} = 1$. In that case, it follows from a discretized counterpart of equation (7) that

$$w^{jk} \equiv \left(v^{jk} + \frac{j\beta}{2} (v^{j+1,k} - v^{j-1,k}) - v_{\text{meas}}^{j/q_s, k/q_t} \right). \quad (29)$$

In order to get the variation $\delta\mathcal{F}$ of $\mathcal{F}$ with respect to $\delta\tilde{v}$, $\delta\beta$ and $\delta v_c^1, \dots, \delta v_c^{n_t}$, a discrete Lagrangian is introduced to avoid the explicit computation of δv^{jk} as a function of $\delta\tilde{v}$, $\delta\beta$ and $\delta v_c^1, \dots, \delta v_c^{n_t}$. It reads:

$$\begin{aligned} \mathcal{L} = \mathcal{F} &+ \sum_{j=1}^{N_s-1} \sum_{k=0}^{N_t-1} \left(\frac{v^{j,k+1} - v^{jk}}{\Delta t} - G(\tilde{v}, \beta; v^{jk}, \sigma^{jk}) \right) \varphi^{jk} \\ &+ \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \left(\sigma^{jk} - \tilde{v} (1 + \beta)^2 \gamma^{jk} \right) \chi^{jk} \\ &+ \sum_{j=1}^{N_s-1} \sum_{k=0}^{N_t-1} \left(\gamma^{jk} - \frac{v^{j+1,k} - v^{j-1,k}}{2\Delta r} \right) \psi^{jk} \\ &+ \sum_{k=0}^{N_t-1} \left(\gamma^{N_s,k} - \frac{v^{N_s-2,k} - 4v^{N_s-1,k}}{2\Delta r} \right) \psi^{N_s,k} \end{aligned}$$

where φ^{jk} , χ^{jk} and ψ^{jk} are Lagrange multipliers. When equations (22, 23) and (25) are satisfied, $\mathcal{L} = \mathcal{F}$ so that $\delta\mathcal{L} = \delta\mathcal{F}$ for any values of variables φ^{jk} , χ^{jk} and ψ^{jk} .

Let us express $\delta\mathcal{L}$ as a function of δv^{jk} , $\delta\sigma^{jk}$, $\delta\gamma^{jk}$, $\delta\varphi^{jk}$, $\delta\chi^{jk}$, $\delta\psi^{jk}$, $\delta\tilde{v}$ and $\delta\beta$. The calculus is performed by renaming indices in sums, using constraints $\delta v^{N_s,k} = 0$, $\delta v^{j,0} = 0$, $\delta\sigma^{0,k} = 0$, $\delta\gamma^{0,k} = 0$ and by introducing the following notations

$$\varphi^{0,k} = \varphi^{N_s,k} = \varphi^{N_s+1,k} = \psi^{0,k} = \chi^{0,k} = 0 \quad (30)$$

(boundary conditions for Lagrange multipliers) and

$$\varphi^{j,N_t} = \psi^{j,N_t} = \chi^{j,N_t} = 0 \quad (31)$$

(“initial” conditions for Lagrange multipliers).

The variation can be decomposed as follows

$$\delta\mathcal{L} = \delta\mathcal{F} + \delta\mathcal{L}_1 + \delta\mathcal{L}_2 + \delta\mathcal{L}_3$$

$$\begin{aligned} \delta\mathcal{F} = & \left(\sum_{j=1}^{N_s} \sum_{k=1}^{N_t} j h_{jk} w^{jk} (v^{j+1,k} - v^{j-1,k}) \right) \delta\beta \\ & + \sum_{k=1}^{N_t} (2h_{0,k} w^{0,k} - h_{1,k} \beta w^{1,k}) \delta v^{0,k} \\ & + \sum_{k=1}^{N_t} 2 (h_{1,k} w^{1,k} - \beta h_{2,k} w^{2,k}) \delta v^{1,k} \\ & + \sum_{j=2}^{N_s} \sum_{k=1}^{N_t} (2h_{jk} w^{jk} + h_{j-1,k} (j-1) \beta w^{j-1,k} \\ & - h_{j+1,k} (j+1) \beta w^{j+1,k}) \delta v^{j,k} \end{aligned}$$

$$\begin{aligned} \delta\mathcal{L}_1 = & \sum_{j=1}^{N_s-1} \sum_{k=0}^{N_t-1} \left(\frac{v^{j,k+1} - v^{jk}}{\Delta t} - G(\tilde{v}, \beta; v^{jk}, \sigma^{jk}) \right) \delta\varphi^{jk} \\ & - \sum_{k=1}^{N_t} \left(\sum_{j=1}^{N_s-1} \frac{\varphi^{j,k-1} - \varphi^{j,k}}{\Delta t} \right) \delta v^{0,k} \\ & + \sum_{j=1}^{N_s-1} \sum_{k=1}^{N_t} \frac{\varphi^{j,k-1} - \varphi^{j,k}}{\Delta t} \delta v^{j,k} \\ & + \sum_{k=1}^{N_t-1} \left(\frac{4}{\Delta r} \left(\sum_{j=1}^{N_s-1} \varphi^{jk} \right) + \frac{\varphi^{2k}}{4\Delta r} \right) \delta\sigma^{1k} \\ & + \sum_{k=1}^{N_t-1} \left(\frac{\varphi^{3k}}{3\Delta r} - \frac{\varphi^{1k}}{\Delta r} - \sum_{j=1}^{N_s-1} \frac{\varphi^{jk}}{\Delta r} \right) \delta\sigma^{2k} \\ & + \sum_{j=3}^{N_s-1} \sum_{k=0}^{N_t-1} \frac{j}{2\Delta r} \left(\frac{\varphi^{j+1,k}}{j+1} - \frac{\varphi^{j-1,k}}{j-1} \right) \delta\sigma^{jk} \end{aligned}$$

$$\begin{aligned} \delta\mathcal{L}_2 = & \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \left(\sigma^{jk} - \tilde{v} (1 + \beta)^2 \gamma^{jk} \right) \delta\chi^{jk} \\ & + \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \chi^{jk} \delta\sigma^{jk} \\ & - (1 + \beta)^2 \left(\sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \gamma^{jk} \chi^{jk} \right) \delta\tilde{v} \\ & - 2\tilde{v} (1 + \beta) \left(\sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \gamma^{jk} \chi^{jk} \right) \delta\beta \\ & - \tilde{v} (1 + \beta)^2 \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \chi^{jk} \delta\gamma^{jk} \end{aligned}$$

$$\begin{aligned}
\delta\mathcal{L}_3 = & \sum_{j=1}^{N_s-1} \sum_{k=0}^{N_t-1} \left(\gamma^{jk} - \frac{v^{j+1,k} - v^{j-1,k}}{2\Delta r} \right) \delta\psi^{jk} \\
& + \sum_{k=0}^{N_t-1} \left(\gamma^{N_s,k} - \frac{v^{N_s-2,k} - 4v^{N_s-1,k}}{2\Delta r} \right) \delta\psi^{N_s,k} \\
& + \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \psi^{jk} \delta\gamma^{jk} \\
& + \sum_{k=1}^{N_t} \frac{\psi^{1k}}{2\Delta r} \delta v^{0,k} \\
& + \sum_{j=1}^{N_s-3} \sum_{k=1}^{N_t} \frac{\psi^{j+1,k} - \psi^{j-1,k}}{2\Delta r} \delta v^{jk} \\
& + \sum_{k=1}^{N_t} \left(\frac{\psi^{N_s-1,k}}{2\Delta r} - \frac{\psi^{N_s-3,k}}{2\Delta r} - \frac{\psi^{N_s,k}}{2\Delta r} \right) \delta v^{N_s-2,k} \\
& + \sum_{k=1}^{N_t} \left(-\frac{\psi^{N_s-2,k}}{2\Delta r} + \frac{2\psi^{N_s,k}}{\Delta r} \right) \delta v^{N_s-1,k}.
\end{aligned}$$

The first terms of $\delta\mathcal{L}_1$, $\delta\mathcal{L}_2$ and $\delta\mathcal{L}_3$ are equal to 0 insofar as equations (22, 23) and (25) are satisfied. The final result can be expressed in the form:

$$\begin{aligned}
\delta\mathcal{L} = & \left(-\left(1+\beta\right)^2 \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \gamma^{jk} \chi^{jk} \right) \delta\tilde{\nu} \\
& + \left(\sum_{j=1}^{N_s} \sum_{k=1}^{N_t} j h_{jk} w^{jk} (v^{j+1,k} - v^{j-1,k}) \right. \\
& \quad \left. - 2\tilde{\nu}(1+\beta) \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \gamma^{jk} \chi^{jk} \right) \delta\beta \\
& + \sum_{k=1}^{N_t} \xi^k \delta v^{0,k} + \sum_{j=1}^{N_s-1} \sum_{k=1}^{N_t} A^{jk} (\varphi, \chi, \psi) \delta v^{jk} \\
& + \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} B^{jk} (\varphi, \chi, \psi) \delta \sigma^{jk} \\
& + \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} C^{jk} (\varphi, \chi, \psi) \delta \gamma^{jk}
\end{aligned}$$

where ξ^k , A^{jk} , B^{jk} and C^{jk} are linear combinations of Lagrange multipliers and source terms originating from $\delta\mathcal{F}$. The Lagrange multipliers are required to satisfy the constraints $A^{jk} = 0$, $B^{jk} = 0$ and $C^{jk} = 0$. This linear system can be solved with a time reversal scheme from $k = N_t$ to $k = 0$ (backpropagation) using boundary conditions (30) and initial conditions (31).

Finally, the expression of the gradient with respect to $\tilde{\nu}$ and β follows:

$$\frac{\partial\mathcal{F}}{\partial\tilde{\nu}} = -\left(1+\beta\right)^2 \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \gamma^{jk} \chi^{jk} \quad (32)$$

$$\begin{aligned}
\frac{\partial\mathcal{F}}{\partial\beta} = & \sum_{j=1}^{N_s} \sum_{k=1}^{N_t} j h_{jk} w^{jk} (v^{j+1,k} - v^{j-1,k}) \\
& - 2\tilde{\nu}(1+\beta) \sum_{j=1}^{N_s} \sum_{k=0}^{N_t-1} \gamma^{jk} \chi^{jk}.
\end{aligned} \quad (33)$$

The gradient with respect to centreline velocities $v_c^1, \dots, v_c^{n_t}$ is obtained by differentiating equation (26). One easily gets by inserting

$$\delta v^{0,k.q_t+i} = \delta v_c^k + (\delta v_c^{k+1} - \delta v_c^k) \frac{i}{q_t}, \quad (34)$$

$$k = 0, \dots, n_t - 1 \quad \text{and} \quad i = 0, \dots, q_t - 1$$

in equation (32) that

$$\frac{\partial\mathcal{F}}{\partial v_c^k} = \sum_{i=0}^{q_t-1} \left(\xi^{k.q_t+i} + \frac{i}{q_t} \left(\xi^{(k-1).q_t+i} - \xi^{k.q_t+i} \right) \right)$$

for $k = 1, \dots, n_t - 1$, and

$$\frac{\partial\mathcal{F}}{\partial v_c^{n_t}} = \sum_{i=1}^{q_t} \frac{i}{q_t} \xi^{(n_t-1).q_t+i}.$$

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