YALES2BIO: a Computational Fluid Dynamics Software Dedicated to the Prediction of Blood Flows in Biomedical Devices

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Abstract— **A high-fidelity computational fluid dynamics software is described. This software is designed to perform numerical simulations of blood flows and flows of red blood cells. After discussing the need for advanced flow in the context of biomedical devices, the numerical method is briefly described and examples are given to show the versatility of the flow solver.**

Keywords— **computational fluid dynamics, blood flows, complex geometries, large-eddy simulations, red blood cells.**

I. Introduction

The interest for medical devices has only been increasing over the last years. This is particularly true in the context of blood flows, where stents and flow diverters, mechanical or tissue heart valves, ventricular assist devices and artificial hearts, are few of the many implantable devices constantly developed and improved. A striking example was the first implant of a full biocompatible artificial heart, developed by the CARMAT society (http://www.carmatsa.com), in France in 2013. One can also mention external devices used either for treatment (dialyzers and extracorporeal circulation) and diagnostics (blood analyzers).

Biomedical Engineering is as fast-growing field and, as in other engineering domains, numerical simulation is expected to be an indispensable tool for the design and the optimization of biomedical devices. However, when the operating fluid is blood (full blood or isolated blood cells), computational fluid dynamics (CFD) faces tremendous challenges, both from the modeling and the numerical points of view (biological membrane modeling, hemoturbulence, flow intermittency, fluid-structure coupling, non-Newtonian rheology,…). Progresses of CFD for blood flows have been dealt with in recent reviews in the context of physiological flows [1-3] and in terms of devices optimization by Marsden [3].

Obviously, numerous numerical approaches already exist [3] and have already provided interesting insights in the flow physics, helping the design of cardiovascular devices. However, in order to really assist the engineers in the development and optimization of such devices, numerical simulation has to improve its treatment of fluid-structure interaction, blood rheology and turbulence, the relative importance of these elements depending on the application. In the context of heart support devices for instance, rheology and turbulence are key components of both their performances and limitations (blood damage, thrombosis).

As stressed by Deutsch *et al.* [4] in 2006, challenges faced by computation of artificial blood pumps are formidable and the experimental approach remains the gold standard for researcher to study blood pumps. However, Fraser *et al.* [5] report a number of computational studies in this field a few years later. Computations use RANS (Reynolds-Averaged Navier-Stokes) modeling to account for the turbulence effects on the flow. However, Fraser *et al.* [5] state that models have rarely been compared and agreement is often qualitative. Recently the American Food & Drug Administration (FDA) started a specific program for the evaluation and the validation of biomedical CFD (https://fdacfd.nci.nih.gov/). Published results of their inter-laboratory study show how turbulence modeling is problematic: as many blood flows at `high' Reynolds number have a complex regime, neither laminar nor fully turbulent, RANS models fail to provide an accurate solution of the full flow [6,7]. This is not the case for more advanced approaches like large-eddy simulations [8] or direct numerical simulations [9].

In addition of being questionable in terms of turbulence modeling, RANS approaches are used to predict thrombosis and blood damage, which are both intimately related to the shear stress history of the cells. In RANS computations, only the mean flow is predicted, which means that the instantaneous shear stress seen by the blood cells is unknown. Any prediction regarding thrombosis and hemolysis based on Lagrangian tracking of particles forced to follow the streamlines obtained by a RANS computation [5] will thus provide incomplete information.

The need for advanced CFD tools is clear at the macroscopic scale; the same statement can be made at the microscopic scale, whether it is to feed macroscopic simulation in high-fidelity data to improve models or to perform numerical simulations of the dynamics of blood cells in devices. One can cite the examples of blood analyzers [10] using the Coulter effect, where red blood cells pass through a small aperture and perturb an electrical field, or microfluidic de-

vices used for cells sorting [11,12]. In these applications red blood cells circulate in devices operating at high velocity, to guarantee a high throughput. The requirements are thus different from microcirculation, where a Stokes flow hypothesis can be made [13-15].

This introduction stresses the need for the development of advanced CFD software to perform high-fidelity numerical simulations of blood flows and flows of red blood cells in the context of the design and development of artificial devices. Here, we focus on systems operating at high speed, which generates turbulence at large scales and adds inertial effects at the scale of the red blood cells. In order to tackle these situations, our group is developing the YALES2BIO software (http://www.math.univ-montp2.fr/~yales2bio/). Its characteristics and first applications are described in the present paper.

II. NUMERICAL METHOD

This section describes the numerical framework of the YALES2BIO solver. YALES2BIO is based on another solver developed at CORIA (UMR 6614): YALES2 (http://www.coria-cfd.fr/index.php/YALES2). YALES2 is a massively parallel finite-volume research code that solves the Navier-Stokes equations on unstructured meshes. It is dedicated to computations of turbulent flows [16-18], in particular bounded domains. The incompressible Navier-Stokes equations are solved using a projection method [19]. The fluid velocity is first advanced using a 4th-order central scheme in space, and explicit low-storage four-step Runge-Kutta scheme in time [16,20]. The divergence-free velocity at the end of the time-step is obtained by solving a Poisson equation for pressure, to correct the predicted velocity. A Deflated Preconditioned Conjugate Gradient algorithm is used to solve this Poisson equation [18]. Turbulence is accounted for by direct simulations or large eddy simulations, using advanced models as the sigma model [21], which properly reproduces the turbulence damping near the walls. This description is valid for both the YALES2 and the YALES2BIO solvers.

A. YALES2BIO: macroscopic blood flows

In order to predict the blood flows in large vessels, an Arbitrary Lagrangian-Eulerian (ALE) method has been developed [20]. It has specifically been used to compute flows in computational domains of known boundary velocity. This technique was used in our group to perform patient-specific simulations of the flow in arteries [22] and hearts [20,23], combining medical imaging (magnetic resonance imaging or CT scan) and CFD. This technique was first developed in the OCFIA project (http://www.ocfia.org). The arterial movements are extracted from a medical exam, thanks to a registration algorithm [23]. Wall movements are not predicted by fluid-structure interaction, but measured directly on a patient. Once the boundary movement is known, blood flow prediction comes down to a fluid problem, solved using YALES2BIO with an ALE technique.

Valves movement in the heart could also be accounted for using this method. However, complications in terms of mesh managements become overwhelming. Even when the valves movement is supposed to be known and imposed, their opening and closure would necessitate the use of series of mesh with different connectivity. An alternative, adopted in YALES2BIO, is to treat these thin structures as immersed boundaries [24]. The numerical method is described in detail by Chnafa *et al.* [20].

B. YALES2BIO: microscopic blood flows

In order to compute flows of red blood cells in microfluidic devices, possibly with complex geometries, an unstructured immersed boundary method has been developed [25]. It is based on the ideas by Peskin [24], adapted to be used in conjunction with unstructured grids. Red blood cells are represented thanks to a Lagrangian mesh that follows the displacement of the membrane. The membrane is displaced by the carrying fluid. When the membrane deforms, its stress state is computed using a finite-element solver [26] and membrane nodal forces are obtained. These forces are then regularized over the Eulerian fluid grid to mimic the effect of the membrane on the fluid. This technique has been used to compute vesicles, capsules and red blood cells under flow [25,27,28]. Contrary to numerous approaches to compute the dynamics of microscopic objects under flow [13-15,29], the present approach solves the Navier-Stokes equations, which enables to predict the red blood cell dynamics in microfluidic systems using the inertial focusing principle [11,12] or more generally in devices operating at large velocity [10].

III. COMPUTATIONS

A. High-velocity macroscopic blood flows: the example of the flow in the left heart

In order to demonstrate the performances of the YALES2BIO solver to compute high-speed macroscopic blood flows, we will describe the recent large-eddy simulation of the flow in a left heart by Chnafa *et al.* [20,23]. By its complexity, this computation illustrates the versatility of the solver. In addition, although the case considered is not a biomedical device but a physiological case, numerous flow

features encountered in the heart will also be obtained in cases of artificial hearts, for instance.

From a patient medical exam, Chnafa *et al.* [20] reconstructed the geometry and the deformations of a left heart, from the pulmonary veins to the aortic root. Imposing the endocardium and the valves movements as in the medical exam, the computation solves the flow equations and provides a characterization of the flow in the patient-specific left heart. Fig. 1 shows the flow field in the simulation at two salient instants in the simulation, both during diastole.

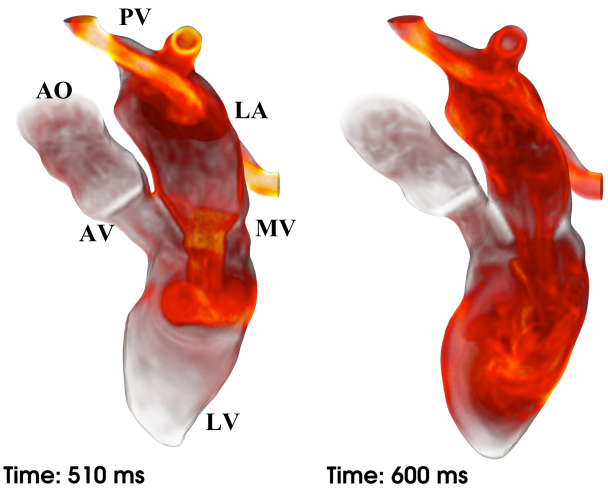

Fig. 1 Flow during diastole in the simulation of the left heart flow [20]. The simulation includes part of the pulmonary veins (PV), the left atrium (LA), left venticle (LV) and the aortic root (AO). Aortic (AV) and mitral (MV) valves are also represented. Two instants are displayed to show the mitral jet (left) and the turbulent flow during diastasis (right).

Chnafa *et al.* [20,23] extensively describe this flow, notably showing a number of non-trivial well-known physiological behaviors that are reproduced in the simulation: the strong mitral jet during the E wave (Fig. 1), the large recirculation cell during late diastole, the back flow through pulmonary veins during the atrium contraction and the large vortical movement in the atrium.

In addition, they demonstrate the presence of cycle-to-cycle variations, localized both in space and time. Variations are prone to occur when jets filling cavities (pulmonary veins jets filling the atrium and mitral jet filling the ventricle) decelerate. There, the flow destabilizes in numerous small vortices (see Fig. 1, right image) and can even become turbulent. Thanks to the high-order non-dissipative numerical scheme, large-eddy simulations are able to predict this intermittent behavior. The flow successively transitions and gets laminar depending on the flow conditions. This feature is of prime interest to study flows at moderate Reynolds numbers, characterized by an intermittent regime.

B. *Red blood cells under flow: the example of the flow in a cytometer*

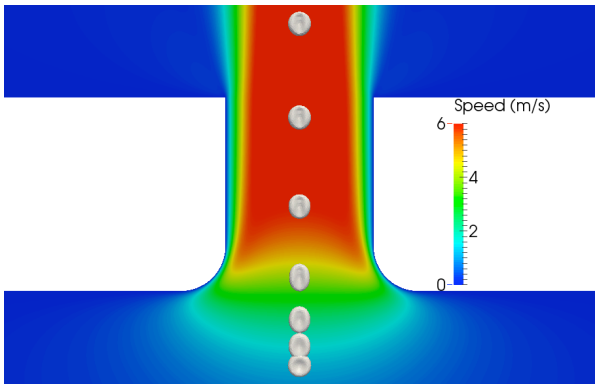

Fig. 2. Simulation of the dynamics of a red blood cell in an industrial cytometer. Sequence of shapes of one red blood cell (from bottom to top) superimposed over the carrying fluid magnitude. The aperture diameter is 50 micrometers and the main flow Reynolds number around 300.

In the context of flows of red blood cells, YALES2BIO is dedicated to the computation of cases where inertial effects are non-negligible [25]. Inertial effects can be used in microfluidic devices for sorting, focusing, ordering and separating cells [11] with a high throughput. They can also be present in a device due to high operating speed.
Inside cytometers based on the Coulter effect, blood counting is performed at high speed (several meters per second) to obtain a short analysis time. As a consequence, red blood cells flow in a device where shear rate are extremely high.
Fig. 2 shows preliminary results of the computation of the dynamics of a red blood cell in an industrial cytometer [27]. The complex computational domain (here only a small part is presented in Fig. 2) and the operating conditions come from the actual configuration of a cytometer from Horiba Medical [10]. Red blood cells enter one by one in a small aperture (Fig. 2). Their presence will perturb an electrical field, which enables counting and sizing of the cells. In order to refine the understanding of the relationship between the red blood cells dynamics (shape, orientation, trajectory,…) and the electrical pulse characteristics, YALES2BIO is used to perform numerical simulations in the industrial cytometer from Horiba Medical.

IV. CONCLUSIONS

A high-fidelity general purpose code dedicated to the computation of blood flows and flows of red cells in complex geometries and at high Reynolds number has been developed. Its performances have been illustrated in two complex flows: the flow in a patient-specific left heart,

which shows intermittency and cycle-to-cycle variations and the flow in an industrial Coulter counter, where red blood cells pass through a small contraction. YALES2BIO is destined to compute flows in biomedical devices in order to help their design and optimization. Future developments will notably include the modeling of thrombosis and hemolysis and of non-Newtonian effects in the simulations.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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