Simulating Biological Flows using Lattice-Boltzmann methods

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ABSTRACT:
In this paper we discuss the need for qualitatively advanced simulation methods for CFD related problems in the bioengineering area and motivate the use of Lattice-Boltzmann methods for these problems. After presenting some theoretical main-features of this technique for single-phase flows as well as basic ideas concerning the implementation of boundary conditions we elusively mention transient direct simulation results for weakly turbulent blood flow. The second part will motivate the use of multiphase extensions of the LB-method to model the generation of thrombosis in blood flow; a new tentative model for this class of problems will be presented together with a numerical example.

1 Introduction

The last decades have brought a vast knowledge concerning important functional mechanisms of physiological flows (mainly blood flow) in the cardiovascular system. Nevertheless there is still a universe of questions requiring further research. This results not only from of the large number of bio-chemical processes involved being non-linearly coupled to each other, but from the fact that at least a minority of these processes results from microscopical and therefore in-
individual physiological and biochemical configurations. This requires at least partially discrete models which could then serve as a basis for future numerical simulations to obtain a detailed understanding of processes such as the generation of atherosclerosis, stenosis, thrombosis and thromboembolism and their impact on the dynamics of the human blood flow.

The definition and experimental verification of such sophisticated biochemical models is still an active topic of research. Therefore it is appropriate that numerical simulation in this field is usually still restricted to use purely continuous and over-simplifying model problems of e.g. Navier-Stokes flow, eventually including more advanced stress-strain relationships due to non-Newtonian properties of blood and/or coupling to elastic artery-walls. Even then the solution of this subclass of biofluid problems requires huge numerical and computational efforts.

In this work we will propose the use of recently developed so-called Lattice-Boltzmann (LB) methods for biological flows. The key motivation for this approach is twofold: First it seems that these methods can be used to simulate 'standard' continuous flow problems with at least similar efficiency as standard Finite Volume or Finite Element approaches and we will refer to a recent numerical example to support this conjecture. In addition in the second part we will present simulations based on a crude model for the generation of thrombosis which serves as an example for using LB-methods as a modelling- and simulation-tool for multiphase and reacting flows extendable by localized and even microscopic biochemical effects. In order to see the difference between LB-methods and other well-known Navier-Stokes discretizations we now give a short theoretical overview over the LB technique. The reader interested in detailed information is referred to the cited literature.

2 A short theoretical overview over the LB - method

The Boltzmann equation

\[
\frac{\partial f}{\partial t} + \vec{v} \nabla f = \Omega
\]  

(1)

used in statistical physics describes the dynamics of a continuous normalized particle distribution function \( f(\vec{x}, \vec{v}, t) \), which is the probability to find a particle with microscopic velocity \( \vec{v}(\vec{x}, t) \). The collision operator \( \Omega \) contains details of the physical interaction between particles and can be of arbitrary complexity. The first step in order to construct an LB-model is to discretize the microscopic velocity space with a discrete set of vectors \( \vec{e}_i \) resulting in a so-called Lattice-Boltzmann equation

\[
\frac{\partial f_i(\vec{x}, t)}{\partial t} + \vec{e}_i \nabla f_i(\vec{x}, t) = \Omega_i(\{f_j(\vec{x}, t) \mid j \in \{1, \ldots, n\}\}), i \in \{1, \ldots, n\},
\]  

(2)

which in fact is a system of \( n \) first order PDEs coupled via \( \Omega_i \). It is known from statistical physics that for a collision operator of minimum complexity to generate fluid behaviour the following (so-called 'STRA' Single Time Relaxation Approximation) form can be introduced

\[
\Omega_i = -\frac{1}{\tau}(f_i - f_i^{eq})
\]  

(3)
\( \Omega_i \) is readily interpreted as a source term resulting from the deviation of \( f_i \) from an equilibrium function \( f_i^{eq} \), which still has to be defined and \( \tau \) is a microscopic relaxation time. The introduction of the minimum set of macroscopic fluid variables (i.e. density \( \rho \) and velocity \( \vec{u} \)) is done by defining

\[
\rho = \sum_{i=1}^{n} f_i \quad \quad \vec{u} = \frac{1}{\rho} \sum_{i=1}^{n} f_i \vec{e}_i
\]  

(4)

Furthermore an Ansatz is made for the equilibrium distribution \( f_i^{eq} \) of the form

\[
f_i^{eq} = \rho[A_i + B_i(\vec{e}_i \vec{u}) + C_i(\vec{e}_i \vec{u})^2 + D_i \vec{u}^2]
\]  

(5)

with constants \( A_i, B_i, C_i \) and \( D_i \) still to be defined. The Lattice-Boltzmann equation (2) can now be discretized in space and time e.g. via a first-order FD scheme resulting in

\[
f_i(\vec{x}_k + \vec{e}_i \delta t, t + \delta t) = f_i(\vec{x}_k, t) + \Omega_i(\vec{x}_k, t) \quad .
\]  

(6)

This set of \( k \times i \) equations can be interpreted as a system of evolution equations for a set of particle distribution functions \( f_i \) evaluated on nodes \( \vec{x}_k \) of a uniform lattice with lattice spacing \( \delta h \) mimicking particle collision at these nodes and particle propagation to neighbouring nodes located at \( \vec{x}_k + \vec{e}_i \delta t \) during \( \delta t \). Usually \( \delta h \) and \( \delta t \) are set to unity.

Demanding that

\[
\sum_{i=1}^{n} \Omega_i = \sum_{i=1}^{n} \Omega_i \vec{e}_i = 0
\]  

(7)

implying a conservation of mass and momentum it can be shown that a multiscale Chapman-Enskog expansion of the kinetic moments of the set of \( f_i \) allows to choose appropriate coefficients in (5) in order to obtain a set of equations for the dynamics of the macroscopic fluid properties. These equations can (in the low Mach number limit \( | \vec{u} | \ll c_s \) with a speed of sound \( c_s \)) be proven to be the incompressible Navier-Stokes equation

\[
\frac{\partial(\vec{u})}{\partial t} + \vec{u} \nabla \vec{u} = -\frac{1}{\rho_0} \nabla p_{\infty} + \nu \nabla^2 (\rho \vec{u})
\]  

(8)

where \( p_{\infty} \) is the incompressible pressure and \( \rho_0 \) is the conserved initial mean density, the continuity equation

\[
\frac{\partial \rho}{\partial t} + \nabla (\rho \vec{u}) = 0
\]  

(9)

and an equation of state

\[
p_{\infty} = \frac{\rho_0^2 c_s^2}{\gamma}
\]  

(10)
For the simulations presented here we used a 2D square grid with nodes connected to their neighbouring nodes by grid vectors $\delta h$ ($\delta t = 1$) given by the $n = 9$ columns of the matrix (in units of $\delta h$

\[
\hat{N}_{2D} = \begin{pmatrix}
0 & 1 & 0 & -1 & 0 & 1 & -1 & -1 & 1 \\
0 & 0 & 1 & . & 0 & -1 & 1 & 1 & -1
\end{pmatrix}
\]

The first column e.g. corresponds to the distribution of $f_1$ which represents the probability distribution of resting particles. The speed of sound for this set of lattice-generating vectors can be computed to be $c_1 = \frac{\delta h}{\sqrt{3} \delta t}$ and the kinematic viscosity $\nu$ is related to the relaxation time $\tau$ via

\[
\nu = \frac{2\tau - 1}{6} \frac{\delta h^2}{\delta t}, \quad (\tau > 0.5)
\]

for the class of models discussed here. The equilibrium distributions for this twodimensional d2q9 model [1] used in the following example are given by

\[
\begin{align*}
    f_1^{eq} &= \rho \left( 1 - \frac{3}{5} \vec{u} \cdot \vec{u} \right) \\
    f_i^{eq} &= \rho \left( \frac{1}{9} + \frac{1}{12} (\vec{e}_i \cdot \vec{u})^2 + \frac{1}{2} (\vec{e}_i \cdot \vec{u})^2 - \frac{1}{6} \vec{u} \cdot \vec{u} \right), \quad i \in \{2, ..., 5\} \\
    f_i^{eq} &= \rho \left( \frac{1}{36} + \frac{1}{12} (\vec{e}_i \cdot \vec{u}) + \frac{1}{8} (\vec{e}_i \cdot \vec{u})^2 - \frac{1}{24} \vec{u} \cdot \vec{u} \right), \quad i \in \{6, ..., 9\}
\end{align*}
\]

Numerical experiments have shown (e.g. [2]) that under certain assumptions such an LB scheme can be tuned to give second-order convergence in space and linear convergence in time with respect to the exact solution of the corresponding Navier-Stokes problem. No-slip conditions ($\vec{u} = 0$) on solid 'wall'-nodes are applied by swapping all anti-parallel distributions $f_i$ and $f_j$ for which $\vec{e}_i + \vec{e}_j = 0$ in every timestep (so-called bounce-back rule). Dirichlet and von-Neumann type boundary-conditions can be applied via finite differences at flow boundaries. If for example one wants to specify a prescribed pressure $p$ and velocity $\vec{u}$ eq. (10) gives the corresponding density which together with eq. (12) yealds the distributions which are set at boundary nodes. A so-called stress-free BC can be applied (e.g. at a channel outflow) for which $\frac{\partial \vec{u}}{\partial x} = 0$ by computing $\vec{u}(x - \delta h, y, t)$ and using the desired value for the pressure to compute the density again via eq. (10) and the new boundary distributions via eq. (12).

As a numerical example for the use of LB-methods for 'plain' Navier-Stokes problems we used the above approach for the simulation of single phase transient 3D-flow through an artificial heart valve at a peak Reynolds number of almost 2000. A detailed description of the problem and the results is given in [3]. In contrast to [4], where symmetric BC for two directions were used to decrease CPU time and memory usage, the LB-simulation gave detailed insight into the dynamics of symmetry-breaking due to vortex-jet-interaction because no symmetry assumptions had been made. The computed shear stresses, which are regarded as a relevant measure for the danger of thrombosis via platelet generation, compared well to experimental data [5]. The overall conclusion was, that LB-methods are an alternative tool for the simulation of weakly turbulent single-phase physiological blood flows with comparable computational efficiency as standard approaches.
3 A tentative model for thromboembolism using multiphase LB extensions

The formation of a thrombus in reality is a very complicated processes, details of which are partially still unknown. The following is just a rough picture used to develop a numerical model to be introduced later. For a more detailed description of the biochemical processes involved see e.g. [6] and the literature therein.

A platelet plug formation is usually the first step in a transport process of thrombogenic substances. The activated platelets and shear-stress damaged zones of the endothelium emit chemicals which initiate blood coagulation. This process is a complex cascade that results in the formation of fibrin strands. This mesh of fibrin strands is referred to as a thrombus. The coagulation cascade is designed to permit significant amplification of the signal to clot. At the same time, it is important that there are also anti-coagulation (thrombolytic) factors in the blood that rapidly dissolve inappropriate clots. A delicate balance between the pro-clotting and anti-clotting mechanisms is usually maintained. Thrombogenic substances such as thromboxane A2, ADP, and thrombin are responsible for the formation of a thrombus. If their concentration exceed a critical level, they cause platelet adhesion which lead to a thrombus formation. The concentration depends on the local shear rate of the blood flow and the size of the thrombus. The bigger the thrombus, the more the blood flow around the thrombus is disturbed and this may cause higher concentration downstream of the thrombus which may lead to platelet adhesion in this region and a thrombus growth in the downstream direction.

Thromboxane A2 is produced on the thrombus surface in a rate which depends on the size of the thrombus. Trombin is produced on the thrombus surface from prothrombin and is transported by convective diffusion. Thrombin is inactivated by antithrombin III. This inactivation (i.e., a decrease of the thrombin concentration) is greatly increased by heparin.

Regarding clots of thrombic substance as a second phase within the blood it is straightforward to model its generation from transient local shear stresses. Thus we need a multiphase extension of the LB-methods described above. Such extensions have been developed only a few years ago by a few groups targeting at the simulation of multi-phase flows in porous media (e.g., [7, 8]). Again we just give a short outline of the theoretical approach:

In addition to the use of two different 'sorts' of particle distribution functions $f^P$ and $f^T$ representing the blood phase and the thrombus phase respectively, the collision operator in eq. (6) is complemented by a species specific part $\Omega^{(2)}$ of the form

$$\Omega^{(2)} = \frac{\phi}{2} \frac{\langle (\vec{\varepsilon}_i \vec{F})^2 \rangle}{|\vec{F}|^2} - \frac{1}{2},$$

(13)

with a 'colour' gradient

$$\vec{F}(\vec{x}) = \sum_i \vec{\varepsilon}_i [\rho^T(\vec{x} + \vec{\varepsilon}_i) - \rho^B(\vec{x} + \vec{\varepsilon}_i)],$$

(14)
and a scalar quantity $\phi$ which will turn out to be a parameter determining the surface tension $\sigma$ between the two phases ($\sigma \propto \rho \nu \phi$). After computing the change of $f_i^T$ and $f_i^B$ due to collisions via eqs. (3), eq. (13) and (6), the distributions for both phases will be redistributed at each node (while conserving mass and momentum) to maximize the scalar product of the colour flux $\tilde{f}^B = \sum_i (f_i^T - f_i^B) \tilde{e}_i$ and the colour gradient. For sufficiently large $\phi$ this will result in immiscible behaviour of the two phases and the automatic generation of free interfaces. For subcritical $\phi$ a convective-diffusive behaviour of the different species is observed. The density inside single-phase areas will be identical apart from surface tension effects comparable to those described by the Laplace law. The adhesion (i.e. the contact angle) of each phase to wall nodes can be arbitrarily tuned by ‘colouring’ via their distribution $f_i$.

Now all ingredients are at hand to introduce our (for simplicity two dimensional) model for the simulation of thromboembolism. The total local density $\rho$ at a node is now defined as the sum of the blood density $\rho_B$ and the thrombus cloth density $\rho_T$. The generation of the thrombus phase with local density $\rho_T$ during each timestep $\delta t$ is given by

$$\delta \rho_T(\tilde{x}, t) = A \mid \tau_{xy}(\tilde{x}, t) \mid \Theta(\mid \tau_{xy}(\tilde{x}, t) \mid - \mid \tau_{crit} \mid) \Theta(\rho_{Tcrit} - \rho_T(\tilde{x}, t))(1 - \frac{\rho_T(\tilde{x}, t)}{\rho_{Tcrit}})^2$$

(15)

where

$$\tau_{xy}(\tilde{x}, t) = \nu \rho(\tilde{x}, t) \frac{\partial u_x(\tilde{x}, t)}{\partial y} + \frac{\partial u_y(\tilde{x}, t)}{\partial x}$$

(16)

and $\Theta(x) = 1$ for $x > 0$ and 0 otherwise. The annihilation of the thrombic phase for low concentrations of $\rho_T$ and small $\tau_{xy}$ during each timestep $\delta t$ is modelled as

$$\delta \rho_T(\tilde{x}, t) = -B \Theta(\mid \tau_{crit} \mid - \mid \tau_{xy}(\tilde{x}, t) \mid) \Theta(\rho_{Tcrit} - \rho_T(\tilde{x}, t)) \rho_T(\tilde{x}, t)(1 - \frac{\tau_{xy}(\tilde{x}, t)}{\tau_{crit}})^2$$

(17)

The transport coefficient $\nu_T$ for the thrombic species is chosen so that $\nu_T >> \nu_B$ implying that the thrombic fluid phase has a large viscosity compared to that of blood. The model thus contains besides the transport coefficients $\nu_T, \nu_B$ and $\sigma$, the ‘biochemical’ parameters $\rho_{Tcrit}, \tau_{crit}, A$ and $B$. In order to get an idea of the meaning of these parameters some comments seem appropriate. The constant $\tau_{crit}$ has to be obtained from experiments and might eventually depend on the shear-stress history. The constants $A$ and $B$ are solely related to chemical reaction rates, $B$ is especially responsible for the localisation of the thrombus formation because for large $B$ the diffusive spreading of low-concentration thrombic mass in regions of low shear-stress is eliminated. $\rho_{Tcrit}$ basically determines how strong a formed thrombus grows at its outer boundary and prevents thrombic mass generation inside a thrombus when $\rho_{Tcrit} < \rho_0$ where $\rho_0$ is the initial density in the flow domain under consideration.

4 Numerical examples

In order to see that the inclusion of the model equations (15) and (17) into the ‘standard’ two-phase LB algorithm allow the simulation of qualitatively sensible thromboembolic processes we
used a simple test geometry of a channel including a predefined stenosis as a source of localized shear stress and a branching. This domain is discretized using 600 x 80 nodes and a parabolic velocity profile and zero pressure gradient as the inflow boundary condition implying $Re = 25$. The variation of the parameter set described above results in a variety of phenomena only two classes of which due to lack of space are shown below. Fig. (1) shows the transient localized development of a thrombus at the place of maximum shear stress predefined by the place of the stenosis at dimensionless times 2.48, 2.96, 6.64 and 20. The equilibrium state is basically reached when the total mass flux in the system is zero because the thrombus has completely occluded the channel. Fig. (2) shows the same system but with decreased parameters A and $r_{crit}$ compared to the first example and parameter B set to zero. The localization of the thrombus formation is now suppressed because the thrombic substance with a sub-critical density $\rho_T$ is transported through the channel by convection and diffusion. Later thrombic bubbles are formed and partially carried away with the flow until they leave the system or stick to the walls. The equilibrium state is similar to the previous example (zero mass flux in the system) but now the overall amount of thrombic mass generated in the system before the occlusion is significantly increased.

Figure 1: Localized thrombus formation at dimensionless times 2.48, 2.96, 6.64 and 20.0
Figure 2: Delocalized thrombus formation at dimensionless times 9.6, 12.0, 18.0 and 32.0

5 Discussion and outlook

In this article we tried to motivate the use of LB methods for biological flow-problems including biochemical reactions and localisation effects. It was shown that even for a crude model of thrombogenesis some essential features observed in real life can be reproduced. Of course a lot of questions are still open such as the ultimate appropriateness of the model, the introduction of non-dimensional biochemical model parameters (analogously to the Reynolds number characterizing viscous flow) and numerical stability of simulations covering the desired parameter phase space. Lots of (eventually semi-analytical) test cases have to be done before simulations can be expected to give quantitatively satisfying results. Yet we feel that as soon as there is a generally accepted set of biochemical equations to describe the above mentioned processes LB-methods will definitely help to find solutions for real-life thrombogenic problems.

References

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