Lattice-Boltzmann Fibrinolysis

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ABSTRACT

Ischemic stroke, and more generally, cardio-vascular diseases, are amongst the top issues in public health. Ischemic stroke results from the occlusion of a brain vessel due to the formation of a thrombus. One way to remove this thrombus is to inject a chemical into the patient's bloodstream, which will breakdown the clot's fibrin fibers: this is called *Intravascular Thrombolysis* (IVT). Since it is hard to get quantitative data from IVT *in-vivo*, lysis experiments are conducted *in-vitro*. We present a novel 3D mesoscopic lattice-Boltzmann (LB) model, which simulates these fibrinolysis experiments. The thrombus is a porous medium described with Walsh's *Partially Bounce-Back* (PBB) dynamic [1], and varies in time as lysis occurs, following Diamond et al. [2]. The model is able to reproduce the observed blood clots permeabilities, and to recover lysis times from the conducted *in-vitro* experiments.

1. Introduction

Ischemic stroke happens when a brain artery gets blocked by an aggregate of blood components, mostly fibrin, red blood cells and platelets, referred to as thrombi. Although thrombi are the result of the natural coagulation process, which is central to prevent bleeding, it has dramatic effect when it occurs in an artery, and stops the transport of oxygen to brain tissues.

Ischemic stroke disease is the 1st cause of disability and 3rd cause of death in civilized countries. It's cause is still not fully understood. Treatment options are thrombolysis and thrombectomy (introduced in 2015). The latter consists in the mechanical removal of the blood clot, through surgery. The former, produces a lysis of the thrombus, namely the chemical breakdown of the clot. This is typically obtained by injecting tissue-Plasminogene-Activator molecules (*tPA*), which induce the formation of plasmin, a molecule that cuts the fibrin strand. Although thrombolysis might seem a straightforward treatment, its success rates is still very low. One of the goals of the H2020 European **INSIST** project [3], is to understand what are the most critical factors that prevent anti-coagulant treatments from being efficient, and to provide "*in silico*" models that simulate all aspects of ischemic strokes.

Since quantitative data on thrombolysis dynamics *in-vivo* is nearly impossible to obtain, we conducted *in-vitro* fibrinolysis experiments. Homogeneous fibrin clots are placed in vertical pipes, and a solution containing the lysing chemical, tPA, is added on the top of it. Due to gravity only, this solution flows slowly through the clot, that acts as a porous medium (see fig. 1).

Here we focus on an in-silico 3-dimensional model of these fibrinolysis experiments. Our approach is based on Lattice-Boltzmann (LB) simulations with the Palabos library [4]. A feature of the present work, is the description of the porous medium. The typical scale of a fibrin strand (fiber radius and length) being much smaller than the artery diameter (10^{-8} m vs. 10^{-3} m), the clotted regions are described at a coarse scale level instead of the pore-scale level. Within the LB approach, a tunable partial bounce-back (PBB) dynamics [1] allows us to implement heterogeneous clots by adjusting their permeability at each grid point (or voxel). This method is shown to yield realistic clot permeability values, and can take into account its dynamical changes during the lysis regime. In particular, the velocity of the lysis front from the experiments could be recovered by the model.

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References

[1] Stuart D.C. Walsh, Holly Burwinkle, and Martin O. Saar. A new partial-bounceback lattice-Boltzmann method for fluid flow through heterogeneous media. *Computers & Geosciences*, 35(6) :1186–1193, June 2009.

[2] S.L. Diamond and S. Anand. Inner clot diffusion and permeation during fibrinolysis. *Biophysical Journal*, 65(6) :2622–2643, December 1993.

[3] Praneeta R. Konduri, Henk A. Marquering, Ed E. van Bavel, Alfons Hoekstra, Charles B. L. M. Majoie, and The INSIST Investigators. In-Silico Trials for Treatment of Acute Ischemic Stroke. *Frontiers in Neurology*, 11, September 2020.

[4] Jonas Latt, Orestis Malaspinas, Dimitrios Kontaxakis, Andrea Parmigiani, Daniel Lagrava, Federico Brogi, Mohamed Ben Belgacem, Yann Thorimbert, Sébastien Leclaire, Sha Li, Francesco Marson, Jonathan Lemus, Christos Kotsalos, Raphaël Conradin, Christophe Coreixas, Rémy Petkantchin, Franck Raynaud, Joël Beny, and Bastien Chopard. Palabos : Parallel Lattice Boltzmann Solver. *Computers & Mathematics with Applications*, April 2020.

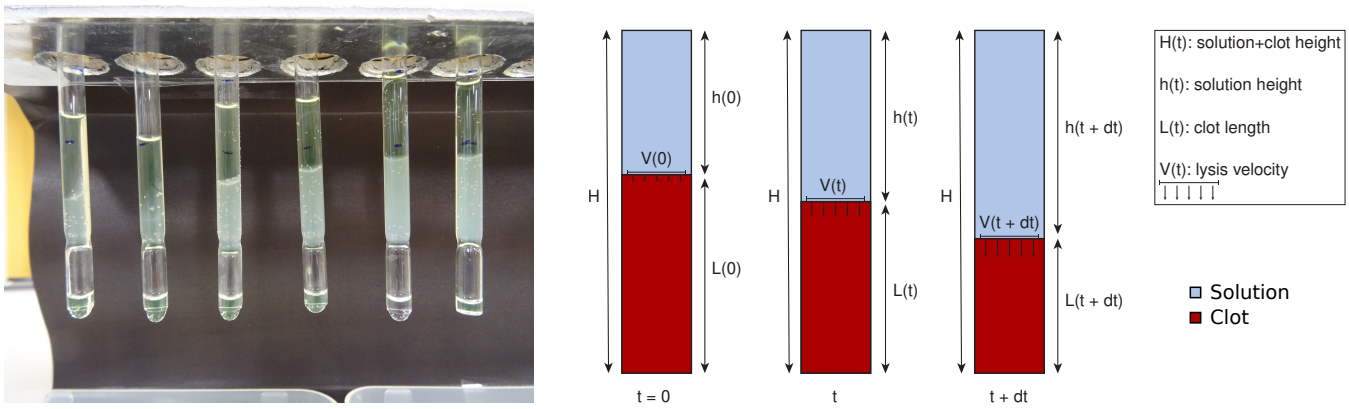

Fig. 1 Setup of the fibrinolysis experiments conducted at the Laboratory for Experimental Medicine of the Université Libre de Bruxelles. Homogenous fibrin clots are placed in vertical pipes, and a solution containing tPA is constantly added on top of it, so that the level stays always the same. The solution penetrates slowly through the clots, and dissolve them gradually. A clear clot-solution interface can be observed, referred to as the lysis front‘.