Coupling scheme for a high-performance multiscale blood flow simulation workflow

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1. Introduction

Increasingly many scientific questions, that need modelling solutions, target processes residing on multiple scale levels. This is especially true in the domain of biomedicine, where understanding a given disease, or the effects of a treatment might involve numerous components. For a single problem blood flow mechanics can be just as important as cellular trafficking or sub-cellular biochemical signalling. One such problem presents itself with the disease of brain aneurysms. These are focal dilatations on major brain arteries with a chance to burst. The outcome of a rupture event can be devastating for the patient. The treatment usually involves endovascular brain surgery and the placement of a blood flow diverter implant, with the intent to thrombose the dilatation and therefore to close it out from the active circulation. In the following, a multiscale, multicomponent model will be presented that aims to model aspects of the thrombus formation mechanism after the medical intervention. The sub-models are fully developed and operational, and the couplings are currently under development. The model structure is discussed from the viewpoint of inter-model communication and requirements for the execution environment for the model components.

2. Models and scales

The whole model-structure consists of several sub-models each capturing the influence of a biological process from a different scale level. For an overview of the scales of the described components see the Scale Separation Map in Fig. 1. The scale level of the medical applications is the level of the 3D macroscopic component, therefore we consider this level to be central. Blood flow on the whole human body level is often represented by 1D or 1.5D models. In our work it is simulated by a simple 1.5D network model which describes the connectivity graph of the major arteries and takes into account the local radii of the vessels. It is a computationally low-cost representation based on the method of characteristics and it allows to incorporate wave propagation and various patient specific tunings (e.g. the length and stiffness of the specific arterial sections). In case the shape of the local wave-form is of lesser importance, or to reduce the model complexity, it can be substituted by 0D models (i.e. Windkessel model). The local macroscopic description of the diseased vessel is based on patient-specific medical records (CT-Angio) and is represented in 3D. In this typically few cm^3 sized volume the fluid mechanical effects dominate. They are modelled with *HemoFlow* a lattice Boltzmann based flow solver [1] that has built in capability for virtual flow diverter insertion as well. This scale level is governed

by the fluid mechanical effects, and to go further with incorporating more biological processes, smaller scales need to be involved. Blood flow on a cellular level dictates the local rheological properties, the transport of chemicals, the shear stresses on the vessel wall or on the surface of a growing thrombus. In our coupled system this scale level is modelled with the open-source cellular modelling toolkit *HemoCell* [2] (www.hemocell.eu). Finally, the smallest scale, the sub-cellular scale (not included in this work) typically involves the transport and interaction of proteins (i.e. von Willebrand transport and binding and interactions with glycocalyx).

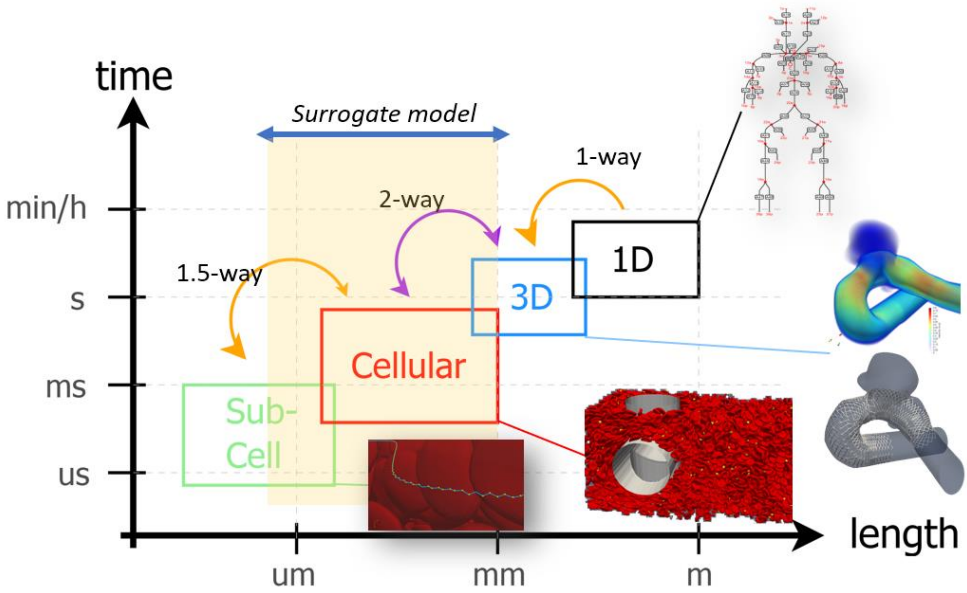

Figure 1 *Scale-separation map of the blood models that address the different contributing processes. In decreasing spatial scale order: 1.5D full body network. 3D macroscopic flow including a virtually implanted flow diverter in HemoFlow. Cellular level flow around the struts of the flow diverter in HemoCell. Sub-cellular transport and uncoiling of a von Willebrand ultra-large protein chain coupled with HemoCell.*

There is one further component that doesn't involve additional scale levels, instead it overlaps fully with the cellular, and partly with the 3D macroscopic levels (denoted with coloured area in Fig. 1). In this range a surrogate model is employed that represents the cellular level components as statistical distributions. The dynamics of these distributions are governed by an advection diffusion-type equation which was calibrated using a database of cellular flow computation results [3]. This significantly reduces the computational costs as the cellular level is by far the most expensive to simulate.

3. Inter-model information exchange and model execution

The 1.5D flow network model is designed for serial, single core execution due to its relatively low computational cost. (Alternative solutions exist that can exploit shared memory parallelism). In our work the growing thrombus inside the aneurysmal sac does not influence significantly the flow in the parental artery (as opposed to e.g. a growing stenosis), therefore this component reduces to a pre-generated static time-series of inflow signals. The next component, the 3D

macroscopic model, is an MPI parallel code and has a single distributed instance running throughout the simulation. It is strongly coupled with the surrogate model which computes the local cell densities and provides the local viscosity, and availability of chemical components (e.g. platelets) for the thrombus formation. While the surrogate represents events from a smaller scale level, it is running in a 1:1 scale coupling in space and time with the macroscopic model and they exchange information at every iteration. For efficiency reasons, these two models are distributed to the same MPI processes (denoted as a dashed frame in Fig. 2) using the same spatial decomposition.

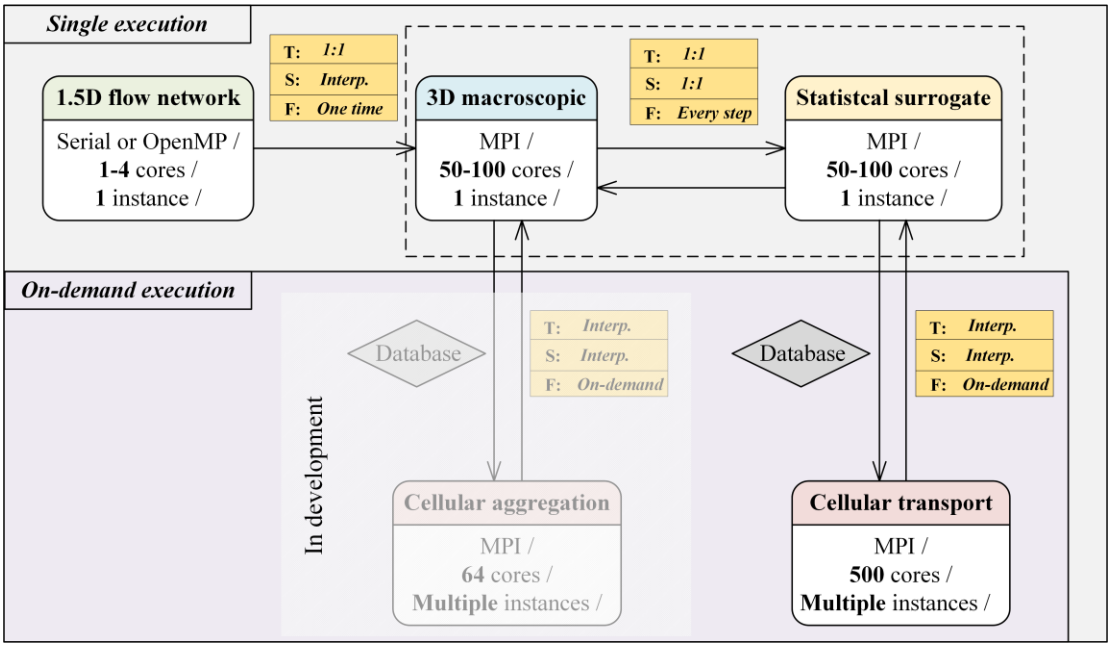

Figure 2 *Coupling and execution chart of the sub-models. The boxes each represent a model targeting one biological process, and describes the type of parallelisation, the typical number of used cores and the number of instances executed during one simulation. The arrows denote the information exchange between and list three properties:* ***T****: coupling type on time-scale,* ***S****: coupling type on the spatial scale,* ***F****: frequency of the information exchange.*

There are cases when the surrogate model cannot provide sufficiently accurate information. For instance, in the vicinity of important small-scale geometric features, such as near the struts of a flow diverter, where the local viscosity and the cell transport differs. In this case a cellular level model is invoked which computes a small repeating section of the flow diverter mesh and the surrounding flow. Based on the average cell densities and flow velocity and direction as input, a new local viscosity is computed and fed back to the macroscopic model.

Similarly, there is a cellular level model currently in development which accounts for the chemical interactions and cell binding, for instance on the surface of the growing thrombus. It informs the macroscopic model of the local thrombus growth rates at various sampled points on the surface of the thrombus. The coupling to the macroscopic and surrogate model is made possible by a specific boundary condition that can maintain a constant influx of cells [4]. The execution of the macroscopic model is suspended during the execution of the cellular models.

Note that the volume of the exchanged information between the macroscopic and cellular levels

are limited to technically a few numbers (e.g. local flow velocity, viscosity, cell density). Furthermore, the parameter space for these is also small and bounded, therefore a dynamically filled intermediate database (look-up table) can significantly reduce the computational cost and can provide reusable information for subsequent simulations. A further way to reduce the cost is to use load-balancing on the cellular scale models [5].

4. Discussion

Apart from the individual model components, the coupled model structure presents several significant challenges both on the computational and on the execution side. Current "mock" pilot executions are running inside one scheduling system allocation that allows for a predefined number of cellular level model executions. This can quickly become too restrictive: e.g. as the thrombus surface is changing, the number samples on it with the cellular level model should change along. We plan to enable dynamic instance creation of sub-models with the help of the QCG Pilot Manager. The internal communication of the models is possible through simple file interfaces due to the relative low amount of exchanged data. With further developments, the inter-model communication is planned to be handled by the currently under-development MUSCLE 3 coupling library. Advanced required features to be developed include the possibility for a dynamically changing the number of communication ports for the 3D macroscopic model to accommodate the change in the number of running cellular model instances. Finally, this leads to one of the most complicated questions. While the individual model components are scalable on the execution platform and can compute larger domains on more cores, an upcoming overarching challenge is to ensure that the whole coupled multiscale structure is scalable as well.

References

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