Center for Biomedical Computing

Abstract

The Center for Biomedical Computing is devoted to three research tasks: computational middleware, robust flow solvers, and applications to biomedical fluid flow problems. These highly integrated topics represent a broad, a medium, and a specialized scope, respectively, of advancing the current state of computational fluid dynamics.

The computational middleware is meant to be a useful "Matlab-like" set of tools generally applicable to computational scientists for rapid prototyping of multi-physics software based on partial differential equations. The flow solvers part aims to advance the computational middleware in the specific direction of robust adaptive implicit finite element methods for viscous and turbulent fluid flow. The application part will use the flow solvers in combination with the computational middleware to attack challenging biomedical flow problems.

This composition of three main themes ensures results of different flavor. First, the computational middleware will be generally useful and has the potential of achieving substantial impact in science. Second, the flow solver part continues research of outstanding quality and usefulness in fluid dynamics. Finally, the application part addresses a new and vital class of challenging physical problems where mathematical modeling is in its initial stages. The three parts also span the range of natural science research, from generic application-independent tools via methods for a wide class of applications (fluid flow) to specific physical problems.

The group behind this project has an excellent track record for developing computational middleware and numerical methods, and applying these tools to solve problems in natural science. For both the computational middleware and flow solver parts, we intend to invite very promising young researchers from outstanding groups for long-term stays in the center and thereby help to increase the scientific quality of our group. Biomedical flow investigations will be done in close collaboration with scientists with vast experience in this field.

1 Background and Motivation

Computational science applies the computer as a laboratory for investigating theoretical models of Nature. The computational scientist's interests lie in scientific investigation, and usually not in studying the technical details of numerical solution methods and software. However, today's challenging scientific problems frequently involve very complicated mathematical models and a corresponding complexity in numerics and software. The need for time-consuming and expensive labor by numerics and programming experts represents a major obstacle to the increased adoption of advanced mathematical models and computational methods by scientists.

In a broad sense, the goal of the center is to facilitate access to complex models for scientists. We will achieve this goal by focusing on selected fields in biomedical computing, and by bringing together excellent researchers in scientific software development, numerical methods, and biomedical applications. Our aim is to produce results that have potentially high impact, with a special focus on developing open-source reusable software tools of wide applicability for solving partial differential equations (PDEs), highly stable and easy-to-apply methods for laminar and turbulent flow, and advanced computer models for use in biomedical research. The long-term, multidisciplinary, and focused work needed to produce such results can be achieved only by a project-specific center of sufficient size. Equal in importance to the specific results mentioned is the training of a number of postdoctoral researchers and PhD students, as well as the building of general national competence in key ICT topics and computational fluid dynamics.

The research in the center will be grouped into three main categories: computational middleware, robust flow solvers, and applications to biomedical flow problems. We will here motivate these principal ingredients and outline what we see as fundamental and worthwhile research problems. In a later section, "Project Plan", we shall go more into detail and specify the goals and subgoals of each research topic.

1.1 Computational Middleware

The maturity of scientific software is measured in terms of the level of abstraction available to the user. In the field of scientific software, the goal is to provide easy-to-use, efficient, and reliable pieces of code to computational scientists. Typically, the computational scientist today does not worry about how the sine function is computed on her computer, but she might be concerned about how the Laplace equation is solved. We predict that in the near future, most scientists will also be able to utilize black-box software for the Laplace equation and similar problems. It is a formidable challenge for scientific software developers to push the limits of complexity and abstraction, such that scientists can analyze more complicated problems. The goal of the center is to contribute heavily to this development within a specific branch of computational science.

Many will agree that Matlab [32] constitutes the single most important contribution to computational science during the last two decades. Matlab encapsulates complicated high-quality numerical libraries and offers robust algorithms in a user-friendly environment that supports both simulation and visualization. We may call this *computational middleware*, in the sense that generally applicable numerical methods are available in robust code without being restricted to particular physical problems. The contents of Matlab are basically tools for linear algebra and ordinary differential equations, though more advanced toolboxes for a few special disciplines do exist. Most tasks within these problem domains are solved quickly and conveniently in Matlab, either by interactive statements or by small programs (scripts). For example, the computational scientist may define a system of ordinary differential equations, call some robust black-box solver, and visualize the solution with just a few commands. This working style allows rapid exploration of mathematical models without the mess of technicalities that were required before systems such as Matlab became available. In particular, the computational scientist does not need expert knowledge of the numerical solution of ordinary differential equations or numerical linear algebra.

Unfortunately, computational science problems are frequently much more complicated than those which Matlab can handle in a convenient way. An environment is needed in which robust solvers for partial differential equations are available, and can be combined conveniently to solve complex multiphysics problems. Such problems have traditionally been solved by comprehensive special-purpose codes. This approach will still be required for many problems where particular features impose special requirements on the numerics. However, many problems can be explored by combining "standard models", such as the Laplace/Poisson equation, the convection-diffusion-reaction equation, the equations of elasticity, the Navier-Stokes equations, and Maxwell's equations, with some problem-specific set of "constitutive laws" entering the coefficients in the standard models. Solution methods and implementations exist for all these models, with varying degrees of efficiency, user-friendliness, robustness, and generality. Sometimes, the computational scientist will prefer to use open source research code, or a flexible generic library for generating new software, while on other occasions she may need a commercial solver. If the environment can encapsulate different codes as reusable components and provide a simple way of connecting them, scientists would have *computational middleware at the partial differential equation level*. We propose to develop the first generation of this type of middleware. As explained below, this is a natural and novel step to be taken in international research on software for partial differential equations.

Over the last three decades, there have been many successful attempts to build computational middleware to ease the numerical solution of partial differential equations. For instance, ELLPACK [40] was an outstanding contribution for its time and provided a "PDE-language" for defining problems at a high level of abstraction, with subsequent generation of Fortran codes. In the 1990s, several efforts were made to build generic and flexible libraries for the solution of PDEs, using the C or C++ language and object-oriented programming [2, 14, 15, 16, 19, 21, 24, 35, 37]. The idea was that such libraries could enable a PDE problem to be solved at a high level of abstraction by programming in C++ directly, rather than in a specialized "PDE language". The cited libraries differed in scope: some focused on flexible and efficient parallel algorithms for linear and nonlinear algebraic systems [37]; some explored (single) scalar or vector PDEs very convenient [15, 19, 24]; some acted as tools for exploring new numerical methods (such as adaptivity and multigrid) in a range of applications [2, 21, 35]; while others addressed special equations with cutting edge numerics [14, 16].

In the last ten years, several important improvements to the cited library technology have emerged – for example, deal.II [8], Sundance [41], COMSOL Multiphysics [7], and FEniCS [17]. All of these and previous attempts had the goal of solving very complex PDE problems. However, at present, the tools available are mainly geared towards the mentioned standard models, and not combinations of them. The provision of a software layer on top of these tools that supports the "plug-and-play with equations" philosophy for multiphysics problems, has to date received less attention, although some recent successful approaches have emerged [7, 41]. and deployment of such a software layer is a natural next step in the evolution of PDE software technology. To enable Matlab-style user-friendliness, the software layer should be implemented in a powerful high-level scripting language, such as Python [25]. We will address this topic by building on our own extensive experience in the field, by inviting internationally leading young scientists for long stays in the center and by distributing our software as part of the FEniCS suite.

1.2 Robust Flow Solvers

Modeling and predicting fluid flow is a major issue in many branches of science and technology. Our focus is on incompressible viscous flows. The dynamics of incompressible viscous flows of Newtonian fluids are fundamentally described by the three-dimensional and time-dependent solutions to the Navier-Stokes equations. These are properly referred to as Direct Numerical Simulations (DNS). DNS solutions describe not only laminar flows, but also the inherently chaotic turbulent motion of a fluid that occurs when the ratio between inertial and viscous forces (the Reynolds number) is sufficiently large. As such, this method constitutes the most fundamental numerical approach to scientific studies of turbulence created by Nature.

Some important biological flows are turbulent only in some regions that may move in space and time, and the DNS approach is very promising for this kind of computationally challenging flow transition problems. On the other hand, at high Reynolds number turbulent flow, DNS is not a computational tool for practical flow predictions, because of the massive requirements on the spatial and temporal resolution, and hence the computational cost [39]. In practice, these difficulties are circumvented by employing a statistical description of the turbulence motion – for example, RANS [10] or LES [39] models. These models are mathematically highly nonlinear and the complexity varies greatly – see, for example, [11]. However, from a numerical and software point of view, these flow models, which differ widely physically, can be brought into a common mathematical framework such that the software we need to solve the equations in the different models can be built from the same basic PDE components. For example, a typical numerical RANS model based on operator splitting can be built from a Stokes solver, an advection solver, and a set of convection-diffusion-reaction solvers.

In addition to turbulent motions, many flow problems are also highly influenced by free surfaces, thermal effects, multiple phases, and deformable structures. The fluid properties in many biomedical flows are also no longer strictly Newtonian. These features all add to the complexity of the set of model equations to be considered. Our idea is to address the added complexity by ”factorizing” models into software components. This requires the models to be written in a context-independent way and the use of operator splitting to express the solution strategy as a series of steps that involve only fundamental PDE components. The development of such software technology demands a clear distinction between physical, mathematical, numerical, and implementational issues in a given flow problem.

The construction of solution methods for laminar and turbulent flow models can benefit greatly from the previously described computational middleware, because it allows the computational scientist to compose a solution strategy by connecting ready-made PDE solver components. However, solving complicated fluid flow equations by simply connecting software components often runs into problems concerning stability. It is, therefore, necessary for the computational scientist to have access to robust solvers and robust ways of combining components. This requirement calls for research on robust numerical methods.

There are two approaches to increased robustness that we will focus on: (i) adaptive numerical methods with error estimation, and (ii) partly or fully implicit methods. Adjusting the degree of implicitness in a flexible way, combined with error estimators for determining the quality of the numerical solution, will be powerful tools when constructing new solution methods for challenging fluid flow problems.

An advanced solver for flows such as in the human heart, will involve turbulence, say a second-moment closure model, coupled with a finite-strain elasticity model for the flexible walls. The overall simulation software may then be built of a set of convection-diffusion solver components, a Poisson solver component, and a large-deformation elasticity or visco-elasticity solver, all from the computational middleware toolbox, combined with components for error estimation and grid adaptation. The combining of these components will use a set up for varying the degree of implicitness, which can be enabled by a fully implicit formulation where the equation splitting is done through block preconditioning [26, 46]. For the computational scientist, such an approach yields a continuum of solution strategies, ranging from the most simple and well known ones to new and more implicit schemes with increased robustness. Building these solvers independently from scratch would be very time-consuming and technically complicated, while our suggested software and numerical approach handles complexity through a hierarchy of manageable pieces.

The software components that constitute a compound fluid flow solver are normally applicable to a wide range of flow problems and can be used even in other physical applications where the mathematics and numerics are the same. Therefore, it is natural to perform research on adaptive methods, error estimation, and implicit solvers from a point of view where the results are applicable to a wide class of incompressible viscous flow problems. The evaluation of the developed methods will naturally employ simple case studies from various industrial and scientific branches of fluid dynamics. However, applying the software and numerical methodology to challenging real-world problems is extremely resource-consuming; hence, it is necessary to narrow our focus to a couple of very specific applications. We have chosen these from the emerging field of biomedical fluid flow.

1.3 Biomedical Flow

Computational biofluid mechanics is an emerging field that is already beginning to have an impact on the design of medical devices, the development and planning of surgical procedures, and the enhancement of the scientific understanding of human development, disease and aging. Within the broad field of biofluids, there is a wide range of important application areas, but the vast majority fall within the focus of this project – namely, laminar and turbulent incompressible viscous flows.

The need for robust and flexible software for computational fluid dynamics is especially great in biomedical flow applications. The flows are three-dimensional, geometries are complex and variable, and the fluid flow problem must frequently be solved in conjunction with other coupled physical problems, such as the following: finite deformations of the heart and vascular walls; transport processes in the airways and vasculature, including reaction-diffusion processes; and two-phase flow in the microvasculature and during aerosolized drug delivery. This complexity means that standard application packages, which may be suitable for the general class of fluid flow problems, become difficult to integrate and couple with nonstandard sources of data and other computational models.

While biomedical fluid flows are invariably viscous and incompressible (including airway gas flows), in other ways they are very diverse. For example, Reynolds numbers in the circulation vary by six orders of magnitude. Blood flow around the heart valves, due to arterial stenosis (narrowing) and in the chambers of the heart, is complex and often turbulent. Flow in the small arteries is laminar but strongly affected by their branching structure and the non-Newtonian viscous properties of blood, as well as the biological effects of fluid shearing forces on the vascular endothelium and its consequent impact on vascular geometry by altering smooth muscle tone. Microvascular flow is two-phase, since the smallest blood vessels can actually be smaller than the diameter of a red blood cell at rest. Transport between the vessel, the surrounding tissue, and the lymphatics is very important. There are, in addition, other important classes of biomedical flow problems. While blood flow through devices such as left ventricular assist devices (LVADs) may or may not be affected by fluid-structure interactions, flow through the heart valves is. Fluid-structure interactions are critical to normal cardiac function and flows, and the deformability of large arteries and veins is also important to normal pressure and flow waveforms.

There are a host of important problems related to normal and pathological blood flow that require state-of-the-art computational approaches, and these either have only recently become feasible or still depend on new developments. These problems include the design of pumps and LVADs to avoid thrombosis (clotting) and minimize hemolysis (breakdown of red blood cells) – see, for example, [1] – as well as the optimization of patient-specific surgical procedures to correct the adverse and often life-threatening hemodynamic effects of congenital cardiac and vascular abnormalities [38]. Although years of surgical experience has improved outcomes from these procedures, even successful operations may result in abnormal loads on the heart and vessels that increase the risks of aneurysm or cardiac hypertrophy and failure. Similarly, computational models that couple the mechanics of the heart wall and valves to the blood flow have not advanced sufficiently to explain fundamental phenomena and solve clinical and design problems. In fact, these efforts have stalled due to a lack of modern, robust, and flexible numerical tools.

Airway flows from the mouth and nose through the trachea and bronchial network to the gas exchange compartments of the lung are a growing area for research. Particularly important questions relate to the effects of airway diseases, such as emphysema and asthma, and the challenges of optimizing the delivery of aerosolized drugs to the lungs. Because the drugs and the flows interact with the airways themselves, the physical processes are linked intimately to the biological ones.

An important opportunity for biomedical flow computations arises from the fact that a variety of biomedical imaging modalities, especially ultrasound and magnetic resonance imaging (MRI), are readily sensitized to motion and thus well-suited to imaging biofluid flows and perfusion. Examples include the following: phase contrast velocity-encoded MR imaging of circulatory blood flows; contrast enhanced MR imaging of airway flows; Blood Oxygen Level Dependent (BOLD) imaging of regional brain perfusion; and Doppler echo imaging of blood flow in the great vessels, the chambers of the heart and across the valves, even *in utero*.

In addition, tomographic imaging modalities and angiography can provide detailed, subject-specific vascular or airway anatomical data. Together with the rapid performance increase in computers and computational techniques, these imaging techniques open up new possibilities for detailed, even person-specific, biomedical modeling.

2 Project Plan

2.1 Computational Middleware

We recently began to collaborate with the partners in the FEniCS project: Chalmers Technological University, University of Chicago, Argonne National Laboratories, The Royal Institute of Technology (KTH, Stockholm), Texas Tech University, and Delft University of Technology. All software development in the center, as well as the publication and distribution of associated written material, will be done in close cooperation with these partners and will be included as modules in the FEniCS suite. We have already managed to hire Dr. Anders Logg, an outstanding young scientist and a key developer of FEniCS modules, for a long stay at Simula to conduct this work. In addition, Drs. Matthew Knepley and Barry Smith (Argonne) and Prof. Robert Kirby (Texas Tech Univ.) will be invited collaborators in the center and will actively support our research. The Simula team (in particular Cai, Bruaset, Langtangen, Lines, Mardal, Skavhaug, and Sundnes) has a strong expertise in computational middleware, and the team will benefit greatly from close interaction with the aforementioned international experts.

There will be four subprojects on computational middleware. The first, **PDE Components**, aims to encapsulate a PDE solver in a way that makes it easy to combine the component with other PDE components. Typically, this middleware involves a standardized application programming interface (API). One possibility is to base the API on ideas from the Common Component Architecture (CCA) work in the US for coupling multi-institutional, multicode, and multiphysics projects [13]. We wish to perform the coupling in Python to make the programming user-friendly, flexible, and powerful. This approach means that we need to develop a library of Python tools for interfacing PDE solvers written in the standard scientific computing languages Fortran, C, and C++. In particular, there is a strong need for a unified way of handling input and output data in a heterogeneous collection of PDE codes. All input related to a problem must be defined in one place, with automatic propagation of information to various codes. Output, typically discrete scalar and vector fields over grids, from different codes should be stored in a common, standard format.

In the second subproject, **Fluid Flow Components**, we will use the developed API and Python tools to encapsulate high-quality software for the PDE components that are needed for building incompressible flow simulators, both for pure flow problems and for flow with deformable geometries. This work includes encapsulating Navier-Stokes solvers with various degree of implicitness (also including commercial codes wherever feasible), convection-diffusion-reaction solvers, Poisson solvers, and large-strain elasticity solvers. These four classes of components are sufficient to build solvers for many turbulence schemes, heat transfer, solute transport, and fluid-structure interaction problems. For certain free-surface tracking methods, it would also be convenient to have a reliable solver for the level-set evolution equation or VOF formulations.

The goal of the third subproject, **Library Components**, is to offer the computational scientist the tools to build her own solver for a specific PDE or PDE system. This work will basically make use of some carefully chosen existing libraries, such as DOLFIN [17], Diffpack [24], PETSc [37], and Trilinos [45], and enable the solver to be built at a high level of abstraction in Python. This subproject will need to further develop DOLFIN, FFC, SyFI, PyCC and related software. If successful, the subproject may be the dominating contribution from the computational middleware part of the project.

There is a strong and ever-increasing need for parallel computing in computational fluid dynamics. Those parts of the center that deal with software, methods, and applications must, therefore, exploit parallel algorithms and hardware, to ensure that the results are applicable to real-world computational science problems. This is the topic of the fourth subproject, **Parallel Computing**. Following our plan of a hierarchical structure for software development, parallel algorithms will be particularly important in the computational middleware, where it will be integrated into all three subprojects listed above. We will focus on two natural ways to incorporate parallelism in computational middleware. The first and easiest approach is to apply sophisticated parallel libraries such as PETSc or Trilinos, whenever linear algebra problems (matrices and vectors) arise. This approach is straightforward and strongly mimics the serial numerical algorithms, but may in certain cases result in unsatisfactory scalability due to the lack of PDE-awareness in the parallel linear algebra libraries.

The second parallelization approach is subdomain-oriented and will be based on overlapping and nonoverlapping domain decomposition, where the original PDE problem is split into a set of "independent" subproblems. The resulting parallelized methods are often numerically superior to their serial counterparts, while achieving better parallel efficiency. We have extensive experience with creating generic software for a subset of this class of methods; namely, additive Schwarz iterations with coarse grid correction and overlapping subdomains [3, 27]. For many fluid flow problems this approach performs very well [3, 4], although fluid-structure interactions in biomedical flows obviously also call for nonoverlapping subdomains. We have already made detailed plans for how the methodology can be flexibly implemented in Python, and have recently started an activity to build a generic framework. This *parallel middleware* runs the domain decomposition algorithm on overlapping domains, using PDE solvers as black boxes. This is an extension of the successful parallel computing framework we have already developed for Diffpack [27].

The key scientist guiding the development of parallel computing tools in the center will be Prof. Scott Baden from the University of California, San Diego (and San Diego Supercomputer Center) in collaboration with Assoc. Prof. Xing Cai at Simula. The former will act in a part-time capacity, while the latter will work almost full-time on parallel middleware and applications of parallel computing in the described context. Our collaboration with key PETSc developers (Knepley, Smith) will clearly strengthen parallel computing in the center. Research involving parallel performance depends on the target hardware, which will mainly be the national supercomputers consisting of large PC clusters. Through international collaboration we will seek the possibility to also address other architectures, for instance, clusters of shared memory machines.

A key issue in computational middleware is run time optimization, for example, memory locality, I/O, and load balancing. In coupled components another issue arises: "cross component optimization". That is, each PDE component should not be optimized separately, but in the context in which it is used together with other components. Professor Baden will address run time support issues to these ends, starting with a specific application and generalizing from there. Baden's Thyme software, possibly in combination with LLNL's ROSE tool, will be central in this work.

Other research challenges in the computational middleware project concern how to design a PDE solver API; how to exchange scalar and vector fields efficiently between different software components; and how to implement the tools such that user friendliness and computational efficiency are achieved at the same time. These are known to be challenging tasks even for scalar computers, and are complicated considerably when parallel hardware is to be employed. The results from our efforts on these topics will, therefore, naturally find their way into scientific papers. However, more important is the development and distribution of the software tools. By making the software open-source and putting effort into documentation, for instance in books (as we have very successful experience with in the past), the research results might have a much broader impact than that which papers alone can achieve. We will also attract interest to the field of PDE software in general and our contributions in particular by organizing workshops and short courses.

Milestones. The main milestones of the computational middleware project will be releases of the software packages described above.

- June 2008. Organize workshop on computational middleware.
- January 2010. Software release, PDE components.
- June 2010. Software release, fluid flow components.
- January 2012. Software release. Library components.

We plan to publish a joint proceedings from the workshops covering computational middleware, robust flow solvers and biomedical applications. This publication is listed as a milestone in the biomedical applications project below.

2.2 Robust Flow Solvers

The research on robust flow solvers is organized as four subprojects. Two of these deal with adaptive numerical methods for laminar and turbulent flow, based on error estimation techniques, where very promising new methods have recently developed by the group around Prof. Claes Johnson at Chalmers University of Technology [20]. A key member of this group, Prof. Mats Larson at Umeå University, will be a principal investigator conducting the research on error estimation and adaptivity. Personnel at Simula (Cai, Langtangen, and Mardal, in particular) have considerable experience with numerical methods for fluid dynamics, and together with collaborators at the University of Oslo and internationally (specific names are listed later), we foresee an extended team that is well-balanced with respect to the four areas of theory, algorithms, software, and validation.

Adaptive Solvers. Technology for the simulation of fluid flow has developed rapidly during the last decade, to the extent that dynamic flow simulations can now be used in many realistic applications. Central to this development are adaptive mesh refinement techniques based on *a posteriori* error estimates. In such estimates, the error in goal quantities of particular interest can be estimated in terms of the residual of the computed solution and a dual weight. The dual weight carries stability information, and indicates in which regions the residual needs to be reduced. It is computed numerically by solving the linearized dual problem [20]. Access to fast computers and storage makes it possible to store the computed time-dependent flow field and solve the linearized dual problem, making robust solvers based on advanced *a posteriori* error estimates increasingly relevant for practical computations. Examples of relevant goal quantities include the lift and drag coefficients of bluff bodies and force distributions on surfaces. Highly robust flow solvers may be built using adaptive mesh refinement based on *a posteriori* error estimates. We will further develop and implement adaptive flow solvers for the full range of incompressible fluids. Important open issues include coupling to turbulence models, the use of more complex elements (for instance, boundary fitted anisotropic elements), and the construction of efficient adaptive strategies. A key collaborator will be Dr. Johan Hoffman, an outstanding young scientist currently at KTH.

Adaptive FSI. Many applications, for instance the dynamic simulation of the heart, involve fluid structure interactions (FSI) where one needs to solve the flow field coupled with a structure model. In such problems, the robustness of the flow solver is very important. As described above, adaptivity may be used, with the goal functionals specified by the data passed from the flow solver to the structure model. In the same way, an adaptive procedure may be constructed for the structure model. The adaptive procedure is then tailored precisely for accurate computation of the interaction between the fluid and the structure. Such coupled adaptive procedures are now emerging [6, 30]. Furthermore, recent studies [12] of time-splitting algorithms for reaction-diffusion problems indicate that the dual stability information may be used to determine the extent to which an implicit solver coupling of the fluid and structure is necessary. Preliminary results in this direction are reported in [28], where the strength of the couplings in a MEMS device involving electrostatics, heat transfer, and elasticity is investigated.

We propose to develop adaptive coupled FSI solvers based on such *a posteriori* error estimates. Subtasks include the development of *a posteriori* error estimates for the coupled problems targeting accurate computation of the coupling terms; implementation of the robust solvers; and development of techniques for determining a suitable degree of implicitness in the coupling.

We expect that adaptivity will prove to be a technology essential for addressing coupled multiphysics problems where the different physics require different resolution and automatic tuning of discretization parameters is necessary.

Another important part of FSI simulations is the handling of complex, moving geometries. Basically, the methods for such moving boundary problems divide into Eulerian and Lagrangian methods. The Lagrangian method is the standard choice in many finite element applications involving moderate geometry changes and is suitable for simulating the flow in elastic vessels. Progress in developing the Eulerian method has been rapid over the last few years, and it is now possible to avoid difficulties with mesh generation and mesh quality. Recent progress makes it possible to formulate Eulerian finite element methods on very complex moving geometries, for instance represented using level sets [29]. Since meshing is easier in Eulerian than in Lagrangian methods, the former are ideal for adaptive mesh refinement. We will develop *a posteriori* error estimates and adaptive algorithms for such methods.

Implicit Coupling of Solvers. This subproject aims to develop a flexible degree of implicitness in flow solvers. The project will be pursued by the Simula team (in particular Cai, Langtangen, Mardal, and Skavhaug) in strong collaboration with Prof. Stefan Turek in Dortmund, and Prof. Ragnar Winther and Prof. Kenneth Karlsen at the Center of Mathematics for Applications, University of Oslo. Turek, Winther, and Karlsen are leading international scientists who together cover both software and theory for flow computations. Our idea is to first formulate a fully implicit method for the Navier-Stokes equations combined with a set of convection-diffusion-reaction equations. By using block preconditioning of the resulting algebraic system, as outlined in [46, 26], we can split the system via various choices of preconditioners. Some simple choices will reproduce classical methods of Chorin type, or a fully implicit solver, while other choices will yield new methods where the degree of implicitness can be chosen through the block preconditioner. The application of this idea to the Navier-Stokes equations is known, but not taken advantage of in software. We intend to focus on extending the idea to more general systems of PDEs and develop accompanying software components.

Adjusting the degree of implicitness in compound FSI solvers is expected to be a key ingredient for improving convergence and attaining the stability and reliability that a scientist in computational biomedicine will need. At present, it remains an open question how to do this with block preconditioning in the case of multidomain FSI. We have invited Trond Kvamsdal and Runar Holdahl (leading national scientists in the FSI field) to join the Simula team to produce reliable FSI solvers for confined flow with elastic boundaries. Moreover, we will collaborate with Dr. Anna-Karin Tornberg and her group at KTH to strengthen our FSI research.

Laboratory Experiments and Validation. In any numerical software, a careful procedure must be included that can verify that the mathematical equations have been solved correctly. The group behind the present project have extensive experience with methods for numerical code verification. We will take an initiative to establish benchmark methodologies for various PDE solver components, including those of relevance to bioflows.

The next phase concerns validation to establish how well the models describes real-world phenomena. Such validation requires comparison with laboratory experiments and carefully conducted studies based on DNS. Some experimental data for benchmark cases are available in the literature, but we will also conduct custom-designed physical experiments at the lab facilities at the University of Oslo (Prof. John Grue and Assoc. Prof. Atle Jensen) and at SINTEF and the Norwegian University of Science and Technology (NTNU) in Trondheim (Prof. Hellevik and collaborators). Direct numerical simulations data will be obtained by scientists at the Norwegian Defence Research Establishment (FFI). The center will establish close collaboration with Prof. B. Anders Pettersson Reif and other senior scientists from the Turbulence and Flow Physics group at FFI.

Milestones. The main outputs from the robust flow solvers project will be journal publications and contributions to the software components released from the computational middleware project.

- June 2009. Organize workshop on robust flow solvers.
- April 2007-January 2012. Study implicit solvers for Navier-Stokes equations. This is a key element of our approach to develop robust flow solvers, and also an area where we already hold considerable knowledge. It will be a focus area for the entire first five-year period.
- April 2008-April 2009. Navier-Stokes solvers with adaptivity and error estimation. This is another important building block for achieving the desired robustness, and will be studied in parallel with the implicit solvers.
- January 2011-January 2014. Exploration of turbulence models. We want to explore various models for turbulent flow, with particular focus on their applicability for bioflows and the transition from laminar to turbulent flow.
- January 2011-January 2014. Fluid flow solvers, deformable geometries. Deformable, moving boundaries are a characteristic feature of biomedical flows. Robust flow solvers for fluid-structure interaction problems will be studied in detail.

2.3 Biomedical Flow

Simula Research Laboratory has worked with computational techniques for biomedical problems for several years – see, for example, [31, 42] and references therein. Until recently, the main focus has been on heart electrophysiology and mechanics, but an important result of this work is a considerable knowledge base of biomedical issues in general. Of even greater importance are close connections to world-leading research communities in the bioengineering field. Along with the group's work on traditional flow problems, this knowledge base will form the foundation for the research on biomedical flows. Prof. Andrew McCulloch at the University of California, San Diego, will be a visiting scientist in the center, with responsibility for the biomedical applications. Several researchers at Simula (in particular, Lines, Mardal, Skavhaug and Sundnes) have experience with biomedical applications, and we have set up collaborations with medical research communities in Norway (specific names are listed below). An important task for this activity will be to strengthen and extend our collaboration with top international groups in the specific field of bioflow computing. Excellent candidates include the group of Prof. Alfio Quarteroni in Lausanne, Prof. Tom Hughes in Austin, Prof. Charles Peskin at Courant, and Prof. Charles Taylor at Stanford.

Below, we outline nine different topics for research in biomedical flows. These are to be taken as a list of possible subprojects at the time of this writing and not as delivarables. All the suggested applications are clinically highly relevant and represent different subsets of the many fluid flow challenges listed above.

Fundamental Flow Features. Before attacking complicated biomedical flow or FSI applications, it is important to establish an understanding of fundamental flow features of relevance to such applications. Here we may mention oscillatory boundary layers, flow around bifurcations, particle transport, and aspects of turbulence. Although biomedical flows for the most part are laminar, turbulence occurs in certain occasions, especially related to diseases, and this might be a focus point of the center since little work has been conducted on turbulent biomedical flows. Results on topics such as transition to/from turbulent spots, turbulent particle transport, non-stationary turbulence, and non-Newtonian fluids are of fundamental interest far beyond biomedical applications. Many of our collaborators will naturally contribute to investigating more fundamental fluid mechanics topics.

Flow Through a Left Ventricular Assist Device. Implanted left ventricular assist devices (LVADs) are increasingly being used to prolong the life of patients whose hearts are so weak that they would otherwise not live long enough to receive a heart transplant. Given the shortage of donor hearts, LVADs are also envisioned to become an alternative to heart transplants as a terminal treatment for heart failure.

Among the biomedical flow cases that we will consider, this one is the closest to conventional industrial flow computations. In essence, the device is a small pump, which is implanted to assist or even completely replace the life-supporting pumping function of the ventricles. Particular challenges for the VADs include a very limited size, as well as the biological risks of infection, blood clots, and hemolysis. Hemolysis and the formation of blood clots will be directly connected to the properties of the blood flow, and are therefore highly relevant to study with computational techniques [47, 50].

A natural progression of the project will be to first study the pumping device itself and see how different designs will affect the critical parameters of flow output, clot formation, and maximum shear stress. Since we are interested in microscopic features of the flow, the application of the advanced turbulence models described above may be crucial for the result. Additional challenges arise from the complicated geometry of the pumps, which results in complicated, localized flow patterns that are resolved most efficiently with adaptive meshing techniques.

The second step of the project will be to model the inflow and outflow regions of the LVAD. The flow patterns in these regions will be important for the loading and remodeling of the cardiovascular system, which may be critical for the continued functioning of the system. Initial studies of this kind can be done with fixed boundaries.

A third step of this project is to couple the results to the flow in the complete ventricles, as described in a separate project below. This coupling will lead to an extremely challenging flow computation, involving full fluid-structure interaction in addition to the challenges already mentioned.

Airway Flow and the Distribution of Inhaled Suspensions. This application has huge clinical potential, but has received limited attention in the literature. Drug administration through the airway system has widespread applications, in particular for lung and airway diseases, such as asthma. However, the potential of this is much greater than is utilized at present, and it is believed that a large number of substances can be administered through the airways safely and conveniently. To utilize this potential, it is important to have detailed knowledge of how the substances are distributed through the airway system, and computational studies are a necessary tool for obtaining this knowledge. One striking example is the Norwegian company Optinose [34, 9], which is developing a new system for drug administration through the nose and uses computational studies to optimize such parameters as flow velocity and particle size.

Studies of flow in the airways are challenging for a number of different reasons. The geometry is highly complex, the flow is turbulent, and modeling the suspended substances creates additional challenges. Depending on the application of interest, it may also be necessary to model the uptake of the substance in the airways. We want to perform simulations of several parts of the airway system, such as the nose and the lungs, and to be clinically relevant the study must include both healthy and diseased airways; see e.g., [51]. We want to study the effect of such parameters as different drop sizes from the nebulizer, fast versus slow breathing and deep versus shallow breathing, etc. Although the answers to many of these questions may seem rather intuitive, experimental results have revealed that they are not, and computational techniques stand out as a promising tool to increase our knowledge in this area.

Transport of Aerosols. Transport of aerosols and vapor in airway flows It has long been recognized that particle inertia throws dense particles out of regions of high vorticity and leads to accumulation in the straining- flow regions in turbulent flows. The size of inhaled aerosols (i.e., droplets or solid particles) is on the other hand in the order of only a few microns with negligible inertia. These particle sizes correspond to the smallest turbulent scales, and the traditional view has been that these are perfectly advected by the airflow. Recent studies, however, indicate that the tendency to cluster is evident even at particle separations in the order of a few microns. Since the clustering of aerosols enhances the rate of coagulation or coalescence, it affects the site of deposition in the respiratory system. This may for instance influence the effectiveness of administrating pharmaceutical drugs by inhalation, as well as influence the health hazards posed by chemical, biological or radioactive aerosols. Other important physical processes that will be considered are deposition of aerosols and evaporation of liquids accompanied by possible aerosolization. The study will be based on numerically generated turbulent flows by means of direct numerical simulations of unbounded and bounded flows. An important partner here is Prof. Reif and his co-workers at FFI.

FSI Simulation of the Mitral Valve. The hemodynamics in the left ventricle and in the vicinity of the mitral valve in particular, is of extreme importance due to the relevance on global functionality of the heart. The highly interactive nature of blood flow and mitral leaflet motion makes this an interesting and challenging FSI problem.

We have developed a novel and promising constitutive model for the mitral leaflets. This is a hyperelastic transversely isotropic membrane shell model which accounts for the collagen fiber orientation in the mitral leaflets. The model has been implemented in a nonlinear finite element solver and produced results which agree well with ultrasound recordings. Further, both physiological and pathological conditions for the mitral leaflets may be represented by the model.

Multiscale Modeling of the Circulatory Dynamics. The simulation the whole cardiovascular system (or even large parts) by solving 3D coupled equations for blood flow and vessel wall interaction, is not computationally feasible in the foreseeable future. However, in most regions only the gross flow features will be of interest (e.g., pressure and flow wave propagation). Full 3D FSI models are often only strictly required in localized regions, typically in the vicinity of bifurcations and aneurysms. This principle calls for a coupling between 3D models and hierarchies of reduced models (comprised by networks of 1D pipes and lumped parameter models).

A potential further development of the network model is to extend it to a multiphase code. This would open for simulation of the transport of various constituents in the blood, such as O_2, CO_2, glucose, and other nutrients. Vital for such a model would be the modeling of production/consumption of the particular constituent in question.

Application of Multiscale Models to Modality to the Fetal Circulatory System. At present, hemodynamic assessment of the venous circulation in the fetus is an integral part of a thorough ultrasound evaluation. Subsequent to the introduction of the umbilical vein and its pulsatile pattern was discovered in the comprised fetus, other parts of the venous system have been explored for possible diagnostic use: the inferior and superior vena cava, ductus venosus, hepatic veins, pulmonary veins, and intracranial veins. A versatile 1D network model adapted to the fetal venous system would be an invaluable research tool to provide a better understanding of the physiological mechanisms. In particular, a network model with a 3D model of the umbilical vein ductus venosus bifurcation would be a very interesting and useful application. Professor Torvid Kiserud at Department for Obstetrics and Gynaecology at The University of Bergen, will be an important collaborator in this project.

Cardiac Fluid-Structure Interaction. We want to link models of blood flow in the ventricles, atria, and around the valves with electromechanical models of the ventricular and atrial walls. As described above, this is an extremely challenging application, which involves full fluid-structure interaction between the partly turbulent blood flow and the actively contracting, thick-walled, nonlinearly elastic heart wall. However, the potential clinical impact of such simulations is also huge, and important advances in this direction have already been made – see, for example, [5, 33, 36, 48, 49]. The modeling may provide important knowledge of the interaction between properties of the heart wall and flow parameters, and in its most advanced stage may also link directly to information on the scale of the heart cells. The computational tools can be applied to normal hearts as well as to congenital malformations of the heart and great vessels, and to surgical procedures to correct them, such as the Fontan procedure. The results will be important for understanding the cardiac system and have applications in surgical planning and even drug development.

Prof. McCulloch's research group at the UCSD will be important partners in this project. We have also established contact with the Heart and Lung Clinic at the National Hospital of Norway, led by Prof. Otto Smiseth, and with the Laboratory for Human Circulatory Physiology at the Department of Physiology, University of Oslo. Their role will be to provide experiments and measurements that are needed for this activity, and to help guide the research in directions with clinical relevance.

Blood Flow in the Circle of Willis. Simula as well as Kvamsdal and Holdahl have recently initiated a collaboration with Dr. Tor Ingebrigtsen at the University Hospital of Northern Norway, with the intention of simulating blood flow in the Circle of Willis and its role in the formation of cerebral aneurysms. Computer simulations of flow in the circulatory system is a field of great international interest – see, for example, [18, 22, 23, 43]. Predicting the formation and eventual rupture of cerebral aneurysms is extremely important in clinical practice, and the circulation in the Circle of Willis has a number of particular features that require special studies. The small diameter of the relevant vessels makes simulations with rigid boundaries a good approximation for a first approach to uncover flow conditions that lead to formation of cerebral aneurysms. The flow can be considered laminar, but the simulations are challenging because of the complicated geometry and irregular flow patterns in the Circle of Willis. A simplified flow model, based on the reduced basis finite element method, may be of great interest for parametric studies of the influence of geometrical features on the flow. Another computational direction is to study the large-deformation growth and eventual rupture of cerebral aneurysms, which increases the scope of the simulations to a complicated FSI problem. Although many excellent computing groups address aneurysms, our advantage is close contact with the medical community and the possibility to get patient-specific data (through Ingebrigtsten). This makes it likely to publish computational results in medical journals.

Data Aquisition and Imaging Techniques. All of the proposed projects link closely with clinical imaging and measurement. In addition to the collaborators mentioned above, we have established connections with the Department of Radiology at the National Hospital of Norway, which may provide high-quality imaging data. We also have close connections with leading national experts on ultrasound imaging.

Milestones.

- June 2007. Organize workshop on biomedical flows.
- June 2010. Organize workshop on biomedical flows.
- April 2007-April 2010. Study of biomedical flows on fixed geometries.
- April 2010-April 2014. Study biomedical flows with deformable geometries, and fluid-structure interaction.
- January 2011. Publish a joint proceedings from the workshops on computational middleware, flow solvers and biomedical applications.
- Januar 2012. Publish a book on biomedical flow computations.

3 Project Team and Management

The center will be led by Prof. Hans Petter Langtangen, with Dr. Joakim Sundnes as deputy manager.The center has recruited an experienced administrative manager, Tom Atkinson. Four researchers will work full-time in the center and be project leaders for software, methods, biomedical applications, and the outreach of results. Senior principal investigators will be responsible for the scientific work and conduct the research projects: Langtangen will take care of computational middleware, robust flow solvers constitute the responsibility of Larson, while McCulloch will handle the biomedical applications.

Simula will host the center. Simula has large office facilities at IT Fornebu, with all the necessary infrastructure for a world-class research center. The center will require an expansion of the current office areas, and this is available in direct proximity to the current facilities. Simula also has professional and stramlined systems for personell handling and administrative tasks, which will all apply also for the new center.

In addition to the scientific seniors who are employed in the center or involved as collaborators, the center will receive advise from Simula's Scientific Advisory Board. This board holds strong expertise on software issues and general information technology, and currently has two members that are experienced in biomedical computing. Depending on the development in the center and our need for advise, we will also consider to add an additional member with relevant knowledge for the center.

Recruitment of Women. Particular emphasis will be placed on recruiting female researchers to the center. The research group behind this project has been involved in biomedical computations for more than ten years, and this activity has a very good track record in recruiting female students at the Masters and PhD levels. Among the total number of students graduated from this activity, the proportion of female students is 75% at Masters level and 40% at PhD level. For postdoctoral projects completed within the group, the proportion of women is 33%. These numbers should be compared with a national average of about 13%[1] at the undergraduate and Master level and 18%[2] at the PhD level in informatics. We have not yet performed any active recruitment of women, but the center will focus on this issue as the second most important goal after excellent research. The strategy for recruiting talented female researchers is described further in a separate document.

Previous Work by the Group. The Department of Scientific Computing at Simula Research Laboratory originates from a research group jointly at the Department of Informatics, University of Oslo, and at SINTEF ICT. Over the last 15 years, this group has performed multidisciplinary research at the intersection of computer science, numerical mathematics, mechanics, and biomedicine.

The group's work has been evaluated twice by panels consisting of top international scientists. In the evaluations of both ICT research in Norway in 2001 and Simula in 2004, the group received the highest grade ("Excellent"). Prof. Kenneth Karlsen, who holds a part-time position in the group, and Dr. Joakim Sundnes, both received the highly prestigious Outstanding Young Investigator award in 2004.

A particular focus has been to develop numerical methods and implementation techniques that allow a large class of partial differential equation problems to be solved by the same computer code. This approach has increased software reliability, simplified verification procedures, reduced the implementation resources, and enhanced maintenance. The methodology has been exemplified and supported through the Diffpack programming environment, which was distributed and commercialized internationally, and used by such universities and companies as Cambridge, Stanford, Intel, and Daimler-Chrysler, to mention but a few.

Besides this particular application, the group has, in collaboration with others, addressed various fluid flow problems, especially water waves and two-phase flow. At the moment, the group is working on extending the previous methodologies to multidomain, multiphysics, and multiscale problem settings.

Over the last decade, the group has established a strong international position regarding the simulation of the electric activity in the heart. This work has recently been expanded to cover the coupling to the mechanical motion of the heart, and has yielded a solid foundation of biomedical knowledge and contacts that will be necessary to attack advanced biomedical flow problems.

In addition to papers in high quality journals, the group has had a particular focus on publishing books and software as well as organizing scientific meetings.

[1]Source: NSD/DBH *http://dbh.nsd.uib.no.*
[2]Source NIFU STEP *http://www.nifustep.no.*

Budget. The center has a ten-year perspective, and an annual budget of approximately 11.5 million NOK. Of this amount, about 4.0 MNOK will be funded from Simula. Our original request for financial support was 11.5 MNOK, but this amount was reduced to 7.5 MNOK by the Research Council of Norway. Most of the budget will be spent on salaries for the foreign researchers whom we plan to invite to the center, and on stipends for PhD students and postdoctoral researchers. As described above, the focus of the tasks undertaken by the center will be threefold. In Table 1 we present a suggested budget for each task, divided into two-year periods. In the first years of the center, the main focus will be on Computational Middleware and Robust Flow Solvers, while the focus on Biomedical Applications will be stronger towards the end of the ten-year period. The personell costs displayed in the budget arise from a base of five full time research positions, in addition to the center management. There will be three part-time researcher positions, three scientific programmers, and about three post-docs and three to five PhD students. Estimated start and end dates for the PhD students and PostDocs are given in Table 2.

	2007-2008	2009-2010	2011-2012	2013-2014	2015-2017
Total Budget	20531	23456	23996	25110	27011
Own funding	7367	8456	8995	10110	10175
From research council	13164	15000	15000	15000	16836
Administration:					
Salaries management	2925	3344	3344	3344	3762
Equipment	500	400	400	400	200
Workshops and seminars	800	600	600	600	600
Purchase of services	400				
Computational middleware:					
Researchers	3045	3480	2957	2088	2349
Postdoctoral researchers	2436	2784	1566	174	
PhD students	1480	1924	1184	1184	1332
Programmers	2275	2113	650		
Visiting researchers	325	393	393	393	442
Robust flow solvers:					
Researchers	1827	2088	2088	2088	2349
Postdoctoral researchers	1218	1392	2610	2784	1740
PhD students	1036	1776	2368	2368	1332
Programmers		487	1950	1950	1463
Visiting researchers	610	786	786	786	841
Biomedical applications:					
Researchers	1309	1496	1670	2888	3249
Postdoctoral researchers				1392	2784
PhD students			1036	1628	2664
Programmers				650	1463
Visiting researchers	344	393	393	393	442

Table 1: Approximate allocation of the budget, in 1000 NOK, for each activity within the center. Each column specifies the total budget for two years of operation. Because of the startup the second quarter of 2007, the final column also includes the first quarter of 2017.

4 Expected Results

As described in the separate publication plan, results from the center will be disseminated through traditional scientific channels, including journals and conferences. The group behind this project has a particular focus on publishing books and software to increase the awareness and impact of the research results. We also have a good track record in organizing short courses, international scientific meetings, and workshops at conferences. Moreover, the group and its collaboratators have strong interests in teaching, especially with reforming more traditional courses to take advantage of computer simulations. All of these outreach activities will naturally

	Start	End		Start	End		Start	End
PhD 1	20070801	20100731	PhD 2	20070801	20100731	PhD 3	20080101	20101231
PhD 4	20100101	20121231	PhD 5	20100101	20121231	PhD 6	20110401	20140331
PhD 7	20110401	20140331	PhD 8	20130101	20151231	PhD 9	20130101	20151231
PhD 10	20140401	20170331	PhD 11	20140401	20170331	PhD 12	20140401	20170331
PostDoc 1	20070401	20090331	PostDoc 2	20070801	20090731	PostDoc 3	20070801	20090731
PostDoc 4	20090401	20110331	PostDoc 5	20090801	20110731	PostDoc 6	20090801	20110731
PostDoc 7	20110401	20130331	PostDoc 8	20110801	20130731	PostDoc 9	20110801	20130731
PostDoc 10	20130401	20150331	PostDoc 11	20130801	20150731	PostDoc 12	20130101	20141231
PostDoc 13	20150401	20170331	PostDoc 14	20150401	20170331	PostDoc 15	20150101	20161231

Table 2: Approximate start and end dates for the PhD students and Post Docs that will be employed in the center.

be in the center's focus. In addition, we need to be active with recruitment and popular presentations of research for students and a public audience.

The potential impact of our expected scientific achievements will reflect the different scopes of the three principal activities in the center. The computational middleware is envisioned to have a broad impact in computational science, by providing generally applicable tools for solving partial differential equations at a high level of abstraction. The more specialized scope of the robust flow solvers will result in knowledge and software components for a wide variety of fluid flow problems, with important applications in industry and science. Finally, the highly specialized focus for the work on biomedical applications has the potential to solve specific problems that are of interest in bioengineering and medicine. The think that the main criterion for the success of this project is two-fold: (i) that we become able to address biomedical flow problems that lie beyond the reach of present computational tools, and (ii) that the generic and specific software is distributed and used internationally.

National Competence Building. The importance of marine research in Norway has led to a strong scientific tradition in fluid mechanics, with respect to both applications and solution methods. Nevertheless, research on robust numerics and state-of-the-art techniques is, as explained above, currently weak (with the exception of the leading spectral element efforts at FFI and NTNU). To import this solution technology to the vast set of marine applications in Norway, we suggest inviting leading international scientists to Simula and initiate collaborations. The CoE project will fund both these scientists and an appropriate number of PhD students and postdoctoral researchers to work with them. This is an efficient way of building important competence in Norway and of pursuing novel research on ICT that has far-reaching applications, including those aspects of Norwegian industry that deal with the marine environment. Despite the existence of several excellent fluid dynamics groups in Norway, with which we have very good contact, we intend to use this CoE to open up a new application area in biomedicine. Hopefully, we will be able to attract the fluid dynamics groups' interest, with respect to both the developed solution methodology and new areas of application.

Why a Center Is Necessary. The research in the center has three main ingredients: software, methods, and biomedical flow applications. Initial research in the directions outlined in this document could well be realized by applying for several smaller projects. However, with small, short-term projects it is virtually impossible to reach the challenging goals of our three topics. We want the software to be widely applicable and be of sufficient quality for international distribution. We want the methods for flow problems to successfully solve demanding flow cases in the human body. We want to satisfy the need for realistic biomedical case studies to receive substantial work with input data and validation.

For these goals to lie within our reach, we need top international scientists who interact with our local group. It takes time to build effective communication across disciplines such as mathematics, numerical methods, scientific software, fluid mechanics, and bioengineering. The partial attention one gets from contributors to small projects is insufficient. In the center, scientists will work full-time on the problems and establish the necessary intensity that is required to make progress with multidisciplinary topics. Inviting top scientists to Oslo for longer stays and bringing their attention to our modeling activity demands an exciting project of significant size, with long-term goals and stable funding.

Another important concern is that real-world problems, such as flow in the heart, involve a substantial amount of development work in addition to underlying academic investigation. This development work (extracting human body data, tuning of numerical strategies, validation) is difficult to fund in small projects on pure research. The same goes for bringing research software to the professional state required for international distribution. With a CoE of this size, these development tasks can be given the necessary attention and funding.

5 Progress Since First Application Round

Several initial steps have been taken to build a relevant network for the center and increase our knowledge about biomedical flows. We gave an international summer school at Svalbard in May 2006, where we provided an introduction to modeling blood flow in the human body for about 40 participants. This summer school also provided valuable contacts in biomedical computing. During the last year, Prof. Mats Larson has directed much of his research towards bioflows, and he has, in particular, successfully worked with adaptive mathematical representations of geometries for the human body. Another key researcher in this project, Dr. Johan Hoffman, has already successfully attacked blood flows with his adaptive numerical technology [20]. His highly-talented collaborator for many years, Dr. Anders Logg, is already employed as a postdoctoral researcher at Simula.

Python as a computing platform for PDE solvers has been explored at Simula. In particular, the prestigious simulator for the electrical activity in the heart has recently been reimplemented as a combination of Python and C++, using ideas originating from this project. The group is currently working towards extending these ideas to solve the nonlinear elasticity equations that describe the mechanical function of the heart muscle. Other ideas about the computational middleware part of the project are currently being explored for ODE applications together with Dr. Steven Lee at LLNL. In February 2007, we will contribute some of our recent progress related to this project in a minisymposium “From Molecule to System: Removing obstacles to structurally based multi-scale models”, organized by Scott Baden, at the SIAM CSE conference.

The ongoing collaboration with Prof. McCulloch’s group at UCSD has been strengthened further, and resulted in a recently submitted paper on numerical algorithms for simulating coupled electromechanics problems [44]. Researchers in McCulloch’s group have recently coupled finite element models of the heart to advanced lumped parameter models of the circulatory system, which is an important step on the way to full FSI simulations of the pumping heart.

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