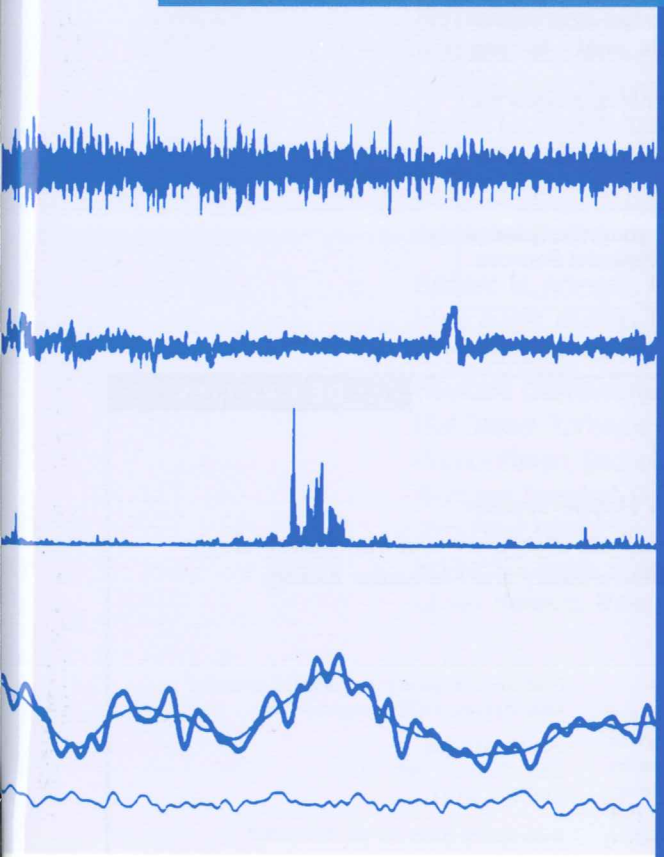
ISSN 0013-5585 ISSN (Internet) 1862-278X CODEN BMZTA7

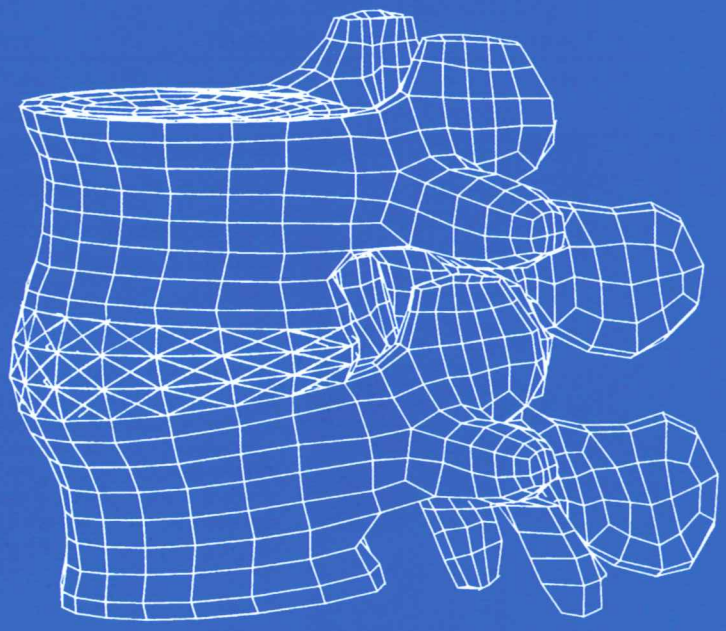
54 – 5 (2009)

# Biomedizinische Technik

## Biomedical Engineering

Gemeinschaftsorgan
der Deutschen Gesellschaft für Biomedizinische Technik im VDE,
der Schweizerischen und der Österreichischen Gesellschaften
für Biomedizinische Technik





**Special issue:**
**Smart Life Support**

Editor:
Steffen Leonhardt

de Gruyter
Berlin · New York

health technologies

Biomed Tech 2009; 54:269–281 © 2009 by Walter de Gruyter • Berlin • New York. DOI 10.1515/BMT.2009.031

Review

# Methods of design, simulation, and control for the development of new VAD/TAH concepts

## Methoden zur Konstruktion, Simulation und Regelung für die Entwicklung von neuen VAD/TAH-Konzepten

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### Abstract

Cardiovascular diseases are a major cause of death worldwide. If medical treatments fail to restore adequate blood flow in a patient, mechanical support is needed. To date, many different types of blood pumps have been developed, but only few are clinically available. This review article describes the challenges involved in this field of research and gives an overview of the development process. Past developments as well as current and new technologies and approaches applied are summarized. Finally, a perspective for improved devices is discussed.

**Keywords:** computational electromagnetics; computational fluid dynamics; control design; total artificial heart (TAH); ventricular assist device (VAD).

### Zusammenfassung

Herz-Kreislauf-Erkrankungen sind die häufigste Todesursache weltweit. Wenn eine hinreichende Durchblutung mit konventionellen Therapien nicht gewährleistet werden kann, ist eine mechanische Kreislaufunterstützung notwendig. In der Vergangenheit wurde eine Vielzahl von Blutpumpen entwickelt, von denen sich jedoch nur wenige klinisch etabliert haben. Dieser Artikel beschreibt die Herausforderungen bei ihrer Konstruktion und gibt eine Übersicht über den Entwicklungsprozess. Bisherige Entwicklungen, aktuelle und zukünftige Technologien und Lösungsansätze werden zusammenfassend dargestellt. Abschließend werden Verbesserungspotentiale bei der Blutpumpenentwicklung diskutiert.

**Schlüsselwörter:** Herzunterstützungssystem (VAD); Kunstherz (TAH); Magnetfeldsimulation; Regelungstechnik; Strömungssimulation.

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### Introduction

Cardiovascular diseases are a major cause of death worldwide [63]. If medical treatments fail to restore adequate blood flow in a patient, mechanical support is needed. Ventricular assist devices (VADs) and total artificial hearts (TAHs) re-establish sufficient perfusion in patients with advanced heart failure when medication and other surgical therapies, such as valve replacement or ventricular reconstruction, have reached their limits. In cases where the function of the natural heart is only partially impaired, a VAD can be implanted in various configurations. These can be divided into left heart assist, right heart assist, and biventricular assist for both sides. Blood is taken either from the atrium or ventricle and expelled into the arterial system. As an example, Figure 1 illustrates an option for left ventricular assist. The implanted pulsatile device (3) draws blood from the left atrium (7) through an artificial inflow valve (6) and pumps it through the outflow valve (4) into the aorta (5). Energy is supplied from an external battery (1) and transferred to the VAD through a percutaneous cable (2).

If heart failure is more advanced partial support by a VAD cannot re-establish sufficient blood flow. Additionally, some patients already have thrombus formation in the diseased heart. In these cases the only option is a TAH. Figure 2 gives an insight how a TAH system can be implanted. After resection of the failing heart, the TAH (1) is connected to the remains of the natural atria, as well as to the aorta and pulmonary artery. The TAH is controlled and supplied by an implanted battery controller unit (2) which is charged from a bigger external battery (4) by a transcutaneous energy transmission system (3). During TAH implantation, blood flow is maintained by a heart lung machine.

Prevalent indications for VAD and TAH interventions are dilated cardiomyopathy, coronary heart disease, and

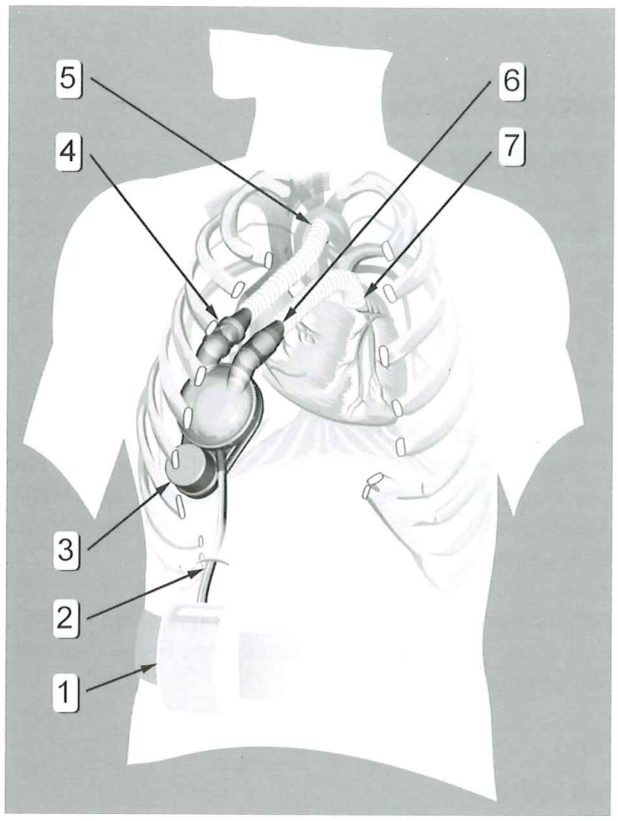


**Figure 1** Schematic of implanted VAD.
1, external battery; 2, percutaneous cable; 3, implanted pulsative device; 4, artificial outflow valve; 5, aorta; 6, artificial inflow valve; 7, left atrium.

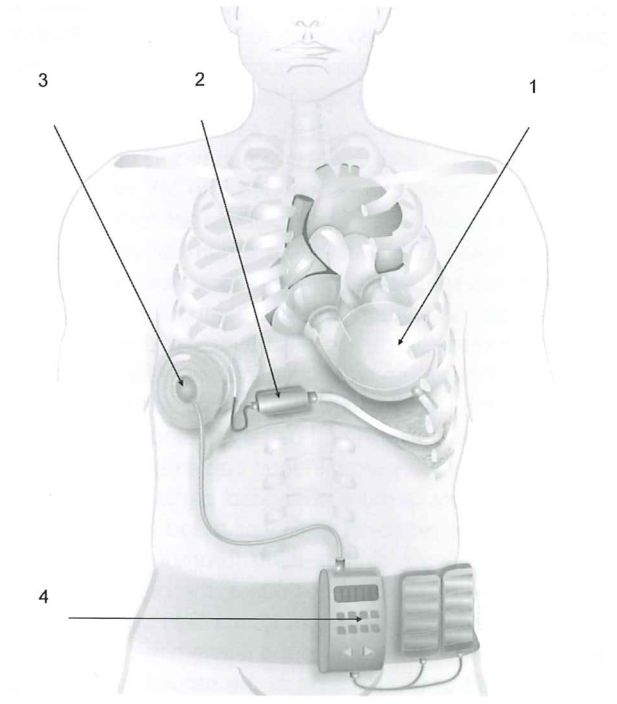


**Figure 2** Schematic of implanted TAH.
1, total artificial heart; 2, implanted battery controller unit; 3, transcutaneous energy transmission system; 4, external battery.

inflammatory cardiomyopathy. Four different types of therapies with these devices exist:

- bridge to bridge – the most acute application providing time to choose the appropriate therapy,
- bridge to recovery – the use of a VAD with the perspective that the natural heart recovers to normal function by temporarily unloading the muscle,
- bridge to transplant – improvement of perfusion until a donor heart is found, and
- destination therapy (DT) – unlimited assistance or replacement for patients that are not eligible for heart transplantation.

Recently, however, the latter two classifications have been somewhat distorted, as some patients initially classed as bridge to transplant remain on the device for extended periods, whilst others listed as DT might improve their condition to become transplant candidates. In 1999, Rose et al. [48] demonstrated that mechanical circulatory support (MCS) has its advantages over conventional treatments, even if the device used is not the most advanced. In spite of these findings, there is a large gap between the number of patients who could benefit from MCS and the actual number of VAD implantations. Some main causes include:

- system size resulting in maximally invasive operations and low patient comfort,
- high risk of thromboembolic events and hemolysis,
- low durability and reliability, and
- high system costs.

Alternatives, such as stem cell therapy or tissue engineered prosthesis, are still far from clinical standard therapy.

Over the past few decades, many different VADs and some TAHs have been developed and a small number of them are already available for patients; however, the potential for improvement is still huge. Each device has its certain advantages and suitable applications, but also its disadvantages. Furthermore, the selection of the most appropriate device for an individual patient is difficult. For example, heart recovery or waiting time for a heart transplantation is not easy to predict. Whereas biocompatibility and durability need to be further improved, other factors, such as timing of implantation and interaction to the organism and circulation system, have to be investigated. The development of a blood pump is a highly complex and interdisciplinary process in which many requirements have to be fulfilled.

Requirements for VADs and TAHs include:

- hemocompatibility (hemolysis, thrombogenicity, material-induced reactions),
- miniaturization,
- durability,
- implantation configuration (anatomical fitting),
- inflammation/infection protection,
- hemodynamics (cardiac output, pulsatile or continuous flow),
- quality of life (mobility, noise, usability, maintenance/control interval, adverse reaction of required medication),
- costs.

As some of these criteria are concurring, a compromise has to be found for every intended application. VADs and TAHs are considered as technical systems. As such, their methodical engineering is generally divided

into four phases: planning, drafting, design, and elaborating [27].

## Planning

If an advanced VAD or TAH is to be developed, the specific advantages in relation to current devices have to be initially defined. This phase should be completed with close cooperation between medical doctors and engineers. Medical competence is required as experience with available devices is crucial to determine the exact need for improvement. Engineers and scientists should provide knowledge of what is technically possible and find new solutions for the problem. As a result of the planning phase, the applicable specifications are defined for the new device, as a basis for the subsequent drafting and design processes.

## Drafting

The drafting phase mainly comprises the conceptual design and validation, which results in the proof-of-concept. In general, concepts are designed qualitatively and submitted to feasibility studies. The most promising design is then followed and initially validated. For blood pumps, concept validation includes functional, hydraulic, short-term durability and pilot animal testing.

## Design phase

In the design phase, a concept is further detailed with particular regard to the following aspects. Blood flow within the pump as well as in the inflow and outflow conduits has to be designed in such a way that the required output can be generated, whereas areas of flow stagnation, regurgitation, and high shear stress are avoided. Hydrodynamic performance is needed to efficiently support the heart and a detailed analysis of the flow field gives information on hemolysis and risk of thrombosis. This flow design is achieved by the use of computational fluid dynamics (CFD) [19, 62]. Furthermore, the motor that converts electrical energy into mechanical energy has to be designed with the aid of computational electromagnetics. Here, magnetic fields in the motor or bearing system are simulated and the construction of these components is optimized. Both CFD and computational electromagnetics often apply the finite element method (FEM) for simulation. After functional elements, such as the blood flow path and the actuator, have been designed, they have to be integrated into a blood pump with supporting housing and connectors. This step is assisted by structural FEM analysis. In parallel to the mechanical design, control design methods can be evaluated to develop a control for pump output regulation. These aspects will be described in more detail in the following sections.

## Numerical analysis (FEM)

In 1956, the first relevant application of the FEM was performed by Clough [17] in the context of structural analysis of airframes. Having shown its potential, the FEM has been progressively applied in almost all domains of science and technique, in particular structure dynamics, electromagnetics [55], fluid dynamics [19], heat transfer [56], and acoustics. In contrast to earlier analytical approaches, nonlinearities and the coupling of different physical problems can be taken into account. Moreover, transient computations can be performed to describe the dynamics of the systems under consideration. Virtually, the only limitation to the complexity of the numerical models is the computation time, which can take several weeks. Nowadays, the FEM has become an ubiquitous technique in engineering and next to finite volume methods a widespread and powerful tool for virtual prototyping of complex systems. Extensive applications are found in mechanical engineering for the computation of stresses and deformations, or the determination of structural dynamics and natural frequencies by means of modal analysis [59].

## CFD simulations

CFD has been used since the 1960s to analyze fluid flows. Different numerical approaches can be applied, with the FEM being one of them (Table 1). In the context of the device design process, CFD is a tool that can guide an engineer's decisions towards an improved design. For heart assist device design, it is required to achieve both minimally blood damaging behavior and good hydraulic performance. One major advantage of CFD over experimental techniques is the ability to evaluate designs with respect to these requirements in short times and at an early stage. CFD can therefore reduce the costs and time required for the validation of a device design as well as the risks for the patient. CFD is also used in later stages of the design process with an objective to improve an already existing design. CFD were seriously envisaged as a design tool for blood pumps in the 1990s. Since then, the design of blood pumps and other medical devices involving blood flow, such as oxygenators, and artificial heart valves, has increasingly benefited from CFD. Today, CFD is generally used as a complementary tool in the design process of blood pumps. It is primarily used to predict the flow of blood through the device, to evaluate shear stresses, and to compute hydraulic pump performance.

For a rotary blood pump, the computation has to take into account a moving impeller and unsteady flow

**Table 1** Solvers and discretization methods.

| Solver | Discretization method |
|---|---|
| CFX-TASCflow (Ansys) | Finite volume |
| STAR-CD | Finite volume |
| FLUENT | Finite volume |
| SIMPLE algorithm | Finite volume |
| SMAC algorithm | Finite difference |
| XNS | Finite element |

through a three-dimensional domain with complex geometry. Rapid progress in the computational power of modern computers, and the development of CFD techniques and blood models, has made the analysis of blood flow through VADs possible. However, for a TAH with a design that mimics the heart's pulsation, the computational analysis is far more complex, due to the continuously deforming flow domain. CFD analysis in the field of TAHs is very rare and not yet common practice today. The same holds true for the simulation of the natural heart. Here, we will focus on the role of CFD as a design tool for rotary VADs.

## Blood damage and rheological blood modeling

One major concern of a blood pump design is its hemocompatibility. The non-physiological flow situation in a pump and the foreign materials in contact with blood lead to a deterioration of the blood. It is important to optimize pumps so that this damage is minimized. To date, no consensus exists concerning a common procedure for the quantitative assessment of blood damage. Blood damage can occur as hemolysis or thrombosis. Hemolysis, the release of hemoglobin from the erythrocyte into the plasma due to premature red blood cell damage, can lead to kidney failure and is a common issue in blood pumps. CFD has to assist the engineer in keeping the hemolysis rates at a reasonably low level to exclude a serious health risk for the patient.

Thrombosis is by far a more dangerous complication. Platelet activation induced by contact with foreign material and exposure to shear stress [6] as well as surface roughness [36] can cause thromboembolic complications inside and outside the VAD, such as stroke.

Blood is a highly complex fluid. Its main constituents are plasma, white and red blood cells, and platelets. Although blood is a multiphase fluid it can be modeled as a homogeneous fluid if it flows through openings with a diameter more than two orders of magnitude greater than the size of a red blood cell [12]. This is usually the case for VADs. The highly deformable red blood cells make up for 99% of the total cell volume and determine the rheological behavior of blood. At low shear rates, blood behaves like a shear-thinning, thixotropic, and nonlinear viscoelastic fluid. However, it could be shown that at shear rates above 100 $s^{-1}$, blood can be modeled as a Newtonian fluid. In VADs, the prevalent shear rates are typically two orders of magnitude higher and the Newtonian assumption may be therefore justified. In CFD studies of VADs, blood is then assumed as an incompressible fluid with constant viscosity. For CFD studies of low shear blood flow through human blood vessels or artificial organs, more complex models of the rheology of blood, e.g., shear-thinning or viscoelastic models, are commonly applied. CFD in the blood flow field can be applied both for analysis of microscale phenomena, e.g., the modeling of discrete blood cells as they travel through capillaries, or on a macroscale, where a continuum with locally constant properties is assumed. For heart assist devices, the number of blood cells flowing through the device is high, and accordingly the continuum approach is chosen. The transport of mass and momentum at macroscale are governed by conservation laws which can be expressed in the form of partial differential equations, the Navier-Stokes equations. In general, CFD studies of blood pumps assume isothermal conditions and therefore the energy transport equation is not solved. To solve the Navier-Stokes equations numerically, the physical domain is replaced by a discretized computational domain, where the sets of equations can be approximated by simple algebraic equations.

## The CFD process

The CFD process is structured into three steps: pre-processing, solving, and post-processing. During the pre-processing step, a computational mesh is generated and boundary conditions are set. It requires the experience and expertise of the CFD engineer to construct a good mesh with adequate refinement and to set boundary conditions that adequately represent the physical problem. For most applications of blood flowing through a heart-assist device, the Navier-Stokes equations for mass and momentum conservation have to be solved. According to Navier-Stokes, the flow of a viscous incompressible fluid occupying a time-varying $n_{sd}$-dimensional domain $\Omega_t$ with boundary $\Gamma_t$ is characterized by the velocity $\mathbf{u}(\mathbf{x}, t)$ and pressure $p(\mathbf{x}, t)$ fields satisfying:

$$\rho(\mathbf{u}_{,t}+\mathbf{u}\cdot\nabla\mathbf{u}-\mathbf{f})-\nabla\cdot\boldsymbol{\sigma}(\mathbf{u}, p)=\mathbf{0} \text{ on } \Omega_t, \quad (1)$$

$$\nabla\cdot\mathbf{u}=0 \text{ on } \Omega_t, \quad (2)$$

where $\mathbf{f}$ is the body force, such as gravity, and the fluid stress is given as:

$$\boldsymbol{\sigma}(\mathbf{u}, p)=-p\boldsymbol{I}+\boldsymbol{T}(\mathbf{u}),\ \boldsymbol{T}(\mathbf{u})=2\mu\boldsymbol{E}(\mathbf{u}), \quad (3)$$

where $\boldsymbol{E}(\mathbf{u})$ is the symmetric part of the velocity gradient $\nabla\mathbf{u}$. The fluid density $\rho$ and dynamic viscosity $\mu$ are assumed to be constant. The essential and natural boundary conditions on subsets of the boundary $\Gamma_t=(\Gamma_t)_g\times(\Gamma_t)_h$ are imposed as $\mathbf{u}=\boldsymbol{g}$ on $(\Gamma_t)_g$ and $\mathbf{n}\cdot\boldsymbol{\sigma}(\mathbf{u}, p)=\boldsymbol{h}$ on $(\Gamma_t)_h$. Together with an initial condition on $\mathbf{u}$, they complete the mathematical statement of the problem.

The solver replaces the transport equations in partial differential form with algebraic equations, to obtain a final numerical representation of the physical problem in the discretized computational domain, which is shown in Figure 3 for the DeBakey axial blood pump. If several processors are used in parallel to solve the equations, the elements of the computational mesh have to be distributed among the processors, as shown in a sample partitioning of the DeBakey blood pump in Figure 4. Discretization techniques used in CFD are the finite element, finite volume, and finite difference methods. Numerical solvers have to be robust and efficient. The output of the solver is a set of numbers corresponding to the values of each field variable, such as velocity components or pressure, at each point of the mesh. These data must be

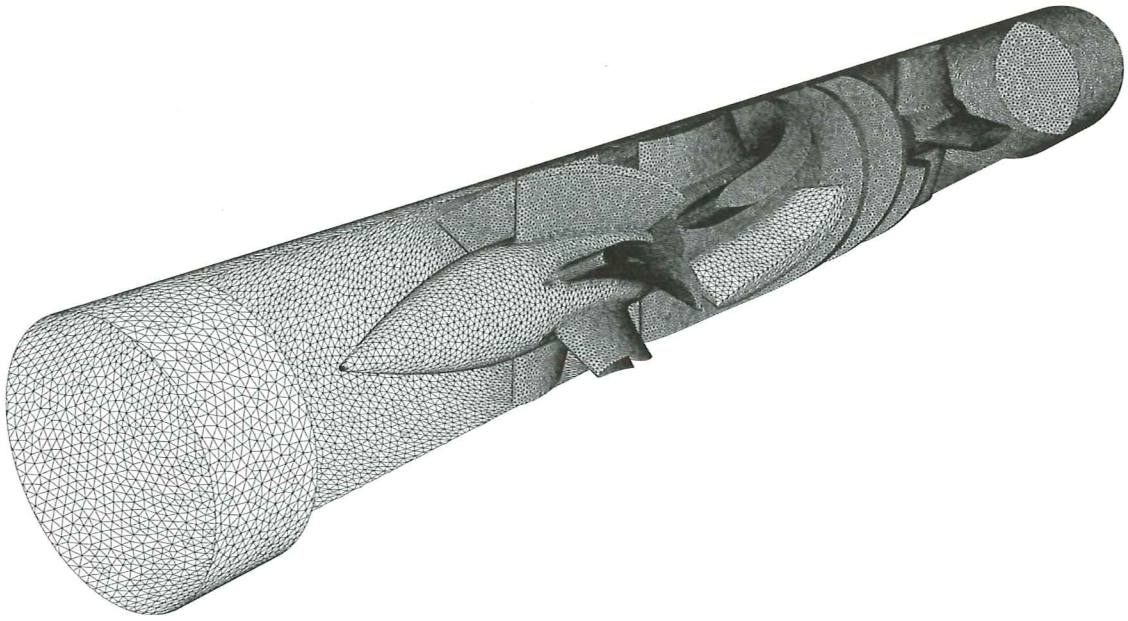

**Figure 3** Computational domain of a DeBakey VAD with 5 million elements.

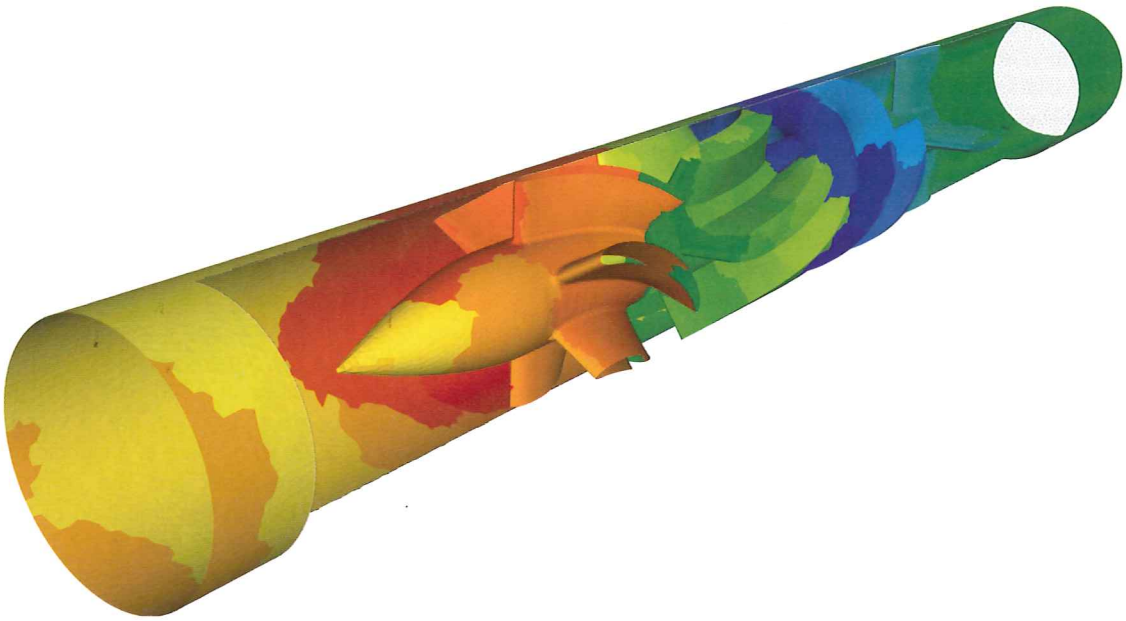

**Figure 4** DeBakey VAD element partitions for 1024 processors.

reduced to some meaningful subset, or processed further to obtain the desired predictive quantities. For example, a subset of pressures and cell-face areas is used to compute the averaged pressure over a pump's surface, as shown in Figure 5.

Commercial post-processing tools allow for visualization, data extraction, and manipulation. In particular, the solver has to be well chosen as it is the centerpiece of the CFD study. Table 1 shows a selection of solvers that were used by the research groups cited in this article and their discretization methods. Most research groups have been working with commercially available solvers, such as CFX-TASCflow, STAR-CD or FLUENT. All of those solvers are based on a finite-volume discretization. The numerical results presented in this article were obtained by means of the finite element flow solver XNS, an in-house [9] developed finite element CFD code. Commercial solvers have the advantage that they have a user-friendly graphical user interface and they are often offered in a package with pre-processing and post-processing capabilities. However, the code remains hidden from the user. Self-developed solvers can be programmed in a more flexible way, and it is possible to implement own continuum models, such as a thrombosis model. Also, the computed results are more understandable for the user as they can have insight into the code and see how it was programmed.

Massively-parallel computing is enabling computational engineering analyses of unprecedented complexity to be performed. Computations that take days to be com-

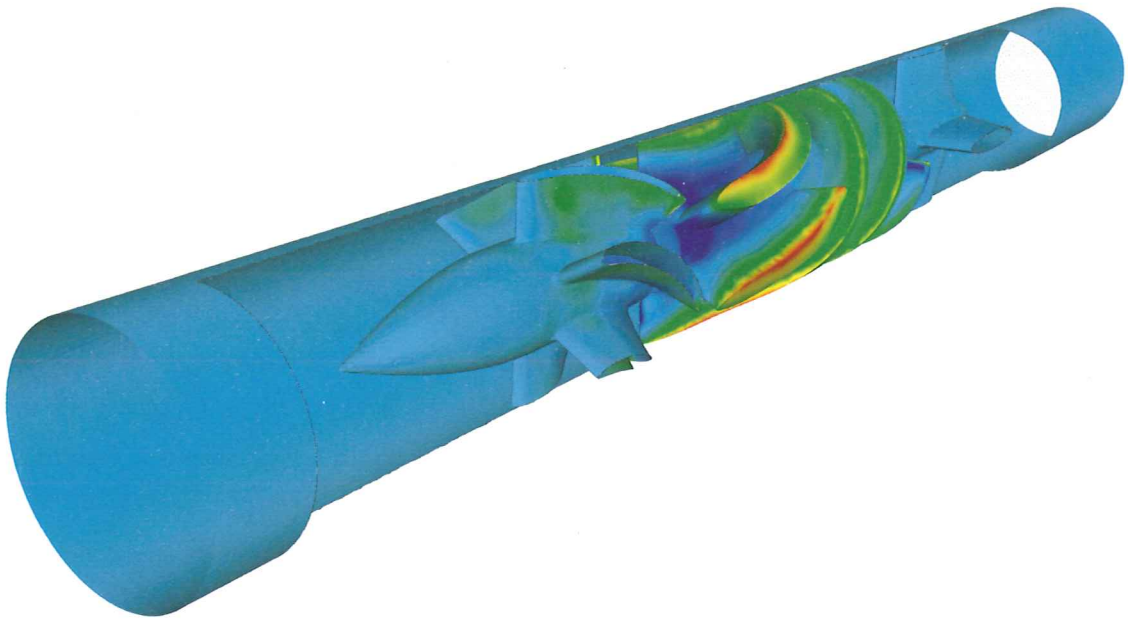

**Figure 5** Sample pressure distribution on a DeBakey VAD.

puted on a single or a few processors are performed in a few hours when a modern supercomputer platform becomes available. Here again it is an advantage to work with a self-developed solver, because the code generally has to be optimized for scalability. In a scaling study, the XNS code was optimized and blood pump simulations were typically performed on 2048 or more processors on the JUGENE supercomputer at the Jülich Supercomputer Center, Jülich, Germany.

### Flow field characterization and pump performance

Flow field characterizations of VADs have been undertaken by many research groups. CFD has been successfully applied to compute the flow field and compare it to experimental flow visualization via particle tracking velocimetry and particle imaging velocimetry (PIV) [3, 41], to numerically predict gap flow in centrifugal blood pumps [1, 40], to predict retrograde leakage flow in the gaps [64], to improve the design of the inlet guide vanes [15] and impeller [18], to compare different impeller designs [67], and finally to study hydrodynamic bearing forces [3, 10, 46]. Design improvements in the above-mentioned studies are generally based on the engineer's intuition and the role of CFD is to validate the proposed design modifications of single components.

Although CFD modeling of blood pumps has seen great progress in the past decade, CFD studies alone are not sufficient to realize a successful design. The numerically predicted results have to be validated by measurements. In most cases these measurements come from *in vitro* experiments in a mock circulation loop. The function of a blood pump is to provide the human body with the required blood flow defined in the planning phase. Simulations have to predict the performance of a pump under operating conditions. Therefore, it is necessary to determine the pressure head (pressure difference between inflow and outflow) and the flow rate at a given rotational speed of the impeller.

Most published CFD papers on blood pumps are concerned with computing and improving hydraulic performance. A list of authors that have published CFD analysis results in the field of VADs can be found elsewhere [7]. Figure 7 shows exemplary CFD results from our group for the centrifugal GYRO pump as shown in Figure 6. The numerical data are compared to experimental data that were generated using a mock loop as described previously [8]. The rotational speeds of the impeller used are 1800, 2000, and 2200 rpm. Figure 7 shows the range of flux values for all simulations, and these are plotted along with the experimental performance curves. It can be seen that, for angular velocities of 1800 and 2000 rpm, the experimental and computed curves are in close agreement; however, at 2200 rpm, there is a significant difference between the experiment and the computational model. This might be due to the limitation of the Smagorinsky turbulence model used here at the higher rotation rate, and consequently higher Reynolds number. Nevertheless, the satisfactory agreement at lower angular speeds is an indication that the computational anal-

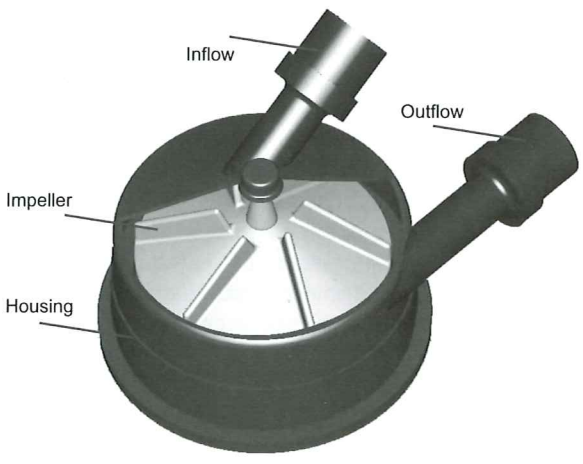


**Figure 6** GYRO centrifugal pump.

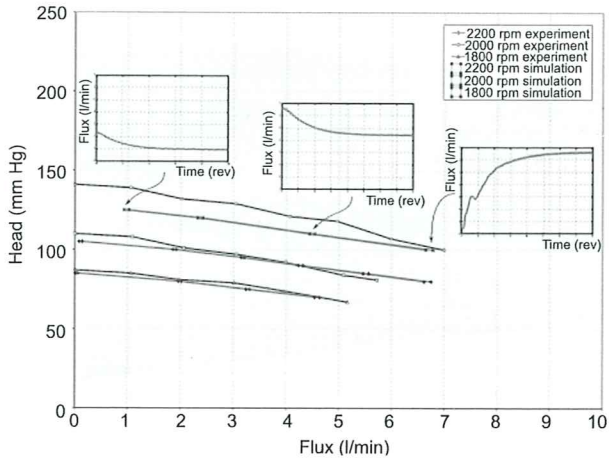


**Figure 7** Hydraulic performance of the Gyro pump: experiment (black) versus simulation (shaded).
Some time histories of the flux are also shown. Adapted from Behr et al. [8]. Copyright John Wiley & Sons. Reprinted with permission.

ysis can be used in the design phase to conduct preliminary studies of pump performance.

For other blood pump applications, Kameneva et al. and Song et al. [31, 50] have stressed the importance of the role of turbulence for blood pump analysis and it could be shown that the accuracy of CFD results can depend to a high degree on the chosen turbulence model.

### Hemolysis prediction

As an additional benefit, CFD has the potential to predict hemolysis in the pump. Most CFD studies of hemolysis use a Lagrangian approach where individual red blood cells are tracked through the pump and the blood damage is accumulated along the pathline. Most blood pumps induce high shear stress zones in the gap areas between blades and housing which provoke hemolysis. Below a shear stress of 42,000 $s^{-1}$, red blood cell membranes do not rupture but they can stretch and form pores through which hemoglobin leaks [60]. The stretching of the membrane has been experimentally shown, under steady-shear conditions, to be a function of shear and exposure time.

From these measurements, Giersiepen et al. [24] derived an empirical correlation to predict the hemolysis in the form of a power-law model according to Eq. (4) where $\Delta Hb/Hb$ is the plasma-free hemoglobin compared to the overall amount of hemoglobin in blood, $\tau$ is shear stress and $t$ is exposure time:

$$\frac{\Delta Hb}{Hb} = C\tau^a \Delta t^b \qquad (4)$$

Since then, Giersiepen's correlation has been used in most of the hemolysis studies undertaken for blood pumps. Other models that have been used in CFD studies are those by Heuser and Opitz [29] and Grigioni et al. [25]. An attempt to compare the accuracy of the different models was made by Gu and Smith [26]. Yet another description of hemolysis was proposed by Klaus et al. [33].

In all these correlations it is important to note that they were derived from steady experiments, whereas the loading of the blood cells in blood pump is a highly time-dependent phenomenon. As red blood cells travel through the pump, the shear stress varies. It has been shown that even high shear stresses will not lead to hemolysis if the exposure time is small [11]. The red blood cell membrane takes time to deform and this is not taken into account by a shear-based Lagrangian particle-tracking approach. Typically, CFD based hemolysis predictions for medical devices overpredict hemolysis.

We have developed a strain-based model for hemolysis [4] that describes the deformation history of a single red blood cell as it is tracked through the device. The mathematical description of the three-dimensional red blood cell model is based on physical properties of red blood cells. The tank-treading phenomenon of the red blood cell membrane around the cell's interior, which leads to a reduction of shear stress, is also integrated into the model. With our model we endeavor to better represent the complex rheological behavior of blood.

Even if CFD is not able to predict absolute hemolysis values, it is a valuable tool to compare the hemolysis levels for different pump designs. CFD can reliably predict the regions where hemolysis is most likely to occur.

Figure 8 shows the cross-section of the DeBakey axial blood pump and Figure 9 the simulated geometry of the blood flow path. With the aid of "Virtual Reality" techniques, single red blood cells and their actual deformation and orientation can be visualized [28]. Hemoglobin release from a red blood cell, which is represented as transparent ellipsoid and its main axes, is indicated by small marker particles. As a result of the CFD study, it could be shown that, although some hemolysis is caused by the high shear stresses in the gap between the impeller blades and the housing due to the high particle velocity and thus low residence time in the impeller region, hemolysis takes place primarily in the region of the diffuser. Furthermore, it could be observed that some particles recirculate between diffuser and impeller increasing their chance of hemolytic destruction.

### Thrombosis prediction

The complex interplay of the phenomena that influence the thrombosis makes its computational prediction a dif-

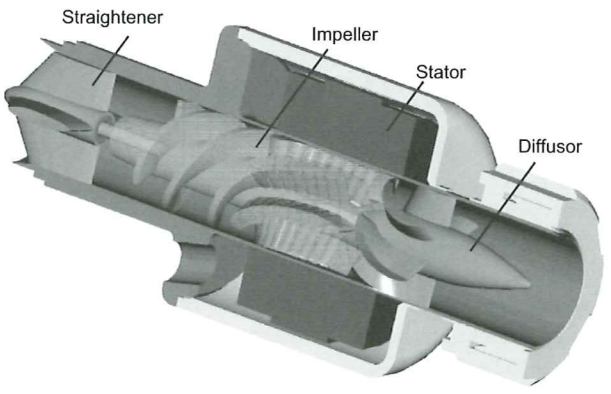


**Figure 8** MicroMed DeBakey axial pump. Modified image reproduced with permission of MicroMed Cardiovascular, Houston, TX, USA.

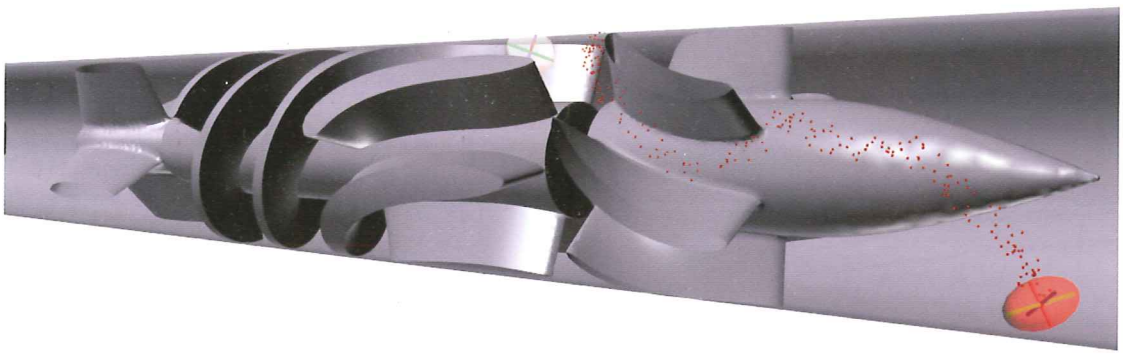

**Figure 9** Hemoglobin release from red blood cells traveling through the DeBakey pump.

ficult task. Therefore, few CFD thrombosis predictions in blood pumps currently exist. The few existing studies assume a simple shear stress and exposure time-dependent behavior of platelets and compute a platelet damage value. However, first approaches and CFD validations of more complex thrombosis models exist for simpler flow cases. Sorensen et al. [51] have presented a platelet-mediated thrombosis model to describe formation and growth of mural thrombi on biomaterials. It is a diffusion-advection based approach, taking into account red cell-enhanced transport, platelet activation, and kinetics of platelet deposition. For simple two-dimensional flow cases, good results could be achieved for the model. However, in the future, more complex models will have to be developed to also include flow disturbances due to thrombus growth, thrombus disruption by fluid forces, and the coagulation cascade. In fact, all of the mentioned separate aspects have already been simulated with CFD tools or otherwise computed, but today no unified approach to thrombosis quantification exists.

### Automated shape optimization

Most traditional CFD approaches include a trial-and-error approach. A promising future approach for the analysis of blood pumps is automated design optimization [2], where automated optimization algorithms perform shape changes to the parametric model of the device. The flow field is newly computed at each step until the optimal shape for a prescribed design objective is obtained. Automated shape optimization was first applied in the field of blood pumps by Antaki et al. [2] and Burgreen et al. [14] and applied to reduce adverse leakage flow of a centrifugal blood pump impeller by Wu et al. [64].

## Further applications for numerical approaches

Whereas in CFD the common numerical approach is the method of finite volumes (Table 1), in general computing physical phenomena the finite element method has


**Figure 10** Sound pressure distribution of an electrical servomotor.

become the most widespread tool. Figure 10, for instance, depicts the sound pressure distribution radiated by an electric servomotor. It has been computed with the open source FE environment iMOOSE [57]. The amplitude of the sound pressure as well as the direction of sound emission can be assessed from the Figure. Acoustic hotspots (black regions), concentrated in the front and rear hemispheres, can then be identified and counter-measures, e.g., modifications of the housing, can be taken at the design stage already without the need of an expensive and time-consuming prototyping [23, 30].

In medical engineering, the FEM is often used to compute stress and deformation in implants for durability analysis. Thus, predictions about the lifetime expectation of implants and their impact on the human body can be made with a minimum of expensive and ethically questionable animal experiments. In particular in the development of VADs and TAHs, the FEM offers the potential for a significant gain in reliability. Besides the prevention of life-threatening situations, such as material failure, hemolysis, or thrombus induced by blood damage, the patient's quality of life can be significantly improved as well. Conventional TAHs, implanted in the human body so far, are relatively heavy and large. They are thus only to a limited extent suitable for women and children. Some types of TAHs and VADs induce blood suction, increasing the risk of atrial collapse and consequently low pump output. As the influence of continuous versus pulsatile blood flow on the human body is not well known, this topic is still subject of research. The power supply of such devices also requires having electric wires penetrating through the skin with an increased risk of infection. Finally, the presence of mechanical bearings severely limits the durability.

The discussion above shows the high demand for FE virtual prototyping in medical engineering. After a first rough dimensioning by means of conventional analytical formulae, the FEM has the ability to optimize the device in all aspects. In addition to durability investigations, the impact on the human body can be predicted by analyzing the heat dissipation in the active implants and its evacuation towards surrounding tissue and blood, as well as the blood flow itself. Comfort of patient's life can be increased, and the risk of infection is reduced simultaneously by transcutaneous inductive energy supply. Noise, excited by the valves and motor of the TAH, can be predicted and acoustic counter-measures taken. Finally, the actuator itself can be optimized, reducing weight and size and maximizing efficiency.

By means of the FEM an innovative TAH prototype has been developed, achieving most of the requirements without expensive and time-consuming experimental layout [35]. Throughout the development, durability and redundancy have especially been taken into account to achieve the desired 5-year life expectancy of the TAH. The optimization of the electromagnetic circuit to reduce the weight and dimensions of the TAH while simultaneously increasing efficiency could only be performed by means of the FEM. For VAD/TAH development, the FEM is a very powerful tool to engineer customized solutions, with maximal durability and life comfort and a significantly reduced need for expensive prototyping and animal testing.

## Control design

As already mentioned in the introductory part, the design of a controller can start right after the drafting phase accompanying the mechanical design. Although the controller is "only" a software part of a VAD/TAH, it has a major influence on the overall functionality. However, its role is often underestimated. A good collaboration between control engineers, mechanical engineers, and medical doctors is crucial to find optimal solutions and avoid layout-associated problems. The control problem is closely linked to the system configuration. Whilst the main problem for continuous flow VADs is suction, its analogy for pulsatile VADs is the synchronization of the VAD with the natural heart. This designated application area of the VAD/TAH might additionally influence the operation mode. A DT-dedicated TAH would ideally behave like a natural heart and therefore be endured with a "physiological control mode". Several experts in the field recommend a pulsatile blood flow especially in long-term applications. Therefore, the speed of rotary blood pumps for DT could be controlled in a pulsating manner to generate a pulsatile flow.

The following section exemplarily presents some of the developments in this field including – as far as available – a short description of the underlying device. The control concepts dealing with suction are various. Suction takes place when the pump speed is not decreased in the case of a reduced blood return, leading to an atrial or ventricular collapse. Therefore, the upper bound for the pump speed is the speed that induces suction in the ventricle, whereas the lower bound is the speed that still realizes the required perfusion. As suction is a common and well-known problem of continuously pumping devices, various control algorithms concerning this problem have already been invented. For example, Vollkron et al. [58] developed a suction detection system based on the pump flow signal. They analyzed the pump flow signal on a beat-to-beat basis in the time domain, derived various criteria for suction, and designed an expert system. The data basis consists of experiences with left ventricular assist device (LVAD) patients in different states. The exact type of LVADs was not specified.

A control strategy consisting of a coarse and a fine part was developed by Ohuchi et al. [43]. The coarse part aimed at the determination of the target pump speed. The fine-tuning of their control strategy featured the avoidance of suction. They worked with a tripod-supported sealless centrifugal blood pump, driven by a DC brushless motor, which was designed at their laboratory [68]. Ferreira et al. [21] presented a suction detection system based on a combination of two frequency-, four time-based and one time-frequency-based indices using the pump flow signal. The classification of a condition as "no suction", "moderate suction", and "severe suction" is implemented with discriminant analysis. In the *in vivo* study they worked with the WorldHeart LVAD.

As mentioned before the control problem for pulsatile VADs is the synchronization of the VAD with the natural heart. In general, one can distinguish two different control modes for pulsatile VADs: asynchronous and synchronous control modes [61]. In the asynchronous control mode, the VAD rate is not synchronized with the heart rate. An example of this realization can be found in the literature [22], where a "fixed rate" and a "full fill/full eject" (FFFE) algorithm is implemented. The FFFE algorithm mimics the Frank-Starling mechanism. In the synchronous control mode the rate of the VAD is synchronized with the natural heart rate. Typical of this is the so-called "counterpulsation mode" meaning that the VAD works opposite in phase to the natural heart. The device used in [22] is an implantable electromagnetic linear-VAD. An example for a synchronous control mode can be found in [66], where Yoshizawa et al. aimed to find the optimal operating point for a pneumatic VAD. The synchronization of the VAD with the natural heart was defined as a precondition. Three additional conditions for the optimal operating point were defined: avoiding thrombosis, hemolysis, and usage of the FFFE algorithm for the determination of the outflow volume as well as minimizing the driving energy.

A differing control algorithm can be found in [20]. Here Drzewiecki et al. studied the optimal timing for a pneumatic LVAD based on a cardiovascular and atrio-aortic-LVAD model. For these authors, optimal timing meant that the oxygen consumption of the left ventricular is minimized and the support of the circulation is maintained. Additionally, they took weaning of the patient's heart from the LVAD into account. They concluded that the ejection of the VAD should start immediately after the closing of the aortic valve and that maximum filling of the pump should be realized. Their results imply that synchronous pumping of a VAD is a better solution for a patient.

In the case of a TAH, the native heart is removed and therefore the challenges regarding control differ from those of a VAD. As already mentioned, the designer must distinguish whether the TAH is intended as a "bridge-to-transplant" or a "destination therapy" solution. In the case of a "bridge to transplant", and therefore a hopefully short-term solution, it might be sufficient if the TAH is able to maintain an appropriate and consistent flow rate. However, if the TAH is actuated for a longer period of time, it becomes obvious that the optimal control solution is to copy the physiological control algorithm of the native heart. When taking into consideration the native heart's reliance on chemo and mechanical receptors to alter physiological output, and that the mechanical heart may replicate these receptors with pressure and flow sensors, the control problem becomes clearer as each sensor is confronted with drift and reliability problems, and might contribute to thrombus formation [38].

To overcome the sensor problem, Ogawa et al. [42] presented a control technique of a continuous flow artificial heart based on the estimation of flow rate and pressure head with an autoregressive with exogenous input model (ARX model). For the determination of the necessary parameters for the ARX model, they made identification experiments in a mock circulatory loop. According to Ogawa et al. [42], they used a centrifugal blood pump (TERUMO, Capiox).

Others tried to gain a direct access to the nerve signals (e.g., [37, 52]). Mabuchi et al. [37] studied the possibility of using the skin sympathetic nervous activity (SSNA) for the control of a TAH. With their experiment, they could demonstrate that in principle it is possible to control a TAH with the SSNA as they gained hemodynamic data which were similar to those recorded from the subject. Subsequently, in a follow-up study [52], they tried to record a goat's cardiac sympathetic and vagal nerve at rest, during exercise, and during administration of a vasopressor or depressor, but had trouble to record clear signals during exercise, and concluded that their data were insufficient for a final evaluation.

As there have been many different approaches featuring this control problem, this section can only be an extract of what has been done so far. The interested reader might be in favor of further reading, e.g., [13, 16, 32, 34, 43, 53, 65].

## Prototype design

After defining the concept of the device and pre-investigations using CFD and FEM simulations are finished, first prototypes are to be manufactured. The prototypes have to prove the functionality of the device, including the performance of the actuator, anatomical fit, sealing ability, and many more. The results and experiences obtained by the use of the prototypes have a high impact on future development iterations. Furthermore, the prototypes are used to validate the simulations.

## Elaboration phase

After the design of the VAD or TAH is finished and first prototypes have been manufactured, the results of simulation have to be validated. To validate the three-dimensional flow within the pump, PIV can be applied. PIV is a laser-optical measurement method which is based on the tracking of particle patterns within a transparent test fluid. The particles are illuminated in quick succession by a thin layer of laser light. High speed cameras take a picture of the particles each time. By comparison of two successive images, the movement of the particles can be detected. Together with the known time interval between the laser pulses, the velocity is estimated. Using two cameras in a stereoscopic approach, the third velocity component perpendicular to the light sheet can be calculated. (For more information about PIV, refer to Raffel et al. [47].)

As an example, Figure 11 shows the mean diastolic velocity of blood flow within a pump chamber of a TAH. The results can be compared to CFD simulations to readjust the simulation parameters [39]. Using a validated simulation, small changes in the design can be investigated numerically without producing a new prototype of the device. Hydraulic performance tests are carried out by connecting the pumps to mock loops, which simulate the hydraulic resistances of the natural circulation sys-

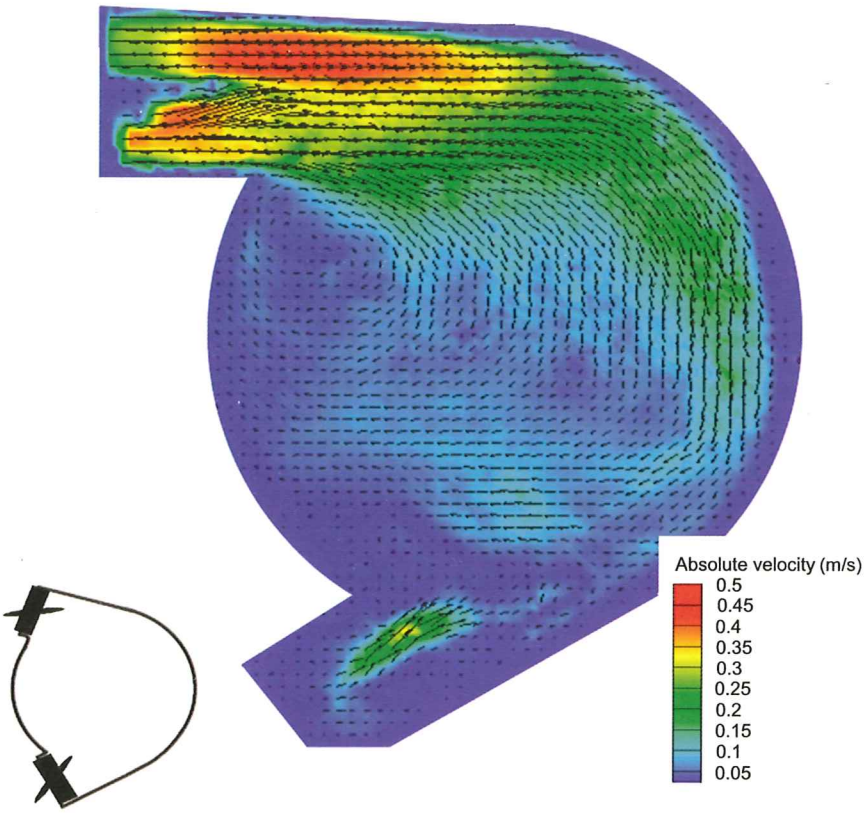


**Figure 11** Velocity vector field during diastole in a TAH.

tem. Here the pump can be exposed to either physiological or pathological situations of the circulatory system (e.g., [45, 54]). To validate the control system, special mock loops can be used which cannot only represent a certain condition but also the transition, e.g., between rest and physical work of a patient. Active mock loops that provide such functionality are still the subject of research. To date, performance of VAD and TAH control systems have usually not been tested *in vitro*. Particularly for long-term devices precise prediction of wear is difficult. Therefore, durability is usually tested in component based setups. Hemocompatibility is then evaluated in laboratory blood tests. Routinely, the flow and material induced blood damage is measured by means of the increase in plasma free hemoglobin in a closed circuit [5]. As a next step, animal trials are performed to pre-evaluate clinical aspects, such as ease of implantation (anastomosis, deairing, fitting), long-term *in vivo* performance or hemocompatibility [49]. Furthermore, the control systems can be extensively tested in this setup [44]. Design steps are performed iteratively until all applicable specifications are fulfilled. This is the state of "design freeze". Subsequently, the production and pre-market approval of the device need to be established prior to commercialization.

## Conclusion

The development of new VADs or TAHs is a major challenge. The majority of the projects over the years did not reach clinical application. The reasons are manifold, i.e., inadequate specifications, pre-clinical device related problems, false medication protocols, high manufacturing and/or development/clinical regulatory costs, as well as competition. Fund raising for the development of such devices is difficult as the development takes a long time and carries a high risk to finally fail in the clinical application. New developments are therefore often initiated in university environments with public funding.

New technologies are now becoming available for blood pump development. CFD has a steadily growing potential as more computational power, new models for blood rheology, models for blood damage, and new efficient techniques for automatic design optimization become available. The same applies for advances in motor and control design. These new technologies offer significant advantages to develop better VADs and TAHs (e.g., smaller, more durable, less thrombogenic, less noisy, improved physiologic control, and high operational safety) more efficiently.

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Received January 19, 2009; accepted June 15, 2009; online first September 3, 2009