The Journal of Open Source Software

svZeroDSolver: A modular package for lumped-parameter cardiovascular simulations

Karthik Menon[1*], **Jakob Richter**[1*], **Martin R. Pfaller**[1*], **Jonathan Pham**[1], **Emilin M. Mathew**[1], **Kaitlin E. Harold**[1], **Nicholas C. Dorn**[1], **Aekaansh Verma**[1], and **Alison L. Marsden**[1¶]

1 Stanford University, Stanford, CA, United States of America ¶ Corresponding author * These authors contributed equally.

DOI: 10.xxxxxx/draft

Software

- Review
- Repository
- Archive

Editor: Open Journals

Reviewers:

- @openjournals

Submitted: 01 January 1970
Published: unpublished

Summary

Computational modeling of cardiovascular blood flow has emerged as a valuable tool in the diagnosis and treatment of cardiovascular disease (Menon, Hu, et al., 2024). While simulations of blood flow can be performed using various high and low-fidelity techniques, lumped-parameter or zero-dimensional modeling is a low-order technique that is widely used in various applications that require quick estimation of bulk flow quantities, such as flow and pressure at specific anatomical locations (Pfaller et al., 2024).

We introduce `svZeroDSolver`, an efficient and modular package for performing lumped-parameter (zero-dimensional) simulations of cardiovascular blood flow. As part of the `SimVascular` open-source project, `svZeroDSolver` and `SimVascular` together allow users to go from medical imaging to fast zero-dimensional evaluations of patient-specific hemodynamics. `svZeroDSolver` is written in C++ using a modular object-oriented framework. Simply specifying a `.json` dictionary of lumped-parameter "blocks" – such as blood vessels, junctions between blood vessels, and boundary conditions (along with their associated parameters) – allows the code to automatically assemble and solve the governing equations corresponding to the user-specified vascular model. In addition, the package includes Python and C++ interfaces to facilitate its use with other software packages. For example, it can be integrated into Python-based optimization and uncertainty quantification applications (Lee et al., 2024; Menon, Zanoni, et al., 2024; Richter et al., 2024; Zanoni et al., 2024). It can also be interfaced with high-performance C++/Fortran software for high-fidelity cardiovascular flow simulations, where `svZeroDSolver` can conveniently provide lumped-parameter boundary conditions (Menon et al., 2023; Menon, Khan, et al., 2024). `svZeroDSolver` includes an application, called `svZeroDCalibrator`, to automatically calibrate parameters of a given zero-dimensional model to recapitulate hemodynamics at specific anatomical locations from independent measurements or high-fidelity simulations – thus improving the accuracy of zero-dimensional models (Richter et al., 2024). It also includes graphical interfaces to interactively create lumped-parameter models for simulations, as well as to visualize the simulated anatomy and hemodynamics.

Statement of need

The ability to non-invasively quantify patient-specific hemodynamics via computational simulations has been shown to improve patient outcomes and reduce invasive clinical procedures in large randomized clinical trials (Taylor et al., 2023). Computational modeling is also a promising tool for non-invasive and personalized optimization of clinical treatments and surgery (Marsden, 2014).

Previous work has used a variety of techniques to model cardiovascular blood flow, all of which can be broadly categorized based on their level of fidelity. High-fidelity models generally involve simulations of the full three-dimensional flow-field within anatomical regions of interest (Menon, Hu, et al., 2024; Updegrove et al., 2017). While these are the most accurate and informative, they are computationally expensive (each simulation can take several hours or days on hundreds of CPU cores) and therefore not feasible for use within typical clinical settings or for applications, such as optimization, which often require thousands of evaluations. On the other end of the spectrum, lumped-parameter or zero-dimensional models provide information about bulk hemodynamics, such as flow rate and pressure, at specific anatomical regions of interest. While these models are not spatially-resolved, they are very valuable in applications that require near real-time quantification of bulk hemodynamics, as well as applications that rely on thousands of repeated model evaluations, such as optimization and uncertainty quantification (Lee et al., 2024; Menon, Zanoni, et al., 2024; Richter et al., 2024; Zanoni et al., 2024). They are also used in conjunction with high-fidelity simulations where lumped-parameter models are used as boundary conditions (Menon et al., 2023; Menon, Khan, et al., 2024).

`svZeroDSolver`, which is a part of the `SimVascular` open-source project, is a new open-source software package that enables fast evaluation of zero-dimensional hemodynamics. One major challenge in zero-dimensional modeling that `svZeroDSolver` addresses is that different clinical applications (and individual clinical cases within the same application) often require unique anatomical arrangements of blood vessels, heart valves, etc. Moreover, distinct anatomical configurations are governed by a distinct set of governing equations. Therefore, it is common for users to implement application-specific solvers which simulate the equations governing a specific application or anatomical configuration. In contrast, the modularity of `svZeroDSolver` allows users to easily create arbitrary anatomical configurations by arranging a library of available "blocks", following which the software automatically assembles the equations governing the user-specified configuration.

Another unique feature of `svZeroDSolver` is its ability to easily interface with other C++ and Python packages. This has been used in previous work on uncertainty quantification [Zanoni et al. (2024);Lee et al. (2024);Richter et al. (2024);menon2024personalizeduncertainty] as well as in multi-scale simulations coupling three-dimensional hemodynamics with zero-dimensional representations of downstream circulation (Menon et al., 2023; Menon, Khan, et al., 2024). The C++ interface has been coupled with high-fidelity multi-physics solvers `svSolver` and `svFSI`, which are part of the widely used `SimVascular` open-source software project for cardiovascular biomechanics simulations (Updegrove et al., 2017; Zhu et al., 2022). `svZeroDSolver` has also been integrated into the graphical user interface of the `SimVascular` project. This allows users to leverage the functionality in `SimVascular` to generate three-dimensional patient-specific anatomical models from medical images, and subsequently perform patient-specific zero-dimensional simulations of blood flow by automatically converting the three-dimensional anatomy into a zero-dimensional model (Pfaller et al., 2022). The automatic conversion of arbitrary patient-specific anatomies to zero-dimensional simulations is possible to due the modular nature of `svZeroDSolver`. Using this pipeline, previous work has demonstrated accelerated convergence of three-dimensional simulations when using corresponding zero-dimensional simulation results as initial conditions (Pfaller et al., 2021).

In addition, `svZeroDSolver` includes several applications to augment its functionality. The `svZeroDCalibrator` application improves the accuracy of zero-dimensional models by optimizing the parameters of blood vessels to recapitulate observed hemodynamics from measurements or high-fidelity simulations. This allows users to build more accurate zero-dimensional models than those typically based purely on the anatomy of the vascular region of interest (Richter et al., 2024). The `svZeroDGUI` application is a web-based graphical interface that allows users to create zero-dimensional simulations by interactively dragging-and-dropping individual blood vessels, heart chambers, boundary conditions, connections between these blocks, etc. Another graphical application, `svZeroDVisualization`, is an interface to visualize the lumped-paramater structure of given anatomical models as well as the simulated hemodynamics within each block. Together, these graphical interfaces make `svZeroDSolver` intuitive for a wide range of users, potentially expanding its use from research to intructional and clinical contexts. The functionality and accuracy of `svZeroDSolver` is assessed using continuous integration tests on GitHub, and has also been verified by comparing with high-fidelity three dimensional simulations (Pfaller et al., 2022). This combination of features makes `svZeroDSolver` uniquely applicable to a wide range of applications in cardiovascular biomechanics.

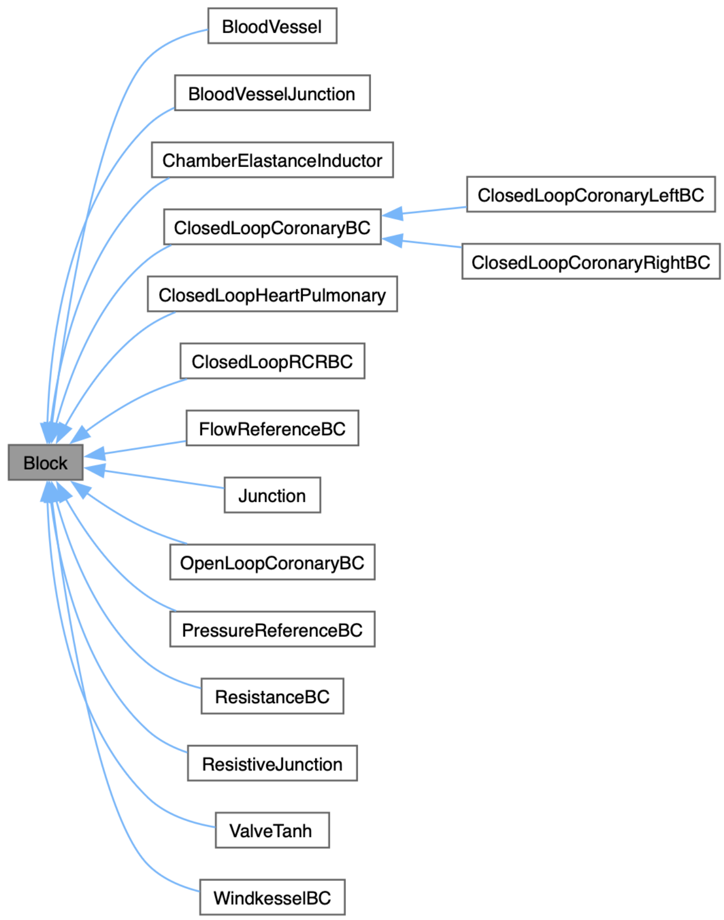

Figure 1: Various zero-dimensional "blocks" included in `svZeroDSolver` at the time of writing.

Software details

`svZeroDSolver` relies on a collection of "blocks" to set up the governing equations for a given anatomical configuration. Each block is inherited from a `block` class, as illustrated in Figure 1, and is governed by a "local" set of equations with associated degrees-of-freedom. The solver parses through an input configuration `.json` file, which lists the blocks, their parameters, and the blocks' connectivity, and then automatically assembles the local equations and degrees-of-freedom for each block into a global system of equations. The governing equations and circuit representation for each block are available in the documentation. For example, see the documentation for a blood vessel block.

The zero-dimensional simulations performed by `svZeroDSolver` are governed by non-linear differential-algebraic equations. We integrate these equations in time using the implicit generalized-alpha scheme (Jansen et al., 2000), with Newton-Raphson iterations to solve the linearized system. Under the hood, these linearized governing equations for each block are implemented as local contributions to a system of linear (matrix) equations, which are then assembled into a global linear system based on the user-specified configuration. Details on the modular implementation of the blocks, along with their governing equations, are provided in the documentation's Developer Guide. We use the Eigen package to represent and solve these sparse linear systems (Guennebaud et al., 2010). Mathematical details on this implementation are provided in the `SparseSystem` and `Integrator` classes in the documentation.

`svZeroDSolver` currently has implementations of different types of blood vessel blocks with non-linear resistors to model vascular stenoses, junctions between blood vessels, a heart valve block modeled using a hyperbolic tangent function, a cardiac chamber block modeled as a time-varying capacitor and inductor, and several different boundary condition blocks including simple flow, pressure and resistors blocks, windkessel boundary conditions, coronary boundary conditions that include the intramyocardial pressure experienced by coronary arteries, as well as closed-loop versions of windkessel and coronary boundary conditions that allow a user to build a closed-loop circulation model (H. Kim et al., 2010; H. J. Kim et al., 2009; Menon et al., 2023; Menon, Khan, et al., 2024; Mirramezani et al., 2019; Vignon-Clementel et al., 2006). The input to `svZeroDSolver` is a `.json` file which specifies the simulation parameters (number of time steps, cardiac cycles, etc.), the types of blocks to be included in the specific model, the boundary conditions, and how the blocks are connected (typically using `junction` blocks). Each of these blocks generally requires several parameters which can be specified using a steady value or a list of time-varying values. The solver can either run simulations for a specified number of time steps and cardiac cycles, or until the difference in mean quantities between consecutive cardiac cycles is below a given threshold.

The documentation for `svZeroDSolver` is automatically built on GitHub using Doxygen. It includes instructions for installation, user guides for `svZeroDSolver` and its various applications, as well as mathematical and graphical descriptions of each zero-dimensional block that is implemented in the solver. Examples of configuration files to run `svZeroDSolver` simulations using the various available blocks are in `svZeroDSolver/tests/cases`. The repository also includes examples demonstrating the simple API for interfacing between `svZeroDSolver` and external C++ software packages in `svZeroDSolver/tests/test_interface`. Details on creating zero-dimensional simulations from three-dimensional models using the `SimVascular` graphical interface are available on the SimVascular documentation.

Future development plans include functionality to specify time-varying block parameters as mathematical expressions using the exprtk package. We are also expanding the available blocks to more accurately model hemodynamics, such as by using data-driven models for pressure losses at arbitrarily shaped vascular junctions (Rubio et al., 2024). In addition, we plan to extend the `svZeroDGUI` application to interactively create custom zero-dimensional boundary conditions for three-dimensional simulations. The development team actively implements new features, blocks and test cases to build on the capabilities of svZeroDSolver and ensure its accuracy and speed.

Acknowledgments

This work was supported by grant ???, by the National Heart, Lung, and Blood Institute of the National Institutes of Health under Award Numbers R01HL141712 and K99HL161313, and the Stanford Maternal and Child Health Institute.

References

Guennebaud, G., Jacob, B., & others. (2010). *Eigen v3*. http://eigen.tuxfamily.org.

Jansen, K. E., Whiting, C. H., & Hulbert, G. M. (2000). A generalized-alpha method for integrating the filtered navier–stokes equations with a stabilized finite element method. *Computer Methods in Applied Mechanics and Engineering*, *190*(3), 305–319. https:

//doi.org/10.1016/S0045-7825(00)00203-6

Kim, H. J., Vignon-Clementel, I. E., Figueroa, C. A., Ladisa, J. F., Jansen, K. E., Feinstein, J. A., & Taylor, C. A. (2009). On coupling a lumped parameter heart model and a three-dimensional finite element aorta model. *Annals of Biomedical Engineering*, *37*(11), 2153–2169. https://doi.org/10.1007/s10439-009-9760-8

Kim, H., Vignon-Clementel, I., Coogan, J., Figueroa, C., Jansen, K., & Taylor, C. (2010). Patient-specific modeling of blood flow and pressure in human coronary arteries. *Annals of Biomedical Engineering*, *38*, 3195–3209. https://doi.org/10.1007/s10439-010-0083-6

Lee, J. D., Richter, J., Pfaller, M. R., Szafron, J. M., Menon, K., Zanoni, A., Ma, M. R., Feinstein, J. A., Kreutzer, J., Marsden, A. L., & Schiavazzi, D. E. (2024). A probabilistic neural twin for treatment planning in peripheral pulmonary artery stenosis. *International Journal for Numerical Methods in Biomedical Engineering*, *40*(5), e3820. https://doi.org/https://doi.org/10.1002/cnm.3820

Marsden, A. L. (2014). Optimization in cardiovascular modeling. *Annual Review of Fluid Mechanics*, *46*, 519–546. https://doi.org/10.1146/ANNUREV-FLUID-010313-141341

Menon, K., Hu, Z., & Marsden, A. L. (2024). Cardiovascular fluid dynamics: A journey through our circulation. *Flow*, *4*, E7. https://doi.org/10.1017/flo.2024.5

Menon, K., Khan, M. O., Sexton, Z. A., Richter, J., Nguyen, P. K., Malik, S. B., Boyd, J., Nieman, K., & Marsden, A. L. (2024). Personalized coronary and myocardial blood flow models incorporating CT perfusion imaging and synthetic vascular trees. *Npj Imaging*, *2*(9). https://doi.org/10.1101/2023.08.17.23294242

Menon, K., Seo, J., Fukazawa, R., Ogawa, S., Kahn, A. M., Burns, J. C., & Marsden, A. L. (2023). Predictors of myocardial ischemia in patients with kawasaki disease: Insights from patient-specific simulations of coronary hemodynamics. *Journal of Cardiovascular Translational Research*, *16*, 1099–1109.

Menon, K., Zanoni, A., Khan, O., Geraci, G., Nieman, K., Schiavazzi, D. E., & Marsden, A. L. (2024). *Personalized and uncertainty-aware coronary hemodynamics simulations: From bayesian estimation to improved multi-fidelity uncertainty quantification*. https://arxiv.org/abs/2409.02247

Mirramezani, M., Diamond, S. L., Litt, H. I., & Shadden, S. C. (2019). Reduced Order Models for Transstenotic Pressure Drop in the Coronary Arteries. *Journal of Biomechanical Engineering*, *141*(3), 31005. https://doi.org/10.1115/1.4042184

Pfaller, M. R., Pegolotti, L., Pham, J., Rubio, N. L., & Marsden, A. L. (2024). Chapter 20 - reduced-order modeling of cardiovascular hemodynamics. In T. C. Gasser, S. Avril, & J. A. Elefteriades (Eds.), *Biomechanics of the aorta* (pp. 449–476). Academic Press. https://doi.org/https://doi.org/10.1016/B978-0-323-95484-6.00016-6

Pfaller, M. R., Pham, J., Verma, A., Pegolotti, L., Wilson, N. M., Parker, D. W., Yang, W., & Marsden, A. L. (2022). Automated generation of 0D and 1D reduced-order models of patient-specific blood flow. *International Journal for Numerical Methods in Biomedical Engineering*, *38*(10). https://doi.org/10.1002/cnm.3639

Pfaller, M. R., Pham, J., Wilson, N. M., Parker, D. W., & Marsden, A. L. (2021). On the periodicity of cardiovascular fluid dynamics simulations. *Annals of Biomedical Engineering*. https://doi.org/10.1007/s10439-021-02796-x

Richter, J., Nitzler, J., Pegolotti, L., Menon, K., Biehler, J., Wall, W. A., Schiavazzi, D. E., Marsden, A. L., & Pfaller, M. R. (2024). *Bayesian windkessel calibration using optimized 0D surrogate models*. https://arxiv.org/abs/2404.14187

Rubio, N. L., Pegolotti, L., Pfaller, M. R., Darve, E. F., & Marsden, A. L. (2024). *Hybrid physics-based and data-driven modeling of vascular bifurcation pressure differences*. https:

//arxiv.org/abs/2402.15651

Taylor, C. A., Petersen, K., Xiao, N., Sinclair, M., Bai, Y., Lynch, S. R., UpdePac, A., & Schaap, M. (2023). Patient-specific modeling of blood flow in the coronary arteries. *Computer Methods in Applied Mechanics and Engineering*, *417*, 116414. https://doi.org/https://doi.org/10.1016/j.cma.2023.116414

Updegrove, A., Wilson, N. M., Merkow, J., Lan, H., Marsden, A. L., & Shadden, S. C. (2017). SimVascular: An Open Source Pipeline for Cardiovascular Simulation. *Annals of Biomedical Engineering*, *45*(3), 525–541. https://doi.org/10.1007/s10439-016-1762-8

Vignon-Clementel, I. E., Alberto Figueroa, C., Jansen, K. E., & Taylor, C. A. (2006). Outflow boundary conditions for three-dimensional finite element modeling of blood flow and pressure in arteries. *Computer Methods in Applied Mechanics and Engineering*, *195*(29-32), 3776–3796. https://doi.org/10.1016/j.cma.2005.04.014

Zanoni, A., Geraci, G., Salvador, M., Menon, K., Marsden, A. L., & Schiavazzi, D. E. (2024). Improved multifidelity Monte Carlo estimators based on normalizing flows and dimensionality reduction techniques. *Computer Methods in Applied Mechanics and Engineering*, *429*, 117119. https://doi.org/https://doi.org/10.1016/j.cma.2024.117119

Zhu, C., Vedula, V., Parker, D., Wilson, N., Shadden, S., & Marsden, A. (2022). svFSI: A multiphysics package for integrated cardiac modeling. *Journal of Open Source Software*, *7*(78), 4118. https://doi.org/10.21105/joss.04118