



Explorative Visual Analysis of Spatio-temporal Regions to Detect Hemodynamic Biomarker Candidates

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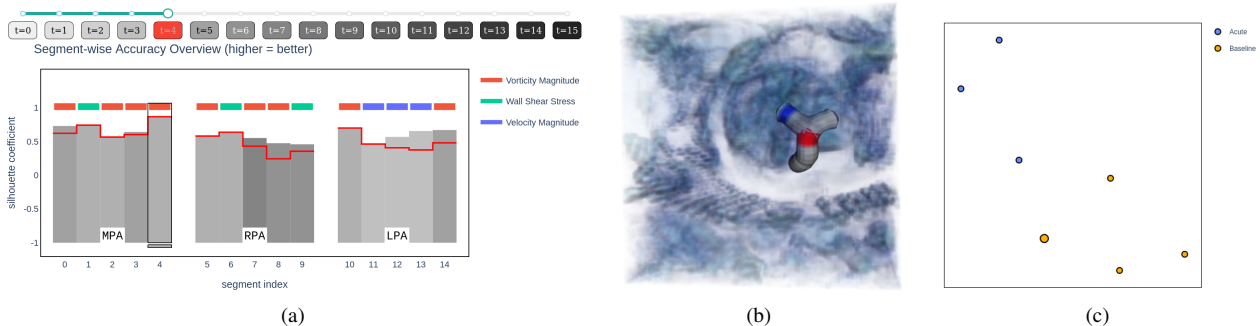


Figure 1: Biomarker candidate overview plot (a) for the main (MPA), right (RPA) and left (LPA) pulmonary artery of the Sepsis dataset. Selected (red) and hovered regions (blue) are highlighted in the anatomical view (b). The quality of the current biomarker can be assessed in the low-dimensional embedding (c), where each subject is represented as colored dot.

Abstract

Biomarkers are measurable biological properties that allow for distinguishing subjects of different cohorts such as healthy vs. diseased. In the context of diagnosing diseases of the cardiovascular system, researchers aim - among others - at detecting biomarkers in the form of spatio-temporal regions of blood flow obtained by medical imaging or of derived hemodynamical parameters. As the search space for such biomarkers in time-varying volumetric multi-field data is extremely large, we present an interactive visual exploration system to support the analysis of the potential of spatio-temporal regions to discriminate cohorts.

1. Introduction

Measurement techniques such as four-dimensional phase-contrast magnetic resonance imaging (4D PC-MRI) allow for a non-invasive assessment of the cardiovascular system. Acquired images, i.e., time-resolved blood flow vector fields, are then used within animal cohort studies to find the cause and effect of conditions such as sepsis within the hemodynamics of the captured vessel's lumen. Typ-

ically, individual animals are split into a control and possibly multiple groups of various conditions or condition progression. A researcher's task then can be described as to find a suitable biomarker that allows him/her to classify an individual to its proper cohort. Depending on the prior knowledge about the disease model, the researcher may either try to confirm a hypothesis or try to form a new hypothesis that lays the foundation to more extensive research. To achieve this, relevant hemodynamical parameters, spatial regions, and time frames need to be identified and tested for their potential

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to serve as biomarker, which results in an extremely large search space.

We propose an interactive visual exploration system that supports the analysis of the potential of spatio-temporal regions to serve as a biomarker, thus, to discriminate cohorts. The ongoing exchange with our collaboration partners from the cardiovascular imaging group motivated the preliminary work that we present in this poster abstract.

2. Related Work

Cohort studies are an active field of research and are identified to be an open challenge in medical visualization [GSG*, PL20]. Population-based studies are aided by visualization frameworks and tools in the fields of prostate cancer [BSM*15] and brain imaging [JBF*20, SBR*21], among others. Blood flow data, in particular, only has recently been addressed by Meuschke et al. [MNB*21], who presented GUCCL, the first framework for guided investigation of aortic blood flow data. They extract features using Bloodline [KGGP19] on which they apply machine learning methods to define relevant features that best distinguish predefined cohorts and analyze these features using combinations of overview visualizations and detailed views. A sufficient amount of data is required to extract the features which, often times, is not available due to ethical guidelines and restrictions regarding animal studies. As only aorta blood flow was considered by the authors, it is unclear how the approach scales to more complex vessel networks. We want to address these issues by capturing the vessel's hemodynamics in small spatio-temporal regions, on each of which we apply the silhouette score [Rou87] that calculates the biomarker potential for each input parameter, such as vorticity magnitude or wall shear stress.

3. System Design

Two cohort studies were conducted by our collaboration partners. The goal hereby was to analyze the effect of (1) right heart overload condition in rats [NLG*21] and (2) of sepsis in mice, with respect to selected hemodynamic parameters.

We therefore developed a system that allows for finding and evaluating biomarker candidates. To make subjects within the cohort study comparable to each other, we first create a parametrization of the centerlines of the vessel's lumen. The centerline of each vessel branch then can be divided into an arbitrary number of segments, e.g., according to a medical textbook. By aggregating data within each segment using the mean, median or maximum value (or possibly others), and concatenating all branches, we convert the data into a linear layout. After this step, we obtain one feature vector for each cohort member, each time frame, and each hemodynamic parameter.

Given the predefined cohorts, the task of finding a good biomarker can also be expressed as to maximize inter-cohort and to minimize intra-cohort similarities, both of which are used to calculate the silhouette score which we propose to use for this purpose. We calculate the pairwise (dis-)similarities between respective feature vectors using the field similarity by Fofonov et al. [FL19]

which we chose in favor of other metrics based on gradients or correlation, since the authors could demonstrate that it can preserve properties that are desirable for low-dimensional embeddings. This property is important as we create low-dimensional embeddings from them using uniform manifold approximation and projection (UMAP) [MHM18]. This technique preserves neighborhoods, allowing for visually determining the quality of the biomarker candidate (cf. Figure 1(c)). It also supports selecting a subset of subjects that the biomarker should be found for.

To give an overview of the entire domain, we derive a novel overview visualization (cf. Figure 1(a)) from this linear layout that facilitates assessing the potential of each hemodynamic parameter in each spatio-temporal region to serve as a biomarker. For each region, the pair of time frame and parameter that yields the best accuracy for that segment are encoded by bars using a gray scale for the time frame and a colored box above the bars for the parameter. For the sepsis data, the highest silhouette score was found at time frame $t = 4$ near the bifurcation in the main pulmonary artery and vorticity field, which allows for a separation of the baseline and acute cohorts. A red line shows the accuracy for the currently selected time frame. The currently selected biomarker is highlighted by black frames around the selected segment with boxes below the frame that encode the selected time frames. The selected parameters are omitted due to clutter. As the overview plot is using the linear representation, we provide an anatomical plot (Figure 1(b)) that serves as context showing a single subject, time frame, and hemodynamic parameter. Red colors indicate the current biomarker candidate, blue the hovered segment. Juxtaposed functional box plots provide insight into the temporal evolution of a selected parameter for all cohorts. For preliminary results and a demonstration of the interactive exploration, please refer to the supplemental material.

4. Conclusion and Future Work

The silhouette score was chosen as an accuracy measure as it measures the inter-cohort separation as well as the intra-cohort similarity. However, the silhouette score only works well on spherical clusters and is highly discontinuous. Therefore, we have to investigate further, if the silhouette score is suitable for the given task and look for alternatives. Apart from the silhouette score further quantitative measures like statistical tests should be included in the overview plot. Furthermore, only single segments were analyzed in the overview plot. Combinations of segments, time frames, and/or parameters could also be visually analyzed. Lastly, we will conduct experiments with domain experts to further evaluate our tool.

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References

- [BSM*15] BERNARD J., SESSLER D., MAY T., SCHLOMM T., PEHRKE D., KOHLHAMMER J.: A visual-interactive system for prostate cancer cohort analysis. *IEEE computer graphics and applications* 35, 3 (2015), 44–55. [2](#)
- [FL19] FOFONOV A., LINSEN L.: Projected field similarity for comparative visualization of multi-run multi-field time-varying spatial data. In *Computer Graphics Forum* (2019), vol. 38, Wiley Online Library, pp. 286–299. [2](#)
- [GSG*] GILLMANN C., SMIT N. N., GRÖLLER E., PREIM B., VILANOVA A., WISCHGOLL T.: Open challenges in medical visualization. [2](#)
- [JBF*20] JÖNSSON D., BERGSTRÖM A., FORSELL C., SIMON R., ENGSTRÖM M., WALTER S., YNNERMAN A., HOTZ I.: Visualneuro: A hypothesis formation and reasoning application for multi-variate brain cohort study data. In *Computer Graphics Forum* (2020), vol. 39, Wiley Online Library, pp. 392–407. [2](#)
- [KGGP19] KÖHLER B., GROTHOFF M., GUTBERLET M., PREIM B.: Bloodline: A system for the guided analysis of cardiac 4d pc-mri data. *Computers & Graphics* 82 (2019), 32–43. [2](#)
- [MHM18] MCINNES L., HEALY J., MELVILLE J.: Umap: Uniform manifold approximation and projection for dimension reduction. *arXiv preprint arXiv:1802.03426* (2018). [2](#)
- [MNB*21] MEUSCHKE M., NIEMANN U., BEHRENDT B., GUTBERLET M., PREIM B., LAWONN K.: Gucci-guided cardiac cohort investigation of blood flow data. *IEEE Transactions on Visualization and Computer Graphics* (2021). [2](#)
- [NLG*21] NAHARDANI A., LEISTIKOW S., GRÜN K., KRÄMER M., HERRMANN K.-H., SCHREPPER A., JUNG C., MORADI S., SCHULZE P. C., LINSEN L., ET AL.: Pulmonary arteriovenous pressure gradient and time-averaged mean velocity of small pulmonary arteries can serve as sensitive biomarkers in the diagnosis of pulmonary arterial hypertension: A preclinical study by 4d-flow mri. *Diagnostics* 12, 1 (2021), 58. [2](#)
- [PL20] PREIM B., LAWONN K.: A survey of visual analytics for public health. In *Computer Graphics Forum* (2020), vol. 39, Wiley Online Library, pp. 543–580. [2](#)
- [Rou87] ROUSSEEUW P. J.: Silhouettes: a graphical aid to the interpretation and validation of cluster analysis. *Journal of computational and applied mathematics* 20 (1987), 53–65. [2](#)
- [SBR*21] SUGATHAN S., BARTSCH H., RIEMER F., GRÜNER E. R., LAWONN K., SMIT N. N.: Interactive multimodal imaging visualization for multiple sclerosis lesion analysis. *Eurographics*. [2](#)