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研究課題名(和文) A mechanical study of lumen formation through membrane bleb regulation under hemodynamic influence

研究課題名(英文) A mechanical study of lumen formation through membrane bleb regulation under hemodynamic influence

研究代表者

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研究成果の概要(和文)：私は、実験に基づく血流イメージングと数値流体力学(CFD)を用いて、ゼブラフィッシュの微小血管ネットワークにおける血圧と壁せん断応力(WSS)の時空間分布を計算する方法を確立した。

血球除去の実験では、胚の血流は血液粘度の低下に応じて血流量を維持する傾向が観察されCFDを適用したところ、ネットワーク圧力とWSSが低下することがわかった。遺伝子変異により血管径を小さくした場合、実験では血流速度が低下することが確認され、CFDを用いるとネットワーク圧の維持と圧力の低減のどちらの状況でも流量の減少傾向に合致することが示された。その結果、血管径を小さくするシナリオではWSSは維持されることがわかった。

研究成果の学術的意義や社会的意義

In situ blood viscosity, wall shear stress and blood pressure are difficult parameters to measure in microvessels. This combined methodology that employs both experiment and computational modeling provides a key tool for quantification of mechanical parameters involved in vascular morphogenesis.

研究成果の概要(英文)：I established a method for calculating spatiotemporal distributions of blood pressure and wall shear stress (WSS) in a zebrafish microvascular network using experiment-based blood flow imaging and computational fluid dynamics (CFD).

With this technique I could study how pressure and WSS are regulated in zebrafish with different blood network geometry and different blood viscosity levels. In the experiment with blood cell removal, embryonic blood flow was observed to have a tendency to maintain blood flow rates in response to the blood viscosity reduction. Applying the CFD, we found that this scenario led to lowered network pressure and WSS. When vessel diameters were reduced by genetic mutation, blood flow rates were observed to be reduced in experiments. Using the CFD, it was indicated that both situations of network pressure maintenance or pressure reduction fit the flow rate reduction trend. Consequently, WSS in vessel reduction scenarios was either maintained.

研究分野：Microhemodynamics

キーワード：Microhemodynamics Hematocrit asymmetry Wall shear stress Vascular morphogenesis Membrane blebbing RBC mechanics Endothelial mechanics Vascular mechanics

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1. 研究開始当初の背景

The role of mechanical forces arising from blood flow in shaping blood vessels during embryonic development is a subject of expanding interest. Primarily, advancements in this field is hampered by the difficulty in measuring these mechanical forces in situ in a biological specimen. This makes it difficult to establish quantitative assessments of the levels of mechanical stimuli pertaining to specific angiogenic and morphogenesis outcomes during vascular remodeling.

2. 研究の目的

The purpose of this research was to construct a methodology for quantification of mechanical forces that arise during a lumen expansion process.

3. 研究の方法

We employed experiments for imaging blood flow levels in zebrafish embryos. We related the flow velocities to the computational fluid dynamics solver, in order to calculate the wall shear stress and blood pressure related to the observed flow levels for a given network geometry.

4. 研究成果

(1) A semi-automated blood flow imaging method was established for high throughput analysis of growth and hemodynamic trends in zebrafish populations. This work provides the overarching spatiotemporal systemic hemodynamic trends and vascular network level adaptations in response to local lumen morphogenesis (Fig. 1).

(2) We have established a methodology pipeline to predict high resolution distribution of wall shear stress (WSS) and blood pressure in a zebrafish trunk lumen network at 54 hours post-fertilization (hpf). 3D model of the vessel lumen network in silico was constructed from confocal imaging of the fluorescently labelled blood lumen through microangiography. Blood flow map pertaining to the vessel lumen network was reconstructed by our in-house developed CFD code after iterating model boundary conditions to match blood flow velocity data obtained from particle tracking velocimetry of red blood cells (RBCs) under high-speed camera imaging (Fig. 2).

(3) Hemorheological and lumen size alteration effects on network blood flow and forces: We studied with the CFD, network flow adaptations in response to blood viscosity and RBC concentration changes, namely how network pressure changes reduces under network constraints of blood flow maintenance, which leads to WSS reduction in the network (Fig. 3). The hemodynamic constraints applied in the model were obtained from experimental observations of network flow parameters between wild-type versus altered networks. Additionally, we also showed how different network optimizations can lead to diametrically opposite effects on WSS distribution after lumen size reduction is applied to a network (Fig. 4).

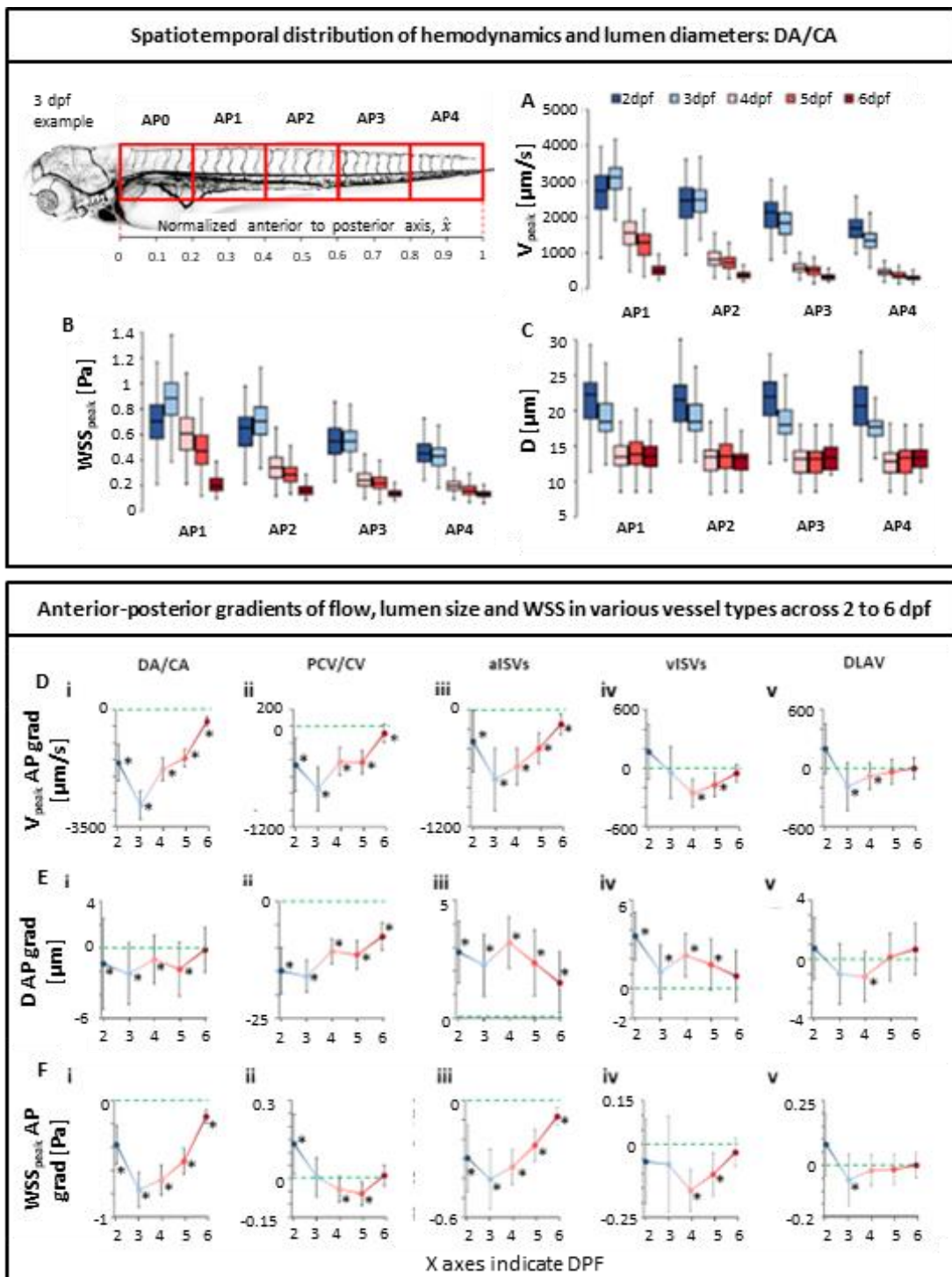


Figure 1. Growth and hemodynamic adaptation trends in zebrafish between 2 to 6 dpf. aISV, arterial intersegmental vessel; CA, caudal artery; DA, dorsal aorta; DLAV, dorsal longitudinal anastomotic vessel; CV, caudal vein; PCV, posterior cardinal vein; vISV, venous ISV;

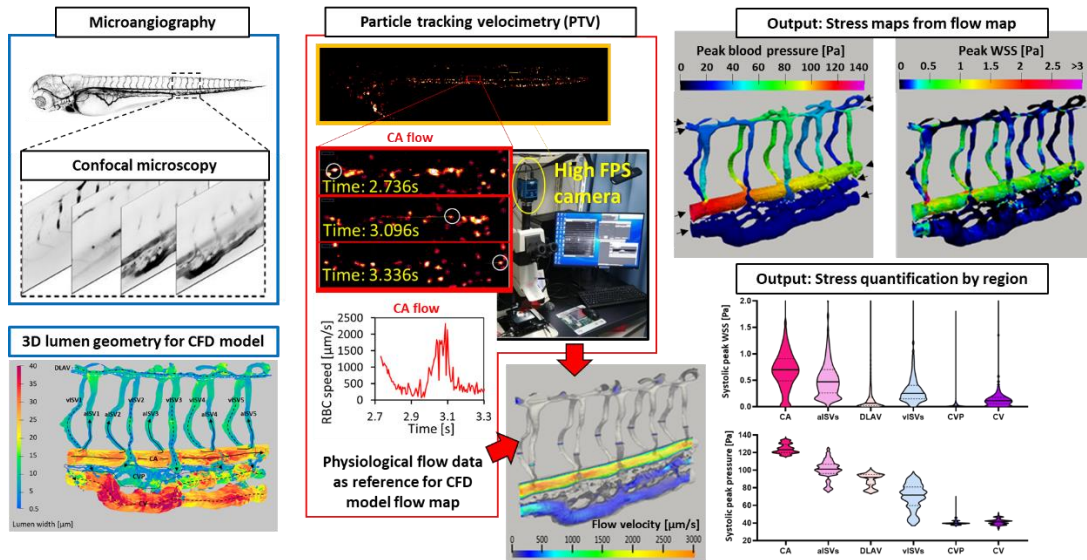


Figure 2. Combining RBC velocity data and lumen geometry from experiments with CFD modeling to generate WSS and pressure analysis in various vessel types in the zebrafish trunk vascular network.

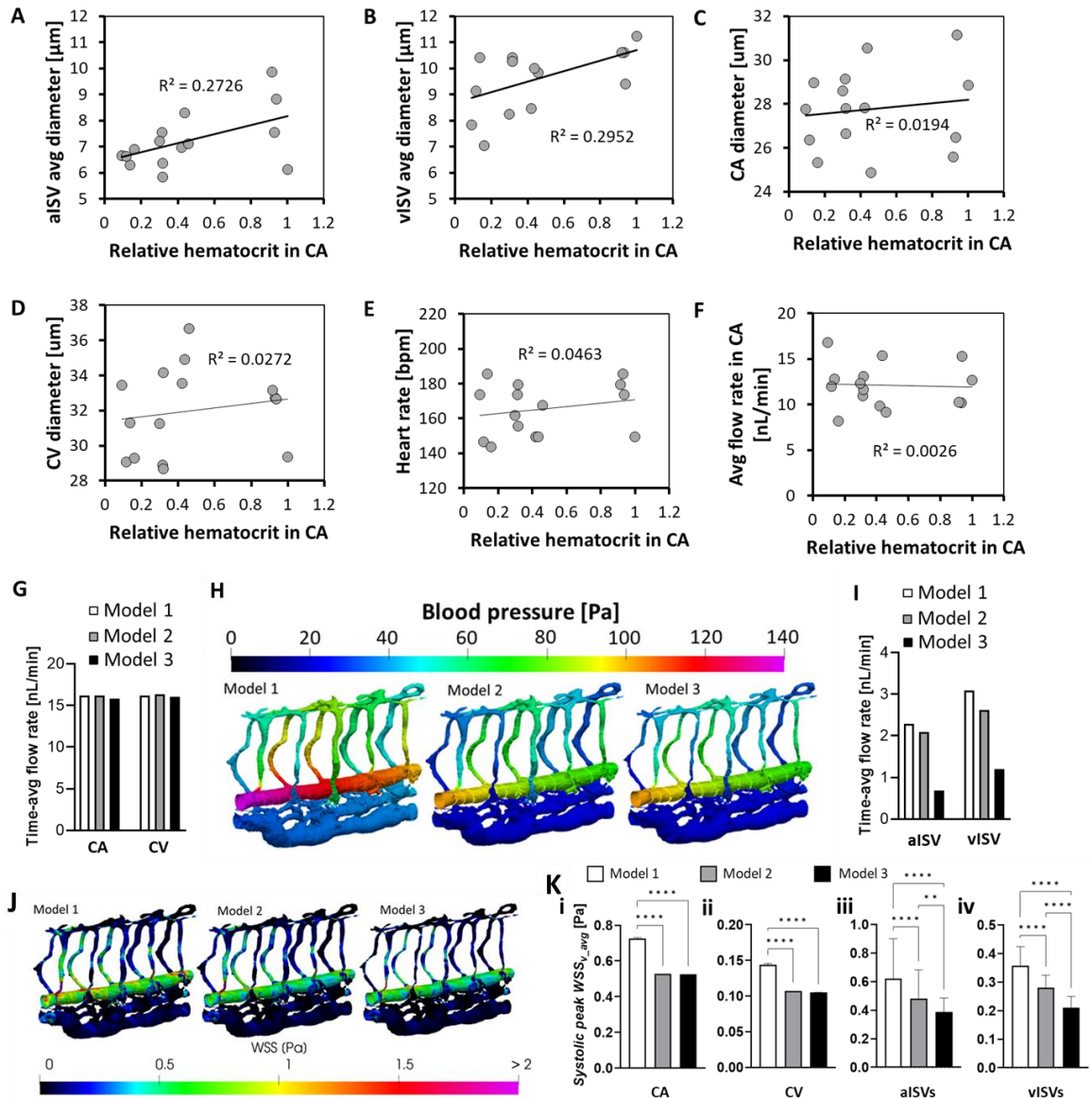


Figure 3. Flow, WSS and morphological effects of RBC removal in the zebrafish lumen network

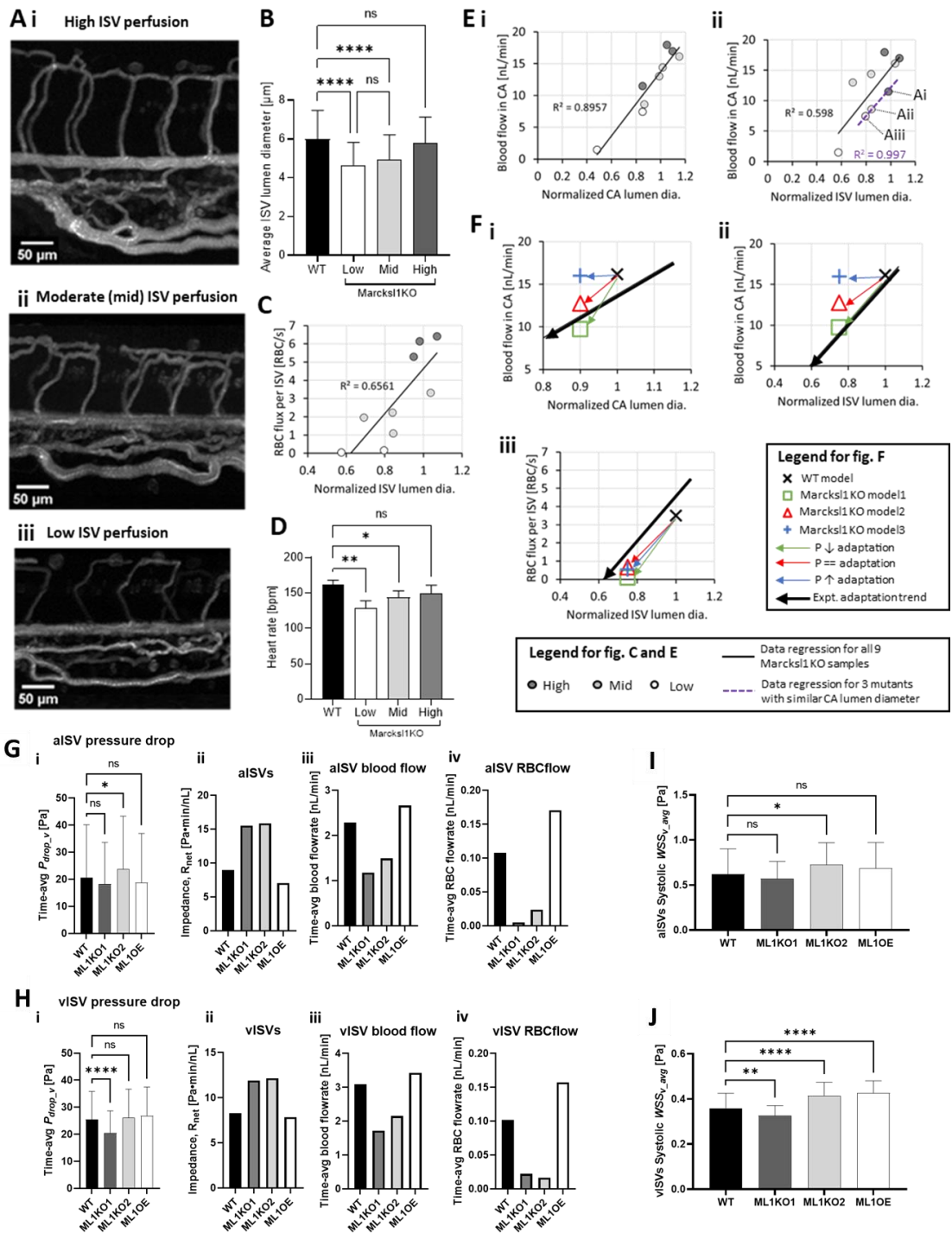


Figure 4. Effect of lumen diameter reduction on hemodynamics in *Marcks-like 1a* and *1b* double knock-out zebrafish.

5. 主な発表論文等

〔雑誌論文〕 計2件（うち査読付論文 2件/うち国際共著 2件/うちオープンアクセス 2件）

1. 著者名 Maung Ye Swe Soe, Kim Jung Kyung, Carretero Nuria Taberner, Phng Li-Kun	4. 巻 13
2. 論文標題 High-Throughput Imaging of Blood Flow Reveals Developmental Changes in Distribution Patterns of Hemodynamic Quantities in Developing Zebrafish	5. 発行年 2022年
3. 雑誌名 Frontiers in Physiology	6. 最初と最後の頁 1 to 21
掲載論文のDOI（デジタルオブジェクト識別子） 10.3389/fphys.2022.881929	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

1. 著者名 Maung Ye Swe Soe, Phng Li-Kun	4. 巻 519
2. 論文標題 A cell-and-plasma numerical model reveals hemodynamic stress and flow adaptation in zebrafish microvessels after morphological alteration	5. 発行年 2022年
3. 雑誌名 bioRxiv	6. 最初と最後の頁 1 to 41
掲載論文のDOI（デジタルオブジェクト識別子） 10.1101/2022.12.07.519059	査読の有無 有
オープンアクセス オープンアクセスとしている（また、その予定である）	国際共著 該当する

〔学会発表〕 計4件（うち招待講演 0件/うち国際学会 1件）

1. 発表者名 Maung Ye Swe Soe and Phng Li-Kun
2. 発表標題 Mapping hemodynamic forces in zebrafish vascular networks through numerical modeling
3. 学会等名 RIKEN 26th Interdisciplinary exchange evening
4. 発表年 2023年

1. 発表者名 Maung Ye Swe Soe and Phng Li-Kun
2. 発表標題 Mapping hemodynamic stresses in microvascular networks using microscopy and numerical modeling
3. 学会等名 RIKEN BDR Organoid Project Annual Meeting
4. 発表年 2022年

1. 発表者名 Maung Ye Swe Soe and Phng Li-Kun
2. 発表標題 Mapping hemodynamic forces in zebrafish vascular networks through numerical modelling
3. 学会等名 55th Japanese Society of Developmental Biology Annual Meeting (国際学会)
4. 発表年 2022年

1. 発表者名 Maung Ye Swe Soe and Phng Li-Kun
2. 発表標題 Mapping hemodynamic forces in zebrafish vascular networks through numerical modelling
3. 学会等名 RIKEN BDR Retreat 2022
4. 発表年 2022年

〔図書〕 計0件

〔産業財産権〕

〔その他〕

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6. 研究組織

氏名 (ローマ字氏名) (研究者番号)	所属研究機関・部局・職 (機関番号)	備考
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7. 科研費を使用して開催した国際研究集会

〔国際研究集会〕 計0件

8. 本研究に関連して実施した国際共同研究の実施状況

共同研究相手国	相手方研究機関
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