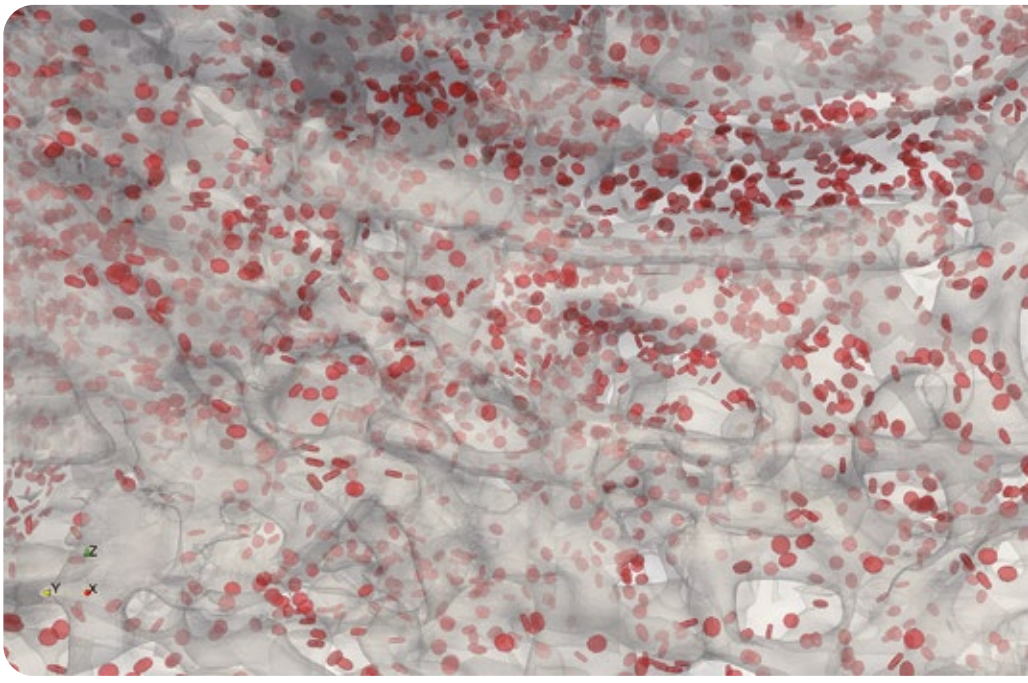
Cellular blood flow modelling towards precision healthcare for placental disorders

Disorders of the placenta are among the leading causes of pregnancy complications, resulting in insufficient oxygen and nutrients reaching the fetus. Researchers at the University of Edinburgh have used the power of ARCHER2 to carry out detailed modelling of placental blood flow, with the aim of being able to identify minute anatomical changes in the placenta that may lead to potential complications.

A Global Healthcare Challenge

Preterm births, or premature labour (babies born before 37 weeks of pregnancy), impose a significant healthcare challenge even in developed nations such as the UK. Approximately one in ten UK babies is born prematurely. This not only necessitates immediate neonatal care but also burdens the public sector with a direct added cost of over £1.24 billion annually, not to mention other incremental societal costs. In the most severe scenarios, extreme premature deliveries can lead to stillbirths, causing devastating grief and trauma for families.

The current prenatal and antenatal care systems, while effective in certain ways, fall short when it comes to predicting or treating placental dysfunction, which refers to insufficient supply of oxygen and nutrients to the fetus through the mother's placenta and constitutes a leading cause of pregnancy complications. This challenge is amplified in low-risk populations as adverse deliveries in these cases could not be predicted by pre-existing maternal risk factors.



www.archer2.ac.uk

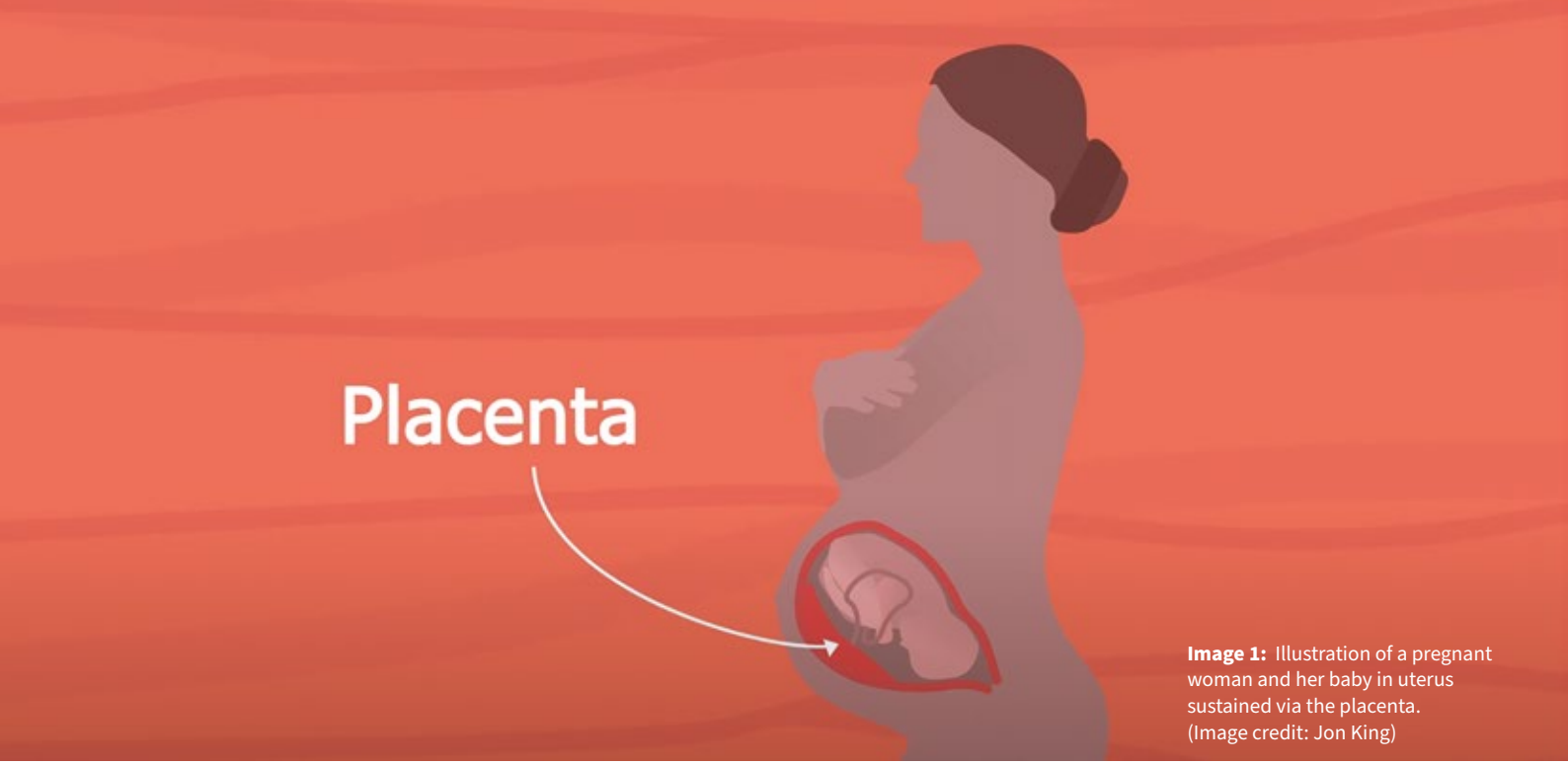


Image 1: Illustration of a pregnant woman and her baby in uterus sustained via the placenta. (Image credit: Jon King)

Hurdle and Innovation

Much of the difficulty in early detection and effective treatment of pregnancy complications arises from a lack of fundamental understanding of the placenta's role in managing blood flow and the transport of nutrients, such as oxygen, sugar, and salts [1]. Traditional studies using animal models cannot offer clear insights due to the distinct evolutionary nature of the human placenta. Thanks to advancements in high-end computing, machine learning, and placenta imaging, we are on the brink of a breakthrough. Known as in silico technologies (ISTs), these digital methods offer a way to study the human placenta in great detail without the limitations of traditional research, potentially revolutionizing our understanding of this transient yet vital organ.

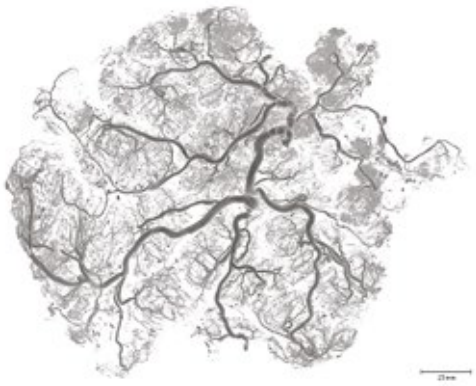


Image 2: Placental cast of the vascular tree connected to the umbilical cord through which oxygen and nutrients are transported from the mother to the baby.

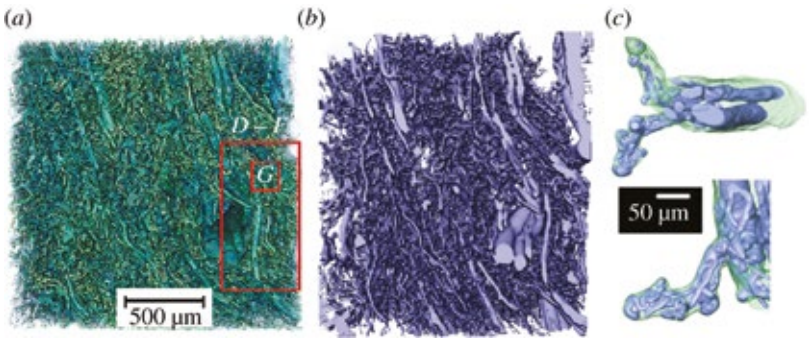


Image 3: Synchrotron micro-CT images showing multiscale structures of the placental tissue [2]. (a) 3D rendering of a cropped placental tissue volume. (b) Fetal vascular network embedded in the cropped tissue. (c) A zoom-in view of the winding capillary vessels enclosed by the villous tissues.

We are developing computational models to delve deep into the placenta's structure and function

Cause for Collaboration

Bringing together researchers and experts from the Universities of Edinburgh, Manchester, and McMaster University, our team is set on a mission. We are developing computational models to delve deep into the placenta's structure and function, based on anatomical changes in the placenta that are potentially associated with compromised nutrient transport during pregnancy [2]. While many studies have explored the blood circulation in human placentas at a larger scale, our focus is on the minute changes during pregnancy that could indicate or predict potential complications, such as pre-eclampsia (PE) and fetal growth restriction (FGR).

Call for Supercomputing

Our approach involves creating detailed models of blood flow and red blood cell transport within placenta-like structures, either reconstructed from actual after-birth placental tissues or artificially designed to mimic the biological architecture [3]. Faithful capture of the microscopic details of cellular blood flow through the intricate placenta tissue, which has not been achieved before, demands the power of thousands of CPU cores facilitated by top-tier supercomputing facilities like ARCHER2. The software at the heart of our simulations, HemeLB (*https://github.com/hemelb-codes/hemelb*), is an open-source tool that is continually evolving to meet the needs of the broader scientific community interested in computational physics and biological fluids [4,5].

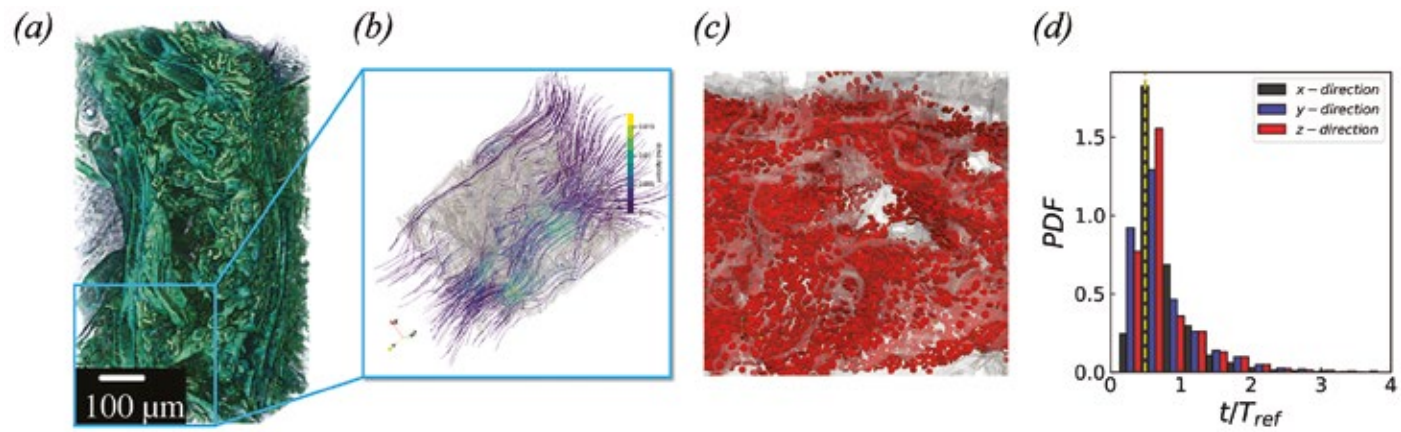
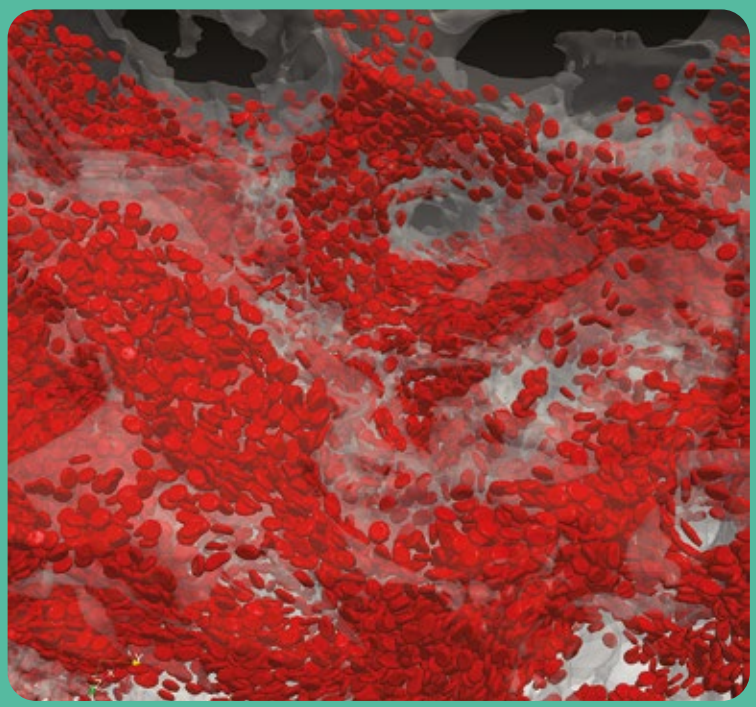


Image 4: Workflow of HemeLB simulations modelling cellular blood flow in the human placenta. (a) 3D geometry rendered from synchrotron micro – CT images of placenta tissues. (b) Simulation of flow, pressure and stresses in reconstructed vascular or porous domains. (c) Simulation of red blood cell perfusion throughout the flow domain. (d) Quantification of cell residence and nutrient transport.



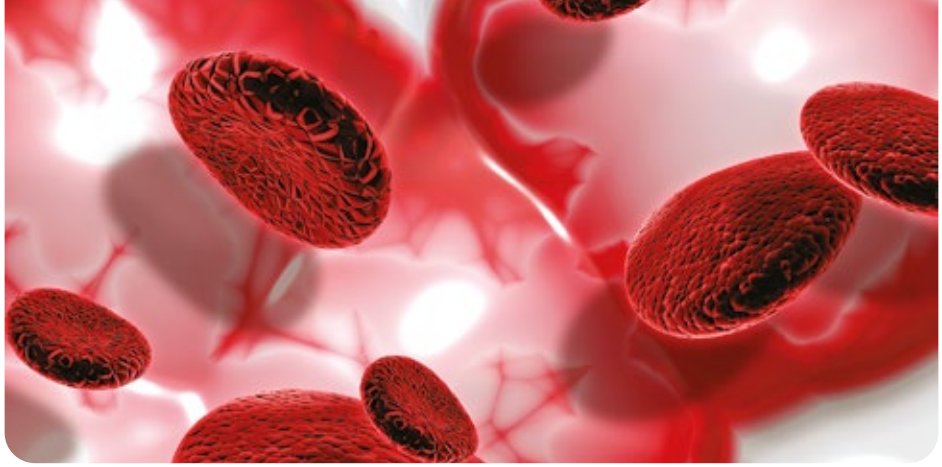
The Road Ahead

Our vision is to craft a comprehensive framework integrating medical imaging and placental blood flow modelling. We also work closely with experimentalists and clinicians on optimising life-supporting devices such as “artificial placenta” for supporting extremely premature infants. With these, we aim to usher in a new era of efficient diagnosis and cost-effective treatment for pregnancy complications, ensuring a safer journey for both mothers and their unborn children.

Image 5: A snapshot of the simulation where maternal blood flow in the intervillous space of human placenta is modelled using HemeLB on ARCHER2.

References:

[1] Q. Zhou, E. Doman, K. Schirrmann et al. Curr. Opin. Biomed. Eng. **22**:100387 (2022)
[2] W. M. Tun, G. Poologasundarampillai et al. J. R. Soc. Interface **18**:20210140 (2021)
[3] Q. Zhou et al. Inter face Focus **12**:20220037 (2022)
[4] Q. Zhou et al. J. R. Soc. Interface **18**:20210113 (2021)
[5] Y. Rashidi, G. Simionato, Q. Zhou et al. Biophys. J. **122**:1526-1537 (2023)



Resources:

InSilicoUK Pro-Innovation Regulations Network (2023) '*Unlocking the power of computational modelling and simulation across the product lifecycle in life sciences: A UK Landscape Report*'

UK Fluid dynamics Report (2021) '*Our Fluid Nation: The Impact of Fluid Dynamics in the UK*'

UK Government Office for Science (2018) '*Computational Modelling: Technological Futures*'

Chief Medical Officer annual reports (2014) '*The Health of the 51%: Women*'

Chief Medical Officer annual reports (2012) '*Our Children Deserve Better: Prevention Pays*'

Authors:

Qi Zhou (School of Engineering, Institute for Multiscale Thermofluids, University of Edinburgh)

Eleanor Doman (Department of Mathematics, University of Manchester)

Igor L. Chernyavsky (Department of Mathematics, University of Manchester;
Maternal and Fetal Health Research Centre, School of Medical Sciences, University of Manchester)

Oliver E. Jensen (Department of Mathematics, University of Manchester)

Miguel O. Bernabeu (Centre for Medical Informatics, Usher Institute, University of Edinburgh;
The Bayes Centre, University of Edinburgh)

Timm Krüger (School of Engineering, Institute for Multiscale Thermofluids, University of Edinburgh)

Acknowledgement:

We gratefully acknowledge Prof. Anne Juel from the Manchester Centre for Nonlinear Dynamics (University of Manchester), Prof. Edward D. Johnstone from St Mary's Hospital (Manchester University NHS Foundation Trust) and Prof. P. Ravi Selvaganapathy from McMaster University (Hamilton, Canada) for valuable collaboration and partnership on this project. The high-resolution images of placenta tissue architecture were generously provided by Win Min Tun.

UKRI EPSRC grants EP/T008806/1, EP/T008725/1; UK Consortium on Mesoscale Engineering Sciences (EP/X035875/1, EP/R029598/1).

Contact Details:

Lead author: Qi Zhou: **q.zhou@ed.ac.uk**

PI: Timm Krüger: **timm.krueger@ed.ac.uk**

https://www.biofm-research.com/research

About ARCHER2

ARCHER2 is the UK's National Supercomputing Service, a world class advanced computing resource for UK researchers. ARCHER2 is provided by UKRI, EPCC, HPE and the University of Edinburgh. ARCHER2 is the latest in a series of National Supercomputing Services provided to UK researchers.

More ARCHER2 case studies can be found at:
https://www.archer2.ac.uk/research/case-studies/

epcc | Hewlett Packard Enterprise | UKRI Engineering and Physical Sciences Research Council Natural Environment Research Council | THE UNIVERSITY of EDINBURGH | www.archer2.ac.uk