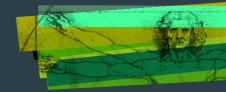
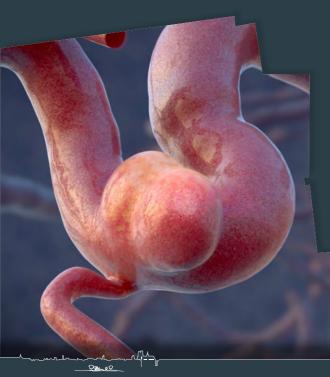
# LE STUDIUM CONFERENCES

TOURS | 2022



# 13-14 December 2022 **Cardiovascular Modelling: Basic Science to Clinical Translation**



## LOCATION

Hôtel de Ville de Tours Salle Anatole France Place Jean Jaurès, 37000 Tours - FR

# **CONVENORS**

# Dr Alberto Marzo

#### LE STUDIUM VISITING RESEARCHER

FROM University of Sheffield - UK

IN RESIDENCE AT Imaging and Brain laboratory (iBrain) / INSERM, University of Tours - ER

# Dr Ayache Bouakaz

Imaging and Brain laboratory (iBrain) / INSERM, University of Tours - FR

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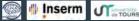
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LE STUDIUM













### **CONVENORS**

Dr Alberto Marzo, LE STUDIUM Visiting Researcher FROM: University of Sheffield - UK IN RESIDENCE AT: Imaging and Brain laboratory (iBrain) / INSERM, University of Tours - FR

Dr Ayache Bouakaz, Imaging and Brain laboratory (iBrain) / INSERM, University of Tours - FR

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LE STUDIUM Loire Valley Institute for Advanced Studies • Région Centre-Val de Loire • FR



Cardiovascular Modelling: Basic Science to Clinical Translation

# EDITO

Created in 1996 on the CNRS campus in Orleans La Source, LE STUDIUM has evolved to become a multidisciplinary Loire Valley Institute for Advanced Studies (IAS), operating in the region Centre-Val de Loire of France. LE STUDIUM has its headquarters in the city centre of Orleans in a newly renovated 17th century building. The amazing facilities are shared with the University of Orleans. In 2014 new developments and programmes linked to the smart specialisation of the Centre-Val de Loire region came to strengthen existing IAS cooperative relationships with the local and the international community of researchers, developers and innovators.

LE STUDIUM IAS offers to internationally competitive senior research scientists the opportunity to discover and work in one of the IAS's affiliate laboratories from the University of Tours, the University of Orleans, National Institute of Applied Sciences (INSA) Centre Val de Loire and ESAD Orléans, as well as of nationally accredited research institutions located in the region Centre-Val de Loire (BRGM, CEA, CNRS, INSERM, INRA, IRSTEA). Our goal is to develop and nurture trans-disciplinary approaches as innovative tools for addressing some of the key scientific, socio-economic and cultural questions of the 21st century. We also encourage researchers' interactions with industry via the IAS's links with Poles of Competitiveness, Clusters, Technopoles, and Chambers of Commerce etc.

LE STUDIUM has attracted over two hundred LE STUDIUM RESEARCH FELLOWS and LE STUDIUM RESEARCH PROFESSORS for long term residencies. In addition to the contribution in their host laboratories, researchers are required to participate in the scientific life of the IAS through attendance at monthly interdisciplinary meetings called LE STUDIUM THURSDAYS and gathering members of the regional scientific community and industries.

For the period 2015-2021, LE STUDIUM operates with an additional award from the European Commission in the framework of the Marie Skłodowska-Curie Actions (MSCA) with the programme MSCA-COFUND for the mobility of experienced researchers. LE STUDIUM is also the official partner of the Ambition Research and Development 2020 (ARD 2020) initiated by the Region

Centre-Val de Loire, that supports the specialisation strategy around 5 main axes: biopharmaceuticals, renewable energies, cosmetics, environmental metrology and natural and cultural heritage.

Researchers are also invited and supported by the IAS to organise, during their residency and in collaboration with their host laboratory, a two-day LE STUDIUM CONFERENCE. It provides them with the opportunity to invite internationally renowned researchers to a cross-disciplinary conference, on a topical issue, to examine progress, discuss future studies and strategies to stimulate advances and practical applications in the chosen field. The invited participants are expected to attend for the duration of the conference and contribute to the intellectual exchange. Past experience has shown that these conditions facilitate the development or extension of existing collaborations and enable the creation of productive new research networks.

The present LE STUDIUM CONFERENCE named "Cardiovascular Modelling: Basic Science to Clinical Translation" is the 124<sup>th</sup> in a series started at the end of 2010 listed at the end of this booklet.

We thank you for your participation and wish you an interesting and intellectually stimulating conference. Also, we hope that during these days in our region some of you will see an opportunity to start a productive professional relationship with LE STUDIUM Loire Valley Institute for Advanced Studies and research laboratories in the Centre-Val de Loire region.

> Yves-Michel GINOT Chairman LE STUDIUM

# INTRODUCTION

Neurological and cardiovascular diseases are the leading cause of death globally. The use of computer models to simulate the functioning of the human body is viewed increasingly as one of the most promising tools to embrace and better understand the complexity of human pathophysiology, and therefore improve prevention, diagnosis, and treatment of human disease.

A significant motivating factor for deployment of biomedical codes in clinical management of cardiovascular disease is the development of human digital twins. Such models would allow personalised guidance for healthcare, disease diagnosis and treatment, and wellbeing for specific individuals.

The symposium will focus on characterization of blood flows using modelling as well as imaging tools (e.g., ultrasound) and its links to vessel wall mechanics and cardiovascular disease. This is an area that sees participation and expertise from different fields including vascular biology, fluid mechanics, computer science, medicine, but also imaging, medical device and software certification and regulation for translation into healthcare.

The scientific literature in this field offers a rich spectrum of research, from basic science focusing on detailed mathematical, numerical and experimental descriptions of vascular pathophysiology, to applied research where similar approaches are used to test clinical hypotheses.

The impact of such a tremendous, cross-disciplinary effort is starting to emerge, with such approaches starting to have an impact on healthcare.

The event will aim to promote discussion and shine light on current and emerging research trends in the computational and experimental characterization and role of cardiovascular blood flows, arterial and venous wall mechanics, its correlation with vascular disease, with a specific emphasis on their application to unsolved clinical challenges and translation into healthcare.

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# CONVENORS

#### Alberto Marzo

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Dr Marzo is an Associate Professor of Cardiovascular Biomechanics at the University of Sheffield, UK. His research expertise is firmly rooted in Engineering and Mathematics in the context of computational biomechanics, with a PhD on the mechanics of flow through elastic vessels from the University of Sheffield, a David Crighton Research Fellowship at the University of Cambridge, and participation in several EU/UK projects, focusing on cardiovascular flow characterisation and development of computational frameworks. His expertise has a strong emphasis on clinical interpretation and translation, with his time spent as Clinical Scientist for the UK National Health Service. This experience gave AM exposure to the UK healthcare system, where he has witnessed the often-difficult clinical perception of innovation, and the resulting challenges relating to technology adoption.

#### The role of collaterals in treatment of intracranial aneurysms

Intracranial aneurysms are balloon-like focal deformations of a blood vessel in the brain, carrying an inherent risk of rupture and bleeding with severe consequences for the patient. A minimally invasive treatment option consists of deploying a medical device (Flow Diverting Stent or FDS) to trigger blood coagulation inside the aneurysmal sac to stop or prevent any existing or potential bleeding. In certain circumstances this treatment causes the occlusion of the arteries surrounding the aneurysm, leading to permanent and often irreversible damage (stroke). There is a strong consensus in the literature that the underlying causes might be associated with stent-induced adverse alterations to blood flow in the vascular network surrounding the aneurysm. Using a 3D-0D multidimensional patient-specific models of blood flow through an extended portion of the Circle of Willis, this study explores the possible role of collateral networks that are often associated with FDS-induced post-treatment complications. The long-term aim is that of providing guidance to clinicians towards a safer and more effective treatment of this condition.





Figure 1 (Left) Patient-specific model of blood flow a typical cerebral network with a saccular aneurysm in the middle cerebral artery and a typical flow-diverter stent (Surpass by Stryker).

(Right) Pressure contours predicted by a N-S based fluid solver that includes the effects of collateral network via a fully coupled lumped-parameter model



#### Ayache Bouakaz

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Ayache Bouakaz obtained his DEA degree (MSc) and his PhD in acoustics in 1992 and 1996 at the National Institute of Applied Sciences in Lyon, France (INSA Lyon). In 1998, he joined Pennsylvania State University at State College, PA, USA as a post-doc for 2 years. From December 1999 to November 2004, he held a position of associate professor at Erasmus Medical Center in Rotterdam, the Netherlands. His research focused on ultrasound imaging, ultrasound contrast agents and transducer design.

In 2004, he obtained a position as an Inserm researchere (CR1) and since 2009, he has held the position of research director in the Inserm Imaging and Brain unit, where he heads the ultrasound imaging and therapy group. His research focuses on imaging and therapeutic applications of ultrasound.

Ayache Bouakaz is a "chair professor" at the Jiaotong University of Xi'an in China since 2017. He is the general chair of the international conference IEEE International Ultrasonics Symposium (IEEE IUS) 2016 in Tours, France and co-general chair of the IEEE IUS 2021 edition and he was the vice-president of the IEEE UFFC society from 2017-2021.

He has published more than 135 articles in peer-reviewed journals, more than 100 articles published in conference proceedings and has filed 9 patents.

# **SPEAKERS**

#### **Ivan Benemerito**

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Dr Benemerito is a research associate at The University of Sheffield and the INSIGNEO institute for in silico medicine. Following the award of his PhD from The University of Sheffield, during which he studied the contact mechanics of the ankle joint during walking activities, he shifted fields of application to cardiovascular biomechanics. He is interested in combining deterministic techniques with statistical approaches to investigate the sensitivity of complex computational models to uncertain input parameters, and to develop methodologies that can be translated to the clinical practice with minimum modifications to existing clinical practices.

# Identification of biomarkers for distal perfusion following an ischaemic event: a combined mechanistic-statistical approach

An ischaemic stroke (IS) is an occlusion of a major cerebral vessel. It often causes severe reduction to the perfusion of downstream districts and the consequent death of tissues. The effects of middle cerebral artery (MCA) occlusion are partially mitigated by the action of the leptomeningeal anastomoses (LMAs), small arterioles which provide continuity of perfusion through diversion of flow from the anterior and posterior brain districts. Extensive LMAs networks are linked to better post-IS outcomes. The action of these vessels, which are active and can be observed only during an ischaemic event, induces modifications in the blood velocities of adjacent vessels. Transcranial Doppler ultrasound (TCD) can monitor the blood velocity in these major arteries but fails in detecting signals from the LMAs and to estimate the efficacy of their action in restoring distal perfusion. 1D computational models can simulate the cerebral circulation and identify biomarkers that correlate with the level of distal perfusion. In this study we have developed a deterministic1D model of the brain circulation which includes the LMAs, and combined its predictions with the use of Gaussian Process emulators and Sobol's sensitivity analysis to identify TCD biomarkers for distal perfusion in case of MCA stroke. We identified four biomarkers related to velocity pulsatility whose values can be associated with poor perfusion in the distal MCA regions.



#### Sara Bridio

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I got my Master Degree in Biomedical Engineering at Politecnico di Milano in 2018. I'm currently a PhD candidate in Bioengineering at Politecnico di Milano, under the supervision of Prof. Francesco Migliavacca, and I will defend my thesis in early 2023. The topic of my research is the development of computational models of the treatments for stroke, from high-fidelity finite-elements models, to reduced order models. Part of my research was carried out within the EU Horizon2020 project INSIST (IN Silico trials for treatment of acute Ischemic STroke). In July 2022 I received the Young Researcher Prize at the European Solid Mechanics Conference in Galway (Ireland) with a work on the investigation of the impact of thrombus composition on the outcome of thrombectomy procedures.

# Dimensionality reduction and kernel optimization for the prediction of thrombectomy outcomes

Endovascular thrombectomy (EVT) is the main treatment for acute ischemic stroke, aiming at removing the thrombus from a cerebral artery with a stent-retriever. The treatment must be performed in the first few hours from symptoms onset, allowing a short time window for preoperative planning. Computational simulations of EVT can predict the treatment outcome but require a long computational time. In this work, a classification model is proposed, trained on high-fidelity EVT simulations, for providing fast estimates on the success of the procedure. The training dataset is composed of 94 finite-elements patient-specific EVT simulations, containing cases with successful (thrombus removed) and unsuccessful (thrombus not removed) outcomes, which are highly unbalanced: 81 successful against 13 unsuccessful EVTs. The proposed strategy is made of two steps. First, a dimensionality reduction approach is used to parametrize the vascular anatomies with few dimensions. Then, given as inputs the anatomy description and the thrombus properties for each virtual patient, a kernel function is trained, based on a restricted semidefinite positive optimization, with which clusters are created according to the EVT success. With the obtained tool, once data describing a new patient is available, it is processed through the trained kernel so that the results may approach either the successful or the unsuccessful cluster. suggesting a higher or lower probability of success of a possible EVT intervention.



# Diederik Bulters

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Professor Bulters is a consultant neurosurgeon specialising in vascular conditions. His group's main themes are risk prediction for unruptured intracranial aneurysms and reducing brain injury from haemoglobin after subarachnoid haemorrhage.

He is past president of the British Neurovascular Group, has held grants from the NIHR, EPSRC, Innovate UK, MRC, European Union, RCS and several medical charities and has been chief and principal investigator for many randomised trials of new drugs, cell therapies and surgical techniques.

His interest in unruptured aneurysms focuses on risk prediction, new imaging techniques to stratify risk, including vessel wall imaging and dynamic contrast enhanced imaging, and the influence of modifiable risk factors including aspirin, blood pressure and cholesterol.

#### Risk of Aneurysm Rupture study - rationale and opportunities

Unruptured intracranial aneurysms (UIA) are common. However, only some subsequently rupture. Prophylactic treatment is possible but reserved for those with a rupture risk high enough to justify this. The problem is that our estimates of risk are not accurate enough, and do not stratify patients into sufficiently high and low risk groups, to base these treatment decisions on.

The best natural history data comes from the PHASES study. This has not been validated, and given the heterogeneity in the populations, methods and biases of the constituent studies, there is a need to do so. There are also many predictors not considered in PHASES, and PHASES is based on short term follow up (mostly 1 year) with little data on long term rates relevant to patients. We therefore designed the Risk Of Aneurysm Rupture (ROAR) study with the aims to: 1) test the accuracy of PHASES, 2) evaluate additional predictors, 3) assess long-term rupture rates.

ROAR is a longitudinal multicentre study that identifies patients with UIA in neurosurgery units and determines rupture events using national databases of hospital admissions and deaths. This design enables long term follow-up in a large cohort of 20,000 patients (11,000 to date).

In this presentation we will describe the design of ROAR and discuss the opportunities to identify different imaging markers of risk of rupture provided by a cohort that is expected to identify several hundred aneurysms with baseline MRA that subsequently rupture.



#### **Gaetano Burriesci**

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Gaetano is Chair of Bioengineering at UCL (UK) and Group Leader of Bioengineering at Ri.MED Foundation (Italy). He studied Mechanical Engineering at the University of Palermo (Italy) and completed his PhD in biomechanics on a joint project between the same university and the University of Sheffield (UK), where he was then appointed Research Associate. Subsequently, he joined SorinGroup (now Corcym) as Research Manager, before taking his position at UCL. His main research interests lie in the field of cardiovascular engineering and medical devices development, where Gaetano has made major progresses that have found application into largely adopted therapeutic approaches.

# Design, development and preclinical validation of a novel transcatheter aortic valve concept

This talk describes the design, development and preclinical assessment of a new polymeric aortic valve suitable for transcatheter implantation. The device consists of three polymeric leaflets and an adaptive sealing cuff, supported by a fully retrievable self-expanding wire frame made from superelastic NiTi alloy. A parametric design procedure based on numerical simulations was implemented to identify design parameters providing minimum stress levels and operating energy for the valve leaflets. The wireframe was optimised to minimise the stress levels during valve delivery and provide adequate anchoring. Valve prototypes were manufactured by thermomechanical processing of the NiTi wire and automated dip-coating of the polymeric components. The hydrodynamic performances of the valves were assessed in a cardiac pulse duplicator, in compliance with the ISO5840-3 standard, and compared to two reference valves suitable for equivalent implantation ranges. A valve prototype was implanted in orthotopic position of an acute ovine model, confirming retrievability, secure valve anchoring, adequate leaflets motion, and no interference of coronary flow or mitral valve function.

The proposed valve system demonstrated excellent hydrodynamic performance with significant reduction in paravalvular leakage and the potential to mitigate complications related to imprecise valve positioning. This new concept may offer a safer and more economical TAVI solution to a broader range of patients.



#### Emmanuelle Chaigneau

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I graduated in 2001 from ESPCI-ParisTech, a french "grande ecole", providing a master-level multidisciplinary training with a major in physics.

For my PhD I studied neurovascular coupling with 2-photon microscopy imaging and became a Doctor in Philosophy from Sorbonne University (Paris 6) in 2005.

Then I worked as a post-doc research fellow, mainly in University College London, and I performed research and development both in microscopy and in neuroscience.

In 2015 I got a permanent position at INSERM in Paris, and since I have been focusing at research and development of microscopy and modelling tools to study neurovascular coupling in the laboratory of Serge Charpak.

# Investigation of functional hyperaemia with an experiment-based model of brain vasculature

Functional hyperemia is the local increase in blood flow that occurs in response to local activation of neurons. In the olfactory bulb, functional hyperemia involves complex velocity changes resulting from vessel dilations at several levels of the vascular tree. Disentangling the effects of dilations occurring at each level is difficult as diameter changes cannot be selectively manipulated in vivo. Experiment-based modelling can provide further insight in this question.

The vasculature was divided into four functional units according to the kinetics of the diameter changes of individual vessels. A four-level network was then developed by reducing all vessels in each of these physiological units into an equivalent tube. The diameter of each equivalent tube was set so that its resistance matches the resistance of the physiological unit. A formal mathematical model was developed to calculate the flow in each compartment as a function of the diameters of each compartment.

In response to diameter changes whose kinetics followed experimental measurements, the model predicted RBC velocity dynamics in the compartments that were in line with the experimental results. Furthermore, the model allowed to manipulate the inputted diameter changes and test their impact on the velocity and flow changes. Our modeling faithfully shows that RBC velocity dynamics in the olfactory bulb results from the timing and relative changes of diameter that occur in the different vascular compartments.



#### **Benjamin Csippa**

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Benjamin Csippa is a research associate at the Budapest University of Technology and Economics in the Department of Hydrodynamic Systems. He holds a BSc degree in Mechanical Engineering (2014) and an MSc in Fluid and Solid mechanics (2017). He is a doctoral candidate at the Pattanyús Ábrahám Géza doctoral school of mechanical engineering sciences.

# Measurement-supported computational framework for the hemodynamic investigation of flow diverter treatments

Flow diverters (FDs) have been studied numerically from their developmental stages. There is an emerging need to design numerical tools for future in silico trials. These trials might even offer additional insights into flow-diverter treatments. The aim of this paper is to present a measurement-supported numerical workflow that automates the virtual deployment and subsequent hemodynamic analysis of flow diverters and to investigate the effect of flow diverter deployment variability on post-treatment flow reduction.

Virtual deployment of FDs was calculated for five patients by a mechanistic spring-network model and user interactions. Computational fluid dynamic simulations were performed in non-treated and 16 deployment scenarios, including two device types in nominal and oversized conditions. The flow diverter was approximated as a homogeneous porous layer, with parameters obtained from laboratory measurements.

A patient-specific power-law relationship was obtained between the linear hydrodynamic resistance coefficient and the flow reduction. In nominal scenarios, a significantly larger average post-treatment flow reduction was obtained for the 64-wire configurations than for the 48-wire configurations. Surprisingly, the average post-treatment flow reduction in oversized scenarios was the same for 64- and 48-wire device types.

In this study, the 64 wire configurations in nominal sizing produced a significantly higher posttreatment flow reduction, replicating the result of other in-vitro studies. With more development, validation, and verification, the presented tool could be suitable for future in-silico trials.

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#### **Thomas Feaugas**

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Thomas Feaugas is a PhD candidate working at Eden Tech in collaboration with Milano-Bicocca University on microfluidic devices for biomedical applications. He is a biomedical engineer graduated from Ecole des Mines de Saint-Etienne and Polytechnique Montreal, where he specialised in microfluidic science. He is developing microfluidic vascular networks capable of reconstructing the human circulatory system as closely as possible. The objective is to design and prototype networks that allow efficient and sustainable extracorporeal blood circulation. A part of his project involves numerical simulations of blood flow in microfluidic systems to assess the thrombogenicity of a specific blood pathway and associated mechanical forces.

# Design of artificial vascular devices: hemodynamic evaluation of shear-induced thrombogenicity

Blood-circulating devices such as ECMOs or prosthetic heart valves have offered lifesaving opportunities for advanced cardiovascular and pulmonary failures. However, complications involving thromboembolism and hemolysis considerably reduce their implementation time and require heavy anticoagulant treatment. Circulating platelets and von Willebrand factor (vWF) play an essential role during hemostasis, although they are among the main constituents of a thrombus. Pathological and uncontrolled transport of these two major players, amplified by mechanical forces such as shearing forces, facilitate acute thrombus growth compromising the device integrity. In this study, we investigate how design features can affect local hemodynamic properties of the blood flow. More specifically, we use Computational Fluid Dynamics (CDF) numerical simulations to evaluate thrombogenic performances of devices associated with defined patterns. We show that leveraging both local hemodynamic analysis, nature-inspired architectures can greatly contribute into the development of predictive models of device thrombogenicity. When integrated in the early phase of the design, such evaluation would pave the way for optimised blood circulating systems with effective thromboresistance performances, lifetime implantation and reduced burden for patients.



#### Nada Ghorab

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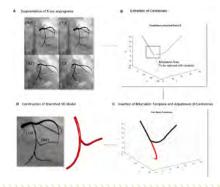
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Nada Ghorab is a second year PhD student in the Mathematical Modelling in Medicine Group at the University of Sheffield. She completed her Master of Engineering degree in Bioengineering at The University of Sheffield, with a specialisation in cardiovascular computational fluid dynamics. Her passion for this area of research emerged after multiple technical and research internships, which included multi-disciplinary collaboration with experts in relevant fields. Currently, her research is about modelling bifurcations and integrating multiple imaging modalities, mainly Optical Coherence Tomography (OCT) and X-ray Angiography, to better model diseased coronary arteries, and perform computational fluid dynamic simulations to guide treatment pre and post procedures.

# Modelling Coronary Bifurcations: Using angiograms to produce CFD models that predict blood flow – the methodology.

Image-based physiological models are starting to translate into clinical cardiological practice. Typically, these models are single-lumen reconstructions based on two 2D x-ray images during coronary angiography. These neglect luminal (stenosis) detail and bifurcation points, both of which are challenging to model, but are important when simulating physiology. The aim of my study is to develop a method that produces 3D, patient-specific models incorporating high resolution luminal data and bifurcations. Centreline and radius information are extracted from angiography to provide the skeleton. The bifurcation area is modelled using a template characterised using the proximal and distal bifurcation points and radii, cubic Hermite interpolation and Frenet orientation in 3D space.

The template position is optimised and merged with the skeleton, producing a branched CFD- compatible model. This is the first demonstration of this novel method. The method is being validated (n = 5 bifurcations) against a novel digital phantom based on human coronary anatomy (see figure) using the Hausdorff Distance between the centrelines, bifurcation angle and the luminal area. Ultimately, this method may provide the basis for models of human coronary physiology with next- level accuracy regarding ischaemia predictions and wall shear stress modelling.



(A) digital phantom;
(B) centreline extraction;
(C) template insertion and centreline adjustment;
(D comparison between phantom and reconstruction



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Graduated in 2021 for Medical Engineering at Eindhoven University of Technology where he created a onedimensional close-loop circulation model, able to compute the pressure and flow waves in both arteries and veins. He started doing his PhD in the same year under the supervision of professor Frans van de Vosse and dr. Wouter Huberts. Whilst doing his PhD and being part of the In Silico World project, he's currently working on the creation of an in Silico clinical trial.

#### An in Silico clinical trial on coronary fractional flow reserve as a replacement for the original clinical trial: a feasibility study

In Silico clinical trials have great potential for replacing clinical trials. In this study, we aim to demonstrate the feasibility of conducting in Silico clinical trials by generating virtual patients, and reproducing a clinical trial in which the clinical benefit of fractional flow reserve (FFR) measurements was demonstrated (i.e., the FAME study [1]) for patients suffering from coronary artery disease. Here, we will present the strategy we envision to demonstrate the clinical benefit of the FFR using in Silico trials only. In addition, we will present preliminary results regarding model development.

An one-dimensional pulse wave propagation model (PWPM) that is capable of computing patient specific FFRs has been developed. Sensitivity analysis will be conducted to prioritize parameters for model personalization. Geometric information will be extracted from angiograms, whereas patient-specific parameters will be estimated by using a machine-learning model that is trained using angiograms, demographics, and pressure losses across stenoses. The latter will be based on FFR measurements or 3D computational fluid dynamic simulations. A synthetically generated training set will be used to assure a large enough dataset and sufficient coverage of the heterogeneity within the population. Secondly, the parameters can be varied to generate virtual patients. In the future, the model output will be transformed into a clinically relevant output (i.e., mortality and morbidity) through a transfer function. Furthermore, the approach will be evaluated on an independent set of real clinical trial data.

The results show that the PWPM can accurately model coronary pathophysiology. The computed FFR values are plausible compared to clinical findings, which typically show an FFR below 0.8 around a stenosis severity of  $\geq$  50/60% [2]. Overall, it can be concluded that this model is ready for the next step in our devised methodology and can be used as a virtual cohort generator to recreate the FAME1 study in Silico.

#### References

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Tonino, P.A.L. et al., N Engl J Med. 2009; 360(3):213-224.
 Kang, S. et al., Circ Interventions. 2011. 4(1), 65-71.
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Prof. dr. Alfons Hoekstra is full professor Computational Science & Engineering and director of the Informatics Institute at the University of Amsterdam. He is also a member of the Computational Science Lab. His research focusses on Virtual Human Twins, mainly in the Cardiovascular domain, on Multiscale Modeling of Complex Systems, and on High Performance Computing. He is editor of the Journal of Computational Science.

#### Towards In-Silico Stroke Trials

Emerging applications of the Virtual Human Twin are In-Silico Trials, where actual (pre-) clinical trials are reproduced in-silico. The goal is to better design clinical trials, or to reduce or speed up clinical trials, and maybe even to partly replace them. In a pre-clinical setting in-silico trials could also contribute to refining, reducing or even replacing animal studies. In this lecture the concept of in-silico trials will be introduced in relation to acute ischemic stroke, where a new revolutionary treatment option that became available only in 2015 has now led to a flurry of clinical trials, and where in-silico trials could potentially contribute in further improving treatment options for patients. A multiscale model for brain perfusion will be introduced that forms the basis for modelling acute ischemic stroke. Also treatment models (thrombectomy and thrombolysis) will be highlighted, and how to bring all these components together into an in-silico stroke trial. Finally, some proof of concepts results obtained with the current prototype will be discussed.



#### **Guillaume Lacoin**

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I have been a science thesis student for three years in the IBrain lab. My objective is to evaluate the contribution of ultrafast Doppler imaging, and elastography, as intraoperative imaging for the surgical management of gliomas. I have a master's degree in acoustics and specialize in medical ultrasound imaging.

# Intraoperative ultrasound plane wave Doppler imaging allows better definition of gliomal infiltration

Tumoral neoangiogenesis is an important prognostic criterion of diffuse gliomas. Preoperative perfusion MRI of gliomas in often biased by proximity of sulci or dura mater. Intraoperative ultrasound allows direct exploration of the operative field, but no quantification of the vascularization has ever been proposed with ultrasounds. Our objective was to develop a sensitive intraoperative method to quantify tumoral vascularization.

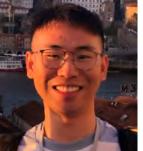
We studied 20 patients with brain glioma included in the ELASTOGLI clinical trial currently underway in our institution (CPP 2018-A01237-48). We used intraoperative ultrasound (5,6MHz US frequency probe (SL10-2), Aixplorer® Super Sonic Imagine). We developed a robust adaptive blood filtering called multi-layered adaptive neoangiogenesis intra-operative quantification (MANIOQ) and estimated the fractional moving blood volume (FMBV) and vascular index (VI). An in vivo analysis of the periphery of the B-mode hyper signal area allows to measure the vascular infiltration extent of the brain tumors. We excluded sulci as not to introduce a bias in quantification.

We showed that FMBV and VI was much higher in tumoral structure (BHS) than adjacent regions for all grades. These two parameters inside tumoral structure was increasing according to the grade. We also showed that vascular infiltration around of the healthy brain was more extensive for grade 3 and 4 (up to 15 mm from FMBV parameter) than for grade 2 glioma (up to 10 mm).

We developed a quantitative imaging method for quantification of tumor vascularization, which allows a better definition of tumoral infiltration and could help in tumor grading. This new imaging modality opens new perspectives, both from a surgical and oncological point of view, to the use of intraoperative ultrasound.

JP.Remenieras, UMR 1253, iBrain, Université de Tours, Inserm, Tours - FR

I.Zemmoura, UMR 1253, iBrain, Université de Tours, Inserm, Tours - FR / CHRU de Tours, Neurosurgical Department, Tours - FR



#### Weiqiang Liu

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Research Assistant, Inria Saclay Île-De-France (2021-present) Master's in Biomedical Engineering and Biomechanics, Institut polytechnique de Paris (2020-2022)

#### 3D blood flow simulations for understanding cerebral vasculopathy in sickle cell patients

Sickle cell disease (SCD) is the most common severe inherited disease and SCD-related cerebral vasculopathy (CV) can lead to ischemic stroke, especially in childhood patients from 2-5 years old. The main risk factor for developing CV is the acceleration of the cerebral arterial blood flow. Such risk could be clinically assessed with time-mean of maximum velocity (TMMV) measured by transcranial Doppler in the distal part of internal carotid artery (ICA). We propose a CFD 3D-0D simulation workflow to investigate the hemodynamics difference in SCD patients across age.

3D blood flow simulations with mean inlet flow rate 5mL/s are performed for 15 patients: 5 patients under 5 years old (UF), 5 childhood patients over 5 years old (OF), and 5 adult patients (AD). TMMV value, mean shear rate and Dean number (De) of different arterial segments (Fig. A) in each patient are calculated.

Results show that for a given flow rate, TMMV values (Fig. B) and mean shear rate (Fig. C) in the siphon region of ICA in UF group are significantly higher than those of OF and AD groups, explaining high risk of stroke in early childhood patients. TMMV values are strongly correlated with Dean number (Fig. D): high flow rate, large curvature, and small diameter contribute together to generate high blood velocity. Wall shear stress and blood flow patterns have also been investigated to better understand the pathophysiological mechanisms of CV.



#### Francesco Migliavacca

Politecnico di Milano

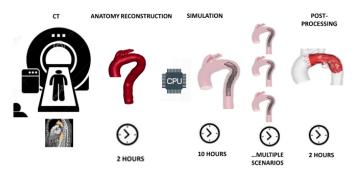
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MSc in Mechanical Engineering and PhD in Bioengineering from Politecnico di Milano. Research Assistant at the Cardiothoracic Unit of Great Ormond Street Hospital for Children in London in 1994 and 1997-99. Consultant and Research Scientist at the Pediatric Cardiac Surgery Department of the University of Michigan, Ann Arbor, MI, USA in 2000 and 2001. At present, he is a Professor of Bioengineering and the Coordinator of the Section of Biological Engineering at the Department of Chemistry, Materials and Chemical Engineering 'Giulio Natta' of Politecnico di Milano. His major recent research activities include the fluid-structure behaviour of stent-like devices. He received the medal 'Le Scienze 2001' in Engineering and was awarded the European Society of Biomechanics Perren Award in 2004.

#### Moving aorta: From bench Tests to bedside

The Thoracic Endovascular Aortic Repair (TEVAR) is the preferred treatment option for thoracic aorta pathologies. Computational models play a key role in procedural planning and must be reliable. High-fidelity simulations to model commercial stent-grafts and reproduce the procedure will be presented. Experimental tests to calibrate Nitinol and PET stent-graft material parameters adopted in the numerical simulation will be described. Explicit FE simulations to reproduce the TEVAR procedure into idealized and patient-specific aortas will be illustrated. Firstly, to validate the deployment simulation, a stent-graft is experimentally released into an idealized aortic phantom and subjected to CT scan. The same stent-graft and aortic model are used for the simulation. The experimental and simulation results are qualitatively and quantitatively compared. Then, the validated TEVAR procedure is applied to deformable patient-specific pathologic aortas reconstructed from clinical CT images. Some insights into fluid-structure interaction simulations of the TEVAR behaviour will be illustrated. This workflow can be used for pre-operative planning of the mini-invasive procedure.





#### Ana Paula Narata

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Dr Ana Narata is a Consultant Neuroradiologist at the General Hospital of Southampton and Senior Clinical Lecturer at the University of Southampton over the past 3 years.

With Neurosurgery training in Boston, United States, and Neuroradiology in Paris and Limoges, France, Dr Ana Narata has been working exclusively as a Neuroradiologist since 2002. Her international reputation was built during the period she was Senior Neuroradiologist at the University Hospital of Geneva, Switzerland, and the University Hospital of Tours, France, being considered an expert in complex intracranial stenting procedures and a pioneer in the treatment of Stroke.

As well as clinical practice, Dr Ana Narata has developed an academic career with interest on flow dynamics and correlated research about intracranial aneurysms and Stroke. Her expertise in supporting the development and performing the benchmark of medical devices are now recognized worldwide.

# Imaging to create virtual humans: the importance of models to improve the management of vascular pathologies

The presentation will cover the importance of virtual models to improve the management of Neurovascular pathologies. Some examples of past projects will be exposed but also the expectations for the future.

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#### **Clément Papadacci**

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Clement Papadacci received his PhD in acoustics in Paris in 2014 under the supervision of Mathias Fink, Mathieu Pernot and Mickael Tanter. During this period, he developed ultrafast ultrasound imaging of the heart and a new method to image fiber orientation using the spatial coherence of ultrasonic waves.

After his PhD, he spent two years as a postdoctoral fellow in Pr. Konofagou's lab at Columbia University in New York. He pursued his research on 3D ultrafast ultrasound and developed new applications such as 3D quasistatic and myocardial elastography.

In 2017, he obtained a tenured researcher position at Inserm within the Physics for Medicine Paris laboratory, where he continues to work on translational research from basic ultrasonic theory to clinical application. At the beginning of 2022, he was awarded an ERC Starting Grant for the Microflowlife project. During this project, he will develop a new ultrasonic array with diffracting lenses to image whole organ micro-flows using ultrasound localization microscopy.

He has been granted 3 patents in the field of ultrasonic imaging (4 more are currently pending) and has published more than 15 papers in ultrasonic, clinical, and high-impact factor journals.

#### 3D ultrafast ultrasound applications for human heart characterization

Non-invasive and objective quantification of the state of the heart by ultrasound is key to enable an early and specific diagnosis of cardiovascular disease. In a first part, I will present the simultaneous measurement of cardiac indexes through ultrafast three-dimensional imaging that promises to improve clinical practice. In a second part, the deformation that will be evaluated in three dimensions to allow in particular to detect lesions in the heart. In a third part, the observation of natural waves induced by valve closures will allow an evaluation of their speed that is related to the rigidity of the heart, an intrinsic parameter of the heart muscle. Next, threedimensional ultrafast imaging will be used to assess the direction of the cardiac fibers using the acoustic signature of the medium. Finally, I will introduce a new technology to enable clinical measurement of heart stiffness in patients.



#### Giulia Pederzani

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I'm a postdoctoral researcher in the Mathematical Modelling in Medicine group at the University of Sheffield. I hold a BSc and MSc in Mathematics, and a PhD in Computer Science. I'm interested in the application of mathematical and computational methods to model biological processes and help solve clinical problems. I focus on the cardiovascular system, from multiscale modelling (cell to tissue level) of how the structural constituents of the arterial wall change in vasospasm to working on the mathematics behind the VIRTUheart™ software suite, with a focus on the image reconstruction process to improve the accuracy of the 3D geometry and thus the predictions from CFD analysis.

# Digital Coronary Phantoms as Gold Standard Method for Software Validation and Improvement

Digital coronary phantoms are mathematically defined 3D clouds of points representing (networks of) coronary arteries. They are easily and highly customisable, and fast to generate. Their mathematical definition allows them to be a perfectly known ground truth which is ideal for software or model validation. We developed a phantom of the main vessels in the left and right coronary trees, based on anatomical knowledge and consultation from the cardiologists in our group. We demonstrate its use in an error propagation study on the software VirtuHeart™, which reconstructs 3D coronary geometry from a pair of angiographies and uses computational fluid dynamics analysis to compute fractional flow reserve (FFR). The software has been previously validated clinically [2] and using a 3D printed phantom [3]. The digital phantom has allowed us to run a more in-depth study on how different sources of error affect (i) the accuracy of 3D geometry reconstruction, and (ii) the estimation of FFR, as well as suggest algorithmic improvements to prioritise for software development. The code to generate and use the phantom will soon be made available as open source software in hope that it is used by the community for model refinement and validation.

Pederzani et al., Fluids, 2022; 7 (6).
 Morris et al., J Am Coll Cardiol Intv. 2013; (2):149-157.
 Solanki et al., Scientific Reports, 2021; 11 (1).

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#### Anna Ramella

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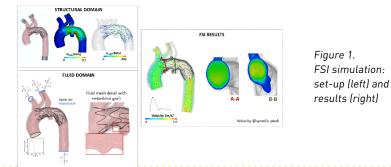
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I obtained the MSc degree in Biomedical Engineering at Politecnico di Milano in April 2020 with a final mark of 110/110 cum laude. I'm currently enrolled in the second year of the PhD in Bioengineering at Politecnico di Milano (Department of Chemistry, Materials and Chemical Engineering 'Giulio Natta') under the supervision of professor Francesco Migliavacca. My research focuses on the numerical modelling of cardiovascular devices behaviour. In particular, I'm currently developing a tool to model the clinical Thoracic Endovascular Aortic Repair procedure using both the Finite Element Analysis and Fluid-Structure Interaction simulations that can be used by clinicians in the pre-procedural planning phase.

#### On the modeling of the tevar procedure: a detailed FEA-FSI methodology

Thoracic Endovascular Aortic Repair (TEVAR) is a procedure to treat thoracic aorta pathologies. Despite its increasing use, many stent-graft (SG) related factors are still to be understood. In this context, reliable computational models play a significant role. In this presentation, commercial SG models are calibrated with experimental tests: the Nitinol stent is discretized with beam elements and the fabric PET graft with triangular membrane elements. An explicit Finite Element (FE) TEVAR procedure simulation is developed and validated with an ad-hoc experimental setup. Then, the numerical model is applied to a patient-specific case. The aorta is segmented from CT images, discretized with tetrahedrons and modelled as isotropic hyperelastic material. The results of the FE simulation are compared with postoperative CT images. To study the post-TEVAR patient-specific hemodynamics, a strongly coupled, 2-way, boundary-fitted FSI simulation is performed. For the fluid domain, velocity is imposed to the inlet and 3-elements Windkessel circuits are assigned to each outlet. The SG is embedded into the fluid mesh volume. For the structural domain, the device and aorta configurations and stress/strain distributions were imported from the FE simulation. SG sealing and velocity can be analysed. This FEA-FSI methodology is useful for investigating the TEVAR complications and designing new devices or supporting clinical decisions.





#### Ahmet Sen

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Ahmet SEN is a Ph.D. candidate in cardiovascular blood flow modelling at École des Mines de Saint- Étienne. During his Ph.D. project, he mostly focuses on the use of machine learning and 1-D blood flow analysis for the detection of ischemic stroke. He is currently a visiting researcher at King's College London as part of his doctoral program. At King's, he conducts research on the use of machine learning for cerebrovascular topology detection and acceleration of computational models.

# Understanding the relationship between anatomical variations of the circle of Willis and hemodynamics using machine learning

Each year cardiovascular disease causes an estimated 17 million deaths worldwide, accounting for one-third of all deaths worldwide. Many of these diseases cause permanent damage due to obstruction of normal cerebral blood flow. In many instances, the biggest challenge is the urgent time frame needed for restoring normal blood flow. Because of this, surgical planning is key but, in general, uncertainties due to the lack of patient's data and time pose important barriers. An important uncertainty is not knowing the anatomical variation of the circle of Willis (CoW) of the patient being treated.

Although imaging technologies such as MRI and CT scans are currently used to obtain detailed patient-specific geometries, these methods are expensive and time-consuming. We propose an alternative machine learning-based technology, which can detect CoW anatomical variations from inexpensive hemodynamic data such as Doppler ultrasound, obtained at the patient's carotid arteries. In our study, an in-silico model, which was previously developed using Nektar1D, was used. The seven most common CoW anatomical variations are described in the model. For each variation, we assume a wide range of patient-specific data such as arterial diameters, heart rate, and cardiac output. For each model, simulated hemodynamic data (blood flow, pressure) was obtained at 8 locations (left and right branchial, vertebral, carotid, and middle cerebral arteries). Next, this data was used in a CNN-MLP hybrid model to inversely determine the correct anatomical variation. Machine learning predicts the correct topology in 90% of the cases.



#### **Redouane Ternifi**

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Redouane TERNIFI is an Ultrasound Research Scientist at Bracco Suisse. His research interests focus on ultrafast ultrasound imaging, super-resolution ultrasound imaging, and contrast-enhanced ultrasound imaging. Before moving to Geneva, he was a Senior Research Fellow, in the Department of Physiology and Biomedical Engineering at Mayo Clinic (Rochester, MN, USA) developing new ultrasound imaging and signal & image processing techniques for visualizing and quantifying microvascular flow in high spatial and temporal resolution, and its application in a wide range of clinical diseases. Dr Ternifi has published over 35 peer-reviewed journal papers.

#### Super-Resolution Ultrasound Imaging: Current Research and Applications

There are several pathologies that can profoundly alter the microvascular system, such as neurologic diseases and cardiovascular diseases. However, medical imaging on this scale is currently not possible due to the limitations of the imaging modalities. A recent development in contrast-enhanced ultrasound, known as ultrasound localization microscopy (ULM), demonstrated that capillary-sized blood vessels can be imaged in vivo, improving the resolution by more than 10-fold. Using the ULM technique, which is inspired by optical microscopy, the transcranial imaging of cerebral vascular blood flow has been enabled and bypasses the classical trade-off between penetration and resolution in ultrasound imaging. The location of individual injected MBs and the tracking of their displacement can be used to generate micrometer-scale blood vessels and velocity maps. In this presentation, we are going to introduce the main steps and the major steps involved in the process, such as clutter filtering, microbubble separation, tracking, and localization, and then outline the most relevant applications and their future perspectives within the clinical context. There is now evidence that these super-resolution ultrasound imaging techniques are being applied preclinically and clinically to assess and quantify the cerebral blood flow in stroke, aneurysms, neurodegenerative diseases, and several other diseases.



#### **Philippe Trochet**

#### **FUJIFILM Visualsonics**

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Philippe Trochet - Applications Specialist at FUJIFILM Visualsonics, Inc.

Engineer in Physics, Philippe Trochet has joined VisualSonics Company in 2008. He is an expert in High frequency imaging and Photoacoustic imaging technologies in preclinical research on small animals. His expertise helps researchers in their studies investigating the mechanisms of disease progression or the quality of interventional procedures.

#### Innovative imaging for cardiovascular diseases

Animal models form an essential part in many research areas such as developmental biology, cancer research, cardiology, inflammation, or virology.

Therefore, state of the art in vivo imaging modalities in Preclinical Imaging Facilities form the basis for true translational research.

This seminar will focus on the Vevo F2 LAZR-X imaging capabilities, covering non-invasive and pain free applications for early detection, sizing, volumetric quantification, dynamic imaging, hypoxia assessment, etc. in various animal models with an outlook to clinical use.

This talk will outline the cardiovascular research area showing possibilities and published results.



#### **Ning Wang**

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Ning obtained his MSc (Distinguish) and BEng (First Class Honours) degree in Mechanical Engineering from University College London (UCL) in 2021 and University of the West of Scotland (UWS) in 2020. Ning joined the University of Sheffield as a Ph.D. student in Dr. Marzo's group at Department of Mechanical Engineering since 2021, he is also supervised by Prof. Sourbron in Department of Infection, Immunity and Cardiovascular Disease. He was awarded a full scholarship by University of Sheffield Research Scholarship (Faculty of Engineering) for his Ph.D. project on the use of modelling and MRI data to improve the diagnosis of kidney disease.

# Determining image accessible biomarkers for non-invasively distinguishing hypertensive from diabetic renal injury through a mechanistic model and MR imaging

Hypertension and diabetes as two common comorbidities that independently cause chronic kidney disease (CKD) showing similar symptoms in clinical. It is not currently possible to distinguish between these two pathologies non-invasively, which ultimately impacts their clinical management. Our research is based on the hypothesis that a mechanistic model can be reliably adopted to identify biomarkers capable of distinguishing between these two aetiologies, non-invasively, using renal doppler ultrasound or phase-contrast magnetic resonance imaging data. Using a 1-D whole-circulation blood flow model (openBF) that includes a comprehensive renal network (Figure 1A), we modelled a healthy virtual population of variant ages. We then described differential changes induced by diabetes and hypertension on blood viscosity, lumen radius, vascular stiffness, peripheral resistance and compliance. A flow parameter commonly measured in the clinic, the Resistive index (RI), was used to quantify changes in the blood velocity waveform of the renal artery induced by the two conditions.

RI values for a virtual population of 2000 individuals show different distributions for modelled hypertension and diabetes from an early stage of the two conditions. Differences in RI distributions become more significant at later stages of progression (Figure. 1B). These early results show the potential of this clinically-aligned biomarker in improving clinical management of CKD.

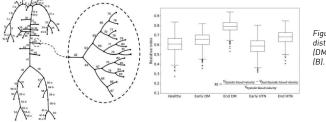


Figure. 1 1-D vascular model (A) and distribution of RI for healthy, diabetic (DM) and hypertensive (HTN) individuals



#### Gabor Zavodszky

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Gabor Zavodszky is an assistant professor of high-performance multi-scale computing at the University of Amsterdam and assistant professor at the Budapest University of Technology. His research focuses on designing and developing HPC models targeting biomedical challenges, primarily focusing on cardiovascular diseases. He participated in several H2020 projects and is currently the co-PI and work package leader in CompBioMed2. He leads the development of two major biomedical codes: HemoCell, the open-source cellular blood flow simulation framework, and VascuTreat, a medical device deployment simulation which is currently being used as clinical decision-making support tool.

# Components of the high-risk thrombotic blood flow environment, from cells to organs

The formation of a thrombus inside one of our arteries is the root cause for several high-mortality cardiovascular diseases, and is the underlying cause of 1 in 4 deaths worldwide. The process of the formation has been linked to the emergence of disturbed flow conditions, although the detailed characterisation of these flows and their connection to biological processes is not yet available. In this talk I will discuss our recent findings on the links between the initial phase of the formation process and the properties of the surrounding blood flow. The mechanical conditions are strongly connected to biological processes through mechanosensing components of the circulation (in particular via vWF and endothelial cells), therefore the fluid mechanical quantities of main interest are those interacting with these agonists. I will summarize the results of in silico and in vitro cell-scale measurements to give a quantitative description on these flow conditions in terms of elevated shear and elongational flows. Furthermore, I will discuss macroscale in silico and in vivo results that show how these cellular level events, that connect mechanics to biology, manifest on the scale of the disease, and provide possible ways forward to translate this knowledge to clinical practices.

LE STUDIUM LECTURES TOURS | 2022



# Mardi 13 Décembre 2022 - 18h30 Innover aujourd'hui pour guérir demain : diagnostics et thérapies personnalisés



Hôtel de Ville de Tours Salle Anatole France Place Jean Jaurès 37000 Tours

# INTERVENANTS

### **Dr Jean-Michel Escoffre**

Laboratoire Imagerie et Cerveau (iBrain) / INSERM, Université de Tours - FR

#### Prof. Damien Lacroix

Institut de Médecine In Silico (Insigneo), Université de Sheffield -UK

Conférence grand public en lien avec la conférence :

Cardiovascular Modelling: Basic Science to Clinical Translation

#### NFORMATIONS

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# **PUBLIC LECTURE**

## INNOVER AUJOURD'HUI POUR GUÉRIR DEMAIN : DIAGNOSTICS ET THÉRAPIES PERSONNALISÉS LECTURE



Jean-Michel Escoffre

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Jean-Michel Escoffre est Chargé de Recherche – Inserm au sein du laboratoire iBrain (UMR 1253, iBrain, Université de Tours, Inserm, Tours).

Depuis 2003, ses principaux intérêts de recherche se situent dans les domaines des méthodes de délivrance de médicaments et de gènes (des mécanismes aux applications cliniques). Actuellement, il travaille sur la délivrance de molécules thérapeutiques par ultrasons guidée par imagerie ultrasonore.

#### La révolution ultrasonore à l'assaut des neuropathologies

Les neuropathologies (maladies neuropsychiatriques, neurodégénératives, neurovasculaires et neurooncologiques) constituent aujourd'hui un problème majeur de santé publique et un fardeau socio-économique. Avec le vieillissement de la population, l'incidence de ces pathologies augmentera significativement au cours des prochaines années. Aujourd'hui, les traitements de ces pathologies sont soit inefficaces ou soit inexistantes. Depuis les années 1990, la communauté scientifique, et en particulier les acousticiens médicaux, développe et valide des alternatives thérapeutiques qui reposent sur l'utilisation d'ultrasons : Ultrasons focalisés de haute intensité, délivrance de molécules thérapeutiques par ultrasons, thérapie sonodynamique, radiosensibilisation ultrasonre... La révolution des traitements des neuropathologies passera-t-elle par les ultrasons ?

LE STUDIUM

Loire Velley



#### **Damien Lacroix**

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Damien Lacroix est Professeur de Génie Biomédical au Département de Génie Mécanique de l'Université de Sheffield (Royaume-Uni) et Directeur Adjoint de l'Institut de Médecine In Silico (Insigneo). Ses intérêts scientifiques se centrent sur la biomécanique avec le développement de modèle numériques qui permettent de mieux comprendre l'influence des efforts mécaniques à travers nos activités physiques sur l'évolution du développement des cellules et tissues en relation à certaines maladies comme les hernies discales, la dégradation du cartilage et la dégénération des tissues.

#### Notre jumeau numérique ou comment personnaliser diagnostics et traitements.

L'approche traditionnelle de la médicine est de traiter tous les patients de la même manière : si vous avez une fracture du col du fémur, recevez une prothèse aux formes normalisées ; si vous avez un accident cardiovasculaire, débouchons vos artères avec la mise en place d'une endoprothèse. Et pourtant nous sommes tous différents. Nos problèmes ne sont pas les mêmes et par conséquent les solutions ne devraient pas l'être non plus.

Avec le développent de modèles numériques personnalisés, nous nous dirigeons vers un futur où nous allons pouvoir déterminer de manière plus précise et spécifique pour chaque personne la prévention et le traitement d'ostéoarthrite, d'hernie discale, de fracture du fémur, d'une crise cardiaque, du diabète ou d'Alzheimer pour ne citer que quelques maladies.

Durant cette conférence nous présenterons les nouvelles technologies qui seront à même d'intégrer la complexité du corps humain pour pouvoir prévenir et guérir les maladies de plus en plus de gens partout dans le monde dans les 20 prochaines années.

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## PAST LE STUDIUM CONFERENCES

## 2022

Prof. Feng Huang, Dr Eric Robert & Dr Augusto Stancampiano

On-line Meeting on Artificial Intelligence for Plasma Science

#### 29-30 November 2022

Dr David Crottès, Prof. Christophe Vandier & Prof. Stéphane Petoud Ion channels in pathological context, new methods and diagnosis tools 21-23 September 2022

Prof. Rita Singh & Dr Pascale Crépieux Gonadotropins in the Physiopathology: Current advances in the Mechanisms of Action 14-15 September 2022

Dr Duangjai Tungmunnithum, Dr Christophe Hano & Prof. Leslie Boudesocque-Delaye NaDES for biomass valorization: new insight of a green technology 6-7 September 2022

Dr Kathia Zaleta & Prof. Patrick Vourc'h RNA therapeutics and Neuroscience 24-25 May 2022

Dr Cynthia Gabbay, Dr Brigitte Natanson & Dr Valentina Litvan

Jewishness between Latin America and Europe: Languages in Contact, Linguistic Imaginaries and Translation 16-17 May 2022

Dr Duangjai Tungmunnithum & Dr Christophe Hano

**1st Franco-Thai Seminar on Phytocosmeceutical Research and Applications** 11 May 2022

Dr Franciska Vidáné Erdő, Dr Franck

Bonnier & Prof. Emilie Munnier Skin Models in Cosmetic Science: Bridging Established Methods and Novel Technologies 7-8 April 2022

## 2021

Dr Robert Courtois De la séduction à l'agression ? La question du harcèlement 29-30 November 2021

Prof. Adrian Wolstenholme, Prof. Georg von Samson-Himmelstjerna & Dr Cédric Neveu New approaches to get around roundworms 29 November - 1 December 2021

Dr Valérie Hayaert, Hélène Jagot & Christophe Regnard Justice en scène(s) 11-12 October 2021

Dr Raphaël Cahen, Prof. Pierre Allorant & Prof. Walter Badier Law(s) and International relations : actors, institutions and comparative legislations

15-17 September 2021

Prof. Eugeen Schreurs, Prof. Philippe Vendrix & Wendy Wauters Music and Lived Religion in the Collegiate Church of Our Lady in Antwerp (1370 - 1566). A Multidisciplinary Study in a European context 2-4 September 2021

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Dr Cristina Del Rincon Castro & Dr Elisabeth Herniou 2021 International Congress on Invertebrate Pathology and Microbial Control & 53rd Annual Meeting of the Society for Invertebrate Pathology 28 June - 2 July 2021

Dr Edurne Serrano-Larrea, Dr Conchi Ania

## PAST LE STUDIUM CONFERENCES

& Dr Encarnacion Raymundo-Piñero Challenges and opportunities in materials for green energy production and conversion 15-17 June 2021

Prof. Maxwell Hincke & Dr Sophie Réhault-Godbert Innate immunity in a biomineralized context: trade-offs or synergies? 23-24 March 2021

Dr Rebecca Tharme & Prof. Karl Matthias Wantzen Managing riverscapes and flow

regimes for biocultural diversity

20-21 January 2021

### 2020

Dr Magdalena Malinowska & Dr Arnaud Lanoue Exploring the molecular diversity of grape, a source of natural ingredients 3 December 2020

Dr Jean-François Deluchey & Prof. Nathalie Champroux What are our lives worth to a neoliberal government? Capitalism, War and Biopolitics in the Pandemic Era

18 - 19 November 2020

Prof. Pieter Hiemstra & Dr Mustapha Si-Tahar Novel host- and microbiota-directed strategies for treating respiratory infections

24 - 25 September 2020

Dr Emilio Maria Sanfilippo & Xavier Rodier FAIR Heritage: Digital Methods, Scholarly Editing and Tools for Cultural and Natural Heritage 17-18 June 2020

Dr Margriet Hoogvliet & Prof. Chiara Lastraioli Spatial Humanities and Urban Experiences During the Long Fifteenth Century 11 Mai 2020

Dr Thimmalapura Marulappa Vishwanatha & Dr Vincent Aucagne Challenges and prospects in chemoselectuve ligations: from protein synthesis to site-specific conjugation 27-29 January 2020

Dr Arunabh Ghosh & Prof. Fouad Ghamouss Towards Futuristic Energy Storage; paving its way through Supercapacitors, Li-ion batteries and beyond 22-24 January 2020

## 2019

Dr Yuri Dancik & Dr Franck Bonnier Skin Models in Cosmetic Science: Bridging Established Methods and Novel Technologies

2-4 December 2019

Dr Eric Robert, Dr Jean-Michel Pouvesle & Dr Catherine Grillon International Meeting on Plasma Cosmetic Science 25-27 November 2019

25-27 November 2019

Prof. Richard Freedman & Prof. Philippe Vendrix Counterpoints: Renaissance Music and Scholarly Debate in the Digital Domain

14-16 November 2019

Prof. Manuela Simoni, Dr Frédéric Jean-Alphonse, Dr Pascale Crépieux & Dr Eric Reiter Targeting GPCR to generate life, preserve the environment and improve animal breeding: technological and pharmacological challenges

16-18 October 2019

Prof. Akkihebbal Ravishankara & Dr Abdelwahid Mellouki

## PAST LE STUDIUM CONFERENCES

Dr Mauro Simonato & Dr Jérôme Rousselet Species spread in a warmer and globalized world 18-20 October 2017

Dr Sophie Heywood & Dr Cécile Boulaire 1968 and the boundaries of childhood 12-14 October 2017

Prof. Mihai Mutascu & Prof. Camelia Turcu Globalization and growth in eurozone: new challenges

28-29 September 2017

Dr Mauro Manno & Prof. Richard Daniellou The role of glycosylation on serpin biology and conformational disease 27-29 September 2017

Prof. Salvatore Magazù, Prof. Francesco Piazza, Dr Sivakumar Ponnurengam Malliappan, Dr Emilie Munnier Recent advances in basic and applied science in cosmetics 3-5 July 2017

Dr Maria Clotilde Camboni & Prof. Chiara Lastraioli The dynamics of the relationship with the more recent past in early modern Europe: between rejection and acknowledgement 20-22 June 2017

Dr Sohail Akhter & Prof. Chantal Pichon Messenger RNA therapeutics: advances and perspectives 22-23 March 2017

Prof. Gary Gibbons & Prof. Sergey Solodukhin **GARYFEST: Gravitation. Solitons and Symmetries** 22-24 March 2017

## 2016

Dr Mohammed Ayoub & Dr Eric Reiter Antibodies Targeting GPCRs, Recent Advances and Therapeutic Challenges 24-25 November 2016

Prof. David Koester, Dr Bernard Buron & Dr Jean-Philippe Fouguet Practical Engagements and the Social-Spatial Dimensions of the Post-Petroleum Future 7-9 November 2016

Dr Jorge Gutierrez & Dr Philippe Frank

Lipids, Nanotechnology and Cancer 10-12 October 2016

Dr Ferenc Kàlmàn & Dr Éva Jakab Tóth Being Smart In Coordination **Chemistry: Medical Applications** 26-28 September 2016

Dr Satvaiit Phadke. Dr Chandrasekaran & Prof. Mériem Anouti Future strategies in electrochemical technologies for efficient energy utilisation

7-9 September 2016

Prof. Peter Bennett & Prof. Philippe Vendrix Sacred/secular intersections in earlymodern European ceremonial: Text, music, image and power 11-13 July 2016

Prof. Leandros Skaltsounis & Prof. Claire Elfakir **Olive Bioactives: applications and** prospects

4-6 July 2016

Dr Mikhail Zubkov & Dr Maxim Chernodub Condensed matter physics meets relativistic quantum field theory

## 13-15 June 2016

Prof. Brown-Grant. Dr Carmassi. Prof. Drossbach. Prof. Hedeman, Dr Turner & Prof. Ventura Inscribing Knowledge on the Page: Sciences, Tradition, Transmission and Subversion in the Medieval Book

6-9 June 2016

Prof. Gary Gibbons & Prof. Sergey Solodukhin Classical and quantum black holes 30-31 May 2016

## PAST LE STUDIUM CONFERENCES

Climate, air quality, and health: longterm goals and near-term actions 28 June 2019

Dr Wolfram Kloppmann N and P cycling in catchments: How can isotopes quide water resources management?

18 June 2019

Dr Carmen Díaz Orozco & Dr Brigitte Natanson Forging glances. Images and visual cultures in XIXth century Latin America

28-29 May 2019 -

Dr Marcelo Lorenzo & Prof. Claudio Lazzari New avenues for the behavioral manipulation of disease vectors 21-23 May 2019

Dr Agnieszka Synowiec & Dr Christophe Hano **Biological Activities of Essential Oils** 13-15 May 2019

Prof. Yiming Chen & Prof. Driss Boutat 2019 International Conference on **Fractional Calculus Theory and** Applications (ICFCTA 2019) 25-26 April 2019

Prof. Temenuga Trifonova & Prof. Raphaële Bertho On the Ruins and Margins of European Identity in Cinema: European Identity in the Éra of Mass Migration 2-3 April 2019

Dr Patrizia Carmassi & Prof. Jean-Patrice Boudet Time and Science in the Liber Floridus of Lambert of Saint-Omer 27-28 March 2019

Dr Vincent Courdavault & Prof. Nathalie Guivarc'h Refactoring Monoterpenoid Indole Alkaloid Biosynthesis in Microbial Cell Factories (MIAMi) 5-6 February 2019

Dr Denis Reis de Assis & Prof. Hélène Blasco Induced Pluripotent Stem Cells (iPSCs): From Disease Models to Mini-Organs 28-30 January 2019

## 2018

Prof. Igor Lima Maldonado & Prof. Christophe Destrieux Frontiers in Connectivity: Exploring and Dissecting the Cerebral White Matter

5-6 December 2018

Dr Marius Secula, Prof. Christine Vautrin-Ul & Dr Benoît Cagnon Water micropollutants: from detection to removal 26-28 November 2018

Prof. Guoxian Chen & Prof. Magali Ribot Balance laws in fluid mechanics, aeophysics, biology (theory, computation, and application) 19-21 November 2018

Dr Volodymyr Sukach & Prof. Isabelle Gillaizeau **Progress in Organofluorine Chemistry** 15-17 October 2018

Jens Christian Moesgaard, Prof. Marc Bompaire, Bruno Foucray & Dr Guillaume Sarah Coins and currency in the 10th and 11th centuries: issuing authorities. political powers, economic influences 11-12 October 2018

Dr Norinne Lacerda-Queiroz & Dr Valérie Quesniaux Malaria - Current status and challenges 27-28 September 2018

Dr Renaud Adam & Prof. Chiara Lastraioli Lost in Renaissance

20-21 September 2018

Prof. Abdelwahid Mellouki & Dr Véronique Daële The 6th Sino-French Joint Workshop on Atmospheric Environment

10-12 September 2018

## PAST LE STUDIUM CONFERENCES

Prof. Emre Erdem & Dr Guylaine Poulin-Vittrant Frontiers in Nanomaterials for Energy Harvesting and Storage 27-29 August 2018

Prof. Graeme Boone & Prof. Philippe Vendrix Affective horizons of 'song' in the long fifteenth century 27-28 June 2018

Prof. Bilal Haider Abbasi. Prof. Nathalie Guivarc'h & Dr Christophe Hano Modern aspects of Plant in Vitro Technology 27 June 2018

Prof. Marek Łos & Dr Catherine Grillon Stem cells & cancer stem cells: **Regenerative medicine and cancer** 11-13 June 2018

Dr Ewa Łukaszyk & Prof. Marie-Luce Demonet Transcultural Mediterranean: in search of non-orthodox and nonhegemonic universalism(s) 30-31 May 2018

Prof. Vladimir Shishov & Dr Philippe Rozenberg Wood formation and tree adaptation to climate 23-25 May 2018

Dr Ján Žabka & Dr Christelle Briois Advances in Space Mass Spectronometry for the Search of Extraterrestrial Signs of Life 16-18 May 2018

Dr Massimiliano Traversino Di Cristo & Prof. Paul-Alexis Mellet From Wittenberg to Rome, and Beyond Giordano Bruno: Will, Power, and Being Law, Philosophy, and Theology in the Early Modern Era 26-27 April 2018

Dr William Horsnell & Dr Bernhard Ryffel Neurotransmitters: non-neuronal functions and therapeutic opportunities 26-28 March 2018

Prof. Eric Goles & Prof. Nicolas Ollinger **Discrete Models of Complex Systems** 19-21 March 20182017

#### 2017

Dr Kristina Djanashvili & Dr Éva Jakab Tóth Is Multimodal Imaging an Invention with a Future? The Input of Chemistry 11-13 December 2017

Dr Emmanuel Saridakis & Dr Marc Boudvillain Structural biology and biophysics of **RNA-protein complexes** 13-15 November 2017

Prof. Franco Pierno & Prof. Chiara Lastraioli The Runaway Word. Languages and **Religious Exile in the Renaissance** 7-8 November 2017

#### 2015

Dr Gyula Tircsó & Dr Éva Jakab Tóth Medicinal flavor of metal complexes: diagnostic and therapeutic applications

7-9 December 2015

Prof. Erminia Ardissino & Dr Elise Boillet Lay Readings of the Bible in Early Modern Europe 24-26 November 2015

Prof. Kathleen Campbell & Dr Frances Westall Habitats and inhabitants on the early Earth and Mars

17-18 November 2015

Prof. Marion Harris & Dr David Giron Insects, pathogens, and plant reprogramming: from effector molecules to ecology 5-7 October 2015

Dr Aravik Hambardzumvan & Dr Sylvie Bonnamy Bioinspired molecular assemblies as protective and delivery systems 7-9 September 2015

## PAST LE STUDIUM CONFERENCES

Dr Peter Arensburger & Dr Yves Bigot Analysis and Annotation of DNA **Repeats and Dark Matter in** Eukaryotic Genomes

### 8-10 July 2015

Prof. Scott Kroeker & Dr Pierre Florian Nuclear Waste Disposal: Designing Materials For the End of Time 27-29 May 2015

Prof. Gary Gibbons & Prof. Sergey Solodukhin **Entanglement, Holography and Geometry** 17 April 2015

Prof. Kari Astala & Dr Athanasios Batakis Loire Valley Workshop on Conformal Methods in Analysis, Random Structures & Dynamics 12-16 April 2015

#### 2014

Dr Natalia Kirichenko & Dr Alain Roques Insect invasions in a changing world 17-19 December 2014

Dr Aleiandro Martinez & Dr Philippe Rozenberg Natural and human-assisted adaptation of forests to climatic constraints: the relevance of interdisciplinary approaches 18-19 November 2014

Dr Magnus Williamson & Prof. Xavier Bisaro Reconstructing Lost Spaces: acoustic, spatial, ceremonial contexts 30-31 October 2014

Dr Edouard Asselin & Dr Patrick D'Hugues Copper, a strategic metal? The present and future of resources, processing and recycling 14-15 October 2014

Dr C. Oshman & Dr G. Poulin-Vittrant Piezoelectric micro and nanostructures and their applications 25-26 September 2014

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Dr Eric Reiter 3rd International Congress on **Gonadotropins & Receptors - ICGRIII** 7-10 September 2014

Dr Robin Beech & Dr Cédric Neveu NemaTours: bringing worms together 17-18 July 2014

Prof. Gary Gibbons & Prof. Sergey Solodukhin Gravitation, Solitons & Symmetries 20-23 May 2014

Dr Charles Sennoga & Dr Ayache Bouakaz Targeted ultrasound contrast maging and drug delivery

19-20 May 2014

Dr Igor Leontyev & Dr Louis Hennet Heterogeneous catalysis: recent advances in preparation and characterization

31 March - 1 April 2014

#### 2013

Prof. Chandani Lokuge & Prof. Trevor Harris Postcolonialism now

4-5 February 2013

Dr Fabrizio Gherardi & Dr Pascal Audigane Geochemical reactivity in CO geological storage sites, advances in optimizing injectivity, assessing storage capacity and minimizing environmental impacts

25-26 February 2013

Prof. Marcos Horacio Pereira & Prof. Claudio Lazzari Vector-borne diseases : a multidisciplinary approach 8-9 April 2013

Prof. Marc Hillmyer & Prof. Christophe Sinturel Bottom-up approaches to Nanotechnology 29-31 May 2013

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