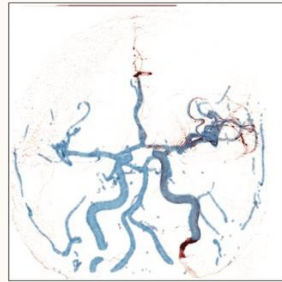


42ème Colloque

SFBT



Société Francophone de Biologie Théorique

Lundi 22 juin 2026

## Multiscale Modeling and Analysis in Biomedical Imaging

### Session 1: AI for Glioma Imaging: Data, Models, and New Learning Paradigms

#### 9h15 Pierre Fayolle (Visio from Corea)

##### Improving Virtual Contrast Enhancement Method using Longitudinal Data,

P. Fayolle<sup>2,4,5</sup>, A. Bône<sup>5</sup>, N. Debs<sup>5</sup>, P. Robert<sup>5</sup>, P. Bourdon<sup>3,4</sup>, R. Guillevin<sup>1,2,4</sup>, D. Helbert<sup>3,4</sup>

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Gadolinium-based contrast agents (GBCAs) are widely used in magnetic resonance imaging (MRI) to enhance lesion detection and characterisation, particularly in the field of neuro-oncology. Nevertheless, concerns regarding gadolinium retention and accumulation in brain and body tissues, most notably for diseases that require close monitoring and frequent GBCA injection, have led to the need for strategies to reduce dosage.

A deep learning framework is proposed for the virtual contrast enhancement of full-dose post-contrast T1-weighted MRI images from corresponding low-dose acquisitions. The contribution of the presented model is its utilisation of longitudinal information, which is achieved by incorporating a prior full-dose MRI examination from the same patient. A comparative evaluation against a non-longitudinal single session model demonstrated that

the longitudinal approach significantly improves image quality across multiple reconstruction metrics. Furthermore, experiments with varying simulated contrast doses confirmed the robustness of the proposed method. These results emphasize the potential of integrating prior imaging history into deep learning-based virtual contrast enhancement pipelines to reduce GBCA usage without compromising diagnostic utility, thus paving the way for safer, more sustainable longitudinal monitoring in clinical MRI practice.

#### 9h35 Xavier Le Guillou

##### GliomAI: building a real-world radiogenomic dataset, defining MRI preprocessing trade-offs, and evaluating multi-task learning in glioma

Xavier Le Guillou Horn<sup>0,2,4</sup>, Benjamin Beouche Helias<sup>1</sup>, Carole Guillevin<sup>1,2,4</sup>, Lucie Karayan Tapon<sup>0</sup>, Céline Thomarat<sup>1,4</sup>, Clément GIRAUD<sup>1,2,4</sup>, Mathieu Naudin<sup>1,2,4</sup>, Jean Lorain Perromat<sup>1</sup>, Brahim Borni<sup>1</sup>, Marie Coutant<sup>1</sup>, Jihan Alameddine<sup>3,4</sup>, François Lecellier<sup>3,4</sup>, Rémy Guillevin<sup>1,2,4</sup>

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The clinical deployment of AI in glioma is hindered by three major limitations: scarcity of well-curated radiogenomic datasets, lack of standardized MRI preprocessing, and poor generalization of single-task models. We report three complementary works: (i) the construction and curation of a real-world radiogenomic dataset (GliomAI), (ii) a critical analysis of MRI preprocessing strategies, and (iii) the development and evaluation of a multi-task learning (MTL) approach.

**Dataset (GliomAI):** We retrospectively collected adult patients with diffuse glioma who underwent preoperative MRI and molecular profiling (2020–2024). Imaging includes T1-weighted contrast-enhanced and FLAIR for all patients, with ADC available in the vast majority, acquired across multiple vendors and field strengths. Molecular data integrate CGH arrays, MGMT promoter methylation, and targeted sequencing, with partial availability of TERT promoter status. Data were curated, cleaned, and labeled, including derived radiogenomic variables.

**MRI preprocessing:** We conducted a structured literature review to analyze preprocessing steps (resampling, skull stripping, registration, intensity normalization). Preprocessing is approached as a trade-off depending on downstream tasks (radiomics vs deep learning), modalities, and data heterogeneity, rather than a fixed pipeline.

**Multi-task learning:** We evaluated ResNet10 and ResNet18 architectures, with and without attention masking (bounding-box-based), in both single-task and multi-task settings. Tasks included: IDH status, 1p/19q co-deletion, and grade (3 tasks), extended to six tasks by adding MGMT methylation, Ki-67 class (4 classes), and tumor type. We also assessed the impact of clinical metadata (age, sex) as model inputs.



The GliomAI dataset includes 568 patients, all with T1c and FLAIR, ~99% with ADC, and multimodal molecular profiling (CGH array, MGMT methylation, targeted sequencing), with TERT promoter status available in a subset (~250 patients). The preprocessing analysis highlights that no single pipeline is optimal: choices depend on the target task, with a critical trade-off between standardization and preservation of biologically relevant signal. MTL models demonstrated improved stability compared to single-task approaches across heterogeneous data. Attention mechanisms improved localization performance, while inclusion of clinical metadata increased performance but raised concerns about shortcut learning.

This work illustrates that robust AI in glioma requires the joint consideration of data curation, preprocessing strategy, and model design.

Rather than proposing a fixed pipeline, we highlight the importance of task-driven choices and explicit trade-offs to achieve clinically relevant and generalizable models.

## 9h55 Jihan Alameddine & Insha Asheem

### Multi-Scale Consistency Learning for Semi-Supervised Binary Glioma Segmentation on 7T MRI

Jihan Alameddine<sup>3,4</sup>, Insha Asheem<sup>2,4</sup>, Carole Guillevin<sup>1,2,4</sup>

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7T MRI provides exceptional spatial resolution for glioma delineation, but manual annotation of a single volume requires up to 12 hours of expert time, severely limiting the availability of labelled data. Furthermore, deep learning models trained on standard 3T MRI fail to generalize to 7T acquisitions due to substantial differences in image contrast, noise characteristics, and spatial resolution, making direct transfer impractical. We propose MS-CL, a semi-supervised framework that trains on annotated and unannotated 7T volumes simultaneously.

The method uses three parallel 3D U-Nets, each processing the same volume at a different resolution (0.5, 1.0, and 2.0 mm), and combines their outputs through an adaptive learned fusion. For annotated cases, a supervised loss based on Tversky and Focal criteria corrects predictions against the ground truth mask. For all cases — including unannotated ones — a cross-scale consistency loss forces the three networks to agree, providing a training signal without requiring labels.

## 10h15 Matthieu Coupet

### Structural Constraint Learning in Biomedical Imaging: Towards Annotation-Free Learning Through Latent Prediction

Matthieu Coupet<sup>2,4</sup>, Mathieu Naudin<sup>1,2,3</sup>, Christine Fernandez<sup>3,4</sup>, Carole Guillevin<sup>1,2,4</sup>

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Learning robust longitudinal representations in brain imaging remains a major challenge, particularly for gliomas, due to the limited availability of annotations and the complexity of their inter-patient variability. In this work, we propose a self-supervised learning approach based on Joint Embedding Predictive Architecture (JEPA) to model the distribution of healthy brain tissue in multi-modal MRI.

Our method learns to predict latent representations of masked regions from their spatial context, without requiring annotations. Unlike classical reconstruction approaches, the model focuses on semantic coherence between regions, enabling the capture of fine anatomical structures and inter-modal relationships. Each modality is predicted from its own context but is also informed by other contrasts, which induces cooperative interaction and strengthens the coherence of latent representations.

During inference, latent prediction errors are projected into the image space to generate anomaly maps, highlighting regions that deviate from the learned model of healthy tissue. This enables unsupervised detection of anomalies, particularly in the context of gliomas, which are characterized by diffuse alterations and heterogeneous contrasts.

We evaluate our approach using internal and public clinical databases (notably BraTS), covering several modalities of anatomical brain MRI (T1, T1ce, FLAIR), and show that latent error maps correlate with pathological regions while remaining robust to variations in intensity and contrast. Finally, we introduce an analysis of the model's training "difficulties," revealing intrinsically complex anatomical areas and paving the way for improved interpretability of self-supervised systems in medical imaging.



## Session 2: Mathematical Modeling of Brain Metabolism

### 10h55 Baptiste Zuber

#### Mathematical model of lactate shuttle between glioblastoma and neurons

Baptiste ZUBER, Laurence CHERFILS, Cyrille ALLERY

LASIE - CNRS UMR 7356, University of La Rochelle

World Health Organization classifies gliomas, brain tumors arising from glial cells, into different grades. Among grade IV gliomas are glioblastomas, the most aggressive brain tumors, for which noneffective therapies currently exist. Recent studies have highlighted the importance of lactate in tumor growth dynamics. Building on the work of Thomas Daubon and collaborators on the lactate shuttle between glioblastoma cells and neurons, we are developing a mathematical model describing the temporal evolution of tumor cell density, lactate concentration, and glutamate concentration. In this new approach, tumor cell density is divided into two compartments representing two distinct cellular phenotypes:

glycolytic cells and oxidative cells. These two cellular phenotypes influence lactate production and consumption. Variations in lactate levels, in turn, affect the concentration of and invasion of tumor cells. Once validated, this model will make it possible to test new therapies *in silico*.

In this presentation, I will describe the mathematical model and present numerical simulations reproducing the *in vitro* evolution of glioblastoma.

### 11h15 Landoline Bonin

L. Bonnin<sup>2,4</sup>, E. Lemarie<sup>3</sup>, N. Boildieu<sup>3</sup>, L. Pellerin<sup>3</sup> and C. Guillemin<sup>1,2,4</sup>

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Non-invasive classification of gliomas using multi-nucleus MRI spectroscopy: a comparative study with histological biopsy

One of the main challenges in brain cancer diagnosis is the need for an invasive procedure, a histological biopsy, which confirms the presence of a brain tumor and classifies it, that is, determines its grade and oncotype, in order to guide the treatment strategy.

At the same time, MRI is routinely used to visualize and characterize the tumor non-invasively, that is, to describe its characteristics such as size, location, and appearance.

This raises the question: why not use only non-invasive MRI to confirm and classify, in addition to characterizing, brain tumors?

This retrospective study included 25 patients with gliomas of various oncotypes and grades. The examinations were performed using a 3T high-field MRI scanner with a semi-LASER multi-nuclear spectroscopy MRI sequence.

Tumor spectroscopic profiles, including glycolytic, lactate, and acid-base parameters, as well as energy balance and proliferation markers, were then analyzed to classify brain tumors virtually and non-invasively.

Furthermore, the results of these virtual biopsies were validated by histological biopsies performed on the patients, by comparing the tumor classifications obtained via spectroscopy with those derived from histological analysis, particularly through the expression of lactate monocarboxylate transporters.

A comparative statistical analysis was then performed to evaluate the diagnostic performance of virtual biopsy compared to histological biopsy.

Our results show that virtual MRI biopsy can classify the oncotype and grade of certain brain tumors with performance comparable to that of histological biopsy.

However, future studies involving a larger number of patients and including a wider range of brain tumors are needed to validate these results.

In addition, another line of research aimed at evaluating the ability of virtual MRI biopsy to confirm the presence of brain tumors is being considered. This study will include patients with non-tumor conditions who have undergone multi-nuclear spectroscopy semi-LASER MRI as well as histological biopsy.

MRI is a promising method for non-invasively classifying and characterizing brain tumors. It could thus reduce the need for invasive biopsy in brain diagnostics.

### 11h35 Hala Ali

#### Signal Processing and Artificial Intelligence in Brain Imaging: Applications to the Detection and Monitoring of Alzheimer's-Type Dementias.

Hala Ali<sup>1,2</sup>, Pascal Bourdon<sup>1,2</sup>, Christine Fernandez-Maloigne<sup>1,2</sup>

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Magnetic resonance spectroscopy (MRS) is a non-invasive imaging technique that provides valuable biochemical information about brain metabolism and has strong potential to support the early detection of neurodegenerative diseases such as Alzheimer's disease. However, accurate metabolite quantification at clinical 3T field strength remains challenging due to spectral overlap, baseline distortions, and weak low-concentration metabolite signals. To overcome these limitations, a physics-informed deep learning approach is developed by combining neural network-based spectral analysis with prior knowledge of MRS signal formation. By improving the accuracy and interpretability of metabolite estimation, this framework aims to support the reliable extraction of metabolic biomarkers associated with neuronal integrity, neuroinflammation, oxidative stress, and neurotransmitter imbalance, contributing to early diagnosis and disease monitoring.



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## 11h55 Clément Giraud

### Separating the contributions of brain compartments with spatial statistics

Clément Giraud<sup>1,2,3</sup>, Arnaud Poinas<sup>2,3</sup>, Rémy Guillevin<sup>1,2,3</sup>

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Magnetic Resonance Spectroscopic Imaging (MRSI) enables non-invasive mapping of brain metabolism, offering valuable insights into tissue biochemistry in both healthy and pathological conditions. However, its clinical interpretation remains limited by partial volume effects, as the relatively large voxel size leads to the mixing of multiple anatomical compartments within a single measurement. This overlap results in heterogeneous metabolic signals that are difficult to attribute to specific tissue types.

To overcome this limitation, we propose a statistical framework designed to separate anatomical contributions within MRSI voxels. The method builds upon the Geographically Weighted Regression (GWR) framework, adapted to model metabolite concentrations as a function of predefined anatomical segmentations. This approach enables spatially localized estimation of tissue-specific metabolic profiles. Furthermore, to account for spatial variability in spectral quality across the MRSI grid, we introduce a progressive weighting scheme based on signal-to-noise ratio (SNR) and full width at half maximum (FWHM). This strategy replaces conventional binary thresholding, allowing for a more nuanced integration of data quality into the model.

The method was evaluated on a cohort of healthy volunteers to assess its general performance. The model demonstrated high goodness-of-fit across most metabolites ( $R^2$  ranging from 0.81 to 0.87), with lower performance observed for lactate ( $R^2 = 0.37$ ), likely due to its low concentration and higher variability in healthy tissue. In addition, the proposed weighting scheme significantly improved robustness to spectral degradation, reducing the median relative error from 3.06% to 1.11% and the maximum error from 96.6% to 36.6%. The framework was further applied to a glioblastoma case, where strong performance was observed for all metabolites ( $R^2 > 0.90$ ).

In this clinical application, the model enabled a clear separation of metabolic profiles between tumor tissue, necrotic regions, and healthy tissue. It also revealed spatially heterogeneous metabolic patterns within pathological regions, highlighting its ability to capture intra-tissue variability. These findings support the relevance of the proposed approach for improving the interpretability of MRSI data in complex pathological contexts.

Overall, this framework provides a physiologically meaningful representation of brain metabolism by explicitly accounting for partial volume effects and anatomical heterogeneity. The progressive weighting strategy enhances robustness to variable data quality, while the model's interpolation capability enables retrospective alignment of voxel-wise measurements with regions of interest. By providing both local and global quality metrics, the method ensures transparency and supports its potential integration into routine clinical workflows.

## Session 3: Imaging and Reconstruction for Diagnostic Assistance

### 14h00 Hayssam Abd Alaziz Obeid

#### Characterization of Brain Activity in Healthy Subjects Using 7 Tesla Functional MRI

Hayssam Abd Alaziz Obeid<sup>0</sup>, Guilherme Medeiros Machado<sup>0</sup>, Benoit Tremblais<sup>1,4</sup>, Frederic Ravaut<sup>0</sup>, Carole Guillevin<sup>2,3,4</sup>, Céline Thomarat<sup>2,4</sup>, Christine Fernandez-Maloigne<sup>1,4</sup>, David Helbert<sup>1,4</sup>

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This work aims to characterize brain activity in healthy subjects using 7 Tesla functional MRI data. The approach is based on estimating dynamic functional connectivity in order to capture temporal variations in brain activity during the acquisition. From connectivity matrices computed over successive time windows, a clustering method is applied to identify recurring brain states. The analysis then focuses on the temporal dimension by studying the sequence of these states, their transitions, and their organization over time. In parallel, a spatial characterization is performed for each state by analyzing the involved functional brain networks. This approach highlights that linking spatial and temporal analyses provides a better understanding of brain activity in healthy subjects and helps to better characterize how a healthy brain functions.

### 14h20 Martin Valls

#### Autoregressive-based Latent Brownian Bridge Diffusion for 3D Brain MRI Translation

Martin Valls<sup>1,2</sup>, Salif Ngom<sup>1,2</sup>, Pascal Bourdon<sup>1,2</sup>, Christine Fernandez<sup>1,2</sup>, Guillaume Herpe<sup>2,3</sup>, David Helbert<sup>1,2</sup>

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The synthesis of missing Magnetic Resonance Imaging (MRI) contrasts from limited acquisitions remains a key challenge in clinical practice, particularly for volumetric data where full 3D scans are costly and time-consuming. Recent diffusion-based approaches have shown promising results for medical image translation, but most operate on 2D slices or rely on computationally intensive 3D models, limiting their clinical usability. In this work, we introduce a unified latent diffusion framework for 3D brain MRI translation that effectively balances volumetric consistency and computational efficiency. Our approach leverages a Brownian bridge diffusion process in latent space to model global transformations between source and target volumes. To further enforce structural coherence across slices, we incorporate an autoregressive transformer that performs latent correction and explicitly captures inter-slice dependencies. This combination enables the modeling of both global



anatomical alignment and local structural consistency, while significantly reducing computational cost compared to full 3D diffusion models. We evaluate our method on clinical brain MRI datasets and compare it with state-of-the-art approaches. Results show improved anatomical fidelity, enhanced volumetric coherence, and increased robustness to inter-subject variability and acquisition artifacts. These findings highlight the potential of our framework for efficient and reliable 3D MRI synthesis in real-world clinical workflows.

## 14h40 Karim Abdoul Diallo

### MS-AttUNet: A Multi-Scale Attention U-Net for Automated Multiple Sclerosis Lesion Segmentation in 7 Tesla FLAIR MRI

Karim Abdoul Diallo<sup>1,3</sup>, Hugo Hardoy<sup>2</sup>, Mathieu Naudin<sup>2,3</sup>, Carole Guillevin<sup>2,3</sup>

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Ultra-high-field 7 Tesla (7T) MRI offers superior visualization of multiple sclerosis (MS) lesions compared to conventional 3T imaging, revealing cortical and juxtacortical lesions that are largely invisible at lower field strengths. However, automated segmentation of these lesions on 7T FLAIR images remains challenging due to pronounced B1+ field inhomogeneity, altered tissue contrast, and an extreme lesion-size distribution ranging from sub-millimeter cortical foci to large periventricular plaques within the same volume. We propose MS-AttUNet, a 3D segmentation network specifically designed for single-sequence 7T FLAIR MRI. Our method introduces three contributions: (i) Multi-Scale Attention Gates with parallel dilated branches that jointly attend to lesions across the full-size spectrum, (ii) a Size-Aware Loss that mitigates the gradient dominance of large lesions over small ones, and (iii) deep supervision on fine decoder levels to improve small-lesion delineation. We additionally describe a 7T-specific data augmentation pipeline that substantially improves generalization on this small-cohort, single-site dataset. Trained and evaluated on 92 patients acquired on a Siemens Magnetom Terra 7T scanner at the University Hospital of Poitiers (69 for training, 23 for independent testing), MS-AttUNet achieves a mean Dice Similarity Coefficient of 0.682 on 5-fold cross-validation, outperforming both Attention U-Net (0.648) and the self-configuring nnU-Net framework (0.654). On the independent test cohort, MS-AttUNet reaches DSC = 0.652, surpassing nnU-Net (0.633) while producing substantially higher voxel-wise recall (0.70), a clinically valuable property for lesion-burden monitoring.

## Session 4: Anatomical and Vascular Imaging: Geometry, Segmentation, and Flow Modeling

### 15h00 Florian Mahiddini

Florian MAHIDDINI<sup>0</sup>, Aymane EL FARDI<sup>0</sup>, Dina RAZAFINDRALANDY<sup>0</sup>, Aziz HAMDOUNI<sup>0</sup>, Dr. Alexandre SMIRNOFF<sup>1</sup>, Carole GUILLEVIN<sup>2,3,4</sup>, Céline THOMARAT<sup>2,4</sup>

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### Topological characterization of anatomical structures for neural network-based identification in laparoscopic imaging

Automatic identification of anatomical structures in laparoscopic images is a central challenge in AI-assisted surgery. In procedures such as cholecystectomy, real-time recognition of key landmarks – the cystic duct, the common bile duct, the hepatocystic triangle – is essential to prevent iatrogenic injuries. While deep learning models have shown strong segmentation performance, their robustness degrades under the large inter-individual morphological variability. Standard convolutional networks, operating on local pixel-level patterns, cannot encode the global geometric constraints that remain consistent across patients.

We propose in this work a hybrid pipeline combining persistent homology with deep neural networks for anatomical structure identification in laparoscopic images. Sublevel-set filtrations are applied to intensity fields of surgical frames, yielding persistence diagrams that encode the global topology of anatomical structures in a provably stable representation. Building on the pioneering application of TDA to endoscopic imagery by Dunaeva et al., these topological descriptors are vectorized into learnable features via persistence images and Betti curves, then fused with standard convolutional feature maps using differentiable topological layers and topology-aware loss functions.

The resulting model jointly optimizes local pixel-level accuracy and global topological consistency with the target anatomy.

We present results on real intraoperative laparoscopic datasets. Evaluation focuses on anatomical structure segmentation and detection, benchmarking our TDA-enriched architecture against pretrained CNNs. We report gains in detection accuracy, and show that topological features provide complementary information that convolutional features alone fail to capture, improving both quantitative performance and the interpretability of anatomical predictions. This work is conducted jointly by LaSIE (Université de La Rochelle) and the DACTIM-MIS team LMA (Université de Poitiers / CHU de Poitiers).



## 15h40 Yacouba Kone

### An End-to-End Geometric Pipeline for Circle of Willis Analysis from TOF-MRA

Yacouba Kone<sup>1,2</sup>, Thierry Urruty<sup>1,2</sup>

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The Circle of Willis (CoW) is a central arterial network whose configuration influences cerebral blood flow and is associated with cerebrovascular diseases.

Automated CoW analysis from TOF-MRA remains challenging due to limited resolution, partial-volume effects, and vessel truncations.

We propose a fully deterministic end-to-end geometric pipeline addressing both anatomical variant classification and quantitative vessel measurements jointly.

Starting from an existing segmentation model used without retraining, truncated distal segments are restored via constrained fast-marching.

Diameters are estimated using multi-angle FWHM profiles with PCA-based tangent estimation. Bifurcation angles are derived from geodesically averaged centerline tangents.

Variants are assigned through rules combining graph connectivity and diameter thresholds.

On the 300 annotated CROWN cases, the pipeline achieves a diameter MAE of 0.22 mm ( $r = 0.79$ ) and angle MAE of  $11.55^\circ$  ( $r = 0.54$ ), reducing prior best results by 50% and 59%.

Vessel completion raises measurement availability from 30% to 100% for M2 segments and 20% to 100% for vertebral arteries.

## 16h00 Clément Thomas

### Multimodal 2D/3D registration of TOF-MRA and X-ray cerebral angiographies, validation in a clinical cohort

Clément THOMAS<sup>1,2,3</sup>, Julien DAMBRINE<sup>2,3</sup>, Guillaume HERPE<sup>1,2,3</sup>, Mathieu NAUDIN<sup>1,2,3</sup>,

Carole GUILLEVIN<sup>1,2,3</sup>, Rémy GUILLEVIN<sup>1,2,3</sup>

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Multimodal image registration between three-dimensional Time-of-Flight magnetic resonance angiography (TOF-MRA) and two-dimensional digital subtraction angiography (DSA) remains a challenging task due to differences in dimensionality, contrast mechanisms, and acquisition geometry.

We propose a 2D–3D multimodal registration framework in which the 3D TOF-MRA volume is projected into 2D representations and subsequently aligned with biplanar DSA acquisitions (anteroposterior and lateral views). The registration relies on a deformable transformation model based on radial basis functions, allowing flexible spatial correspondence between modalities. Optimisation is performed using a gradient-based approach, ensuring efficient

convergence. The method was evaluated on a cohort of clinical data acquired in routine practice, reflecting real-world imaging conditions.

This study demonstrates the feasibility of a 2D–3D multimodal registration approach between TOF-MRA and DSA in real-world clinical conditions. These findings pave the way for future developments, particularly in the context of haemodynamic analysis derived from cerebral angiographic data.

## 16h40 Valentin Thomas

### Segmentation, registration, and modeling of blood flow in the coronary arteries

Valentin Thomas<sup>2</sup>, Clément Thomas<sup>1,2,3</sup>, Céline Thomarat<sup>1,2</sup>, Carole Guillevin<sup>1,2,3</sup>, Julien Dambrine<sup>2,3</sup>

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This work focuses on the hemodynamic modeling of coronary arteries based on medical imaging. The first step involves segmenting the vessels to extract their geometry from the images. This geometry is then used to perform a 2D/3D registration, allowing data from coronary angiography (2D) and CT scans (3D) to be aligned and a coherent representation of the artery to be reconstructed. Based on this reconstruction, a blood flow model is established, based on simplified fluid mechanics assumptions. Healthy segments are described by Poiseuille's law, while bifurcations are handled using Murray's law to distribute flow rates. The objective is to estimate pressure losses along the vascular network. Particular attention is paid to cases of stenosis, where classical assumptions are no longer valid. The work thus aims to construct a coherent model, while identifying its domains of validity and its physical limitations.



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17h00 Pr Luc Pellerin

**Astrocyte-Neuron Lactate Shuttle: Concept, Evidence and Role(s)**

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For a long time, glucose was considered the sole brain energy substrate predominantly used by neurons to satisfy all their energy needs. A new view emerged in the late 90's with the proposal of the astrocyte-neuron lactate shuttle. Originally based on *in vitro* observations, it receives over the last three decades several supporting evidence both *in vitro* and *in vivo*. The main concept proposes that astrocytes respond to signals (essentially of neuronal origin but not exclusively) by enhancing their lactate production. In parallel, active neurons take up lactate present in the extracellular space and oxidize it as their main source of energy. The process is supported by cell-specific expression of isoforms for key enzymes and transporters. Thus, astrocytes express the monocarboxylate transporters MCT1 and MCT4, the latter being adapted for lactate efflux in a glycolytic environment, while neurons express the high affinity transporter MCT2. As such, the concept does not preclude the use of glucose by neurons but questions its exclusive use as an energy source. In addition to its role as an essential energy substrate, lactate is emerging as a critical signal acting either through receptors, redox mechanisms or epigenetic regulation via lactylation. The mechanism by which one of the major neuronal signals, the excitatory neurotransmitter glutamate, triggers a glycolytic response of astrocytes has been described in detail. Thus, glutamate uptake via high affinity, Na<sup>+</sup>-dependent glutamate transporters cause a rise in intracellular Na<sup>+</sup> concentrations that will activate the glial  $\beta_2$  subunit of the Na<sup>+</sup>,K<sup>+</sup> ATPase. This stimulation is sufficient to promote glucose uptake by astrocytes. Due to their high expression of PKM2, a critical factor that determines the degree of aerobic glycolysis notably in cancer cells, astrocytes from different brain regions are geared to exhibit a strong glycolytic profile and will preferentially produce lactate, especially upon stimulation, either from extracellular glucose or from glycogen. This metabolic specialization of astrocytes can subserve different functions, such as activity-dependent energy substrate supply, regulation of excitability, modulation of synaptic transmission or glucose sensing. A range of *in vivo* experiments have demonstrated that astrocytes represent a prominent site of glucose uptake in active brain regions. Moreover, it was shown that astrocyte-derived lactate and its uptake by neurons is essential to sustain brain responses, as visualized by functional magnetic resonance imaging *in vivo*. In parallel, it was shown by different approaches and in different brain regions that astrocyte-derived lactate and its uptake by neurons is necessary to support neurogenesis as well as learning and memory processes. New evidence indicates that lactate shuttling between astrocytes and neurons is implicated in numerous central functions such sleep regulation, hypothalamic control of food intake, social interactions or decision making. Despite being often misportrayed by its detractors, the astrocyte-neuron lactate shuttle has proven its usefulness and expanded beyond neuroenergetics, becoming a leading concept in neurobiology.



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