

The unprecedented advances in modern machine learning offer the potential for faster and more accurate data-driven analyses. However, ideal algorithmic setups often fall short in practice, particularly in diverse healthcare environments: (1) Real-world processes must conform to physical laws and constraints. (2) Factors such as artifacts and variations in complex real-world systems necessitate robust and adaptive models. (3) Clinical contexts introduce further challenges, including privacy requirements, missing data, differing protocols among clinical cohorts, and varying levels of accessible healthcare resources across regions. Therefore, the successful deployment of any approach depends on both modeling *and* data: theoretical foundations ensure methodological soundness, and enhance the model's applicability; meanwhile, to achieve generalizable representations, data-driven models must rely on extensive, inclusive data.

My research lies at the intersection of Machine Learning (**ML**), Computer Vision (**CV**), Data Science (**DS**), and Medical Image Computing (**MIC**), aiming to advance foundational theories for learning and representation, and establish general frameworks that support complex real-world systems. **Motivated by practical applications**, I am dedicated to **developing robust and adaptable AI algorithms that effectively handle diverse and imperfect real-world data**, and **applying them to unlock new capabilities for reliable and accessible healthcare systems** (Fig. 1). Drawing on my interdisciplinary background and expertise, I have been focusing on:

- (A) ***ML/CV Theory & Algorithms:*** Physics-driven learning for time-varying dynamic systems.
- (B) ***Interdisciplinary MIC Research:*** Modality-agnostic foundation models for imperfect data.
- (C) ***Clinical Applications:*** Perfusion image analysis, stroke detection and diagnosis, low-field MRI.

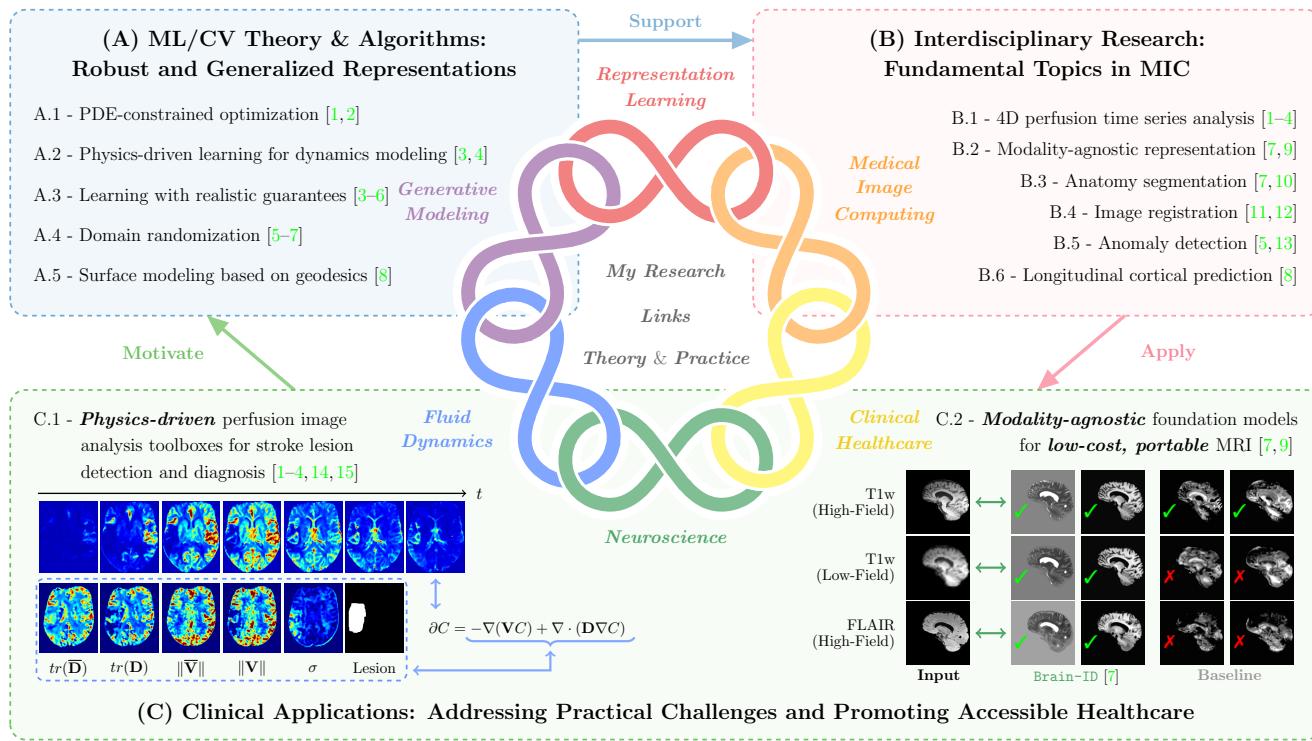


Figure 1: My research bridges theories, algorithms, and applications. **Motivated** by real-world applications, I leverage my interdisciplinary expertise in machine learning, computer vision, mathematics, and physics, to **support** various application areas. I strive for foundational approaches that provide interpretability and efficiency, ultimately **applying** them for practical challenges.

In each of the following sections, I will systematically introduce my research, and illustrate how my current and future work *cycles around* advancing ML/CV fundamentals (Fig. 1.A), enhancing MIC algorithms (Fig. 1.B), and promoting real-world clinical applications (Fig. 1.C).

Physics-Driven Formulation for Time-Varying Dynamic Systems

[Motivation] Blood vessels are vital for brain function, delivering oxygen and nutrients to neuronal tissues. Blockages, such as those occurring during a stroke, can disrupt blood flow and cause severe neurological damage. By visualizing blood flow dynamics through the injection of a contrast agent, perfusion imaging allows clinicians to detect ischemic changes early, and identify at-risk tissue, facilitating timely treatment decisions and improving patient outcomes. Traditionally, perfusion image analysis examines contrast agent dynamics per voxel, which *ignores* the spatiotemporal relations of perfusion dynamics, and *requires* tedious computation of an arterial input function (AIF) that varies greatly across different approaches.

From fluid dynamics to brain perfusion. Inspired by computational fluid dynamics, I proposed PIANO [1], the first spatiotemporal perfusion imaging approach based on advection-diffusion partial differential equations (PDEs) for characterizing blood perfusion. PIANO treats the spatiotemporal relations of brain perfusion as an *inverse optimization problem*, by estimating the *intrinsic* velocity and diffusion fields that govern the time-varying dynamics of contrast agents. In [2], I demonstrated the framework’s ability to accurately differentiate fluid flow and mass diffusion. Connecting fluid dynamics theory with perfusion imaging, PIANO unlocks tremendous new capabilities: it (1) eliminates the need for patient-wise AIF computation; (2) is *invariant* to factors affecting conventional perfusion imaging methods, such as variations in contrast agent injections over individuals; and (3) allows for a *continuous* reconstruction of the 4D perfusion process via interpretable physics fields (i.e., velocity and diffusion), which can reduce scanning time and radiation exposure. By revealing invariant physics, PIANO offers deeper insights into the distribution of brain perfusion, and enables population-based research in clinical cohort studies [15].

I proposed the first physics-driven spatiotemporal approach (Fig. 1.A.1) that estimates underlying physics from perfusion dynamics (Fig. 1.B.1), which bypasses the patient-specific, labor-intensive AIF computation in traditional perfusion image analyses (Fig. 1.C.1).

Physics-driven learning towards interpretable, rapid, and accurate diagnosis. Time is critical in patient care, especially in acute settings such as stroke. Leveraging deep learning to accelerate perfusion image analysis is compelling, yet non-trivial. High-resolution 4D perfusion images, which usually span more than 1 minute (≈ 60 time points), impose a heavy computational burden. In YETI [3], I introduced a “virtual boundary condition” to guarantee the inflow and outflow *consistencies* between spatiotemporal subdomains (patches) during training with mass transport of the entire brain volume. YETI reduces the inference time from 1 hour (with PIANO) to under 5 seconds per case, while improving anomaly detection performance by $\approx 30\%$. Collaborating with radiologists, I further developed the SONATA approaches [4, 14], which directly model regions of abnormality that can directly be used to better localize potential lesions.

I developed a series of physics-driven deep learning frameworks (Fig. 1.A.2) that achieve faster and more accurate stroke lesion detection performance (Fig. 1.C.1).

Learning with Realistic Guarantees

[Motivation] Gaps exist between the idealized theories and the unpredictability of real-world scenarios. My research is motivated by the pursuit of rigorous algorithms that incorporate real-world knowledge, to ensure their well-posedness while simultaneously improving application performance.

Regularization-free representations with realistic constraints. A physics-related framework must adhere to physics principles. For example, blood flows through the vessels of the circulatory system, maintaining its normal functions. This is a result of the incompressibility of blood, governed by divergence-free (DF) velocities. Similarly, diffusion tensors that govern mass diffusion should be symmetric positive semi-definite (SPSD). How can we learn under such realistic constraints without forcing additional regularizations that might compromise model performance? In [3], I derived regularization-free representation theorems that map the velocity vectors and diffusion tensors with DF and SPSD constraints into their *constraint-free* latent spaces through surjective projections. The introduced theorems guarantee that

models learn velocity and diffusion fields with their DF and SPD properties *by construction*. I further extended these representations to out-of-distribution scenarios [4, 14] by explicitly modeling abnormalities through disentangled representations. The proposed regularization-free learning not only ensures the well-posedness of the estimated physics fields, but also enhances stroke lesion detection performance.

I introduced representation theorems (Fig. 1.A.2) that achieve regularization-free training of deep learning models, while ensuring realistic requirements and improving performance.

Appearance-conditioned pathology encoding. Medical imaging utilizes varying modalities to visualize tissues and organs' internal structure and function for diagnosing abnormalities and treating diseases. Magnetic resonance imaging (MRI), a cornerstone of modern medical imaging, highlights specific parts of soft tissue through contrasts to assist clinicians in identifying tumor growths or other pathologies. Based on the imaging principles behind MRI, I proposed PEPSI [5], a representation learning approach for MRI that can be trained without requiring real images with pathology. PEPSI uses a synthetic data generator that encodes priors on the appearance of pathology conditioned on different MR contrasts. With minimal fine-tuning on small real datasets, PEPSI achieves $\approx 20\%$ improvements in anomaly detection, and $\approx 60\%$ reduction in training convergence time. PEPSI also demonstrates significant advantages for clinical applications, such as stroke lesion detection [6], and white matter hyperintensity segmentation [13].

Leveraging priors on the appearance of pathology, I proposed representation models for images with potential abnormalities (Fig. 1.A.3-4), which train on synthetic data and are proven effective in detecting stroke lesions and white matter hyperintensities (Fig. 1.B.5).

Towards Safe, Reliable, and Accessible Healthcare

[Motivation] The collection and quality of medical images often face practical limitations from both internal and external factors. My goal is to develop robust and generalizable foundation models that are adept at handling diverse medical data, contributing to a safe, reliable, and accessible healthcare system.

Learning from interpretable simulations. Internal factors are intrinsic to data and are usually infeasible to measure, such as noise, artifacts, physics fields that drive the perfusion dynamics, etc. In [3, 4, 14], I developed a series of advection-diffusion simulators to generate pseudo-perfusion time series, built from directional vessel trees and diffusion tensors with structural anisotropy. This allows for direct supervision of the predictions of velocity and diffusion, thereby explicitly guiding the models towards correct directions and enhancing their *interpretability*, while the underlying physics of real-world perfusion images remains unknown. Through transfer learning, models pre-trained on pseudo-perfusion processes can seamlessly adapt to real perfusion imaging datasets of limited size, while consistently achieving superior performance in stroke lesion detection compared to the state of the art.

I built time series generators to boost model interpretability and performance (Fig. 1.C.1).

Modality-agnostic foundation models. External factors also hinder the collection of medical data, e.g., privacy concerns, labor-intensive labeling, variations in clinical protocols, and the medical devices unaffordable in Low-Income Developing Countries (LIDCs). I introduced Brain-ID [7], a representation learning model trained on enriched, diverse data generated through domain randomization. Brain-ID is highly attuned to anatomical structures, while remaining resilient to variations in external imaging appearances such as imaging modalities, poses, resolutions, and artifacts. Trained entirely on synthetic data, Brain-ID seamlessly applies to real images and various downstream tasks. Importantly, its high-resolution features exhibit exceptional robustness in challenging clinical scenarios, including low-field and small-sized datasets, opening up possibilities for applications in affordable, low-field MRI, and making high-resolution image analysis accessible to LIDCs. I further proposed BrainFM [9], a modality-agnostic foundation model that establishes a unified formulation across image modalities including CT and MRI.

I proposed foundation models that are robust to image modalities, resolutions, noise (Fig. 1.A.4, 1.B.2), and are particularly effective with low-field and small datasets (Fig. 1.C.2).

Future Directions

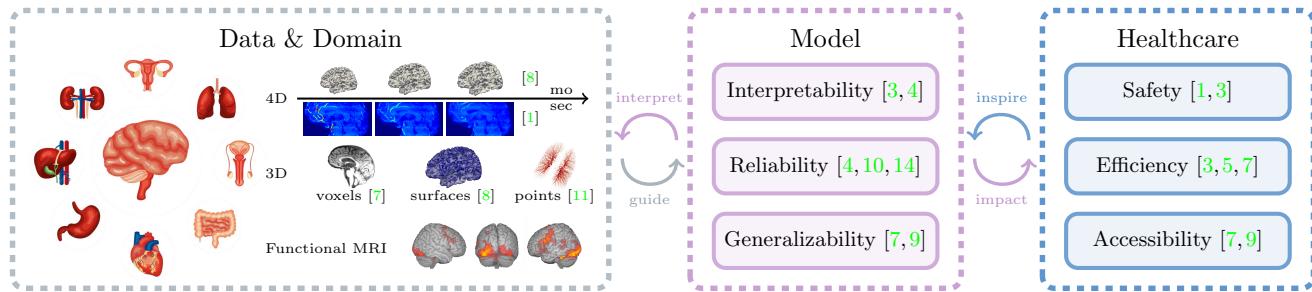


Figure 2: My future research communicates between modeling and data, to benefit modern healthcare.

Backed by data, my future research will continue to advance modern healthcare, by developing generalized frameworks that deliver valuable theories, practical algorithms, and novel real-world applications (Fig. 2).

Foundational theory of physics-driven learning for multi-modal biomedical data. My prior research introduced physic-driven formulations for dynamics modeling in the human brain [1, 3, 4, 14, 15]. With the support of data and expertise from collaborating hospitals, I am eager to delve deeper and wider into both theoretical advancements and novel applications: (1) The invertible nature of my physics-driven models for perfusion dynamics naturally opens up opportunities for reasoning about biomedical *functionality*. Aiming for more reliable models for patient diagnosis and treatment, I plan to explore more comprehensive physics-driven learning approaches that support both the inverse estimation of intrinsic physics, and the forward prediction of patient outcomes based on real-time interventions, such as combining multi-modal data from interventional DSA (digital subtraction angiography) and functional MRI. (2) As general frameworks for time-varying dynamics, my models can be adapted to various data types (e.g., meshes [8], point clouds [11]) and domains (e.g., myocardial and liver perfusion). I am particularly interested in addressing the unique and long-standing challenge of liver perfusion which, unlike perfusion in other organs, is supplied by multiple sources (i.e., hepatic artery and hepatic portal vein).

Interpretable, reliable, and generalizable foundation models. As a critical challenge in AI for healthcare, the lack of large-scale datasets hinders the widespread adoption of data-driven models, causing redundant efforts such as re-training and labor-intensive annotations. Through domain randomization, my work [5, 7, 9] eliminated the need for extensive labels, which marks an initial stride toward generalizable foundation models for medical image analysis. My goal is to address the following topics systematically: (1) How can we simulate diverse and unbiased data to bridge the domain gap between synthetic and real data, while also addressing the data bias in the real world [16]? (2) How do we distill knowledge from foundation models to new tasks/domains without requiring supervision and additional annotations? (3) How can we accurately measure uncertainties and ensure the reliability of foundation models [17]?

Safe, efficient, and accessible healthcare. (1) Safety and Efficiency. Current MRI exams typically last 45–60 minutes, which can induce anxiety and claustrophobia due to the confined space of scanners; CT exams result in radiation exposure and lifetime risk of cancer. Achieving continuous temporal modeling [1, 3], my work unlocked the possibilities of reducing scanning time while maintaining consistent physics representations, leading to safer and faster scanning. (2) Accessibility. High-powered MRI machines cost at least \$3 million, restricting MR diagnosis to only 10% of the world; patients in intensive care units (ICUs) are also too vulnerable to undergo scanning in traditional MRI machines. Low-field MRI scanners are more affordable, and often portable for use in ICUs, yet their images cannot provide the most detailed results. My research [7, 9] demonstrated the promising potential of reconstructing high-quality images from low-field MRI data. I am committed to further enhancing the diagnostic performance of low-field MRI to match that of conventional high-field MRI, from both modeling and data perspectives, thereby ultimately expanding access to MRI for patients in ICUs and LIDCs.

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