2025 Work Progress by the Imaging & Computing Lab

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At the **Imaging & Computing Lab (ICL)**, we focus on several major research directions: perfusion MRI, medial imaging analysis, and translational research in brain development and neurodegenerations. Our work spans multiple subfields, including ASL sequence development, image reconstruction, denoising, machine learning, resting-state fMRI pattern recognition, Alzheimer's disease, pain, sleep, and addiction.

In 2025, we published 15 papers—**just shy of** our average goal. Some of our core projects, such as MR pulse sequence development, are incredibly time-consuming (often requiring up to three years for a single publication), making them highly vulnerable to funding fluctuations. Compounding these challenges is a drastically shifting political environment, which has made it increasingly difficult to recruit and retain top-tier lab members. For instance, Dr. Bo Li was forced to leave the lab due to an unprecedented and entirely bizarre visa issue. Bo and I frequently worked until 10:00 PM to test our sequences; his departure has nearly halted all sequence-related projects.

Looking toward 2026, I anticipate these external challenges may intensify. While I remain cautiously optimistic about achieving significant research outcomes, I must also confront the mounting pressure of financial constraints within the lab. Below is a brief summary of the work we accomplished in our recently published papers.

Imaging Computing Lab（ICL）主要从事以下 3 个方向的研究：1.脑灌注成像，2.医学图像处理，3.脑发育与脑疾病。方向一涉及序列开发和图像重建；方向二涉及去噪、机器学习、和静息态脑功能研究。

2025 年 ICL 成员共发表论文 15 篇，大体覆盖以上三个方向，产出勉强达到平均水平。当然有个别方向是因为项目本身的原因。比如序列开发从设计到编程到测试再到收数据基本上要 2 年的时间，然后写文章发表还要 1 年左右。这方面要特别感谢李波博士经常奋战到晚上 10 点。不幸的是在我们刚看到胜利前景时，李波竟然因为签证问题被迫离开马大（一言难尽）。2026 年将继续承受基金短缺和人力不足的巨大压力。能否将压力转变成动力将是成败的关键。以下是主要论文列表及简要介绍。

Section I: MRI technique development and machine learning.

1. Li, Yiran, Paul S. Jacobs, Dushyant Kumar, Anshuman Swain, Neil Wilson, John Detre, Ravinder Reddy, and Ze Wang. "Transformer Enabled Half Z-spectrum Sampling B0 Inhomogeneity Correction for GluCEST and NOE MRI." *Chemical & Biomedical Imaging* (2025).
   Intro: Chemical exchange saturation transfer MRI is an important tool to measure low-concentration molecules in the brain but needs calibration data acquired at different settings to calibrate the quantification results caused by system imperfection. This calibration process prolongs the total scan time. We have previously proposed a deep learning-based approach to substantially shorten this process through sparse sampling and deep-learning prediction. In this follow-up study, we extended the previous work to further cut the calibration process by half and to reduce the image blurring issue using Transformers.
   化学交换饱和转移（CEST）磁共振成像是测量大脑中低浓度分子的重要工具，但需要获取不同设置下的校准数据，以校正由系统缺陷导致的定量结果。这一校准过程延长了总扫描时间。此前，我们提出了一种基于深度学习的方法，通过稀疏采样和深度学习预测显著缩短了这一过程。在本项后续研究中，我们扩展了之前的工作，利用 Transformer 架构进一步将校准时间缩短了一半，并减轻了图像模糊问题。

2. Yinghua Fu, Li Jiang, John A Detre, Ze Wang, Alzheimer's Disease Classification Using Multi-Level Graph Convolutional Neural Networks Generated from a Mutual Information-based Functional Connectome, Journal of Alzheimer’s Disease, 2025, 106(3):1021-1035. PMC12344501.
   Intro: Deep neural networks have been widely used in translational research. Motivated by the fact that different brain regions interact with each other both spatially and temporally and that brain works at different levels of graph-like networks, we designed a network to automatically extract the spatio-temporal brain features at different levels and to build a multi-level graph networks using resting state fMRI. The graph networks are built upon the connectomes calculated from the multi-level spatio-temporal features using several different distance metrics. We then applied this network to predict Alzheimer’s Disease status. Our results

show that the multi-level graph networks outperformed many other existing networks and the mutual information-based one had the best performance.

深度神经网络已广泛应用于转化医学研究。受“大脑不同区域在空间和时间上相互作用”以及“大脑在不同层级的图网络（graph-like networks）维度上运行”这两点启发，我们设计了一个网络，利用静息态 fMRI 自动提取多层级的时空脑特征，并构建多级图网络。这些图网络是基于多个不同距离度量，通过多级时空特征计算出的连接组（connectomes）构建而成。随后，我们将该网络应用于阿尔茨海默病的辅助诊断。结果表明，这种多级图网络的表现优于许多现有网络，其中基于互信息的网络效果最佳。

3. Hangfan Liu, Bo Li, Yiran Li, Manuel Taso, Dylan Tisdall, Yulin Chang, John A Detre, Ze Wang. MUSIC: Multi-coil unified sparsity regularization using inter-slice correlation for arterial spin labeling MRI denoising, Pattern Recognition Letters, 2025.

   Intro: Arterial Spin Labeling (ASL) Perfusion MRI is the only non-invasive non-contrast-based technique to measure regional cerebral blood flow (CBF) but it has a relatively low signal-to-noise ratio, which can be further reduced when the baseline CBF is low, or the transit time is long, or the echo-time is long. In this paper we developed a method to utilize the inter-channel and inter-slice correlation to denoise ASL MRI through sparse and low-rank regularization. While this method works on image slices, a new extension will zoom into voxel level, making it more powerful to include the non-local spatial low rankness to further enhance the performance.

   动脉自旋标记（ASL）灌注磁共振成像是唯一一种用于测量局部脑血流量（CBF）的无创、无需对比剂的技术，但其信噪比较低；当基线 CBF 较低、传输时间较长或回波时间较长时，信噪比会进一步降低。在本文中，我们开发了一种利用通道间和层面间相关性的方法，通过稀疏和低秩正则化对 ASL 磁共振图像进行去噪。虽然该方法目前局限于图像层的去噪，但新的扩展研究(我们称之为 LACS)将深入到体素级别，使其能够结合非局部空间低秩性，从而进一步提升性能。

4. Muhammad Nadeem Cheema, Lei Zhang, Anam Nazir, Yiran Li, John A Detre, Ze Wang. Transformer-based arterial spin labeling perfusion MRI denoising. The

Visual Computer, 2025, 1-11, https://doi.org/10.1007/s00371-025-04061-x. PMCID: PMC12366763.

Intro: This paper used Transformers to replace the convolutional neural networks (CNN) used in our first deep learning-based denoising method for arterial spin labeling perfusion MRI. The use of Transformers substantially removed the image blurring issued of the CNN based approach.

数年前我们提出了一个基于卷积神经网络的动脉自旋标记灌注磁共振成像去噪方法。一个遗留问题是卷积神经网络的输出图像会有一定程度的模糊化，从而降低空间分辨率。这篇文章中我们用了 Transformer 来去噪。结果表明这种改进能显著消除以往基于卷积网络的方法中存在的图像模糊问题。

5. Bo Li, Xiao Liang, Manuel Taso, Yulin Chang, John A Detre, Ze Wang. A single oscillating waveform-based gradient delay estimation. MRI, 2025, 119: 110367. PMC12168186.

   Intro: MRI depends on the gradients to define the precise data acquisition locations. However, there is always a mismatch between the real position and the expected location calculated based on the ideal situation. One major cause of this mismatch is the delay of the gradients after they are turned on. In this paper we proposed a method to estimate and correct such a delay. The method, which we called SODA, was extended from the one previously published by Robison et al. in MRM 2010. The major improvement is that SODA can estimate the delay using a single oscillating gradient waveform rather than two waveforms. For spiral imaging, SODA can be performed without additionally acquired calibration data.

   MRI 依靠梯度场来确定数据采集位置。然而，实际位置与预期位置之间总会存在偏差。造成这种偏差的一个主要原因是梯度场开启后的延迟。在本文中，我们提出了一种用于估计并校正这种延迟的方法。该方法被称为 SODA，是在 Robison 等人 2010 年发表于 MRM 的研究基础上扩展而来的。SODA 的主要改进在于，它可以仅使用单个振荡梯度波形来估计延迟，而无需使用两个波形。对于螺旋成像（Spiral imaging），SODA 无需额外采集校准数据即可使用。

Section II: resting state fMRI research

Resting state fMRI analysis is an ongoing research interest in our group. We continued this journey in 2025 with a substantial effort. We proposed two methods and made several translational progresses. Related work was mainly performed by Dr. Donghui Song and Dr. Gianpaolo Del Mauro.

静息态功能磁共振成像数据分析是我们关注的一个研究方向。2025 年，我们继续深耕这一领域，提出了两种新方法，并取得了多项转化医学方面的进展。相关工作主要由宋东辉博士和 Dr. Gianpaolo Del Mauro 完成。

6. Ozerk Turan, Jonathan Garner, Amal Isaiah, Thomas Ernst, Ze Wang, and Linda Chang, Fitbit-measured sleep duration in young adolescents is associated with functional connectivity in attentional, executive control, memory, and sensory networks, ***Sleep***, 2025, 48, 9, zsaf088.

   Intro: In a paper published in Lancet Child & Adolescent Health in 2022 (Yang et al., https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00188-2), we identified long-lasting adverse effects of insufficient sleep on brain, behavior, and mental health. In this work, we restudied sleep duration effects on brain connectivity using objective sleep measures acquired with smart watch. The findings are consistent with those based on subjective sleep assessment.

   在 2022 年发表于《柳叶刀-儿童青少年健康》（*Lancet Child & Adolescent Health*）的一篇论文中(Yang et al., https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(22)00188-2)，我们发现睡眠不足对大脑、行为和心理健康具有长期的负面影响。这篇发表于《睡眠》的文章是与同事 Linda Chang 教授团体合作的结果。原本计划申请到 NIH 基金之后再系统性的拓展之前的工作。但事与愿违一直没拿到任何资助。在这篇文章中我们利用智能手表获取的客观睡眠指标，重新研究了睡眠时长对大脑连接的影响。研究结果与基于主观睡眠评估所得出的结论是一致的。

7. Ze Wang. Resting state fMRI-based temporal coherence mapping. ***Imaging Neuroscience***. 2025, 3: IMAG.a.15. PMC12319858.

   Intro: Temporal correlation indicates the system's memory, the capability to integrate information across time. Human brain relies on temporally correlated activity to function. A loss of such temporal coherence may indicate deficits of high-order brain functions such as inhibition control, working memory, and

executive functions because high reliability and predictability are critical to those functions. In this paper, we proposed a new technique to quantify the long-range temporal correlation/coherence as well as the balance between correlation and anti-correlation. Based on large data from the human connectome project, we found that coherence in the fronto-parietal regions and other areas is highly reproducible. They decrease with age and positively correlate with cognitive functions. We have released the corresponding tool in https://github.com/zewangnew/ICLtbx.

时间相关性反映了系统的“记忆”能力，即跨时间整合信息的能力。人脑依靠时间相关的活动来维持正常功能。这种时间相干性（temporal coherence）的丧失可能预示着高阶脑功能的障碍，例如抑制控制、工作记忆和执行功能，因为这些功能极度依赖系统的高度可靠性和可预测性。在本文中，我们提出了一种新技术，用于量化长程时间相关性/相干性，以及正相关与负相关之间的平衡。基于人类连接组计划（HCP）的大数据，我们发现额顶叶区域及其他区域的相干性具有高度的可重复性。这些指标随年龄增长而下降，并与认知功能呈正相关。相应的计算工具可以从 https://github.com/zewangnew/ICLtbx 处下载。在同样的网址我们还提供了一系列有意思的计算工具，包括 TCM 的跨工具拓展工具。

8. Aldo Camargo, Gianpaolo Del Mauro, Ze Wang. Cross Entropy Gradient Analysis for Alzheimer's Disease Assessment, ***Journal of Alzheimer’s Disease***, 2025, in Press.

   Intro: rsfMRI-based brain entropy (BEN) mapping has emerged as a potentially useful tool to characterize irregularity or uncertainty of regional brain activity. Our previous work has demonstrated the high reliability of this new metric, its associations with neurobiological parameters, diseases, and cognitive functions, and the sensitivity to stimulant and neuromodulations. Those studies focused on regional BEN. In this study, we characterized cross-regional brain entropy. Among the many possible properties of cross entropy, we focused on the spatial gradients. Using data from healthy elderlies, patients with amnestic mild cognitive impairment and Alzheimer’s Disease, we reported a disease stage-related cross entropy gradient change, suggesting a disease progression-related reduction of cross-regional information sharing.

基于静息态 fMRI (rsfMRI) 的脑熵 (BEN) 映射已成为表征区域脑活动不规则性或不确定性的潜在有用工具。我们之前的研究已经证实了这一新指标的高度可靠性、其与神经生物学参数、疾病及认知功能的关联，以及对刺激和神经调节的敏感性。以往的研究主要集中在区域性脑熵上，而本研究中，我们对跨区域脑熵进行了表征。在跨熵的众多可能属性中，我们重点关注了其空间梯度。利用来自健康老年人、轻度认知障碍患者和阿尔茨海默病患者的数据，我们发现了与疾病恶化程度相关的渐进式跨熵梯度下降。这个发现意味着随着阿尔茨海默型的痴呆症的恶化，大脑相应部分的信息共享越来越小。

9. Gianpaolo Del Mauro, Ze Wang, rsfMRI-based Brain Entropy is negatively correlated with Gray Matter Volume and Surface Area. ***Brain Structure and Function***, 2025, 230(2):35. PMC12414511.
10. Gianpaolo Del Mauro, Yiran Li, Jiaao Yu, Peter Kochunov, Landrew Samuel Sevel, Jeff Boissoneault, Shuo Chen, Ze Wang, Chronic pain is associated with greater brain entropy in the prefrontal cortex. ***Journal of Pain***. 2025， 32：105421. PMC12414511.

    Intro: Pain is an essential survival mechanism, acting as an internal alarm system to alert the body to actual or potential tissue damage. Meanwhile, pain becomes an immense challenge when it transitions from a temporary symptom to a chronic condition. Chronic pain is a leading cause of disability worldwide, contributing to diminished quality of life, lost economic productivity, and secondary health crises such as the opioid epidemic. A big challenge in pain research is the lack of an objective marker to evaluate the subjective pain. Previous studies have assessed neuroimaging as a potential tool for assessing pain but are limited by the use of task activation and small sample sizes. Resting state fMRI has been used to identify connectivity networks related to pain but the inter-regional nature of connectivity makes it difficult to infer regional alterations. In our previous large HCP data-based study (see **https://doi.org/10.1002/jnr.25341**), we identified age-modulated pain intensity related brain entropy increase in healthy individuals. In this study, we aimed to assess chronic pain related brain entropy changes using over 30000 subjects' data from the UK Biobank. Our main findings are: 1). Chronic pain is linked to higher brain entropy in the prefrontal cortex and other brain

regions; 2) Pain widespreadness is linked to higher brain entropy in the occipital cortex; 3) Chronic headache and general diffused pain are linked to higher brain entropy. These findings suggest the use of regional brain entropy as an objective measure to assess chronic pain.

痛觉是一种至关重要的生存机制，它充当内部警报系统，提醒身体存在实际或潜在的组织损伤。然而，当疼痛从临时症状转变为慢性病症时，它便成为了一个巨大的挑战。慢性疼痛是全球范围内致残的主要原因，导致生活质量下降、经济损失，并引发阿片类药物流行等次生健康危机。疼痛研究中的一大挑战是缺乏客观指标来评估主观疼痛。以往的研究曾评估将神经影像学作为评估疼痛的潜在工具，但受限于任务激活实验设计以及样本量较小的问题。静息态 fMRI 已被用于识别与疼痛相关的连接网络，但连接指标的跨区域特性使得推断特定区域的改变变得十分困难。在我们之前一项基于 HCP 大数据的研究中（参见 https://doi.org/10.1002/jnr.25341），我们发现健康个体中存在受年龄调节的、与疼痛强度相关的脑熵增加。在本研究中，我们旨在利用来自 UK Biobank 的 3 万余名受试者数据，评估慢性疼痛相关的脑熵变化。我们的主要发现包括：1) 慢性疼痛与前额叶皮层及其他脑区的脑熵升高有关；2) 疼痛的广泛程度与枕叶皮层的脑熵升高有关；3) 慢性头痛和全身弥漫性疼痛与脑熵升高有关。这些发现表明，区域脑熵可以作为评估慢性疼痛的一个客观指标。

11. Panshi Liu, Donghui Song, Xinping Deng, Yuanqi Shang, Qiu Ge, Ze Wang, Hui Zhang. The Effects of Intermittent Theta Burst Stimulation (iTBS) on Resting-State Brain Entropy (BEN). ***Neurotherapeutics***. 2025, 22(3): e00556.
Intro: resting state fMRI-derived brain entropy (BEN) mapping has emerged as a sensitivity probe for cognitive function and disease research. One important question is whether regional BEN can be causally modulated so that we may have a way to treat disease through changing the disease-related regional BEN. We have previously published several papers supporting this possibility. In this paper, Panshi and Donghui studied the intensity effects of repetitive trans-cranial magnetic stimulation (rTMS). They used an open dataset from openneuro. An Intermittent Theta Burst Stimulation (iTBS) rTMS protocol was used to deliver stimulation. Our findings suggest that BEN is sensitive to the effects of iTBS, with different stimulation intensities having distinct effects on neural activity. Notably,

subthreshold iTBS may offer more effective stimulation. This research highlights the crucial role of stimulation intensity in modulating brain activity and lays the groundwork for future clinical studies focused on optimizing therapeutic outcomes through precise stimulation intensity.

基于静息态 fMRI 的脑熵 (BEN) 映射已成为认知功能和疾病研究中一种灵敏的探测工具。一个重要的问题是：区域脑熵是否可以被因果性地调节？如果可以，我们或许就能通过改变与疾病相关的区域脑熵来治疗疾病。我们此前已发表多篇论文支持这一可能性。在本文中，我们研究了重复经颅磁刺激 (rTMS) 的强度效应。他们使用了来自 OpenNeuro 的公开数据集，并采用间歇性爆发式磁刺激 (iTBS) 这一 rTMS 协议进行刺激。我们的研究结果表明，脑熵对 iTBS 的效应非常灵敏，且不同的刺激强度对神经活动产生的影响截然不同。值得注意的是，阈下强度的 iTBS 或许能提供更有效的刺激。这项研究突显了刺激强度在调节大脑活动中的关键作用，并为未来旨在通过精确调节刺激强度来优化治疗效果的临床研究奠定了基础。

12. Donghui Song, Xin-ping Deng, Da Chang, Ze Wang, Altered resting-state brain entropy by repetitive transcranial magnetic stimulation across the human cortex, ***Cerebral Cortex***, 35, 7, 2025, bhaf171: https://doi.org/10.1093/cercor/bhaf171
Intro: This is another paper showing the rTMS-induced regional BEN changes.

13. Donghui Song, Ze Wang. *The relationships of resting-state brain entropy (BEN), ovarian hormones and behavioral inhibition and activation systems (BIS/BAS)*. ***Neuroimage***, 312, 121226, https://doi.org/10.1016/j.neuroimage.2025.121226. 2025.
14. Donghui Song, Ze Wang. Age-dependent effects of intranasal oxytocin administration were revealed by resting brain entropy (BEN), ***Behavioral Brain Research***, 2026, Vol. 500, 115985.