

GUANGDONG AND HONG KONG UNIVERSITIES

“1+1+1” Joint Research Collaboration Scheme

粵港高校「1+1+1」聯合資助計劃

Fusing Imaging and Spatial-Temporal Complexity Measures for Early Alzheimer's Detection and Neuromodulation

HKBU PI: Changsong Zhou^{1,2,3}

BNBU PI: Jianglun Wu⁴

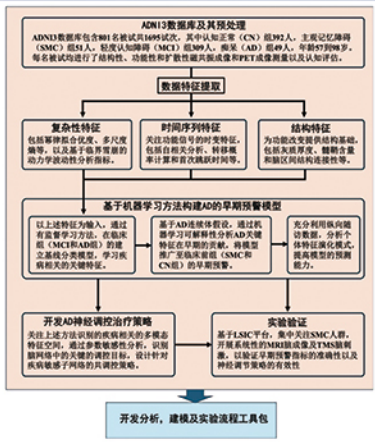
1. Department of Physics, Hong Kong Baptist University, Kowloon Tong, Hong Kong;
2. Centre for Nonlinear Studies and Beijing-Hong Kong-Singapore Joint Centre for Nonlinear and Complex Systems (Hong Kong), Institute of Computational and Theoretical Studies, Hong Kong Baptist University, Kowloon Tong, Hong Kong;
3. Life Science Imaging Centre, Hong Kong Baptist University, Kowloon Tong, Hong Kong
4. Faculty of Science and Technology, Beijing Normal-Hong Kong Baptist University

Introduction and Objectives

As populations age, Alzheimer's disease (AD) is set to become a major global health challenge, with its early stages often remaining unnoticed, leading to missed opportunities for timely diagnosis and intervention. To address this issue, this project will develop a predictive framework by integrating multimodal brain imaging with spatial-temporal complexity analysis of brain activity. We aim to:

- Establish an early warning indicator system for AD;
- Develop data-driven neuromodulation strategies;
- Verify the effectiveness of neuromodulation strategies.

Research Plan and Current Progress



Current Progress:

- **Data preprocessing:** HKBU team has started processing the ADNI data
- **Data analysis:** HKBU team has been working on brain criticality in healthy population, which will be extended to aging population; BNBU team has been working stochastic signal analysis methods.
- **Data modeling:** HKBU team has developed personalized Ising model of brain and stiff network modeling of brain network and cognition. BNBU team has developed modeling of geometric folding.
- **TMS experiment:** HKBU team has done pilot study of neuromodulation using TMS.

Representative Result 2: Stiff Network Modeling

Individual differences in cognitive abilities pose a long-standing challenge in systems neuroscience, because it remains difficult to identify which components of inter-individual brain variation are most relevant to cognition. Here we introduce **Stiff Network Modeling**, a sensitivity-based framework that decomposes large-scale brain networks into eigennetworks organized by their cognitive-performance relevance. Using fMRI data collected during working memory and language tasks from a large participant sample, we identified a topologically coherent brain network pattern whose coordinated variation is most strongly aligned with individual differences in cognitive task performance. Importantly, the same network-level representation provides a cross-scale link between functional dynamics, structural connectivity, cortical microstructure, and transcriptomic gradients. These findings demonstrate that individual cognitive abilities are organized along specific neural network patterns. Stiff Network Modeling provides an integrated framework for understanding individual differences in large-scale brain structure and dynamics. A manuscript will be submitted to Nature Neuroscience.

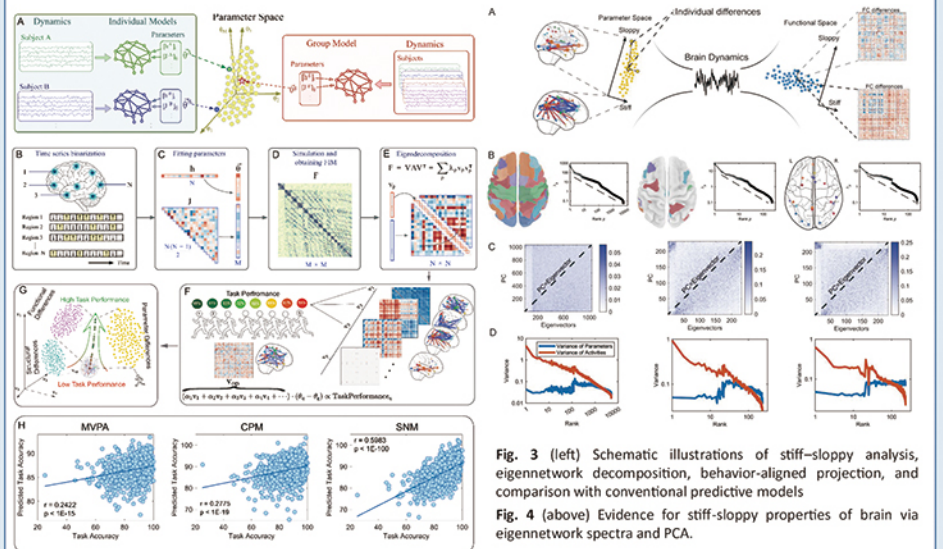
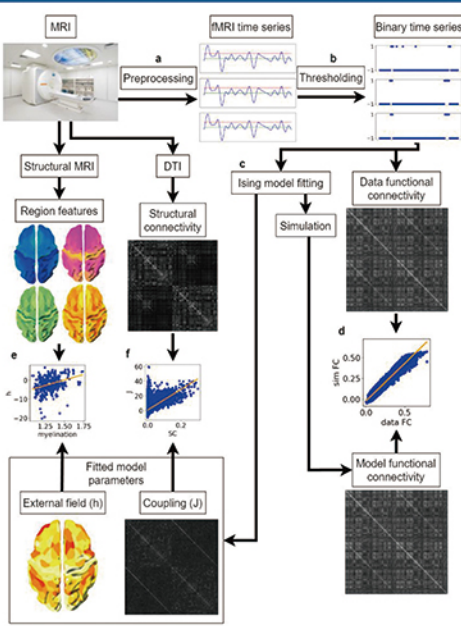


Fig. 3 (left) Schematic illustrations of stiff-sloppy analysis, eigennetwork decomposition, behavior-aligned projection, and comparison with conventional predictive models
Fig. 4 (above) Evidence for stiff-sloppy properties of brain via eigennetwork spectra and PCA.

Representative Result 1: Personalized Brain Model



How can we build individualized, biophysically interpretable models relating structure and function in the human brain? To address this, we enhance Ising model fitting for high-resolution fMRI by incorporating node heterogeneity and an optimized, two-stage Boltzmann learning approach. We systematically analyze the impact of binarization thresholds and the external field on model fit and biological relevance, examining correlations with brain structure measures like myelination. This personalized modeling bridges traditional connectomics with region-focused translational research, offering a powerful framework to understand individual differences in brain network organization and function. The work has been accepted for Publication in *NeuroImage*.

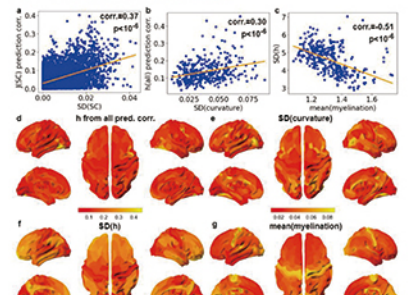
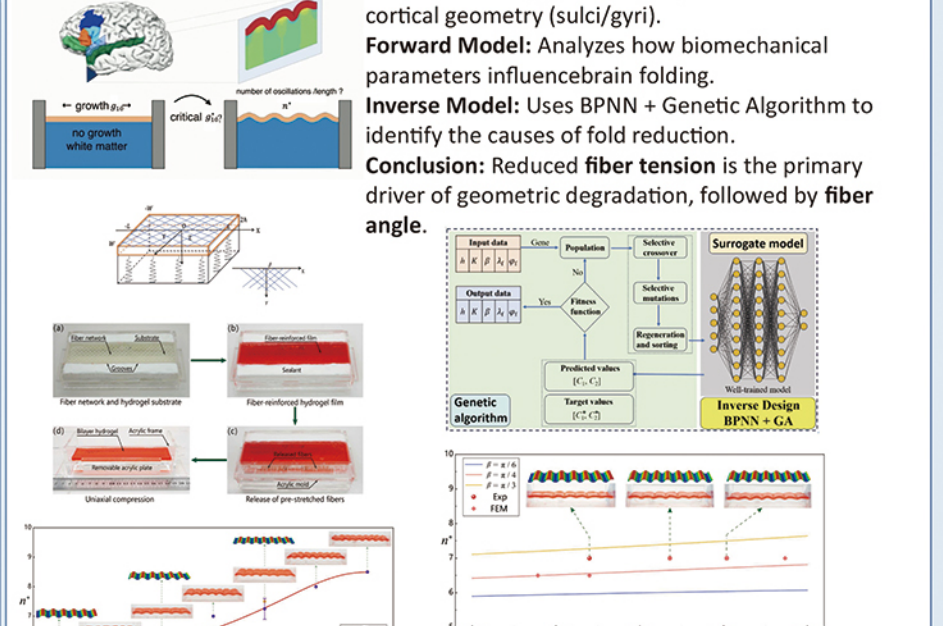


Fig. 2. Spatial trends in variability and predictability of Ising model parameters.

Representative Result 3: Geometric Modeling



Problem: AD degrades both cognitive function and cortical geometry (sulci/gyri).
Forward Model: Analyzes how biomechanical parameters influence brain folding.
Inverse Model: Uses BPNN + Genetic Algorithm to identify the causes of fold reduction.
Conclusion: Reduced fiber tension is the primary driver of geometric degradation, followed by fiber angle.

Fig. 5 (Left & Bottom Right): Folding mechanisms of the film-substrate system.
Fig. 6 (Below) Mechanisms of fold reduction in the system.

Project relevant works/outcomes:

1. Sijia Zhao, Sofia Toniolo, Qian-Yuan Tang et al., Remote digital cognitive assessment for aging and dementia using the Oxford Cognitive Testing Portal OCTAL, *Npj Digital Medicine* (published).
2. [Sijia Zhao, Rong Ye, Qian-Yuan Tang et al., Evidence for a distinct domain from 11,243 individuals across health and neurocognitive disorders, *Translational Psychiatry* (accepted).
3. Adam Craig, Sida Chen, Qian-Yuan Tang, Changsong Zhou*, Personalized whole-brain Ising models with structure-correlated node heterogeneity: optimized data binarization and improved fitting workflow, *NeuroImage* (published).
4. Christopher Gabaldon, Adrià Mulero, Rong Wang, Daniel A. Martin, Sabrina Camargo, Qian-Yuan Tang, Ignacio Cifre, Changsong Zhou, and Dante R. Chialvo, *Communication Biology* (under review).
5. Sida Chen, Siqi Yang, Zhao Chang, Taro Toyozumi, Werner Sommer, Lianchun Yu*, Qian-Yuan Tang* and Changsong Zhou*, Stiff network modeling for brain-behavior relationship: revealing behavior-sensitive dimensions of large-scale brain network underlying individual differences. *Nature Neuroscience* (to submit).
6. Xiaoyi Chen*, Danlei Zhu, Wujian He, et al., Wrinkling evolution of growing fiber-reinforced biological tissues with pre-tension, *Journal of the Mechanics and Physics of Solids* (Published)
7. Congshan Liu*, Wenxiang Tao, Xinyu Wang, Bin Wu, Xiaoyi Chen*, Chaofeng Lyu*, Prescribed wrinkling pattern evolution in growing film substrate biological systems by prestrain, *Acta Mechanica Sinica*, (accepted).
8. E. Pruchnicki, Xiaoyi Chen, Y. Gao, V. Eremeyev, Homogenization and dimensional reduction for nonlinear multilayered plates including biological growth when the plate thickness and the size of the heterogeneities are not of the same order of magnitude, *Mathematics and Mechanics of Solids* (accepted).
9. Xiaoyi Chen*, Hao Wang, Xinyu Wang, et al., Mechanics-informed inverse design for wrinkle control in fiber-reinforced bilayers, *Materials Today Communications* (accepted).
10. Yuhui Guo, Jianglun Wu*, Space-time fractional stochastic partial differential equations driven by Levy white noise, *Journal of Mathematical Analysis and Application* (under review)

