



## **ISTBI** Newsletter

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## BMC Medicine: Cellular transcriptional alterations of peripheral blood in Alzheimer's disease

Alzheimer's disease (AD), a progressive neurodegenerative disease, is the most common cause of dementia worldwide. Accumulating data support the contributions of the peripheral immune system in AD pathogenesis. However, there is a lack of comprehensive understanding about the molecular characteristics of peripheral immune cells in AD. In a study published on 29 August 2022 in BMC Medicine, Prof. Xing-Ming Zhao at ISTBI and his research team found the cellular transcriptional alterations of peripheral blood in Alzheimer's disease.

To explore the alterations of cellular composition and the alterations of intrinsic expression of individual cell types in peripheral blood, the researchers performed cellular deconvolution in a large-scale bulk blood expression cohort and identified cell-intrinsic differentially expressed genes in individual cell types with adjusting for cellular proportion. The researchers detected a significant increase and decrease in the proportion of neutrophils and B lymphocytes in AD blood, respectively, which had a robust replicability across other three AD cohorts, as well as using alternative algorithms.

The differentially expressed genes in AD neutrophils were enriched for some AD-associated pathways, such as ATP metabolic process and mitochondrion organization. The researchers also found a significant enrichment of protein-protein interaction network modules of leukocyte cell-cell activation, mitochondrion organization, and cytokine-mediated signaling pathway in neutrophils for AD risk genes including CD33 and IL1B. Both changes in cellular composition and expression levels of specific genes were significantly associated with the clinical and pathological alterations. A similar pattern of perturbations on the cellular proportion and gene expression levels of neutrophils could be also observed in mild cognitive impairment (MCI). Moreover, an elevation of neutrophil abundance in the AD brains was noticed. The study revealed the landscape of molecular perturbations at the cellular level for AD. These alterations highlight the putative roles of neutrophils in AD pathobiology.

#### » Full Article:

Li, Y., Sahakian, B.J., Kang, J. et al. The brain structure and genetic mechanisms underlying the nonlinear association between sleep duration, cognition and mental health. Nat Aging 2, 425-437 (2022). https://doi.org/10.1038/s43587-022-00210-2

#### [About the Authors]





#### Prof. Xing-Ming Zhao

Xing-Ming Zhao is Professor at Institute of Science and Technology for Brain-Inspired Intelligence, Fudan University; Deputy Director of Key Laboratory of Computational Neuroscience and Brain-Inspired Intelligence, Ministry of Education; Executive director of Zhangjiang International Brain Bank; Shanghai Youth Science and Technology Star; candidate of Shanghai Pujiang Talent Program; IEEE Senior Member; IEEE SMC TCon Systems Biology Co-Chair; IEEE SMC

Shanghai Chapter Chair; ACM SIGBio China Vice Chair; CCF Senior Member; Deputy Director of Professional Committee of Bioinformatics and Artificial Life, Chinese Association of Artificial Intelligence; Standing member of Technical Committees of Bioinformatics, China Computer Federation; Director of Technical Committees of Bioinformatics, Shanghai Computer Society; etc.



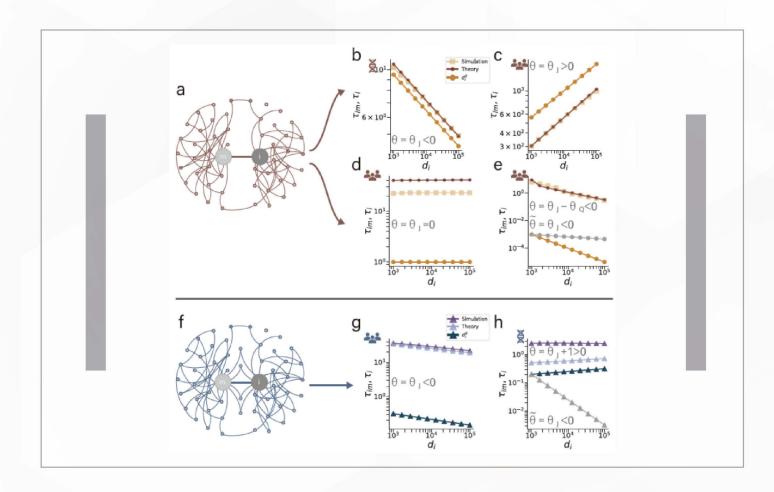
# Biological Psychiatry: Depression associated with a 51% higher risk of dementia

On 5 September 2022, the collaborated research between Prof. Jianfeng Feng and Dr. Wei Cheng at ISTBI collaborated and Prof. Jintai Yu at Huashan Hospital, "Depression, Depression Treatments, and Risk of Incident Dementia: A Prospective Cohort Study of 354,313 Participants", was in Biological Psychiatry.

In this prospective cohort study, 354,313 participants aged 50 to 70 years were recruited from the UK Biobank between 2006 and 2010, and were followed-up until 2020, with a total of 4,212,929 person-years. The researchers initially studied the effect of depression on dementia incidence across four subgroups characterized by courses of depressive symptoms. Then, 46,820 participants with depression diagnose were further categorized into the treated and untreated groups. The researchers compared the risks of dementia among different depression treatments groups in all participants that depressed as well as four courses of depressive symptoms by performing survival analyses.

Results indicated depression was associated with a 51% higher risk of dementia, among which the increasing, chronically high and chronically low courses were associated with

framework predicts genuine scaling exponents, no matter if the propagation dynamics is dominated by hubs, by the path length, or by basic motifs. For paths with large average degree, as abundant in social and other empirical networks, the prediction of propagation time using asymptotic scaling as proposed by existing literature may be orders of magnitude off, as the scaling exponent may fall in an unrelated universality class. They have overcome this inconsistency by introducing two topology-independent exponents that quantify the universality class of the local response dynamics on networks.



#### △ Response time scaling for local propagation.

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#### » Full Article:

Bao, X.#, Hu, Q.#, Ji, Peng\* et al. Impact of basic network motifs on the collective response to perturbations. Nat Commun 13, 5301 (2022). https://doi.org/10.1038/s41467-022-32913-w

#### [About the Authors]





Peng Ji received his Ph.D. in theoretical physics from Humboldt University of Berlin in 2015 with Professor Jurgen Kurths, and then worked at the Potsdam Institute for Climate Impact Research in Germany. He joined Fudan University at the end of 2016 as a young researcher, and became a professor in 2021. He has won honorary titles such as Pujiang Talent (2017), Shanghai University Distinguished Professor-Oriental Scholar (2018), Oriental

Scholar-Tracking Program (2021). His current research interests include human brain and zebrafish imaging analysis, neural network models, nonlinear dynamics analysis of complex networks, etc. He has published a series of articles in journals such as Nature Physics, Nature Communications, Physics Reports, Physical Review Letters as the first or corresponding author in recent years.

increased dementia risk while no association was found in the decreasing course. Compared to those who were depressed but untreated, receiving depression treatments corresponded to a hazard ratio of 0.7. Among the three detrimental courses, treatments for increasing and chronically low symptoms of depression were associated with a 42% and 29% lower risk of dementia while the reduction effect for chronically high symptoms was insignificant.

The negative association between depression treatment and incident dementia was significant in the increasing and chronically low course, highlighting the necessity of timely interventional strategies before depression progress to a chronically severe state.

#### » Full Article:

Yang, Liu, Yue-Ting Deng, Yue Leng, Ya-Nan Ou, Yu-Zhu Li, Shi-Dong Chen, Xiao-Yu He, et al. "Depression, Depression Treatments, and Risk of Incident Dementia: A Prospective Cohort Study of 354,313 Participants." Biological Psychiatry, 2022. https://doi.org/10.1016/j.biopsych.2022.08.026.

#### [About the Authors]





### Prof. Jianfeng Feng

Jianfeng Feng is Chair Professor at Shanghai National Centre for Mathematic Sciences, Dean of Institute of Science and Technology for Brain-inspired Intelligence and Dean of School of Data Science at Fudan University. He has been developing new mathematical, statistical and computational theories and methods to meet the challenges raised in Brain Science and mental health researches. Recently, his research interests are mainly in big data analysis,

mining for neuroscience and brain diseases and developing brain-inspired algorithms and theory. He was recognized as one of the Chinese Most Cited Researchers in Neuroscience of 2019 and one of the Chinese Most Cited Researchers in Mathematics of 2020 and 2021 by Elsevier. He was also named the 2020 World's Top 2% Scientists by Stanford University.

#### [About the Authors]





#### Dr. Wei Cheng

Wei Cheng is now a Young Principle Investigator at Institute of Science and Technology for Brain-Inspired Intelligence, Fudan University. He obtained a Ph.D. in Applied Mathematics from Fudan University, supervised by Prof. Jianfeng Feng. Dr. Cheng completed postdoctoral fellowship at the Department of Statistics of Fudan University from Jul, 2016 to April, 2018, during which he visited University of Warwick, UK as exchange scholar for one year. Dr. Cheng is

the recipient of National Scholarship for Doctoral Students, The National Natural Sciences Foundation of China, Shanghai Sailing Program Research Grant, among many other awards and grants in the last five years.



# Nature Communications: Impact of basic network motifs on the collective response to perturbations

Dr. Peng Ji at ISTBI, Prof. Jan Nagler at Frankfurt School of Finance and Management et al. studied how basic network motifs determine the perturbation spreading in networks. The study was published on 8 September 2022 in Nature Communications.

They have developed analytical tools that allow to capture the impact of simple undirected motifs on the system dynamics. The developed framework not only helps disentangle joint effects but provides a deeper understanding of the interplay of self-dynamics, interaction dynamics, and topological properties. This analysis suggests a radical departure from the previously proposed concepts of distance-limited propagation and degree-limited propagation. In distance-limited propagation the response time scaling is said to be dominated by the propagation path length but not by the edge density along the path. Vice versa, for degree-limited propagation the response time scaling is said to be dominated by the mean degree, but not the propagation path length. They have demonstrated by independent methods that when the propagation is drastically slowed, or accelerated, that may not necessarily result from edges or hubs but from cycles, in particular triangles. This analysis is based on a network decomposition into independent edges and edges as part of motifs. The developed

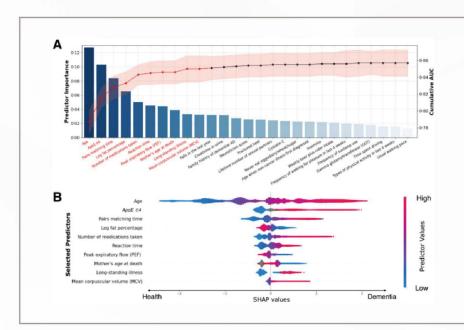


## eClinicalMedicine: Predict dementia ten years in advance

Recently, research teams lead by Prof. Jianfeng Feng at ISTBI and Prof. Jintai Yu at Huashan Hospital developed an ML-based UKB-DRP model with solid predictive power for incident dementia and AD within five, ten, and much longer years, which can be used to identify individuals at high risk of dementia and AD in the general population. The study was published in eClinicalMedicine on 23 September 2022.

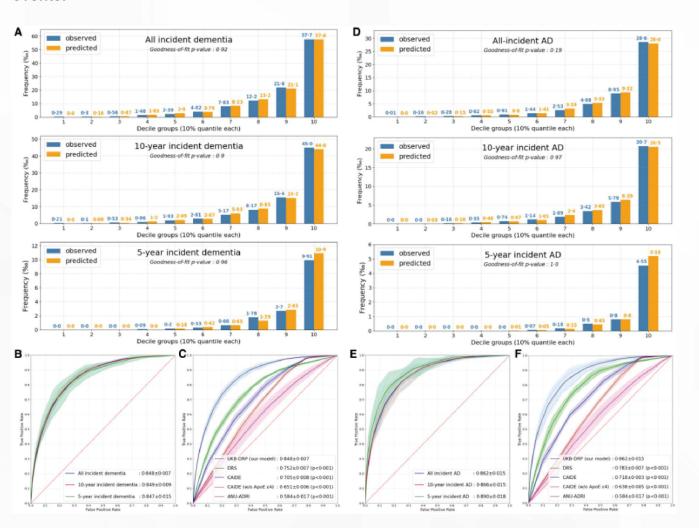
In this longitudinal population-based cohort of the UK Biobank (UKB), 425,159 non-demented participants aged 40-69 years were enrolled from 22 recruitment centers across the UK between March 1, 2006 and October 31, 2010. During a median follow-up time of 11.9 years, 5,287 participants developed dementia. The researchers implemented a data-driven strategy to identify predictors from 366 candidate variables covering a comprehensive range of cognitive, biological, behavioral, genetic and environmental factors and determined top ten predictors for model development.

A novel UKB dementia risk prediction (UKB-DRP) model comprising ten predictors including age, ApoE ε4, pairs matching time, leg fat percentage, number of medications taken, reaction time, peak expiratory flow, mother's age at death, long-standing illness, and mean corpuscular volume was established.



△ Predictor selection and SHAP visualisation of modelling on all incident dementia population

The UKB-DRP model showed superior prognostic accuracy compared with previously published CAIDE, DRS, and ANU-ADRI. The model achieved AUCs of around 0.85 in predicting dementia incidence within five, ten, and much longer years. The model's performance was better in AD predictions with all AUCs more than 0.86. In addition, the model was well-calibrated with predicted probabilities perfectly plotted against the observed proportions of events.



△ Performance of the UKB-DRP and existing prediction scales.

Compared with the models established based on variables obtained from elaborate neuropsy-chological tests, expensive whole genome sequencing (WGS), invasive lumbar puncture, or brain positron emission tomography (PET) imaging, the UKB-DRP model is solely based on the easily accessible predictors which can be collected from quick questionnaires, physical measures, and simple blood tests. Therefore, this prediction model can be widely applied to medical institutions at different levels.

The web application was made accessible online at <a href="https://jiayou0907.shinyapps.io/UKB-DRP-Tool/">https://jiayou0907.shinyapps.io/UKB-DRP-Tool/</a>.



#### △ A stylized representation of the UKB-DRP tool

#### » Full Article:

You J, Zhang YR, Wang HF, Yang M, Feng JF, Yu JT, Cheng W. Development of a novel dementia risk prediction model in the general population: a large longitudinal population-based machine-learning study. eClinicalMedicine. 2002. doi:10.1016/j.eclinm.2022.101665



# 13 projects approved for funding by the National Natural Science Foundation of China (NSFC)

On 8 September 2022, the National Natural Science Foundation of China (NSFC) announced the funding decisions of 2022. ISTBI has 13 projects approved for funding support, which is a record high number, receiving a total funding amount of 8.68 million yuan. This year, ISTBI's overall application success rate is 48%, with the General Program success rate being 66% and the Young Scientists Fund success rate being 50%.

○ General Program supports scientists engaged in basic research on self-selected topics to conduct innovative research and promote a balanced, coordinated and sustained development of all disciplines.

Successful Applicants (4): Qiang Luo (Research Professor), He Wang (Research Professor), Shanfeng Zhu (Research Professor), Chun-Yi Lo (Young Principal Investigator)

◇ Young Scientists Fund supports young scientists to freely select their research topics within the funding scope of NSFC to conduct basic research, particularly focus on fostering the ability of young scientists to independently undertake research projects and conduct creative research, stimulates their creative thinking and trains backup talents for basic research.

Successful Applicants (6): Jingqi Chen (Young Principal Investigator), Hao Li (Young Research Associate), Zijian Hao (Postdoc Fellow), Yuchao Jiang (Postdoc Fellow), Yingnan Nie (Postdoc Fellow), Yijie Zhao (Postdoc Fellow)

○ The Research Fund for International Young Scientists (RFIS-I) supports international scientists with foreign citizenship who are ready to conduct basic research in China's mainland.

Successful Applicants (2): Anna Maria Cuscó Martí (Postdoc Fellow), Joern Alexander Quent (Postdoc Fellow)



Fudan "Innovation China" Center for Brain-inspired Intelligence (International Collaboration and Innovation) approved by China Association for Science and Technology

In September 2022, the China Association for Science and Technology announced the creation of the first 194 "Innovation China" centers in three categories, including International Collaboration and Innovation, Industry-Academia Collaboration, and Business Incubation. Applied by ISTBI and recommended by the Shanghai Association for Science and Technology, Fudan "Innovation China" Center for Brain-inspired Intelligence (International Collaboration and Innovation) is launched, being one of the 16 approved International Collaboration and Innovation centers across China and the first "Innovation China" center in Shanghai.

Fudan "Innovation China" Center for Brain-inspired Intelligence (International Collaboration and Innovation) specializes in frontier research in brain-inspired artificial intelligence, intelligent diagnosis and treatment, autonomous driving, and intelligent robots. Through attracting world-top experts and constructing an international research collaboration platform, the Center aims to make breakthroughs in collaborative research, talent recruitment and training, transfer and transformation of scientific and technological achievements on a global level.

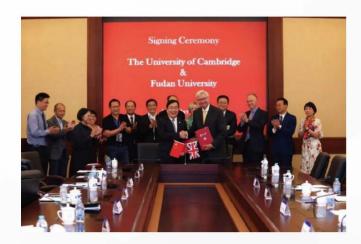


#### [ISTBI Global and Industrial Partnerships]

ISTBI forms a close network of global partnerships with prestigious higher education institutions and research institutions around the world, such as the University of Cambridge, the University of Oxford, King's College London, the University of Sydney, Charité Universitäts Medizin Berlin, and the Institute of Physical and Chemical Research (Riken), to join efforts in aspects of strategic alliance, collaborative research, academic exchange, and talent training.

In 2018, jointly applied by ISTBI, the University of Cambridge and the University of Oxford, the Overseas Expertise Introduction Center for Discipline Innovation of Computational Neuroscience and Brain-Inspired Intelligence ("111 Center") was approved by the Ministry of Education of China, serving as an avenue for bringing in oversea experts and supporting technology transfer. Over the past five years, ISTBI researchers published over 200 high-level papers with international collaborators.





△ Signing Ceremony: Memorandum of Understanding between Fudan University and the University of Cambridge (Left)



△ Signing Ceremony: Memorandum of Understanding between Fudan University and the University of Sydney (Right)

Towards the goal of improving international influence and reputation in the field of brain-inspired intelligence, ISTBI actively supports its faculty to carry out international collaboration activities, organizing 44 international academic events such as conferences, seminars, and workshops, sponsoring hundreds of incoming and outgoing international academic visits, and hosting over a hundred visiting lectures.

Since its establishment, ISTBI has invested in recruiting top scholars from around the world to build an international multidisciplinary research team. The foreign faculty has had 5 Distinguished Professors, 2 Distinguished Research Professor, 1 Honorary Professor, 5 Adjunct Professors, 2 Young Principle Investigators and 6 Postdoc Fellows, including recipients of the APS (Association for Psychological Science) William James Fellow Award, the Brain Prize, the Humboldt Prize, the Royal Society Wolfson Research Merit Award and other international awards, and scientists who are selected into the Highly Cited Researchers, the World's Top 2% Scientists, the Highly Cited Chinese Researchers, and other internationally notable ranking lists.

ISTBI has been working in partnerships with leading enterprises, including State Grid Power, USTC, and SAIC Motor, continuously improving the pattern of innovative academia-industry collaboration. Since 2020, ISTBI has established a joint AI laboratory with FAW (Nanjing) and a joint autonomous driving research center with Mogo Auto to accelerate frontier research and technology transfer.



△ Launching Ceremony: Fudan-FAW Joint Laboratory of Artificial Intelligence



△ Launching Ceremony: Fudan-Jihua Joint Laboratory of Artificial Intelligence Algorithms

## ISTBI "Current Progress in Brain and Intelligence Science" Symposium

On 28 October, PIs at the ISTBI gathered together to share their current research progress in brain and intelligence science at a one-day symposium.







Speakers	Title
Jianfeng FENG	Towards precision medicine: Subtyping brain disease
Xiao CHANG	Brain dysconnetivity in schizophrenia and reinforcement-related disorders
Jie ZHANG	Dynamic brain at different spatial scales
Jingqi CHEN	Uncovering the missing genetic links of neuropsychiatric disorders—ongoing efforts from big-data to bench
Deniz VATANSEVER	Cognitive maps and the neural mechanism of mental navigation
Miao CAO	Understanding the neurodevelopment of language processing
Yuwei JIANG	Accessing the hierarchy of linguistic and non-linguistic processing in different levels of consciousness
Zhuoyi SONG	Combining modelling and inference to investigate functional neural information processing
Wei CHENG	Neurophysiological subtypes of schizophrenia
He WANG	Imaging-based quantification of vascular morphology and flow
Deniz VATANSEVER	Round-table discussion I

Speakers	Title
Gunter SCHUMANN	The Horizon Europe Project environMENTAL: Introduction and first results
Valerie VOON	The promise of neuromodulation: from modifiable biomarkers to proof-of-concept to clinical therapeutic outcomes
Luis Pedro COELHO	The role of small proteins of the global
Shouyan WANG	Intelligent and digital intervention: From technology to clinical application

#### ISTBI "Current Progress in Brain and Intelligence Science" Symposium

On 29 October, the ISTBI Early-Career Researcher Symposium took place in the East Wing of Guanghua Towers. Whilst our past academic events were mostly organized by the PIs, this symposium was organized by the postdoctoral fellows, aiming to promote idea exchange among early-career researchers and instigate cross-disciplinary collaboration within the institute.

Speakers	Title
Prof. Tielin Yang	Causal relationship between brain imaging-derived phenotypes and human diseases
Dr. Chao Xie	Shared Neural Basis Underlying Comorbid Psychopathology: Systematic Investigation of a Neuropsychopathological NP Factor
Dr. Anna Cuscó	Exploring the pet gut microbiome within a large-scale investigation of animal gut metagenomes
Dr. Jörn Alexander Quent	Neuroimaging of mental navigation using virtual reality environments
Dr. Kaixiang Zhuang	The brain's control-default hubs support diverse functional interaction for creative thinking
Dr. Yunman Xia	Development of functional connectome gradients during child-hood and adolescence
Prof. Jiayi Zhang	Visual cortex encodes timing information in humans and mice
Dr. Yang Qi	Computing with correlated neural variability: neural coding, learning, and inference
Dr. Ronghui You	DeepMHCII: A Novel Binding Core-Aware Deep Interaction Model for Accurate MHC II-peptide Binding Affinity Prediction
Dr. Ming Yang	A Brief Guide of Business Venture in China: from Laboratory to Market
Dr. Rencheng Zheng	Automatic Liver Tumor Segmentation on Dynamic Contrast Enhanced MRI Using 4D Information: Deep Learning Model Based on 3D Convolution and Convolutional LSTM
Dr. Svetlana Ugarcina	Challenges in metagenomic annotation of antibiotic resistome

In addition to the presentations, 20 posters of research progress contributed by other postdoctoral fellows were showcased at the venue. Attendees voted for the Best Presentation Awards and the Best Poster Awards, recognizing the followings:



Best Poster Awards: Dr. Qing Ma, Dr. Chun Shen, Dr. Xinran Wu

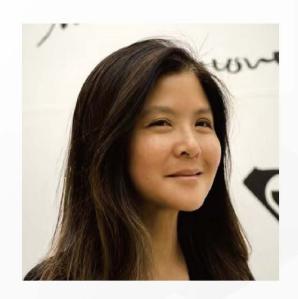


Best Presentation Awards: Dr. Yang Qi, Dr. Yunman Xia, Dr. Kaixiang Zhuang



#### Scientist at ISTBI

## Distinguished Research Professor: Valerie Voon



Valerie Voon is a Distinguished Professor at the ISTBI, Fudan University and is a Medical Research Council Senior Clinical Fellow at the University of Cambridge. Her research group spans Cambridge and Shanghai focusing on interventional experimental psychiatry identifying modulation-responsive biomarkers towards precision neuromodulation. Her work is theory-driven anchored on cognitive neuroscience - the functional bridge between brain and behaviour - particularly impulse control and flexibility and its relationship with addiction cues and negative emotions.

She uses multimodal approaches including imaging, neuromodulation, physiology, pharmacological challenges, and computational modeling. She has published over 200 articles including in high level journals such as Neuron, Lancet Neurology, Molecular Psychiatry, Biological Psychiatry and Brain. She is the President of the British Neuropsychiatry Association.





△ Brain-inspired Intelligence Themed Forum - 2021 World Artificial Intelligence Conference



