



中国科学院深圳先进技术研究院
SHENZHEN INSTITUTES OF ADVANCED TECHNOLOGY
CHINESE ACADEMY OF SCIENCES



深港脑科学创新研究院
SHENZHEN-HONG KONG
INSTITUTE OF BRAIN SCIENCE

中国科学院深圳先进技术研究院脑认知与脑疾病研究所

用心建设湾区 用脑造福世界
Greater Bay Area, One World, One Brain!

中国科学院深圳先进技术研究院

Shenzhen Institute of Advanced Technology Chinese Academy of Sciences

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2025年度报告

2025 ANNUAL REPORT 年度报告

中国科学院深圳先进技术研究院脑认知与脑疾病研究所
The Brain Cognition and Brain Disease Institute
Shenzhen Institutes of Advanced Technology Chinese Academy of Sciences

中国·深圳



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深港脑科学创新研究院
SHENZHEN-HONG KONG
INSTITUTE OF BRAIN SCIENCE

深圳先进院

SIAT

中国科学院深圳先进技术研究院

Shenzhen Institutes of Advanced Technology
Chinese Academy of Sciences



中国科学院深圳先进技术研究院（简称“深圳先进院”）成立于2006年，由中国科学院、深圳市人民政府和香港中文大学三方共建，是中国科学院在粤港澳大湾区布局建设的国家战略科技力量。

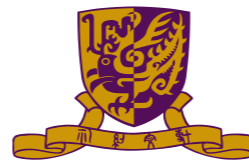
作为深圳首个国立科研机构，深圳先进院创新构建了以科研为主的集科研、教育、产业、资本为一体的微型协同创新生态系统，坚持聚焦科技创新需求，高效推进科学研究与产业发展一体设计、一体推进。深圳先进院聚焦“四个率先”和“两加快一努力”目标任务，全力以赴抢占科技制高点，重点布局医学成像设备与科学仪器、合成生物与生物制造、集成电路材料与封装三大主攻方向以及脑机接口与智能系统、脑解析与灵长类模型、医疗器械与医疗装备、智能医药与健康数据、先进材料与碳中和等多个新兴方向，不断孕育科技新动能。

探索国家需求、科技前沿与产业发展三者最大公约数，深圳先进院积极承担重大科技任务、产出重大科研成果、开展重大成果转移转化，形成出成果、出人才、出经验的良好机制。着力打通科技制高点到科技成果转化融合点的“两点一线”路径，抢占科技竞争和未来发展的制高点。

面向国家重大需求方面，深圳先进院牵头新建医学成像科学与技术系统全国重点实验室、定量合成生物学全国重点实验室，参与共建集成电路材料全国重点实验室、脑认知与类脑智能全国重点实验室，全力抢占科技制高点；面向经济主战场方面，牵头组建国家高性能医疗器械创新中心、国家生物制造产业创新中心，不断推动产业技术的升级迭代。

面向世界科技前沿方面，深圳先进院牵头建设深圳先进电子材料国际创新研究院、深港脑科学创新研究院、深圳合成生物学创新研究院三大基础研究机构，以及深圳合成生物研究、脑解析与脑模拟两大科技基础设施，均已投入使用，为建设粤港澳大湾区科技创新中心和综合性国家科学中心提供有力支撑。

展望未来，深圳先进院将始终聚焦主责主业，持续深化改革，加快突破关键核心技术，努力攻克世界级科学难题，为推进高水平科技自立自强、在国际竞争中赢得主动作出新的更大贡献。



Introduction to SIAT

Who We Are

Founded in 2006, The Shenzhen Institutes of Advanced Technology (SIAT), an affiliated institute of the Chinese Academy of Sciences (CAS), was established through a collaboration among CAS, the Shenzhen Municipal Government, and the Chinese University of Hong Kong (CUHK).

SIAT's mission is to enhance the innovation capacity of the equipment manufacturing and service industries in the Guangdong-Hong Kong-Macao Greater Bay Area (GBA), promote the development of emerging industries with proprietary intellectual property, and evolve into a world-class industrial research institute.

IBT Interdisciplinary Research Fields

Focusing on the multidisciplinary integration of Information Technology and Biotechnology, SIAT comprises nine affiliated institutes and over 50 research centers:

1. Shenzhen Institute of Advanced Integration Technology (SIAIT) – CAS and CUHK
2. Institute of Biomedical and Health Engineering (IBHE)
3. Institute of Advanced Computing and Digital Engineering (IACDE)
4. Institute of Biomedicine and Biotechnology (IBB)
5. Institute of Brain Cognition and Brain Disease (IBCBD)
6. Institute of Synthetic Biology (iSynbio)
7. Institute of Advanced Electronic Materials (IAEM)
8. Institute of Technology for Carbon Neutrality (ITCN)
9. Institute of Scientific Instrumentation (under development)

Currently, SIAT is leading the establishment of two national key laboratories, three national innovation centers, and 79 provincial and municipal innovation platforms.

Youthful yet Exceptionally Skilled Research Team

Over the past 19 years, SIAT has made significant strides in talent development, academic research, and technology commercialization. By December 2025, the institute had grown to 2,340 staff members and 2,388 graduate students. The average age of the staff is 34, with 795 having overseas study or work experience, and 73 scholars have been recognized among the top 2% of global scientists. Additionally, more than 100 distinguished foreign professors serve as part-time visiting or chief scientists at SIAT.

Transforming Research into Impact

SIAT is committed to transforming scientific and technological advancements. It has incubated 2,030 companies and holds equity stakes in 386 of them. These enterprises primarily focus on six key sectors: next-generation information technology, new energy, synthetic biology, artificial intelligence, new materials, and high-end medical devices.

Establish An Open Innovation Ecosystem for Global S&T

SIAT's international cooperation is anchored in the GBA while extending its reach globally, fostering an ecosystem for international scientific collaboration. It boasts extensive partnerships with overseas entities across 53 countries and regions, encompassing over 520 programs with 98 institutions. SIAT has established close collaborations with many globally renowned universities and research institutions, particularly in fields such as translational medicine, novel energy storage, biomaterials, synthetic biology, and brain science. These partnerships have led to the creation of long-term collaborative platforms, underscoring the effectiveness of SIAT's international engagement.

Hub for Scientific Innovation and Reform

Consistently serving as a hub for innovation, SIAT integrates various strengths and innovative policies under the dual initiatives of the GBA and the pioneering demonstration zone of socialism with Chinese characteristics to promote interdisciplinary collaboration.

Looking ahead, SIAT aims to leverage the collaborative strengths of the CAS, the Shenzhen Municipal Government, and the Chinese University of Hong Kong to create an open and innovative platform that welcomes scientists and researchers from all sectors and countries, fostering seamless collaboration and cutting-edge scientific research.

所长致辞

A MESSAGE FROM THE DIRECTOR

王立平 所长
Director Liping Wang

深圳先进院脑认知与脑疾病研究所 所长
深港脑科学创新研究院 创院院长



大脑被誉为宇宙间最复杂的物体。脑科学研究是当前国际科技热点，也是我们理解自然和自身的“终极前沿”，习近平总书记在全国科技创新大会、两院院士大会、中国科协第九次全国代表大会上的讲话中指出：“脑连接图谱研究是认知脑功能并进而探讨意识本质的科学前沿，这方面探索不仅有重要科学意义，而且对脑疾病防治、智能技术发展也具有引导作用。”

在深圳市政府的大力支持下，基于深圳先进院的优势资源，脑认知与脑疾病研究所于2016年正式成立。2019年，深圳先进院与香港科技大学共同牵头，汇聚深港多方脑科学研究力量，建设了深港脑科学创新研究院，这是深圳市以脑科学领域合作为模版，推动深港科技协同创新共同体建设的新起点和新示范。

深港脑院经过这几年的发展，紧密围绕国家脑科学的战略布局聚集了深港两地五家单位优势的脑科学研究力量，形成了分可独立作战，聚可合作攻关的70多个研究团队，已发表在国际顶级期刊的SCI论文超900篇；深港脑院还牵头成立了全国首家脑科学产业创新中心，推动成立了总规模11.6亿元的脑科学产业基金，用于支持脑科学与脑技术产业的转化与应用。

未来，脑所/深港脑院将以服务粤港澳大湾区建设、社会主义先行示范区建设及综合性国家科学中心的建设为目标，通过提升区域脑与健康科学领域的源头创新能力、人才培养能力、产业推动能力、科研支撑能力和战略咨询能力，为将我国建设成为世界主要科学中心和创新高地做出实质贡献。

The human brain is hailed as the most complex entity in the Universe. Brain research is a global focus of science and technology, representing humanity's ultimate quest to understand nature and itself.

Supported by the Shenzhen Municipal Government and leveraging SIAT's strengths, the Brain Cognition and Brain Disease Institute (BCBDI) was founded in 2016. In 2019, SIAT and HKUST co-led the establishment of the Shenzhen-Hong Kong Institute of Brain Science (SHKIBS), a benchmark for Shenzhen-Hong Kong sci-tech collaboration in brain science.

Aligned with national brain science strategies, SHKIBS has integrated strengths from five Shenzhen-Hong Kong institutions, forming over 70 teams capable of independent and collaborative research. It has published over 900 top-tier SCI papers, initiated China's first "Industrial Innovation Center for Brain Science and Technology", and launched a 1.16-billion-RMB industry fund to boost tech transformation.

Moving forward, BCBDI and SHKIBS will serve the Greater Bay Area, Pilot Demonstration Zone and National Science Center. By enhancing capacities in original innovation, talent cultivation, industrial promotion, research support and strategic consultation, they will contribute to building China into a global sci-tech hub.

脑认知与脑疾病研究所

Brain Cognition and Brain Disease Institute

中国科学院深圳先进技术研究院脑认知与脑疾病研究所（以下简称“脑所”）于2014年11月16日揭牌并在2016年11月19日正式去筹成立。

脑所下设脑功能图谱与行为研究中心、脑认知与类脑智能研究中心、神经发育与退行性脑疾病研究中心、内尔神经可塑性诺奖实验室、神经系统疾病转化研究中心和脑信息中心等6个研究中心。

脑所定位于融合整体观和还原论方法，围绕既定“脑发育、退行与行为”“脑体互作”“脑机接口与脑科学新技术”“临床前研究与临床转化”等四个研究方向，利用神经科学新技术及跨物种动物模型，通过对脑状态与机体调控的研究，为类脑智能以及脑疾病早诊优治新策略研究提供源头理论和技术支撑。

目前，依托中国科学院深圳先进技术研究院，脑所牵头建设了深圳市基础研究机构“深港脑科学创新研究院”，深圳市重大科技基础设施“脑解析与脑模拟重大科技基础设施”，以及深圳市脑科学技术产业创新中心。

脑所目前已形成一支多学科交叉汇聚的脑科学科研团队，人员规模500余人。团队聚集了包括德国科学院院士及诺贝尔生理学或医学奖获得者等9人，国家杰青、长江、国家重点引进人才工程专家及“四青”人才等骨干63人。团队骨干分别来自于斯坦福大学、剑桥大学、哈佛大学、加州大学伯克利分校、杜克大学等著名学府，背景横跨生物、物理、化学、医学、信息学等学科，国际影响力与日俱增。

成立至今，获批国家省部地方等各级项目超950项，获批金额近19亿元；共发表包括*Nature*、*Science*、*Cell*、*Nature Biotechnology*、*Nature Neuroscience*、*Nature Communications*、*Neuron*、*Molecular psychiatry*等国际顶级期刊在内的SCI高水平论文约900篇，申请专利近1300项，获授权专利350余项。

脑所积极开展境内外创新深度合作：已开拓与香港科技大学，加拿大不列颠哥伦比亚大学、法国INRA、德国洪堡大学等的科研合作与人才培养；正在实施中国科学院脑科学国际大科学合作培育计划；筹划“一带一路”国际科学组织联盟项目等。

The Institute of Brain Cognition and Brain Diseases (BCBDI), Shenzhen Institutes of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS), was officially founded on November 19, 2016, and now has a research team of over 500 members.

BCBDI has six research units and focuses on four research directions: Brain Development, Degeneration & Behavior, Brain-Body Interaction, Brain-Computer Interface and New Technology Development, Preclinical Research & Clinical Translation.

Affiliated with SIAT (CAS), BCBDI spearheads the development of three key Shenzhen-based platforms: Shenzhen-Hong Kong Institute of Brain Science, Shenzhen Brain Science Infrastructure, and Shenzhen Industrial Innovation Center for Brain Science and Technology. Based on the above platforms, BCBDI dedicates itself to brain health.

Since its establishment, BCBDI has secured more than 950 research projects at national, ministerial, provincial and municipal levels, with a total approved funding of nearly 280 million USD (approx. 1.9 billion RMB).

BCBDI has expanded and deepened international collaborations in research and talent training with HU Berlin (Germany), INRA (France), HKUST (Hong Kong, China), MIT (USA) and UBC (Canada).

脑所架构

BCBDI Organization



深港脑科学创新研究院

Shenzhen-Hong Kong Institute of Brain Science

深港脑科学创新研究院（简称“深港脑院”）是依托深圳先进技术研究院（以下简称“先进院”）建设的非独立法人机构，是深圳市布局的十大基础研究机构之一，也是首家深港两地共同建设的深圳市基础研究机构。深港脑院于2019年1月正式授牌成立，香港科技大学校长叶玉如担任深港脑院名誉院长，先进院脑研究所所长王立平研究员担任深港脑院院长。深港脑院由先进院与香港科技大学共同牵头建设，其他共建单位包括南方科技大学、深圳大学、北京大学深圳研究生院。深港脑院将以国家重大需求、创新驱动发展为牵引，以解析大脑基本原理和脑疾病发病机制为核心目标，以多物种动物模型及脑结构和脑功能图谱解析建设为核心任务，汇聚粤港澳大湾区生物、医疗健康领域的科研与产业优势资源，建设成为在国际上具有重要影响力、在国内学术领域占据一席之地的脑科学基础研究及产业转化基地，助力深圳成为国家脑健康、生物医药领域创新驱动发展的中坚力量。



脑设施简介概况

Shenzhen Brain Science Infrastructure

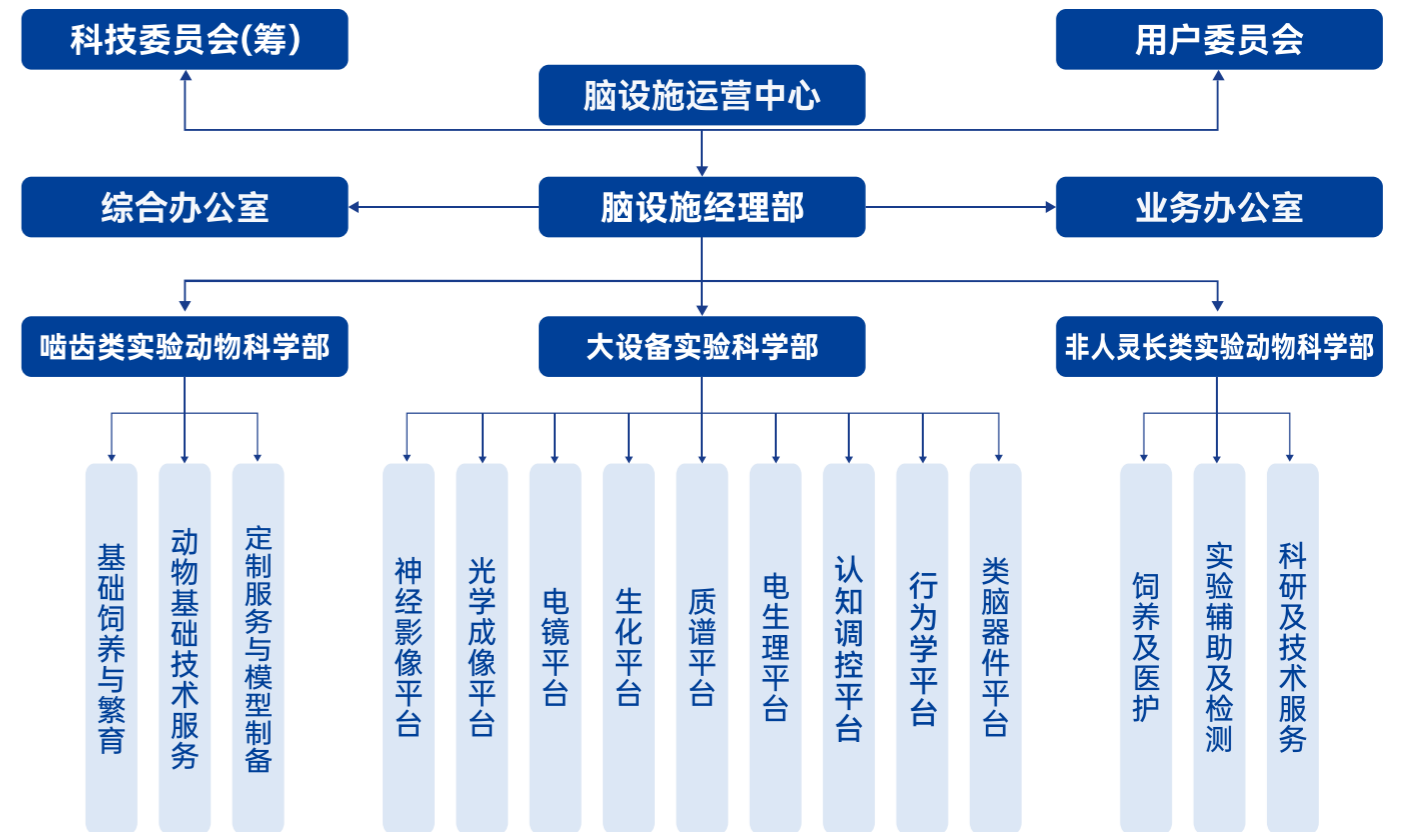
深圳市脑解析与脑模拟重大科技基础设施（脑设施）于2020年获深圳市发展和改革委员会批复，由中国科学院深圳先进技术研究院牵头建设，为光明科学城启动区的重点建设项目。脑设施总建筑面积5万余平方米，包含脑编辑、脑解析和脑模拟三大技术模块，具备跨物种动物模型的制备以及跨尺度神经结构功能解析的能力。



依托中国科学院深圳先进技术研究院脑认知与脑疾病研究所（脑所）和深港脑科学创新研究院（深港脑院），脑设施已组建了三大科学部（非人灵长类实验动物、啮齿类实验动物、大设备）和九大技术平台，致力于支撑深圳综合性国家科学中心和粤港澳大湾区国际科技创新中心的建设，将为脑科学与类脑智能领域的基础和临床前研究、产业生态打造提供全面的技术支撑，并实现信息和资源的高效共享。

脑设施组织架构

Organizational Structure of Shenzhen Brain Science Infrastructure



建设进展 (三科学部+九大平台)



深圳市脑科学技术产业创新中心

Shenzhen Industrial Innovation Center For Brain Science And Technology

深圳市脑科学技术产业创新中心（简称“脑创中心”）是由深圳市和光明区政府投资建设，由中国科学院深圳先进技术研究院及深港脑科学创新研究院负责技术支撑和运营管理，核心任务是构建一个以创新企业孵化服务为引领、共享技术平台为依托、耐心资本为支撑以及资源整合应用示范为特色的未来产业高质量培育平台。脑创中心聚焦脑科学、脑技术、脑健康、脑疾病及脑智能领域和技术产业转化发展中的关键痛点，建立起“需求方出题，科技界答卷”的创新合作模式，实现“创新、创业、创投、创意”四创合一融合发展格局，致力于成为以脑与生命健康产业为特色的服务全国、辐射全球的新质生产力集聚高地。



自2022年正式运行以来，脑创中心成功建立了创新链、产业链、金融链、人才链、服务链、政策链“六链融合”的高效创新发展生态体系，并始终秉持“以人为本”理念耕耘前沿产业，通过“破圈、赋能、联通”增加有效科技供给，以“共享、创新、服务”推动脑科学未来产业高质量发展。

脑创中心核心业务高质量发展

- > 孵化器进驻超**58**家，毕业**8**家
- > 孵化器企业历史融资超**15**亿元
- > 推动成立**1.6**亿元种子基金，**10**亿元脑科学产业基金
- > 对外输出**5**个城市（重庆、杭州、嘉善、德清、芜湖）



重庆 脑科学与类脑智能中心项目对接合作引进

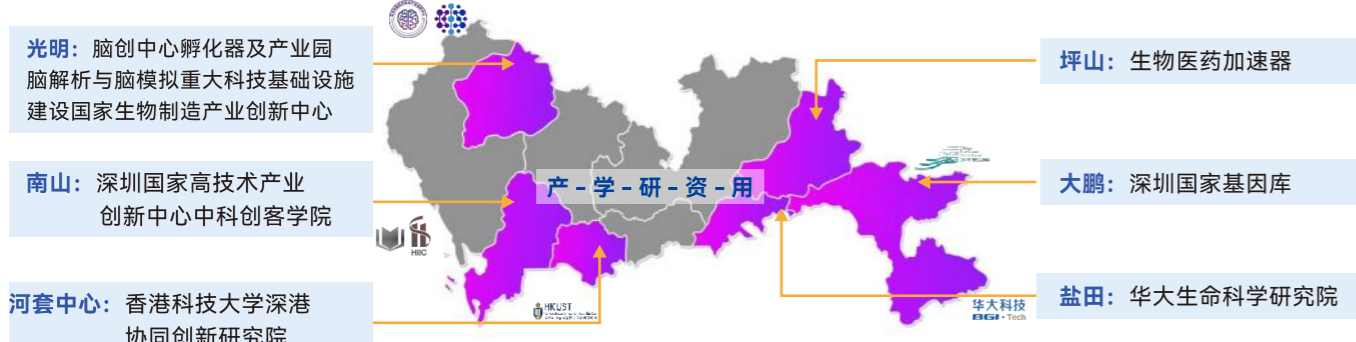
杭州 未来科技城“深-杭”双城联动赋能产业发展

嘉善 共建引才工作站

德清 与中国老龄基金会共同打造银发经济新示范

芜湖 携脑科学企业赴芜湖开展座谈会

脑科学与脑健康“一极多中心”产业布局



成果转化服务

携智入驻
产业投资基金
共享技术平台
专项政策支持

临床医学转化

深圳市第二人民医院
深圳市儿童医院
深圳大学总医院
中山大学附属第七医院

行业科技赋能

科普教育
智慧社区
睡眠市场
电子烟市场

BCBDI RESEARCH CENTERS

中心介绍

- Center for Brain Connectome and Behavior
- Center for Cognitive Science and Intelligence Technology
- Center for Neurodevelopmental and Neurodegenerative Diseases
- Shenzhen Neher Neural Plasticity Laboratory
- Translational Research Center for the Nervous System
- Interdisciplinary Center for Brain Information

脑功能图谱与行为研究中心

Center for Brain Connectome and Behavior

愿景/Mission:

致力推动AI辅助的动物行为学检测以及与自由移动小动物活体成像与电生理记录以及与光遗传/化学遗传融合技术，并用以解析调控本能行为的神经环路机制，脑认知原理，并探索脑体互作的神经调控规律及其在稳态失衡下的变异特征，为神经系统疾病与其他系统共病提供新的干预靶点。

We are committed to advancing AI-assisted animal behavioral analysis by integrating in vivo imaging and electrophysiological recording in freely moving small animals with optogenetic and chemogenetic approaches. Leveraging these cutting-edge technologies, we aim to elucidate the neural circuit mechanisms underlying innate behaviors and the fundamental principles of brain cognition. In parallel, we investigate the neural regulatory frameworks governing brain-body interactions and their dynamic alterations during homeostatic disruption, with the ultimate goal of identifying novel intervention targets for neurological disorders and their comorbidities with other physiological systems.

研究方向/Key research areas:

- 本能行为的脑连接图谱解析与新技术开发
- 中枢与外周器官互作的结构与功能解析
- 脑疾病与其他系统疾病共病机制研究
- Developing New Technologies to decode Brain Atlases and Connectomics underlying Innate Behaviors
- Structural and Functional Basis of Brain-Body Interactions
- Mechanisms of Brain Disorders and Comorbidity with Peripheral Systems

正高级/副高级 Principal/Associate Investigators



脑智能中心

Center for Cognitive Science and Intelligence Technology

愿景/Mission:

本中心专注于神经科学与智能技术之间的跨学科研究。我们的目标是通过运用神经科学的理论方法，信号处理，机器学习和材料科学，了解特定认知过程背后的大脑功能以及它们的功能异常如何导致脑部疾病。并为此开发调节大脑活动和恢复受损神经功能的技术工具和方法。

Our center focuses on the interdisciplinary research between neuroscience and intelligence technology. Employing the theories and methods of neuroscience, signal processing, machine learning and material science, we aim to understand the functions of the brain underlying specific cognitive processes and how their malfunctioning can lead to brain disorders. With this aim, we develop technological tools and methods for modulation of brain activities and restoration of impaired neural functions.

研究方向/Key research areas:

- 认知的神经环路和计算机制的研究
- 用于脑部疾病的新型调节工具和机器识别的开发
- 神经信号处理和类脑健康技术的研究
- Neural Circuits and Computational Mechanisms of Cognition
- Development of Novel Intervention and Machine Recognition for Brain Diseases
- Neural Signal Processing and Brain-Inspired Health Technologies

正高级/副高级 Principal/Associate Investigators



神经发育与退行性脑疾病研究中心

Center for Neurodevelopmental and Neurodegenerative Diseases

愿景/Mission:

探讨神经发育和神经退行性疾病的病理生理机制，并开发用于诊断、治疗和预后的新型生物标志物和治疗干预措施。

To explore the pathophysiological mechanisms underlying neurodevelopmental and neurodegenerative diseases, and to develop novel biomarkers and therapeutic interventions for diagnosis, prognosis and treatment.

研究方向/Key research areas:

- 神经元发育和可塑性的分子基础
- 神经发育和神经退行性疾病的病理生理学
- 诊断和预后的生物标志物以及新的干预策略
- Molecular Basis of Neuronal Development and Plasticity
- Pathophysiology of Neurodevelopmental and Neurodegenerative Diseases
- Biomarkers for Diagnosis and Prognosis, and Novel Intervention Strategies

正高级/副高级 Principal/Associate Investigators



陈宇
Yu Chen



陈岳文
Yuewen Chen



高亮
Liang Gao



洪伟
Wei Hong



叶涛
Tao Ye



李寅虎
Yinhu Li



Bernhard Schaefer



屈雪琪
Xueqi Qu

神经系统疾病转化研究中心

Translational Research Center for the Nervous System

愿景/Mission:

开发神经环路研究、基因递送和理解新的分子机制的关键技术和工具，开发生物标志物和靶向药物，及基于系统生物学的方法等，以满足神经科学研究、神经系统疾病诊断和治疗的需要。

Developing key technologies and tools for researches on neural circuits, delivery of genes, understanding new molecular mechanism, developing biological markers and targeted drugs, systems biology-based approaches, etc., to meet the needs of neuroscience research, diagnosis and treatment of nervous system disorders.

研究方向/Key research areas:

- 基于脑科学和神经系统疾病的诊/防/治需求为导向，开发多组学研究技术、解析神经环路的示踪工具和疾病细胞基因治疗的关键递送载体
- 围绕神经退行性疾病解释致病机制，推进靶向药物和神经调控干预、成像检测等技术研究
- 研发并建立用于监管和评价基于病毒载体的细胞基因治疗制剂的新技术方法和标准体系
- Guided by brain science and neurological diseases: development of multi-omics technologies, neural circuit tracing tools and key delivery vectors for cell and gene therapies
- Elucidating pathogenic mechanisms of neurodegenerative diseases and advancing research on targeted drugs, neuromodulatory interventions and imaging technologies
- Developing and establishing novel technology and system for the supervision and evaluation of viral vector-based cell and gene therapy

正高级/副高级 Principal/Associate Investigators



徐富强
Fuqiang Xu



叶克强
Keqiang Ye



孙毅
Yi Sun



张志珺
Zhijun Zhang



刘北明
Pakming Lau



曹罡
Gang Cao



廖春雨
Chunyu Liao



贾凡
Fan Jia



王华东
Huadong Wang



刘青
Qing Liu



杨欣
Xin Yang



肖珂
Ke Xia



钱政江
Zhengjiang Qian



景波
Bo Jing



林坤章
Kunzhang Lin

深圳内尔神经可塑性诺奖实验室

Shenzhen Neher Neural Plasticity Laboratory

愿景/Mission:

内尔神经可塑性实验室致力于研究脑疾病的神经可塑性机制，并利用现代神经科学的先进技术来开发潜在的治疗靶点。

Neher Neural Plasticity Laboratory is committed to study the neural plasticity mechanisms of brain diseases and develop potential therapeutic targets by using state-of-art technologies in modern neuroscience.

研究方向/Key research areas:

- 神经可塑性机制研究
- 突触可塑性在学习和记忆中的作用
- 药物成瘾的神经可塑性机制
- 生理和病理条件下疼痛回路的神经可塑性
- Mechanistic Study on Neural Plasticity
- Role of Synaptic Plasticity in Learning and Memory
- Neural Plasticity Mechanisms of Drug Addiction
- Plasticity of Pain Circuits in Physiological and Pathological Conditions

正高级/副高级 Principal/Associate Investigators



Erwin Neher



朱英杰
Yingjie Zhu



周涛
Tao Zhou



黄天文
Tianwen Huang



孟志强
Zhiqiang Meng



鲍进
Jin Bao



陈祖昕
Zuxin Chen



张淑雯
Shuwen Chang



陈波
Bo Chen



陈子君
Zijun Chen



邓潇斐
Xiaofei Deng



马征
Zheng Ma



陈高伟
Gaowei Chen

脑信息中心

Interdisciplinary Center for Brain Information

愿景/Mission:

脑信息中心致力于理解大脑的交叉学科研究。中心旨在通过发展与应用交叉学科手段来获取、分析和理解大脑连接组与调控的多模态信息，来揭示大脑在多个时空尺度下信息处理的基本机制，从而帮助理解大脑功能与相关疾病。

The ICBI focuses on interdisciplinary research towards understanding the brain. By using and developing interdisciplinary approaches to acquire, analyze and understand multi-modality information of brain connectome and regulation, the center aims to reveal basic mechanisms of brain information processing at multiple spatial and temporal scales, to help understand brain functions and treat brain diseases, and to inspire the next generation artificial intelligence.

研究方向/Key research areas:

- 神经突触的分子架构以及突触传递与可塑性机理
- 大脑中细胞组织规则以及神经系统的连接图谱
- 学习、记忆以及相关脑疾病的神经环路基础
- 高分辨高通量光-电显微成像技术、高灵敏电生理电化学探测器及元件、高性能数据处理算法与工具等前沿神经科学技术
- Molecular Architecture of Synapses and Mechanisms of Synaptic Transmission and Plasticity
- Cellular Organizational Principles of the Brain and Connectome of the Nervous System
- Neural Circuit Basis of Learning, Memory and Associated Brain Diseases
- Cutting-edge Neuroscience Technologies: High-resolution and High-throughput
- Opto-electronic Microscopy, High-sensitivity Electrophysiological and Electrochemical Detectors and Components, High-performance Data Processing Algorithms and Tools.

正高级/副高级 Principal/Associate Investigators



毕国强
Guoqiang Bi



孙坚原
Jianyuan Sun



张小康
Xiaokang Zhang



徐放
Fang Xu



陈培华
Peihua Chen



申雪峰
Xuefeng Shen



肖彦洋
Yanyang Xiao



李宝强
Baoqiang Li



王瑶
Yao Wang



周航
Hang Zhou



马鲲鹏
Kunpeng Ma

BCBDI
RESEARCH
PROGRESS

科研成果

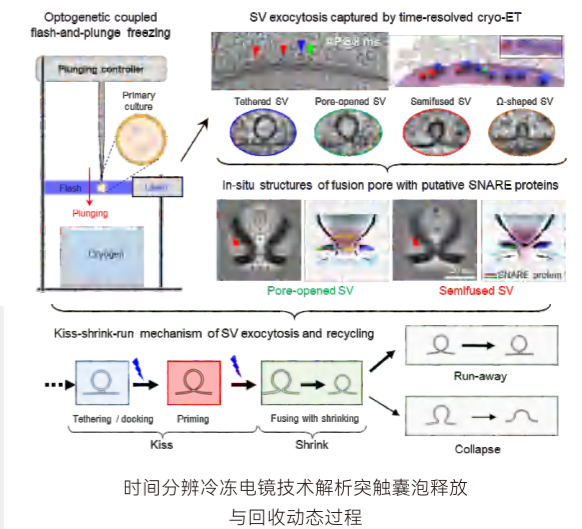
脑所2025年度代表性研究成果

脑所瞄准脑科学与脑疾病重大问题，围绕国家科技发展战略需求，聚集脑疾病与脑科学重大前沿科学问题，以源头创新为核心驱动，以脑疾病的诊断干预策略和脑认知的神经基础为核心科学问题，在“大脑智能发生的神经机制”、“大脑健康与神经稳态维持”、“脑图谱解析与调控新技术”等三个重点领域取得的阶段性重要进展。

01 “亲吻-收缩-逃逸/融合”：破解神经突触传递机制

"Kiss-shrink-run" unifies mechanisms for synaptic vesicle exocytosis and hyperfast recycling

脑信息中心毕国强、刘北明、陶长路团队，联合美国加州大学洛杉矶分校周正洪团队、南方科技大学王培毅团队、深圳先进院孙坚原团队，通过自主研发的毫秒级时间分辨原位冷冻电镜成像技术，破解了神经信息传递过程中，突触囊泡释放与快速回收的生物物理过程——“亲吻-收缩-逃逸/融合”（Kiss-Shrink-Run/Collapse）。这一成果统一了半个世纪以来学界关于突触囊泡释放与回收机制的两个争议模型，为理解神经信号传递、神经可塑性及相关脑疾病机理提供全新视角。



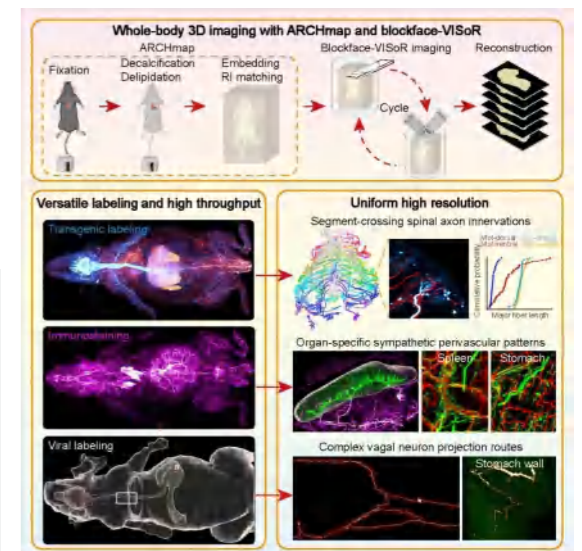
成果全文信息:

Tao CL^{#*}, Tian CL[#], Liu YT[#], Lu ZH[#], Qi L, Li XW, Li C, Shen X, Gu ML, Huang WL, Liu S, Yang LQ, Liao Z, Ma X, Wu J, Sun J, Wang P, Lau PM[†], Zhou ZH[†], Bi GQ[†]. "Kiss-shrink-run" unifies mechanisms for synaptic vesicle exocytosis and hyperfast recycling. *Science*. 2025 Oct 16;390(6770):eads7954. Epub 2025 Oct 16. (IF=45.8)

02 世界最快的小鼠全身亚细胞分辨率高清三维成像技术

High-speed mapping of whole-mouse peripheral nerves at subcellular resolution

脑信息中心毕国强、刘北明团队，联合合肥综合性国家科学中心人工智能研究院在大尺度生物组织三维显微成像领域取得重大突破。团队合作成功开发出世界最快的小动物全身亚细胞分辨率高清三维成像技术，实现了周围神经系统精细图谱的高效绘制。这项突破性的技术不仅有助于建立周围神经连接图谱研究的新范式和解析神经调控结构的基础性问题，也在发育生物学、系统解剖学和生物医药等领域具有重要应用前景。



成果全文信息:

Shi MY[#], Yao Y[#], Wang M[#], Yang Q[#], Ding L, Li R, Li Y, Huang H, Yang CY, Zhou Z, Zhu Z, Wen P, Dai F, Zeng X, Zhang KM, Guo Y, Sun ZA, Xia H, Ren Z, Cakmak YO, Zhang M, Xu F, Qu L, Zhu Q^{*}, Lau PM[†], Xu C^{*}, Bi GQ[†]. High-speed mapping of whole-mouse peripheral nerves at subcellular resolution. *Cell*. 2025 Jul 10;188(14):3897-3915.e20. (IF=42.5)

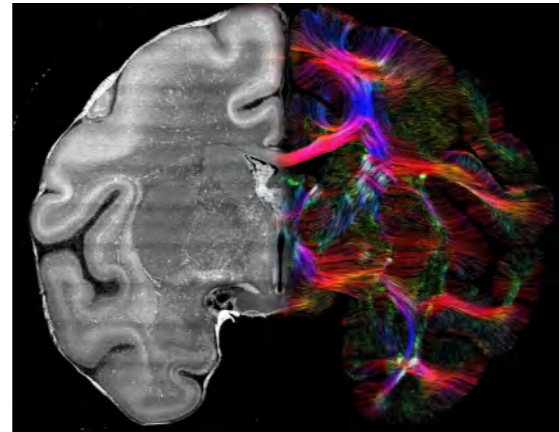
03 细胞尺度全脑纤维重建新技术

Whole-brain reconstruction of fiber tracts based on cytoarchitectonic organization

脑信息中心徐放、肖彦洋、毕国强团队提出了一种基于细胞结构方向信息解析脑内神经纤维走向的新方法CABLE (cytoarchitecture-based link estimation)，实现了在灵长类动物乃至人类脑组织中以细胞尺度完整重建全脑三维神经纤维通路。该方法突破了传统扩散磁共振成像在毫米级分辨率下精度的局限，同时规避了轴突病毒示踪通量低、难以整脑应用的瓶颈，为高精度脑连接图谱构建提供了新的技术路径。

成果全文信息:

Zhang, Y., Song, T., Yang, CY. et al. Whole-brain reconstruction of fiber tracts based on cytoarchitectonic organization. *Nature Methods* 22, 2639-2648 (2025). (IF=32.1)



左侧是尼氏染色的猕猴脑切片，右侧是尼氏染色经过CABLE计算得到的纤维图像

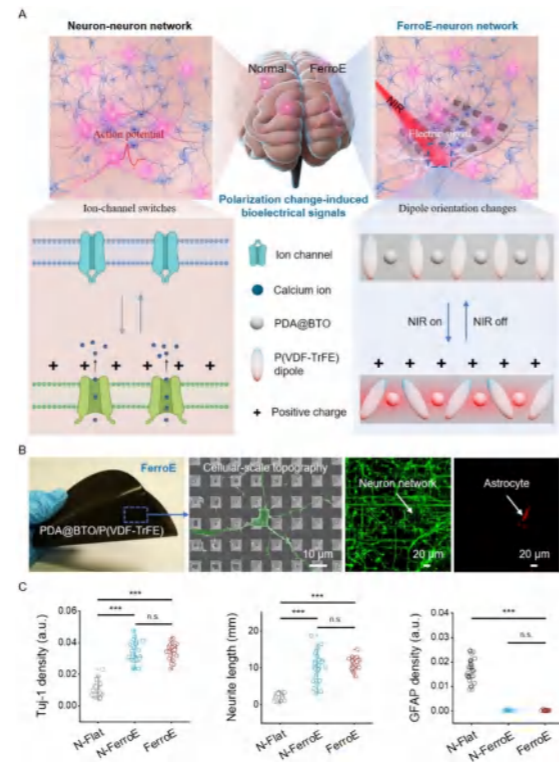
04 自适应生物界面的类神经铁电生物电子

Neuron-inspired ferroelectric bioelectronics for adaptive biointerfacing

深圳先进院脑所鲁艺与医工所杜学敏团队合作，研发了一种类神经界面材料与铁电生物电子器件 (Ferroelectric bioelectronics, FerroE)，融合了神经元偏好的柔性及拓扑结构特性，以及类神经元行为 (如极化变化产生电信号和高密度神经网络的形成)，实现了与神经系统的无缝整合和自适应通信。这类具备神经元偏好特性和行为的类神经界面材料与器件，将为下一代脑机接口、组织工程材料和生物医学器件的发展带来新机遇。

成果全文信息:

Wang Fang[#], Wang Lulu[#], Zhu Xule, Lu Yi*, Du Xuemin*. Neuron-inspired ferroelectric bioelectronics for adaptive biointerfacing, *Advanced Materials*, 2025, 37, 2416698. (IF=26.8)



类神经界面材料与铁电生物电子器件 (FerroE) 设计与神经元的无缝整合

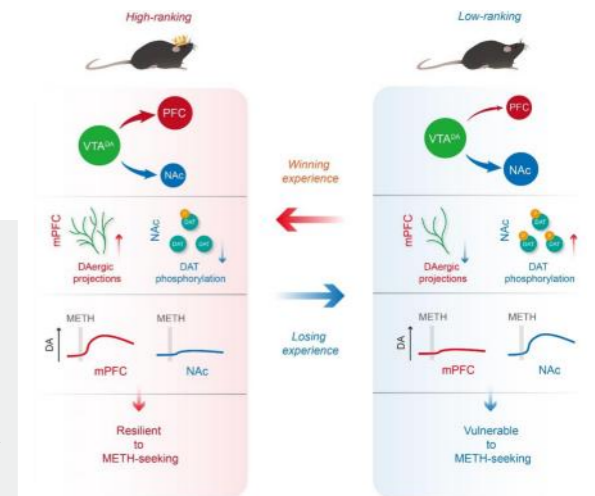
05 社会因素调控成瘾易感性的神经环路机制

Social rank modulates methamphetamine-seeking in dominant and subordinate male rodents via distinct dopaminergic pathways

内尔诺奖实验室朱英杰研究团队发现，两条多巴胺神经通路在成瘾的发生发展中起了非常关键的作用，“中脑-边缘”多巴胺通路促进毒品成瘾的形成，而“中脑-皮质”多巴胺通路抑制成瘾行为的发生；更重要的是，在社会竞争中获得胜利的体验可以重塑这两条多巴胺通路，并降低毒品成瘾行为。该研究为成瘾易感性的社会因素提供了新的机制解释和理论模型，并为成瘾的干预治疗提供了新的方案。

成果全文信息:

Xiaofei Deng[#], Wei Xu[#], Yutong Liu[#], Haiyang Jing, Jiafeng Zhong, Kaige Sun, Ruiyi Zhou, Liang Xu, Xiacong Wu, Baofang Zhang, Wanqi Chen, Shaolei Jiang, Gaowei Chen, Yingjie Zhu*. Social rank modulates methamphetamine-seeking in dominant and subordinate male rodents via distinct dopaminergic pathways. *Nature neuroscience*. 2025 May 12;28(6);1268-1279. (IF=20)



社会因素调控成瘾易感性的神经环路机制

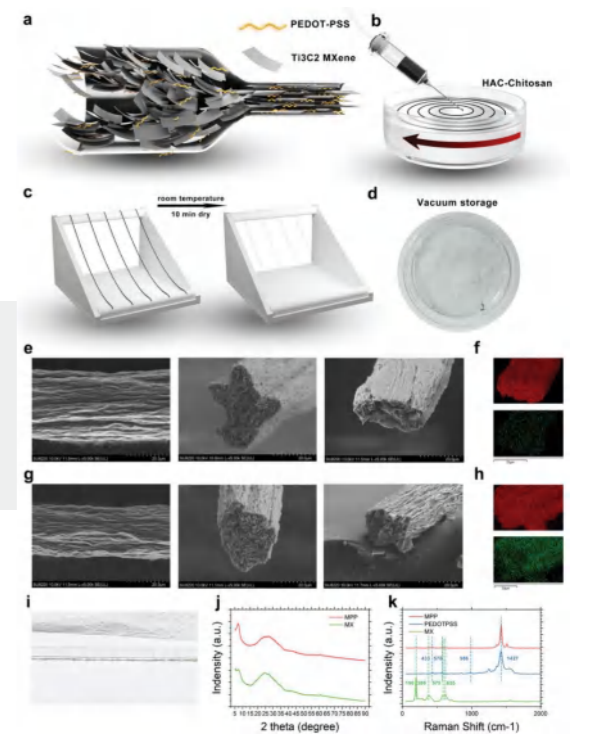
06 研发电学性能突破新高的液晶MXene神经电极

High-Performance MXene/PEDOT-PSS Microscale Fiber Electrodes for Neural Recording and Stimulation

脑信息中心都展宏团队通过应变控制两步纺丝技术，在壳聚糖凝胶液中实现MXene纳米片的液晶级有序排列，制备出MXene纤维电极 (MX) 及MXene/PEDOT-PSS复合电极 (MPP)，相关研究成果发表在 *Advanced Functional Materials*。MPP电极综合电学性能显著优于现有神经电极材料，该前沿技术的研发在体表电生理记录、大脑皮层记录及脑深部刺激方面均有应用，有望为帕金森病等运动障碍疾病的早期诊断提供跨尺度动态监测新工具，同时也可作为癫痫闭环调控及迷走神经刺激等转化研究提供关键技术支撑。

成果全文信息:

S. Gou, P. Li, S. Yang, G. Bi, Z. Du, High-Performance MXene/PEDOT-PSS Microscale Fiber Electrodes for Neural Recording and Stimulation. *Advanced Functional Materials*. 2025, 35, 2424236. (IF=18.5)



两步凝固法制备纤维电极及材料基础表征

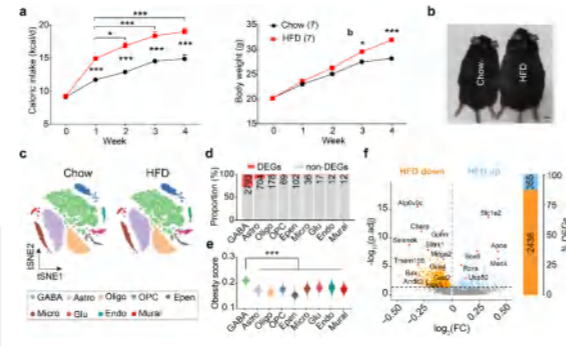
07 高脂饮食导致外侧隔核功能失调进而加剧肥胖的新机制

High-fat diet disrupts a septal control on feeding to promote obesity in male mice

内尔诺奖实验室朱英杰团队发现高脂饮食会通过下调外侧隔核脑区中的超极化激活环核苷酸门控通道1 (Hcn1)，抑制该区域神经元活性，并同时降低谷氨酸脱羧酶2 (Gad2) 的表达，从而减弱外侧隔核对下游脑区的抑制性调控。过表达Hcn1与Gad2能够增强外侧隔核神经元活性，恢复γ-氨基丁酸 (GABA) 水平，并有效阻止高脂饮食引发的暴饮暴食及肥胖表型。该研究阐明了饮食因素如何破坏大脑进食抑制系统的神经环路，为理解肥胖发生的中枢机制提供了新的理论依据。

成果全文信息:

Jiang S, Lai S, Jing H, Wu X, Li F, Chen B, Bao J, Wang L, Chen G, Zhu Y. High-fat diet disrupts a septal control on feeding to promote obesity in male mice. *Nature communications*. 27 Dec. 2025, doi:10.1038/s41467-025-68010-x. (IF=15.7)



长期高脂饮食导致外侧隔核功能失调进而加剧肥胖的机制

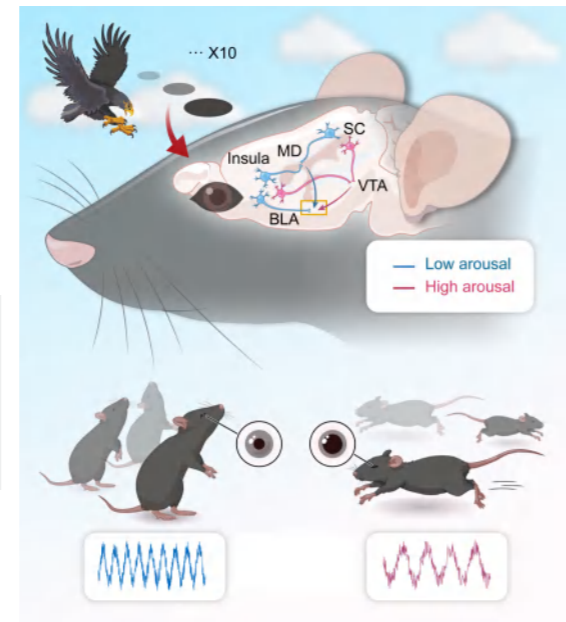
08 本能恐惧反应个体差异的神经环路机制

Neural Circuit Underlying Individual Differences in Visual Escape Habituation

脑图谱中心王立平、刘雪梅团队首次揭示了快速逃避和快速习惯化两种行为反应分别由两条神经通路介导；鉴定出背内侧丘脑 (MD) 整合视觉恐惧信息，通过降低威胁刺激唤醒度促进习惯化，是本能恐惧行为异质性的枢纽调控核团。该成果将精神疾病中恐惧反应的个体差异与行为适应性相联系，将为理解精神疾病个体易感性及精准干预提供了新视角。美国纽约大学Dayu Lin在Neuron撰文评述，肯定该研究“从神经环路层面揭示了应对重复威胁的多样化策略的神经基础”。

成果全文信息:

Liu X, Lai J, Han C, Zhong H, Huang K, Liu Y, Zhu X, Wei P, Tan L, Xu F, Wang L. Neural circuit underlying individual differences in visual escape habituation. *Neuron*. 2025 Jul 23;113(14):2344-2357.e5. (IF=15)



恐惧反应个体差异的神经环路机制

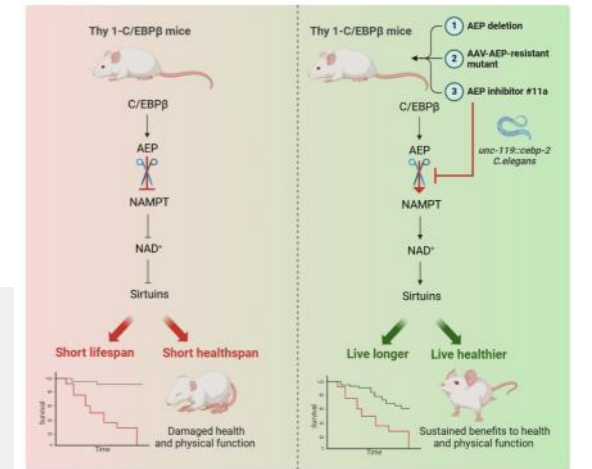
09 神经元C/EBPβ/AEP通路作为脑衰老干预的新型分子靶点

Neuronal C/EBPβ Shortens the Lifespan via Inactivating NAMPT

脑转化中心叶克强教授团队首次揭示C/EBPβ-AEP-NAMPT蛋白酶级联反应在脑衰老过程中发挥核心驱动作用。C/EBPβ/AEP通路可特异性剪切NAMPT，破坏细胞内NAD⁺稳态，进而导致神经功能衰退并加速机体衰老。该结论已在原代细胞、线虫及转基因小鼠等多类模型中获得验证。靶向调控该信号轴有望为延缓脑衰老及防治阿尔茨海默病等年龄相关疾病提供新的干预策略。

成果全文信息:

Bowei Li, Zhongyun Xie, Mengmeng Wang, Shuke Nie, Zhengjiang Qian, Xin Meng, Xia Liu, Seong Su Kang, Keqiang Ye*. "Neuronal C/EBPβ Shortens the Life Span via Inactivating NAMPT", *Advanced Science*, 2025, 12(21):e2414871. (IF=14.1)



Thy 1-C/EBPβ转基因小鼠寿命缩短机制及干预策略示意图

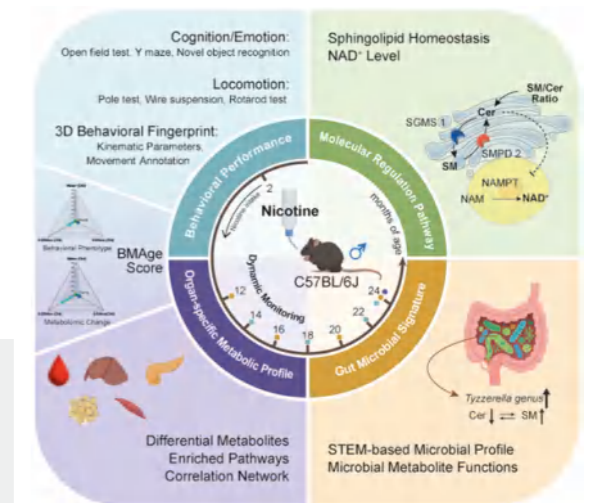
10 终生饮用尼古丁对小鼠衰老相关运动及代谢功能的动态调控

Nicotine reprograms aging-related metabolism and protects against motor decline in mice

脑图谱中心刘欣安与内尔诺奖实验室陈祖昕团队系统揭示了终生饮用尼古丁动态影响小鼠生命健康及代谢功能，尼古丁通过协调重塑糖脂与鞘脂代谢、提升能量代谢，引发系统性代谢重编程，从而增强机体抵抗运动衰老的能力。复旦大学刘铁民教授指出，“在衰老与代谢研究领域，尼古丁的作用一直存在争议，而本研究通过系统化、长程化的动物实验给出了颇具突破性的答案”。上海交通大学医学院蔡时青研究员评价，该工作为“尼古丁在非烟草路径下的生理功能研究提供了高质量、系统性、多维度的数据资源，拓展了其在衰老和代谢调控研究中的基础研究边界，具有重要的科学参考价值”。

成果全文信息:

Shuhui Jia^a, Xiaoyuan Jing^a, Ruoxi Wang, Mengke Su, Pei Wang, Yingxin Feng, Xiaohu Ren, Longfang Tu, Ping Wei, Zhen Lu, Yicong Jia, Feng Hong, Zhizhun Mo, Jiemeng Zou, Kang Huang, Caiyun Yan, Qianhui Zou, Liang Wang, Guoping Zhong, Zhi Zeng, Qiuliyang Yu, Wen Su, Xifei Yang, Fan Pan, Jianzhi Wang, Liping Wang, Lijun Kang, Paul J. Kenny, Zuxin Chen* and Xin-an*. Nicotine reprograms aging-related metabolism and protects against motor decline in mice. *Advanced Science*, 2025, 12(40): e15311. (IF=14.1)



长期饮用尼古丁通过代谢重编程对抗小鼠运动衰老

11

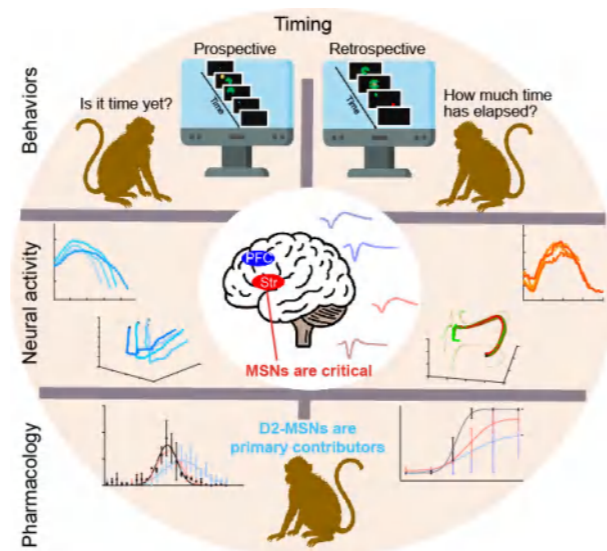
灵长类时间感知的神经基础

Medium Spiny Neurons Mediate Timing Perception in Coordination with Prefrontal Neurons in Primates

脑智能中心戴辑团队利用在体电生理和药理学干预技术，结合眼动行为监测技术，发现猕猴大脑采用绝对编码模式、相对编码模式两种不同策略，分别在回顾性及前瞻性计时中表征时间信息，其中纹状体中棘状神经元 (MSN) 尤其是D2-MSN在两种计时过程中起着关键作用。该研究揭示了时间信息在灵长类动物大脑中的神经表征机制，有望为改善阿尔茨海默、帕金森、精神分裂症等脑疾病患者的认知和运动功能提供潜在的干预靶点。

成果全文信息:

Xinhe Liu, Zhiting Zhang, Lu Gan, Panke Yu, Ji Dai*. "Medium Spiny Neurons Mediate Timing Perception in Coordination with Prefrontal Neurons in Primates", *Advanced Science*, 2025, 12:2412963. (IF=14.1)



本研究的行为范式、大脑编码前瞻性和回顾性计时的特点以及表征时间信息的关键神经元类型

12

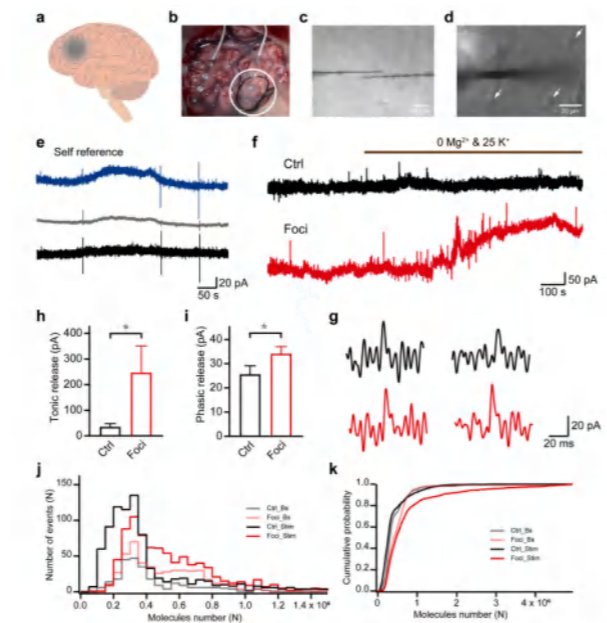
新型超快传感器首次实时捕捉人脑异常谷氨酸信号

Pathological glutamate release profiles in the epileptogenic zones of patients revealed by a novel ultra-fast glutamate sensor

脑信息中心申雪峰团队开发出了一种新型、快速、低成本的超快谷氨酸传感器，并将传感器应用于六名局灶性皮质发育不良型癫痫患者的切除脑组织上，首次在人类脑组织中记录到量子化谷氨酸释放事件，且发现致病灶内的量子化释放事件幅度显著大于对照区域，且刺激后会出现更多大尺寸的释放事件。这表明癫痫灶内的谷氨酸能神经突触出现显著的功能异常，倾向于释放更多递质，从而造成癫痫病理状态下的兴奋/抑制失衡

成果全文信息:

Zhao S², Li C², Zheng Y², Wang F, Wang Y, Ma K, Li Y, Zhang L, Zhang X, Gao J, Yao Y, Chen P*, Sun J*, Shen X*. Pathological glutamate release profiles in the epileptogenic zones of patients revealed by a novel ultra-fast glutamate sensor. *Biosensors and Bioelectronics*. 30 Dec. 2025, doi: 10.1016/j.bios.2025. 118332. (IF=10.5)



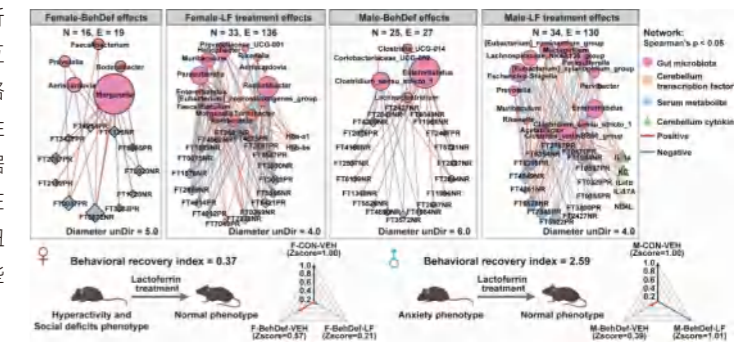
癫痫患者致病组织中谷氨酸动力学的实时监测

13

母代孕前压力应激影响子代成年后精神行为的脑体互作网络机制

Unraveling Sexually Dimorphic Offspring Behaviors: Maternal Premating Stress and the Neuro-Microbial-Metabolic Network

脑所/深港脑院刘欣安、陈祖昕和王立平团队合作，系统解析了母代孕前压力-焦虑状态导致子代成年后情绪行为异常的脑体互作网络机制。本研究构建了一个“肠道微生物群通过神经-代谢网络介导母体情绪应激对子代产生性别特异性精神行为影响”的系统性理论框架，并从微生物组、代谢组、转录组与神经电生理多层证据中验证了这一脑体互作网络机制。研究结果强调了肠道菌群稳态在维持神经-代谢联动网络中的关键作用，并提示不同菌群网络枢纽可能参与介导性别特异性的精神行为表型。未来将进一步解析这些关键微生物在跨代情绪与行为调控中的作用。



乳铁蛋白改善子代小鼠的行为评分及微生物-神经-代谢网络特征

成果全文信息:

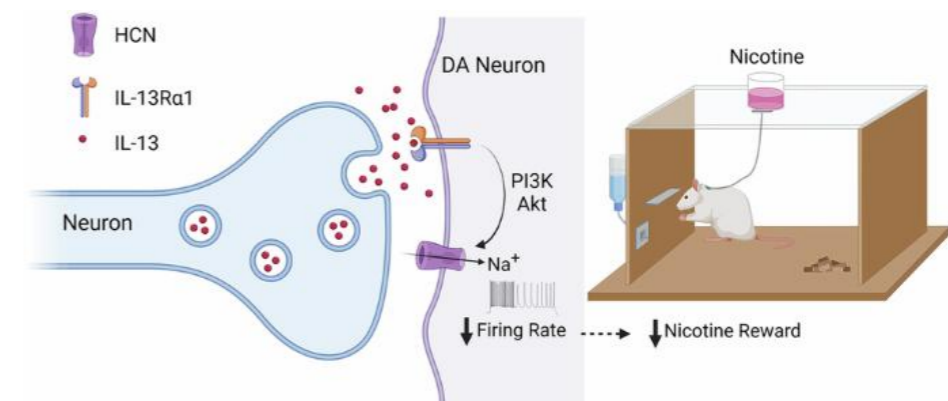
Xiaoyuan Jing², Zhibin Xu², Qixing Yang², Yan Jiang², Jintao Wang, Ruoxi Wang, Yuantao Li, Rouxuan Zhou, Liping Wang*, Zuxin Chen*, Xin-an Liu*. Unraveling Sexually Dimorphic Offspring Behaviors: Maternal Premating Stress and the Neuro-Microbial-Metabolic Network. *Molecular Psychiatry*. 2025.Dec 10. (IF=10.1)

14

神经免疫信号直接调控多巴胺神经元及尼古丁成瘾机制

Interleukin 13 signaling modulates dopaminergic functions and nicotine reward in rodents

内尔诺奖实验室陈祖昕与脑图谱中心刘欣安团队联合国内外机构，首次系统揭示了免疫炎症因子白细胞介素-13 (IL-13) 能抑制尼古丁对多巴胺神经元的兴奋效应，并显著降低尼古丁自给药行为。这一发现不仅揭示了免疫炎症因子在奖赏及成瘾行为中的重要作用及关键分子靶点，也为解释急性疾病（如重感冒）后部分吸烟者吸烟量下降甚至成功戒烟的现象提供了潜在机制。未来，靶向 IL-13/IL-13Ra1 信号通路有望成为戒烟及其他药物成瘾干预的新策略。



IL-13 (囊泡神经递质) 经 IL-13Ra1 通路调控多巴胺神经元与尼古丁成瘾

成果全文信息:

Liu XA, Aguirre CA, Yang Q, Ren J, Wang L, Ju F, Guo H, Wang J, Liu L, Li Z, He J, Xu Z, Shi C, Cintron-Colon R, Michel T, Wood M, Margetts AV, Pollock TA, Vilca SJ, Tuesta LM, Di Angelantonio S, Basilico B, De Stefano ME, Xia J, Wei P, Li S, Yang X, Wang L, Delorme-Walker VD, Marcondes MCG, Parsons L, Conti B, Chen Z. Interleukin 13 signaling modulates dopaminergic functions and nicotine reward in rodents. *Molecular Psychiatry*. 2025 Aug 7. (IF=10.1)

脑认知与类脑智能全国重点实验室

State Key Laboratory of Brain Cognition and Brain-inspired Intelligence Technology

实验室概况

脑认知与类脑智能重点实验室是按照全国重点实验室标准，经中国科学院批准成立，依托于中国科学院脑科学与智能技术卓越创新中心，并与中国科学院自动化研究所、中国科学院深圳先进技术研究院共建。该实验室得到了国家、中国科学院以及地方政府的大力支持，预期将获得充足的资金和政策扶持，以推动实验室的建设和发展。



研究方向

实验室的主要研究方向集中在解析大脑抽象推理与灵活决策的神经机制，并探索相应的算法原理。这一研究方向不仅具有重要的科学意义，而且有望推动通用类脑智能系统的发展，为人工智能领域带来革命性的进展。实验室已承担和拟承担多项重大科研项目，包括中国科学院先导专项（B类），这些项目将进一步巩固实验室在脑科学与智能技术领域的领先地位。

创新成果

发现了时间空间信息的编码和互作原理

科技创新2030重大项目

中国科学院B类先导专项 "大脑灵活决策功能的神经机制"

深圳先进院牵头1项子课题

重大问题：大脑推理与决策的神经机制

Neuron, 2025a
刘雪梅/王立平

Neuron, 2025b, Accepted
刘雪梅/王立平

Neuron, 2025c, Accepted
王立平

Advanced Materials, 2025a
鲁艺

Nature Communication, 2024
王成

Advanced Materials, 2025b
鲁艺

建设规划

实验室计划建设一系列先进的研究平台和实验设施，以满足科研工作的需要。这些平台不仅将服务于实验室内部的研究项目，也将对外开放，促进与地方产业的合作与交流。结合南山区的人工智能等未来产业需求，实验室将致力于推动科研成果的转化应用，预期将对地方经济发展产生显著贡献。

在场地建设方面，实验室将根据研究需求和发展规划，合理规划和建设必要的实验空间和设施，确保科研工作的顺利进行。此外，实验室还将积极参与国内外学术交流，不断提升自身的科研水平和国际影响力。

广东省脑连接图谱重点实验室

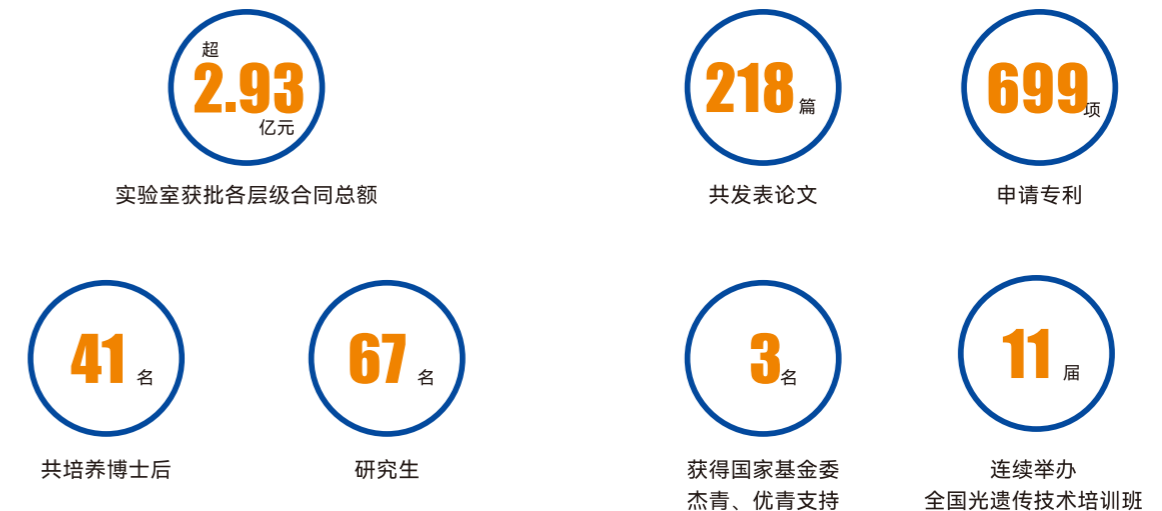
Guangdong Provincial Key Laboratory of Brain Connectome and Behavior

总体定位与研究方向

紧密围绕脑图谱结构与功能解析这一国家重大战略布局，从重大脑疾病的社会需求出发，以大脑介观尺度神经环路标记、示踪、调控和功能读取技术的开发与应用为特色，围绕脑连接图谱的结构和功能解析，脑连接图谱与脑疾病和脑连接图谱解析新技术和新工具的研究方向，聚焦国际脑科学研究的前沿，打造脑连接组学领域国际一流的创新研究平台，使之成为服务粤港澳脑科学专业人才培养、学术交流基地和资源开放共享的创新载体。



2017-2025研究水平与成果贡献



光遗传技术的交流促进了最大程度的技术与资源共享为研究人员提供了更广泛的合作和协作平台

队伍建设与人才建设

1. 形成了一支充满活力、具有创新精神的团队，实验室固定人员35人，高级职称人员23人；
2. 高端人才吸引与学科交叉合力实验室研究实力的强化与综合创新的推动；
3. 培养卓越人才，助力科技创新与团队综合能力增强。

三个方向的学科带头人交叉合作密切

<p>脑连接图谱结构功能</p>  <p>王立平 研究员</p>  <p>屠洁 研究员</p>  <p>普渝婷 研究员</p>	<p>脑连接图谱与脑疾病</p>  <p>杨帆 研究员</p>  <p>李翔 研究员</p>  <p>谭力铭 研究员</p>	<p>脑科学新方法新技术</p>  <p>鲁艺 研究员</p>  <p>路中华 研究员</p>  <p>蔚鹏飞 研究员</p>
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管理与开放运行情况

广东省脑连接图谱重点实验室学术委员会 (按姓氏音序排列)

					
王以政 院士(主任)	程和平 院士	段树民 院士	时松海 院士	颜宁 院士	赵继宗 院士

				
谯小维 教授	陈宇 研究员	鲁友明 教授	罗敏敏 教授	唐亚梅 教授

				
王立平 教授	王韵 教授	武胜普 教授	薛天 教授	张建国 教授

批复3项开放课题，通过合作吸引人才（国家杰出青年科学基金获得者）

SIAT与Broad研究所签署合作备忘录，双方将在脑科学等领域建立深入合作

与法国马赛大学、意大利EMBO、澳大利亚莫纳什大学等实验室开展国际合作，联合发表文章

BCBDI
RESEARCH
TEAMS

研究团队



王立平

Liping Wang PRINCIPAL INVESTIGATOR

Associate Investigators

Xuemei Liu, Qingqing Liu

Assistant Investigators

Zhijie Wang, Jijia Zhang, Wenjie Zhao, Juan Lai,
Xiaofen Li, Tingmei Wang, Shuxian Yang, Pufang Fan

Postdocs

Moxuan Luo, Peilei Shen,
Jinling Zhong, Yunhua Zheng,
Xulin Li, Yakun Bo, Shuaiyu Wang,
Jiaoyang Wang

Central and Peripheral Neural Mechanisms Underlying Innate Behaviors

Mental disorders such as depression and post-traumatic stress disorder are recognized as one of the leading challenge in global health. Understanding the neural circuits underlying fear and stress-related mental disorders are the important emerging fields in neuroscience research. The dissection of the interplay between these functional circuits and peripheral systems will emerge

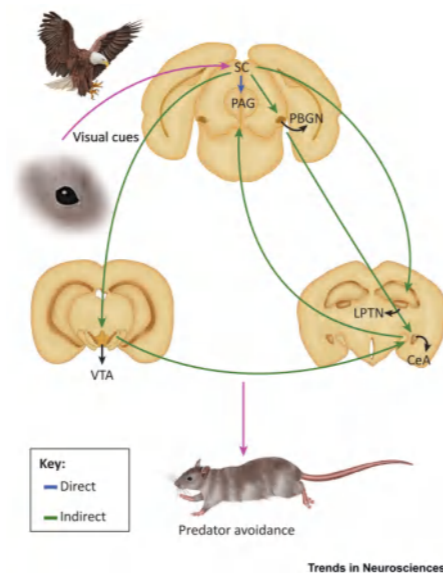
knowledge of causal mechanisms subserving mental disorder mechanisms presently hidden from view. It will also contribute to the identification of possible biomarkers and to the development of new cognitive or behavioral intervention targets for mental disorders.

The Neural Circuits of Innate Defensive Responses

Animal's brain has complex innate structures driving adaptive behaviors without requiring extended learning. However, the brain connectivity and processing mechanism of these innate structures are still largely unknown. Liping Wang's lab focuses on dissecting the connections and functions of highly organized subcortical neural structures processing visual threat, so called "innate fear circuits".

The looming paradigm used on mice is one of the most essential ways to study innate fear responses induced by visual cues. Studies from Liping Wang's lab have already described several parallel neural circuits originating from the multisensory integration center superior colliculus (SC) and participating in processing looming-induced defensive responses under certain conditions. His team identified a neural circuit projecting from SC to the mice pulvinar, that abstracts the key features of threat signal and directly innervates lateral amygdala (LA) activity, which in turn mediates mice freezing response with the absence of a shelter. Another neural circuit originating from the deep layers of SC that reaches ventral tegmental area (VTA) GABAergic neurons and leads to central amygdala nucleus (CeA), mediating visually evoked flight to nest responses. They also identified two escape behaviors in mice—persistent escape (T1) and rapid habituation (T2)—linked to unique arousal states under

repetitive looming stimuli, revealing neural circuits underpinning adaptive threat responses and individual variability. In 2023, his team published a review article describing the circuitry between subcortical brain regions involved in mediating defensive behaviors, and discussed the intersection of peripheral systems involved in internal states with the neurocircuits that underlie defence responses against predatory threat.



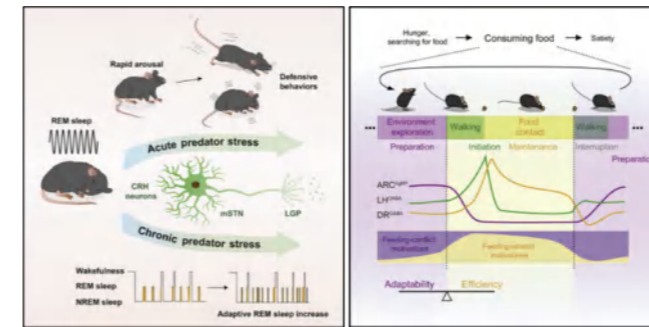
Trends in Neurosciences

The Systematic Mechanisms Underlying the Integration of Innate Behaviors

Innate behaviors, such as sleeping, eating, defense against predator and reproduction, are extremely important for individual and species survival. They are genetically hardwired and evolutionarily conserved across species from simple to complex animals. Under certain conditions, organisms need to optimize behavioral choices to cope with the external environment threats and internal needs.

A recent study from Liping Wang's lab has identified a basal ganglia circuit that promotes arousal and defensive behaviors in response to threat, and that enables sleep adaptations in the face of prolonged predatory stress. This study offers a potential evolutionary explanation of the prominent co-occurrence of increased rapid eye movement (REM) sleep and stress-related mental disorders, and elucidates the underlying neurobiological mechanism.

His team also delineated that feeding is fragmented and divergent motivations for food consumption or environment exploration compete throughout the feeding process. An iterative activation sequence of agouti-related peptide (AgRP)-expressing neurons in arcuate (ARC) nucleus,



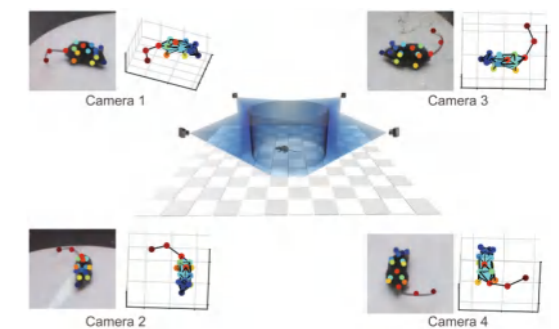
SELECTED PUBLICATIONS:

- Xiaoyuan J[#], Zhibin X[#], Qixing Y[#], Yan J[#], Jintao Wang, Ruoxi Wang, Yuantao Li, Rouxuan Zhou, **Wang L***, Zuxin Chen*, Xin-An Liu*. (2025) Unraveling Sexually Dimorphic Offspring Behaviors: Maternal Premating Stress and the Neuro-Microbial-Metabolic Network. *Mol Psychiatry*. doi: 10.1038/s41380-025-03378-2.
- Liu X[#], Lai J, Han C, Zhong H, Huang K, Liu Y, Zhu X, Wei P, Tan L, Xu F, **Wang L***. (2025) Neural circuit underlying individual differences in visual escape habituation. *Neuron*. doi: 10.1016/j.neuron.2025.04.018.
- Ye J[#], Xu Y[#], Huang K[#], Wang X[#], **Wang L***, Wang F*. (2025) Hierarchical behavioral analysis framework as a platform for standardized quantitative identification of behaviors. *Cell Reports*. doi: 10.1016/j.celrep.2025.115239.
- Zhou X[#], Xiao Q[#], Liu Y, Chen S, Xu X, Zhang Z, Hong Y, Shao J, Chen Y, Chen Y, **Wang L***, Yang F*, Tu J*. (2024) Astrocyte-mediated regulation of BLA WFS1 neurons alleviates risk-assessment deficits in DSC1-N mice. *Neuron*. doi: 10.1016/j.neuron.2024.03.028.
- Tseng YT[#], Schaefer B[#], Wei P[#], **Wang L***. (2023) Defensive

GABAergic neurons in the lateral hypothalamus (LH), and in dorsal raphe (DR) orchestrate the preparation, initiation, and maintenance of feeding segments respectively, via the resolution of motivational conflicts. This iterative neural processing sequence underlying the competition of divergent motivations further suggests a general rule for optimizing goal-directed behaviors.

Behavioral Analysis Using 3D-Motion Learning Framework

Classical behavioral tests often suffer from several drawbacks including non-uniform measuring paradigms, variability in apparatus use, and a tedious and time-consuming manual or semi-manual evaluation of recordings. The automated machine-learning based animal motion capture system and 3D behavior decomposition framework developed in Liping Wang's lab, enables an unbiased characterization of autism spectrum disorder (ASD)-related phenotypes and detection of subtle differences between mouse groups, which often escape the human observer or are not sufficiently captured with traditional software to assist the evaluation of classical behavioral tests.



- responses: behaviour, the brain and the body. *Nat Rev Neurosci*. doi: 10.1038/s41583-023-00736-3.
- Liu Q[#], Yang X[#], Luo M[#], Su J, Zhong J, Li X, Chan R H M, **Wang L***. (2023) An Iterative Neural Processing Sequence Orchestrates Feeding. *Neuron*. doi: 10.1016/j.neuron.2023.02.025.
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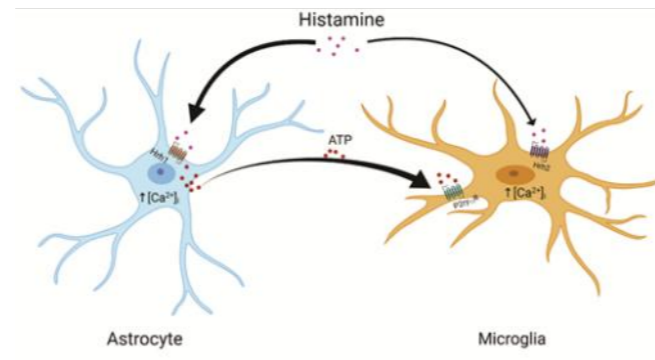
Glial cells function in physiology and disease

The Kettenmann lab has been studying the functions of all the three major types of glial cells in the brain, the astrocytes, oligodendrocytes and microglial cells. One goal is to analyze how astrocytes and oligodendrocytes are connected via gap junctions to form a panglial network and how this network influences neuronal function in the white and in the grey matter. A major focus of the lab is on the role of microglial cells in the normal and in the pathologic brain. The Kettenmann team found that microglial cells can express classical neurotransmitter receptors

formerly considered to be a hallmark of neurons. Activation of these receptors influences microglial functions. Within the context of pathology they are currently studying the importance of microglial cells in stroke, Alzheimer's disease and psychiatric diseases. Another line of research addresses the question how microglia interact with glioma cells. They aim to understand this interaction on a molecular level with the goal to identify therapeutic targets.

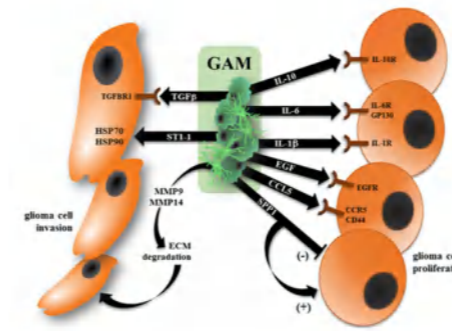
Microglial responses to neuronal activity

Microglial cells were considered as pathologic sensors and their functions was solely associated with brain diseases. In the last years it has become evident that they also play a role in synaptic modulation during development and plasticity as we summarized in a recent review. Moreover, we have shown that microglial cells do not only express the receptor systems of immune cells such as for chemokines and cytokines, but have functional receptors for the classical neurotransmitters such as for GABA, serotonin or histamine as we have demonstrated for microglial cells not only in cell culture, but also in acutely isolated brain slices. Most of these receptors are linked to Ca^{2+} signalling, thus Ca^{2+} activity is an important readout of microglial activity. We have therefore generated two novel mouse lines where microglial Ca^{2+} activity can be recorded by an intrinsic, microglia-specifically expressed Ca^{2+} sensor. These lines have been transferred to Shenzhen and are currently in the breeding facility. With these novel mouse lines we could recently identify mechanisms by which microglia communicate with astrocytes and neurons. We found that astrocytes respond to histamine via activation of histamine H_{rH1} receptors which leads to a release of ATP. This signal is sensed by microglia triggering an increase in Ca^{2+} and resulting in an increase of phagocytic activity. We now plan to use this mouse model to study the response of microglial cells using the Ca^{2+} activity as a read-out in awake mice confronted with visual stimulation. In collaboration with Liping Wang and Jie Tu's research group we will analyze the fear induced response behavior.



The role of microglia in glioma

One of the most common primary brain tumors are glioma. So far there are few effective therapies for these cancers, and patients with malignant glioma fare poorly, even after surgery, chemotherapy and radiation. Over the past decade, it is now appreciated that glioma contain a high proportion of non-cancerous cell types, in particular microglia and infiltrating macrophages which can make up for 30% of the tumor mass. We have in the last years identified a number of interacting mechanisms by which glioma cells reprogram the microglia/macrophages into a pro-tumorigenic phenotype. In turn microglia/macrophages promote glioma growth by several mechanisms which we and other groups have identified.



We have recently studied the role of TREM-2 in this glioma-microglia interaction. TREM-2 is a major risk factor in Alzheimer's disease. We found that TREM2 promotes glioma progression in male but not female animals. The accumulation of glioma-associated microglia/macrophages (GAMs) and CD31+ blood vessel density is reduced in male TREM2-deficient mice. A transcriptomic analysis of glioma tissue revealed that TREM2 deficiency suppresses immune-related genes. Thus, the TREM2-dependent crosstalk between GAMs and the vasculature formation promotes glioma growth.

In addition to mouse models, we are now using human iPSC-derived microglia to analyze these interactions in a system which is closer to the patient situation. This model allowed us to identify a new interaction partner between glioma, CCL18 which is expressed in human, but not in rodents.

These human iPSC-derived microglia technology has now been established in the Shenzhen lab and we will use it not only for the study of glioma microglia interaction, but also for the interaction of human microglial cells with human neurons.

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Decoding brain circuits and plasticity

The brain consists of myriad neurons that connect with one another through heterogeneous and plastic synaptic connections to form complex yet ordered circuits. Neuronal activity within and across these circuits shapes their connectivity and underlies perception, emotion, decision and learning in animals and human. Towards understanding this complex system, we are developing and applying cutting-edge light and electron microscopy techniques, as well as AI-based data processing methods, to explore brain circuits across multiple spatiotemporal scales.

Through analyses of the acquired multi-modality data, the goal is to understand the structure, dynamics and function of brain circuits and the logic behind, and to inspire the next generation artificial intelligence.

Current research directions include: (1) Synaptic architecture and mechanisms of plasticity; (2) Brain mapping and circuit basis of learning and memory; (3) New imaging and analysis techniques and their biomedical applications.

In situ structure and organization of GABA_A receptors in hippocampal inhibitory synapses revealed by cryo-electron tomography

Information processing in the brain depends on specialized organization of neurotransmitter receptors and scaffolding proteins within the postsynaptic density. However, how these molecules are organized *in situ* remains largely unknown. CryoET imaging can preserve the cells in native states and has an order of magnitude of higher resolution compare to the super-resolution optical microscopy. We developed template-free classification of oversampled sub-tomograms techniques to analyze cryo-electron tomograms of hippocampal synapses. We identified type-A GABA receptors (GABAARs) in inhibitory synapses and determined their *in situ* structure at 19-Å resolution. These receptors are organized hierarchically: from GABAAR super-complexes with a preferred inter-receptor distance of 11 nm but variable relative angles, through semi-ordered, two-dimensional receptor networks with reduced Voronoi entropy, to mesophasic assembly with a sharp phase boundary. These assemblies likely form via interactions among postsynaptic scaffolding proteins and receptors and align with putative presynaptic vesicle release sites. Such mesophasic self-

organization might allow synapses to achieve a 'Goldilocks' state, striking a balance between stability and flexibility and enabling plasticity in information processing. This work represents the first nanometer-resolution observation at the inhibitory synaptic receptors and a critical step towards resolving the atomic details of the brain.

Developing new techniques and data streamline for high-throughput whole-brain imaging

Biological volumes are of high content of fine structures. We work on developing tools for resolving the structures at subcellular resolution. One of the most complicated biological volumes is the brain which plays a central role in physiological functions. We have established an ultrahigh-speed volumetric imaging method to resolve one mouse brain at unprecedented 2 hours/brain speed at sub-micron resolution. We are currently developing new methods for other organs including the spinal cords, liver, spleen, heart, kidney and other tissues. High-throughput microscopy results in huge amount of image data. We are taking advantages of artificial intelligence for extracting information and knowledge from petabytes of images of mouse and primate brain, to generate broader understanding of brain connectivity and general rules of neural circuitry organization.

Mapping the mesoscopic connectome of rodents and primates

Based on technologies described above, we are aiming at establishing mesoscale connectomes of rodents and especially

primates as reference for general neuroscience research. We are particularly interested in neocortical organization and micro-circuits governing the information flow while primates are performing intelligent tasks.

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Development of tools for neuro-circuit studies and therapeutical purposes

Our group has been working on the development of virus-based tools for neuro-circuit and therapeutical purposes. By combining current advances in the related fields, including neurobiology, molecular & cellular biology, virology, neuroimaging and bioengineering, we have been focusing on developing tools

with low toxicity, high sensitivity, flexibility, simplicity, cell specificity, controllability in spread direction and ranges. Hundreds of the tracers have been commercialized and used by thousand of labs across the world. More attentions are going to be paid to the development of vectors for therapeutical purposes.

Efficient retrograde labeling and astrocyte-directed transduction of AAV11 vector

Viral tracers that enable efficient retrograde labeling of projection neurons are powerful vehicles for structural and functional dissections of the neural circuit and for the treatment of brain diseases. Currently, some recombinant adeno-associated viruses (rAAVs) based on capsid engineering are widely used for retrograde tracing, but display undesirable brain area selectivity due to inefficient retrograde transduction in certain neural connections. An easily editable toolkit to produce high titer AAV11 was developed and exhibits potent and stringent retrograde labeling of projection neurons complementary to AAV2-retro. Furthermore, GfaABC1D promoter embedding AAV11 is superior to AAV8 and AAV5 in astrocytic tropism in vivo. These properties make AAV11 a promising tool for mapping and manipulating neural circuits and for gene therapy of some neurological and neurodegenerative disorders.

Sindbis virus with G285S mutation in nsP1 as a stable vector for gene delivery

Neuroscience, gene therapy, and vaccine have all benefited from the increased use of viral vectors. Sindbis virus (SINV) is a notable candidate among these vectors. However, viral vectors commonly suffer from a loss of expression of the transgene, especially RNA viral vectors. A directed evolution approach by continuous passage of selection was used to identify adaptive mutations that help SINV to stably express exogenous genes. Two adaptive mutations that are located at aa 285 (G to S) of nsP1 and aa 422 (D to G) of nsP2 were found, respectively. Further study showed that G285S was sufficient for SINV to stabilize the expression of the inserted gene, while D422G was

not. Combined with AlphaFold2 and sequence alignment with the genus Alphavirus, it was found that G285S is conserved. These results demonstrated an efficient approach to greatly augment the gene delivery capacity of viral vectors, which will be useful to neuroscience and oncolytic therapy.

Oncolytic Viral Therapy for Glioma by Recombinant Sindbis Virus. The characteristics of glioblastoma, such as drug resistance during treatment, short patient survival, and high recurrence rates, have made patients with glioblastoma more likely to benefit from oncolytic therapy. The therapeutic effect of the SINV virus carrying different combinations of IL-12, IL-7, and GM-CSF on glioma in a glioma-bearing mouse model was evaluated. It was restricted to the injection site in the tree shrew brain and did not spread throughout the whole brain. In addition, SINV-induced apoptosis in conjunction with the stimulation of the immune system by tumor-killing cytokines substantially suppressed tumor development. Furthermore, SINV carrying IL-7 and IL-12 had the most notable glioma-killing effect. These results suggest that SINV has a significant safety profile as an oncolytic virus and that combining SINV with cytokines is an efficient treatment option for malignant gliomas.

A rabies virus-based toolkit for efficient retrograde labeling and monosynaptic tracing

Recombinant rabies viral vectors allow for the retrograde labeling of projection neurons and cell type-specific trans-monosynaptic tracing, making these vectors powerful candidates for the dissection of synaptic inputs. Although several attenuated rabies viral vectors have been developed, their application in studies of functional networks is hindered by the long preparation cycle and low yield of these vectors. An improved production system for the rapid rescue and preparation of a high-titer CVS-N2c-ΔG virus was developed.

The results showed that the new CVS-N2c-ΔG-based toolkit performed remarkably: 1) N2cG-coated CVS-N2c-ΔG allowed for efficient retrograde access to projection neurons that were unaddressed by rAAV9-Retro, and the efficiency was six times higher than that of rAAV9-Retro; 2) the trans-monosynaptic efficiency of oG-mediated CVS-N2c-ΔG was 2-3 times higher than that of oG-mediated SAD-B19-ΔG; 3) CVS-N2c-ΔG could delivery modified genes for neural activity monitoring, and the time window was 3 weeks; and 4) CVS-N2c-ΔG could express sufficient recombinases for efficient transgene recombination. These findings demonstrate that new CVS-N2c-ΔG-based toolkit may serve as a versatile tool for structural and functional studies of neural circuits.

Applications of the tools in neuroscience

The tools developed have been broadly used to answer various types of questions, through collaboration or technical support. Here are some examples of recent collaborations: 1) Using viral tools, it was revealed that a subset of layer 5 neurons in somatosensory cortex receives spinal inputs through a direct spino-cortical circuit bypassing the thalamus, and thus define these neurons as spino-cortical recipient neurons (SCRNs), and the branches from spinal ascending axons formed a kind of disciform structure with the descending axons from SCRNs in the basilar pontine nucleus (BPN), which represents a noncanonical pathway, allowing a fast sensory-motor transition of the brain in response to noxious stimuli (Cell Research, 2023); 2) The tracing tools were used to demonstrate that newborn neurons were

integrated into the micturition neural circuits and reconnected higher brain centers and lower spinal cord centers to control voiding, and participated in the restoration of the lower urinary tract function, even in the absence of long-distance axonal regeneration, which implied that neurotrophin3-loaded chitosan biomaterial substantially recovered bladder function after complete spinal cord injury (Biomaterials, 2023); 3) The tracing tools revealed that potentiating astrocyte Ca²⁺ signaling in the hippocampal cornu ammonis 1 (CA1) enhances the strength of temporal association of episodic memory formation, which are mediated by astrocytic α4 subunit-containing nicotinic acetylcholine receptors (α4-nAChRs) via mechanisms involving NMDAR co-agonist supply (Cell Reports, 2023); 4) Using rAAV encoding cre-dependent hm3D and cre-dependent anterograde transsynaptic viral tracer H129ΔTK-TT combined with fMRI on DAT-cre or CamKIIα-cre transgenic rats, it was found that more regions responded to selective activation of VTA CamKIIα-positive neuron than that of dopaminergic neurons, and multiple cortical and subcortical brain regions are structurally and functionally connected by VTA dopaminergic and CamKIIα-positive neurons (Journal of Translational Medicine, 2023); 5) Using viral tools, it was revealed that unilateral activation of glutamatergic neurons in the paraventricular hypothalamic nucleus (PVH) induced bilateral elevation of intraocular pressure (IOP) and the ipsilateral IOP increased more noticeably, which implied that PVH may play an important role in IOP upregulation via glutamatergic neurons (Investigative Ophthalmology & Visual Science, 2023).

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Molecular and cellular mechanism of synaptic transmission

Dr. Sun's primary interest is to understand the presynaptic mechanism of synaptic short term plasticity and how it impacts neuronal information encoding. The major focus is on the molecular and cellular mechanism and consequence of regulation of neurotransmitter release in single vesicle, single active zone and single neuron perspectives. His laboratory uses an interdisciplinary approach with combination of biophysics and molecular biology to explore the mechanism for presynaptic secretory machinery to

achieve synaptic transmission.

He is particularly interested in 1). The nature of quantal signal at central synapses and the mechanisms that link the quantalized synaptic transmission to neuronal information encoding. 2). The molecular mechanism that determines the vesicle release probability, releasable vesicle availability at nerve terminal during various neural activities.

Dissection of the complete kinetic structure of recycling vesicle pool at the Calyx of Held synapse under in vivo-like activities

Synaptic transmission at mammalian central synapses has ongoing background activity at physiological temperature. The recycling vesicle pool, with proper kinetics, ensures sustained synaptic transmission. However, the kinetic structure of recycling vesicle pool has never been quantitatively analyzed before, and most studies were performed at room temperature and under resting conditions. With the combination of presynaptic capacitance measurement and postsynaptic EPSC recording on calyx of Held synapses at physiological temperature, we studied vesicle recycling under sustained presynaptic stimulation. The kinetics of vesicle reuse was revealed by impeding transmitter refilling with folimycin. We found that more than 90% of vesicles in nerve terminals are involved in recycling but they were not homogeneously competent for immediate reuse. A significant surface pool of vesicles, assayed as an increased capacitance, was detected with different levels corresponding to different stimulation intensities. We kinetically dissected the recycling vesicle pool as sequentially connected sub-pools (readily priming pool, readily releasable pool, surface pool and post-endocytic pool) and depicted the complete kinetic structure. The

sizes and transition rates among these sub-pools were dynamically regulated by neuronal activity, in order to ensure efficient synaptic transmission. Our work provides the first quantified kinetic description of synaptic vesicle trafficking along the complete recycling pathway, and sheds new insight into the impact of the vesicle recycling machinery on stable and reliable synaptic transmission under variable levels of neuronal activity.

Loose-Patch Amperometry at Single Nerve Terminal

Neuronal information is majorly encoded chemically at synapses and the elementary unit of synaptic transmission is the contents of neurotransmitter released from single vesicle. However, the contents of quantal neurotransmitter have never been precisely estimated at synapses, which largely prevent our understanding the nature of quantal neurotransmitter release and its impact on neuronal information processing. In order to break through the technical bottleneck of precisely counting quantal neurotransmitter molecules, we developed a new approach in combination of electrophysiology and electrochemistry to measure intact quantal content of single vesicles. An etched submicro-carbon fiber electrode for electrochemical detection was designed to be enclosed in an electrophysiologically used

glass pipette. The glass pipette allowed the electrochemical electrode to access the release site, and amperometric recordings were made within the enclosed space at the electrophysiological loose-patch mode. Our study showed that the intact quantal release could be successfully detected at the dopaminergic varicosities by this loose-patch amperometric measurement in real time with negligible leakage.

Subquantalized synaptic transmission

The classic Katz's quantal theory states that the synaptic transmission is built up statistically of small all-or-none units, corresponding to an individual synaptic vesicle which are identical in size. In the light of this theory, miniature represents the basic unit, or quantum, from which the evoked response is composed. However, the nature of quantal events is still unknown and a variety of controversial and conflicting hypotheses of quantal transmission in the CNS were produced, mostly due to the complication of multiple sourced synaptic inputs and attenuated postsynaptic currents recording at central neurons. Here, we overcame this problem by taking advantage of

single synaptic bouton recording. We recorded spontaneous mEPSCs at single synaptic boutons of early age developing calyx synapse, micrometer size Ca²⁺ uncaging induced minis at single boutons of juvenile calyx synapse and micrometer size channelrhodopsin-2 activation evoked minis at single boutons of mature PB-CeAL synapse. In combination of the approaches of autocorrelation of the histogram of minis, the standard deviation of subquantal estimation and recombined noise analysis, we searched and identified subquantalization of single minis and developed a method to estimation the size of subquantal unit. It seems that subquantalized single minis can be observed in all three different preparations, not only at early developing synapses but also mature synapse; not only in spontaneous minis but also in evoked minis; not only at calyx, but also other type of synapse. We thus propose that the subquantalization can be a ubiquitous feature of synaptic transmission. Our study suggests that vesicle release based minis not be a real 'quantum' in synaptic information transfer and procession. Instead, the process of synaptic transmission could be regulated with higher precision and capacity than Katz quantal theory predicted.

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The neural mechanism and intervention strategy of opioid addiction

Drug addiction is a major global problem characterized by compulsive drug seeking and use despite harmful consequences. Both the rewarding effect of a drug and the desire to avoid severe withdrawal symptoms motivate drug-seeking behavior. We have identified a glutaminergic projection from the paraventricular nucleus of thalamus (PVT) to the nucleus accumbens (NAc) that

contributes to opiate withdrawal. Further study provides an input-output connectivity framework for understanding the role of NAc subcircuits in mediating reward and aversion. We also found that social rank modulates vulnerability to drug addiction via distinct dopaminergic pathways. Winning experiences can remodel the dopamine system and suppress drug-seeking behavior.

Winning experiences reduce drug-seeking behavior through remodeling of the dopamine system

Social status has a profound impact on mental health and propensity towards drug addiction. However, the neural mechanisms underlying the effects of social rank on drug-seeking behavior remain unclear. Here, we found that dominant male rodents (based on the social-rank tube test) had denser mesocortical dopaminergic projections and were more resistant to methamphetamine (METH)-seeking, whereas subordinates

had heightened dopaminergic function in the mesolimbic pathway and were more vulnerable to METH-seeking. Optogenetic activation of the mesocortical dopaminergic pathway promoted winning and suppressed METH-seeking in subordinates, whereas lesions of the mesocortical pathway increased METH-seeking in dominants. Elevation of social rank with forced-win training in subordinates led to remodeling of the dopaminergic system and prevented METH-seeking behavior. These results provide a framework for understanding the neural basis of the impact of social status on drug-seeking.

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Dissecting the mechanism of central neural regulation of bone metabolism

Central nervous system plays important roles in maintaining the homeostasis of human body and regulating the physiological functions of peripheral organs. However, the mechanism of central neural regulation of bone metabolism remain unclear. Our research interests are mainly focused on how different neural circuits and neurotrophic factors exert influences on bone metabolism in disease models. In previous studies, we have identified a GABAergic neural circuit in the ventromedial hypothalamus (VMH) mediates chronic stress induced bone loss.

On this basis, we found that the burst firing of VMH neurons was closely related to anxiety and energy metabolism abnormalities in mice. In addition, we demonstrated that optogenetic regulation can inhibit the excessive secretion of human parathyroid hormone and prevent bone loss. Currently, we are using cutting-edge technology including optogenetics, chemogenetics and neural tracing to dissect the underlying mechanism of crosstalk between the brain and the bone.

Skeleton interception and regulation

Skeleton interception and regulation refer to how the skeletal system responds to mechanical forces, hormonal signals, and environmental changes, maintaining bone homeostasis and function through feedback mechanisms involving the nervous system. This process includes direct cellular sensing, regulation by local factors, and remote control by the central nervous system.

In mechanical load sensing, osteoblasts and osteoclasts sense forces through mechanosensitive channels or integrin receptors,

with shear stress promoting bone formation. Chemically, bones respond to hormones like PTH, vitamin D, and estrogen for bone formation; while inflammatory factors such as TNF- α and IL-6 accelerate bone resorption. Bone regulation involves local factors (e.g., TGF- β , IGFs, Wnt proteins), neural regulation through the sympathetic and parasympathetic systems, and endocrine axes, including the brain-gut-bone axis. Studies show that neuronal activity changes in the hypothalamus can influence bone density.

As research progresses, these findings may lead to more effective strategies for preventing and treating bone diseases.

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Synaptic plasticity and its modulation

Synapse is one of the most important structures where neurons communicate with each other and neuronal circuit is formed. Synaptic plasticity is a general hardware implementation of learning and adaptation in the nervous system. Representation of the changing world and algorithms for adaptations are encoded in the diversity and complexity of synaptic plasticity. In addition,

dysfunction of synapse and plasticity underlie the majority of neuronal diseases, like developmental disorder, mental disorder and aging. Our group is trying to understand rules of synaptic plasticity and its modulation, especially focusing on the modulatory factors in homeostatic plasticity.

Homeostatic synaptic plasticity

A major challenge faced by neural circuits is to maintain proper neural processing while enabling effective information storage mediated by activity-dependent synaptic plasticity. This is not trivial, because plasticity of synaptic connections alters the flow of information between neurons. Furthermore, activity-dependent synaptic plasticity, namely long-term potentiation (LTP) and long-

term depression (LTD), creates positive feedback which when uncompensated lead to network instability. Homeostatic synaptic plasticity tunes presynaptic and postsynaptic strengths to maintain network stability in a slow time scale, for example, in a day-night cycle. We have evidences that homeostatic synaptic plasticity is both innate and subject to external stimuli. We are currently investigating the underlined mechanisms and their roles in diseases.

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Molecular basis underlying neuronal plasticity and neurodegeneration

Cognitive functions depend on the precise neural network formed by neurons in the brain. The precise organization of synaptic proteins and the spatial and temporal coordination of synaptic signaling events are central topics in neurobiology. The focus of the laboratory is to understand the molecular basis of synapse

development and plasticity in the central nervous system, and the pathophysiology of neurodegenerative diseases (e.g. Alzheimer's disease). The laboratory will also investigate the biomarkers for the diagnosis and prognosis of Alzheimer's disease and novel approaches for disease intervention.

Wiring of the brain: Neuronal migration, differentiation, and integration

We found that cytoskeletal regulators downstream of neurotrophin signaling (e.g. chimaerin, ARMS, Axin) control the critical multipolar-bipolar transition during neuronal migration and regulate axon and dendrite specification. Moreover, we demonstrated that Axin is crucial for regulating the elimination rate of dendritic spines. We recently revealed the mechanisms through which Eph receptor controls the maturation of synapses via Cdk5 kinase and showed that the two activators of Cdk5 play differential roles.

evidence of the existence of additional AD risk factors in the APOE locus. We are currently analyzing the associations between genotypes and multidimensional biomarkers to develop a scoring system for patient stratification, and using systems approaches and candidate approaches to decipher the AD-associated biomarkers and the underlying pathophysiological mechanisms.

Alzheimer's disease biomarkers: Genetics and beyond

Through a multi-institutional collaboration, we completed the first whole-genome sequencing project of AD in the Chinese population and identified novel risk genes associated with the alteration of immune pathways. Our follow-up study provided compelling

Peripheral-central communications in AD: Microbiome and metabolome

With self-developed complex-network modeling, we determined the optimal window period and bacterial candidates for gut microbiome (GM) manipulation in the AD mice, facilitating the interventions for AD by targeting the "gut-brain axis". In recent, we further constructed mediation analysis-pipeline on the basis of microbiome and metabolome, elucidated the GM-associated metabolic landscapes from peripheral to central tissues, and deciphered the regulatory mechanisms of the GM-metabolite-brain axis under the pathogenetic pressure of AD.

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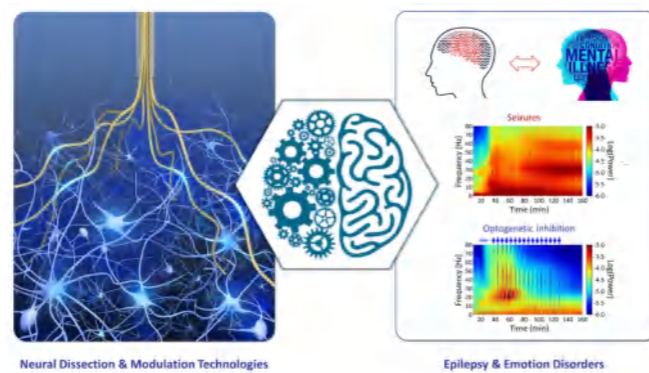
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Novel probes and sensors for neural circuit dissection

The brain is the most complicated biological structure in the known universe, which consists of numerous interconnected neurons which form complex and highly ordered neural circuits. To investigate the complex brain processing mechanisms at the functional level, researchers can directly measure and manipulate the activities of specific neurons or neural circuits in living, behaving animals using optogenetics. However, there is a great gap between brain research and the technologies available to use. To bridge this gap, the research of our group mainly focuses on: (1) novel research tools and techniques for neural recording and modulation, including flexible optogenetics, bio-sensors & bio-actuators, electrode arrays and neural interfaces; (2) functional dissection and modulation of specific neural circuits involved in neuropsychological diseases (epilepsy and emotion disorders).



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Neural circuits under mental disorders

Mental health issues are highly prevalent globally, with more than 10% of the world's population, or hundreds of millions of people, experiencing some form of mental health problem during their lifetime. Astrocytes, through their complex interactions with neurons, have a profound impact on neural networks and behavior. Understanding the specific regulatory mechanisms of astrocytes in different brain regions is crucial for comprehending and treating various mental disorders. Dr. Tu Jie's research team has long focused on investigating the neural circuits, cellular, and molecular mechanisms underlying behavioral abnormalities in mental disorders, exploring the glial cell mechanisms in these conditions:

1.The team elucidated the central nervous system circuit mechanisms of anxiety disorder induced by chronic stress

(*Molecular Psychiatry*, 2021, Corresponding Author), and clarified the role of astrocytes in this process (*Neural Regeneration Research*, 2024, Main Corresponding Author; *Cell Reports*, 2017, Co-Author).

2.They described how impaired "astrocyte-neuron" interactions in specific neural circuits lead to cognitive and behavioral abnormalities associated with mental disorders (*Neuron*, 2024, Main Corresponding Author).

3.The team explored the molecular mechanisms behind impaired "glial cell-neuron" interactions and proposed that neuronal autophagic flux is regulated by ubiquitin homeostasis, with its imbalance contributing to cognitive and emotional dysfunctions (*Autophagy*, 2025, Main Corresponding Author).

SELECTED PUBLICATIONS:

(* corresponding author; #equal contribution)

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Neural information processing and neural engineering

The lab develops novel tools for neural engineering and studies the information processing underlying specific neural pathways. Our work aims to help understand how the brain processes the neural information arising from neurons and the neural circuits to complete the tasks that requires emotional and cognitive processing. 1b do

Novel neural stimulation tools

In collaboration with materials scientists, we fabricated flexible device based on the triboelectric nano-generator which can generate pulses suitable for neural stimulation. This device used electronic-skin materials and can harvest energy from human motion, therefore we developed a self-powered electronic skin for neuroscience and biomedical engineering applications. The self-powered electronic skin can be coupled with different sensors that can detect odors, vision and tactile touch. Inspired by the biological olfactory systems, we designed the structure of the odorant sensing units and the self-powered device can respond to odors. The artificial olfactory receptor can detect different odors can when it is connected to the brain, it can lead to behavior changes. We also demonstrate that the self-powered device can be extended to neural stimulations by producing reproducible excitatory postsynaptic potentials.

this we employ a range of technological developments including electrophysiology, novel materials and computational methods. Development of novel neural stimulation tools and understanding of neural information processing contribute to brain-machine interactions and brain-inspired intelligence.

Prefrontal-subcortical information processing

Recent electrophysiological studies in rodents have implicated hippocampal-prefrontal connectivity in anxiety, spatial learning and memory-related tasks. In human patients with schizophrenia and autism, robust reduced connectivity between the hippocampus (HPC) and prefrontal cortex (PFC) has been reported. We measured the directional information processing in mice by Granger causality, a mathematical tool that has been used in neuroscience to quantify the oscillatory driving relationship between the ventral HPC (vHPC) and the PFC in two anxiety tests and between the dorsal HPC (dHPC) and the PFC in social interaction test. The current findings indicate that directed oscillatory activities between the PFC and the HPC have task dependent roles during exploration in the anxiety test and in the social interaction test. Currently we are combining optogenetic/pharmacogenetic tools and in vivo electrophysiology to manipulate the thalamic areas that bridge the information relay between the HPC and the PFC.

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Molecular mechanism of prion-like proteins in neurodegenerative diseases

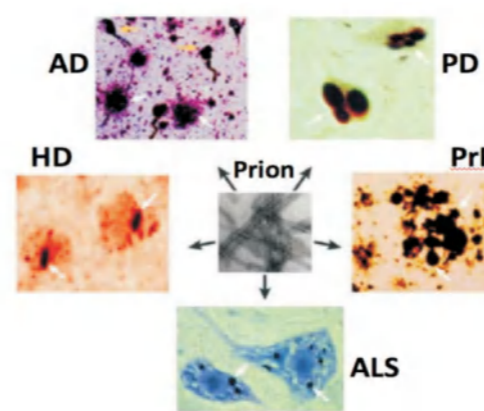
Neurodegenerative diseases are a group of conditions that cause the progressive loss of nerve cells in the brain and spinal cord, leading to damage or death of neurons and subsequent loss of cognitive, physical, and behavioral abilities. Caused by various factors, including genetic mutations, environmental toxins, and aging, neurodegenerative diseases include Alzheimer's disease,

Parkinson's disease, and amyotrophic lateral sclerosis (ALS). Our overall research goal is to determine how prion-like proteins, such as amyloid beta, TDP-43 and α -Synuclein, are involved in various neurodegenerative diseases, and to enhance drug development based on information of their function and structure.

Prion: Disease and Non-disease Function

Prions, or proteins that assume self-perpetuating and highly aggregated conformations, underlie infectious neurodegenerative diseases in humans as well as a variety of neurodegenerative disorders connected with protein amyloids, examples of which include Alzheimer's disease, Huntington's disease, Parkinson's disease, and Amyotrophic Lateral Sclerosis. However, some fungal prions have been found non-toxic and beneficial. The hypothesis

that prions have physiological roles is also supported by our recent work in the nervous system. However, the molecular mechanisms for regulation of these prion-like proteins is largely unknown. Knowledge of these mechanisms is essential to inform diagnosis and treatment of a number of conditions, and would also considerably promote understanding of the normal functioning of the nervous system.



Neurodegenerative diseases and Aging

Aging is the primary risk factor for neurodegenerative diseases, such as Alzheimer's and Parkinson's. As the brain ages, it experiences a decline in neural function, decreased neural plasticity, and a weakened blood-brain barrier. This makes it more susceptible to damage from accumulated neurotoxic proteins like amyloid beta and tau in Alzheimer's disease or alpha-synuclein in Parkinson's disease. Furthermore, age-related decreases in neurotrophic factors and immune function can impede neuronal repair mechanisms. The result is a heightened vulnerability to neurodegeneration, leading to cognitive and motor dysfunction. Therefore, a better understanding of the mechanisms underlying the aging process is crucial for the development of effective strategies to prevent or delay neurodegenerative diseases.

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m⁶A is the most abundant reversible modification existing on eukaryotic mRNA and ncRNA, and was found to be involved in nearly every step of RNA life circle, including splicing, transport, translation and decay. As a new post transcriptional regulation pathway, m⁶A affects a lot of biological processes. Whereas the

exact role of m⁶A in regulating different brain functions and disease are largely unknown. Combining RNA/m⁶A-seq, proteomic analysis, genetic mouse model, behavioral assay, and electro-physiological recording, we will investigate the mechanism of how m⁶A was participated in different brain functions and diseases.

🧠 m⁶A facilitates hippocampus-dependent learning and memory through YTHDF1

N⁶-methyladenosine (m⁶A), the most prevalent internal RNA modification on mammalian messenger RNAs, regulates the fates and functions of modified transcripts through m⁶A specific binding proteins. In the nervous system, m⁶A is abundant and modulates various neural functions. Whereas m⁶A marks groups of mRNAs for coordinated degradation in various physiological processes, the relevance of m⁶A for mRNA translation in vivo remains largely unknown.

Here we show that, through its binding protein YTHDF1, m⁶A promotes protein translation of target transcripts in response to neuronal stimuli in the adult mouse hippocampus, thereby facilitating learning and memory. Mice with genetic deletion of

YTHDF1 show learning and memory defects as well as impaired hippocampal synaptic transmission and long-term potentiation. Re-expression of YTHDF1 in the hippocampus of adult YTHDF1-knockout mice rescues the behavioral and synaptic defects, whereas hippocampus-specific acute knockdown of YTHDF1 or Mett13, which encodes the catalytic component of the m⁶A methyltransferase complex, recapitulates the hippocampal deficiency. Transcriptome wide mapping of YTHDF1-binding sites and m⁶A sites on hippocampal mRNAs identified key neuronal genes. Nascent protein labelling and tether reporter assays in hippocampal neurons showed that YTHDF1 enhances protein synthesis in a neuronal-stimulus dependent manner. In summary, YTHDF1 facilitates translation of m⁶A-methylated neuronal mRNAs in response to neuronal stimulation, and this process contributes to learning and memory.

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The key technologies for High Performance Brain-Computer Interface and Neuromorphic Intelligence

Our group has been working on:

1. Neuro-electronic and Neuro-photonic technologies for high bandwidth Brain-Computer Interface
2. Neural circuit mapping and decoding technologies for neural network simulation and neuromorphic computing
3. Neuromorphic device and system development for humanoid robotics.

🧠 Reverse-engineer the brain to advance artificial intelligence

The approach of working backwards from measurements of the functioning system to engineer models of how that system works is called reverse engineering. Discovering how the human brain works in the language of engineers will not only lead to transformative AI. It will also illuminate new approaches to helping those who are blind, deaf, autistic, schizophrenic, or who have learning disabilities or age-related memory loss. Armed with an engineering description of the brain, we will see new ways to repair, educate, and augment our own minds.

🧠 Nano-enabled neural interfaces

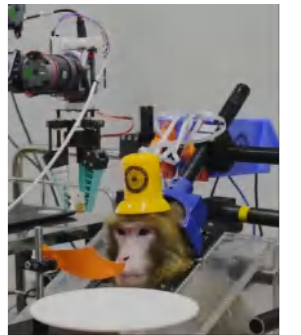
Advances in microscopy and molecular strategies have allowed researchers to gain insight into the intricate organization of the mammalian brain and the roles that neurons play in processing information. Despite vast progress, therapeutic strategies for neurological disorders remain limited, owing to a lack of biomaterials for sensing and modulating neuronal signalling in vivo. Therefore, there is a pressing need for developing material-based tools that can form seamless biointerfaces and interrogate the brain with unprecedented resolution. The architecture of the NAc in controlling reward and aversion.



The cover illustrates a bioresorbable silicon-based optoelectronic thin film for the selective excitation or inhibition of neural activities in peripheral and central nervous tissues.
(Image: Xing Sheng, Tsinghua University)

🧠 Brain-Computer interface system

Brain-Computer interface (BCI) system aims to restore lost function in patients with neurological and neuropsychiatric disorders by creating a direct control pathway to the brain to read out neural activity, interact with an external device, and in some cases write in neural information by stimulating the brain. The BCI creates a closed-loop control system in which the brain is the controller, deciding on its control commands in the form of neural activity to move the neuroprosthetic limbs based on sensory feedback and movement goals.



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Memory and Spatial Navigation

Our group focuses on understanding construction of the memory system and how the stored experiences are used to guide future learning and behavior.

The hippocampus is the core of a neural memory system providing an objective spatial framework within which the items and events of an organism's experience are located and interrelated. Since the breakthrough discovery of grid cells in the medial entorhinal

cortex (MEC), the general wisdom is that MEC provides the hippocampus with the necessary spatial signal. However, the behavioral correlates of the cells in the lateral entorhinal cortex (LEC), which, together with MEC, constitute the main cortical gateways to the hippocampus, are largely unexplored. We found that LEC neurons encode egocentric information about external items, such as the boundaries of the environment and 3D objects.

Current and future research areas include

- (1) Using microendoscopic calcium imaging in freely moving animals to associate the activity of navigation cells with behavior;
- (2) How does information about external items interface with the

hippocampal spatial representation?

- (3) The transformation between egocentric and allocentric information.

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Psychiatric Neuroscience Research in Non-human Primates

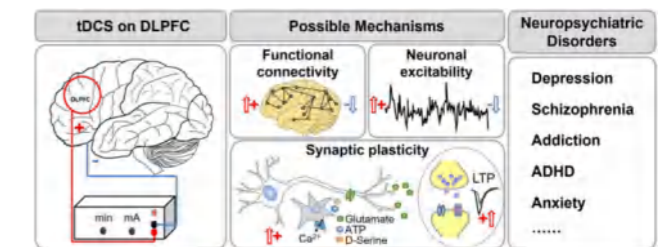
Our long-term goal is to identify the neural mechanisms of neuropsychiatric diseases such as drug addiction, depression and anxiety. We use classic behavioral pharmacological approaches, sophisticated electrophysiology as well as cutting edge neuronal modulational technologies such as optogenetics, TMS, tES and

FUS to discover the responsible neural circuits for these diseases in non-human primate models. In addition, we assess the therapeutic effects of new technologies in advanced animal models.

Neural Mechanisms of the Psychiatric Diseases

Psychiatric diseases, such as depression, anxiety, schizophrenia, addiction etc., affect hundreds of millions of people in the world. Most of these diseases need more effective treatments. Our lab is interested in understanding brain mechanisms of these diseases and how to modulate the neural activity to restore the brain functions. To do this, we are trying to develop advanced rodents and primate animal models and evaluation systems to better mimic the conditions in human patients. Using proper animal models, we test the therapeutic effects of various chemical compounds and neuromodulation techniques.

In future studies, we will use intracranial micro injection, extracellular electro-physiology, and other neural circuits modulation tools to investigate the circuitry level mechanisms of these brain diseases.



DLPFC is a target for neuromodulation of psychiatric diseases (Li et.al., 2022).

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Neural Mechanisms Underlying Sleep and Cognition

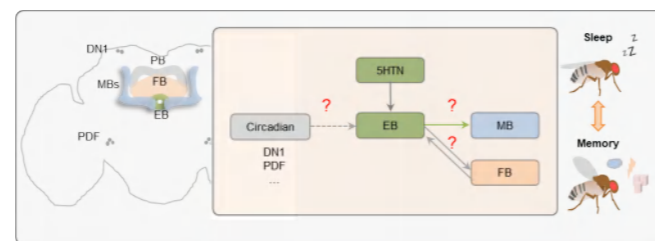
Sleep, learning and memory are complex phenomena that are of great importance for survival. Although sleep architecture has a profound impact on learning and memory, the molecular mechanism and neural circuits are still largely unknown. Dysfunctions in sleep and cognition are usually associated with neurodegenerative disorders, such as Alzheimer's disease. To

investigate the molecular and cellular basis of the interaction between sleep and memory, we employ fruit fly *Drosophila melanogaster* as the animal model and apply multidisciplinary approach, including behavioral, genetic, anatomical and imaging techniques. We also study the same questions through cross-species verification.

Integrated Neural Circuits of Sleep and Memory Regulation

Memories are affected by physiological processes, including the most paramount physiological process, sleep. Sleep plays a critical role in gating and stabilizing memories, evidenced from detrimental impacts of sleep deprivation on cognitive abilities in many stages of memory processing. In turn, learning experience can drive sleep need. Thus, investigation of the interactions between sleep and memory is one of the greatest challenges in neuroscience, which worth substantial efforts. Sleep in *Drosophila* is well-documented, and exhibits almost all the hallmarks as in mammals, including circadian and homeostatic regulation, attenuated responsiveness, and the existence of distinctive sleep stages. Despite current understanding of MB circuits, a certain amount of MB wake promoting and sleep promoting neurons still remain uncharacterized how functionally integrated in both regulations. Besides the MB, the central complex (CX) also has been

shown in multiple physiological regulations, including sleep and memory. CX composes of four central brain neuropils, from anterior to posterior are the noduli, the ellipsoid body (EB), the fan-shaped body (FB) and the protocerebral bridge (PB). The FB and EB are illustrated of their participation in sleep regulation, such as sleep amount, sleep structure as well as sleep homeostasis. However, mechanisms how sleep affects memory remain largely elusive.



Current Projects in Liu Lab (Wu and Liu, 2023)

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Neural Mechanisms of Pain

Pain is a multi-dimensional unpleasant experience that strongly affects daily life, and pain treatment is still a huge medical challenge nowadays. To understand the neural mechanisms of pain, we will selectively label and manipulate specific group of target neurons via intersectional mouse genetic tools, in both peripheral and central nervous system, and decipher the pain

circuits by combined anatomical, electrophysiological, opto-/chemogenetic and behavioral approaches. We will also study the interaction of pain and body homeostasis/autonomic systems. Our findings will provide new insights for the development of new pain relievers and analgesic strategies.

Neural Circuits Driving Exteroceptive v.s. Interoceptive Reactions to Painful Stimuli

Animals and humans display two types of response to noxious stimuli. The first includes reflexive defensive responses (exteroceptive, sensing external environment) that prevent or limit injury. When the first-line response fails to prevent tissue damage (for example, a finger is burnt), the resulting pain invokes a second-line coping response—such as licking the injured area to soothe suffering (interoceptive, sensing own body changes). However, the underlying neural circuits that drive these two strings of behaviour remain poorly understood. We found spinal neurons marked by coexpression of TAC1Cre and LBX1F_{lpo} drive coping responses

associated with pain. Ablation of these neurons led to the loss of both persistent licking and conditioned aversion evoked by stimuli (including skin pinching and burn injury) that—in humans—produce sustained pain, without affecting any of the reflexive defensive reactions that we tested. This selective indifference to sustained pain resembles the phenotype seen in humans with lesions of medial thalamic nuclei. Consistently, spinal TAC1-lineage neurons are connected to medial thalamic nuclei by direct projections and via indirect routes through the superior lateral parabrachial nuclei. Our study therefore reveals a fundamental subdivision within the cutaneous somatosensory system, and challenges the validity of using reflexive defensive responses to measure sustained pain.

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Circuit Dynamics Underlying Brain Function and Disorders

Lau lab focuses on the dynamics of neuronal synapses and networks, and the neural circuitry mechanisms underlying brain disorders, especially those related to emotional stress.

We employ electrophysiological and optical approaches to study the dynamics of neuronal network in vitro and in vivo. Pharmacological and optogenetic manipulations are used to modulate neuronal circuit dynamics and to establish animal models of emotion-related disorders, such as anxiety, depression, and autism. To systematically dissect neural circuits involved in such disorders, we also develop and apply high-throughput system-wide mapping techniques based on tissue clearing and

high-speed 3D imaging (VISoR) in collaboration with Dr. Guoqiang Bi's group.

Current research directions include: (1) Emergence of reverberatory activity with conserved firing patterns in neuronal networks through activity-dependent synaptic plasticity; (2) Brain-wide activity mapping and neural circuitry mechanisms in animal models of depression, anxiety, and autism; (3) The mind-body problem – how mental conditions interact with functional and diseased states of internal organs through central-peripheral connectivity.

Neural circuit mechanisms in brain disorders

Depression is a severe psychiatric disorder with wide prevalence and low recovery rate. Previous studies have identified various brain regions associated with depression, but no unanimous conclusions were drawn owing to individual difference of patients and restricted resolution of neuroimaging techniques in clinical investigations. Therefore, a systematic and quantitative whole-brain activity map of depression is needed to further understand the disorder.

Combining c-fos immunostaining and VISoR fast imaging, we have obtained the activity map of subcortical brain regions in two depression models, the congenital depressive Wistar Kyoto rats and chronic social defeat mice. We have further examined the connectivity between core circuit regions and demonstrated their critical roles in regulating depression-like behaviors. Other ongoing research projects in the lab include neural circuits of autism and self-injurious behavior.

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High resolution cell biology of membrane protein complexes and drug discovery

Recent advances in Cryo Electron Microscopy allow investigating problems that have been difficult/impossible to solve via other structural biology methods. In particular, it has been possible to degerming the structure of non-crystalline membrane protein at true-atomic resolution of better than 2.5 Angstrom, which enables a mechanistic understanding of mechanisms and opens

opportunities for rational drug design. Even more exciting, it is now possible to use sub-tomogram averaging from cryo electron tomograms to visualize the in-situ structure of membrane proteins at high resolution directly within membranes, which is critical for maintaining native conformations and functionality.

Snap Molecular Building Blocks of Brain Computing

Synapses are specialized devices where learning and memory occur and the efficient transmission of synaptic signals relies on the delicate structure and complex molecular composition of the synapses. However, the small size (several hundred nanometers in

diameter) and heterogeneous nature of the synapses pose significant challenges in direct observation of the molecules inside synapses. Based on the proposed processing technique for in situ cryo-electron tomography, for the first time we observe individual GABAA receptors and their organization on the synaptic membrane, endowing the brain's ability for information processing.

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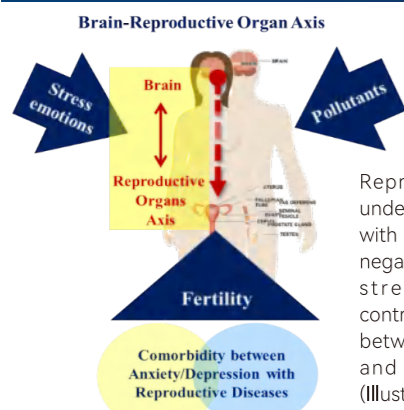
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Brain-Reproductive Organs Axis and Its Role in Homeostasis

The body and the nervous system together form one integrated system, whether healthy or diseased. Reproductive functions including hormone production, gametogenesis and sexual behaviors are under sophisticated central and peripheral

regulations. We focus on the study of the brain-reproductive organs axis at the neural circuitry/neuroendocrine level, which might shed light on future discoveries and potential clinical benefits, especially in stress-associated reproductive diseases.



Reproductive functions are under sophisticated regulation, with both internal stressors like negative emotions and external stressors like pollutants contributing to the comorbidity between emotional disorders and reproductive diseases (Illustration by Lei Li).

Locus Coeruleus: A Modulation and Integration Brainstem Hub and Its Roles in Innate Defensive Behavior, Balancing, and Reproduction.

The locus coeruleus (LC), located in the pons of the brainstem, is the principal site for the brain synthesis of norepinephrine. Our tracing data showed that the LC is one of the central targets of ovarian innervation. The locus coeruleus noradrenergic system is the most extensively studied stress-activated modulatory system with its widespread outputs. We demonstrated that the visually evoked innate defensive response was modulated by a locus

coeruleus-superior colliculus (LC-SC) projection (Li et al., 2018; Li et al., 2018; Montardy et al., 2022; collaboration with LP Wong group). We also reported the locus coeruleus-vestibular nuclei (LC-VN) projection and its roles in stress-disturbed posture and balancing function (Wei et al., 2021). LC was also the central mediator of gut microbiota metabolite – indole in its anxiogenic effect (Mir et al., 2024). As a central nucleus connected to ovarian innervation, further roles of the LC in reproductive regulation are supported by NSFC funding and are currently under investigation.

Negative Effects of Microplastics on Brain and Reproductive Health

Microplastics and nanoplastics are environmental pollutants of great concern in recent years, with the largest pollution coming from the ocean, known as "marine PM2.5." There is an urgent need for biological assessments and mechanistic studies of the effects of microplastics/nanoplastics on brain health and reproductive health. Our lab is actively involved in this field with intensive international collaboration, supported by the Alliance of International Science Organizations (ANSO). Our collective efforts and progress were presented at the Belt and Road Forum for Young Scientists during the First Belt and Road Conference on Science and Technology Exchange 2023 (Lu et al., 2021, cited by the WHO 2022 report; Ho et al., 2022; Lo et al., 2023; Yang et al., 2023; Li et al., 2022; Tsukazawa et al., 2022; Lai et al., 2022; Lin et al., 2024a; Lin et al., 2024b).

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Sexual Dimorphism in Neuroethological Differences and Their Underlying Mechanisms

Understanding how sex differences in the brain contribute to distinct neuroethology characteristics, from molecular mechanisms to neural circuits, is a major challenge in neuroscience. Animals have developed distinct natural behaviors, many of which show sexual dimorphism. Moreover, many neuropsychiatric disorders exhibit sex differences in terms of prevalence and clinical features. Our approach combines machine learning-based behavioral

analysis with neural circuit tracing and modulation techniques to address three primary goals: 1) developing and advancing data-driven techniques for behavioral genomics analysis, 2) investigating the distinct features of sex-specific neuroethology and their underlying mechanisms; 3) elucidating variations in neuroethology and their neural mechanisms across different brain states.

Hierarchical Behavioral Analysis Framework (HBAF) as a platform for standardized quantitative identification of behaviors

Behavior is composed of modules that operate based on inherent logic. Understanding behavior and its neural mechanisms is facilitated by clear structural behavioral analysis. Here, we developed a hierarchical behavioral analysis framework (HBAF) that efficiently reveals the organizational logic of these modules by analyzing high-dimensional behavioral data. By creating a spontaneous behavior atlas for male and female mice, we discovered that spontaneous behavior patterns are hard-wired,

with sniffing serving as the hub node for movement transitions. The sniffing-to-grooming ratio accurately distinguished the spontaneous behavioral states in a high-throughput manner. These states are influenced by emotional status, circadian rhythms, and lighting conditions, leading to unique behavioral characteristics, spatiotemporal features, and dynamic patterns. By implementing the straightforward and achievable spontaneous behavior paradigm, HBAF enables swift and accurate assessment of animal behavioral states and bridges the gap between a theoretical understanding of the behavioral structure and practical analysis using comprehensive multidimensional behavioral information.

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Brain Wiring by Nature and Nurture

Our brain is the most complicated organ in our body, which comprises billions of neurons and trillions of neuronal connections with remarkable spatiotemporal specificity. Furthermore, it also comprises similar number of glia cells and complex network of blood vessels that support and modulate neuronal networks. This highly complicated yet organized structure gives rise to all our thoughts, emotions and actions. How is such a complicated

structure established during development has been a central question in neuroscience. Disruptions of brain development lead to numerous brain disorders, such as ASD, ADHD, and schizophrenia. Regulation of brain wiring occurs at different scales from genome to behavior. We aim to reveal a unifying logic from nanoscale to macroscale that underlies the brain wiring regulated by nature and nurture.

Regulation of brain wiring

It has been accepted that both genetic and environmental factors regulate brain wiring. However, we do not know the exact relationships between individual factors and wiring phenotypes. Recent establishment of several comprehensive clinical cohort databases in the US and Europe, and new methods for multidimensional data analysis offer us an unprecedented opportunity to reveal new insights into this question, providing objects for mechanistic studies.

Latest advances in spatial biology have revealed, at single cell level, co-variation of cellular transcriptome with structural and functional features of neuronal networks along spatial axes across the whole brain. We are studying whether and how experience regulates this spatial molecular and cellular organization, as well as its relationship to patterns of neuronal connectivity and physiology across brain regions, and influence to behavior. This research system will offer

mechanistic insights into how brain wiring is regulated by nature and nurture, and render new insights in brain disorders.

Regeneration of the visual pathway

Glaucoma and optic nerve injury are major causes of irreversible vision loss. These diseases co-feature neuronal cell death and axon loss, resembling brain degenerative diseases such as Alzheimer's Disease and Parkinson's Disease. Furthermore, the eye is part of the CNS. With relatively simple structure and tissue environment compared to the rest of the brain, it is possible that breakthroughs on CNS regeneration will be easier in the visual system. We are trying to apply combinatorial strategies used by normal development to regenerate the visual pathway, in both rodent and non-human primate models. Similar strategies has been shown to successfully regenerate mouse spinal cord after injury, giving us more confidence in this research direction.

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Neuronal and Functional Regulation in the Non-human Primates

We are interested in understanding the neural circuits of visual perception, attention, consciousness, and emotion in nonhuman primates (NHP), and how we can regulate these basic functions by manipulating the activities of specific neurons or pathways. To this end, we use several novel neuromodulation techniques, including optogenetics and chemogenetics, in combination with traditional electrophysiology, MRI, and behavioral experiments to uncover

how visual information is encoded in the brain, how attention modulates perception, how emotion interacts with cognition, and how these functions can be manipulated in the behaving monkeys. Eventually, we hope our findings can help pave the way for extensive translational studies and clinical applications in the near future.

Multi-channel Recording in Deep Regions of Monkeys

Previously, it was very difficult to record neural activity from deep brain regions (e.g., the Amygdala, Inferior Temporal Cortex) in behaving monkeys using traditional techniques. We have successfully applied the semi-chronic technique to enable long-term recording from the amygdala in awake monkeys. This technique allows us to obtain multiple-channel (128 channels) signals from almost anywhere in a monkey's brain (up to 42 mm deep) for several months. In addition, while the system can hold signals very stable for a long time, it allows adjusting the position for each recording electrode at any time, even after all the electrodes have been implanted. We are now using this technique to study how the monkey amygdala encodes facial expression,

olfactory valence, and integrates multisensory information.

Primate Preoptic Neurons Drive Hypothermia and Cold Defense

Activating a subpopulation of neurons in the preoptic area (POA) by a chemogenetic strategy reliably induces hypothermia in anesthetized and freely-moving macaques. Comprehensive monitoring of physiological parameters reveals that such hypothermia is accompanied by autonomic changes, including a rise in heart rate, skeletal muscle activity, and correlated biomarkers in blood. Consistent with enhanced ambulatory movement during hypothermia, the animals show a full range of cold defense behaviors. Resting-state fMRI confirms the chemogenetic activation of POA and charts a brain-wide network of thermoregulation.

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The main research of Ye lab includes: 1. Molecular Mechanism of neurodegenerative diseases' pathologies; 2. Development of small molecular drugs for treating neurodegenerative diseases; 3. Identification of early diagnosis biomarkers for neurodegenerative diseases. Employing the counter-screening of high-throughput TrkB receptor-dependent anti-apoptotic drugs, Ye lab discovered a specific small molecular TrkB agonist 7,8-dihydroxyflavone (7,8-DHF) in the first time. It mimics the cognate TrkB ligand BDNF by binding to TrkB and selectively activating the receptors. It creatively solves the technical problem that BDNF cannot be taken orally or across the blood-brain barrier (BBB) to enter the brain. Mounting evidence supports that 7,8-DHF exerts remarkable therapeutic effects in Alzheimers disease (AD), Parkinson's disease

(PD), depression, osteoporosis and many other diseases after oral administration. The optimized prodrug R13 and the synthetic second generation derivative CF3CN exhibit improved in vivo stability and more potent TrkB agonistic activities. In addition, Ye lab was the first to discover delta-secretase (AEP), which cleaves both APP and Tau simultaneously, in addition to cleavage of a-Synuclein, driving both AD and PD pathogenesis. Inhibition of delta-secretase effectively treats AD and PD in mouse disease models. Remarkably, his lab established that C/EBPβ/AEP signaling is not only the core driving force for various age-related neurodegenerative diseases but also mediating the aging process and longevity

Inhibition of δ-secretase improves cognitive functions in mouse models of Alzheimer's disease

Delta-secretase, also known as asparagine endopeptidase (AEP) or legumain, is a lysosomal cysteine protease that cleaves both amyloid precursor protein (APP) and tau, mediating the amyloid-β and tau pathology in Alzheimer's disease (AD). Professor Ye's research team reported the therapeutic effect of an orally bioactive and brain permeable δ-secretase inhibitor in mouse models of AD. They performed a high-throughput screen and identified a non-toxic and selective δ-secretase inhibitor, termed compound 11, that specifically blocks δ-secretase but not other related cysteine proteases. Chronic treatment of tau P301S and 5XFAD transgenic mice with this inhibitor reduces tau and APP cleavage, ameliorates synapse loss and augments long-term potentiation, resulting in protection of memory. Therefore, these findings demonstrate that this δ-secretase inhibitor may be an effective clinical therapeutic agent towards AD.

Asparagine endopeptidase (AEP) cleaves a-synuclein and mediates pathologic activities in Parkinson's disease.

The pathological features of Parkinson's disease (PD) mainly include the absence of dopaminergic neurons in the substantia nigra and the accumulation of Lewy bodies in the remaining dopaminergic neurons.

Lewy bodies are formed by aggregation of hyperphosphorylated or truncated a-Synuclein. Professor Ye's research team found that AEP is activated in the PD patient brains and cleaves human a-Synuclein at N103 in an age-dependent manner. Inhibition of AEP-mediated cleavage of a-Synuclein reduces the pathological role of a-Synuclein. These findings support the role of AEP as a key mediator of a-Synuclein-related pathological effects in PD.

C/EBPβ regulates delta-secretase expression and mediates pathogenesis in mouse models of Alzheimer's disease.

Delta-secretase cleaves both APP and Tau to mediate the formation of amyloid plaques and neurofibrillary tangle in AD. Professor Ye's team showed that a CCAA'Penhancer-binding protein (C/EBPβ), an inflammation-regulated transcription factor, acts as a key age dependent effector elevating both delta-secretase AEP and inflammatory cytokines expression in mediating pathogenesis in AD mouse models. They found that C/EBPβ regulates delta-secretase transcription and protein levels in an age-dependent manner. Overexpression of C/EBPβ in young 3xTg mice increases delta-secretase and accelerates the pathological features including cognitive dysfunctions, which is abolished by inactive AEP C189S. Conversely, depletion of C/EBPβ from old 3xTg or 5XFAD mice

diminishes delta-secretase and reduces AD pathologies, leading to amelioration of cognitive impairment in these AD mouse models. Thus, these findings support that C/EBPβ plays a pivotal role in AD pathogenesis via increasing delta-secretase expression.

FSH blockade improves cognition in mice with Alzheimer's disease.

Alzheimer's disease has a higher incidence in older women, with a spike in cognitive decline that tracks with visceral adiposity, dysregulated energy homeostasis and bone loss during the menopausal transition^{1,2}. Inhibiting the action of follicle-stimulating hormone (FSH) reduces body fat, enhances thermogenesis, increases bone mass and lowers serum cholesterol in mice. Professor Ye's team show that FSH acts directly on hippocampal and cortical neurons to accelerate amyloid-β and Tau deposition and impair cognition in mice displaying features of Alzheimer's disease. Blocking FSH action in these mice abrogates the Alzheimer's disease-like phenotype by

inhibiting the neuronal C/EBPβ-δ-secretase pathway. These data not only suggest a causal role for rising serum FSH levels in the exaggerated Alzheimer's disease pathophysiology during menopause, but also reveal an opportunity for treating Alzheimer's disease, obesity, osteoporosis and dyslipidaemia with a single FSH-blocking agent.

Development of an a-synuclein positron emission tomography tracer for imaging synucleinopathies

Synucleinopathies are characterized by the accumulation of a-synuclein (a-Syn) aggregates in the brain. Positron emission tomography (PET) imaging of synucleinopathies requires radiopharmaceuticals that selectively bind a-Syn deposits. Professor Ye's team developed a promising PET tracer F0502B for imaging aggregated a-Synuclein (a-Syn), providing a tool to improve the understanding of disease progression and monitor the therapeutic efficacy in clinical trials.

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Neural Mechanisms of Affective Disorders and Drug Addiction

It has become increasingly imperative to develop more effective treatments for neuropsychiatric disorders. Given the evident heterogeneity of individuals suffering from neuropsychiatric disorders, my lab is interested in understanding why some people are more prone to these conditions (susceptible), but others do not (resilient). Specifically, we investigate the neurophysiological basis of individual variations in response to drugs of abuse and chronic stress, a well-known risk factor for affective disorders. Utilizing rodent models and advanced techniques, including cell type-specific

electrophysiological, viral-mediated gene transfer, circuit-dissecting optogenetic and circuit-mapping molecular profiling approaches, we study the molecular, cellular and neural circuit mechanisms underlying individual variations in drug addiction and affective disorders. The long-term goal of our research is to identify novel drug targets and develop innovative treatments for substance-use and affective disorders based on the understanding of individual variations.

Segregation of Susceptibility and Resilience to Stress

Prolonged stress can cause a variety of psychiatric disorders, including major depressive disorder. However, this occurs in some individuals (susceptibility), but not in others (resilience). We were able for the first time to segregate susceptible and resilient behavioral phenotypes in a chronic social defeat stress (CSDS) mouse model (Cell 2007).

Dopamine Mechanism of Susceptibility and Resilience

We revealed the heterogeneity of ventral tegmental area (VTA) dopamine (DA) neurons in response to CSDS. We observed that in susceptible mice (Fig 1), VTA DA neurons projecting to medial prefrontal cortex (VTA-mPFC) displayed a decreased firing rate, whereas the nucleus accumbens-projecting VTA DA neurons (VTA-NAc) exhibited hyper-activity. Optogenetically mimicking the firing alterations of these circuits induced depression-related behaviors. In contrast, the resilient mice exhibited an unaltered firing activity in both of these circuits (Naure 2013; Nat Neurosci 2014). Strikingly, the unchanged baseline activity of VTA-NAc neurons in the resilient group was maintained via an increased excitatory I_h current and counteractively increased inhibitory K^+ channel currents, a homeostatic E/I balance that was absent in VTA-mPFC DA neurons (Science 2014). Interestingly, the firing activity of VTA-amygdala (AMG) neurons was decreased in both susceptible and resilient mice, indicating that this projection circuit may not contribute to the

segregation of stress susceptible and resilient phenotypes (Nature Commun 2022). These studies reveal the circuit-specific adaptations and functional heterogeneity of VTA DA neurons in response to CSDS.

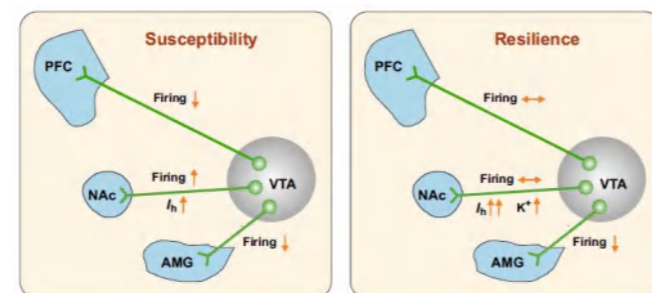


Figure 1. The neuroadaptations of midbrain dopaminergic circuitry in response to CSDS. (by Ming-Hu Han)

We further explored possible extrinsic synaptic contributions to these projection-specific neuroadaptations. Specifically, we investigated the locus coeruleus (LC) contribution to the homeostatic E/I plasticity observed in the VTA-NAc circuit of resilient mice (Fig 2). Our data showed that the firing activity of LC neurons projecting to the VTA (LC-VTA) was increased selectively in the resilient group when compared to stress-naïve control and susceptible mice. Optogenetic activation of LC-VTA neurons reversed depression-related behaviors in previously defined susceptible mice. Moreover, our circuit-specific molecular profiling studies in DAT-Cre mice showed that $\alpha 1$ - and $\beta 3$ -adrenergic receptors were enriched in VTA-NAc DA neurons as

compared to whole VTA DA neurons, suggesting that LC-VTA neurons connect to the NAc through $\alpha 1$ and $\beta 3$ receptors in the VTA. Our current work supports the hypothesis that LC-VTA norepinephrine circuit neurons contribute to the active resilience mechanism (K^+ channel compensation) in VTA-NAc DA circuit neurons predominantly through the $\alpha 1$ - and $\beta 3$ -adrenergic receptors expressed in VTA-NAc DA neurons (Biol Psychiatry 2019).

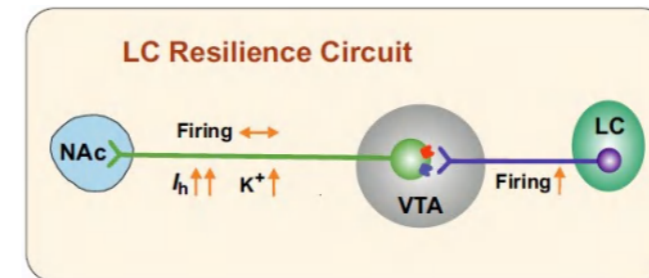


Figure 2. Working hypothesis of LC-VTA-NAc resilience neural circuit. (by Ming-Hu Han)

Taking together, our studies suggest that K^+ channels play an active role in mediating resilience. We thus further evaluated KCNQ subtype of K^+ ion channels and demonstrated that systematically applied KCNQ opener retigabine (ezogabine) was able to normalize the hyperactivity of VTA-NAc neurons in susceptible mice, and showed significant antidepressant effects in CSDS model and patients with major depressive disorder (Nat Commun 2016; Mol Psychiatry 2020; Am J Psychiatry 2021). Our studies have provided important novel information in the growing field of resilience research.

Individual Variations in Alcohol Drinking Behaviors

Alcohol-use disorders create an enormous global health burden that ranks number two in the mental, neurological and substance-use disorders, which again indicates an imperative need for more effective treatments. In contrast to most drugs of abuse, there are intriguing individual behavioral variations in alcohol use: some

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individuals consume alcohol for decades in a controlled manner without developing dependence, but others have an uncontrollable desire to consume, resulting in a severe form of alcohol-use disorders. Understanding the neural mechanisms that underlie such differences afford the unique potential for developing personalized therapeutic strategies and provide highly useful drug targets for the treatment of alcohol-use disorders.

Previous efforts to understand the neurological mechanism of drinking variations in an animal model have utilized rodents with variable gene backgrounds. Similar to stress response, it is interesting that there is also variability of alcohol drinking behaviors in genetically identical inbred mice. In our studies, we observed that in C57BL/6J mice, a strain typically used in alcohol research because of its high ad libitum consumption of alcohol, 10-15% of the population displayed low alcohol drinking behaviors. This provides us with an exceptional model to explore the neurophysiological mechanisms that underlie the individual variations in alcohol drinking behaviors. Intriguingly, our in vivo electro physiological recording study showed that the firing rate and bursting properties of VTA DA neurons were significantly higher in low alcohol drinking mice compared to those in alcohol-naïve control group and high alcohol drinking mice. Optogenetically mimicking the increased firing activity in previous high alcohol drinking mice reduced alcohol drinking behaviors. Based on these observations, we further investigated the firing properties of VTA-mPFC and VTA-NAc circuit neurons, and dissected the functional roles of these circuit neurons in mediating alcohol drinking behaviors. Toward identifying possible therapeutic targets for alcohol-use disorders, we first replicated the in vivo firing changes in VTA slice preparation affording us the opportunity to explore the underlying ionic mechanisms. Our slice recording data showed that VTA-NAc neurons displayed a control-like firing activity, which was also maintained by a re-established E/I balance (Nat Commun 2017). These molecular, cellular and neural circuit studies stated above provide highly useful and novel information, both for improving our knowledge of variable alcohol drinking behaviors and for identifying new drug targets to develop effective treatments for alcohol-use disorders.

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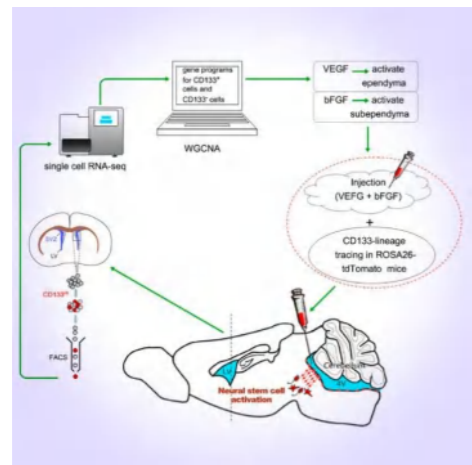
CNS Neural Repair via Stem Cells: Systems Biology-based Approaches

Through many years of research on embryonic and adult neural stem cells (NSC), mesenchymal stem cells (MSC), and pathological conditions including Rett Syndrome, an autism spectrum disorder (ASD), neurodegenerative disorders such as ALS, PD, and AD, as well as traumatic spinal cord injury (SCI), Yi Sun's team realized that neural inflammation plays a pivotal role in pathogenesis of all of the aforementioned pathological conditions. Using systems biology-

based approaches, we unveiled the fundamental underlying logic for neural repair, and established the theory of interaction loops amongst "gut-circulation immunity-CNS immunity-Neuronal function". We also initiated large-scale single cell transcriptome based immune typing, to facilitate preventative and precision medicine.

Brain Dormant adult neural stem cells (NSC) throughout the ventricular surface are seeds for new neurons to repair injured CNS

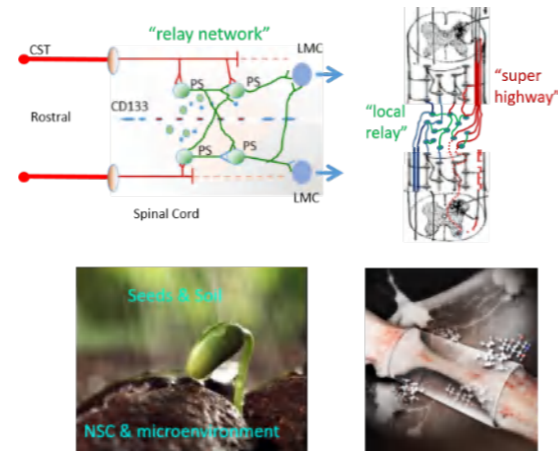
The scarcity of tissue-specific stem cells and the complexity of their surrounding environment have made molecular characterization of these cells particularly challenging. Through single-cell transcriptome analyses, we revealed the existence of dormant ependymal NSCs throughout the ventricular surface of the adult mouse CNS, as well as signals abundant after injury for their activation.



An illustration of uncovering molecular properties of Dormant adult neural stem cells in the adult mouse forebrain neurogenic zone via single cell transcriptome analyses. (Image from Luo et al. Cell. 2015)

Changing the inflammatory CNS microenvironment could promote NSC to differentiate into neurons, forming nascent circuits, and resuming neural function

The CNS injury environment, such as the one after spinal cord injury (SCI), is often inhibitory and inflammatory, limiting the ability for activated NSCs to differentiate into neurons to form nascent circuits. We postulate that the fundamental underlying logic for neural repair could be through establishment of non-inflammatory and neural trophic CNS microenvironment via

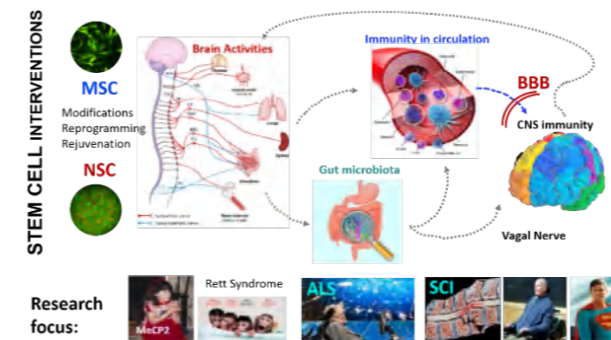


An image of promoting neural function/plasticity via changing the inflammatory CNS microenvironment.

small/macro molecules, biomaterials, exosomes, or stem cells, to enable residual neurons to compensate functions of damaged neural circuits through plasticity, or to allow NSC, endogenous or exogenous, to produce new neurons, forming nascent relay networks to integrate into broken circuits to restore neural function.

Interaction Loops amongst "Gut/circulation immunity-CNS immunity-Neuronal function"

Based on our previous studies on both neurodevelopmental and neurodegenerative disorders, as well as CNS injury, we

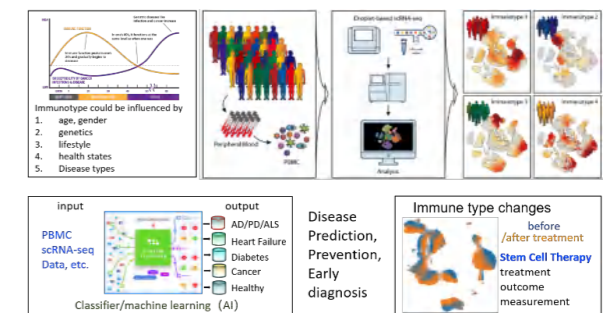


An image of Interaction Loops amongst "Gut/circulation immunity-CNS immunity-Neuronal function" (for diagnosis and treatment of CNS diseases via the periphery).

established the theory of interaction loops amongst "gut-circulation immunity-CNS immunity-Neuronal function", which provides the bases for targeting CNS diseases via the periphery.

Immune-typing facilitate preventative and precision medicine

We initiated single cell transcriptome-based immune typing of individuals with different age, gender, and pathological conditions, aiming at targeting CNS diseases via the periphery, including reprogramming monocytes into therapeutic cells.



An image of immune typing (facilitating preventative and precision medicine).

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The precise diagnosis and treatment for depressive disorder

Major depressive disorder (MDD) is the most common severe mental disorder and ranks second in the total global burden of human diseases. However, so far, its diagnosis still depends on clinical manifestations and reliable biomarkers of clinical diagnostic are still under investigation. Thereby, it is an urgent scientific problem how to screen and verify the function of candidate biomarkers through multiple dimensions and multi-

omics, which can penetrate BBB for the intervention of central target. In addition, based on previous research findings, it is of great significance to develop a novel strategy for brain stimulation that offers high efficacy and precision but has minor side effects, in which, we also devote oneself to research and develop the neuroregulation of intelligent closed loop.

The screening and verification of candidate biomarkers through multiple dimensions and multi-omics for MDD diagnosis and treatment

Based on clinical patients and well-matched healthy controls, we adopted the "extreme trait strategy" and multiomics sequencing, combined with bioinformatics and machine learning techniques to screen plasma candidate biomarkers. The multiple validations (including duplicate validation, independent sample validation, disease-specific validation and central and peripheral consistency validation) were used to further identify biomarkers for the diagnosis and treatment of depression. Most recently, we determined brain-derived biomarkers in plasma exosomes of the patients of depressed, and determined the levels of candidate biomarkers in the cerebrospinal fluid of depressed rhesus monkeys and brain tissue of depressed mice, respectively, and analyzed the correlation with the brain-derived biomarkers in plasma exosomes for determining the CNS origin. For example, proteomically identified vitamin D-binding protein (VDBP), which in plasma microglia-derived extracellular vesicles (EVs) was verified as a selective potential biomarker for MDD.

Using the candidate molecular-conditioned knockout mice or overexpressed mice to determine their susceptibility or resistance to chronic stress-induced depression-like behavior. Neurobiological techniques combined with in vivo optogenetics, chemogenetics and neural tracer techniques were used to gradually determine the mechanisms of pathways and neural circuitry of candidate molecules involved in the pathogenesis of depression. Moreover, we have been establishing an overall research system and made progress in stages for the targeted intervention of candidate molecules by central delivery of penetrate blood-brain barrier for MDD. For example, we have determined that a circular RNA directly encodes protein and confirmed its involvement in the causal mechanism of depression. In addition, based on the risk loci discovered by previous meta-GWAS, we will further elucidate the SPN role in the development of depression by affecting transcription factor binding ability and subsequently affecting promoter activity to regulate target gene expression.

The functional verification of candidate biomarkers molecules for diagnosis and treatment of depression

Magneto-mechanical effect of magnetic micro hydrogel for improvement of magnetic neuro-stimulation and antidepressive effect and mechanism in mice model

Superparamagnetic iron oxide (SPIO) nanoparticles play an

important role in mediating precise and effective magnetic neuro-stimulation and can help overcome limitations related to penetration depth and spatial resolution. However, nanoparticles readily diffuse in vivo, decreasing the spatial resolution and activation efficiency. We employed a microfluidic means to fabricate injectable microhydrogels encapsulated with SPIO nanoparticles, which significantly improved the stability of nanoparticles, increased the magnetic properties, and reinforced the stimulation effectivity with a long-term safe residency in the cortex up to 22 weeks in mice model. The electrophysiological

analysis of brain slices showed that the magnetic microhydrogels offer significant advantages in terms of neural activation relative to dissociative SPIO nanoparticles. The intervene strategy and system is offered for performing magnetic neuro-stimulation with an improved prospect for biomedical translation. In addition, we have founded that the selective activation of ABCA1/ApoA1 signalling in the primary visual cortex by the magnetoelectric stimulation rapidly ameliorates depression-like behaviours via regulation of synaptic plasticity in mice model.

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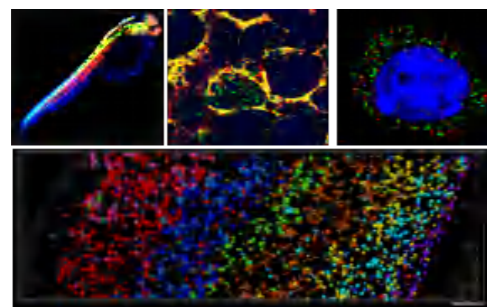
Development of Single-Cell Multi-omics Technologies and Their Application in 'Neuro-Immune-Infection' System Biology

Professor Gang Cao's team focuses on the development of state-of-art single cell multi-omics technologies, including (single-cell) spatial omics, (single-cell) three-dimensional genomics and (single-cell) connectomics and their application in "Neuro-immune-infection" system biology and diagnosis. We aim to: 1) develop novel methods for System neuroscience research: such as single cell resolution connectome; in situ single-cell sequencing, novel techniques for interactome and epigenomics (Especially 3D genomics); 2) Understand the molecular mechanism of the interaction of neurotropic pathogens with host cells and immune

response, particularly the neuronal regulation of immune response; 3) Optimization and application of the above-mentioned new neural circuits tracing tools, in situ single-cell sequencing and the epigenomics technologies, to delineate the genetic, epigenetic landscape and physiologic function of specific neural circuits at single neuron level, especially depression and autism; 4) dissecting the neural circuits regulating immune response to understand autoimmune diseases and immunoregulation against infection from neuroscience perspective.

High-throughput π -FISH (fluorescence in situ hybridization) technology

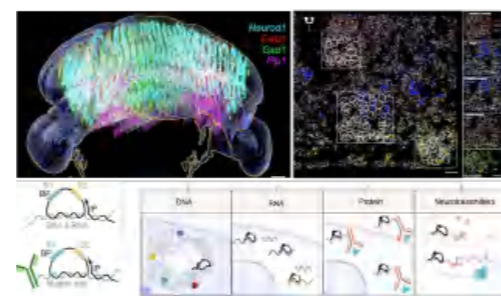
Our team has developed a novel multiplex fluorescence in situ hybridization technique (π -FISH) which enables the precise co-detection of DNA, mRNA, lncRNA, miRNA, rRNA, and proteins at the tissue in situ level. This in situ detection method has several merits such as high hybridization efficiency, strong signal amplification, low background noise, high specificity and high detection throughput. It has been successfully applied to the detection of the androgen receptor splice variant 7 (ARV7), a biomarker for androgen therapy resistance for prostate cancer. (Nature Communications, 2023, Featured Article).



Medium throughput in situ hybridization platform

Single-cell resolution spatial multi-omics technology (Mip-Seq)

Our team has successfully developed an efficient high-throughput pair-wise in situ sequencing spatial genomics technology. We have established an in situ spatial-omics platform by designing padlock probes to target RNA directly. We have updated the traditional single barcode strategy to dual barcode, which allows the interpretation of 10 signals in a single round of sequencing. Therefore, we can decode 10N genes by N rounds, while the capacity of the traditional in situ sequencing is 4N. These innovations significantly improve the detection efficiency and throughput and reduce the cost of in situ sequencing.



Single-cell MIP-Seq technology

(This technology enables the mapping of spatial transcriptomes at single-cell resolution for hundreds of genes, in situ sequencing of specific molecular groups, and identification of mutations at specific loci.)

Development of innovative technologies for spatial genomics, connectomics, interactomics, and functional genomics screening

Our team has developed a cost-effective and efficient chromosomal conformation capture technique, DLO Hi-C (Nature Genetics, 2018, highlight article). and single-cell spatial genomics technique SCI-DLO Hi-C (Nature Communications, 2022). Meanwhile, we have constructed a novel yeast two-hybrid system (RLL-Y2H) based on plasmid fusion and high-throughput sequencing technology, enabling high-throughput interactomics screening of "library versus library" (Nucleic Acids Research, 2018). We have also developed a high-throughput functional genomics screening technology based on CRISPR/Cas10 (Genomics, Proteomics & Bioinformatics, 2021). Using these technologies, we have elucidated the interplay mechanism

between PRV and the host genome (Science Advances, 2021) and the crosstalk between spleen and nervous system (Neuron, 2022, highlight article). Notably, we are developing methods for System neuroscience research: such as single cell resolution connectome for neural circuits tracing and delineate the genetic, epigenetic landscape and physiologic function of specific neural circuits at single neuron level, especially depression and autism.

Development of Tumor Diagnostic Reagent Kits Based on Gene in Situ Detection Technology

Based on our self-developed gene in situ detection technologies we have developed a series of tumor diagnostic kits These kits have high sensitivity, specificity, and accuracy, which can cover any locus in the genome and diverse transcriptome with single-cell or single-molecule resolution, facilitating the detection of relevant biomarkers at the molecular level and the diagnosis of corresponding diseases. Among which, 20 kits have issued with cFDA medical device certifications. Meanwhile, a series of DNA and RNA probe kits have been developed for both basic research and clinical testing.

SELECTED PUBLICATIONS:

(* corresponding author; * equal contribution)

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曾渝婷

Tseng Yu-Ting PRINCIPAL INVESTIGATOR



Neuro-Immune-Cardiac Interactions in Sleep and Defensive Behaviors

Our lab investigates the fundamental functional units of neural circuits and peripheral organs, with a focus on sleep and defensive behaviors in both health and disease. We apply advanced behavioral and physiological analyses to infer internal states at the

organismal level under controlled conditions. Through these approaches, we aim to elucidate neuro-immune-cardiac interactions during sleep and uncover how sleep supports diverse physiological functions essential for overall health

Neural Circuits Co-regulating Innate Fear and REM Sleep

REM sleep is characterized by high brain activity and rapid eye movements, but also by muscle atonia. Given these features, is it advantageous for animals to engage in REM sleep when a predator is nearby? In 2022, we found that REM sleep increased in response to predator threats, regulated by corticotropin-releasing hormone (CRH) neurons in the medial subthalamic nucleus (mSTN). Projections from the mSTN to the external globus pallidus (GPe) serve as an effector pathway for both threat-coping responses and REM sleep expression^{2,4}. We further propose that REM sleep enables animals to “rehearse” or simulate adaptive responses to danger in a protected, offline state, while simultaneously maintaining emotional balance. Insights into the role of REM sleep in animals may therefore illuminate human sleep in the context of modern stressors and prevalent sleep disturbances¹.

Exploring the Brain's Mechanisms and Mental Health Interventions: A Holistic Perspective

This reviews explore how various peripheral signals—driven by factors such as infection, nutrient deficiency, and reproductive needs—shape and regulate innate defensive behaviors³. These signals include inflammatory cytokines, gastrointestinal hormones, gut microbiota, and sex hormones. The authors emphasize the intricate network of interactions between the brain and peripheral systems, aiming to clarify the regulatory mechanisms of defensive behaviors and the pathophysiology of anxiety and fear-related psychiatric disorders. Together, these works establish a foundation for future studies of the physiological basis of behavior and highlight the growing interest in brain-body interactions, while underscoring that key mechanisms of brain-periphery communication remain unresolved. Systematic dissection of these pathways may yield insights into health maintenance and inform new interventions for fear-related psychiatric disorders.

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ASSOCIATE INVESTIGATOR Yan Huang

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Human Neuroscience and Brain Disease

- Abnormal attentional processing associated with brain diseases (e.g., anxiety, depression, ADHD);
- Noninvasive regulation by TMS or tES, e.g., attention enhancement, emotional improvement;
- Emotions and cognition of children and adolescents.

Is individual attentional bias positive or negative? It depends on trait anxiety

Whether the general population shows a positive or negative bias – this issue has always been controversial. A new study discloses that emotional bias is mainly determined by individuals' trait anxiety level. The study, published in *Social Cognitive and Affective Neuroscience*, was carried out by Dr. HUANG Yan's group from SIAT. The aim of this research was to explore the relationship between individuals' trait anxiety and their attentional bias and its neural mechanisms. Seventy adults with varying trait anxiety levels participated in an emotional competition search task. In the competition condition, a happy and an angry face were presented among neutral faces, with one as the target and the other as the distractor; while in the non-competition condition, one happy or

angry face was presented among the neutral faces. The N2pc component of event-related potential (ERP), an attentional selection index, was used to measure attentional bias. Results showed a significant correlation: lower trait anxiety was associated with a stronger positive bias, while higher levels were linked to a more negative bias. Importantly, this anxiety-associated attentional bias specifically manifested in bottom-up processes and the emotion-competition condition. This research offers electrophysiological evidence indicating that individuals' trait anxiety is associated with the direction of attentional bias, and, for the first time, discloses its neural mechanism – emerging in stimulation-driven attentional processes, which has implications for cognitive interventions for anxiety disorders.

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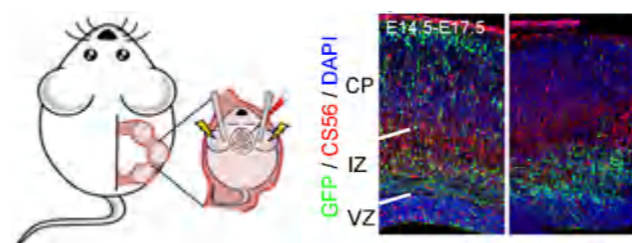
The cellular and molecular mechanisms underlying neurodevelopmental disorders

Neurons undergo changes in morphology and function during development or in response to external stimuli, which are essential for neural signaling and the formation of neural circuits. To support these changes, the cytoskeleton within developing neurons must undergo rapid reorganization to shape their structure and function. However, the cellular and molecular mechanisms underlying cytoskeletal dynamics in these processes

remain poorly understood. In our laboratory, we focus on investigating the roles of key regulators involved in cytoskeletal reorganization during neuronal development. In particular, we are also interested in uncovering the mechanisms behind neurodevelopmental disorders caused by mutations in these critical cytoskeletal regulatory genes.

To ensure the proper direction of information flow within neural circuits, neurons must polarize to form a single long axon for information output and multiple dendrites for signal reception. To achieve these morphological changes, the cytoskeletal structure within neurons must undergo extensive remodeling and reconstruction. Thus, the dynamics of the actin cytoskeleton must be tightly regulated. However, how these positive and negative signals coordinate to regulate dendrite and axon outgrowth remains largely unknown. Coronins are an evolutionarily conserved family of actin-binding proteins, first identified in the actin-rich structures of the amoeba *Dictyostelium discoideum*. Accumulating evidence suggests that coronins are involved in a variety of

biological processes dependent on actin cytoskeletal reorganization, such as cell morphogenesis, migration, and endocytosis. Our recent research focuses on the coronin family and investigates their roles in neuronal polarization, and migration during cortical development.



SELECTED PUBLICATIONS:

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Neuroimmunology

We are interested in investigating the neural-immune interaction in CNS inflammation and homeostasis maintenance of immune system. Specifically focus on (1) understanding the mechanism of infiltrating monocyte in modulating CNS inflammation post

ischemic injury. (2) Deciphering the neural mechanisms in regulating immune cell circadian oscillation at the level of central to peripheral circuit and neural transmitter signal transduction in target cells.

Regulation of infiltrating monocyte-mediated inflammation in CNS injury

The central nervous system (CNS) is considered to be immune-privileged from peripheral immune system in homeostasis. However, in the scenarios of neural injury, infective or degenerative diseases, the activation of microglial and opening of blood brain barrier leads to the leakage of peripheral immune cells and inflammatory factors into CNS which results in exacerbation of inflammation-induced neuronal death or dampened relief of inflammation depending on the inflammatory context.

One of our goals is to clarify the molecular mechanism mediating the transition of infiltrated monocyte from pro-inflammatory to anti-inflammatory status or vice versa regarding to the injury type. Infiltrated monocytes share similar phenotype as the resident microglia cell, however they have shorter life span and stronger plasticity in term of immune regulation. Using monocyte as a cellular target to inhibit the inflammation induced cell death in early stage of CNS injury and the glial scar formation in later stage of CNS injury could be a novel potential therapeutic strategy for CNS repair and regeneration.

Neuronal mechanisms in regulating immune homeostasis

Immune homeostasis is the fundamental function of immune system

in maintaining body healthy status via making the balance from system activation by clearance of damaged cells and pathogens to system inactivation by immune tolerance and resolution of inflammation. One of the aspects of immune homeostasis is manifested as the 24 hours circadian oscillations of immune cell in blood and other organs. Immune cell homing to and egress from immune organs are the key steps in maintaining immune homeostasis and initiation of immune response. Emerging evidence shows that neural signals play important roles in mediating immune cell circadian oscillations and the detailed mechanisms are still not fully understood.

In this subject, we firstly put our efforts in deciphering the unknown neural circuit connection from central nuclei to peripheral innervation in lymph organs such as the cervical lymph nodes. According to the published researches in other lymph organs, we intend to find out the common central nuclei in modulating immune system homeostasis specifically focus on immune cell homing and egress by functional analysis utilizing chemogenetics. In addition, we are also investigating the immune regulatory effects of this circuit in acute inflammation and autoimmune disease models such as sepsis and experimental autoimmune encephalomyelitis. Ongoing studies also focus on understating the cellular and molecular mechanisms at the level of immune cell interaction with stroma cell, e.g. endothelial cell, in lymph organs under the signaling of neural transmitters in homeostasis and disease models.

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Neural-Microbial-Metabolic Interactions in Behaviors and Diseases

Recent years have witnessed the rise of the neuro-peripheral interactions as a major topic of research interest in biology. For example, studies have revealed that the gut-brain axis influences normal physiology and contribute to various CNS diseases, such as Alzheimer's disease, Parkinson's disease, stress & depression

and autism, et al. Accumulating data now indicate that the peripheral systems communicate with the CNS potentially through neural, endocrine and immune pathways — and thereby influences brain function and behaviors.

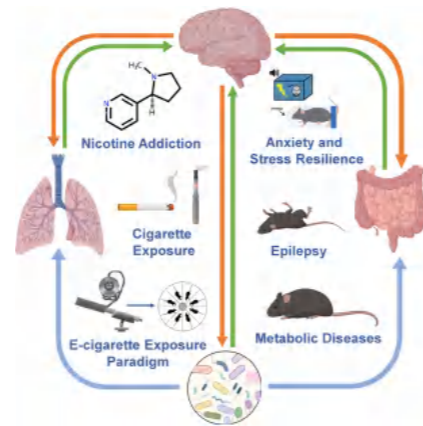
The Microbiome-Organ-Brain Axis in Health and Disease

Emerging evidences suggest that metabolism is tightly regulated by both central and peripheral system. For the details of underlying mechanisms are largely unknown, we aim to understand how the CNS and visceral organs interplay in the pathology of mental disorders, such as anxiety, addiction, epilepsy, metabolic diseases, et al. Recently, we explained the role of the brain-gut axis in epilepsy and stress resilience by multi-omics profiling and found dose-dependent action of cordycepin affected adipose metabolism under stress exposure via the microbiome-gut-brain-adipose axis.

The Central-Peripheral Homeostasis in Smoking

Tobacco use leads to nicotine addiction that is characterized by urges to use the drug despite the accompanying negative health and socioeconomic burdens. Previous work have revealed that nicotine affects metabolic homeostasis by altering the activity of specific neural circuits. Meanwhile, electronic cigarette use has been increasing dramatically worldwide and more than 8,000 flavors of e-cigarettes are currently marketed. We investigate whether the

central-peripheral homeostasis, such as the microbiota-immune-brain interactions, is involved in the regulation of nicotine addiction. We found the enhancement of menthol flavor in e-cigarette on social functioning, correlating with the central and peripheral immunometabolic disruptions; this raises the vigilance of the cautious addition of various flavorings in e-cigarettes and the urgency of further investigations on the complex interplay and health effects of flavoring additives with nicotine in e-cigarettes.



The Network of Neural-Microbial Interaction

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(* corresponding author; # equal contribution)

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陈祖昕

ASSOCIATE INVESTIGATOR Zuxin Chen

Team Members

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Mengke Su, Cuihan Shi, Qixing Yang, Caiyun Yan

The neuronal mechanism for nicotine addiction and related diseases

1) The neural mechanism of nicotine addiction. We are committed to understanding the neural circuitry, cellular and molecular mechanisms of nicotine addiction. Our ultimate goal is to develop novel drugs for smoking cessation.

2) Brain-body interaction in blood glucose homeostasis. We are conducting in-depth researches to understand the pathogenesis of diabetes from the perspective of central-peripheral mutual

interaction. The ultimate goal is to develop neural modulation tools or drugs for the treatment of diabetes.

The approaches we are utilizing include patch-clamp recordings, optogenetic/chemogenetic, fiber photometry, virus mediated neural circuitry mapping, two-photon imaging, complex behavior analysis.

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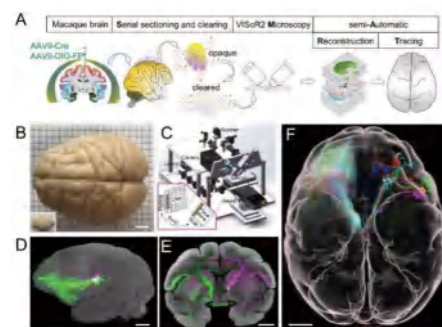
Mesoscopic Connectome Mapping

We focus on mapping the whole-brain connectome at mesoscale with ultrahigh-throughput fluorescent imaging techniques. Deciphering and understanding the infrastructure of the brain is the basis to fully interpret the function of the brain. We work interdisciplinarily with people from physics, chemistry, engineering and computer sciences, aiming at resolving both the organization

of the brain and cellular mechanisms underlying learning and memory. We developed microscopes to mapping the whole brain at sub-micron resolution to image how neurons connected to each other at the brain-wide scale. We are also tracking neuronal activities with calcium indicators and voltage indicators to uncover mechanisms how neuronal firing encode information.

 Developing new techniques and data streamline for high-throughput whole-brain imaging

Biological volumes are of high content of fine structures. We work on developing tools for resolving the structures at subcellular resolution. One of the most complicated biological volumes is the brain which plays a central role in physiological functions. We have



established an ultrahigh-speed volumetric imaging method to resolve one mouse brain at unprecedented 2 hours/brain speed at sub-micron resolution. We are currently developing new methods for other organs including the spinal cords, liver, spleen, heart, kidney and other tissues. High-throughput microscopy results in huge amount of image data. We are taking advantages of artificial intelligence for extracting information and knowledge from petabytes of images of mouse and primate brain, to generate broader understanding of brain connectivity and general rules of neural circuitry organization.

 Mapping the mesoscopic connectome of rodents and primates

Based on technologies described above, we are aiming at establishing mesoscale connectomes of rodents and especially primates as reference for general neuroscience research. We are particularly interested in neocortical organization and micro-circuits governing the information flow while primates are performing intelligent tasks.

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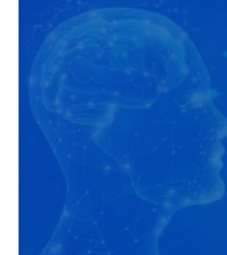
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ASSOCIATE INVESTIGATOR



Detection of Single Synaptic Vesicle Release and virus entry

Neurotransmitters in synaptic vesicles are the carrier of neural information. The neurotransmitter quantal release depends not only on the size of vesicles and the number of transmitters in a single vesicle, but also on the fusion mode and dynamic characteristics of vesicles fusion, which is critical in synaptic transmission mechanism, neural information coding and

neurological diseases. Our major focus is to understand the molecular and cellular mechanism of neurotransmitter release from a single vesicle, with novel and high-accuracy techniques and methods.

Cell-attached capacitance recording technique was employed to detect a single virus entry into the cells.

 Cell-attached Capacitance technique

The cell-attached capacitance recording technique is a powerful technique that has been successfully used to resolve single vesicle fusion and fusion pore conductance. A single vesicle as small as 50 nm in diameter during exocytosis or endocytosis can be detected by cell-attached capacitance indicating fusion or retrieval of vesicles with the plasma membrane. The admittance measurement provides the membrane capacitance change that increases in proportion to the membrane area because of the incorporation of the vesicle into the patch membrane or decrease due to the vesicle budding off from the plasma membrane. Now, we successfully detected the vesicle fusion and glutamate release from a single synaptic vesicle in the Calyx of Held synapse, which have never been achieved before.

 Detection of a single Coronavirus (COVID-19) entry

The first cases of COVID-19 were previously documented in December 2019 in Wuhan City. Since then, COVID-19 has raged globally, posing a huge threat to human health and severely damaging the world economy.

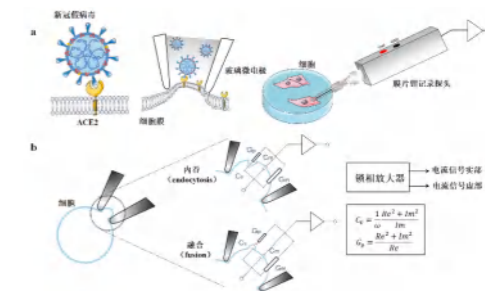
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(* corresponding author; # equal contribution)

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There are two distinct SARS-Cov-2 entry pathways. Virus binding to ACE2 induces conformational changes in S1 subunit and exposes the S2 cleavage site in the S2 subunit. Firstly, if the target cell expresses insufficient TMPRSS2, or a virus-ACE2 complex does not encounter TMPRSS2, the virus-ACE2 complex is internalized via clathrin-mediated endocytosis. Secondly, in the presence of TMPRSS2, S2 cleavage occurs at the cell surface. Fusion between viral and cellular membranes forms a fusion pore through which viral RNA is released into the host cell cytoplasm.

We firstly detected a single coronavirus entry into the host cells by the cell-attached capacitance recording technique successfully. The host cells include HEK293T cells, human lung alveolar type II epithelial cells, Laryngeal epithelial cells.





申雪峰

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Mechanism of synaptic vesicle release and novel analytical techniques

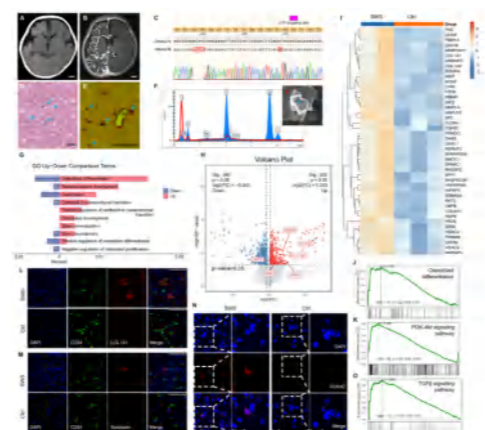
Goal of our work is to understand the molecular and cellular mechanism of synaptic vesicle release and to develop novel analytical techniques to study single cells, single synapses and exocytosis in vivo and in brain slice. Currently, the research in our lab is primarily focused on: (1) Developing micro-/nano-scale

analytical techniques for real-time monitoring of single cells and single synapses, (2) Developing novel enzymatic/non-enzymatic sensing tools to measure the neurotransmitters and metabolites, and (3) Exploring their use in the study of synaptic activities under pathological conditions (e.g. epilepsy).

Vascular Ossification in the Developing Brain

This study represents the first documented case of brain calcification (BC) presenting as ectopic ossification in a pediatric patient with Sturge-Weber Syndrome (SWS) at four months of age. Using proteomics and immunofluorescence, we demonstrated the presence of bone matrix proteins and osteogenic cells, which may originate from the endothelial cells with GNAQ mutations via the epithelial-to-mesenchymal transition and osteoblast differentiation processes, leading to vascular ossification in the developing brain of the pediatric patient with SWS. In addition, we identified impaired tight junctions and blood-brain barrier integrity at the affected brain vessels, potentially an indirect consequence of BC development in patients with SWS, indicating a critical role of BC in the regulation of epilepsy onset and cognitive decline. Nonetheless,

the precise mechanisms of BC in SWS and its roles in neurological symptoms remain elusive, underscoring a vital avenue for further studies.



Analysis of brain lesions from a 4m-old SWS patient

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Molecular Mechanisms and Intervention Strategies of Alzheimer's Disease

The age-related accumulation of amyloid β -protein ($A\beta$) is a key initiating event in AD. $A\beta$ exhibits diverse disease-relevant pathological activities and is as a primary therapeutic target. However, there remains uncertainty about which $A\beta$ species are the most disease-relevant and what drivers their formation. Our research aims to elucidate the molecular mechanisms and pathological consequences underlying peptide self-assembly-induced covalent crosslinking of $A\beta$, as well as how cellular components, proteins, lipids, and other factors modulate $A\beta$

aggregation behavior and its downstream neurotoxic effects. Our research also focuses on developing next-generation anti- $A\beta$ monoclonal and nanobody-based therapeutics with enhanced efficacy in inhibiting $A\beta$ aggregation, promoting pathogenic $A\beta$ clearance, and neutralizing its neurotoxicity. We also explore the efficacy and mechanisms of physical interventions (e.g., electroacupuncture, magnetic stimulation) for neuromodulation and AD treatment, and develop novel antibody delivery strategies to boost brain accumulation and reduce side effects.

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贾 凡

Fan Jia

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Virus-based advanced technology for neural circuit and medicine

Dr. Jia focuses on developing the virus-based advanced technology for brain research, gene therapy, cancer therapy, test and vaccine. Virus is a special smart and powerful microbe, which has harmful and useful aspects, just like a double-edged sword, for human and animals. The useful aspect has been applied in the fields of basic research and medicine by deleting harmful aspect, e.g. Pseudorabies virus and Rabies virus have been used to mapping neural circuit, Adeno-associated virus has been used for

curing genetic disease, Lentivirus has been used for preparing modified immune cells (CAR-T), Herpes simplex virus has been modified to destroy cancer, etc. However, some problems are still needed to be resolved, such as high toxicity, low efficiency, complex production protocol, high-cost, etc. Therefore, I focus on these points for developing i) novel and high-efficient virus-based tools, ii) convenient and powerful production protocol

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Development of Viral Vector-mediated Neural Circuit Tracer & Oncolytic Virus Drugs

(1) Transsynaptic tracing of neural circuits using neurotropic viruses is widely used in defining the synaptic organization of neural networks. Through systematic modification and optimization, we are focusing on the development of rigorous, low toxic and high-brightness transmulti-/monosynaptic HSV1 H129 and HSVMac tracing systems.

(2) Oncolytic virotherapy has become one of the most potential treatments for malignant tumors. Engineered HSV oncolytic virus drugs T-VEC (2015) and G47Δ (2021) were approved for melanoma and glioma treatment in the US and Japan, respectively. We are focusing on the development of novel HSV oncolytic viruses for solid tumors therapy.

Brain-wide neuronal circuit connectome of human glioblastoma

Glioblastoma (GBM) infiltrates the brain and can be synaptically innervated by neurons, which drives tumour progression. We applied rabies virus-mediated and herpes simplex virus-mediated trans-monomer tracing to systematically investigate circuit integration of human GBM organoids transplanted into adult mice. We found that GBM cells from multiple patients rapidly integrate into diverse local and long-range neural circuits across the brain. Beyond glutamatergic inputs, we identified various neuromodulatory inputs. CHRM3 activation promotes GBM cell motility, whereas its downregulation suppresses GBM cell motility and prolongs mouse survival. Together, these results reveal the striking capacity for human GBM cells to rapidly and robustly integrate into anatomically diverse neuronal networks of different neurotransmitter systems.

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A direct spino-cortical circuit bypassing the thalamus modulates nociception

Nociceptive signals are usually transmitted to layer 4 neurons in somatosensory cortex via the spinothalamic-thalamocortical pathway. We found a subset of layer 5 neurons receives spinal inputs through a direct spino-cortical circuit bypassing the thalamus, defined as spino-cortical recipient neurons (SCRNs). Morphological studies revealed that the branches from spinal ascending axons formed a kind of disciform structure with the descending axons from SCRNs in the basilar pontine nucleus (BPN). The direct spino-cortical circuit represents a noncanonical pathway, allowing a fast sensory-motor transition of the brain in response to noxious stimuli. potential treatment of refractory HSV-1-associated diseases.

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Development of Multiphoton Microscopy for Quantitative Imaging of Neurovascular Activities

Our team has focused on the developments of multiphoton imaging techniques and computational methods, which are capable of μm -resolution, quantitative and absolute measurements of vascular and neuronal structure and physiological activities in live rodent brain. With these techniques,

we are interested in studying the regulation of cerebral microvascular oxygen delivery, functional connectivity, and cellular dynamics in the healthy and diseased conditions.

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Neuroprotection and neurorepair after ischemic brain injury

Our group focuses on the pathological changes as well as molecular and cellular mechanisms of various ischemic brain injuries including hypoxic-ischemic encephalopathy, transient ischemic attack and ischemic stroke. We are particularly interested in hypothermia-based treatment, which prevents neuronal death and promotes neurorepair after ischemic injury. We are also

developing novel methods in replacement of traditional hypothermic therapy to avoid side effects. In addition, in vivo monitoring of oxygen level and vasculogenesis by multi-photon microscopy during and after ischemic injury is also of high interest in our research area.

Mammalian Cold-inducible RNA-binding Proteins As Novel Therapeutic Targets of Ischemic Injury

There are only two known mammalian cold-inducible RNA-binding proteins which can be robustly stimulated by mild to moderate hypothermia. The two homologous proteins, RBM3 and CIRP, have shown multiple functions in neuroprotection and neurogenesis after

ischemic injury, involving the regulation of unfolded protein response, IGF2 signaling and cell cycle. We have screened small molecules which specifically increase the protein level of cold-inducible RNA-binding proteins and thereby present as potential drugs for stroke treatment. After a success in in vitro stroke model, now we are testing the efficacy and safety of these compounds in in vivo stroke model, and expecting to promote these drugs for clinical trials in the future.

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(* corresponding author; # equal contribution)

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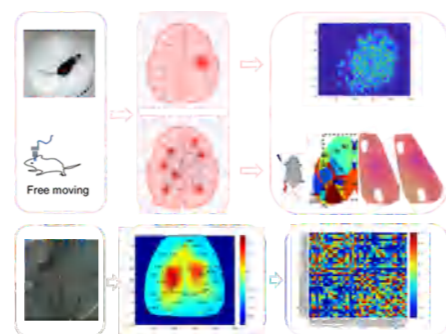
Mesoscale functional mechanisms in brain diseases

We focused new methods of whole brain mesoscale functional imaging. In free-moving animals, we can simultaneously image full-cortical scale fluorescence signals without damaging the skull, and could image deep brain nuclei and full-cortical scale

fluorescence signals at same time, and we also could combine optogenetics and ultra-speed imaging with this kind of methods to study the brain diseases (Alzheimer's disease, ADHD, Parkinson's disease, Autism and depression) at the mesoscale level.

Functional screening from single cell resolution to mesoscale

The whole-brain structural imaging has developed well, but these imaging methods often do not have the temporal resolution that required for biological function studies. Lack of functional imaging methods and instruments at the mesoscale level. Recently, our laboratory has developed multiple fluorescence imaging methods and equipments from single-cell resolution to mesoscopic scale, which are important for the decode of brain and brain diseases.



(Top) Endoscope calcium imaging monitors cell assembly and cell activity with single-cell resolution, and (bottom) mesoscale imaging monitors fluorescent biological signals in freely moving mice responding to different behavioral tests.

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Molecular Mechanism of Synaptic Transmission and Plasticity

Liquid-liquid phase separation (LLPS) of macromolecules is a biological phenomenon that enables the dynamic regulation of numerous cellular processes. The formation of LLPS is driven by multivalent interactions and intrinsically disordered regions (IDRs). IDRs are protein sequences that do not form stable three-dimensional conformations, allowing them to adapt to their environment and perform a wide range of functions. Although approximately 58% of the proteins in the human proteome contain

IDRs, their functions remain largely unexplored. We are interested in understanding how IDRs drive phase separation and how they participate in regulating synaptic plasticity. By combining state-of-the-art super-resolution light microscopy and functional electrophysiology, we aim to decipher the role of IDRs in regulating synaptic function and further provide insight into how disease-related mutations lead to neurodevelopmental disorders.

Synaptic Plasticity Mediated by Liquid-Liquid Phase Separation

Phase separation is a process by which biomolecules, such as proteins and RNA, demix into distinct liquid-like compartments within cells. These biomolecular condensates lack membranes and are formed through weak multivalent interactions, enabling dynamic and reversible assembly. Recently, many researcher show that phase separation plays a critical role in organizing cellular biochemistry, particularly in regulating synaptic functions. AMPA receptors (AMPA) are glutamate receptors critical for fast excitatory synaptic transmission in the brain. Their trafficking is tightly regulated to control synaptic strength, a process essential

for learning and memory. Emerging evidences suggests that phase separation is intricately linked to the regulation of AMPAR trafficking. This connection is mediated through scaffolding proteins and liquid-like condensates at postsynaptic densities (PSDs). We discovered that the IDRs of PSD proteins promote phase separation through multivalent interactions. In addition, during synaptic plasticity induction, LLPS undergoes activity-dependent modulation, which influences condensate properties and AMPAR dynamics. Our study revealed a novel mechanism how LLPS regulates synaptic plasticity, which opens avenues for targeted therapeutic interventions in conditions such as autism spectrum disorder (ASD).

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朱凯川

Kaichuan Zhu SENIOR ENGINEER

Neuropathophysiological mechanisms of neurodegenerative diseases

The research of Dr. Zhu focuses on understanding the neuropathophysiological mechanism of neurodegenerative diseases, e.g., Alzheimer's disease, using in vivo two-photon microscopy and in vivo electrophysiology. The ultimate goal is to explore the potential signature and early biomarkers in the early pre-symptomatic stage and eventually help for the clinical

diagnosis. Dr. Zhu also interesting in exploring the mechanism of neurodegenerative diseases affect memory formation and consolidation. Dr. Zhu is also involved in Shenzhen Brain Science Infrastructure and is responsible for the operation management and technical training of experimental animal platforms.

BACE1 is critical for normal synaptic function

BACE1 (Beta-site amyloid precursor protein cleaving enzyme 1) is a promising drug target for the treatment of Alzheimer's disease. Prolonged BACE1 inhibition interferes with structural and functional synaptic plasticity in mice, most likely by altering the metabolism of BACE1 substrates, SEZ6 (Seizure protein 6). SEZ6 is predominantly cleaved by BACE1, and Sez6 knockout mice share some phenotypes with BACE1 inhibitor-treated mice. Furthermore, knocking out Sez6

in a small subset of mature neurons also prevented the structural postsynaptic changes induced by BACE1 inhibition. Chronic BACE1 inhibitor treatment did not alter long-term potentiation in CA1 neurons of Sez6^{-/-} mice. Our results suggest that SEZ6 plays an important role in maintaining normal dendritic spine dynamics. Furthermore, SEZ6 is involved in BACE1 inhibition-induced structural and functional synaptic alterations.

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(* corresponding author; * equal contribution)

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刘青

ASSOCIATE INVESTIGATOR Qing Liu

The neural circuit basis of normal brain functions as well as disorders

Multidisciplinary approaches including neural circuit tracing with neurotropic viruses, electrophysiology, fiber photometry, and behavioral assessment, combined with optogenetic and chemogenetic techniques, have been used to investigate the neural circuit basis of normal brain functions such as learning, memory, and sensory perception, to reveal the influence of specific neural circuits on the onset and progression of neurological and psychiatric disorders, offering new strategies related to early warning and treatment of these disorders. For example, we identified that the three most prominent inputs for the mitral/tufted cells (M/TCs), the excitatory projection neurons of the olfactory bulb (OB), came from the anterior olfactory nucleus (AON), the piriform cortex (PC), and the basal forebrain (BF), similar to the granule cells (GCs), the most abundant

population of inhibitory interneurons in the OB. However, M/TCs received proportionally less input from the primary olfactory cortical areas, including the AON and PC, but more input from the BF and contralateral brain regions than GCs. Individual BF cholinergic neurons were found using fMOST to innervate multiple layers of the OB, forming synapses on both M/TCs and GCs. Moreover, we revealed that paraventricular hypothalamic nucleus (PVN) sent efferent neural projection indirectly to the autonomic nerve endings in the anterior chamber, and activation of glutamatergic projection neurons in unilateral PVN induced significant bilateral intraocular pressure (IOP) elevation and the ipsilateral increased more noticeably, suggesting a new direction for understanding the pathogenesis of glaucoma and the development of treatment.

SELECTED PUBLICATIONS:

(* corresponding author; * equal contribution)

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廖春雨

Chunyu Liao ASSOCIATE PROFESSOR

Graduate Students

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Research Assistants

Yanhua Liu, Yingying Lin

Our research is focused on developing and optimizing genome editing tools for investigating diseases, as well as establishing diagnostic and therapeutic strategies.

CRISPR-Cas systems are initially discovered as adaptive immune system (defense system) of bacteria and archaea. They have been reprogrammed as powerful tools for genome editing. Nowadays, CRISPR-based technologies have been applied in numerous fields. However, there are still fundamental questions unanswered regarding their biological features and technical limitations. Our long-term goal is to study the molecular mechanism of CRISPR-

Cas and other defense systems, develop and optimize tools, and apply the tools on combating diseases. In the following few years, we will focus on developing tools for studying gut microbiota and interpret their roles in different diseases, such as cancer and neurodegenerative disease. The gained knowledge will be translated into novel diagnostic and therapeutic strategies for alleviating or even curing diseases.

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温士贤

ASSOCIATE INVESTIGATOR Shixian Wen

Artificial Intelligence Systems and Primate Brains

The brain is more powerful than any intelligent machine in existence. Thus, better understanding the mechanisms of the primate brains provides us inspirations to design a better bio-inspired artificial intelligence (A.I.) system. In the opposite, recent technology improvements, such as emerging of deep learning,

enable us to have a better understanding the mechanisms of the primate brains. These two entities form a symbiotic closed loop (Fig.1). My research focuses on designing better bio-inspired A.I. algorithms and using A.I. to better understand the primate brains.

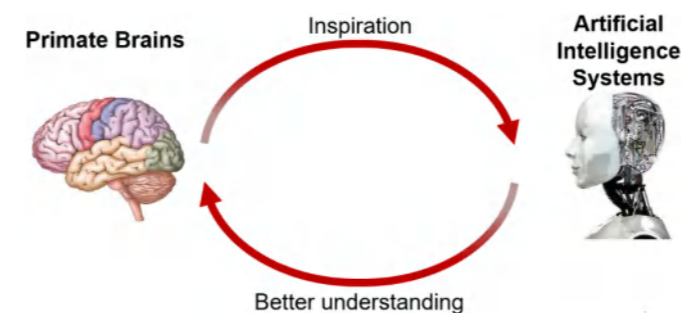


Fig.1. Interaction between Primate Brains and Artificial intelligence system

Designing better bio-inspired A.I. algorithms

The human brain is the gold standard of adaptive learning. It not only can learn and benefit from experience, but also can adapt to new situations. In contrast, deep neural networks only learn one sophisticated but fixed mapping from inputs to outputs. This limits their applicability to more dynamic situations, where the input to output mapping may change with different contexts. Inspired from the Hippocampus (HPC) of the human brain, we have developed

Beneficial Perturbation Network (BPN) to accommodate these dynamic situations and to largely eliminates catastrophic forgetting in the state-of-the-art A.I. systems.

Using A.I. to better understand the primate brains.

To understand the motor control in Primary Motor Cortex(M1), we designed a new spike synthesizer that captures underlying neural attributes of the M1 using a deep generative model. The spike synthesizer can accelerate the training and improve the generalization of brain computer interface decoders.

Using A.I. to screen human diseases.

Many high-prevalence neurological disorders involve dysfunctions of oculomotor control and attention. Here, we have developed eye-tracking method and system for screening human diseases (e.g., Autism, Attention deficit hyperactivity disorder, fetal alcohol spectrum disorder, and Parkinson's disease, Alzheimer's Disease)

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周航

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Research Assistant (incoming)

Biyang Pan, Yilin Lang

Peripheral and central mechanisms underlying development and maintenance of chronic pain

Chronic pain is a global epidemic, impacting over 20% of the population, surpassing the prevalence of cardiovascular diseases, cancers, and diabetes combined. Unfortunately, there is a lack of effective drugs for treating chronic pain. In our laboratory, we employ advanced technologies such as chemo/optogenetics, circuit tracing, two-photon microscopy, and multi-channel

photometry to explore both peripheral and central mechanisms underlying the development and persistence of chronic pain. Our goal is to identify circuitry, cell-type-specific elements, and molecular targets that could serve as potential avenues for more effective pain management.

Research highlight: a sleep-active central pathway crucial for pain chronicity

Chronic pain is highly comorbid with sleep disorders. However, the neural pathway underlying this association has remained elusive since it was first precisely documented in humans by Johns Hopkins University researchers in 1975. Recently, we identified a sleep-active pathway connecting the parabrachial nucleus, basal forebrain, and primary somatosensory cortex (S1) that plays a crucial role in the generation and maintenance of chronic

neuropathic pain in a mouse model. The hyperactivation of this pathway during non-rapid eye movement (NREM) sleep following peripheral nerve injury causes neuronal hyperactivation and pain-related synaptic plasticity in the S1, perpetuating neuropathic pain. Targeted inactivation of this pathway specifically during NREM sleep can alleviate pain hypersensitivity. These findings shed light on the underlying mechanisms linking sleep disorders and pain chronicity, implying potential therapeutic avenues for pain management.

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冯博

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Bo Feng

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Research Assistants

Ziquan Sun



Molecular basis underlying neurodegenerative diseases

Neurophysiological homeostasis serves as the foundation for maintaining normal brain function, sustaining the stability of the internal environment through the coordinated holistic regulation of peripheral organs and systems. Once this homeostasis is disrupted, it lead to various psychiatric disorders and

neurodegenerative diseases. The focus of the laboratory is to understand the molecular mechanisms of neurodegenerative diseases (e.g. Alzheimer's disease, Parkinson's disease) from the perspectives of synapse loss and brain-body interaction, and on developing related drug targets.

The interaction between glial cells and neuronal synapses and its role in neurodegenerative diseases

We discovered that planar cell polarity proteins signaling is targeted in Alzheimer's disease. We identified monoclonal antibodies targeting the PCP signaling pathway, demonstrating potential for therapeutic value. Further research revealed that the complement signaling pathway ADAM10-CX3CL1-CX3CR1 is involved in regulating microglial morphology and migration. Activated microglia release inflammatory factors through interactions with neurons, subsequently affecting neuronal excitability and synaptic plasticity, forming a vicious cycle between neuroinflammation and neural network dysfunction. Based on this, the team also identified highly effective and low-toxicity lead compounds targeting specific

inflammatory factors, providing a potential intervention strategy for restoring the homeostasis of the neuroimmune microenvironment.

The synergistic role of the brain and peripheral organs in the onset of neurodegenerative diseases

With the deepening research into the holistic view of the organism, neurodegenerative diseases are often closely linked to systemic metabolic dysfunction. Pathological protein deposits (such as A β and α -synuclein) are found not only in the central nervous system but also in multiple peripheral organs. We focus on the role of pathological protein deposits in peripheral organs in the onset of neurodegenerative diseases and aim to identify new targets for drug intervention from this perspective.

SELECTED PUBLICATIONS:

(* corresponding author; # equal contribution)

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闵文强



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任佳



刘枫源



吴恒玥



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石丽



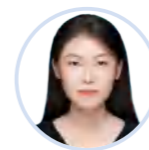
赵新旺



曾雨



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梁世龙



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Division of Non-human Primate Research



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产业化团队

Team for Industrialization



脑所助理团队

BCBDI Administrative Assistants



BCBDI RESEARCH PROJECTS

科研项目

科研项目

BCBDI Research Projects

脑所成立至今，获批国家省部地方等各级项目超950项，获批准金额超12亿元。其中，近三年获批的重要纵向科研项目包括：

国家级项目含脑科学与类脑研究国家科技重大专项1项、国自然重大项目1项/课题3项、国自然重点项目2项、美国脑计划1项、国自然青年科学基金项目（A类）2项、国自然青年科学基金项目（B类）2项、国自然外国学者研究基金项目2项、国自然面上/青年项目43项等。

省部级项目含中国科学院稳定支持基础研究领域青年团队1项、中国科学院先导专项（B类）项目1项/课题2项、中国科学院全球共

性挑战专项2项；广东省脑科学与类脑研究重大科技专项1项、中国科学院所级中外联合研究单元1项、中国科学院-香港地区联合实验室1项、CAS-PIFI国际杰出团队1项、中国科学院国际伙伴计划1项等。

深圳市级项目含深圳市医学研究专项资金揭榜挂帅项目1项、一般项目10项；深圳市基础研究重点项目2项、深圳市概念验证中心1项、深圳市可持续发展科技专项2项、深圳市重点实验室评估后续支持1项等。

项目名称	获批年度	项目层次	项目类别	获批金额 (万元)	负责人	起止日期
压力应激导致节律睡眠紊乱共患情绪异常的机制及干预	2025	国家级	脑科学与类脑研究 国家科技重大专项	4976	王立平	2025.9-2030.8
环境压力应激调控卵巢激素合成的中枢-卵巢神经机制	2025	国家级	国自然重点项目	221	王立平	2026.1.1-2030.12.31
脑介观连接组学	2025	国家级	国自然 青年科学基金项目（B类） [原优秀青年科学基金项目]	200	徐放	2026.1.1-2028.12.31
蛋白质相态调控与神经元功能及病变障碍	2024	国家级	国自然重大项目	1500	毕国强	2025.1.1-2028.12.31
成瘾神经机制及干预策略	2024	国家级	国自然 国家杰出青年科学基金	400	朱英杰	2025.1.1-2029.12.31
认知功能的神经网络调控动力学研究	2024	国家级	国自然 国家杰出青年科学基金	400	鲍进	2025.1.1-2029.12.31
睡眠障碍与恐惧异常的关联机制研究	2024	国家级	国自然 优秀青年科学基金项目	200	曾渝婷	2025.1.1-2027.12.31
Center for Mescale Connectomics	2023	国际	美国脑计划2.0	949	毕国强	2023.10.31-2028.11.1
神经退行性疾病关键分子靶标可视化放射性药物的研发（课题）	2023	国家级	国自然重大项目课题	371	叶克强	2024.1.1-2028.12.31
物理场调控神经振荡的机理及量效关系（课题）	2023	国家级	国自然重大项目课题	300	杨帆	2024.1.1-2028.12.31
电磁场刺激闭环调控大脑皮层异常神经振荡干预（课题）	2023	国家级	国自然重大项目课题	300	蔚鹏飞	2024.1.1-2028.12.31

项目名称	获批年度	项目层次	项目类别	获批金额(万元)	负责人	起止日期
线粒体功能障碍在帕金森病中的作用机制及干预策略研究	2023	国家级	国自然重点项目	218	叶克强	2024.1.1-2028.12.31
卵泡刺激素和ApoE4协同触发女性阿尔茨海默病的发病机制	2023	国家级	国自然 外国学者研究基金项目	160	叶克强	2024.1.1-2025.12.31
正向别构激活GluN2A-NMDA受体治疗中风的新型一类药物开发	2023	国家级	国自然 外国学者研究基金项目	160	王玉田	2024.1.1-2025.12.31
大湾区多物种脑疾病动物模型技术研发平台	2023	广东省	广东省重点领域研发计划 “脑科学与类脑研究” 重点专项（定向委托）	1000	黄天文	2024.1.1-2026.12.31
微塑料跨境传递与脑肠健康影响的多维解析及全球治理合作	2025	中国科学院	全球共性挑战专项	161	李蕾	2026.1.1-2028.12.31
阿尔茨海默病的诊疗策略研究	2025	中国科学院	全球共性挑战专项	149.2	陈宇	2026.1.1-2028.12.31
无创神经调控靶向治疗脑疾病的技术研发及原理解析	2024	中国科学院	稳定支持基础 研究领域青年团队	2000	鲍进	2024.7.1-2029.6.31
图像视觉与情绪的神经编码机制	2024	中国科学院	先导科技专项（项目）	1443.48	鲍进	2024.7.1-2029.6.31
时间概念形成的神经机制	2024	中国科学院	先导科技专项（课题）	598.71	王成	2024.8.1-2026.7.31
情绪信息加工的脑网络空间定位	2024	中国科学院	先导科技专项（课题）	305.82	朱英杰	2024.7.1-2029.6.31
脑科学联合实验室	2024	中国科学院	中国科学院- 香港地区联合实验室	180	王立平	2024.1.1-2028.12.31
CAS-PIFI国际杰出团队-加拿大	2023	中国科学院	CAS-PIFI国际杰出团队	300	王立平	2024.1.1-2026.12.31
中-美脑认知与脑疾病联合研究中心	2023	中国科学院	所级中外联合研究单元	200	王立平	2024.1.1-2026.12.31
靶向小胶质细胞蛋白Gpnmb干预阿尔茨海默病的机制与策略研究	2023	中国科学院	国际伙伴计划	179	Helmut Kettenmann	2024.1.1-2026.12.31
慢性压力驱动的机体功能障碍发生机制与干预策略研究	2025	深圳市	深医专项揭榜挂帅项目	1000	王立平	2026.1.1-2029.12.31
社交竞争胜利降低觅药行为的神经机制及临床转化研究	2025	深圳市	深医专项前沿 探索型一般项目	300	朱英杰	2026.1.1-2029.12.31

项目名称	获批年度	项目层次	项目类别	获批金额(万元)	负责人	起止日期
感觉信息树突整合与阿尔茨海默病神经元过度兴奋的交互机制和治疗策略研究	2025	深圳市	深医专项前沿 探索型一般项目	300	王成	2026.1.1-2029.12.31
神经精神调控工程重点实验室	2025	深圳市	深圳市 重点实验室评估	200	王立平	2025.9.1-2028.8.31
精神障碍下风险认知异常行为的神经机制	2024	深圳市	深医专项一般项目	290	屠洁	2025.1.1-2027.12.31
视觉经验调控视觉脑区发育与脑疾病的机制研究	2024	深圳市	深医专项一般项目	290	谭力铭	2025.1.1-2027.12.31
FCD型癫痫致病灶的神经活动特征及其三维病理结构基础	2024	深圳市	深医专项一般项目	290	孙坚原	2025.1.1-2027.12.31
基20240067 感觉和运动的分子、细胞和环路机制研究	2024	深圳市	深圳市 基础研究重点项目	200	鲍进	2024.12.23-2027.12.22
基20240101 压力应激下中枢-外周互作网络的时空特征及调控机制研究	2024	深圳市	深圳市 基础研究重点项目	200	韩明虎	2024.12.23-2027.12.22
高精度型胞嘧啶碱基编辑器的开发及其在阿尔茨海默症中的应用研究	2024	深圳市	深医专项应用 转化型/生物技术研究	100	叶涛	2025.1.1-2026.12.31
专2023N033 实验动物进出门安全检疫技术研究及应用	2023	深圳市	深圳市 可持续发展科技专项	400	叶涛	2023.11.21-2026.11.20
神经调控骨血管干预骨丢失的机制研究	2023	深圳市	深医专项一般项目	300	杨帆	2024.1.1-2026.12.31
亨廷顿舞蹈症新型靶向多肽药物研发	2023	深圳市	深医专项一般项目	300	王玉田	2024.1.1-2026.12.31
睡眠异常参与心肌梗死后心力衰竭的脑-心轴互作机制	2023	深圳市	深医专项一般项目	300	曾渝婷	2024.1.1-2026.12.31
压力影响精子质量的大脑-睾丸轴神经机制研究	2023	深圳市	深医专项一般项目	300	李蕾	2024.1.1-2026.12.31
深圳市神经系统疾病干预技术概念验证中心	2023	深圳市	深圳市 概念验证中心认定资助	300	孙毅	2021.1.1-2025.12.31
压力应激韧性发生发展的神经机制	2023	深圳市	深医专项一般项目	300	韩明虎	2024.1.1-2026.12.31
专2023N070 精神活性物质成瘾性及毒性机制研究	2023	深圳市	深圳市 可持续发展科技专项	200	徐薇	2023.11.21-2026.11.20

BCBDI
ACADEMIC
ACTIVITIES

学术交流

学术交流

Academic Activities

Seminars(2025)

No.	Time	Speaker	Title
1	Jan-13	Frank Kirchhoff University of Saarland 萨尔大学	Glial transmitter receptors in brain function –How astroglial GABAB receptors contribute to a sex bias in GHB-triggered Absence Seizures.
2	Mar-02	张宏 中国科学院生物物理研究所	多细胞生物自噬起始的分子机制
3	Mar-07	冯欣 中国科学院自动化研究所	新一代活体分子影像技术——磁粒子成像研究进展
4	Mar-21	Xiaoke Chen Stanford University 斯坦福大学	Deconstruction of a Spino-Brain-Spinal Cord Circuit Drives Chronic Mechanical Pain
5	Mar-06	张聪 中国科学院脑智卓越中心	额叶序列工作记忆控制的神经机制
6	Apr-09	Ulrich Schridde Cell Press	Publishing with Cell Press: Turning exciting research into High-Impact publications
7	May-07	白瑞良 浙江大学	脑循环功能磁共振成像进展
8	May-07	何舜平 中国科学院水生生物研究所	在生命的时间树上探寻鱼类物种多样性的演化
9	May-14	刘星 复旦大学上海医学院	情绪和情绪相关记忆的神经环路机制
10	Jun-25	Jingyi Hou侯婧逸 EMBO Press	“Behind the scenes of EMBO press – 走进EMBO 出版社的幕后世界”
11	Aug-04	刘娟 海军军医大学	树突状细胞迁移的代谢调控及自身免疫
12	Aug-04	王强 华南理工大学	线粒体调控胚胎左右不对称的功能机制
13	Aug-04	刘兴国 中国科学院广州生物医药与健康研究院	再探线粒体与细胞核的两套中心法则
14	Oct-17	房泽鹏 北京师范大学	人类高阶丘脑核团通过丘脑-前额叶环路门控意识感知
15	Dec-01	强力 北京大学	The Metabolic Origin of Aging
16	Dec-04	杨竞 北京大学	肿瘤神经科学的过去、现在和未来
17	Dec-01	郭敏 浙江大学	图像算法赋能先进荧光显微成像
18	Dec-27	曹君利 徐州医科大学	麻醉药物非麻醉效应的神经机制
19	Dec-27	曹君利 首都医科大学宣武医院	如何从临床中凝练重大科学问题



2015.11.20-22
第四届全国光遗传技术培训班
The 4th National Workshop on Optogenetic Technology



2016 非人灵长类脑科学未来发展态势国际研讨会
Future Primate Neuroscience Symposium

2016.03.21-23 中国·深圳

2016.3.21-23
首届非人灵长类脑科学未来发展态势国际研讨会



第九届中德前沿科学研讨会
The 9th Sino-German Frontiers of Science Symposium

2016.04.07-10 中国·深圳

2016.04.07-10
第九届中德前沿科学研讨会



第五届全国光遗传学培训班
The 5th National Workshop on Optogenetic Technology

2016.10.28-30 中国·深圳

2016.10.28-30
第五届全国光遗传学培训班



国家自然科学基金委重大研究计划“情感和记忆的神经环路基础”2016年度交流与总结会和国际交流会
International Workshop on NFSC Keynote Research Project "Neural Circuits underling of emotion and memory"

2016.10.31-11.01 中国·深圳

2016.10.31-11.01
基金委年度总结会（深圳）



Nature Conference on Neural Circuitry of Emotion (2016 Shenzhen)

2016.11.18
Nature conference: 情感神经环路国际研讨会



香山会议588次讨论会
The 588th Seminar of Xiangshan Conference Series

2017.03.11-12 中国·深圳

2017.03.11-12
香山会议588次讨论会



2018基金委生命学部神经科学学科战略发展调研第二次会议
The 2nd conference of Research Strategy Development of Neuroscience Department of the NFSC

2018.10.18 中国·深圳

2018.10.18
“2018基金委生命学部神经科学学科战略发展调研第二次会议”在深圳先进院召开



中国神经科学学会神经科学研究技术分会2017学术年会
Satellite Conference of Neurotechnology, 2017 Annual Conference of the Chinese Neuroscience Society

2017.11.18-19 中国·深圳

2017.11.18-19
中国神经科学学会神经科学研究技术分会2017学术年会



中国神经科学学会神经科学研究技术分会2018学术年会
Satellite Conference of Neurotechnology, 2018 Annual Conference of the Chinese Neuroscience Society

2018.12.20-21 中国·深圳

2018.12.20-21
中国神经科学学会神经科学研究技术分会2018学术年会



第六届全国光遗传技术培训班
The 6th National Workshop on Optogenetic Technology

2017.11.20-22 中国·深圳

2017.11.20-22
第六届全国光遗传技术培训班



第七届全国光遗传技术培训班
The 7th National Workshop on Optogenetic Technology

2018.12.22-24 中国·深圳

2018.12.22-24
第七届全国光遗传技术培训班



2019.3.21-23
第二届非人灵长类神经科学研究国际研讨会



2019.08.29-30
首届“大脑-肠道-微生物中法联合国际峰会”



2019.10.29-11.01
中国神经科学学会神经科学研究技术分会2019年学术年会



2019.11.02-04
第八届全国光遗传技术培训班



2019.11.18-20
中国神经科学学会神经科学研究技术分会2020年学术年会



2019.11.20-22
“第九届全国光遗传技术培训班”暨“第五届神经环路示踪技术全国培训班”



2021.04.15
“大湾区成瘾基础与临床”前沿研讨会



2022.08.25
首届脑未来·脑科学与脑技术创新大赛



2021.08.26
脑所-深圳湾实验室联合学术交流研讨会



2022.11.18-23
“中国神经科学学会2021-2022年技术年会”暨“深圳市脑科学学会首届学术年会”暨“第十届全国光遗传技术培训班”



2022.07.09
深圳脑科学学会第一届会员大会第一次会议



2022.12.28-29
第二届国际脑科学前沿与产业大会



2023.03.25-03.26
From Fly to Mouse Symposium



2023.04.08
深澳脑与生命科学前沿(Brain+)研讨会



2023.04.07-04.10
第六届突触传递与神经可塑性国际研讨会暨2023年神经显微成像前沿论坛



2023.03.30-04.01
The Role of Microglia in Health & Disease专题研讨会



2023.04.09-04.10
2023年成瘾与脑科学国际研讨会暨中国药物滥用防治协会成瘾与脑科学分会第一届学术会议



2023.04.21
第三届 生命健康论坛



2023.04.27-04.28
第三届国际脑科学前沿与产业大会暨2023湾区脑科学峰会



2023.05.27-05.29
中国生理学会自主神经专业委员会2023学术年会：“神经-免疫-内分泌-代谢网络相互调控”大会



2023.11.04-11.05
2023“神经药理前沿论坛”



2023.11.16-11.17
湾区脑科学产业创新与合作大会·
2023暨深圳市脑科学学会
第二次年会暨中国神经科学学会
神经科学研究技术分会年会



2023.12.11-12.12
首届粤港澳大湾区生命与健康科学论坛：
“神经科学与老龄化”



2024.01.13
生命·健康-情感障碍主题研讨会



2024.04.18-21
中国生理学会自主神经专业委员会2024学术年会暨第二届“神经-免疫-内分泌-代谢网络相互调控”大会



2024.02.25-28
Application of New Technologies to Non-human Primate Models: Opportunities for International Collaboration



2024.04.24
International Symposium of Life & Health Sciences



2024.05.07-09
神经环路示踪与调控大会暨针灸研究前沿技术创新大会



2024.08.19-21
海峡两岸首届生命科学与健康会议



2024.11.01-04
SMART Symposium-Illuminating the Brain



2024.11.08-10
2024神经药理前沿论坛暨中国药物滥用防治协会成瘾与脑科学分会年会暨深圳市脑科学学会第三次年会



2024.11.05-08
中德-多肽调控的基础与医学研究前沿交叉研讨会



2024.11.14-16
第二届小胶质细胞生理与病理功能专题国际研讨会



2025.04.04-06
中国生理学会自主神经专业委员会2025学术年会暨第三届脑体互动大会



2025.05.27-30
神经环路示踪与调控大会·培训班暨针灸研究前沿技术创新大会



2025.04.06-08
Cell Symposia



2025.11.07-08
神经精神药理交叉前沿论坛暨深圳市脑科学学会第四次年会

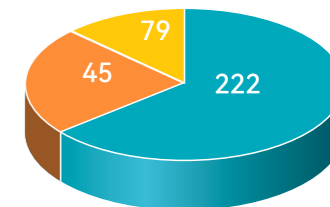
BCBD I UNDERGRADUATE AND GRADUATE EDUCATION

学生培养

学生培养

Undergraduate and Graduate Education

中国科学院深圳先进技术研究院脑认知与脑疾病研究所，依托中国科学院大学，以培养高层次、高素质创新创业人才为教育目标。截至2025年12月，**已培养学生(含所有类型)346人，其中博士研究生79人，硕士研究生222人，本科生45人**。所培养学生获国家、中国科学院、省级、企业等多项奖项。如国家奖学金、中国科学院院长奖、广东省自然科学奖、必和必拓企业奖等，发表Neuron、Nature Communications、Nature Machine Intelligence、PNAS等高水平杂志文章。毕业生多前往苏黎世联邦理工学院、清华大学、加州理工学院、哥伦比亚大学、约翰霍普金斯大学、香港中文大学、华为、腾讯等境内外知名院校和企业就业深造。**脑所目前在培研究生174人，其中博士研究生约占36%**，学生来自香港中文大学、上海交通大学、香港理工大学、香港城市大学、中国科学技术大学、南京大学等全国近30所高等院校。脑所研究生教育以科教融合为特色，注重学生科研创新能力培养，通过各色国际国内学术交流项目，拓展学生视野。从2015年起已举办脑·未来夏令营十一届、中法国际夏令营二届、脑·未来冬令营二届、创新实践X-Lab三届等特色活动，同时与宁波诺丁汉大学、北师大香港浸会大学、中国科学技术大学、南京大学、深圳大学、南方科技大学、山东师范大学等知名高校建立了研究生联合培养计划。



■ 博士研究生 ■ 硕士研究生 ■ 本科生

已培养学生(含所有类型)346人





2015年
第一届脑·未来夏令营



2016年
第二届脑·未来夏令营



2017年
第三届脑·未来夏令营



2018年
第四届脑·未来夏令营



2019年
第五届脑·未来夏令营



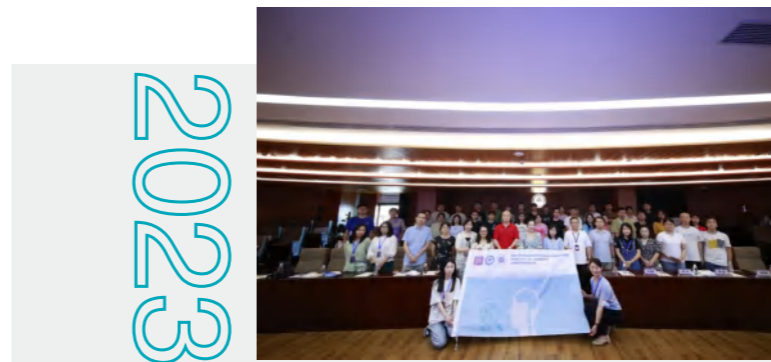
2020年
第六届脑·未来夏令营



2021年
第七届脑·未来夏令营



2022年
第八届脑未来优秀大学生夏令营



2023年
第九届脑·未来夏令营



2024年
第十届脑·未来夏令营



2025年
第十一届脑·未来夏令营

2015年-2025年
十一届夏令营



党团班一体化建设、关爱学生心理健康：

脑所学生专项办（以下简称“专项办”）自2022年5月13日建立以来，已管理400余名学生并联动学生党支部、团支部、各班级开展各类特色活动，如学生迎新暨安全培训会、红色剧本杀、红色观影、学术沙龙、博士生辩论赛、师兄师姐交流会、艺术疗愈等数场活动，有效丰富研究生科研之余的生活，以活动为纽带深入学生群体，建立互信互助的师生关系，营造和谐向上的集体氛围，增强学生归属感。



在学生心理、安全工作上，脑所本年度学生心理普测参与度稳居全院前列，心理事故零发生；事件处置闭环率、台风天住宿地核查率100%；内尔诺奖5班作为晋级团队在由教育处组织的“知信、诚信、守信、立信”科研诚信主题知识竞赛中获得团队三等奖，斩获科研诚信新荣誉。

科技教育高质量发展：基于脑认知规律的未来学习力支持体系

陆续荣获：**广东省**科普教育基地 | **深圳市**科普基地 | **深圳市**优秀校外基地



基地接待超过**10,000**名
中小学及高校学生



“每周半天计划”课程，
研发课程**4**套，覆盖学生近**1000**名



开展**研学、
夏冬令营与科普竞赛**

多种形式传播和宣传 科技教育



CCTV《开讲了》
全网播放量超**1500**万

科技教育课程《脑科学进校园》



小学**600**人 初中**2000**人 高中**2000**人

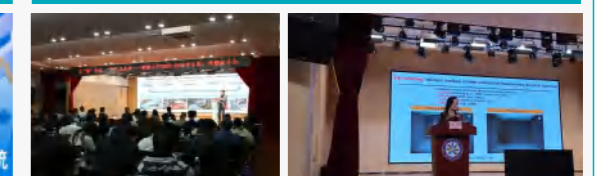
《大脑进校园》和《元认知课程》，覆盖我市**18**所学校，学生**4600**人

教师培训纳入**市级教师继续教育平台**



深圳市是全国首个将脑发育视角下的心理
健康教育纳入**市级教师继续教育平台**的城市

家长讲座：**构建家校共育体系**



面向全市中小学开展**大脑发育家庭教育**，
已覆盖**2500**名家长

BCBDI INDUSTRIALIZATION

成果转移转化

VISoR高通量三维显微成像技术：全方位生物组织成像与分析服务

深圳百会新知科技有限公司是提供生物医学显微成像和大数据服务的专业性平台公司。其核心技术来源于毕国强教授团队研发的同步飞扫高速三维显微成像技术，该技术将大样品成像速度推进到一个新的高度，其核心在于通过对连续运动的透明样品不间断扫描成像，把数据采集速度推到高速相机的极限，从而实现高速扫描成像。这一技术已经开始为中国脑计划项目提供支撑，并参与了美国脑计划2.0灵长类介观图谱项目。

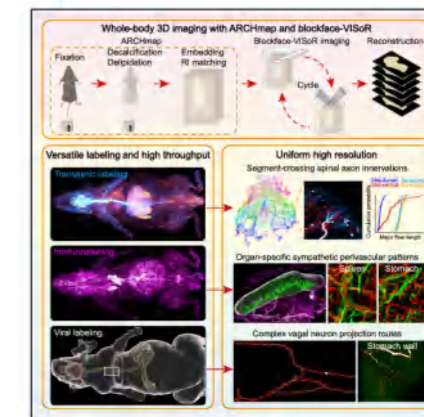


毕国强团队
Nature Biotechnology, 2021

Cell

High-speed mapping of whole-mouse peripheral nerves at subcellular resolution

Graphical abstract



Authors

Mei-Yu Shi, Yuchen Yao, Miao Wang, ..., Pak-Ming Lau, Cheng Xu, Guo-Qiang Bi

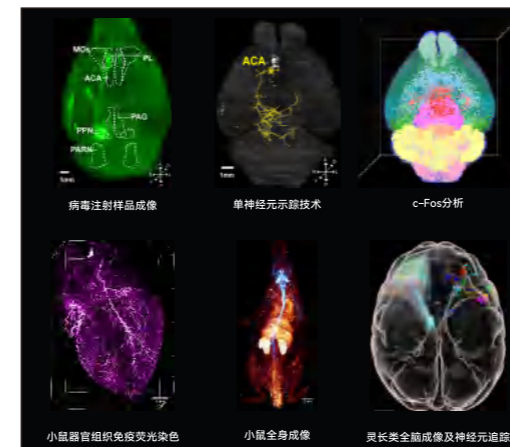
Correspondence

qyzhu@ustc.edu.cn (Q.Z.),
plau@ustc.edu.cn (P.-M.L.),
xuc@ustc.edu.cn (C.X.),
gqbi@ustc.edu.cn (G.-Q.B.)

In brief

A high-speed pipeline enables whole-mouse imaging and mesoscopic analysis of peripheral nerves using transgenic, immunostaining, and viral labeling, providing an effective means to map body-wide structures and intersystem interactions at single-cell resolution relevant to physiology and disease.

毕国强团队
Cell, 2025 (本公司作为共同完成单位，入选2025年度“中国神经科学重大进展”)



核心服务内容

- 样品处理服务（组织透明化服务）
适用于多种组织类型（如脑、脊髓、肠道、肾脏、心脏、全身等）。
- VISoR高通量三维成像服务
0.5小时即可完成 $1 \times 1 \times 2.5 \mu\text{m}^3$ 分辨率的小鼠全脑成像。
- 数据分析服务
通过高性能计算集群及自主开发的算法和软件，实现图像拼接、c-Fos信号提取、图谱配准和神经元形态重建等多种分析。

深圳百会新知科技有限公司在生物医学显微成像和大数据分析领域具有明显的技术优势和专业服务能力，处于行业领先地位，公司自成立以来，已为上百家科研院所、高校、医院等提供了成像及数据分析服务，受到客户的一致好评。

深圳百会新知科技有限公司



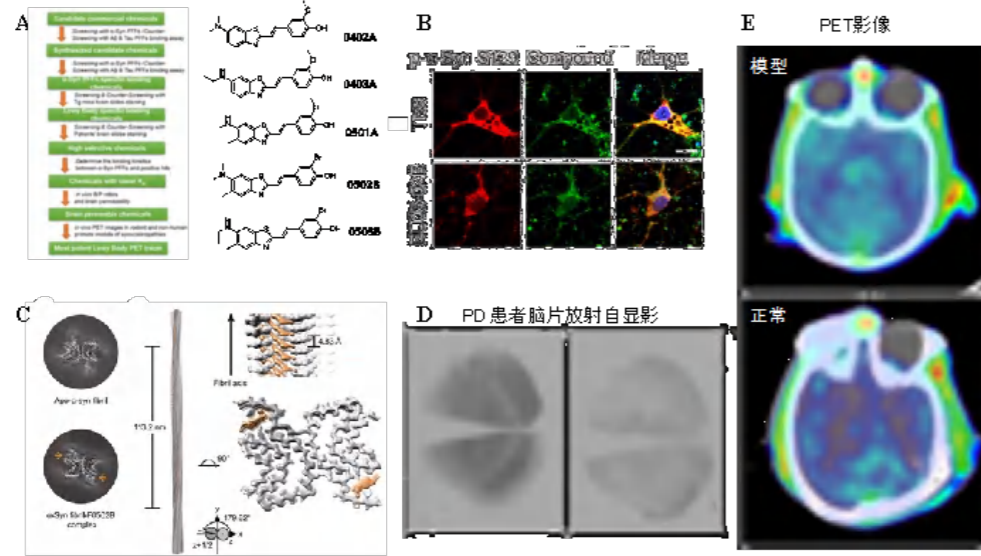
企业简介：

深圳百会新知科技有限公司是提供生物医学显微成像和大数据服务的专业性平台公司，公司致力于以交叉技术实现知识创新，通过优化的新技术实施方案向全社会提供服务。公司在深圳脑科学产业创新中心设立的介观成像平台配备了完善的设备和专业技术人员，可以为客户提供从样品透明处理到三维扫描成像以及数据分析等全流程服务。

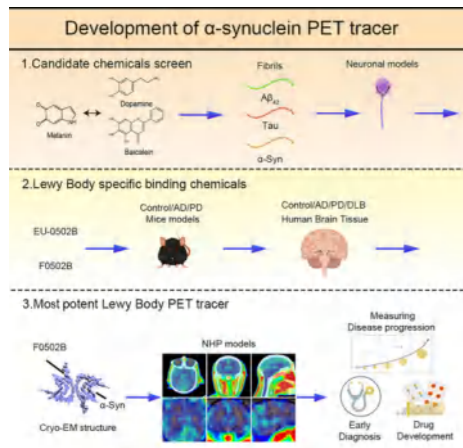
帕金森病诊断的新型PET示踪剂“[18F]-F0502B”加速帕金森病早期精确诊断进程

帕金森病 (Parkinson's disease, PD) 的诊治是当前生物医学领域难以解决的重大难题。目前PD的临床诊断主要依靠患者的临床表现, 缺少高灵敏度及高特异性的分子影像学手段。残存神经元内 α -突触核蛋白 (α -Syn) 沉积形成路易小体是PD的特征性神经病理改变。因此, 本团队基于PD的特征性病理改变, 首次开发的用于PD诊断的新型PET示踪剂“[18F]-F0502B”, 可显像聚集神经细胞 α -Syn聚集体, 这一成果填补了帕金森病影像诊断标志物的空白, 使得帕金森病的早期精确诊断成为可能。

学术成果: 开发了 α -Syn特异性PET探针药物[18F]-F0502B:



A. α -Syn高亲和力候选化合物的体外筛选, 得到先导化合物0502B; B. PD患者死后脑样本验证先导化合物EU0502B和路易小体的结合; C. α -Syn和F0502B结合位点的冷冻电镜解析; D. PD患者死后脑的18F标记F0502B放射自显影, 总结合(左)和非特异性结合(右); E. 非人灵长类[18F]-F0502B-PET影像; E. α -Syn 预制纤维脑内注射模型(上)和正常对照组(下)。



前PET示踪剂项目正在进行研究者临床试验 (IIT), 项目进展顺利, 已获得中科天使、同创伟业等机构投资。

1. 对包括多巴胺衍生物在内的候选化学物质进行了筛选, 以确定它们与 α -Syn纤维的特异性结合。
2. 在小鼠模型和人类脑组织中进一步测试了候选化合物的高度选择性。
3. 确定了示踪剂与 α -Syn聚集体复合物的结构, 并用[18F]-F0502B在活体非人灵长类动物模型中进行了PET显像测试。

叶克强教授团队 *CELL*, 2023

深圳博芮健制药有限公司

企业介绍:

深圳博芮健制药有限公司 (Braegen Pharmaceutical) 公司致力于中枢神经系统(CNS) 领域的创新药和诊断方法开发, 产品管线包括一个临床阶段的创新药和两个临床前阶段已立项IND的小分子药物和PET-CT诊断试剂, 适应症包括阿尔茨海默病 (AD)、帕金森病 (PD)、肌萎缩侧索硬化 (ALS)等多种神经退行性疾病。



以揭秘“大脑黑匣子”为己任, 做病毒载体创新研究的引领者

创新引领发展, 布林凯斯以病毒载体创新研究领导者为目标, 深耕工具研发并斩获系列成果。

嗜神经病毒领域, 成功开发低毒高效逆向跨单突触系统 (RV)、严谨性顺向跨单突触系统 (HSV) 及高亮型/Cre依赖型逆向跨多突触系统 (PRV803/805) 等新品, 以低毒、高敏特性助力中国神经科学研究跻身世界前沿。AAV病毒领域, 打造小胶质细胞高效转染、脑区核团精准标记等领域亟需的新工具, 同时搭建 AI-AAV 辅助定向进化平台, 结合自有高产体系的高库容量与高精度的AAV突变体工程化改造筛选平台, 降本增效开发靶向性新型AAV, 赋能基因与细胞治疗领域发展。

神经科学前沿技术转化平台 —— 平台共享, 合作赋能

2025年, 布林凯斯以技术转化平台为纽带, 深度链接多家顶尖科研团队, 构建起“资源共享、优势互补、协同创新”的合作生态。以开放共赢为导向, 全面开放技术转化平台资源。从核心技术攻坚到科研成果落地, 我们与合作伙伴深度协同, 打通技术转化的关键链路, 实现资源共享、价值共创。全年合作成效显著, 以平台之力赋能科研突破, 以共赢之势推动神经科学领域的技术革新与产业升级。

HaloDA1.0
远红光多巴胺探针, 观测脑内神经递质“多色共舞”
北京大学李毓龙研究员团队

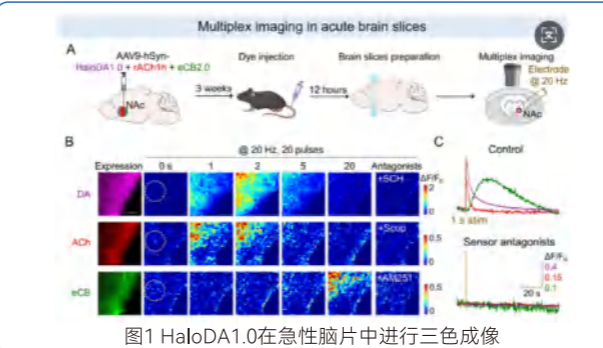


图1 HaloDA1.0在急性脑片中进行三色成像

mYongHong
新一代超稳定超亮红色荧光蛋白
福建医科大学付志飞研究员团队

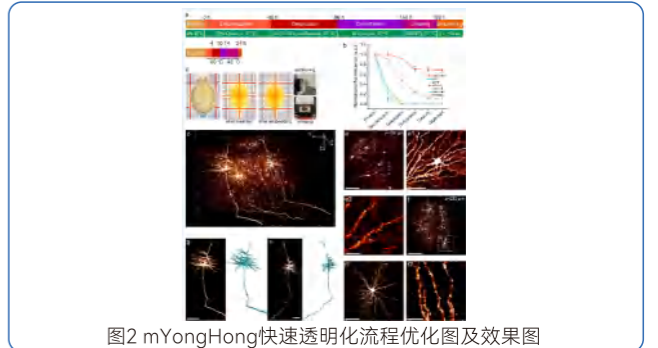


图2 mYongHong快速透明化流程优化图及效果图

SomaFRCaMP1
高性能红色钙成像蛋白, 灵敏度比肩绿色探针
西湖大学 Kiryl Piatkevich 教授团队

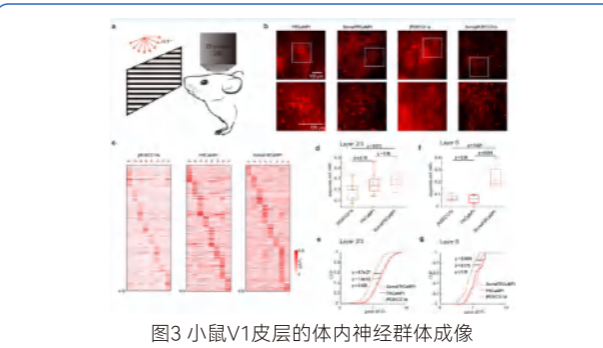


图3 小鼠V1皮层的体内神经群体成像

rAAV-miniBEND
一种用于脑内皮细胞基因递送和脑血管畸形建模的靶向载体
北京脑科学与类脑研究所戈鹏平教授团队

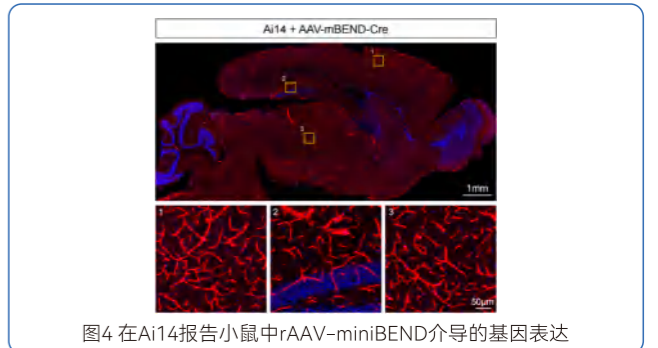


图4 在Ai14报告小鼠中rAAV-miniBEND介导的基因表达

深圳市布林凯斯生物技术有限公司

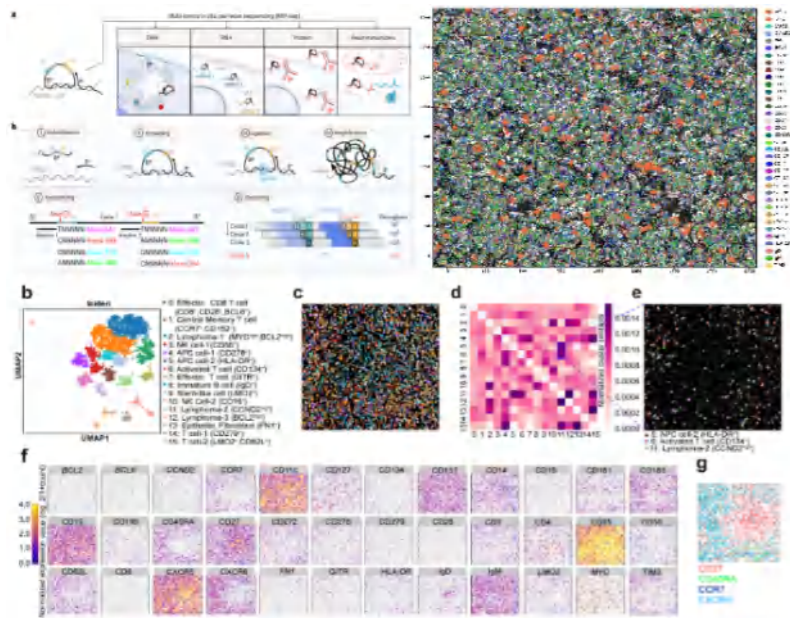
企业介绍:

布林凯斯 (Brain Case) 是一家专注于工具病毒载体研究及转化医学研究的高新技术企业。在过去的十多年时间里, 以揭秘“大脑黑匣子”为己任, 一直致力于工具病毒载体开发及应用策略研究, 在神经环路示踪工具病毒载体 (RV、PRV、HSV、VSV、CAV等)、疾病基因治疗用重组腺相关病毒 (rAAV) 载体研究、肿瘤免疫治疗用溶瘤病毒等研究积累丰富经验, 发展了行业领先的制备系统。公司现有80+人的研发及技术团队, 硕博研究生率超45%, 拥有20多项自主知识产权, 已建成全流程的GMP生产及实验平台, 在深圳、武汉等地建有完善的技术平台。公司开展基于神经环路研究、递送载体技术的基础科研及药物研发服务。



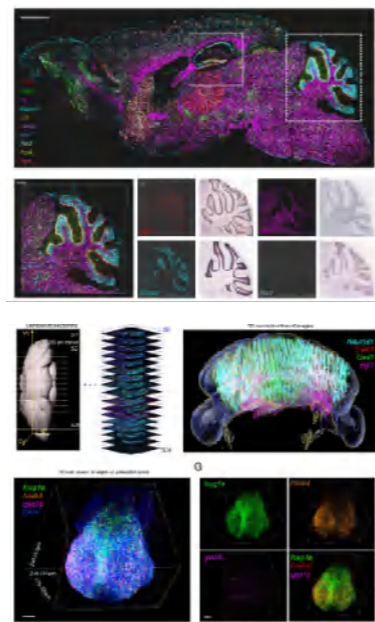
空间多组学技术的开发与在分子病理的应用

随着单细胞测序与大规模组学技术的发展，通过空间组学对生理病理的研究和应用越来越广泛，目前聚焦空间多组学技术平台开发的相对较少，多以欧美国家为主，且检测能力不足，设备昂贵等特点，仅适用于基础科研。因此团队基于原位测序原理开发了一种新型的空间多组学技术（MiP-seq），可以实现在细胞或者组织原位水平上进行高通量、单细胞、单分子、单碱基精度的原位检测，操作更加简便灵活、性价比高，在未来的基础科研与临床精准诊断会有更大的市场前景。



MiP-seq技术原理及使用技术解析弥漫性大B淋巴瘤组织样本中30种蛋白及6种mRNA的空间分布

曹罡团队, *Nature Biomedical Engineering*, 2024



该技术目前已经实现产业化，与科研高校、医院、企业等100多家单位建立合作。



鯤羽（深圳）生物科技有限公司

企业介绍:

鯤羽生物（Spatial FISH）是一家自主创新的国家高新技术企业，核心成员由国家领军人才及毕业于国际一流研究机构组成，硕博比例高达67%，拥有一支高水平、专业化、创新能力突出的技术团队。公司拥有 π -FISH RNA原位检测试剂盒、DNA肿瘤产前检测试剂盒及靶向空间组学（MiP-seq）技术服务产线3套，产品覆盖神经、发育、临床肿瘤等基因检测试剂盒200多种，高通量自动化杂交仪与原位测序仪及全自动成像扫描3大平台，获批医疗器械资质证书30项，申请获批技术专利12项等。同时，与多家三甲医院合作，共同致力于打造下一代分子病理智能远程诊断平台，推动精准诊断、公平医疗发展。鯤羽生物立志打破国外技术垄断，致力建设民族自主创新品牌。

BCBDI
COMMUNIST PARTY AND
COMMITTEE ACTIVITIES

党群团工会活动

2025 党建活动

脑所/深港脑院党总支坚持以习近平新时代中国特色社会主义思想为指引，加强对科研工作的政治引领，以党建促进科研，以科研带动创新，以创新引领基地建设，以基地建设为抓手服务创新驱动发展，切实发挥党组织坚强的战斗堡垒作用。深入学习贯彻党的二十大精神，凝聚思想共识，激发奋进力量，将“两学一做”学习教育常态化、制度化，提升党员党性修养、政治站位和团队凝聚力。



中共中国科学院深圳先进技术研究院
脑所总支部委员会党员大会换届选举



开展“携手脑科学，守护脑健康”
科普活动传递科技力量，弘扬科学家



党员大会选举产生了新一届支部委员会



深入贯彻中央八项规定精神学习教育



前往博药制药有限公司参访交流



东山中学“弘扬攻关精神，探索创新之路”来访研学



赴古田开展“与国同光”抗日战争胜利八十周年”历史教育



SIAT庆祝中国科学院建院76周年主题讲座

党群团 工会活动

脑所/深港脑院团支部在上级党委、团委的领导下，带领全体团员青年学习树牢“四个意识”，坚定“四个自信”，做到“两个维护”；坚持“围绕中心、服务大局、保障发展”的工作思路和原则。一是加强思想学习，夯实组织基础。组织团员青年学习感悟先进事迹，传承红色基因，督促团员学并结合红色基地游览等活动。二是组织团员青年参加院所的系列学术活动，学习科研技能，培养科学思维。关心青年成长，培养青年能力。三是开展志愿活动，爱心传递社会。



★ 志愿服务活动



★ 志愿服务活动



★ 师生观影活动



1-2月



3-4月



5-6月



7-8月



9-10月



11-12月

团建活动

脑所/深港脑院工会小组始终坚持党的领导，紧密结合党建工作，立足岗位做贡献促业务工作。一是组织开展多形式、丰富多彩的文体活动。推进脑所文化建设，营造家园文化。二是开展各项主题活动。积极组织开展职工疗休养等活动，激发员工积极参与。三是采取多种形式引导加强规章制度和业务知识的学习，以达到团结、合规、绩效的效果。



春节拍摄活动



总结活动



运动会



徒步活动



团建活动



团建活动



疗休养活动



篮球活动



羽毛球活动



气排球活动



足球活动



乒乓球活动



大事记
领导关怀
事记总览

领导关怀

Leader's Care



2016.01.06
时任中国科学院副院长谭铁牛院士访问脑所指导工作



2017.12.02
时任中国科学院院长白春礼院士访问脑所指导工作



2019.06.13
时任中国科学院副院长张亚平、深圳先进院创院院长樊建平与
时任UCB校长Santa Ono教授进行会谈



2020.03.10
时任深圳市委书记，现任第二十届中央委员、内蒙古自治区党委书记、
自治区人大常委会党组书记王伟中调研深圳先进院



2018.03.09
时任深圳市委书记，现任第二十届中央委员、内蒙古自治区党委书记、
自治区人大常委会党组书记王伟中调研深圳先进院



2018.03.09
时任深圳市委书记，现任第二十届中央委员、内蒙古自治区党委书记、
自治区人大常委会党组书记王伟中调研深圳先进院



2020.09.23
时任广东省副省长，现任广东省委常委、省委统战部部长王曦调研
深圳先进院



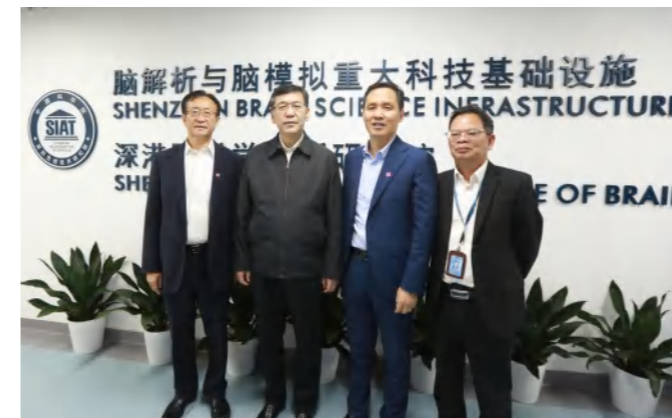
2021.03.08
时任上海市委书记、现任国务院总理李强调研深圳先进院



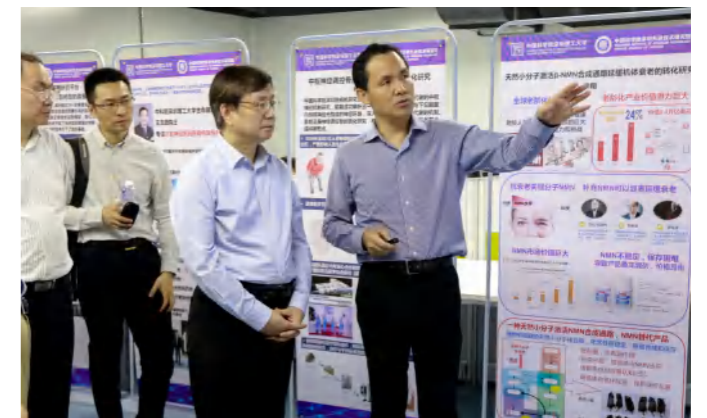
2018.03.29
时任科技部副部长黄卫、时任深圳副市长高自民
与广东省脑连接图谱重点实验室学术委员会成员座谈留影



2019.03.23
时任中国科学院副院长张亚平见证深港脑院“SIAT-UCB院士工作站”
揭牌成立



2021.03.24
时任中国科学院副院长，现任中央科技办主任、科学技术部部长
阴和俊调研深圳先进院



2021.05.18
中国科学院院长、党组书记，学部主席团执行主席侯建国调研
深圳先进院



2021.09.09
时任国家药品监督管理局局长焦红调研深港脑院



2023.09.23
时任广东省副省长张新，深圳市委副书记、市长覃伟中
陪同湖南省党政代表团考察调研深圳先进院



2025.02.18
时任南京市市长，现任内蒙古自治区党委常委、
包头市委书记陈之常等调研脑设施



2025.02.23
中华人民共和国教育部党组书记、部长怀进鹏院士等调研脑设施



2024.02.04
时任广东省副省长，现任广东省委常委、省委统战部部长王曦一行
调研脑设施



2024.05.22
中国科学院副院长、党组副书记吴朝晖调研脑所



2025.3.18
中国科学院副院长、党组副书记吴朝晖调研深圳先进院



2025.08.08
原中国科学院院长白春礼院士到深圳先进院调研



2024.06.25
深圳市委副书记、市长覃伟中等一行调研脑设施



2024.07.15
广东省科技厅王月琴厅长等调研脑设施

事记总览

Events Overview



2015.05.23
北京天坛医院赵继宗院士做学术报告



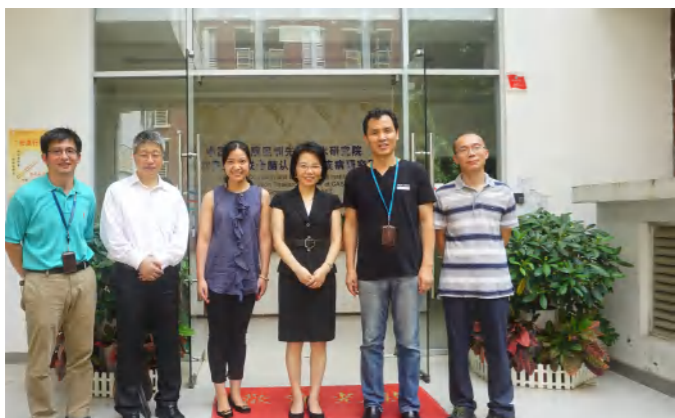
2015.05.23
清华大学药学院鲁白教授来访交流



2015.05.23
香港科技大学校长叶玉如院士做学术报告



2016.03.12
2005年诺贝尔生理学奖得主
Barry Marshall教授来访



2017.09.15
肖瑞平教授、程和平院士等一行来访



2017.11.06
时任深圳市副市长，现任现任深圳市人大常委会副主任、
党组书记高自民调研先进院



2017.12.04
时任深圳市副市长，现任第十四届人民代表大会农村农业委员会
副主任委员艾学峰一行视察



2017.12.22
暨南大学教授、中国科学院院士苏国辉来访交流



2018.03.29
粤港澳脑与智能科学高峰论坛
暨广东省脑连接图谱重点实验室学术委员会成立大会



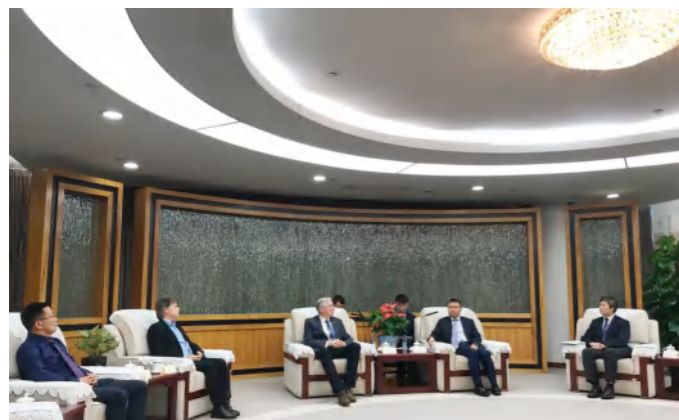
2018.05.23
王立平与朱英杰赴德国与内尔教授
洽谈诺奖实验室建设



2018.06.20
深圳先进院获AAALAC认证揭牌仪式



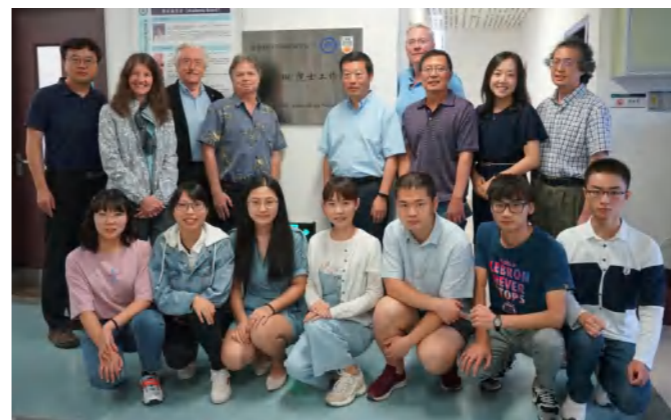
2018.07.26
加拿大UBC王玉田院士访问先进院



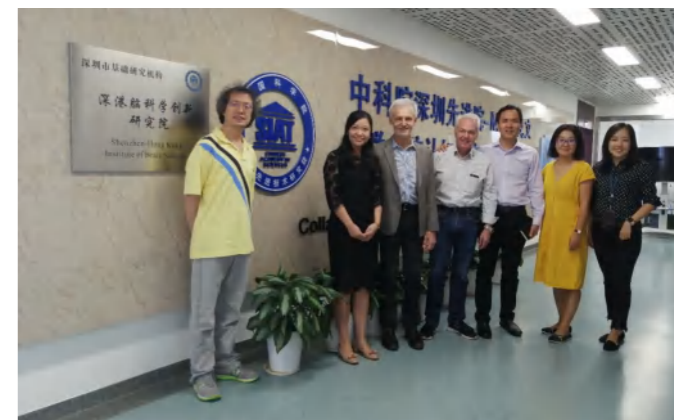
2018.09.30
时任深圳市副市长王立新、时任深圳市科技创新局副局长钟海会见UBC院士团队



2019.01.02
“高时空精准细胞调控技术对脑疾病干预的应用基础研究”获深圳市自然科学奖一等奖



2019.10.08
首批SIAT-UBC联合培养研究生遴选留影



2019.10.23
国际神经科学领域权威期刊Glia主编德国科学院院士Helmut Kettenmann和香港城市大学神经科学系系主任Bruce Ransom教授到访交流



2019.03.23
深圳内尔神经可塑性实验室授牌仪式



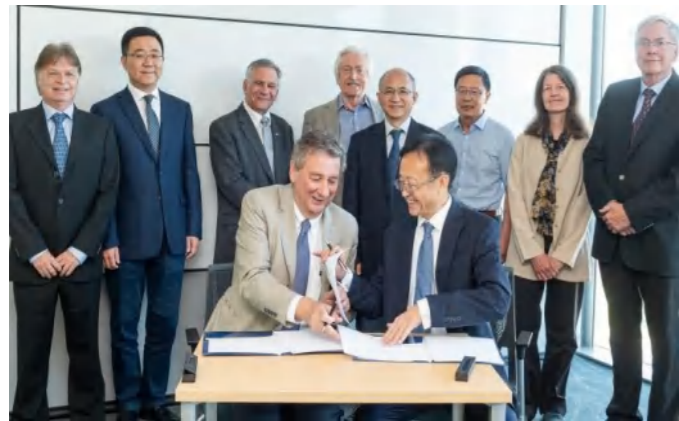
2019.05.31
深港脑科学创新研究院揭牌仪式暨第一届管理委员会第一次会议



2019.11.15
深港脑科学创新研究院第一届学术委员会第一次会议与会领导、专家学者留影



2019.12.06
科技部生物中心张新民主任一行调研深圳先进院



2019.06.13
德莫特·凯莱赫博士和深圳先进院创研院长樊建平签署合作协议



2019.09.10
中国科学院脑联结解析与调控重点实验室申请论证会



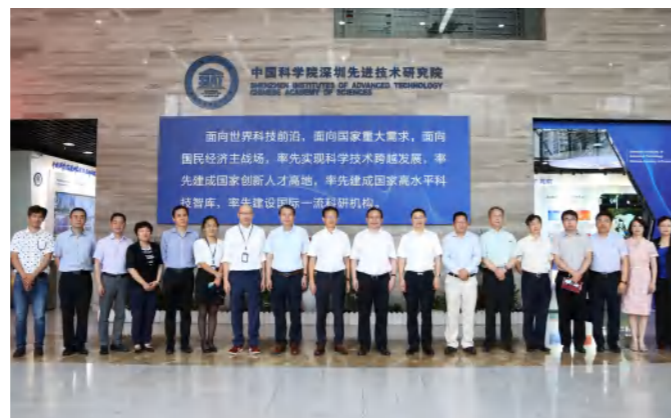
2019.12.18
脑-健康：创新与产业论坛暨脑认知脑疾病学术与产业联盟成立大会



2019.12.18
深圳先进院与荷兰爱思唯尔科技出版集团签署战略合作备忘录



2020.06.06
深港脑科学创新研究院第一届管理委员会第二次会议



2020.07.08
时任南开大学校长，现任全国政协第十四届全国委员会教科卫体委员会副主任、中国工程院院士曹雪涛一行来访深圳先进院



2021.10.26
全国首届脑与健康科技产业大会（B30大会）在深圳光明科学城圆满落幕



2021.12.09
中国工程院院士，河北医科大学副校长、法医学院院长
全国人大常委会，法律委副主任，九三学社中央副主席丛斌来访



2020.09.07
中国科学院脑联结解析与调控重点实验室及
广东省脑连接图谱重点实验室2020年学术委员会



2020.11.05
生命健康与新医药发展产业论坛



2021.12.15
深港脑科学创新研究院第一届管理委员会第三次会议



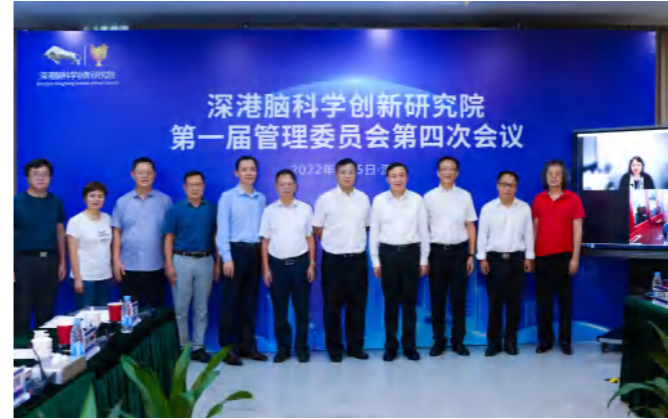
2022.05.27
光明脑科学B30系列论坛——生命科技“内循环”之基石：
千亿量级实验动物产业的挑战、机遇与未来（线上）顺利举办



2021.05.11
NSFC集成项目启动仪式暨项目进展交流会



2021.07.26
时任深圳市科技创新委员会党组书记、主任，
现任深圳市龙华区人大常委会主任王有明调研深港脑院



2022.08.05
深港脑科学创新研究院第一届管理委员会第四次会议顺利召开



2022.08.05
时任深圳市副市长，现任深圳市委常委、秘书长，
市直机关工委书记郑红波一行调研深港脑院



2022.08.19
“大脑进校园”课程大纲编制研讨会



2023.12.29
第二届国际脑科学前沿产业大会顺利举办



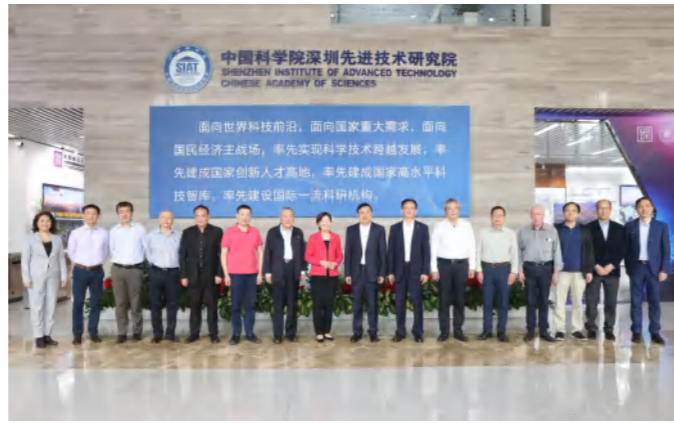
2023.09.25
深港脑科学创新研究院第一届管理委员会第五次会议顺利召开



2023.09.25
深圳市科技创新委员会党组书记、主任张林调研深港脑院



2023.02.14
丹扬、蒲慕明、颜宁三位院士到访深港脑院交流



2023.03.17
深港脑院第一届学术委员会第二次会议暨战略发展研讨会



2023.11.06
中国工程院院士，康复大学校长董尔丹一行参观脑设施



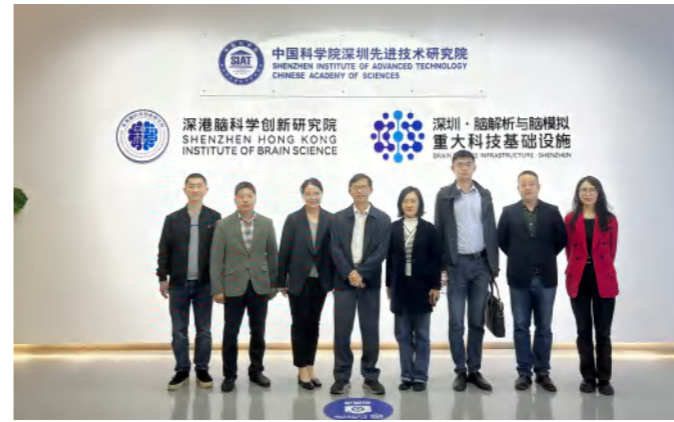
2023.11.16
诺贝尔生理学或医学奖得主Erwin Neher参观脑设施



2023.04.27
第三届国际脑科学前沿与产业大会暨2023湾区脑科学峰会成功举办



2023.04.29
诺贝尔生理学或医学奖得主Thomas C. Südhof参观脑设施



2024.03.15
广东省科技厅副厅长吴世文等访问脑设施



2024.03.29
时任兰州大学校长、中国科学院院士严纯华等调研脑设施



2024.05.17
时任深圳先进院副院长、现任南京大学副校长、
中国科学院院士郑海荣会见诺奖得主Erwin Neher教授



2024.06.12
粤港澳大湾区院士联盟（香港科技界）叶玉如院士等访问脑设施



2025.03.03
中国科学院院士张宏参观脑设施



2025.03.09
中国科学院院士王志珍、顾瑛一行参观脑设施



2024.06.19
时任广东省发展改革委副主任，
现任黑龙江省工业和信息化厅副厅长郭跃华等调研脑设施



2024.07.19
深圳市脑解析与脑模拟重大科技基础设施获国际实验动物评估和
认可委员会（AAALAC）认可



2025.04.17
中国科学院深圳先进技术研究院脑所广东省脑连接图谱重点实验室
2024年度学术委员会



2025.08.15
香港中文大学校长、中国科学院院士卢煜明等调研脑设施



2024.09.23
中国科学技术协会原专职副主席、书记处书记孟庆海等调研脑设施



2024.12.05
第四届脑科学前沿与产业大会暨第五届光明脑科学大会顺利举办



2025.11.29
脑机工程与AI、基础与临床研究创新联合体签约仪式



2025.12.15
深医专项“揭榜挂帅”项目启动会



2025.12.27
国家科技重大专项项目启动暨实施方案论证会



2025.12.27
深港脑科学创新研究院第二届管理委员会、
学术委员会暨国际战略咨询委员会第一次会议



2025.12.28
第五届脑科学前沿与产业大会暨2025深圳脑机接口博览会



2026.01.06
中国神经科学学会中枢与外周互作分会成立



2026.01.06
中国科学院学部咨询项目调研团队程和平院士一行考察脑设施



BCBDI 媒体矩阵



脑所公众号



脑所网站



深港脑院网站



脑设施公众号



脑设施视频号



脑创中心公众号