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Application of Multi-Input Multi-Output Brain-Computer Interface in Cognitive Assessment for Alzheimer's Disease

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Abstract:

This research aims to augment human cognitive abilities, particularly memory function, through the development of innovative prosthetics. The hippocampus, a crucial brain region involved in memory encoding and recall, has been the focal point of numerous studies seeking to develop prosthetics that can restore or enhance memory function in individuals with impairments such as Alzheimer's disease. This review examines two studies that delve into the development and application of hippocampal neural prosthetics, highlighting the potential of these prosthetics to revolutionize the treatment of memory impairments. One study utilized static neural stimulation patterns to enhance memory for specific information content, while another developed a nonlinear Multiple Input Multiple Output (MIMO) dynamic model to predict and stimulate neural activity patterns during memory encoding. Both studies demonstrated significant improvements in memory performance. Additionally, this paper discusses the clinical significance and application prospects of hippocampal neural prosthetics, including the potential for implantable prosthetics and the widespread applicability of MIMO stimulation. Furthermore, the paper explores advanced modeling and classification techniques for neural ensembles and visual memory decoding, including Volterra-type hierarchical modeling, optimal multi-unit stimulation patterns, and a sparse classification model for decoding visual memories. Finally, the paper presents the implementation and evaluation of neural prosthesis systems, including an application-specific integrated circuit (ASIC) design for a hippocampal prosthesis and a high-performance, scalable system architecture for real-time estimation of neural activity. These advancements hold promise for future research and applications in neural prosthetics for memory enhancement.

Keywords: MIMO; Alzheimer's Disease; Hippocampal Prosthesis.

1. Introduction

Alzheimer's Disease (AD), a pernicious neurodegenerative disorder, is characterized by the relentless decline of cognitive abilities, notably memory loss, significantly impacting the quality of life for those afflicted. Amidst the escalating global aging demographic, the prevalence of AD has surged annually, posing a formidable challenge to public health and healthcare systems worldwide. In this context, Brain-Computer Interface (BCI) technology, an innovative neuroengineering domain, has emerged as a pivotal tool in assessing cognitive function, diagnosing brain disorders, and exploring novel therapeutic avenues.

Among various research directions within BCI technology, the Multi-Input Multi-Output (MIMO) model stands out as one of the most important areas, which has garnered substantial attention due to its unparalleled ability to precisely characterize the intricate input-output relationships within complex neural networks. MIMO models the dynamic interplay of multiple neural inputs and their corresponding outputs. This approach offers deeper insights into neural system functioning, which in turn enhances the accuracy and effectiveness of BCI-based cognitive assessments and diagnostic strategies.

This paper delves into various aspects of MIMO BCI in cognitive assessment for Alzheimer's Disease, including current research, emerging trends, and potential future directions. This paper objective is to synthesize the latest research findings, identify key challenges and opportunities, and propose potential directions for future research. By doing so, this paper aims to contribute to the ongoing global efforts to combat AD and advance the development of BCI technology for cognitive function assessment and therapeutic interventions.

2. Advancements in Hippocampal Neural Prosthetics for Memory Enhancement

2.1 Overview of Hippocampal Neural Prosthetics

In recent years, the field of neuroscience has been actively exploring innovative technologies aimed at enhancing human cognitive abilities, particularly memory function. Among these advancements, hippocampal neural prosthetics have emerged as a promising avenue for research. The hippocampus, a key brain region involved in memory encoding and recall, has been the focal point of numerous studies seeking to develop prosthetics that can augment or restore memory function in individuals with impairments [1].

The primary objective of these research efforts is to explore and develop novel methods for improving memory function, with a special emphasis on addressing memory impairments observed in conditions such as Alzheimer's disease and other forms of dementia.Researchers are leveraging neurotechnology advancements to design prosthetics. These prosthetics aim to interface with the hippocampus and stimulate neural activity patterns, thus enhancing memory encoding and recall.

This section reviews two studies that delve into the development and application of hippocampal neural prosthetics. The first study examines the feasibility of using electrical stimulation to enhance memory formation in individuals with hippocampal dysfunction, while the second study explores the potential of using brain-computer interfaces (BCIs) to facilitate memory recall by decoding neural activity patterns in the hippocampus. Both studies underscore the potential of hippocampal neural prosthetics to revolutionize the treatment of memory impairments and pave the way for novel therapeutic interventions.

2.2 Methodological Advancements in Hippocampal Prosthetic Development

2.2.1 Static Neural Stimulation Patterns

One notable study conducted in the field of hippocampal neural prosthetics successfully utilized static neural stimulation patterns to enhance memory for specific information content. This groundbreaking approach involved the calculation of stimulation patterns through modeling based on the subjects' own hippocampal spatiotemporal neural codes. The research team constructed a Memory Decoding Model (MDM) to precisely calculate the stimulation patterns for hippocampal CA1 and CA3 neurons during the encoding phase of the Delayed Match-to-Sample (DMS) task [1].

The MDM was designed to capture the unique neural activity patterns associated with successful memory encoding and to replicate these patterns through electrical stimulation. By delivering targeted stimulation to the hippocampus, the researchers aimed to reinforce the neural representations of specific information, thereby enhancing its subsequent recall.

The results of this study were highly encouraging. They demonstrated significant improvements in memory performance for images in the Delayed Recognition (DR) task, which followed the DMS task. Specifically, 22.4% of subject-category combinations showed significant performance changes, indicating that the static neural stimulation patterns had a measurable impact on memory enhancement.

2.2.2 MIMO Model-Based Electrical Stimulation

Another study in the field of hippocampal neural prosthetics took a unique approach. It developed a nonlinear Multiple Input Multiple Output (MIMO) dynamic model based on neural activity recorded in the CA3 (input region) and CA1 (output region) of the hippocampus during the execution of the Delayed Match-to-Sample (DMS) task [2]. This innovative model was designed to capture the complex relationship between neural activity patterns in the CA3 and CA1 regions and to predict the activation patterns of CA1 neurons during the memory encoding phase.

The researchers utilized this MIMO model to generate electrical stimulation patterns that were specifically tailored to the neural activity patterns observed during successful memory encoding. By delivering targeted stimulation to the hippocampus based on these predicted patterns, the study aimed to enhance memory formation and retention.

The results of this study were highly promising, demonstrating significant improvements in subjects' short-term memory performance in the DMS task. Specifically, electrical stimulation based on the neural activity patterns predicted by the MIMO model led to an average increase of 37% in memory performance. Furthermore, in the subsequent Delayed Recognition (DR) task, subjects demonstrated significantly improved recognition rates for sample images learned during the MIMO stimulation trials, indicating enhanced long-term memory retention.

2.3 Clinical Significance and Application Prospects

The results of these studies suggest that stimulation patterns tailored to specific memory content can enhance memory encoding, providing possibilities for the development of implantable hippocampal neural prosthetics to improve human memory [3]. There are over 50 million individuals worldwide with Alzheimer's disease, with annual costs nearing one trillion dollars. This research offers new ideas for improving memory function in such patients.

Despite significant individual differences among subjects, such as memory function and the location of epileptic foci, MIMO stimulation produced positive effects in most subjects, demonstrating the widespread applicability of this method [3]. Future research should focus on refining the stimulation patterns and exploring the long-term effects of hippocampal neural prosthetics on memory function in a larger and more diverse population. Additionally, investigating the potential of combining hippocampal neural prosthetics with other therapeutic approaches, such as pharmacological treatments, may further enhance their effectiveness in improving memory.

3. Advanced Modeling and Classification for Neural Ensembles and Visual Memory Decoding

3.1 Hierarchical Modeling and Optimal Stimulation Patterns for Neuronal Ensembles

This section delves into the design of optimal stimulation patterns for neuronal populations, utilizing the approach of Volterra-type hierarchical modeling. The method constructs predictive models using input-output data to describe the influence of interactions between multiple input events on the output, with modeling proceeding in ascending order of interaction complexity [4]. The novel concept of “Triggering Likelihood Functions” (TLFs) is introduced to quantify the triggering effects of neuronal activity at different orders (first-order and second-order). These TLFs are calculated from experimental data, considering both intra-neuronal (self-TLFs) and inter-neuronal (cross-TLFs) interactions. Based on TLFs, an Event Triggering Likelihood (ETL) model is constructed to assess the overall impact of a given multi-unit stimulation pattern on the desired behavioral outcome.

By maximizing the utility function Q calculated from ETL, an OMUSP is designed to maximize the likelihood of inducing the desired behavioral outcome, specifically, correct execution of a Delayed Non-Match to Sample (DNMS) task [4]. The research finds that OMUSP is task-specific, meaning that different OMUSPs are designed for different task conditions (e.g., left lever and right lever trials). The effectiveness of OMUSP is validated through actual experiments, showing that compared to random stimulation, applying OMUSP significantly improves animals’ performance in the DNMS task, with an average increase in correct rate of approximately 10% under longer delay conditions.

3.2 MIMO-NMN Approach for Modeling Neural Encoding Dynamics and Functional Connectivity

This section introduces the Multi-Input Multi-Output Neuron Model Network (MIMO-NMN) approach for simulating the dynamic coding and functional connectivity of neural networks. The MIMO-NMN method stands out as a remarkable advancement in neural network modeling due to its significant advantages over traditional models such as the Volterra-Wiener model, Generalized Linear Model (GLM), and Linear-Nonlinear Cascade (LNC) model [5]. Specifically, MIMO-NMN exhibits superior estimation accuracy, allowing for more precise predictions and simulations of neural network behavior. Additionally, it offers enhanced model interpretability, enabling researchers to gain deeper insights into the underlying mechanisms and dynamics of neural networks. Furthermore, MIMO-NMN demonstrates notable strengths in functional connectivity analysis, providing a more comprehensive understanding of how different neural elements interact and contribute to overall network function.

Architecture of the MIMO model is shown in Fig. 1. The construction of the MIMO-NMN model involves analyzing all neuron pairs using Single-Input Single-Output (SISO) NMN, then constructing Multi-Input Single-Output (MISO) models based on the outputs of each SISO model and their cost function values. Multiple MISO models are combined to form the MIMO model, with weak connections eliminated to reduce model complexity. Simulation verification using synthetic data generated from a simulated LNB cascade system shows that MIMO-NMN outperforms traditional NM and GLM methods in estimating linear filters and predicting spike probabilities. At a noise level of 35%, MIMO-NMN‘s predicted spike probabilities aligned with actual spike events at over 90%, while the accuracy of traditional methods significantly decreased. Analysis of human hippocampal data during a delayed match-to-sample (DMS) task further verifies the effectiveness of MIMO-NMN, with an average prediction accuracy exceeding 85%, significantly higher than traditional methods.

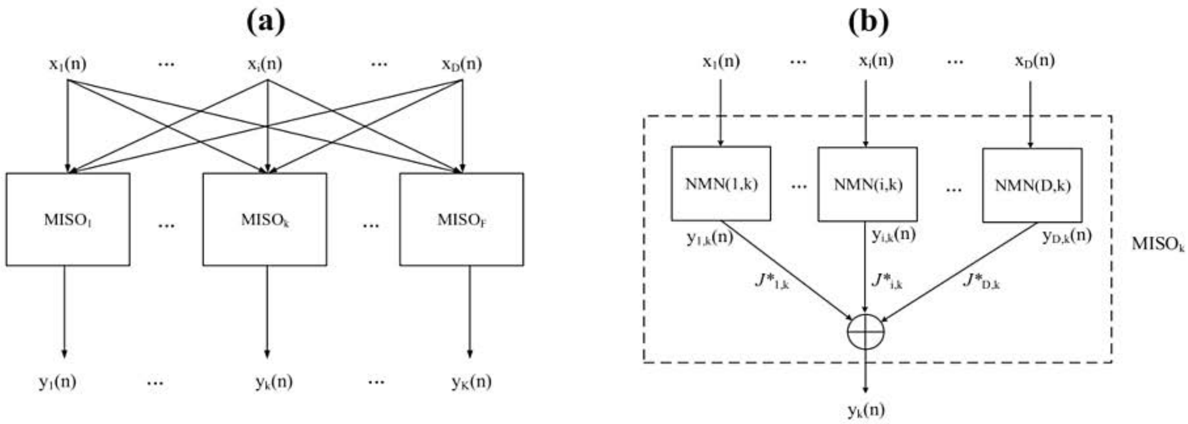

Fig. 1 Architecture of the MIMO model. (a) The MIMO model that has D inputs and K outputs can be divided into several MISO models. (b) In each MISO model, the output yk can be calculated by the weighted sum of the outputs from the SISO NMN model [5].

3.3 Sparse Classification Model for Decoding Visual Memories

Decoding visual memory from human hippocampal spiking activity is challenging. This is due to the high-dimensional input signals and limited data length. Given the large number of neurons and high temporal resolution of hippocampal spiking activity, as well as the limited number of DMS trials, an innovative sparse classification model is proposed to address these challenges. The model utilizes B-spline basis functions for feature extraction of spiking activity, allowing for effective representation of the complex spatiotemporal patterns present in the data. To address the ultra-high-dimensional estimation problems that arise from the high-dimensional input signals, a sparse estimation method with multi-resolution and multi-trial is employed [6]. This approach involves using different temporal resolutions and multiple cross-validations to estimate the model coefficients, which are then optimized using L1-regularized logistic regression to avoid overfitting. By leveraging the sparse nature of the model, people are able to effectively classify visual memory categories and features, even with very limited data points.

The proposed sparse classification model demonstrates efficient classification performance in decoding visual memory categories and features from hippocampal spiking activity. The model is able to effectively classify categories such as „animals," „plants," and „nature," demonstrating significant predictive power even with limited data points. Through the multi-resolution and multi-trial process, a stable Sparse Classification Function Matrix (SCFM) is obtained, indicating good generalization ability of the model. The high Matthews Correlation Coefficients (MCC) achieved across multiple categories, with an MCC of 0.71 for the „animals" category, further verify the classification accuracy of the model. These results demonstrate the effectiveness of the proposed sparse classification model in decoding visual memories from human hippocampal spiking activity, highlighting its potential for use in future research and applications.

4. Implementation and Evaluation of Neural Prosthesis Systems

4.1 ASIC Implementation of a Nonlinear Dynamical Model for Hippocampal Prosthesis

In this section, this paper proposes a novel low-complexity, small-area, and low-power programmable hippocampal neural network application-specific integrated circuit (ASIC) for a hippocampal prosthesis. The ASIC design incorporates five key modules: 1) a low-noise amplifier, 2) an analog-to-digital converter, 3) a spike sorter, 4) a multi-input, multi-output (MIMO) response model, and 5) a charge-metering stimulus amplifier [7].This architecture is based on the MIMO generalized Lagrange-Volterra model, which reduces the core area and power consumption of the chip compared to the traditional parallel multiple-input single-output (MISO) model architecture. MIMO and MISO models are shown in Fig. 2.

To enhance the efficiency of the ASIC, this paper designed a high-efficiency storage space allocation scheme that centralizes the coefficient matrices of all MISO models and stores them using SRAM (Static Random Access Memory). This approach reduces the number of SRAMs used and minimizes wasted storage space. Experimental results demonstrate that the physical area occupied by SRAM has been reduced by 59.38%.

Additionally, this paper developed a new type of low-power convolutional unit. Through resource sharing and operand isolation techniques, this unit significantly reduces both the area and power consumption of the convolutional circuit. The experimental results show that the area of the convolutional unit circuit has been reduced by 72.43%, and power consumption has also been reduced.

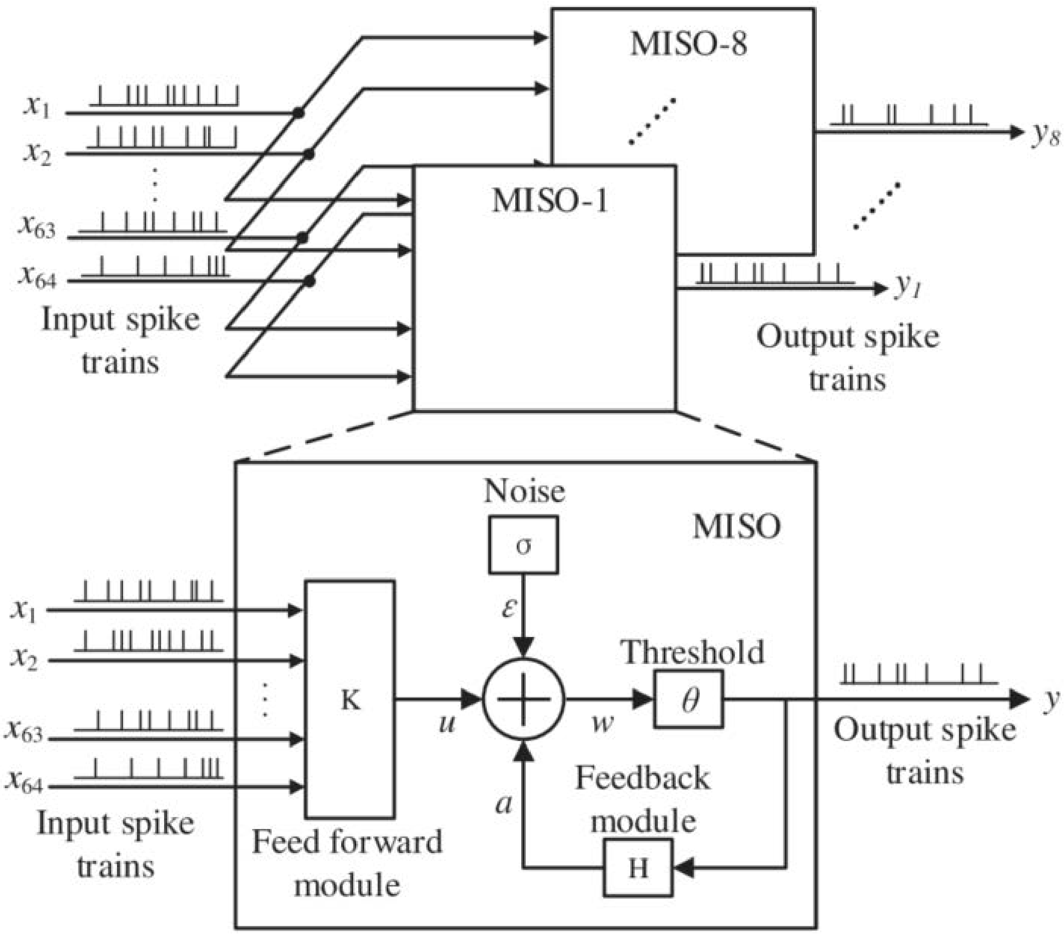

Fig. 2 The MIMO model can be decomposed into multiple independent MISO models. (Top) Structure of a MIMO model. (Bottom) Structure of a MISO model [7].

Furthermore, this paper proposed a low-power Gaussian random number generator module based on the Box-Muller algorithm, with module sharing implemented to further reduce system power consumption. Compared to traditional methods, the power consumption has been reduced by approximately 152.68 times.

The ASIC design has implemented the real-time prediction function of the hippocampal neural network, which can process and transmit neural signals in real-time after being implanted into a biological body by configuring coefficients. Programmability has been achieved, allowing for model training outside the chip, and the trained coefficients can be sent to the ASIC to adapt to different neural signal processing needs.

4.2 High-Performance and Scalable System Architecture for Real-Time Estimation

This section proposes a high-performance and scalable system architecture that primarily investigates a hardware platform based on Field-Programmable Gate Arrays (FPGAs) for real-time estimation of generalized Laguerre-Volterra MIMO models. The Xilinx XC6VSX475T FPGA was chosen as the hardware platform, leveraging its inherent massive parallelism, high-speed data interfaces, and real-time processing capabilities for modeling neural activity [8]. The processing core comprises three main stages: vector convolution and Multiply-Accumulate (MAC) components, pre-threshold potential update units, and gradient computation units.

The hardware platform significantly enhances the data throughput for model parameter estimation, achieving a 3.1-fold increase compared to a C model running on an Intel i7–860 quad-core processor. By optimizing circuit structures and algorithm design, computation precision is improved, ensuring the validity and reliability of results. The hardware platform can be expanded within each stage by utilizing different numbers of processing units and is easily scalable to a multi-FPGA architecture for further enhancing computational capabilities. A four-FPGA network structure is proposed, significantly increasing data throughput through data parallel processing.

The self-reconfiguring platform is shown in Fig. 3. To meet design challenges in future neural dynamics research and enhance the platform's versatility and flexibility, this paper introduces the concept of a hardware IP library. Additionally, this research explores the concept of on-chip self-reconfiguration, enabling the hardware platform to dynamically reconfigure itself according to specific application requirements to achieve an optimal balance of speed, resource utilization, and power consumption.

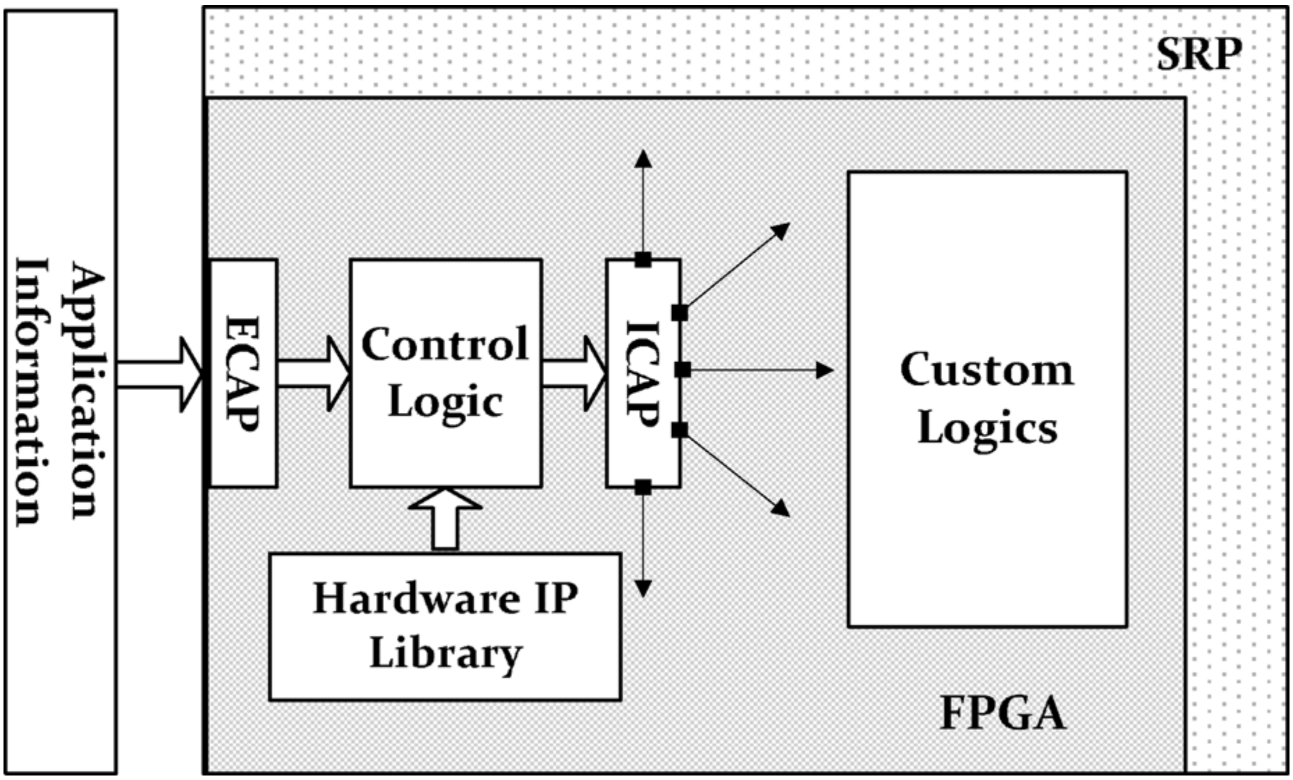

Fig. 3 Self-reconfiguring platform [8].

5. Conclusion

In conclusion, this comprehensive review has highlighted several key advancements in the application of MIMO BCI for cognitive assessment in Alzheimer's Disease (AD). By leveraging advancements in neurotechnology, MIMO BCI offers a promising tool for assessing cognitive function, diagnosing brain disorders, and exploring novel therapeutic avenues. The paper has synthesized the latest research findings, highlighting key advancements in hippocampal neural prosthetics for memory enhancement, advanced modeling and classification techniques for neural ensembles and visual memory decoding, and the implementation and evaluation of neural prosthesis systems. These advancements demonstrate the potential of MIMO BCI to revolutionize the treatment of memory impairments and pave the way for novel therapeutic interventions in AD. The global population is aging, and the prevalence of AD is surging. In this context, continued research and development in this field are crucial to combat the disease and improve the quality of life for those afflicted. The proposed directions for future research aim to contribute to these ongoing efforts and advance the development of BCI technology for cognitive function assessment and therapeutic interventions. With continued dedication and innovation in this field, people stand at the threshold of a new era in AD treatment and prevention.

References

[1] Theodore W. Berger, Dong Song, Rosa H. M. Chan, Vasilis Z. Marmarelis. The Neurobiological Basis of Cognition: Identification by Multi-Input, Multioutput Nonlinear Dynamic Modeling. Proceedings of the IEEE, 2010, 98(3): 356-374.

[2] Hampson RE, Song D, Robinson BS, et al. Developing a Hippocampal Neural Prosthetic to Facilitate Human Memory Encoding and Recall. Journal of Neural Engineering, 2018, 15(3): 036014.

[3] Roeder BM, She X, Dakos AS, et al. Developing a Hippocampal Neural Prosthetic to Facilitate Human Memory

Encoding and Recall of Stimulus Features and Categories. Frontiers in Computational Neuroscience, 2024, 18: 1263311.
[4] Marmarelis VZ, Berger TW, Song D, et al. Design of Optimal Stimulation Patterns for Neuronal Ensembles Based on Volterra-type Hierarchical Modeling. Journal of Neural Engineering, 2012, 9: 066003.
[5] Geng K, Shin DC, Song D, et al. Multi-Input, Multi-Output Neuronal Mode Network Approach to Modeling the Encoding Dynamics and Functional Connectivity of Neural Systems. IEEE Neural Computation, 2019, 31(7): 1327-1355.
[6] Song D, She X, Hampson RE, Deadwyler SA, Berger TW. Multi-Resolution Multi-Trial Sparse Classification Model for Decoding Visual Memories from Hippocampal Spikes in Human. In: Proceedings of the 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Jeju, Korea (South), 11-15 July 2017.
[7] Qiao Z, Han Y, Han X, et al. ASIC Implementation of a Nonlinear Dynamical Model for Hippocampal Prosthesis. Neural Computation, 2018, 30(9): 2472-2499.
[8] Li WXY, Chan RHM, Zhang W, et al. High-Performance and Scalable System Architecture for Real-Time Estimation of Generalized Laguerre-Volterra MIMO Model From Neural Population Spiking Activity. IEEE Journal on Emerging and Selected Topics in Circuits and Systems, 2011, 1(4): 489-501.