Journal of Zhejiang University-SCIENCE B 2026 27(11):1261-1271
www.jzus.zju.edu.cn; www.springer.com/journal/11585
E-mail: jzus_b@zju.edu.cn

Research Article
https://doi.org/10.1631/jzus.B2500462

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SWCNTs/PEDOT:PSS-modified microelectrode arrays reveal striatal–hippocampal neural encoding of movement initiation and place fields during goal-directed navigation

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Abstract: Goal-directed navigation necessitates coordinated interactions among multiple brain regions, with the hippocampus and striatum playing critical roles in spatial representation, movement-related information, and reward-related evaluation. The hippocampus, particularly the cornu ammonis 1 (CA1) region, is renowned for its role in spatial encoding via place cells. The striatum, a basal ganglia nucleus, can integrate cortical, thalamic, and limbic inputs to regulate motor planning, reward valuation, and behavioral flexibility. Despite extensive research, a key challenge remains: the lack of high-spatiotemporal-resolution, high-precision, and multi-channel electrodes that are structurally matched for reliable implantation across multiple brain regions. To address this, we developed two silicon-based microelectrode arrays (MEAs) anatomically tailored for dual-region neuronal electrophysiological recording of the striatum and CA1. By modifying the electrode sites with single-walled carbon nanotubes (SWCNTs)/poly(3,4-ethylenedioxythiophene):poly(4-styrenesulfonate) (PEDOT:PSS) nanocomposites, we significantly enhanced the electrical performance, reducing impedance and phase delay. Leveraging this platform, we demonstrated that neurons in the rat ventral striatum (vStr) contribute to movement initiation, transmitting information to CA1, while CA1 place cells dynamically encode new goal locations and relay spatial information to neurons in the dorsal striatum (dStr). This research provides a reliable platform for exploring the neural interactions between the striatum and hippocampus, establishing a foundation for future studies on neural circuits in complex behaviors.

Key words: Microelectrode array; Electrophysiology; Navigation; Single-walled carbon nanotube; Poly(3,4-ethylenedioxythiophene): poly(4-styrenesulfonate)

1 Introduction

Goal-directed navigation is a complex cognitive process that integrates spatial mapping (Dupret et al., 2010), motivational drive (Syed et al., 2016), reward evaluation (Sosa and Giocomo, 2021), and target selection (Penner and Mizumori, 2012; Tryon et al., 2017) into cohesive behavior. Successful navigation requires animals to dynamically encode environmental cues (place fields), initiate context-appropriate movements, and adjust strategies based on expected rewards. The hippocampal cornu ammonis 1 (CA1) region generates precise spatial representations and transmits contextual information via place cells, receiving inputs primarily from the entorhinal cortex, which encodes spatial and temporal information (Cholvin et al., 2021; Marks et al., 2021). The striatum receives environmental information from the cortex and engages in reciprocal communication with the thalamus, playing diverse roles in reward encoding, motor control, and habitual behavior (Cruz et al., 2023). Although the

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Received Aug. 3, 2025; Revision accepted Dec. 15, 2025;
Crosschecked July 31, 2026; Published online Sept. 23, 2026

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functions of both brain regions have been extensively studied, the temporal dynamics and coding principles governing striatal–hippocampal interactions during navigation remain unclear.

A critical barrier to dissecting these interactions lies in the limitations of conventional neural recording technologies. Traditional tungsten probes and other metal microelectrodes have been widely used in electrophysiological research owing mainly to their straightforward fabrication processes and well-established manufacturing protocols. However, their manufacturing process makes it challenging to scale up channel count and density. In contrast, silicon-based microelectrode arrays (MEAs) offer advantages including customizable shank geometries for anatomical targeting, multiple recording sites, and compatibility with integrated circuits (Zhang et al., 2016; Xu et al., 2024). However, bare electrodes typically exhibit suboptimal impedance (around 1 MΩ), which can lead to a high noise baseline and impair electrophysiological recordings (Cogan, 2008). Consequently, surface modification of electrode sites with conductive materials is essential to optimize the electrochemical performance and signal transduction efficiency of the electrodes. Metallic modifications, such as platinum nanoparticles and gold nanoparticles, can significantly reduce electrode site impedance (Zhang et al., 2016; Lee et al., 2018). In recent years, conductive polymers (CPs) have gained increasing attention for their excellent biocompatibility and good conductivity, making them increasingly used in bio-signal detection (Bettucci et al., 2022). Poly(3,4-ethylenedioxythiophene):poly(4-styrenesulfonate) (PEDOT:PSS) has gained popularity due to its excellent adhesion, biocompatibility, and stable conductivity (Kayser and Lipomi, 2019; Donahue et al., 2020; Huang et al., 2024). However, PEDOT:PSS has a much lower conductivity than metal materials. Single-walled carbon nanotubes (SWCNTs) have superior electrical and mechanical properties and nanoscale size (Rathinavel et al., 2021; Dewey et al., 2024; Park et al., 2024), which make them particularly advantageous for incorporation with PEDOT:PSS, leading to significant improvements in the composite's electrical performance.

To enable synchronous neural signal detection from both the striatum and CA1 neurons, in this study, we designed and fabricated two MEAs tailored to the structural characteristics of these brain regions. The electrode sites were modified with a nanocomposite material, SWCNTs/PEDOT:PSS, to improve both biocompatibility and electrical performance, facilitating high-quality electrophysiological recordings. By conducting goal-directed navigation behavior experiments on rats in a maze, we explored the encoding processes of movement initiation and spatial location perception in these two brain regions, as well as the interactions between their neural signals.

2 Results and discussion

2.1 Characterization of electrode morphology and electrical performance

The custom-made MEAs were designed according to the shape and size of the brain region and fabricated using the micro-electro-mechanical system (MEMS) process (Xu et al., 2024). The detailed fabrication process is described in supplementary materials and methods. The packaged MEAs are shown in Fig. S1. Two MEAs were implanted into the brains of Sprague-Dawley rats (Fig. 1a). The MEAs implanted into the striatum consisted of four shanks, with eight recording sites on each shank, covering both the dorsal striatum (dStr) and ventral striatum (vStr). The probe implanted into the hippocampus targeted the CA1 subregion, with a total of 16 recording sites. Fig. 1b presents top-view microscope images of the tips of the four-shank MEAs following modification with SWCNTs/PEDOT:PSS. Fig. S2 illustrates the details of electrode tips implanted in the striatum and hippocampal CA1 region. The strip-shaped ground electrode has a much larger area than the recording electrode. This design aims to achieve common grounding between the detection equipment and biological tissues, thereby improving the stability of signal recording. The recording electrodes are placed close to the electrode edge, which can reduce the distance to neurons in the direction of the electrode surface and thus enhance the efficiency of signal acquisition. Meanwhile, the small gap reserved between the recording electrodes and the electrode edge can improve the structural stability of the electrode during fabrication and use, preventing damage caused by physical etching, chemical corrosion, and implantation procedures. Scanning electron microscopy images at the nanoscale demonstrate that SWCNTs and PEDOT:PSS are thoroughly mixed and firmly adhere to the surface of the detection sites

(Figs. 1c and 1d). The conductive polymer PEDOT:PSS exhibited good biocompatibility along with conductivity, while SWCNTs showed superior electrical conductivity (Burnstine-Townley et al., 2020). We calculated the specific surface area of electrode sites modified with different materials based on atomic force microscopy (AFM) scans (Macht et al., 2011). The specific surface area of the sites increased to variable degrees after modification with PEDOT:PSS and SWCNTs/PEDOT:PSS, thereby confirming the improvement in their electrochemical performance (Fig. S3).

Fig. 2a shows the impedance characteristics of unmodified and modified electrodes in the frequency range of 10–1 000 000 Hz. At the typical frequency of 1000 Hz, the impedance of the bare electrode was (1666.9±70.4) kΩ (mean±standard error of the mean [SEM], n=10), while after modification with PEDOT:PSS, it was reduced to (121.2±13.1) kΩ. In comparison, the SWCNTs/PEDOT:PSS-modified electrode showed a significant reduction, with an impedance of (19.0±1.1) kΩ (Fig. 2b). Fig. 2c shows that electrodes modified with SWCNTs/PEDOT:PSS had a lower phase delay than bare electrodes. The electrical conductivity of PEDOT originates from the continuous π-conjugated system formed by its molecular conjugated structure, and PSS can enhance its conductive performance. In carbon nanotubes (CNTs), each carbon atom forms strong covalent bonds with three adjacent carbon atoms. The electrons that do not participate in hybridization can move freely within the conjugated system of the entire CNT, providing a structural basis for the electrical conductivity of the material. In addition, CNTs have an extremely high aspect ratio, which enables them to interlock with each other in the network structure formed by PEDOT:PSS, constructing an efficient three-dimensional (3D) conductive network. This network not only allows the material to form a denser microstructure (Fig. S4) but also further increases the specific surface area of the material, ultimately effectively improving the electrical conductivity and optimizing the conductive performance. The modified electrodes were subjected to ultrasonication (180 W) in deionized water and implanted into the rat brain, and their impedance curves were measured (Fig. 2d). The results showed that ultrasonication did not significantly alter the electrode impedance (Fig. 2e),

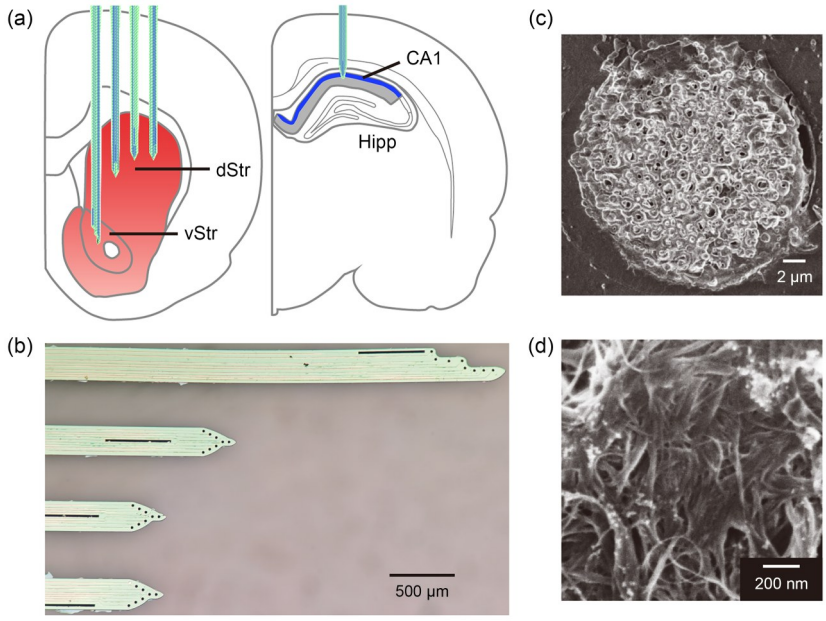

Fig. 1 Electrode implantation schematic diagram and SWCNTs/PEDOT:PSS-modified MEAs. (a) Schematic diagrams of two MEAs implanted in the striatum and hippocampal CA1, respectively. CA1: cornu ammonis 1; Hipp: hippocampus; dStr: dorsal striatum; vStr: ventral striatum. (b) Microscope photographs of four-shank MEAs after modification with SWCNTs/PEDOT:PSS. The black rectangle represents the modified ground electrode, the black circle denotes the modified recording electrode, and the white circle indicates the unmodified bare electrode site. (c, d) Scanning electron microscopy images of the SWCNTs/PEDOT:PSS-modified microelectrode surface at the micrometer scale (c) and at the nanometer scale (d). MEA: microelectrode array; SWCNT: single-walled carbon nanotube; PEDOT:PSS: poly(3,4-ethylenedioxythiophene):poly(4-styrenesulfonate).

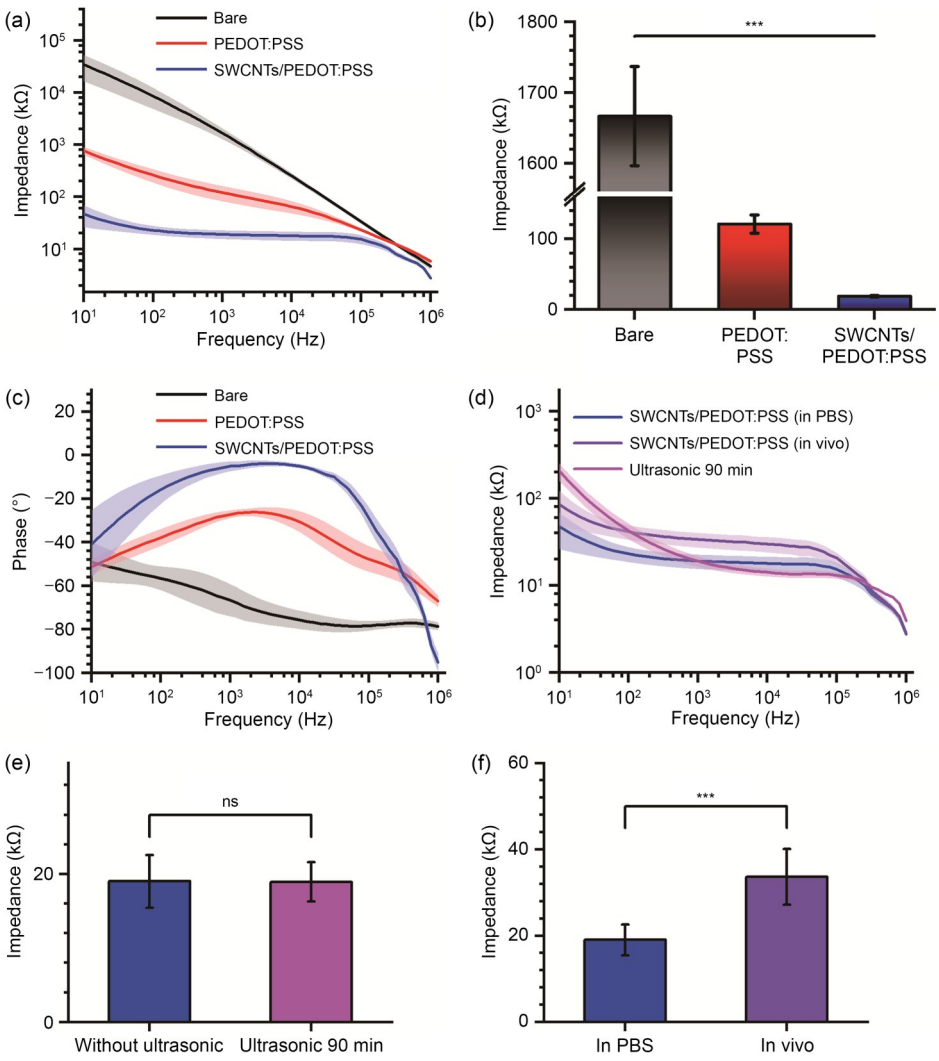

Fig. 2 Electrical characterization of MEAs. (a) Impedance properties of bare and modified electrodes at different frequencies. (b) Impedance characteristics of bare and modified electrodes at 1000 Hz. (c) Phase delay of bare and modified electrodes among different frequencies. (d) Impedance curves of SWCNTs/PEDOT:PSS-modified electrodes measured in PBS, after 90 min of ultrasonication, and in rat brains (in vivo). (e) Impedance comparison between SWCNTs/PEDOT:PSS-modified MEAs before and after 90 min of ultrasonication at 1000 Hz. (f) Impedance comparison between SWCNTs/PEDOT:PSS-modified MEAs tested in PBS (in vitro) and those in rat brains (in vivo) at 1000 Hz. Data are expressed as mean±SEM, n=10; *** P<0.001; ns: not significant. SEM: standard error of the mean; PBS: phosphate-buffered saline; MEA: microelectrode array; SWCNT: single-walled carbon nanotube; PEDOT:PSS: poly(3,4-ethylenedioxythiophene): poly(4-styrenesulfonate).

indicating excellent stability. However, after implantation into the rat brain, the impedance at 1000 Hz increased from (19.0±1.1) to (33.6±2.1) kΩ (Fig. 2f). This increase is likely attributable to the adhesion of brain tissue onto the electrode surface during and after implantation, as well as interactions between the electrode site and the brain tissue environment. Despite the slight rise in impedance, the electrodes remained capable of reliable electrophysiological signal detection. Additionally, we statistically analyzed the signal-to-noise ratio (SNR) of neural signals recorded by the electrodes implanted in the rat brain for 20 d. The electrodes maintained a stable noise baseline and a good SNR over time after implantation, demonstrating the stability of the modified electrodes (Fig. S5).

These findings highlight the exceptional electrical performance of the SWCNTs/PEDOT:PSS-modified MEAs. The lower electrode impedance corresponds to a reduced noise baseline (Cogan, 2008). To further verify the biocompatibility of the MEA electrodes,

MEAs, microwire arrays, and tungsten electrodes were implanted into rat brains. After explantation, immunofluorescence staining was performed for astrocytes, microglia, and neurons (Fig. S6). The fluorescence intensities of different cell types were quantified using ImageJ (Schindelin et al., 2015) (Fig. S7). The results show that the number of glial cells around the MEA implantation site was significantly lower than that around the other two types of electrodes, indicating better biocompatibility and reduced tissue damage. The use of the conductive polymer PEDOT:PSS enhances the electrode's biocompatibility (Ibanez et al., 2018; Zeglio et al., 2019), facilitating improved in situ detection of electrophysiological signals.

2.2 Behavioral experiments and the characteristics of electrophysiological recording signals

After each rat completed training in the maze, two MEAs were implanted into its brain (Fig. 3a). Fig. 3b illustrates the structure of the maze, which comprises a single path and two goal positions (labeled Goals 1 and 2). The rat starts from the red area and, upon reaching the goal position, may receive a piece of peanut as a reward there. The rat's movement path is restricted to a one-way direction (Fig. 3c). Each time the rat starts from the red area and returns to the red area is considered one trial. The experiment was divided into three stages. In Stage 1, rewards were given only at Goal 2. In Stage 2, rewards were given at both Goals 1 and 2. In Stage 3, food rewards were no longer given at Goal 1 (Fig. 3d). Each stage consisted of 20–30 trials, and transitions between stages occurred without any external cueing.

The rats' movement trajectories in the maze are shown in Fig. 4a. The transition from a stationary to a moving state is highlighted by the red line. Figs. 4b and 4c further illustrate the changes in the linearized position and acceleration over 20 s. After movement began, the rat's position and acceleration fluctuated significantly.

Fig. 4d shows that some neurons in CA1 and vStr channels 1–4 (Ch1–Ch4) exhibited denser firing in the seconds preceding movement, while Fig. 4e shows more tightly packed local field potentials (LFPs) during the same period. After movement began, the neuronal firing activity rapidly diminished, and the LFPs returned to slow oscillations. The control group (Ch7) showed firing activity (Fig. 4d) and LFPs (Fig. 4e) of a neuron in the CA1 region that was not related to movement events. Its firing activity was sparse over 20 s, and the LFPs exhibited slow oscillations throughout the period. Neurons in dStr (Ch5 and Ch6), on the other

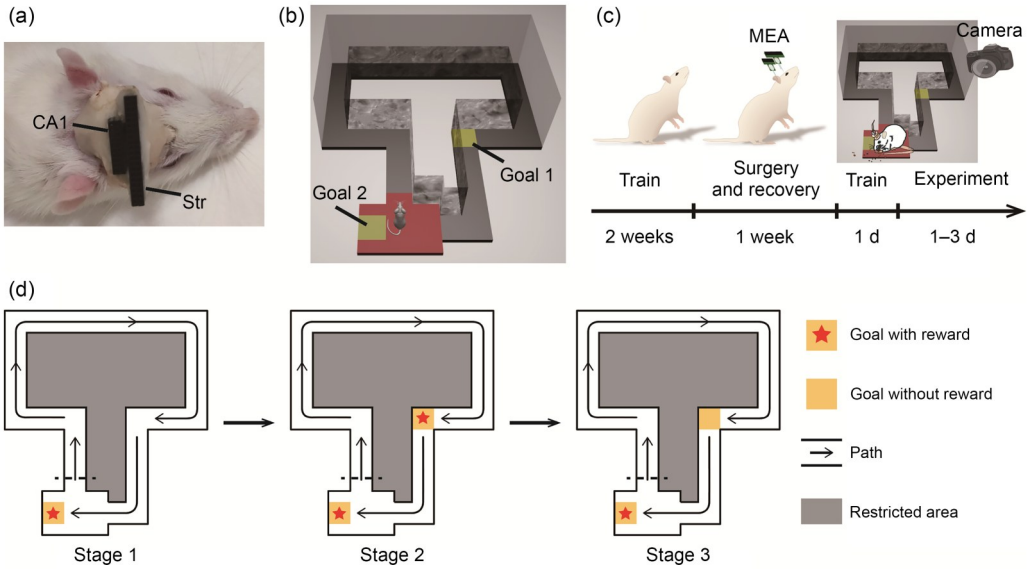

Fig. 3 Schematic diagrams of the experimental procedure and behavioral task. (a) Photographs depicting two microelectrode arrays (MEAs) implanted in the rat brain, with the corresponding brain regions labeled. CA1: cornu ammonis 1; Str: striatum. (b) A three-dimensional schematic diagram of the maze, with two goal positions marked. All walls are black and opaque, with some walls hidden and not depicted. The actual path is black. The colors are used for illustrative purposes. (c) Diagram illustrating the experimental procedure. (d) Three stages of the experimental paradigm. The rat's movement direction is represented by black lines and arrows. The black dashed line represents the starting line of a trial.

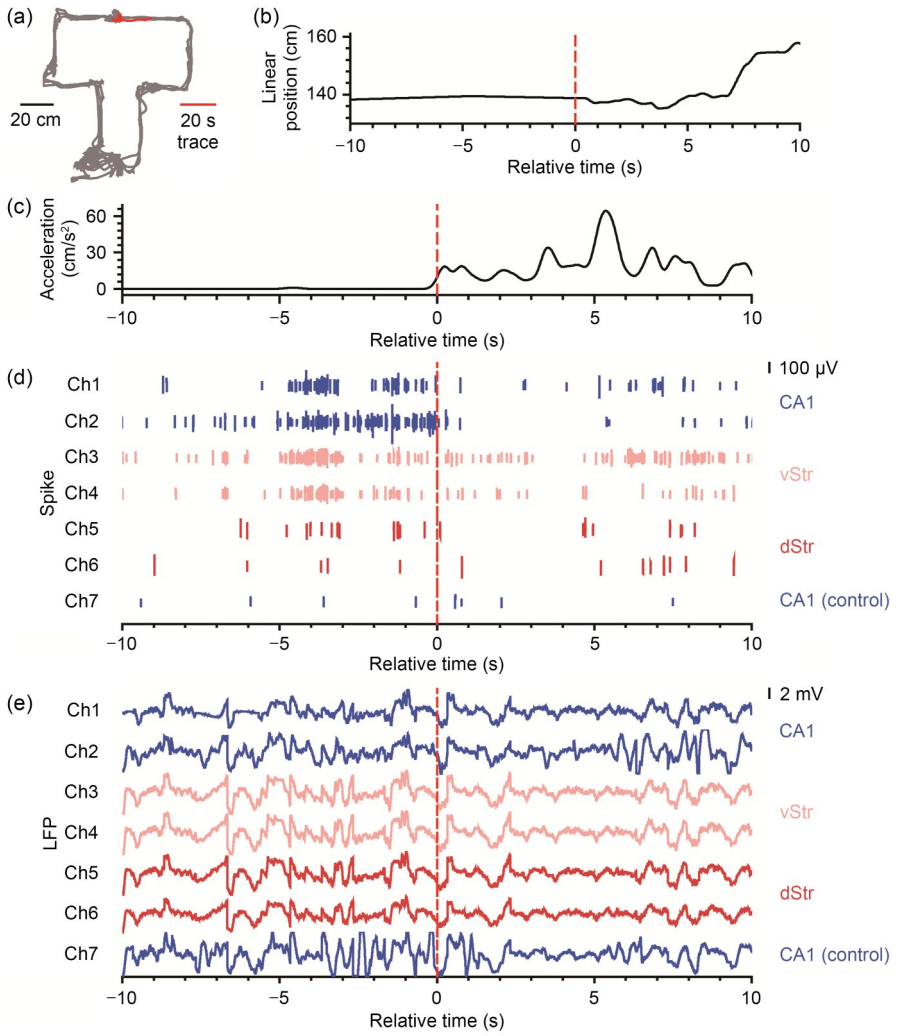

Fig. 4 Spatial trajectories and electrophysiological signals. (a) Movement trajectory of the rat (gray line), with the trajectories 20 s before and after the movement marked by the red line. (b) After converting two-dimensional trajectories into linearized trajectories (Fig. S8), the trajectories within 20 s in (a) are plotted to show the change in the linear position over time. (c) The variation in acceleration over 20 s. (d) The spike trains of neurons across different channels over 20 s. (e) LFP traces across different channels over 20 s. The red dashed line denotes the moment when the motion state changed. CA1: cornu ammonis 1; vStr: ventral striatum; dStr: dorsal striatum; LFP: local field potential; Ch1: channel 1.

hand, did not show this effect as prominently. This result suggests that CA1 and vStr may be involved in the process of movement initiation. Therefore, a quantitative analysis of the movement events was performed.

2.3 Role of vStr neurons in movement initiation and signal CA1 neurons

The movement onset time was identified using a threshold from the acceleration curve (supplementary materials and methods), and acceleration changes were recorded for 20 s before and after the movement began and aligned to the moment of movement onset. The average acceleration waveform is shown in Fig. 5a.

Peri-event time histograms (PETHs) were constructed to depict neuronal firing activities over 20 s period (Figs. 5b–5d). Neurons modulated by movement initiation (supplementary materials and methods) are shown in Figs. 5b (CA1) and 5c (vStr). In the 5 s preceding movement onset, the average firing rate significantly increased across different movement initiation events and rapidly declined to baseline levels after movement began. A total of 10 neurons in CA1 and 12 neurons in vStr were identified as being modulated by movement initiation. In contrast, no neurons in the dStr were found to be modulated by movement initiation (from three rats). Their firing rates exhibited

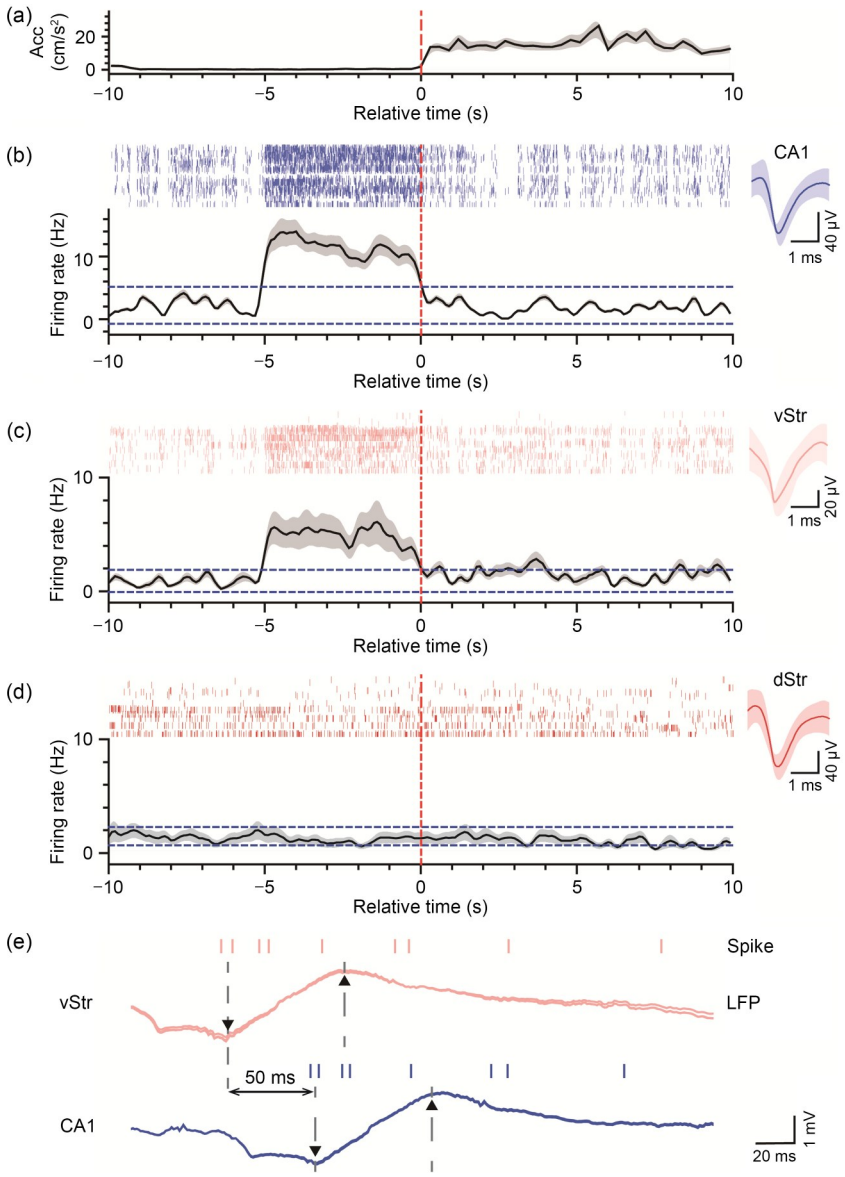

Fig. 5 Firing activities and information transmission before and after movement in CA1 and striatum neurons. (a) The average acceleration curve within 20 s before and after movement onset (*n*=58). The red dashed line denotes the moment of movement onset. (b–d) The firing activities of three neurons from CA1 (b), vStr (c), and dStr (d) over 20 s. The upper panel shows the spike raster for different movement events. Each row represents a single movement event. The lower panel shows the mean firing rate curve. The two blue dashed lines denote the 99% confidence interval of the baseline. A significant difference in the mean firing rate is indicated when the curve exceeds the blue dashed line range (*P*<0.01). The right panel shows the spike waveform. (e) LFP traces from vStr (*n*=3) and CA1 (*n*=3) with peaks and troughs marked by triangles. The displayed LFPs are within the 5 s preceding movement onset. The spike raster is shown above the LFPs and the delay in information transmission between the two brain regions is marked. Data are presented as mean±SEM in (a–d). CA1: cornu ammonis 1; Acc: acceleration; LFP: local field potential; vStr: ventral striatum; dStr: dorsal striatum; SEM: standard error of the mean.

no significant changes over 20 s (Fig. 5d). Fig. 5e shows that the LFPs of vStr neurons preceded those of CA1 neurons by 50 ms. Combined with spike activities, it can be inferred that movement initiation information flows from the vStr to CA1.

The involvement of vStr in movement initiation is consistent with previous findings (Ko and Wanat, 2016; Suzuki et al., 2021; Levcik et al., 2023). Few studies have reported a direct pathway from vStr to CA1. The information transfer between these regions

is likely mediated through indirect pathways, such as projections from the vStr into the thalamus, ventral tegmental area, or prefrontal cortex, which then connect to the hippocampal CA1 region (Bueno-Junior and Leite, 2018; Yang et al., 2018; Douma and de Kloet, 2020).

2.4 Place fields in CA1 and place-related firing in dStr

The calculation of the position firing rate map is detailed in supplementary materials and methods. Note that both the traces and spikes were velocity-filtered to avoid interference from periods of immobility or stopping to consume food rewards (Duvelle et al., 2019). In the hippocampal brain region, neurons that fire collectively at a specific position or several specific positions are referred to as place cells, and the areas where they fire are called place fields. Fig. 6a shows a neuron with stable place fields across three stages, while Fig. 6b shows Cell 2, which exhibits a place field only in Stage 2, and Cell 3, which displays the neuron place firing rate heatmap of different stages. The spatial information content (SIC) represents the amount of spatial information transmitted by each spike, and its calculation method is detailed in supplementary materials and methods. In CA1, the SICs (mean±standard deviation [SD], n=9, from three rats) of place cells across Stages 1–3 were (1.3±1.2), (3.1±1.1), and (2.3±1.6) bits/spike, respectively; in dStr, the SICs (mean±SD, n=5, from three rats) of position-related cells were (0.4±0.2), (0.5±0.2), and (0.4±0.1) bits/spike, respectively (Fig. S9).

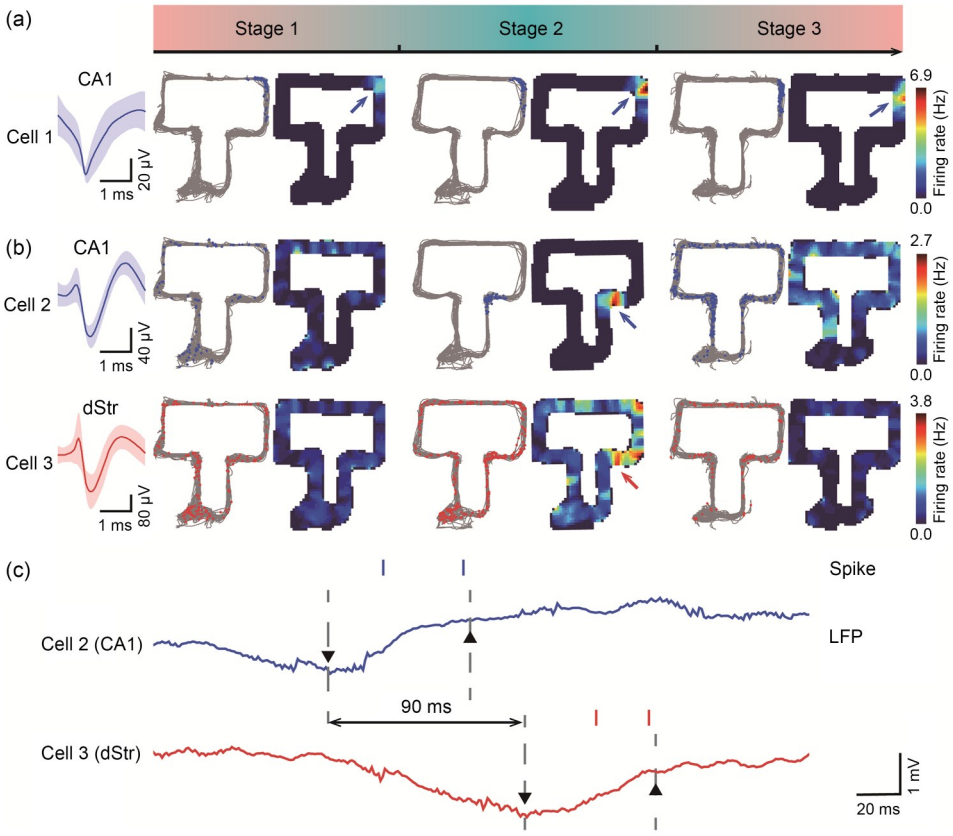

Fig. 6 Spatial firing characteristics of CA1 and dStr neurons across different stages. (a) A hippocampal cell that maintained a stable place field across all three stages. Left: spike waveform. Middle: trajectories (gray line) with spike positions (blue dots) and place firing rate heatmaps for each of the three stages. Right: the color bar of the heatmap. The position of the place field is indicated by a blue arrow. (b) A hippocampal-striatal cell pair. Cell 2 in the hippocampus exhibits a place field (located near Goal 1) during Stage 2, while Cell 3 in dStr shows place-related firing at the corresponding position. The spike positions in Cell 3 are plotted as red dots. The place-related firing position is indicated by a red arrow. (c) The potential information transfer between Cells 2 and 3. LFP traces from CA1 and dStr are shown, with peaks and troughs marked by triangles. The LFPs shown correspond to the period of the place field during Stage 2. The spike raster is displayed above the LFPs. LFP: local field potential; CA1: cornu ammonis 1; dStr: dorsal striatum.

From Stage 1 to Stage 3, the SIC of CA1 place cells first increased and then decreased, which corresponds to the appearance and disappearance of Goal 1. This suggests that neurons in the CA1 region of the rat brain are capable of dynamically learning the changing goal position information in the external environment. Because the SIC of place-related cells in the dStr showed no significant changes among the three stages and the inferred direction of information transferred from CA1 to dStr in Fig. 6c, it is speculated that the spatial information in CA1 aids dStr neurons in encoding other types of information, including rewards and habitual behaviors (Guida et al., 2022; Bech et al., 2023).

3 Conclusions

The designed MEAs are well-suited for the striatal and hippocampal regions. After fabrication using MEMS technology, the electrodes exhibited high spatiotemporal resolution. Coating the electrode sites with SWCNTs/PEDOT:PSS nanocomposites improved their electrical properties, significantly reducing electrode impedance and phase delay, which in turn decreased electrophysiological recording noise, thereby improving the SNR.

Our preliminary data from a goal-directed navigation task in three rats suggest that neurons in the vStr may be involved in movement initiation and could transmit information to CA1 via indirect pathways. Furthermore, the observed activity of CA1 place cells is consistent with a crucial role in learning new goal positions and may facilitate the transmission of spatial information to the dStr. These results provide initial evidence for a potential cross-circuit communication mechanism, which warrants validation in larger-scale studies.

Through a goal-directed navigation task in rats, neurons in the vStr are involved in the initiation of movement and may transmit information to CA1 neurons via indirect pathways. Additionally, place cells in CA1 play a crucial role in learning and representing new goal positions, transmitting spatial information to neurons in the dStr.

MEAs modified with nanocomposites provide an excellent platform for studying neural activity across multiple brain regions. This research lays a foundation for future studies on the functional differences and connections between the hippocampus and striatum. We aim to further explore the information transmission pathways between the hippocampus and striatum, as well as the changes in the encoding of information throughout this process.

Materials and methods

Detailed methods are provided in the electronic supplementary materials of this paper.

Data availability statement

The data that support the findings of this study are available from the corresponding authors upon reasonable request.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (Nos. 62121003, T2293730, T2293731, 62333020, 62171434, and 62471291), the National Key Research and Development Program of China (Nos. 2022YFC2402501 and 2022YFB3205602), the Major Program of Scientific and Technical Innovation 2030 (No. 2021ZD02016030), the Joint Foundation Program of the Chinese Academy of Sciences (No. 8091A170201), and the Scientific Instrument Developing Project of the Chinese Academy of Sciences (No. PTYQ2024BJ0009).

Author contributions

Jin SHAN and Wei XU designed the experiments, fabricated the devices, analyzed the data, and drafted the manuscript. Jinping LUO and Yaoyao LIU contributed to the study concept. Ming LI and Luyi JING assisted with the data analysis. Yu WANG, Shiya LV, and Zhaojie XU assisted with the device fabrication. Juntao LIU, Yiming DUAN, and Qianli JIA assisted with the experiments. Yilin SONG, Mixia WANG, and Xinxia CAI guided the theoretical analysis, reviewed the manuscript, and checked it for final submission. All authors have read and approved the final manuscript, and therefore, have full access to all the data in the study and take responsibility for the integrity and security of the data.

Compliance with ethics guidelines

Jin SHAN, Wei XU, Jinping LUO, Yaoyao LIU, Ming LI, Luyi JING, Yu WANG, Shiya LV, Zhaojie XU, Juntao LIU, Yiming DUAN, Qianli JIA, Yilin SONG, Mixia WANG, and Xinxia CAI declare that they have no conflicts of interest.

All institutional and national guidelines for the care and use of laboratory animals were carried out with the permission of the Beijing Association on Laboratory Animal Care and approved by the Institutional Animal Care and Use Committee at the Aerospace Information Research Institute, Chinese Academy of Sciences (No. AIRCAS-202302-01).

Declaration on the use of generative AI tools

No generative AI tools were used in the preparation of this manuscript.

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Supplementary information

Figs. S1–S9; Materials and methods