scientific reports

OPEN



Biomechanics characterization of an implantable ultrathin intracortical electrode through finite element method

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Neural electrodes are widely used in brain-computer interfaces and neuroprosthesis for the treatment of various neurological disorders. However, as components that come into direct contact with neural tissue, implanted neural electrodes could cause mechanical damage during surgical insertions or while inside the brain. Thus, accurately and timely assessing this damage was vital for chronic implantation, which posed a significant challenge. This study aimed to evaluate the biomechanical effects and clinical application risks of a polyimide-based ultrathin flexible intracortical microelectrode through the finite element method (FEM). It analyzed the electrode-brain biomechanical effects during the electrode's insertion process and under steady-state acceleration with the electrode inside the brain. Furthermore, the study examined the impact of factors including implantation depth (ranging from 5 to 5000 μm), cortical thickness (0.5 mm, 2.5 mm, and 4.5 mm), step displacement (from 1 to 5 μm) during insertion, and acceleration direction (vertical and horizontal) on the electrode's biomechanical effects. The primary findings showed that the 98th percentile Von Mises Strain (ϵ_{qg}) and Von Mises Stress (σ_{og}) in the region of interest (ROI) decreased dual-exponentially with increasing implantation depth and increased linearly with larger step displacements. Compared to the Von Mises strain threshold of 14.65%, as proposed by Sahoo et al., indicating a 50% risk of diffuse axonal injury (DAI), it was recommended to limit the initial step displacement during insertion to 1 μ m, increasing to 5 μ m at deeper locations (over 500 µm) to balance safety and efficiency. Additionally, it was found that cortical thickness had a negligible impact during insertion and while experiencing steady-state acceleration in vivo, with the three fitted curves almost coinciding when cortical thicknesses were 0.5 mm, 2.5 mm, and 4.5 mm. The flexible electrode exhibited excellent mechanical performance under steady-state acceleration in vivo, with ϵ_{98} being less than 0.3% and σ_{98} being less than 50 Pa, although it was more sensitive to horizontal acceleration. Thus, it could be concluded that during long-duration accelerations from transportation modes such as elevators and high-speed trains, the electrode's mechanical effects on brain tissue could be neglected, demonstrating long-term mechanical stability. This research was significant for guiding surgical insertion and clinical applications of flexible electrodes.

Keywords Flexible microelectrode, Biomechanics, Finite element method, Electrode insertion surgery

Neural electrodes have extensive applications in fields including neural signal monitoring, brain-machine interfaces(BMI), and the treatment of neurodegenerative disease^{1,2}. Serving as interfaces between biological tissues and external devices, neural electrodes are crucial components for neural recording and stimulation.

Implantable intracortical neural electrodes are invasive neural electrodes positioned within or even beneath the cerebral cortex^{3,4}. Compared to non-invasive EEG scalp electrodes and epi-dural Electrocorticography (ECoG) cortical electrodes, intracortical electrodes offer advantages both at neural recordings with high spatial resolution, and at neural stimulation with enhanced specificity and selectivity^{4,5}. However, due to their direct contact with biological tissue, implanted neural electrodes still face some challenges during long-term

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implantation, including glial cell response, material degradation, and mechanical tissue damage^{4–6}. Therefore, efforts and optimizations are necessary in the biocompatibility and mechanical compatibility to mitigate clinical risks associated with implantable neural electrodes.

Using biocompatible flexible microelectrodes is one of the most effective strategies for achieving long-term implantation^{7,8}. Thanks to flexible materials^{9,10} and ultra-thin, ultra-fine designs¹¹, flexible electrodes possess significant advantages, including an extremely low elastic modulus and size compatibility with neurons, resulting in higher compliance and better biomechanical matching^{10,12–14}. Additionally, flexible microelectrodes facilitate higher integration and multi-channel capabilities, enabling the simultaneous recording of electrical potentials from thousands of target neurons¹². The substrate materials used in flexible electrodes also often exhibit good biocompatibility, such as polyimide(PI), parylene-C, and hydrogels^{11,12,14,15}. These advantages have led to the widespread application of flexible electrodes in implanted neural electrodes.

Although flexible electrodes could demonstrate excellent performance in long-term implantation, the biomechanical issues cannot be overlooked⁹. The neural tissue is with the elasticity modulus on the order of several kPa, while the thin flexible polymer electrodes of at least tens of MPa^{16,17}. Consequently, flexible neural electrodes could cause mechanical damage to brain tissue. Upon insertion into brain tissue, electrodes can create regions of high stress and strain around them, leading to neuronal deformation through traction and causing mechanical injury^{18,19}. In long-term implantation, inertial forces during acceleration and deceleration indirectly act on brain tissue, resulting in relative displacement between the electrode and brain tissue, potentially causing brain damage²⁰. In addition, the magnitude, direction, and property of applied forces can significantly influence the extent of brain tissue damage¹⁶. Besides, it is worth noting that mechanical damage to brain tissue could lead to diffuse axonal injury (DAI), a common pathological characteristic of mild traumatic brain injury (mTBI) that can result in delayed responses and memory impairments^{19,21}. Therefore, biomechanical analysis of electrodes and assessment of brain mechanical injury are crucial for determining the clinical feasibility of electrodes.

The biomechanical analysis methods for implanted electrodes include both biological and non-biological approaches. Biological methods involve pathological analysis of neural tissue. Histological and cytological analyses of neural tissue slices taken after electrode implantation can assess potential damage to neuronal morphology and function, providing insight into the long-term mechanical effects of electrode implantation on brain tissue²². During the insertion process, high-speed cameras can capture images, supplemented by computer modeling and image processing, to confirm the extent of deformation on the surface of the brain tissue and evaluate its mechanical response²³. But these methods do not yield specific, accurate, real-time stress and strain values for the brain tissue. In contrast, non-biological methods—finite element analysis (FEA), can provide precise numerical calculations of the overall mechanical response of brain tissue^{24,25}. Many studies have utilized FEM to investigate the biomechanical effects of electrodes. For example, Sui et al.²⁶ examined the appropriate structural dimensions and damage mechanisms of silicon microelectrodes under the interaction with tissue mechanics. O'Sullivan et al.²⁷ assessed the effects of various simple geometries, insertion speeds, and surface frictions on the strain of brain tissue during electrode implantation using FEA. Abed et al.²⁸ evaluated the impact of micro-movements of implanted electrodes, thickness of the implant body, and material properties on brain tissue strain.

Numerical analyses can effectively help shorten experimental cycles. However, there are short of numerical analyses based on flexible thin-film electrodes. PI-based thin-film electrodes have widely been implanted intracortically in human applications^{7,17,29,30} and other applications such as epi-retinal prostheses^{31,32}. To this end, in this present study, we characterized the biomechanics of PI-based thin-film electrodes resembling commercial designs. Further, we quantified the biomechanical effects encompassing the insertion process of ultra-thin flexible microelectrodes and steady-state acceleration on the electrodes inside the brain. The findings could shed lights on clinical electrode design and guiding insertion procedures.

Model and method

In 3-D space, the stress-strain constitutive equation³³ is given by:

$$\sigma - \sigma^{0} = D\left(\epsilon - \epsilon^{0}\right) \tag{1}$$

where σ is the stress vector composed of normal stresses and tangential stresses, ϵ is the strain vector composed of normal strains and tangential strains, and D is the isotropic constitutive matrix determined by elastic modulus and Poisson's ratio. σ^0 is the initial stress vector, and ϵ^0 is the initial strain vector.

Von Mises Strain and Von Mises Stress convert the spatial vectors into scalars, facilitating the evaluation and determination of the material's mechanical response. This simplification significantly streamlines the analysis process. Figure 1. illustrates the flowchart of the finite element analysis (FEA) process used in this study. In the FEA software Ansys Workbench 2022R2 (Ansys, Inc., Canonsburg, PA, USA), the analysis is carried out by first establishing the geometry model, performing mesh generation, assigning the material properties, and applying the appropriate boundary conditions and loads for the problem at hand. From this, Von Mises Strain and Von Mises Stress can be directly obtained at each node and further post-processed. It is important to emphasize that mesh independence testing is essential to ensure the accuracy of the solution. These steps are detailed in "Geometry model", "Mesh", "Material", "Load and boundary conditions" and "Brain injury assessment method" and Supplementary Methods.

Electrode design

This paper presents an implantable ultra-thin flexible microelectrode array mimicking the transverse structure with interconnecting traces sandwiched and a ring micro hole aiding insertion at the frontend.



Fig. 1. Flow chart of FEM.

Specifically, the electrode array comprises 132 metal interconnecting traces, each 100 μ m wide, 1.5 μ m thick, and 40 mm long, in correspondence with 128 recording electrode sites (diameter 10 μ m) and 4 stimulation sites (diameter 40 μ m). The electrodes feature a sandwich structure, with PI as the base and upper encapsulation layers, gold as the interconnecting conductor, and Chromium beneath the gold for enhanced gold adhesion. The gold traces are 350 nm wide and evenly spaced to connect the electrode sites with external electronic equipment. The electrode frontends are designed with a ring structure to facilitate implantation by surgical robots.

Unlike traditional rigid metal electrodes that can be directly inserted, flexible microelectrodes require specialized insertion methods to prevent damage to the electrodes and surrounding tissue due to their bendability^{18,34,35}. For instance, the Neuralink company employed robotic systems for rapid electrode insertion⁷. Zhao et al.³⁶ used PEG (polyethylene glycol) to encapsulate fine metal wires for guidance. Arafat et al.³⁷ utilized rotation and guiding techniques for insertion. During the insertion procedure, these methods aimed to enhance the strength of the electrodes or employ tensioning techniques to prevent bending and fracturing of the flexible structures. Similar to Neuralink electrode insertion⁷, we intend to utilize a needle tip to pull on a traction ring located at the frontend of the electrode (Fig. 1.), converting direct pressure into a pulling force for insertion. The surgical process involves the robot gradually pulling the electrode forward, advancing by a few micrometers at a time while making adjustments in milliseconds, ultimately achieving precise implantation in the targeted neural area.

Figure 2. illustrates the layout of the gold interconnecting traces and electrode sites for a single electrode bundle, which includes 6 recording channels and 2 stimulation channels.

Geometry model

Using Ansys DesignModeler, a geometric model of the electrode-brain tissue interface was created, consisting of a flexible electrode and brain tissue. To enhance computational efficiency, the model simplified the electrode by disregarding the mechanical effects of small electrode sites. It represented the 132 gold interconnecting traces (each 0.35 μ m wide) and the surrounding PI as a thin, 94 μ m-wide Au-PI composite layer, forming a sandwich structure with a ring-shaped traction at the frontend (Fig. S1).

The brain tissue model consisted of gray matter (which contains neuronal cell bodies) and white matter (which contains axonal fibers), each exhibiting distinct mechanical properties¹⁶. The pia matter and dura matter were excluded from the model, as electrode implantation occurred after the pia mater was exposed (Fig. S2). Cortical thickness in the human brain varies significantly, both within individuals across different regions and between individuals, ranging from 0.5 mm to 4.5 mm, with an average thickness of 2.53 mm³⁸. Therefore, three cortical thicknesses (0.5 mm, 2.5 mm, and 4.5 mm) were considered to assess the biomechanical effects on electrode performance (Fig. S2a). A region of interest (ROI) of $200 \times 250 \times 50 \ \mu\text{m}^2$ was defined around the electrode tip, with a shallower ROI for implantation depths less than 200 μ m (Fig. S2b,c), as the influence zone of microelectrodes is limited to tens to hundreds of micrometers²⁴.



Fig. 2. Simplified diagram of metal interconnecting traces for single electrode.

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The study also examined the effects of varying electrode insertion depths, applying a dense depth gradient at the gray-white matter interface and the brain surface, where mechanical properties change significantly. The steady-state acceleration analysis focused on implantation depths greater than 200 μ m, with model parameters outlined in Table S1.

Mesh

The model employed swept meshing for the electrode shaft and free tetrahedral meshing for irregular components (e.g., traction ring). Brain tissue meshing used graded element sizes (2 μ m near the electrode, coarser with distance), validated via convergence tests to ensure < 5% relative error in strain results (Fig. S7). Total elements ranged from 400,000 to 1.3 million, depending on implantation depth, with second-order elements ensuring accuracy. Mesh details were shown in Figs. S3, S4.

Material

Electrode materials included PI (E = 2500 MPa)³⁹, Chromium (E = 140 GPa)⁴⁰, and a hybrid Au-PI layer (E = 31.78 GPa)⁴¹ with weighted density and Poisson's ratio (Table S2). Brain tissue can be considered as a compressible viscoelastic solid, with its shear modulus following the Maxwell viscoelastic model (2).

$$G(t) = G_{\infty} + (G_0 - G_{\infty}) e^{-\beta t}$$
(2)

where G(t) represents the time-dependent shear modulus, G_{∞} represents Long-term shear modulus, G_0 represents Short-term shear modulus, and β is the Decay constant.

The mechanical properties of gray and white matter are outlined in Table S3^{42,43}. Specifically, gray matter has $G_0 = 34$ kPa, $G_{\infty} = 6.4$ kPa, while white matter has $G_0 = 41$ kPa, $G_{\infty} = 7.8$ kPa. Both types of tissue have a bulk modulus of 2.19 GPa and a density of 1040 kg/m².

Load and boundary conditions

Accurate FEA relies heavily on proper boundary conditions. This study examines the biomechanical processes involved in the insertion of flexible electrodes and their steady-state acceleration post-implantation. Stepwise insertion simulated robotic traction via vertical displacements ($1-5 \mu m$ per step) on the electrode ring, with the distant brain tissue fixed (Fig. S5a). For steady-state acceleration, vertical (-0.926 m/s^2) and horizontal (1.135 m/s^2) accelerations were applied to the entire system (Fig. S5b), derived from elevator and high-speed train data (Fig. S6). The electrode-brain interface used bonded contact, with skull-fixed electrode tops and constrained distant brain surfaces. More load and boundary conditions settings were shown in Table S4.

Brain injury assessment method

The insertion of flexible electrodes and their subsequent relative displacement with brain tissue can stretch neurons and induce deformation, potentially leading to mechanical brain injury⁶. Neural tissue subjected to the mechanical forces exerted by electrodes may experience DAI that could result in delayed responses and memory impairments. Long, thin axonal structures are particularly vulnerable to stretch injuries caused by the rapid deformation of the brain^{19,21}. Furthermore, the heterogeneity in stiffness at the neural electrode-tissue interface can lead to redistribution and localized amplification of axonal strain⁴⁴. Therefore, assessing brain injuries induced by flexible electrodes is of paramount importance.

To evaluate the potential mechanical brain injuries caused by these electrodes, this study adopts the Von Mises strain threshold of 14.65%, as proposed by Sahoo et al.⁴⁵, which corresponds to a 50% risk of DAI occurrence. Additionally, given that the impact of the electrodes is localized around the brain tissue, the Von Mises Strain value at the 98th percentile of the region of interest (ε_{98}) is selected as the assessment parameter. If ε_{98} exceeds the threshold, the electrodes are considered to have caused brain injury. Conversely, if ε_{98} falls below the threshold, the biomechanical effects of the electrodes are deemed to be within a safe range.

Results

Electrode insertion process

Figure 3. summarizes the mechanical effects of electrode implantation depth and cortical thickness on the brain tissue ROI during the stepwise insertion process of flexible electrodes, with a step size of 1 μ m. ε_{98} exhibits a double-exponential decay with increasing electrode implantation depth (Fig. 3a). ε_{98} is greatest when the electrode is first implanted into the gray matter and then rapidly diminishes with further increases in implantation depth. At an implantation depth of approximately 500 μ m, ε_{98} approaches convergence, with a convergent value around 2.2%. Furthermore, even during the initial phase of insertion when mechanical effects are at their peak, ε_{98} remains below the brain injury threshold of 14.65%, staying within a safe range.

The effect of cortical thickness on the strain response of the ROI during electrode insertion is not significant. The fitting curves for different cortical thicknesses in Fig. 3a are almost superimposed. Despite significant variations in the mechanical properties between the gray matter and the white matter, there is no noticeable change in ε_{98} when the electrode is implanted near the interface.

Figure 3b shows the Von Mises Stress response of the ROI(σ_{98}). In the initial phase of electrode insertion, consistent with the strain response, σ_{98} exhibits a double-exponential decay with increasing electrode implantation depth. However, near the interface between the gray matter and white matter, there is a linear increase in σ_{98} , as reflected in the three fitting curves in Fig. 3b. As the electrode implantation depth increases and moves away from the cortical-white matter interface, the three stress curves nearly overlap, and the ROI stress converges again.

Figure S8 shows the Von Mises Strain distribution maps of the ROI at different electrode implantation depths during the insertion process, with a step size of 5 μ m and a cortical thickness of 2.5 mm. At the initial stage of electrode insertion, when the electrode tip depth is 20 μ m (Fig. S8a), Von Mises Strain in the brain tissue around the electrode tip exceeds the brain damage threshold of 14.65%, with some areas even reaching twice the threshold (as indicated in the map). This suggests that at the initial insertion stage, a 5 μ m step size is likely to cause strain damage to the surrounding brain tissue. As the electrode implantation depth increases to 100 μ m



Fig. 3. Mechanical response of electrode step insertion (UY = $-1 \mu m$): (a) Variation of ε_{98} with electrode implantable depth; (b) Variation of σ_{98} with electrode implantable depth.



Fig. 4. Mechanical response of ROI during electrode insertion at different step displacements (cortical thickness of 2.5 mm): (**a**) Variation of ε_{98} with electrode implantable depth; (**b**) Variation of σ_{98} with electrode implantable depth.

beneath the gray matter (Fig. S8b), although some brain tissue around the electrode still shows Von Mises Strain near the damage threshold (indicated areas), the regions above the threshold are greatly reduced compared to Fig. S8a, and the affected area of the brain tissue decreases significantly.

When the electrode implantation depth exceeds 500 μ m, ϵ_{98} and σ_{98} approach convergence(Fig. 3). This is reflected in the Von Mises Strain maps of the ROI (Fig. S8c,d), where at implantation depths of 500 μ m and 2000 μ m, the brain tissue shows minimal strain damage. The distribution of Von Mises Strain in the ROI in Fig. S8c,d is quite similar, and the extent of the brain tissue affected is comparable.

Figure S9 shows the strain and stress distribution in the ROI during continued stepwise insertion of the electrode near the cortical-white matter interface. The cortical thickness is 2.5 mm, the electrode implantation depth is 2505 μ m, and the step size is 5 μ m. It can be observed that when the electrode is implanted near the gray-white matter interface, the Von Mises Strain does not exhibit a sudden, noticeable change but rather a continuous distribution (Fig. S9a). In contrast, there is a distinct boundary in the Von Mises Stress near the interface, with the stress in the white matter being significantly higher than that in the gray matter (Fig. S8b).

Figure 4. presents the analysis of strain and stress values in the ROI under different step displacements, with a cortical thickness of 2.5 mm. As the electrode step displacement varies, the trends in ε_{98} and σ_{98} remain consistent, though their magnitudes change. When the electrode implantation depth is constant, there is a positive correlation between the mechanical response values of the ROI and the step displacement size; larger step displacements result in greater strain and stress in the ROI. Additionally, with a step displacement of 1 µm,



Fig. 5. Mechanical response of ROI under vertical acceleration: (a) Variation of ε_{98} with electrode implantable depth; (b) Variation of σ_{95} with electrode implantable depth.





 ϵ_{98} remains below the damage threshold throughout the insertion process. However, as the step displacement increases, ϵ_{98} exceeds the threshold in the initial stages of insertion, indicating a higher risk of significant DAI, although ϵ_{98} eventually decreases below the threshold when the implantation depth reaches approximately 500 µm.

Figure S10 shows the Von Mises Strain distribution map of ROI when the electrode implantation depth is 20 μ m and the cortical thickness is 2.5 mm, under different electrode insertion step displacements. The results indicate that as the insertion step displacement increases, both the intensity and the extent of the mechanical impact of the electrode on brain tissue also increase. When the insertion step displacement is between 1 and 2 μ m, the strain distribution in the brain tissue is confined within a few micrometers around the electrode. As the insertion step displacement increases, the strain in the brain tissue exceeds the safety threshold, as shown in Fig. S10 by regions colored from green to red. These high-strain areas are concentrated near the narrow ends of the electrode and rapidly decay with increasing distance from the electrode, remaining within a few tens of micrometers around the electrode.

Steady-state acceleration after implantation

Figures 5 and 6 summarize the steady-state results under steady-state acceleration after electrode insertion and illustrate the fitted curves of ε_{98} and σ_{98} in relation to electrode implantation depth and cortical thickness. Figure 5 presents the stress and strain results for the electrode-brain tissue system subjected to vertical steady-

state acceleration, which is consistent with the acceleration of the Shanghai Tower's elevator. The results indicate a piecewise linear relationship between ε_{98} and the electrode implantation depth. Overall, ε_{98} increases linearly with the electrode implantation depth (Fig. 5a). However, when the electrode tip transitions from the cortical to the white matter region, ε_{98} actually decreases. Despite the increase in strain with implantation depth, the strain induced in brain tissue by vertical elevator acceleration is extremely minimal, less than 0.04%, and can be considered negligible.

Figure 5b shows that under vertical acceleration, σ_{98} increases linearly with electrode implantation depth, without any local decreases due to strain. Consistent with the minimal strain response, the stress values in the ROI are also only a few Pascals.

Additionally, Fig. 5 indicates that cortical thickness has a negligible impact on the mechanical response of brain tissue under vertical acceleration. The stress fitting curves for different cortical thicknesses almost completely overlap (Fig. 5b). The strain fitting curves also show differences only at the cortical-white matter interface, with the curves for the shallow cortical and deep white-matter electrode implantation scenarios nearly overlapping.

Figure 6 presents the numerical results for the electrode-brain tissue system subjected to horizontal steadystate acceleration, with the acceleration level equivalent to that of high-speed rail. Compared to vertical acceleration, the mechanical response of the ROI to horizontal acceleration shows no significant variation with respect to electrode implantation depth. At shallower implantation depths, the brain tissue stress and strain induced by horizontal acceleration are relatively high. As the implantation depth increases, ε_{98} and σ_{98} rapidly decrease, then slowly rise and fluctuate. Additionally, ε_{98} and σ_{98} under horizontal acceleration are quite small, with strain less than 0.3% and stress below 50 Pa. Similarly, the impact of cortical thickness is not significant.

Figure S11 illustrates the strain distribution map of the ROI under steady-state acceleration. Here, the electrode implantation depth is 500 μ m, and the cortical thickness is 2.5 mm. It is evident that the electrode implantation system is more sensitive to horizontal acceleration, with the mechanical response induced by horizontal acceleration being 1–2 orders of magnitude greater than that caused by vertical acceleration. However, despite the greater mechanical effect of horizontal acceleration, the maximum strain values remain very small and are unlikely to have any significant impact on brain tissue. Spatially, the effects of vertical acceleration are primarily concentrated within the inner circle of the electrode traction ring, while the effects of horizontal acceleration are concentrated in the front half of the traction ring.

Discussion

Although this paper does not provide experimental biological validation to demonstrate the credibility of the finite element analysis results, a comparison with a large of literature indirectly supports the reliability of the finite element analysis results for the electrode insertion process. Due to the lack of experimental data and literature regarding the analysis of steady-state acceleration effects during long-term implantation, the accuracy of this part's results remains open to discussion. However, the magnitude and trend of the numerical results obtained can serve as a reference for the clinical application of electrodes.

Electrode insertion process

We have investigated the mechanical response of brain tissue during the electrode insertion process. The designed insertion process is a quasi-static procedure: the flexible PI electrode is to be inserted through a surgical robot, advancing in specified directions by a few micrometers each time. After each advancement, there is a pause of several milliseconds to adjust the direction and step size, allowing the mechanical response of the brain tissue to reach a steady state before the next advancement.

The FEA outcome for the flexible electrode insertion process led us to the following key findings: (1) During the stepwise insertion of the electrode into brain tissue, the mechanical response of the surrounding tissue overall exhibits a double-exponential decay with increasing electrode implantation depth and a linear increase with larger step displacements; (2) The cortical thickness has a negligible impact on the biomechanical effects of the electrode, while the mechanical properties of the brain tissue and the cortical-subcortical boundary play a crucial role in these effects; (3) For thin, flexible PI electrodes, the induced mechanical effects diminish rapidly with spatial distance, remaining confined within several tens of micrometers around the electrode. Each finding has been elaborated upon below, along with a comparative analysis with results from other literature.

There is limited research on the impact of electrode implantation depth on the mechanical interactions between the electrode and brain tissue. Zhang et al.²³ indirectly indicate that neural electrodes implanted at deeper positions result in lower brain tissue strain. The process of microneedle insertion into the skin is similar to that of neural electrode implantation, involving the insertion of micro-sized flexible implants into biological tissue, which can provide valuable insights. Kang et al.⁴⁶ demonstrated that the mechanical effects of microneedle puncture are maximal in the initial stage, rapidly diminishing with increasing depth, while there is a localized rise in tissue stress near the interface between the epidermis and dermis. This result exhibits a similar trend to our first finding.

Furthermore, we found a linear positive correlation between the biomechanical effects of the electrode and the size of the implantation step displacement, which is consistent with the results of Abed et al.²⁸ regarding the mechanical effects of electrode micro-movements. This suggests that during dynamic implantation, the biomechanical effects of the electrode are also linearly correlated with implantation speed, aligning with findings from Andrei et al.⁴⁷ Cansanova et al.⁴⁸ that indicate faster electrode insertion leads to greater tissue damage and brain strain. However, this is not the case in the studies by O'Sullivan et al.²⁷, Bjornsson et al.⁴⁹, and McNamara et al.⁵⁰, where lower insertion speeds resulted in significant tissue damage despite reduced tissue strain. This may be due to longer operation times and damage duration associated with slower insertion speeds, as well

as differences in electrode geometry, friction coefficients, and varying magnitudes of insertion speeds. This highlights the need to carefully control the surgical duration during electrode implantation procedures.

Based on the findings regarding cortical thickness, we speculate that the mechanical influence of flexible microelectrodes is limited to a few tens of micrometers around the electrode. Therefore, variations in cortical thickness at the millimeter scale do not significantly affect the biomechanical impact on the electrodes. However, it remains uncertain whether the influence of cortical thickness can be disregarded for larger metal electrodes and electrode arrays. Notably, at the gray-white matter junction, where the mechanical properties of the surrounding tissue change obviously, there are more pronounced variations in stress and strain.

Steady-state acceleration under implantation

One direction for the development of implanted neural electrodes is to achieve long-term stable implantation, which is crucial for functional recovery in paralyzed patients and human-computer interaction. A significant challenge with long-term electrode implantation is ensuring mechanical compatibility between the neural electrodes and biological tissues to prevent mechanical stimulation and damage to the tissues. Therefore, evaluating the biomechanical compatibility of electrodes before their clinical application is of great importance.

We investigated the effects of sustained acceleration, which may occur during long-term implantation of electrodes (such as in high-speed trains and elevators), on the stability of electrodes during in vivo implantation. We also analyzed the influence of electrode implantation depth and cortical thickness. Our key findings are as follows: (1) Under typical steady-state accelerations from elevators and high-speed trains, the biomechanical effects of flexible PI electrodes inside the brain are minimal; (2) The impact of electrode implantation depth on the mechanical response of brain tissue varies with the direction of acceleration, showing greater sensitivity to horizontal acceleration; (3) Similarly, the effect of cortical thickness on mechanical response is not significant, while the mechanical properties of brain tissue and the gray-white matter interface play a more crucial role.

Although this study did not simulate accelerations during air travel, existing literature suggests that accelerations during takeoff and landing typically range from 0.1 to 0.5 g (as outlined in "Airplane Characteristics for Airport Planning"). These values are comparable to the accelerations we simulated (approximately 0.1 g). Therefore, we chose to focus on long-duration, low-acceleration scenarios to evaluate electrode stability during long-term implantation.

Compared to the strain of over 10% in brain tissue during electrode insertion, the maximum strain under steady-state acceleration is around 0.1%, which can be nearly ignored. We found that under vertical steady-state acceleration, the mechanical response of brain tissue linearly increases with the depth of electrode implantation, a finding not previously reported. In contrast, the variation in mechanical response with implantation depth under horizontal steady-state acceleration is not significant, likely due to the very small cross-sectional area of the electrode (only 1.5 μ m thick), leading to potentially inaccurate results that require further experimental and literature validation. Similarly, like during electrode insertion, the mechanical influence of flexible microelectrodes is minimal, and the impact of cortical thickness is very slight, although there is a localized change at the cortical-white matter interface.

Brain injury assessment and suggestion

There are various methods for assessing mechanical damage to brain tissue, including pathological section analysis and mechanical effect evaluation. To fully leverage the advantages of finite element simulation, which provides accurate mechanical response values, this study references the Von Mises strain threshold of 14.65%, as proposed by Sahoo et al.⁴⁵, indicating a 50% risk of DAI, to evaluate whether electrodes cause mechanical damage to brain tissue, with specific criteria detailed in Sect. 2.6.

Based on our experimental results, using 14.65% Von Mises strain as the criterion for brain injury, we propose the following electrode implantation strategy: during the initial stage of implantation, when the depth is less than 200 μ m, the step displacement of electrode insertion should be controlled at around 1 μ m; for depths between 200 and 500 μ m, the step displacement should gradually increase from 1 μ m to 5 μ m; and for depths greater than 500 μ m, the step displacement should remain at 5 μ m. This implantation strategy ensures safety while also considering the efficiency of electrode insertion, minimizing prolonged exposure of brain tissue to the external environment and reducing the risk of damage and infection.

For the long-term safety assessment of flexible microelectrodes, simulation results indicate that when using transportation methods like elevators and high-speed trains, which involve prolonged acceleration, the mechanical compatibility between the electrodes and brain tissue is excellent, resulting in negligible mechanical impact on the tissue. However, further evaluations of electrode safety are necessary in situations involving shortduration high acceleration, such as head impacts and falls, as well as longer durations of greater acceleration, like those experienced in airplanes and rockets.

Limitations and assumptions

Due to the limitations of experimental methods, the results obtained from FEA require further biological experiments for validation. However, as previously mentioned, it is challenging to monitor and quantify the mechanical impact on brain tissue during the electrode insertion process and in the in-vivo implanted state. Therefore, comprehensive validation of the numerical results presented in this study is difficult through experiments. In our next research phase, we will conduct insertion experiments using OCT (Optical Coherence Tomography) imaging to monitor the deformation of brain tissue in real time and compare with those of the simulations.

During the establishment and analysis of the finite element model, several assumptions and simplifications were made: (1) Brain tissue was modeled as a linear viscoelastic material, although it is typically considered a hyperelastic material^{51,52}; (2) The complex internal metal wiring of the electrode was simplified to a single-

layer structure, and the mechanical effects at the electrode tip were neglected, as detailed in "Mesh"; (3) The electrode implantation was carried out through robotic traction, but the effect of the traction needle was not considered in the simulation; (4) The contact type between the electrode surface and brain tissue was defined as bonded contact, despite the presence of friction and slip; (5) Although most electrode implantation processes are continuous transient puncture processes, the designed electrode implantation process was treated as a discrete, steady-state, stepwise insertion process. Some of these aspects are discussed in more detail in the supplementary materials and will be addressed in future research to thoroughly investigate the mechanical effects of the interaction between the electrode and brain tissue.

Conclusions

This study employs FEM to analyze the biomechanical effects of a novel flexible microelectrode. The electrode is based on a flexible PI substrate and features an ultra-thin profile (thickness of 1.5 μ m). The research focuses on two main aspects: the electrode insertion process and the biomechanical effects under steady-state acceleration in vivo. The geometric structure and metal interconnecting traces of the electrode were simplified. Simulations investigated the effects of electrode implantation depth, gray matter thickness, step displacement, and acceleration direction on the biomechanical responses. The potential mechanical damage to brain tissue caused by the electrode was assessed, leading to promising implantation strategies for clinical guidance. Key conclusions include:

- i. The mechanical response of brain tissue generally exhibits a double-exponential decay with increased implantation depth and a linear increase with larger step displacements.
- ii. The flexible, thin sheet-like electrode is more sensitive to horizontal acceleration, although the mechanical effects remain weak.
- iii. The mechanical influence of the flexible microelectrode is limited to a few tens of micrometers, likely explaining why millimeter-scale changes in gray matter thickness have negligible effects on the electrode's biomechanical response.

Finally, we propose a balanced implantation strategy that ensures safety and surgical efficiency: during the initial phase of implantation, the step displacement should be controlled around 1 μ m, gradually increasing to 5 μ m as the depth of implantation increases. Our findings indicate that the electrode demonstrates excellent mechanical compatibility for long-term implantation, with minimal mechanical responses in brain tissue under steady-state acceleration. This research offers significant guidance and reference for the clinical implantation and application of this electrode and other flexible electrodes.

Data availability

The raw and analysed datasets generated during the study are too large to be publicly shared, yet they are available for research purposes from the corresponding authors on reasonable request. The code used in this study is available from the corresponding author upon reasonable request.

Received: 13 March 2025; Accepted: 28 May 2025 Published online: 06 June 2025

References

- 1. Cogan, S. F. Neural stimulation and recording electrodes. Annu. Rev. Biomed. Eng. 10 (1), 275–309. https://doi.org/10.1146/annur ev.bioeng.10.061807.160518 (2008).
- Lebedev, M. A. & Nicolelis, M. A. L. Brain-Machine interfaces: from basic science to neuroprostheses and neurorehabilitation. *Physiol. Rev.* 97 (2), 767–837. https://doi.org/10.1152/physrev.00027.2016 (2017).
- Jeong, U. J. et al. A minimally invasive flexible electrode array for simultaneous recording of ECoG signals from multiple brain regions. Lab. Chip. 21 (12), 2383–2397. https://doi.org/10.1039/D1LC00117E (2021).
- Pesaran, B. et al. Investigating large-scale brain dynamics using field potential recordings: analysis and interpretation. *Nat. Neurosci.* 21 (7), 903–919. https://doi.org/10.1038/s41593-018-0171-8 (2018).
- Shen, K., Chen, O., Edmunds, J. L., Piech, D. K. & Maharbiz, M. M. Translational opportunities and challenges of invasive electrodes for neural interfaces. *Nat. Biomed. Eng.* 7 (4), 424–442. https://doi.org/10.1038/s41551-023-01021-5 (2023).
- Polikov, V. S., Tresco, P. A. & Reichert, W. M. Response of brain tissue to chronically implanted neural electrodes. J. Neurosci. Methods. 148 (1), 1–18. https://doi.org/10.1016/j.jneumeth.2005.08.015 (2005).
- 7. Musk, E. & Neuralink An integrated brain-machine interface platform with thousands of channels. J. Med. Internet. Res. 21 (10), e16194. https://doi.org/10.2196/16194 (2019).
- Campbell, A. & Wu, C. Chronically implanted intracranial electrodes: tissue reaction and electrical changes. *Micromachines*. 9 (9), 430. https://doi.org/10.3390/mi9090430 (2018).
- Lacour, S. P. et al. Flexible and stretchable micro-electrodes for in vitro and in vivo neural interfaces. *Med. Biol. Eng. Comput.* 48 (10), 945–954. https://doi.org/10.1007/s11517-010-0644-8 (2010).
- Du, Z. J. et al. Ultrasoft microwire neural electrodes improve chronic tissue integration. Acta Biomater. 53, 46–58. https://doi.org/ 10.1016/j.actbio.2017.02.010 (2017).
- Merken, L., Schelles, M., Ceyssens, F., Kraft, M. & Janssen, P. Thin flexible arrays for long-term multi-electrode recordings in macaque primary visual cortex. J. Neural Eng. 19 (6), 066039. https://doi.org/10.1088/1741-2552/ac98e2 (2022).
- Liu, S., Zhao, Y., Hao, W., Zhang, X. D. & Ming, D. Micro- and nanotechnology for neural electrode-tissue interfaces. *Biosens. Bioelectron.* 170, 112645. https://doi.org/10.1016/j.bios.2020.112645 (2020).
- Fedorchenko, A. I., Wang, A. B. & Cheng, H. H. Thickness dependence of nanofilm elastic modulus. Appl. Phys. Lett. 94 (15), 152111. https://doi.org/10.1063/1.3120763 (2009).
- Yin, T., Zhang, G., Qu, S. & Suo, Z. Peel of elastomers of various thicknesses and widths. *Extreme Mech. Lett.* 46, 101325. https://d oi.org/10.1016/j.eml.2021.101325 (2021).
- 15. Kanno, M., Kawakami, H., Nagaoka, S. & Kubota, S. Biocompatibility of fluorinated polyimide. J. Biomed. Mater. Res. 60 (1), 53–60. https://doi.org/10.1002/jbm.1280 (2002).

- Procès, A., Luciano, M., Kalukula, Y., Ris, L. & Gabriele, S. Multiscale mechanobiology in brain physiology and diseases. Front. Cell. Dev. Biol. 10, 823857. https://doi.org/10.3389/fcell.2022.823857 (2022).
- Heo, D. N. et al. Flexible and highly biocompatible nanofiber-based electrodes for neural surface interfacing. ACS Nano. 11 (3), 2961–2971. https://doi.org/10.1021/acsnano.6b08390 (2017).
- Sharafkhani, N. et al. Neural tissue-microelectrode interaction: brain micromotion, electrical impedance, and flexible microelectrode insertion. J. Neurosci. Methods. 365, 109388. https://doi.org/10.1016/j.jneumeth.2021.109388 (2022).
- Shakiba, D., Zhao, W. & Ji, S. Multiscale mechanobiology of brain injury: axonal strain redistribution. *Biophys. J.* 119 (7), 1273– 1274. https://doi.org/10.1016/j.bpj.2020.07.041 (2020).
- Sillay, K. A. et al. Perioperative brain shift and deep brain stimulating electrode deformation analysis: implications for rigid and non-rigid devices. Ann. Biomed. Eng. 41 (2), 293–304. https://doi.org/10.1007/s10439-012-0650-0 (2013).
- Johnson, V. E., Stewart, W. & Smith, D. H. Axonal pathology in traumatic brain injury. *Exp. Neurol.* 246, 35–43. https://doi.org/10 .1016/j.expneurol.2012.01.013 (2013).
- Du, Q., Wang, C., He, G. & Sun, Z. Insertion trauma of a new cochlear implant electrode: evaluated by histology in fresh human Temporal bone specimens. Acta Otolaryngol. 141 (5), 490–494. https://doi.org/10.1080/00016489.2021.1897159 (2021).
- Zhang, W., Tang, J., Li, Z. & Ma, Y. A novel neural electrode with micro-motion-attenuation capability based on compliant mechanisms—Physical design concepts and evaluations. *Med. Biol. Eng. Comput.* 56 (10), 1911–1923. https://doi.org/10.1007/s11 517-018-1826-z (2018).
- Lee, H., Bellamkonda, R. V., Sun, W. & Levenston, M. E. Biomechanical analysis of silicon microelectrode-induced strain in the brain. J. Neural Eng. 2 (4), 81–89. https://doi.org/10.1088/1741-2560/2/4/003 (2005).
- Subbaroyan, J., Martin, D. C. & Kipke, D. R. A finite-element model of the mechanical effects of implantable microelectrodes in the cerebral cortex. J. Neural Eng. 2 (4), 103–113. https://doi.org/10.1088/1741-2560/2/4/006 (2005).
- Sui, X., Han, Z., Zhou, D. & Ren, Q. Mechanical analysis and fabrication of a penetrating silicon microprobe as an artificial optic nerve visual prosthesis. Int. J. Artif. Organs. 35 (1), 34–44. https://doi.org/10.5301/ijao.5000034 (2012).
- O'Sullivan, K. P. & Coats, B. Coupled Eulerian–Lagrangian model prediction of neural tissue strain during microelectrode insertion. J. Neural Eng. 21 (4), 046055. https://doi.org/10.1088/1741-2552/ad68a6 (2024).
- Al Abed, A., Amatoury, J. & Khraiche, M. Finite element modeling of magnitude and location of brain micromotion induced strain for intracortical implants. *Front. NeuroSci.* 15, 727715. https://doi.org/10.3389/fnins.2021.727715 (2022).
- Xue, N. et al. Polymeric C-shaped cuff electrode for recording of peripheral nerve signal. Sens. Actuators B. 210, 640–648. https:// doi.org/10.1016/j.snb.2015.01.006 (2015).
- Xiang, Z. et al. Progress of flexible electronics in neural interfacing A self-adaptive non-invasive neural ribbon electrode for small nerves recording. Adv. Mater. 28 (22), 4472–4479. https://doi.org/10.1002/adma.201503423 (2016).
- Ferlauto, L. et al. Design and validation of a foldable and photovoltaic wide-field epiretinal prosthesis. Nat. Commun. 9 (1), 992. https://doi.org/10.1038/s41467-018-03386-7 (2018).
- Schanze, T. et al. An optically powered single-channel stimulation implant as test system for chronic biocompatibility and biostability of miniaturized retinal vision prostheses. *IEEE Trans. Biomed. Eng.* 54 (6), 983–992. https://doi.org/10.1109/TBME.20 07.895866 (2007).
- Oñate, E. Structural Analysis with the Finite Element Method: Linear Statics. https://doi.org/10.1007/978-1-4020-8733-2 (Springer Netherlands, 2009).
- Wang, L. et al. Functionalized helical fibre bundles of carbon nanotubes as electrochemical sensors for long-term in vivo monitoring of multiple disease biomarkers. *Nat. Biomed. Eng.* 4 (2), 159–171. https://doi.org/10.1038/s41551-019-0462-8 (2019).
- You, X. et al. Progress in mechanical modeling of implantable flexible neural probes. Comput. Model. Eng. Sci. 140 (2), 1205–1231. https://doi.org/10.32604/cmes.2024.049047 (2024).
- Zhao, Z. et al. Parallel, minimally-invasive implantation of ultra-flexible neural electrode arrays. J. Neural Eng. 16 (3), 035001. https://doi.org/10.1088/1741-2552/ab05b6 (2019).
- Arafat, M. A., Rubin, L. N., Jefferys, J. G. R. & Irazoqui, P. P. A method of flexible micro-wire electrode insertion in rodent for chronic neural recording and a device for electrode insertion. *IEEE Trans. Neural Syst. Rehabil. Eng.* 27 (9), 1724–1731. https://do i.org/10.1109/TNSRE.2019.2932032 (2019).
- Fischl, B. & Dale, A. M. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc. Natl. Acad. Sci. 97(20), 11050–11055. https://doi.org/10.1073/pnas.200033797 (2000).
- 39. McKeen, L. W. Polyimides. In Film Properties of Plastics and Elastomers, 147–185 (Elsevier, 2017). https://doi.org/10.1016/B978-0 -12-813292-0.00007-1
- 40. Matweb. (n.d.). Chromium, Cr; Recrystallized. [Dataset]. Retrieved August 23. from https://www.matweb.com (2023).
- 41. Matweb. (n.d.). Gold, Au. [Dataset]. Retrieved August 23. from https://www.matweb.com (2023).
- 42. Zhang, L., Yang, K. H. & King, A. I. A proposed injury threshold for mild traumatic brain injury. J. Biomech. Eng. 126 (2), 226–236. https://doi.org/10.1115/1.1691446 (2004).
- Zhang, L. et al. Recent advances in brain injury research: A new human head model development and validation. 2001-22-0017. https://doi.org/10.4271/2001-22-0017 (2001).
- 44. Alisafaei, F. et al. Mechanisms of local stress amplification in axons near the Gray-White matter interface. *Biophys. J.* **119** (7), 1290–1300. https://doi.org/10.1016/j.bpj.2020.08.024 (2020).
- Sahoo, D., Deck, C. & Willinger, R. Brain injury tolerance limit based on computation of axonal strain. Accid. Anal. Prev. 92, 53–70. https://doi.org/10.1016/j.aap.2016.03.013 (2016).
- Kang, T. et al. The synergistic effect of mechanical vibration for skin puncturing using polymeric microneedles. J. Drug Deliv. Sci. Technol. 71, 103334. https://doi.org/10.1016/j.jddst.2022.103334 (2022).
- Andrei, A., Welkenhuysen, M., Nuttin, B. & Eberle, W. A response surface model predicting the in vivo insertion behavior of micromachined neural implants. J. Neural Eng. 9 (1), 016005. https://doi.org/10.1088/1741-2560/9/1/016005 (2012).
- Casanova, F. In vivo evaluation of needle force and friction stress during insertion at varying insertion speed into the brain. J. Neurosci. Methods. (2014).
- Bjornsson, C. S. et al. Effects of insertion conditions on tissue strain and vascular damage during neuroprosthetic device insertion. J. Neural Eng. 3 (3), 196–207. https://doi.org/10.1088/1741-2560/3/3/002 (2006).
- McNamara, I. N. et al. Electrode sharpness and insertion speed reduce tissue damage near high-density penetrating arrays. J. Neural Eng. 21 (2), 026030. https://doi.org/10.1088/1741-2552/ad36e1 (2024).
- Budday, S. et al. Mechanical characterization of human brain tissue. Acta Biomater. 48, 319–340. https://doi.org/10.1016/j.actbio.2 016.10.036 (2017).
- Bilston, L. E., Liu, Z. & Phan-Thien, N. Linear viscoelastic properties of bovine brain tissue in shear. *Biorheology*. 34 (6), 377–385. https://doi.org/10.1016/S0006-355X(98)00022-5 (1997).

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Funding

This research was supported by the STI 2030-Major Projects (No. 2022ZD0208601), the National Natural Science Foundation of China (No. 62176158) and the STAR Project of Shanghai Jiao Tong University (WH410362603/001).

Declarations

Competing interests

The authors declare no competing interests.

Compliance with ethics guidelines.

This study does not contain any studies with human or animal subjects performed by any of the authors.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/1 0.1038/s41598-025-04737-3.

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