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Mixed ionic-electronic conducting eutectic soft materials for bioelectronics

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Bioelectronic devices represent a rapidly expanding frontier at the interface of materials science, biology, and electronics, with the potential to transform healthcare by enabling seamless communication between living tissues and engineered systems. A central challenge in this field is the design of soft materials that can efficiently transport both ionic and electronic charge carriers, thereby bridging the fundamental mismatch between biological and electronic signal transduction. In this opinion, we argue that eutectic systems offer a powerful yet underexplored platform for engineering mixed ionic-electronic conducting soft materials. Eutectic mixtures, by virtue of their unique phase behavior, tunable molecular interactions, and inherent structural flexibility, provide an exceptional starting point for tailoring materials that combine biocompatibility, adaptability, and functional conductivity. We highlight how eutectic design principles can be leveraged to expand the palette of soft conductors, offering pathways to address persistent challenges such as stability, processability, and integration with complex biological environments. Looking forward, we outline key research directions to unlock the full potential of eutectic-derived conductors in advancing next-generation bioelectronic systems.

Introduction

In biological systems, communication and control rely heavily on ionic currents and electrical signaling, which regulate processes ranging from muscle contraction to sensory perception.[1] Capturing and modulating these signals has long been a central goal in bioelectronics, not only for therapeutic intervention but also for preventive and diagnostic applications. At the core of this challenge lies the development of materials that can seamlessly bridge the ionic nature of biology with the electronic foundation of modern devices.[2] Mixed ionic-electronic conducting soft materials have emerged as a particularly promising class for this purpose, enabling dynamic, biocompatible, and adaptive interactions at the bio-electronic interface. Conducting polymers (CPs) such as poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS), polypyrrole, and polyaniline have played a central role in bioelectronics because they uniquely combine electronic conductivity with the ability to operate in hydrated, ion-rich environments.[3] PEDOT:PSS, in particular, has become the benchmark CP owing to its high electronic conductivity, aqueous processability, and compatibility with biological systems. Its mixed ionic-electronic transport enables efficient coupling between biological signals and electronic devices, lowering interfacial impedance and increasing charge storage capacity.[4] These properties explain why CPs are so often chosen as the electronic component in bioelectronic interfaces.

However, CPs tend to display limited mechanical robustness, showing rigidity, low extensibility, and pronounced brittleness. To bridge the mechanical mismatch between rigid CPs and living tissues, they are frequently incorporated into soft matrices such as hydrogels. In these composites, the hydrogel provides tissue-like mechanics, high water content, and biocompatibility, while the CP network supplies the electronic conductivity needed for recording and stimulation.[5] For example, PEDOT:PSS has been processed into hydrogel scaffolds with tissue-level elasticity and conductivity in the tens of S cm^{-1} range.[6,7] These hybrid systems have enabled significant advances in biosensing and stimulation.

Despite this progress, CP-hydrogel composites still suffer from important drawbacks. Their conductivity is strongly dependent on hydration, making electrochemical performance fluctuate with changes in water content.[8] Hydrogels themselves are prone to dehydration and freezing, which limits their stability outside narrow physiological conditions.[9] To address these limitations, ionogels made of ionic liquids (ILs) were developed, offering high ionic conductivity and improved environmental resilience. Owing to their negligible volatility and permanent ionic content, ILs create a stable conductive medium and

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simultaneously act as effective dopants for CPs, reorganizing their microstructure and increasing charge carrier density.[10] This dual role improved conductivity, flexibility, and long-term electrochemical stability compared with conventional hydrogels. However, IL-based systems introduced new challenges, including cytotoxicity, poor biodegradability, and high production costs, which restrict their use in biomedical applications.[11]

To overcome these issues, attention has shifted to eutectic solvents (ESs), an attractive family of ionically conducting media. ESs share many of the advantageous features of ILs, such as high ionic conductivity, non-volatility, and the ability to modulate CP performance, yet they are cheaper, biodegradable, and often more biocompatible.[12] For interested readers, a recently published critical review provides a comprehensive and balanced discussion of these key aspects of ESs in comparison with ILs.[13,14] This makes them attractive partners for CPs in the design of mixed ionic-electronic conductors. While CPs have historically dominated the bioelectronics space, new opportunities arise from eutectic systems, whose compositional versatility enables fine-tuning of ionic transport. Their intrinsic fluidity and ability to form soft, adaptive phases make them especially attractive for creating bioelectronic interfaces that must conform to complex, dynamic biological environments.[15] These attributes position eutectic-derived conductors as a unique starting point to expand the design space of bioelectronic devices, from recording and sensing to active stimulation and long-term integration with living tissues.

We believe the time has come to move beyond these incremental improvements and consider ESs themselves as a foundational design platform for next-generation soft conductors. By definition, ESs are mixtures of two or more components whose combination lowers the melting point below that of each individual component. Within this broad category, emerging deep eutectic solvents (DESs) form a particular subset where strong hydrogen bonding drives large negative deviations from ideal mixing, producing liquid phases in a broad temperature range and with unique physicochemical properties.[16] The components of these mixtures are usually referred to as hydrogen bond acceptor (HBA) and hydrogen bond donor (HBD), where the HBA is an electron-rich species that accepts hydrogen bonds (typically quaternary ammonium salts) and the HBD is a molecule capable of donating labile protons, such as alcohols, organic acids, or amines. For the sake of clarity, in this opinion, we will use the term ESs to encompass all the eutectic systems, whether they display negative deviations from the thermodynamic ideality or not. The solid–liquid phase diagram of a binary eutectic system and the chemical structure of typical HBAs and HBDs are shown in Fig. 1A and B, respectively. The immobilization of these innovative ionic solvents into solid matrices gives rise to a new family of soft materials, known as

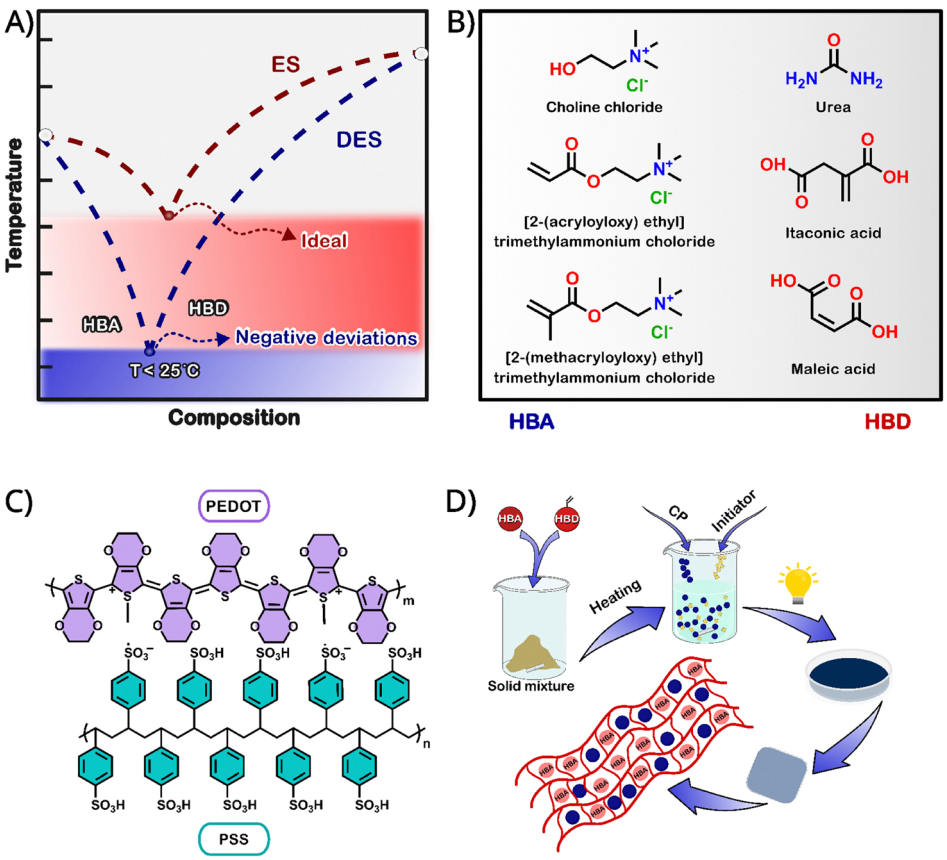

Fig. 1 (A) Solid–liquid phase diagram showing melting point depression during ES and DES formation. (B) Typical examples of HBA and HBD. (C) Chemical structure of PEDOT:PSS. (D) Illustration of polyES–CP preparation, from initial components to a final device.

eutectogels,[15] which are envisioned to transform next-generation implantable and wearable technologies. In our view, this is not merely another incremental addition to the materials library, but rather a paradigm shift that could redefine how we think about the design of soft, stable, and multifunctional conductors for bioelectronics.

Building on this, polymerizable eutectic solvents (polyES) are designed so that one component of the eutectic mixture carries a polymerizable group, typically undergoing free-radical polymerization. This process transforms the liquid mixture into a covalently bonded polymer network that preserves the compositional versatility and ionic functionality of the parent ES while eliminating free-liquid phases. Unlike eutectogels, where the eutectic solvent is only physically immobilized within a supporting matrix, polyES achieve chemical fixation that prevents leakage and phase separation, while also imparting greater mechanical robustness and long-term electrochemical stability.[17] Together, these attributes make polyES a dependable foundation for the development of safe implantable bioelectronic devices. The implications are profound as eutectogels and polyES elastomers could transform not only wearable and implantable sensors but also active stimulation devices. Fig. 1C depicts the representative structure of one of the most popular CP used nowadays, PEDOT:PSS, while Fig. 1D illustrates its combination with polyES and the resulting composite architecture.

Among the wide range of envisioned applications, brain stimulation stands out as a particularly urgent and transformative challenge. Neurological disorders such as Parkinson's disease, epilepsy, and depression demand highly reliable and long-lasting implantable devices, yet current electrode technologies often fail due to mechanical mismatch, electrochemical instability, or chronic inflammatory responses. Because even minor instabilities or leakage events can have severe consequences in the brain's delicate environment, the development of safer and more resilient materials is essential.[18] Mixed conducting polyES offer a promising pathway, as their solid-state nature, tunable ionic-electronic balance, and potential for functionalization could enable interfaces that combine softness with stable performance. In this opinion, we specifically explore how polyES-based systems could be harnessed for brain stimulation, highlighting their potential to overcome the limitations of existing materials and to advance next-generation neural therapies.

Potential applications of mixed conducting PolyES in the nervous system

Mixed conducting polyES-based elastomers could be especially promising for advancing future bioelectronic interfaces in the nervous system. Their anticipated ability to combine ionic-electronic transport with mechanical compliance and solid-state stability suggests new opportunities in neural tissue regeneration, electroencephalographic (EEG) signal recording,

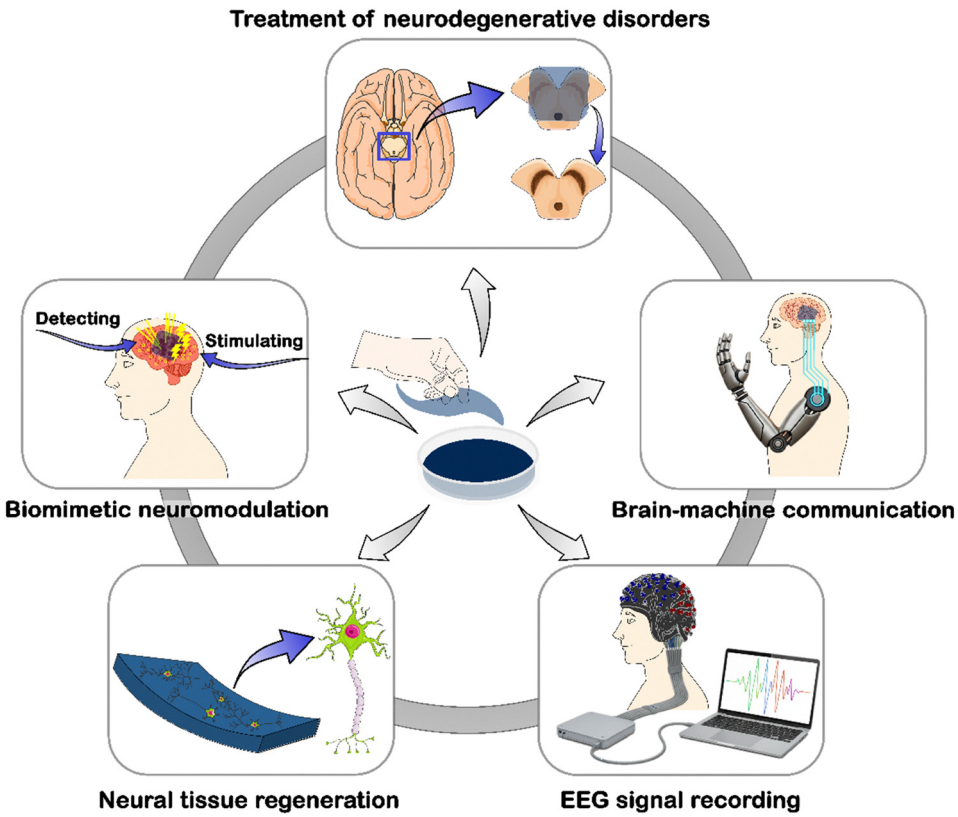

Fig. 2 Schematic illustration summarizing different applications for polyES–CP as a core material in neural bioelectronics.

brain–machine communication, bioinspired neuromodulation, and the treatment of neurodegenerative disorders.[19] All of these applications are represented in Fig. 2 and discussed below. Within this scope, brain-related diseases emerge as some of the most urgent and complex health challenges. Unlike implants in other tissues, neural devices must operate within the extreme sensitivity and intricate organization of the central nervous system, making the demand for safe, reliable, and biocompatible materials particularly acute.

Neurons communicate through ionic fluxes, whereas most synthetic CPs are optimized for electronic charge transport. While mixed ionic-electronic conductors have been developed to mediate this mismatch, their function often remains highly dependent on hydration and unstable ionic environments. CP-incorporating polyES-based elastomers could offer a way forward by providing stable ionic pathways within a solid-state matrix, ensuring consistent performance for long-term neural interfacing.[20]

Because the nervous system relies on a delicately balanced electrical environment, damage to peripheral or central nerves disrupts the propagation of essential signals. Electroactive materials and electrical stimulation provide powerful tools to counteract these effects, since they can modulate local bioelectric fields, trigger action potentials, and guide cellular responses that support nerve repair.[20] These capabilities highlight the promise of targeted neural stimulation, particularly in the treatment of brain disorders, where restoring or modulating circuit activity may help recover lost function and even promote regeneration. Mixed conducting polyES systems could provide a more reliable foundation for neural interfaces, since their solid-state nature combines efficient electronic transport with stable ionic pathways, overcoming the fluctuations and instabilities that limit hydration-dependent conductors. Beyond their role as ionic conductors, the chemistry of polyES can be purposefully tuned to add therapeutic functionality. By selecting components such as vitamins, polyphenols or terpenes, these materials could not only deliver electrical performance but also contribute anti-inflammatory or neuroprotective effects, directly supporting the regenerative processes required in neural implants. Given the strong interactions between HBD and HBA components within the polyES matrix, sustained delivery of these therapeutic molecules could be achieved *via* passive diffusion; alternatively, the system could be engineered to enable electro-responsive release mechanisms. This dual functionality points to a new vision of bioelectronic materials that are not only passive conductors but also active participants in the healing and modulation of the nervous system.[21–23]

Wireless bioelectronic devices could enable effective neural therapies without the need for invasive surgery. By stimulating neurons and enhancing growth factor activity, they promote healing without drugs while reducing many of the risks and complications associated with surgical procedures.[24] Conductive soft materials add another dimension, as they can interact with stem cells and influence their intracellular behavior. Conventional hydrogels are often used to protect implanted cells from the harsh post-stroke environment, improving survival, yet their lack of conductivity limits control over the cellular microenvironment once implanted.[25] Incorporating CPs in hydrogels overcomes this limitation by providing a platform that both shields transplanted stem cells and allows their activity to be modulated through electrical stimulation. However, hydrogels or composites that retain a liquid phase remain unstable over time, since the aqueous component can separate and compromise long-term function. Mixed conducting polyES systems could offer a way forward by combining stable solid-state architecture with electrical functionality, enabling cell-protective scaffolds that remain reliable for chronic therapies.

Brain stimulation therapies represent biologically oriented interventions that can complement or, in some cases, substitute conventional treatments for psychiatric and neurological disorders. Although less widely used than medication or psychotherapy, they hold particular promise for conditions that do not respond to standard interventions, with reported applications in depression, post-traumatic stress disorder, anxiety disorders, Alzheimer's disease, and dementia.[26] Central to all these approaches is the electrode, which must deliver targeted stimulation either transcranially or through implanted devices to modulate neural activity in specific regions of the brain. One of the main barriers to the long-term success of such therapies lies in the stability of the electrode–tissue interface. Over-extended implantation periods, conventional materials often provoke inflammatory responses or lose performance due to poor integration with the surrounding tissue. Recent strategies have explored incorporating bioactive molecules such as adhesion peptides, extracellular matrix proteins, or growth factors directly into electrode coatings to promote neuronal growth and improve stability.[27] Mixed conducting polyES matrices could expand this concept by providing not only tunable ionic and electronic conductivity but also inherent biocompatibility and chemical versatility. These systems can deliver therapeutic effects by incorporating bioactive molecules, whether encapsulated or chosen directly as the HBD or HBA, so that the active species, in either case, provides anti-inflammatory or neurotrophic functionality, with release modulated in a controlled, electrically responsive manner. This dual function would both preserve neuronal survival and maintain low impedance at the electrode interface, offering a decisive advantage over conventional CPs that struggle with long-term stability.[28]

The potential impact of such materials becomes particularly evident when considering neurodegenerative diseases. In Parkinson's disease, pharmacological treatments and surgical interventions such as deep brain stimulation offer temporary symptom relief, but their efficacy often declines over time and can be accompanied by severe side effects. Certain CPs have already shown the ability to promote neuronal proliferation, differentiation, and axonal outgrowth, suggesting a role in neural repair.[29–31] PolyES-based systems could build on these observations, combining stable mixed conduction with the possibility of integrating nanoscale therapeutics such as agents targeting mitochondrial dysfunction in dopaminergic neurons. By coupling localized stimulation with the controlled release of neuroprotective compounds, these materials could simultaneously address the

electrophysiological dysfunction and the underlying neurodegeneration in Parkinson's disease, paving the way for safer and more durable therapies.[32]

Epilepsy presents another area where polyES-based electrodes could provide transformative benefits. Accurate localization of the epileptogenic zone is essential for successful surgical intervention, particularly in the ~30% of patients who do not respond to antiseizure medications. This requires electrodes capable of long-term, high-fidelity signal acquisition without compromising surrounding tissue health. Mixed conducting polyES composites, with their combination of mechanical compliance and long-term electrochemical stability, could improve both the precision of presurgical mapping and the durability of implanted devices. By reducing chronic tissue responses while preserving recording fidelity, these systems hold the potential to enhance surgical outcomes for patients with drug-resistant epilepsy.[33]

From fabrication to implantation: key challenges

Developing polyES-based neural interfaces that can truly rival or even surpass aqueous-based systems is far from straightforward. At the heart of the problem lies an interplay of mechanics, electrochemistry, and biology that is difficult to balance.

Accurate recording of the brain's electrophysiological environment is critical for both the early detection of neurological disorders and the ongoing monitoring of neuronal health. However, in practice, physiological systems may not always tolerate implanted devices. Even if the device has suitable electrical performance, variations in mechanical, chemical, or surface properties can trigger foreign body responses, alter neuronal activity, or impair signal quality.[34–36] These challenges highlight the need to systematically analyze different polymers, polyES formulations, composites, and CPs to identify material systems that minimize adverse biological responses while preserving high-fidelity signal acquisition over long periods.

One of the most persistent hurdles is the mechanical mismatch between traditional conductive materials and the ultra-soft nature of brain tissue. Most metals and CPs have moduli orders of magnitude higher than the brain's 0.1–10 kPa range.[35] This stiffness mismatch may seem minor on paper, but *in vivo* it can trigger chronic inflammation, glial scarring, and neuronal loss. Over time, these biological responses degrade signal fidelity and compromise long-term integration. Even micrometer-scale movements from pulsatile blood flow or head motion can impose enough mechanical stress to initiate neuroinflammation.[37] Couldn't we simply use softer materials? Not without trade-offs, softer materials often sacrifice conductivity, chemical stability, or processing precision. The challenge is to create a material that is simultaneously soft, electrically efficient, chemically stable, and minimally reactive to tissue. Here, hydrophilic functional groups such as –OH, –COOH, –CONH–, $-CONH_2$, and $-SO_3H$ may play a role, promoting water retention and protein-friendly interfaces to encourage cell compatibility.[38,39]

This raises a fundamental question: why do we replace solvent-rich eutectogels, which excel in ionic mobility, with liquid-free polyES? The answer lies in long-term stability. Eutectogels, rich in ES, offer excellent ionic conductivity and high charge injection capacity (CIC), but could suffer from leakage over time.[19] As the ES diffuses into the surrounding tissue, conductivity drops, CIC decreases, and impedance rises, all of which are detrimental to chronic implants. In addition, the uncontrolled release of solvent components could trigger local immune or inflammatory responses, further compromising device safety and long-term performance. By contrast, polyES removes the liquid phase, sidestepping solvent loss entirely. But removing the ionic media comes at a steep price since ionic transport slows dramatically in solid matrices, cutting conductivity and CIC. This is one of the grand challenges in polyES research: to recover high ionic transport without reintroducing instability. We expect that the incorporation of a CP into polyES may help overcome this issue; additionally, promising approaches include tailoring soft and hard monomer ratios, fine-tuning chemical and physical crosslinking, and optimizing HBA/HBD selection to balance mechanical integrity with ion mobility.

A second obstacle is the homogeneous physical dispersion of the CPs within the polyES matrix. As CPs are intrinsically immiscible with the polyES matrix, good dispersibility is required to promote partial interconnection between conductive domains, thereby enabling electronic transport through a percolation threshold mechanism.[40] Poorly dispersed phases can create localized brittleness, electrical "dead zones," and device fragility. Inhomogeneous conductivity not only affects stimulation uniformity but also undermines recording accuracy, making device performance unpredictable. How can this be solved? One approach is to use molecular additives or chemical modifications that encourage ordered conductive pathways.[19] Controlling morphology at the nanoscale could yield scaffolds with consistent mechanical and electrical properties in every region, a key step toward reliable, reproducible devices.

Another underexplored challenge is permeability. For a neural interface to remain functional over time, the material must allow the free exchange of nutrients, waste products, and signaling molecules across the tissue-device interface. Without this transport, metabolic waste can accumulate, proteins can adsorb, and cellular debris can build up, leading to biofouling and a gradual loss of device functionality.[41–43] At present, there is no clear evidence demonstrating whether polyES could maintain such permeability under physiological conditions, and it remains completely unexplored in this application. If polyES surfaces are inherently impermeable, for example, forming smooth, pore-free films, this could pose a significant barrier to long-term biocompatibility, as trapped waste or restricted fluid exchange might trigger immune activation or local tissue stress. Over months or years, this could compromise both signal quality and stimulation efficiency. Addressing this knowledge gap will be critical, since if polyES proves to lack intrinsic permeability, future designs may require engineered porosity, microchannels, or hybrid structures to sustain mass transport and prevent biofouling, thereby preserving device

performance in chronic applications. In one study, ultrasound-induced micro-vibrations from piezoelectric components have been explored to mimic permeability effects, while also stimulating cellular activity and modulating immune signaling pathways. This dual-function approach could address both mass transport limitations and therapeutic stimulation needs.[44] Two-photon polymerization and volumetric 3D printing could expand this design space by enabling sub-micrometer control of internal geometries and heterogeneous architectures, making it possible to create anisotropic pore networks, tortuous microchannels, or gradient-density lattices that tune permeability without compromising stability.[45,46] While the intrinsic permeability of the polyES matrix can be tuned by controlling crosslink density, HBA/HBD selection, and polymer architecture, microfabrication approaches can be employed to create continuous pathways that shorten effective diffusion lengths and enable predictable mass transport through the material. Micro-channels may also mitigate the formation of stagnant boundary layers by providing nearby reservoirs and continuous pathways for ionic/water exchange, thereby reducing local gradients in composition that may otherwise build up adjacent to impermeable regions. On the other hand, polyES matrices can be designed using zwitterionic or polyethylene glycol (PEG)-like monomers to reduce *in vivo* biofouling and manage interface failure.[47–49] These advanced tools could thus enable next-generation polyES-based devices that overcome diffusion barriers and enhance biological integration for improved long-term performance.

Degradation control presents another layer of complexity. In biodegradable systems, the rate must be precisely matched to the intended application; too fast, and the device fails prematurely, too slow, and residual fragments may linger, provoking immune reactions.[50,51] The heterogeneous composition of conductive composites can also cause uneven degradation, leading to unpredictable fragmentation patterns. Engineering at the microscale offers one potential solution, enabling more uniform breakdowns while reducing production costs. Moreover, degradability is not always the goal since short-term diagnostic devices may benefit from fully bioresorbable polyES, whereas chronic implants require non-degradable or hybrid strategies to ensure stability over years.[52] In these long-term applications, electrodes should also be miniaturized to enhance spatial resolution while delivering sufficient charge safely, avoiding irreversible electrochemical reactions. Excessive charge density at an electrode can trigger irreversible electrochemical events, including metal corrosion or dissolution, gas formation, and the generation of potentially toxic byproducts.[27]

Finally, integrating all these performance requirements into a single platform remains a major bottleneck. A mechanically compliant device may lose conductivity; one that is highly conductive may lack permeability; one that is stable over years may be too rigid to avoid immune responses. The central challenge, therefore, is not solving each parameter in isolation, but designing materials that satisfy the full set of mechanical, electrochemical, and biological criteria simultaneously. Fig. 3 provides a graphical summary of some key design challenges of polyES–CP systems.

The long-term effects of repetitive brain stimulation remain poorly understood, highlighting the need for ongoing safety and efficacy studies. Ethical concerns, including consent, privacy, and potential misuse, require careful attention. Collaborative efforts among neuroscientists, engineers, and clinicians, along with clinical trials and regulatory guidelines, are essential to ensure safe and responsible deployment of bioelectronic devices. Also, the long-term effects of implanted electrodes remain uncertain, particularly as the brain undergoes aging, disease progression, or other physiological changes. While conventional metal electrodes (*e.g.*, platinum, iridium) have been studied for decades and are known to face issues of durability, safety, and functional stability, polymer-based electrodes are comparatively newer, and their chronic performance *in vivo* remains largely unexplored.[53,54]

In short, the use of polyES-based materials for neural interfaces remains largely unexplored, and their potential is tempered by interrelated challenges in mechanical compliance, ionic transport, phase homogeneity, permeability, and degradation control. Overcoming these will require deep molecular-level design, advanced processing methods, and close collaboration between materials scientists, neurobiologists, and biomedical engineers. The prize, however, is worth the effort: a new class of neural implants capable of delivering stable, high-fidelity performance for years within one of the body's most demanding environments.

Future strategies and insights for advancing neural interfaces

Moving forward, a deep synergy between materials science, neurobiology, and biomedical engineering will be essential to develop next-generation neural implants that are safe, functional, and effective for both sensing and stimulation. To achieve this, future research should deepen our understanding of key parameters that influence polyES behavior, including functional group density, molecular architecture, crosslinking strategies, and nanofiller reinforcement. Currently, many of these critical factors remain poorly understood or underreported in the literature, limiting the rational design of optimized materials.

While most existing bioelectronic sensors rely on hydrogels or rigid materials, polyES have only recently been explored, and their use has been restricted to ionotronic applications, where they function as solid electrolytes supporting ionic transport without electronic conduction. For example, recent studies have demonstrated polyES as an ionically conducting medium for energy storage and soft ionotronic devices.[17] To the best of our knowledge, mixed ionic-electronic conducting polyES have not yet been reported, representing a significant unexplored opportunity for advancing bioelectronics. There is a pressing need to extend these investigations to brain neural interfaces. It is timely to explore whether these materials can meet the mechanical and electrochemical demands of neural stimulation and recording in brain tissue, which requires ultrasoft,

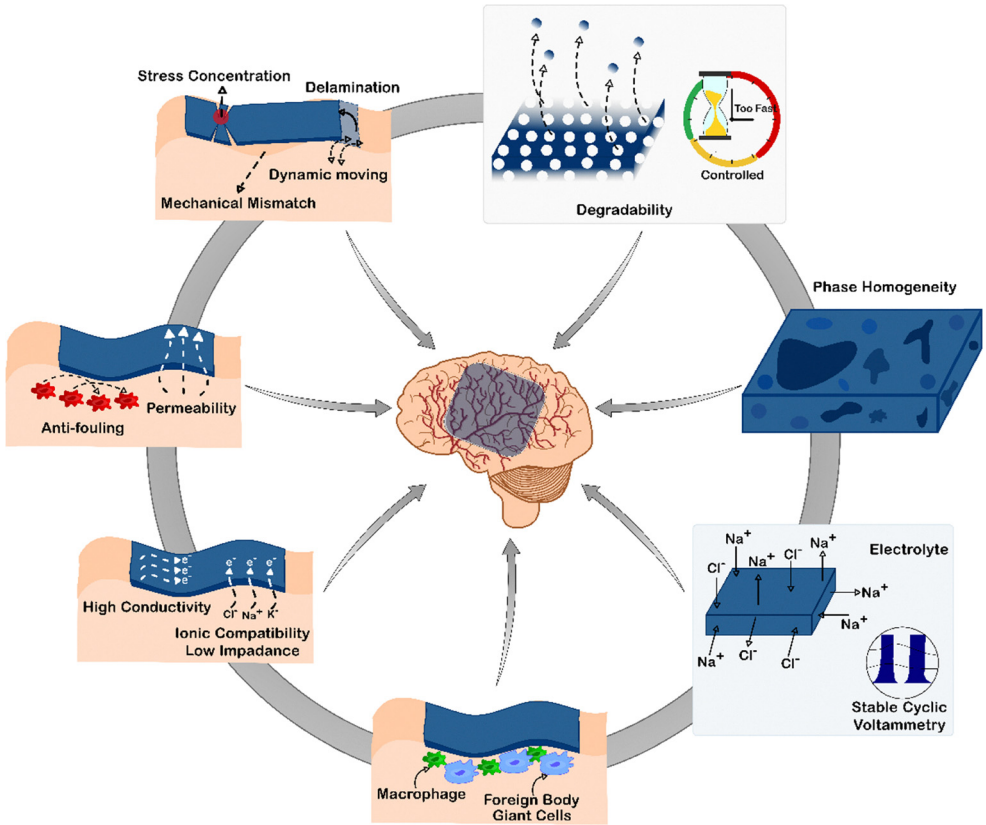

Fig. 3 Schematic illustration summarizing the crucial properties and performance requirements for next-generation neural implants based on polyES–CP materials.

flexible electrodes capable of precise signal acquisition with minimal tissue damage.[55]

In addition to mechanical performance, ensuring long-term stability is essential. Many devices degrade over time due to protein adsorption and cellular fouling on their surfaces, which can impair functionality.[37,41,42,50] Therefore, future studies should investigate how polyES-based devices could perform over extended periods: does the device maintain its function after long-term implantation? If so, efforts should focus on improving surface coatings and doping strategies, such as anti-fouling treatments, to preserve implant functionality and biocompatibility while minimizing immune responses.

Another important consideration is whether reducing the polyES-based device's specific surface area could help. A smaller specific surface area might reduce cell attachment, lower the risk of fouling, and decrease mechanical strain on brain tissue. To achieve this, it would be valuable to explore different fabrication methods aimed at producing smoother surfaces. Possible approaches include printing, melt-blending, and casting. Future work should compare these techniques to determine which yields the smoothest surface and the best overall performance for neural implants.

The biological impact of polyES/CPs extends beyond electrical conduction. Research is needed to elucidate how these materials influence the immune environment, modulate voltage-gated calcium channels (VGCCs), affect signaling pathways like MAPK (MEK/ERK), and promote secretion of bioactive factors. Understanding these interactions will be key to designing bioelectronic devices that actively support neural repair and regeneration.[44,52] An important open question for future studies is to what extent the unique chemical microenvironment of polyES can give rise to interfacial synergistic effects that facilitate bio-signal transduction and lower the associated energetic barriers.

Patient-centered considerations must also guide future development. Given that many neurological diseases predominantly affect the elderly, and older patients often cannot tolerate multiple surgeries, implantable bioelectronic devices should ideally be biodegradable. Copolymerization with biodegradable monomers provides an effective strategy to enhance their biodegradability.[56] Designing mixed conductive materials that remain stable and functional throughout their intended lifespan, then degrade safely without adverse effects, will greatly enhance clinical applicability and patient outcomes.

In summary, the future of neural bioelectronics lies in multidisciplinary collaboration, where advances in materials chemistry, device engineering, and biological understanding converge. Within this landscape, mixed conducting polyES emerge as a promising platform to enable next-generation implants that combine long-term safety with effective neural interfacing.

Author contributions

M. L. Picchio and A. Larrañaga conceived the idea of this opinion. M. Firuzeh and E. Giuzio wrote the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

No primary research results, software or code have been included and no new data were generated or analysed as part of this review.

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References

1 I. Y. Kuo and B. E. Ehrlich, *Cold Spring Harbor Perspect. Biol.*, 2015, **7**, a006023.
2 M. Jia and M. Rolandi, *Adv. Healthcare Mater.*, 2020, **9**, 1901372.
3 O. Bettucci, G. M. Matrone and F. Santoro, *Adv. Mater. Technol.*, 2022, **7**, 2100293.
4 C. F. Jones, L. Resina, F. C. Ferreira, P. Sanjuan-Alberte and T. Esteves, *J. Phys. Chem. C*, 2024, **128**, 11083.
5 M. S. Horrocks, K. E. Zhurenkov and J. Malmström, *APL Bioeng.*, 2024, **8**, 031503.
6 B. Lu, H. Yuk, S. Lin, N. Jian, K. Qu, J. Xu and X. Zhao, *Nat. Commun.*, 2019, **10**, 1043.
7 S. J. K. O'Neill, M. Ashizawa, A. M. McLean, R. Ruiz-Mateos Serrano, T. Shimura, M. Agetsuma, M. Tsutsumi, T. Nemoto, C. D. J. Parmenter, J. A. McCune, G. G. Malliaras, N. Matsuhisa and O. A. Scherman, *Adv. Mater.*, 2025, **37**, e2415687.
8 A. B. Mostert, *J. Mater. Chem. B*, 2022, **10**, 7108.
9 Y. Li, Q. Cheng, Z. Deng, T. Zhang, M. Luo, X. Huang, Y. Wang, W. Wang and X. Zhao, *Polymers*, 2024, **16**, 971.
10 I. E. Jacobs, Y. Lin, Y. Huang, X. Ren, D. Simatos, C. Chen, D. Tjhe, M. Statz, L. Lai, P. A. Finn, W. G. Neal, G. D'Avino, V. Lemaur, S. Fratini, D. Beljonne, J. Strzalka, C. B. Nielsen, S. Barlow, S. R. Marder, I. McCulloch and H. Sirringhaus, *Adv. Mater.*, 2022, **34**, e2102988.
11 Y. Zhuo, H.-L. Cheng, Y.-G. Zhao and H.-R. Cui, *Pharmaceutics*, 2024, **16**, 151.
12 S. P. Ijardar, V. Singh and R. L. Gardas, *Molecules*, 2022, **27**, 1368.
13 J. Afonso, A. Mezzetta, I. M. Marrucho and L. Guazzelli, *Green Chem.*, 2023, **25**, 59.
14 D. N. Jimat and M. H. Hasnuddin, Challenges, Toxicity and Socioeconomic and Environmental Impact Using DES, in *Deep Eutectic Solvents*, ed. D. N. Jimat, Springer, Singapore, 2026.
15 P. A. Mercadal, A. González, A. Beloqui, L. C. Tomé, D. Mecerreyes, M. Calderón and M. L. Picchio, *JACS Au*, 2024, **4**, 3744.
16 L. Mu, J. Gao, Q. Zhang, F. Kong, Y. Zhang, Z. Ma, C. Sun and S. Lv, *Processes*, 2023, **11**, 1986.
17 M. L. Picchio, A. Dominguez-Alfaro, R. J. Minari, J. D. Mota-Morales and D. Mecerreyes, *J. Mater. Chem. C*, 2024, **12**, 11265.
18 J. K. Nguyen, D. J. Park, J. L. Skousen, A. E. Hess-Dunning, D. J. Tyler, S. J. Rowan, C. Weder and J. R. Capadona, *J. Neural Eng.*, 2014, **11**, 056014.
19 P. Zhang, Y. Yang, Z. Li, Y. Xue, F. Wang, L. Shan, Y. Wang, X. Shi, K. Wu and J. Liu, *Adv. Funct. Mater.*, 2025, **35**, 2422869.
20 Y. Sun, Y. Zhang, Y. Guo, D. He, W. Xu, W. Fang, C. Zhang, Y. Zuo and Z. Zhang, *J. Nanobiotechnol.*, 2024, **22**, 244.
21 A. N. Galindo, D. A. Frey Rubio and M. H. Hettiaratchi, *Mater. Adv.*, 2024, **5**, 4025.
22 M. Kaluza, D. Ksiazek-Winiarek, P. Szpakowski, J. Czpakowska, J. Fijalkowska and A. Glabinski, *Int. J. Mol. Sci.*, 2025, **26**, 6477.
23 U. A. Weerasinghe, T. Wu, P. L. Chee, P. Y. M. Yew, H. K. Lee, X. J. Loh and K. Dan, *Green Chem.*, 2024, **26**, 8497.
24 Y. Zhang, Y. Wang, K. Zhao, M. Yang, Z. Ye and X. Zhang, *Discover Electron.*, 2025, **2**, 6.
25 B. Oh and P. George, *Brain Res. Bull.*, 2019, **148**, 10.
26 W. Klomjai, R. Katz and A. Lackmy-Vallée, *Ann. Phys. Rehabil. Med.*, 2015, **58**, 208.
27 D. D. Zhou and E. Greenbaum, *Implantable Neural Prostheses 2: Techniques and Engineering Approaches*, Springer, 2010, vol. 1.
28 W. Duan, U. Aregueta Robles, L. Poole-Warren and D. Esrafilzadeh, *Adv. Sci.*, 2024, **11**, 2306275.
29 H. Yi, R. Patel, K. D. Patel, L.-S. Bouchard, A. Jha, A. W. Perriman and M. Patel, *J. Mater. Chem. B*, 2023, **11**, 11006.
30 S. Song and P. M. George, *Neural Regener. Res.*, 2017, **12**, 1976.
31 M. Bianchi, S. Guzzo, A. Lunghi, P. Greco, A. Pisciotta, M. Murgia, G. Carnevale, L. Fadiga and F. Biscarini, *ACS Appl. Mater. Interfaces*, 2023, **15**, 59224.
32 P. Zhu, Z. Zhao and Y. Gao, *Front. Pharmacol.*, 2025, **16**, 1552586.
33 S. Lagarde, J. Modolo, M. Yochum, A. Carvallo, A. Ballabeni, D. Scavarda, R. Carron, N. Villeneuve, F. Bartolomei and F. Wendling, *Epilepsia*, 2024, **65**, 1744.
34 E. N. Zhang, J.-P. Clément, A. Alameri, A. Ng, T. E. Kennedy and D. Juncker, *Adv. Mater. Technol.*, 2021, **6**, 2000909.
35 H. Dawit, Y. Zhao, J. Wang and R. Pei, *Biomater. Sci.*, 2024, **12**, 2786.
36 K. M. Woeppel and X. T. Cui, *Adv. Healthcare Mater.*, 2021, **10**, 2002150.

37 H. J. Kim, J. H. Koo, S. Lee, T. Hyeon and D.-H. Kim, *Nat. Rev. Mater.*, 2025, **10**, 654.
38 J.-T. Kim, S. M. Cho, D. H. Youn, E. P. Hong, C. H. Park, Y. Lee, H. Jung and J. P. Jeon, *Acta Biomater.*, 2023, **167**, 335.
39 A. Golabchi, B. Wu, B. Cao, C. J. Bettinger and X. T. Cui, *Biomaterials*, 2019, **225**, 119519.
40 N. Tessler, Y. Preezant, N. Rappaport and Y. Roichman, *Adv. Mater.*, 2009, **21**, 2741.
41 Z. Bérces, K. Tóth, G. Márton, I. Pál, B. Kováts-Megyesi, Z. Fekete, I. Ulbert and A. Pongrácz, *Sci. Rep.*, 2016, **6**, 35944.
42 T. D. Y. Kozai, A. S. Jaquins-Gerstl, A. L. Vazquez, A. C. Michael and X. T. Cui, *ACS Chem. Neurosci.*, 2015, **6**, 48.
43 I. Sands, R. Demarco, L. Thurber, A. Esteban-Linares, D. Song, E. Meng and Y. Chen, *Adv. Mater.*, 2024, **36**, 2401750.
44 Q. Wang, Y. Wei, X. Yin, G. Zhan, X. Cao and H. Gao, *Adv. Funct. Mater.*, 2024, **34**, 2400217.
45 M. Malinauskas, A. Žukauskas, S. Hasegawa, Y. Hayasaki, V. Mizeikis, R. Buividas and S. Juodkazis, *Light: Sci. Appl.*, 2016, **5**, e16133.
46 B. E. Kelly, I. Bhattacharya, H. Heidari, M. Shusteff, C. M. Spadaccini and H. K. Taylor, *Science*, 2019, **363**, 1075.
47 Y. Wang, L. Shang, Y. Zhao and L. Sun, *Engineering*, 2022, **13**, 128.
48 M. J. Jensen, A. Peel, R. Horne, J. Chamberlain, L. Xu, M. R. Hansen and C. A. Guymon, *ACS Biomater. Sci. Eng.*, 2021, **7**, 4494.
49 N. Hui, X. Sun, S. Niu and X. Luo, *ACS Appl. Mater. Interfaces*, 2017, **9**, 2914.
50 S. Lv, Z. Xu, F. Mo, Y. Wang, Y. Duan, Y. Liu, L. Jing, J. Liu, Y. Wu, M. Wang, S. Zhang, Y. Liu, J. Liu, Y. Wu, M. Wang, Y. Song and X. Cai, *npj Flexible Electron.*, 2025, **9**, 40.
51 Y. Li, N. Li, N. De Oliveira and S. Wang, *Matter*, 2021, **4**, 1125.
52 B. Cao, Y. Huang, L. Chen, W. Jia, D. Li and Y. Jiang, *Biosens. Bioelectron.*, 2024, **259**, 116378.
53 E. Song, J. Li, S. M. Won, W. Bai and J. A. Rogers, *Nat. Mater.*, 2020, **19**, 590.
54 P. Oldroyd and G. G. Malliaras, *Acta Biomater.*, 2022, **139**, 65.
55 B. Ji, F. Sun, J. Guo, Y. Zhou, X. You, Y. Fan, L. Wang, M. Xu, W. Zeng, J. Liu, M. Wang, H. Hu and H. Chang, *Microsyst. Nanoeng.*, 2023, **9**, 126.
56 M. Castillo-Santillan, P. Quiñonez-Angulo, D. Maniar, J. R. Torres-Lubian, M. C. Gutiérrez, T. Pelras, A. J. J. Woortman, Q. Chen, M. G. Pérez-García, K. Loos and J. D. Mota-Morales, *RSC Appl. Polym.*, 2024, **2**, 403.