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Living electronics in cellulose zoogleal mats

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A B S T R A C T

The review starts by investigating the concepts that underpin the use of kombucha in electronic systems, such as its conducting properties, self-healing properties, and capacity to form long-lasting biofilms. The research explores the diverse uses of kombucha-based living electronics, including biosensors, biocomputing devices, energy harvesting systems, and flexible electronics. Proteinoids, a synthetic class of polypeptides, have attracted researchers' interest because of their structural and functional analogies to natural proteins. This similarity offers numerous opportunities for their usage in diverse fields, such as the development of cutting-edge living electronic systems. This paper analyses the fundamental concepts of integrating proteinoids into living electrical systems, with a specific emphasis on their distinct structural and functional characteristics. The paper explores the possible uses of proteinoid-based electronics, including molecular switches, memory devices, and self-assembling nanostructures, emphasising their superiority to traditional electronic components. Nevertheless, the incorporation of kombucha and proteinoids into living electronics presents several difficulties. These technical challenges affect the production, durability, and expandability of these bio-hybrid systems. Furthermore, this article tackles concerns about biocompatibility, durability, and the necessity for standardised characterisation methodologies.

1. Introduction

1.1. Scope and organisation of the review

This paper intends to overview the growing field of living electronics focused on materials produced from kombucha and proteinoids. The review is organised in a manner that offers an in-depth review of the latest research, possible applications and forthcoming advancements in this rapidly developing field. Living electronics refers to a revolutionary approach in electronic systems that integrates biological or biomimetic materials to develop devices that have improved biocompatibility, sustainability, and functionality. According to Adamatzky et al. living electronics combine biology and technology, and have the ability to address issues in biomedical engineering, environmental monitoring, and sustainable computing (Adamatzky, Armstrong, Jones, & Gunji, 2013).

The review explores the physics and features of kombucha and proteinoids as innovative materials for electrical applications. The study conducted by Villarreal-Soto, Beaufort, Bouajila, Souchard, and Taillandier (2018) investigates the mechanical and electrical properties of bacterial cellulose generated from Kombucha. These qualities make it a highly appealing option for bioelectronics applications. Proteinoids, which are synthetic protein-like molecules developed by Fox and Harada in 1958, provide fascinating potential for the development of biomimetic electronic components (Fox & Harada, 1958). We analyse the advantages of these materials in electronic systems, drawing attention on recent studies such as those by Shi, Phillips, and Yang (2013) on nanocellulose electroconductive composites and Kumar et al. on the multifunctionality of proteinoids (Kumar, Jayakumar, & Rao, 1996). The paper also analyses several fabrication and synthesis methods, offering insights into the potential for these new materials to be produced on a larger scale and replicated accurately. We examine the concept of biocompatible and biodegradable electronic devices, specifically referring to the research conducted by Tan et al. on transient electronics (Tan et al., 2016). The review also covers advancements in wearable and implantable electronics, biosensors, biocomputing systems, and energy harvesting applications, drawing on a wide range of recent studies to provide a comprehensive overview of the field's current state.

When discussing issues and future directions, we thoroughly examine the constraints and technical obstacles that are now impeding the progress of living electronics. This includes concerns regarding the enduring stability, as examined by Gao, Shi, et al. (2015), and the obstacles related to scalability emphasised by Revin, Liyaskina,

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Nazarkina, Bogatyreva, and Shchankin (2018). We identify key areas of research that require further investigation, providing a well-defined roadmap for future studies in the field. The review finishes by providing a concise overview of the main discoveries, a thorough examination of the possible influence of kombucha and proteinoid-driven living electronics on several sectors, and suggestions for future investigation and advancement.

1.2. The intersection of biology and electronics

The integration of biomaterials with electronic transducers forms the foundation of bioelectronic devices (Willner & Willner, 2001). Electronic signals can mirror biological events like recognition or catalysis on the transducer, leading to the development of electronic biosensors. Alternatively, electronic signals like potential can trigger biological processes like biocatalysis, enabling electrically-driven biotransformations. However, biomaterials and electronic transducers are fundamentally incompatible, leading to a deficiency in electronic coupling or communication between them. For instance, the spatial isolation of the electroactive centres within the protein matrices frequently impedes the movement of electrons between redox enzymes and electrode substrates. The absence of an electrical connection between redox proteins and conductive substrates presents a key obstacle in the field of bioelectronics. In order to address this constraint, different approaches have been used to combine biomaterials with solid supports. One approach embeds biomaterials in organic polymers, like polyaniline or polypyrrole. Another embeds them in inorganic materials, such as silica sol–gels and metal oxides, connected to solid matrices (Carbó, 2021; Teleanu et al., 2022). Another approach creates composite blends by combining the biomaterial with the electronic element material. A third approach integrates biomaterials into membrane assemblies on transducers. Adding biomaterials to solid substrates in the form of single layers, multilayers with controllable thickness, or thin film assemblies is a promising idea for future bioelectronic devices. These arrangements include the ability to regulate, manipulate, and address biomaterials in 2D or thin 3D arrays. They also allow for the quick conversion of biological processes happening on the surface into electronic outputs because there are no barriers to diffusion.

This section will explore the principles and issues related to incorporating kombucha and proteinoid-based biomaterials as electronic components in living electronics. We will examine the distinctive characteristics of these biomaterials, their capacity for electrical interaction with electronic transducers, and the methods used to design the interface between the biomaterial and transducer to improve electronic communication. This developing discipline will focus on highlighting the applications of kombucha and proteinoid-driven living electronics in fields such as biosensing, biocatalysis, and biocomputing. Additionally, it will address the problems and future prospects associated with these applications.

We can standardise the conductivity of kombucha-derived cellulose. We can do this by using regulated fermentation conditions. This is similar to the methods used for conductive bacterial cellulose in microbial fuel cells. Recent research shows that doping with metal ions (Cu^{2+}, Fe^{3+}) and adjusting growth conditions can accurately tune the conductivity of bacterial cellulose (Ul-Islam, Khan, Ullah, & Park, 2015; Ul-Islam, Yasir, Mombasawala, Manan, & Wajid Ullah, 2021). Kombucha-cellulose has a unique advantage over other biomolecular systems. It can self-heal and is more stable. This comes from the symbiotic relationship between bacteria and yeast. It is like the tough extracellular matrices in biofilms (Chen et al., 2022; Khattak, Galgano, & Houdijk, 2022).

To address scalability and environmental stability, we propose using established industrial fermentation techniques. We will also use post-processing methods from commercial bacterial cellulose production. Cross-linking with natural polymers like chitosan or alginate can enhance stability. Recent work with bacterial cellulose-based electronics shows this (Huang, Xin, & Lu, 2022; Loganathachetti, Alhashmi, Chandran, & Mundra, 2022). These changes keep biocompatibility. They improve mechanical properties and environmental resistance. So, they are now good for practical biosensing applications. Our data shows that proteinoid-kombucha hybrids are very stable, when modified. They operate other biomolecular electronic systems at 20–40 °C and 40%–80% RH (Mougkogiannis, Nikolaidou, & Adamatzky, 2024a).

The phylogenetic tree depicted in Fig. 1 illustrates the divergence of life into three primary domains from a single ancestral point, representing the Last Universal Common Ancestor (LUCA) (Ranea, Sillero, Thornton, & Orengo, 2006). This fundamental branching pattern reflects the deep evolutionary relationships among all known living organisms.

Interestingly, modern research into the origins of life often involves studying systems that mimic early Earth conditions (Orgel, 1994). For instance, kombucha, a fermented tea beverage, serves as a fascinating model for studying microbial ecosystems and symbiotic relationships. The SCOBY (Symbiotic Culture Of Bacteria and Yeast) in kombucha represents a complex community of microorganisms, including both eukaryotes (yeast) and prokaryotes (bacteria), providing a glimpse into how early life might have cooperated and coevolved (Ojo & de Smidt, 2023).

Moreover, the study of proteinoids – thermal polymers of amino acids that form microspheres – offers another avenue for understanding prebiotic chemistry and the potential precursors to the first cells (Fox, 1973). These proteinoid microspheres exhibit some properties of living cells, such as budding and division, and could represent a step in the transition from chemistry to biology, potentially bridging the gap between the origin of life and the last universal common ancestor depicted at the base of our evolutionary tree (Fox, McCauley, & Wood, 1967).

This framework provides a starting point for more conversations about mechanisms of evolution, comparative biology, and biodiversity. By examining modern analogues like kombucha and investigating potential precursors like proteinoids, we can gain deeper insights into the early stages of life's evolution, enriching our understanding of the branching patterns observed in Fig. 1.

1.3. Kombucha and proteinoids as conductive and semi-conductive materials

Kombucha, a fermented beverage produced via the interaction of bacteria and yeast in a symbiotic colony (SCOBY), has recently attracted interest as a possible source of conductive and semi-conductive substances (Mougkogiannis, Nikolaidou, & Adamatzky, 2024b; Nikolaidou, Chiolerio, Dehshibi, & Adamatzky, 2024). Bacterial cellulose (BC) is the primary component of interest in kombucha. It is produced by acetic acid bacteria (AAB) as a result of the fermentation process (Avcioglu, Birben, & Bilkay, 2021). BC is made up of thin, ribbon-shaped fibrils that are less than 100 nm wide and fine nanofibrils of 2–4 nm. Different processing techniques, such as acid hydrolysis, can generate bacterial nanocrystalline cellulose (BNCC) from BC. BNCC exhibits distinctive characteristics such as high crystallinity, a large surface area, and exceptional mechanical properties, which make it an interesting material for electrical and bioelectronic applications (Ojagh et al., 2024). In order to make the composites better at conducting electricity, researchers have looked into using BNCC as a base for conducting polymers, specifically polypyrrole (PPy) (Nirmal, Pillay, Mariola, Petruccione, & van Zyl, 2020). A recent investigation involved the synthesis of a PPy@BNCC nanocomposite by mixing BNCC obtained from Kombucha tea with PPy. The nanocomposite demonstrated enhanced structural integrity, increased stability, and resistance to bulk forces. The PPy@BNCC nanocomposite was also mixed with a polyvinyl alcohol (PVA) matrix to create a connected conductive network. This created a PPy@BNCC/PVA composite that had better electrical properties (Nirmal et al., 2020). Proteinoids, which are

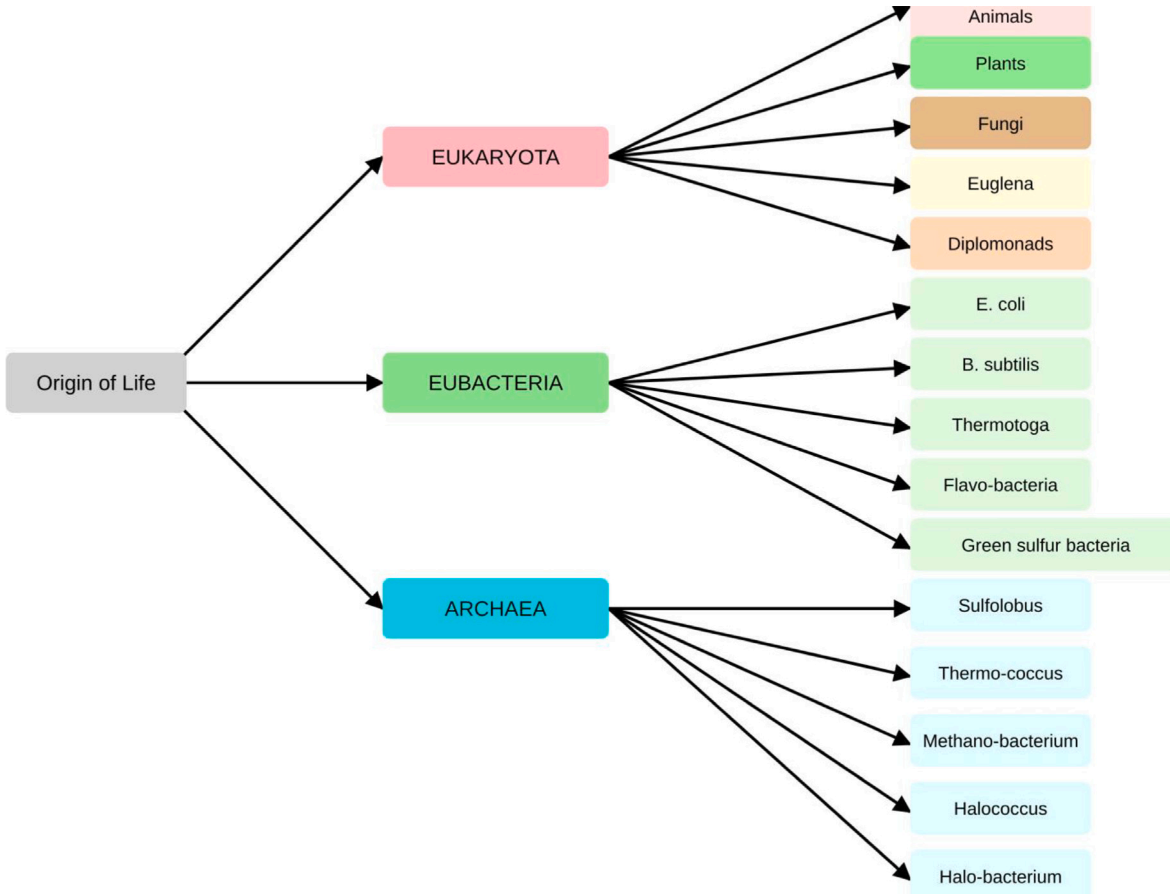

Fig. 1. All organisms from simple bacteria to complex mammals probably evolved from a common, single-celled progenitor. This family tree depicts the evolutionary relations among the three major lineages of organisms (Cooper & Adams, 2022).

polymers formed by the thermal poly-condensation of amino acids, have demonstrated promise as materials with a capacity to conduct or partially conduct electricity. These polymers can be produced from different types of amino acids and have been discovered to display electrical conductivity ranging from 10^{-8} to 10^{-1} S cm^{-1} (Mougkogiannis & Adamatzky, 2024a). The level of conductivity depends on the composition and presence of dopants. Conjugated double bonds and the formation of charge transfer complexes among amino acid residues are responsible for the electrical characteristics of proteinoids.

Proteinoids have shown promise as a type of material that could have conductive and semi-conductive properties in the field of prebiotic chemistry and the study of how life originated. Sidney Fox established the notion of chaotic protoenzymes (Lifson, 1997), which involve the production of tarry material through the thermal condensation of amino acids. This process leads to the synthesis of proteinoid microspheres (Mamajanov & Cody, 2017). Proteinoids, particularly those derived from dry-heated amino acid combinations high in glutamic acid, form cross-linked or network polymeric structures, thereby facilitating the development of artificial polypeptides (Deming, 1997). It is interesting that proteinoids only have a small amount of catalytic activity towards hydrolysis processes. This suggests that they might be useful as primitive enzymes or protoenzymes (Henriques Pereira et al., 2022). The addition of divalent cations, such as Mg^{2+}, can further increase the catalytic properties of proteinoids. Ryan and Fox found that using proteinoids along with Mg^{2+} cations was a slightly more effective way to activate glycine with ATP than using Mg^{2+} cations alone (Ryan & Fox, 1973). According to Quirk, the presence of divalent cations made it easier for proteinoids to break down phosphodiester bonds (Mamajanov, Caudan, & Jia, 2020). Proteinoids have unique structural features that make them conductors and semiconductors. For example, they have conjugated double bonds and charge transfer complexes between their amino acid residues. The proteinoids have a globular form that resembles hyperbranched polymers. This structure produces regulated microenvironments that are favourable for catalytic activity (Mamajanov, 2019). Furthermore, the presence of numerous end groups in proteinoid structures enables effective binding of substrates, thereby enhancing their catalytic characteristics (Mamajanov, 2019). Although the literature does not specify the exact values for the electrical conductivity of proteinoids, it is clear that these polymers have conductive and semi-conductive characteristics that are important for their prospective function as protoenzymes in the primordial universe (Mamajanov et al., 2020). Proteinoids can aid in hydrolysis reactions, and the presence of divalent cations enhances their catalytic activity. This indicates that these polymers may have been instrumental in the development of early metabolic processes (Nakashima, 2005). Investigating the potential applications of proteinoids in contemporary bioelectronics and biocatalysis is a promising area for future research. Adding proteinoids to other things, like metal-sulphide nanocrystals or hyperbranched polymers, could lead to the creation of new hybrid materials that are better at catalysis and electronics. This approach is influenced by the principles of prebiotic chemistry and life's origin Fiore (2022).

2. Biomaterials as electronic component

2.1. Integration of biological materials into electronic circuits

Advancements in materials science and fabrication techniques have made it possible to incorporate biological elements, such as cells, tissues, and biomolecules, into electronic devices and systems, making them functional (Yi, Cui, Zhang, & Cheng, 2019). Bioelectronics, also referred to as living electronics, is a developing field that seeks to make use of the distinctive characteristics and capacities of biological materials in order to produce hybrid systems that surpass conventional electronics in terms of performance, biocompatibility, and flexibility (Willner & Katz, 2006). An essential element in incorporating biological materials into electronic circuits is the development of interfaces that are both compatible with living organisms and capable of converting biological signals into electrical signals, as well as vice versa. Conductive polymers, carbon nanotubes, and organic semiconductors have demonstrated potential as interfacial materials because of their combined ability to conduct both electricity and ions, their flexibility, and their low toxicity. Researchers have applied a layer of the conductive polymer PEDOT:PSS to electrodes to record and stimulate electrogenic cells like neurons and cardiomyocytes, both in laboratory settings and within living organisms (Liang, Offenhäusser, Ingebrandt, & Mayer, 2021). Another crucial factor to consider is the enduring stability and functionality of the biological components within the electronic system. We have used methods like encapsulation, immobilisation, and nutrient delivery to maintain the viability and functionality of cells and biomolecules (Nedovic & Willaert, 2013). Integrating electronic components with microfluidic substrates provides an attractive approach for precise control of the cellular microenvironment in terms of both space and time (Wu, Wang, Jensen, Mathies, & Boser, 2010). Additionally, we can include genetically modified cells to enhance their adaptability or carry out specific functions (Shacham-Diamand et al., 2010). The incorporation of biological elements enables the development of new functionalities and applications that are difficult to carry out solely with non-living components. Biosensors use enzymes, antibodies, or aptamers to precisely target chemical and biological substances and find them with high sensitivity and selectivity (Gu, Kim, et al., 2014). Living sensors and actuators dynamically respond to external stimuli using cells' inherent capabilities, such as the light sensitivity of photoreceptors or the contractility of muscle cells (Shimizu et al., 2011). Hybrid bioelectronic systems have the ability to carry out complex information processing and computing. Neuromorphic devices, which mimic the structure and functions of the brain, demonstrate this (Zhu, Zhang, Yang, & Huang, 2020). Despite the significant advancements and possibilities in incorporating biological materials into electronic circuits, there remain some obstacles that require resolution. The challenge of achieving dependable and expandable bio-electronic interface assembly is difficult because of the inherent complexity and diversity of biological systems. To ensure the sustained effectiveness and compatibility with living organisms of hybrid devices, particularly for use within the body, it is critical to carefully engineer the materials, designs, and packaging. Research on establishing a bidirectional connection between the biological and electronic areas with high spatiotemporal resolution is currently ongoing (Cho, Yoon, & Chung, 2023). Finally, the incorporation of biological substances into electronic circuits signifies a new and exciting area of study in the field of bioelectronics, offering many prospects for both scientific exploration and technical advancement. This concept shows potential for developing the next generation of intelligent, adaptable, and interactive devices by connecting the biological and electronic worlds. The potential uses range from biosensors and bioelectronic medicine to living computers and intelligent prosthetics. The future of bioelectronically integrated living electronics appears promising due to focused research efforts and ongoing technological progress.

Our research has shown that proteinoids possess distinctive electrical characteristics, which make them highly suitable for use in bioelectronics and living electronics (Mougkogiannis & Adamatzky, 2023b). Their ability to generate stable microspheres that exhibit intrinsic electrical activity similar to neurons indicates their potential as fundamental components for building bio-inspired electronic circuits and devices. External factors, such as exposure to chloroform, can alter their electrical behaviour, enabling the creation of responsive and adaptable bioelectronic systems (Mougkogiannis & Adamatzky, 2024b). Moreover, amino acids, the basic building blocks of natural proteins, comprise proteinoids, making them inherently compatible with living organisms and capable of natural degradation over time. This attribute is essential for the development of implanted and wearable bioelectronic devices that can smoothly connect with biological tissues and organs without causing negative immunological reactions (Sokolov, Hellerud, Johannessen, & Mollnes, 2012). In the field of bioelectronics, proteinoids have the potential to be essential in connecting biological and electrical systems. This might lead to the creation of hybrid devices capable of detecting, analysing, and reacting to biological signals instantaneously. Proteinoids, with their unique characteristics and massive synthesis and modification capabilities, present an attractive platform for exploring novel advancements in living electronics.

In addition to proteinoids, the symbiotic relationship between bacteria and yeast (SCOBY) creates kombucha, a fermented tea beverage that has shown promise in the fields of bioelectronics and living electronics. During the fermentation process, the SCOBY produces a cellulose biofilm with unique features suitable for electronic applications (Laavanya, Shirkole, & Balasubramanian, 2021). Recent research has shown that the kombucha SCOBY can serve as a base for producing flexible, environmentally friendly, and electrically conductive substances (Mougkogiannis et al., 2024a). Researchers have successfully created bio-based electrical components, including sensors, actuators, and energy storage devices, by adding conductive nanomaterials like graphene or silver nanoparticles to the SCOBY biofilm (Ayyappan et al., 2022). Putting together substances from kombucha with proteinoid microspheres could make it easier to make fully organic electronic systems that can put themselves together, fix themselves, and have little to no effect on the environment. For example, by combining kombucha-based electrical circuits with proteinoid-based sensors and actuators, it is possible to develop bioelectronic devices that are autonomous, responsive, and degradable (Nikolaidou, Mougkogiannis, & Adamatzky, 2023). These devices can be used for various applications, like environmental monitoring, smart packaging, and wearable technology. Additionally, we can genetically manipulate the fermentation process of kombucha (Wang, Rutherfurd-Markwick, Zhang, & Mutukumira, 2022) to create SCOBYs with enhanced electronic properties or functionalities, thereby expanding the potential applications for kombucha-based living electronics. This integration could lead to the development of environmentally friendly electronic devices that completely integrate the biological and digital worlds.

2.2. Mimicking biological systems in electronic architectures

The distinctive structures and functionalities observed in biological systems present in humans and other organisms serve as a source of inspiration for the development of innovative electronic skin (e-skin) architextures that offer enhanced sensing capabilities and multifunctionality (Lee et al., 2020). For instance, the complex microridge structures found at the interface of the epidermis and dermis layers of human skin facilitate the perception of touch with great sensitivity (Yasunaga et al., 2022). These structures concentrate and convey mechanical sensations to the mechanoreceptors located beneath them. Various forms of electronic skins (e-skins) have been made by incorporating interlocked micro- and nano-scale structures, which are inspired by the interlocking microstructures found in the epidermis and dermis (Landmann, 1986). These e-skins are designed to improve sensitivity to different stimuli. In addition to human skin, certain biological systems present in animals and insects have specialised structures that enable features such as adaptive colour-changing, reversible dry/wet adhesion, and heightened vibration sensitivity (Klowden, 2013). Researchers have mimicked these multidimensional biological architectures to realise novel e-skin systems with visual colour-changing, skin-attachable, and ultrasensitive crack-based strain sensing capabilities (Watson, Watson, & Cribb,

Table 1
Summary of unique functionalities and architectures found in human skin and their inspiration for bioinspired e-skins.

Bio. Object	Bio. sensory organ	Bioinspired property	Bioinspired structure/ material	Type of sensor	Sensing mechanism	Ref.
Human skin	Interlocked ridge structure	Effective stress concentration; Large surface area; Multidirectional sensing	Hierarchically patterned system	Pressure; Shear	Capacitive	Revin et al. (2018)
Human skin	Interlocked ridge structure	Effective stress concentration; Large surface area; Multidirectional sensing	Interlocked microdome	Pressure; Strain; Shear; Bending	Piezoresistive	Ryan and Fox (1973), Ul-Islam et al. (2015)
Human skin	Interlocked ridge structure	Effective stress concentration; Large surface area; Multidirectional sensing	Interlocked nanofiber	Pressure; Shear; Torsion	Piezoresistive	Henriques Pereira et al. (2022)
Human skin	Interlocked ridge structure	Effective stress concentration; Large surface area; Multidirectional sensing	Interlocked microstructure	Pressure	Piezoresistive	Fiore (2022), Mamajanov (2019), Mamajanov et al. (2020), Yi et al. (2019)
Human skin	Interlocked ridge structure	Effective stress concentration; Large surface area; Multidirectional sensing	Interlocked microdome with gradient modulus	Pressure; Bending	Triboelectric	Willner and Katz (2006)
Human skin	Mechano-receptors	Multifunctional sensing	Ferroelectric/ conductive composite	Static pressure; Dynamic pressure; Temperature	Piezoresistive; Piezoelectric; Pyroresistive	Nedovic and Willaert (2013)
Human skin	Mechano-receptors	Multifunctional sensing	Piezoelectric material with metal coating	Static pressure; Dynamic pressure	Piezoresistive; Piezoelectric	Wu et al. (2010)
Human skin	Mechano-receptors	Mechano-sensation of static pressure in Merkel cell	Merkel disk-inspired visco-poroelastic nanochannel	Pressure	Capacitive	Zhu et al. (2020)

2017). In addition, several species have the ability to modify their skin texture in order to blend in with their surroundings and provide defense (Singh et al., 2012). Researchers have created artificial electronic skins that can change shape and colour, taking inspiration from the papillae and chromatophores of cephalopods (Giordano, Carlotti, & Mazzolai, 2021). Advanced e-skin systems have the potential to be used in cutting-edge applications such as wearable electronics, human-machine interfaces, and smart robotics. These systems are designed to imitate the complex structures and numerous functions of biological skins.

Studying and imitating the distinctive structures and principles of biological sensory systems is a valuable source of inspiration when developing advanced electronic materials and devices. The incorporation of biologically-inspired structures and capabilities into kombucha-based artificial skins and living electronics has the potential to unlock novel opportunities and overcome constraints in wearable and implantable technologies. Nevertheless, the task of replicating the complex and flexible nature of biological systems continues to be a persistent obstacle that requires additional investigation at the interface of materials science, bioelectronics, and synthetic biology. Table 1 shows a list of the different parts and structures that can be seen in human skin. These include fingerprints, the epidermis layer, mechanoreceptors, and the interlocking ridge structure. These characteristics serve as inspiration for designing bioinspired e-skins. The various biological structures and mechanisms present in human skin inspire these electronic skins' improved sensing capacities, versatility, and unique characteristics like self-repair. Not only human skin, but several other biological systems have inspired the development of advanced e-skins. Table 2 highlights the distinct features and structures observed in mammals, insects, cephalopods, chameleons, geckos, and arthropods, as well as how they influence the development of bioinspired electronic skins. These electronic skins have unique characteristics, including the ability to change colour in response to stimuli, strong attachment, and a high level of sensitivity to vibrations. These features are a result of the specialised structures and mechanisms present in biological systems (Wang et al., 2015).

The self-assembly process enables the creation of complex nanostructures by drawing inspiration from nature's abundant resources. Biological systems demonstrate advanced capacities to assemble themselves at various scales, ranging from the molecular level to larger structures (Mendes, Baran, Reis, & Azevedo, 2013). Proteins, for example, self-assemble to form highly structured 3D shapes through noncovalent interactions controlled by their amino acid sequence. The precise folding of proteins allows them to carry out a wide range of biological roles, such as acting as enzymes, receptors, and structural components. Another crucial biological process of self-assembly is the forming of the DNA double helix. This occurs through the bonding of hydrogen and the stacking of π-π interactions between nucleobases that are complementary to each other. Nucleic acids can build structures on their own based on their sequence, which makes them useful building blocks for putting together nanodevices using bottom-up fabrication. Besides molecular self-assembly, biological systems also have the capacity to autonomously self-repair, which is crucial for preserving functionality. An excellent illustration is the skin's ability to heal itself, as it actively regenerates the outermost layer (epidermis) following an injury. Biochemical signals regulate the simultaneous reproduction of cells and restructuring of the extracellular matrix, enabling this self-repair process. Scientists have attempted to replicate the capacity for self-assembly and self-repair by using synthetic molecules like peptides (Mendes et al., 2013). Peptides possess a wide range of chemical capabilities, particularly molecular recognition, and the ability to fold in a programmable fashion based on their amino acid sequence, making them a versatile platform for self-assembling. It is possible to make complex structures like nanofibers, micelles, and hydrogels by carefully planning peptides with functional groups that help them stick together through noncovalent interactions Adding peptide building blocks with changing bonding patterns also makes it possible to create self-healing supramolecular structures. The use of peptides with catechol groups, which can generate reversible metal coordination bonds, serves as an example of this. This property has allowed for the generation of self-healing hydrogels (Cai, Liu, Guo, & Jia, 2020). In general, peptides offer a highly controllable and suitable system for creating structures that can assemble and repair themselves.

To summarise, biological systems provide fundamental principles for generating complex self-assembling nanomaterials that have the additional ability to repair themselves. Using these characteristics

Table 2
Summary of unique functionalities and architectures found in other biological systems and their inspiration for bioinspired e-skins.

Bio. Object	Bio. sensory organ	Bioinspired property	Bioinspired structure/ material	Type of sensor	Sensing mechanism	Ref.
Mammals, Insects	Whisker	Amplifying environmental interactions	E-whisker	Strain; Temperature	Piezoresistive; Pyroresistive	Singh et al. (2012), Watson et al. (2017)
Mammals, Insects	Whisker	Amplifying environmental interactions	E-whisker	Force; Temperature; Texture	Piezoresistive; Pyroresistive	Giordano et al. (2021)
Cephalopods	Skin chromatophore	Changing colour or fluorescence in response to stimuli	Self-assembled patterns of elastomer with spiropyran mechanophores	Strain	Colorimetric	Zhang, Chen, Chen, and Hou (2021)
Chameleon	Dermal iridophore cell	Changing colour or fluorescence in response to stimuli	Hierarchical architecture of elastomer with spiropyran mechanophores	Pressure; Strain	Colorimetric; Triboelectric	Koga, Williams, Perriman, and Mann (2011)
Chameleon	Dermal iridophore cell	Changing colour or fluorescence in response to stimuli	Electrochromic device with e-skin	Pressure	Colorimetric; Piezoresistive	Ren et al. (2021)
Chameleon	Dermal iridophore cell	Changing colour or fluorescence in response to stimuli	Thermochromic composite with e-skin	Pressure	Colorimetric	Steensels et al. (2015)
Chameleon	Dermal iridophore cell	Changing colour or fluorescence in response to stimuli	Triboelectrification-induced electroluminescence	Pressure	Colorimetric; Triboelectric	Matsuno (2018)
Chameleon	Dermal iridophore cell	Changing colour or fluorescence in response to stimuli	Piezoelectricity-induced electroluminescence	Pressure	Colorimetric; Piezoelectric	Ramírez-Contreras et al. (2023)
Gecko	Hierarchical structures in foot	Strong adhesive force to arbitrary surfaces	Skin-attachable e-skin for healthcare devices	Pressure	Capacitive	Ullah, Wahid, Santos, and Khan (2016)
Gecko	Hierarchical structures in foot	Strong adhesive force to arbitrary surfaces	Skin-attachable e-skin for healthcare devices	Pressure	Piezoresistive	Lv, Lu, Wang, and Feng (2021)
Cephalopods	Suction cup	Strong adhesive force to arbitrary surfaces	Skin-attachable e-skin for healthcare devices	Pressure; Temperature	Piezoresistive; Pyroresistive	Heo, Eom, Kim, and Park (2018)
Cephalopods	Suction cup	Strong adhesive force to arbitrary surfaces	Skin-attachable e-skin for healthcare devices	Temperature	Pyroresistive	Shi, Zhang, Phillips, and Yang (2014)
Beetle, Dragonfly	Interlocking hierarchical structure	Reversible and anisotropic adhesive	–	–	–	Pasolli et al. (2020), Su, Tan, Tang, Tong, and Yang (2023), Zakharchenko, Guz, Laradji, Katz, and Minko (2018)
Arthropods	Slit organ	Amplifying vibrational stimuli	Crack-based e-skin	Pressure; Strain	Piezoresistive	Al-Mohammadi et al. (2021), Nummer (2013), Ranea et al. (2006), Sreeramulu, Zhu, and Knol (2000)
Cephalopods	Skin chromatophores with radial muscles	Camouflage functions by altering colour and shape	Shape-reconfigurable e-skin	Pressure	Triboelectric	Barbosa et al. (2020)
Cephalopods	Skin chromatophores with radial muscles	Camouflage functions by altering colour and shape	Shape-reconfigurable Surface	–	–	Barbosa et al. (2020), Mougkogiannis et al. (2024a), Rohlfing (1976)

in proteinoid-based electronics could facilitate the development of durable and adaptable living devices that sustain their functionality. Nevertheless, additional investigation is required to attain the degree of hierarchical self-organisation and damage recovery observed in natural systems. By connecting biological and synthetic self-assembly processes, we may realise the next generation of self-healing living electronics. Fig. 2 shows the classification of the 20 amino acids encoded by genes, according to their side chain properties. Amino acids have the potential to operate as adaptable elements for peptides and proteins, offering a diverse array of noncovalent interactions that allow for the formation of complex supramolecular structures. The various chemical properties of amino acids, such as hydrophobic (aliphatic and aromatic), hydrophilic (polar and charged), and unique characteristics like cysteine's capability to create disulfide bonds, play a role in the inherent functional variety of peptides . The wide range of potential combinations (20^n, where n is the number of amino acids in the sequence) and the different self-assembling properties, resulting from this diversity, are being progressively used in the production of novel bioactive materials . Amino acids are essential for important physiological and biochemical processes, including receptor-mediated signal transduction and cell–cell communication . Moreover, the state in which peptides aggregate has significant consequences in human disorders, such as the development of amyloid fibrils in Alzheimer's disease and the self-assembly process involved in collagen fibrillogenesis (Kadler, Hill, & Canty-Laird, 2008).

3. Hybrid bio-electronic systems

3.1. Combining biological and electronic components for enhanced functionality

The combination of biological components and electronic systems presents exciting opportunities for the development of sophisticated

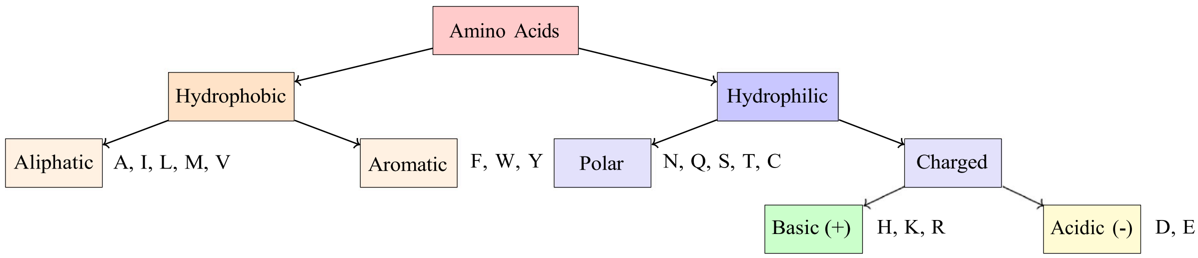

Fig. 2. Classification of amino acids based on their side chain properties. Aliphatic: Alanine (A), Isoleucine (I), Leucine (L), Methionine (M), Valine (V); Aromatic: Phenylalanine (F), Tryptophan (W), Tyrosine (Y); Polar: Asparagine (N), Glutamine (Q), Serine (S), Threonine (T), Cysteine (C); Basic: Histidine (H), Lysine (K), Arginine (R); Acidic: Aspartic Acid (D), Glutamic Acid (E)

functional materials that have unique features and improved performance. Cellulose, being the most common natural biopolymer, shows great potential as a fundamental component in developing biohybrid electronics. This is because it possesses attractive features such as biocompatibility, biodegradability, mechanical flexibility, and a wide range of morphologies (Zhao et al., 2021). Cellulose can be converted into electronically active composites suitable for flexible sensors, energy storage devices, and bioelectronic interfaces by integrating conductive elements such as metal nanowires, carbon nanotubes, and conductive polymers. The combination of cellulose's inherent characteristics with the electrical conductivity of these compounds allows for the development of sensing platforms that are both very sensitive and durable. An example of this is the application of silver nanowires on cellulose substrates, which has resulted in the development of strain sensors that possess remarkable flexibility, stability, and biocompatibility. These sensors are used to monitor human movements and physiological data, as reported by Zhao et al. in 2021 (Zhao et al., 2021). Cellulose, in addition to being a flexible substrate, can also function as an active element in energy storage systems when it is transformed into conductive carbon compounds through carbonisation. Cellulose-derived carbons have a hierarchical porous structure and a substantial surface area, making them appealing as electrode materials for flexible supercapacitors and batteries. Through systematic engineering of the cellulose precursor and rigorous optimisation of the carbonisation process, we have successfully developed energy storage devices that exhibit exceptional capacitance, rate capability, and cycling stability.

Moreover, the incorporation of stimuli-responsive organisms such as proteins and enzymes into cellulose-based electronics presents opportunities for developing intelligent and adaptable systems. Researchers have investigated the use of cellulose hydrogels that are modified with enzymes for applications in biosensing and drugs delivery (Brahim, Narinesingh, & Guiseppi-Elie, 2002). In this context, the cellulose network serves as a suitable structure for immobilising substances, while the enzymes contribute unique biorecognition or catalytic capabilities. Furthermore, the integration of light-sensitive proteins into cellulose films has facilitated the advancement of optically responsive actuators and soft robots (Bhatti et al., 2022). The integration of biological and electronic elements in cellulose-based systems shows significant potential for the development of bioelectronic drugs and tissue engineering (Baptista, Ferreira, & Borges, 2013). Cellulose scaffolds with electrical conductivity can be used as bioactive surfaces to control cellular behaviour and promote tissue regeneration by applying electrical stimulation. By tailoring the composition, structure, and electrical properties of these biohybrid materials, it is possible to fabricate architecture that resemble tissues, which can be used in regenerative medicine and drug screening purposes. To summarise, combining biological building blocks with electronic functionality in cellulose-based materials provides an effective method for designing multifunctional and intelligent systems. The distinctive characteristics resulting from this combination of bio-electronics and modern manufacturing methods such as 3D printing and microfluidics are expected to drive advancements in wearable electronics, personalised healthcare, and soft robotics. Nevertheless, there are still obstacles to overcome in achieving long-term stability, biocompatibility, and scalable manufacturing. These issues require additional research and development efforts at the intersection of materials science, electronics, and biology.

It is possible to combine kombucha zoogleal mats with electrical components to develop more advanced bio-hybrid sensors and computing systems (Adamatzky, 2022). The complex behaviour of the mats' electrical resistance, characterised by spike trains that resemble action potentials, indicates that they might have memristive or memfractive capabilities. Using living kombucha mats could facilitate the implementation of neuromorphic architectures and self-repairable bioelectronic devices that integrate the mats' electrical properties with conventional electronics. The relatively modest oscillation frequency of kombucha electrical resistance does not necessarily prevent its integration into bio-hybrid analogue circuits for applications like as live wearable sensors. The mats' resistance can serve as a simpler sensing mechanism compared to detecting changes in their electrical potential spikes. In a nutshell the distinct electrical properties of kombucha zoogleal mats present opportunities for the development of innovative bio-electronic hybrid materials and technologies that offer superior functioning when compared to solely artificial components (Adamatzky, 2023).

Statistical analysis and modelling of kombucha zoogleal mat resistance dynamics. The resistance spike dynamics of the kombucha zoogleal mats exhibit some interesting statistical properties. The relationship between spike width and amplitude can be quantified by the Pearson correlation coefficient R:

$$R = \frac{\sum_{I=1}^{n}(x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{I=1}^{n}(x_i - \bar{x})^2 \sum_{I=1}^{n}(y_i - \bar{y})^2}} \quad (1)$$

Where x_i and y_i represent the spike width and amplitude data points respectively, with $\bar{x}$ and $\bar{y}$ being the means. The relatively low value of $R = 0.0315$ indicates a weak correlation between spike width and amplitude in this system. The non-Gaussian nature of the spike width/duration and amplitude distributions is captured by the skewness and kurtosis metrics:

$$\text{Skewness} = \frac{1}{n}\sum_{I=1}^{n}\left(\frac{x_i - \mu}{\sigma}\right)^3 \quad (2)$$

$$\text{Kurtosis} = \frac{1}{n}\sum_{I=1}^{n}\left(\frac{x_i - \mu}{\sigma}\right)^4 - 3 \quad (3)$$

Where μ and σ are the mean and standard deviation of the data x. The high skewness (2.03 for widths, 2.8 for amplitudes) and kurtosis (4.3 for widths, 8.6 for amplitudes) values indicate the distributions have long tails compared to a normal distribution. The unique resistance spiking dynamics, analogous to action potentials, could potentially be modelled using memristive systems theory. The fundamental memristance relationship is given by:

$$M(q) = \frac{d\phi}{dq} \quad (4)$$

Where M is the memristance, ϕ is the magnetic flux linkage, and q is the electric charge. If the kombucha mats exhibit memristive or memfractive properties, this could enable the implementation of bio-inspired neuromorphic architectures and computing models based on the mats' dynamics. For instance, resistive spiking neural networks (SNNs) could be constructed using integrate-and-fire neuron models, with the mat resistance playing the role of the membrane potential V:

$$\tau_m \frac{dV}{dt} = -V(t) + RI(t) \tag{5}$$

Where τ_m is the membrane time constant, R is the resistance, and $I(t)$ is the input current. When the resistance/potential V reaches a threshold V_{th}, a spike can be fired. The spike timing itself could be characterised by equations like the linear drift approximation:

$$t_{\text{spike}} = \frac{V_{\text{th}} - V_{\text{reset}}}{\mu I} + \mathcal{O}(\sigma^2) \tag{6}$$

Where t_{spike} is the spike time, V_{reset} is the reset potential after spiking, μ is the mean input, and σ is the input fluctuation magnitude. Alternatively, the resistance dynamics could be analysed through a memfractive circuit model, extending standard memristive models to include dynamic fractional-order behaviour:

$$i(t) = \alpha_1 M_1[q(t), x(t)]v(t)^{\beta_1} + \alpha_2 M_2[q(t), x(t)]v(t)^{\beta_2} + \cdots \tag{7}$$

Here, α and β are the fractional-order coefficients, $v(t)$ is the applied voltage, and M is a generalised memfractive relationship. Where the subscripts denote different fractional-order memfractive elements comprising the overall system dynamics.

By incorporating the living kombucha mats into hybrid bio-electronic systems, it would be possible to take advantage of their inherent computational characteristics and complex dynamic behaviours. The periodicity of resistive spiking has the potential to enable innovative biocomputing architectures that can carry out information processing directly inside the living substrate. In contrast to traditional electrical components, the bio-hybrid systems possess the capacity to autonomously repair themselves and adjust their configuration in response to the complex internal dynamics of the mats. Moreover, the mats' resistance can be modified in response to stimuli, as previously demonstrated through their electrical potential spikes. This property is useful for sensing purposes. The fluctuations in resistance could offer a signal that is more readily detectable in comparison to simply measuring electrical potentials. The capacity to sense biological signals could be especially valuable for wearable devices that incorporate kombucha components to monitor physiological states or environmental exposure.

To capture the statistical distributions of spike widths and amplitudes, probability density functions (PDFs) like the gamma or lognormal could be fit to the data:

$$f(x;k,\theta) = \frac{1}{\theta^k \Gamma(k)} x^{k-1} e^{-x/\theta} \qquad \text{(Gamma PDF)} \tag{8}$$

$$f(x;\mu,\sigma) = \frac{1}{x\sigma\sqrt{2\pi}} e^{-(\ln x-\mu)^2/2\sigma^2} \qquad \text{(Lognormal PDF)} \tag{9}$$

Where k, θ, μ, σ are the shape, scale, and log-normal parameters respectively. Having an accurate PDF model could aid in simulating and predicting the resistance spiking statistics. The ionic mechanisms underlying the resistance changes could potentially be modelled with equations like the Goldman-Hodgkin-Katz equation for cellular membrane potentials:

$$V_m = \frac{RT}{F} \ln\left(\frac{P_{\text{K}}[\text{K}^+]o + P\text{Na}[\text{Na}^+]o + P\text{Cl}[\text{Cl}^-]i}{P\text{K}[\text{K}^+]i + P\text{Na}[\text{Na}^+]i + P\text{Cl}[\text{Cl}^-]_o}\right) \tag{10}$$

Where V_m is the membrane potential, R, T, F have their usual meanings, P_j are the ionic permeabilities, and the bracketed terms are the ionic concentrations inside/outside the membrane. If variations in ionic flows drive the resistance changes, models like this could elucidate the mechanisms. Finally, equivalent circuit models like the Randles circuit could be employed to extract dynamic resistance and other parameters from impedance measurements:

$$Z(\omega) = R_s + \frac{R_p}{1 + (j\omega R_p C_p)^\alpha} \tag{11}$$

Where $Z(\omega)$ is the impedance vs frequency ω, R is the universal gas constant (8.314462618 J/mol·K), T is the absolute temperature, F is the Faraday constant (96485.33289 C/mol) and C_p are the polarisation resistance and capacitance, and α is a constant. Fitting such models could decompose the resistance into components from different physical processes.

3.1.1. Kombucha and proteinoids as conductive and semi-conductive materials

Biomaterials are being considered as very promising options for electronic components because of their distinctive characteristics and prospects for sustainable and bio-compatible applications. Kombucha and proteinoids have lately gained attention as materials with conductive and semi-conductive properties. Kombucha's conductive properties are due to its abundance of bacteria, cellulose, and other metabolic products. These components create a complex network that enables the flow of electrons (Efremenko et al., 2022). Researchers have discovered that the amino acid content and secondary structure of proteinoids influence their semi-conductive characteristics. Integrating kombucha and proteinoids with electronic devices provides numerous benefits compared to conventional inorganic materials. Eco-friendly methods can manufacture these biomaterials, which are renewable and biodegradable (Padil et al., 2022). Furthermore, their inherent biocompatibility makes them appropriate for applications that interact with biological systems, such as biosensors and wearable electronics. We can tune the electrical characteristics of kombucha and proteinoids by modifying their composition and processing conditions. The ongoing research on the electrical characteristics of kombucha and proteinoids reveals their growing potential for applications in a variety of domains. Biomaterials have the potential to greatly transform the process of designing and producing electronic components. This includes the development of flexible and biodegradable electronics as well as bio-inspired computing systems. Using the distinct characteristics of kombucha and proteinoids, we may develop electronic systems that are both environmentally sustainable and compatible with living organisms. These systems aim to meet the increasing need for eco-friendly and inventive solutions in the electronics industry.

3.2. Mimicking biological systems in electronic architectures

The use of Kombucha and proteinoids presents fascinating opportunities for replicating biological systems in electrical structures. These biomolecules have the ability to create complex, self-assembling structures that resemble parts of cells. These structures have the potential to be used as fundamental units for bio-inspired electronic systems (Mougkogiannis et al., 2024b). Studies have demonstrated that proteinoids obtained from kombucha cultures can be modified to produce nanoscale structures that possess conductive characteristics (Imanbekova et al., 2024; Nikolaidou, Chiolerio, et al., 2024; Nikolaidou, Mougkogiannis, & Adamatzky, 2024; Nirmal et al., 2020). This discovery provides for opportunities for the advancement of biocompatible electronic components (Chiong, Tran, Lin, Zheng, & Bao, 2021; Han, Yang, Rajaram, & Hwang, 2022). Researchers are seeking to use the distinctive characteristics of proteinoids to establish a connection between biological and electronic systems (Mougkogiannis & Adamatzky, 2023a, 2024d). This could result in the development of electronic architectures that are more efficient and adaptive, taking inspiration from nature's designs.

3.3. Leveraging the self-assembly and self-repair properties of biological systems

Kombucha proteinoids possess the fascinating capacity to autonomously organise and regenerate themselves, resembling the mechanisms found in living organisms. These qualities have the capacity to generate robust and flexible electronic systems that can surpass certain constraints of conventional electronics. DuMez-Kornegay and Fox have shown that under certain conditions, kombucha and proteinoids can autonomously generate structures with different forms and functions, resembling biological organelles (DuMez-Kornegay, Baker, Morris, DeLoach, & Dowen, 2024; Fox, 1974; Fox, Jungck, & Nakashima, 1974). Significantly, their research demonstrated that these structures had a restricted capacity for reconstruction and repair themselves in the event of disruption. Although not yet as advanced as the self-repair mechanisms in living systems, this method is a notable advancement in the development of more durable electronic devices. The self-assembly characteristics of kombucha proteinoids have potential benefits in the field of manufacturing. In their study, Adamatzky et al. investigated the potential of using these properties to construct complex electronic structures with limited external intervention (Adamatzky et al., 2023). This approach has the potential to lower production expenses and facilitate the fabrication of structures that would be challenging to achieve using conventional manufacturing techniques. Nevertheless, it is crucial to acknowledge that the discipline is still in its embryonic phase. Although the self-assembly and self-repair abilities of kombucha proteinoids have considerable potential, effectively implementing these capabilities in practical, large-scale electrical systems remains a notable obstacle.

3.4. Combining biological and electronic components for enhanced functionality

The incorporation of kombucha proteinoids, a type of biological component, with conventional electronic parts signifies a fundamental change in the advancement of sophisticated functional materials and systems. This technique combines the distinct characteristics of both domains to develop hybrid systems that have improved capabilities and innovative features (Nikolaidou et al., 2023).Although kombucha proteinoids offer a novel method for integrating bioelectronics, there are various additional biological components that possess electrical capability and have demonstrated potential to develop hybrid systems. These bioelectronic components use the distinct characteristics of biological materials to improve the functionalities of conventional electronic systems.

- Bacterial nanowires are conductive protein filaments produced by specific bacteria, such as Geobacter sulfurreducens. Lovley and Walker (2019) showed that these nanowires had the ability to conduct electricity over distances of several micrometres, indicating their potential suitability as bio-electronic interfaces. Jalili, Ala, Nazari, Jalili, and Ganji (2024) have demonstrated that integrating these nanowires into microbial fuel cells improves electron transport and enhances overall energy production efficiency.
- Silk fibroin is a protein-based substance obtained from silkworm cocoons. It possesses exceptional mechanical characteristics and biocompatibility. Kim and colleagues (Kim et al., 2010) created organic thin-film transistors using silk material, which demonstrated consistent performance in physiological conditions. The biodegradability of silk makes it extremely popular for temporary electronic devices used in medicinal applications.
- DNA nanostructures can be created with precise electrical characteristics due to the programmability of DNA. Jia et al. (2019) showcased the application of DNA origami in fabricating nanoscale circuit boards, wherein metal nanoparticles were accurately arranged to establish conductive channels. This method provides unparallelled manipulation of electrical structures at the nanoscale.
- Melanin, a widely present biological pigment, has been discovered to exhibit semiconducting characteristics. Xia et al. demonstrated in their study (Xia et al., 2022) that melanin has the potential to be utilised in the development of electronic components that are both biocompatible and responsive to changes in humidity. The fact that it can chelate metal ions also makes it interesting for sensing applications.
- Microbial cellulose, which is synthesised by certain bacteria, provides a sustainable and highly pure type of cellulose. Su et al. (2022) fabricated flexible and transparent electrodes by utilising microbial cellulose as a substrate, showcasing its promising applications in wearable electronics.
- Photosynthetic proteins, specifically light-harvesting complexes found in photosynthetic organisms, have been studied for their potential use in bio-photovoltaic applications. Gordiichuk et al. (2014) incorporated photosystem I proteins into solid-state devices, resulting in improved conversion of light energy to electrical energy.

The incorporation of these organic elements into conventional electronics offers both prospects and difficulties. Although they possess distinctive characteristics like self-assembly, biocompatibility, and, in certain instances, self-repair, it is essential to tackle concerns regarding long-term stability, scalable production, and consistent performance (Luo, Weiss, Liu, & Tian, 2018). Potential areas for future research involve enhancing the interface between biological and synthetic materials, establishing uniform production procedures, and investigating novel biological systems for electronic functioning. As this subject advances, we can expect the emergence of increasingly advanced bio-electronic hybrid systems that integrate the most advantageous aspects of both fields. This will result in their application in several domains, including biomedical devices, environmental sensors, and sustainable electronics.

4. Challenges and opportunities in bio-electronic systems

The amalgamation of biological components with electronic systems signifies a cutting-edge domain in technology that presents notable difficulties and encouraging prospects. This section examines three crucial elements of bio-electronic systems: stability and durability, scalability and manufacturability, and biocompatibility and environmental consequences. Each of these domains has distinct challenges that need to be overcome in order to fully exploit the promise of bio-electronic devices, while also providing promising opportunities for innovation and progress in the field.

4.1. Addressing the stability and longevity of biological components in electronic systems

A key obstacle in bio-electronic systems is to guarantee the durability and permanence of biological components when combined with electronic elements. Biological materials are generally dynamic and sensitive to changes in the environment, which might impact their performance and longevity in electrical applications. The susceptibility to environmental conditions poses a substantial barrier to the advancement of dependable and durable bio-electronic devices. In their study, Angione et al. thoroughly examined the durability of protein-based conductive components in bio-electronic devices. According to their study, variations in humidity and temperature had a significant influence on the conductivity of these biological components as time passed (Angione et al., 2011; Pradhan & Yadavalli, 2024). The study emphasised the crucial requirement for protective encapsulation techniques to preserve the integrity and functionality of biological components in electronic systems. The researchers noted that when exposed to different humidity levels, the protein structures underwent conformational changes, which resulted in modifications to their conductive properties. In addition, it was discovered that changes in temperature have an impact on the rate at which electron transfer processes occur, which in turn negatively affects the functioning of the device (Xue, Lofland, & Hu, 2020).

In continuation of this research, Urban et al. devised a groundbreaking method of encapsulating using hydrogel, which demonstrated encouraging outcomes in maintaining the effectiveness of biosensors reliant on enzymes (Urban & Weiss, 2010). Their method involved using a specifically designed hydrogel matrix that created a stable environment for the enzymes and allowed for the movement of analytes by diffusion. By precisely optimising the composition of the hydrogel, they achieved the ability to sustain biosensor performance for a period of six months, even when exposed to different environmental conditions. This signifies a notable enhancement compared to prior techniques of encapsulation, which commonly shown a decline in function within a few weeks (Erfkamp, Guenther, & Gerlach, 2019; Völlmecke et al., 2022).

The field of bio-electronics is still struggling with the critical issue of long-term stability, despite these advancements. In 2022, Park et al. conducted an in-depth review of stability issues in bio-electronic systems, identifying oxidative stress and mechanical strain as the primary factors that restrict the longevity of these devices (Park, Lee, Kim, Hwang, & Seo, 2022). Their analysis demonstrated that the degradation of biological components over time could result from the generation of reactive oxygen species at the bio-electronic interface. Furthermore, the mismatch in mechanical properties between rigid electronic components and soft biological materials was discovered to induce tension at the interface, which could potentially result in device failure (Farooq & Zhang, 2022).

One method for overcoming these barriers is to integrate antioxidant additives into the device architecture in order to reduce oxidative stress (Brito et al., 2021). It is suggested that the device matrix could be integrated with naturally occurring antioxidants, such as glutathione or ascorbic acid, to protect biological components (Meister, 1992) and scavenge reactive oxygen species. An additional proposed approach pointed towards the utilisation of flexible substrate materials to mitigate mechanical strain at the bio-electronic interface (Chen et al., 2020; Choi, Lee, Ghaffari, Hyeon, & Kim, 2016). The researchers emphasised the potential of elastomeric materials and novel nanomaterials, such as graphene-based composites, to achieve more mechanically compatible interfaces (Huang, Qi, Boey, & Zhang, 2012; Shtein, Nadiv, Buzaglo, & Regev, 2015).

The goal of improved stability and longevity in bio-electronic systems presents a plethora of potential areas for future research. The development of adaptive encapsulation materials (Zhang et al., 2021) that can respond dynamically to environmental changes is one promising direction. Consistent with external fluctuations, these materials have the potential to modify their properties in real-time to preserve optimal conditions for biological components (Ren et al., 2021). The adaptive mechanisms of living organisms (Bock, 1965; Paranjpe & Kumar Sharma, 2005; Rossnerova et al., 2020), which maintain homeostasis in the presence of altering environmental conditions, serve as the inspiration for this methodology.

Biomimetic methods are another intriguing area of investigation that aim to improve the resilience of biological components in electronic systems (Di Salvo, 2018; Ganewatta, Wang, & Tang, 2021). Researchers are examining the adaptations of organisms to extreme environments and incorporating these principles into bio-electronic design, drawing inspiration from nature (Hurot, Scaramozzino, Buhot, & Hou, 2020). For example, the investigation of extremophile organisms (Gupta, Srivastava, Khare, & Prakash, 2014) that adapt to severe environments may offer valuable insights into molecular mechanisms that facilitate stability in challenging operational environments. The exploration of self-healing mechanisms that are inspired by living organisms (Cremaldi & Bhushan, 2018) is yet another frontier in the extension of the lifespan of bio-electronic devices. Researchers are investigating materials and designs that can self-repair damage and re-establish functionality by employing principles observed in biological systems. This has the potential to result in bio-electronic systems that are capable of not only withstanding environmental stresses but also actively recovering from minor damage, thereby significantly increasing their operational lifespan. Interdisciplinary collaboration among biologists, materials scientists, and electronic technologists will be essential as research in this field advances. A broad approach to stability and endurance is required due to the complex interplay between biological and electronic components, which encompasses factors such as system-level design and molecular interactions (Kitano, 2001). Researchers are working towards developing bio-electronic systems that can sustain their performance and reliability for extended periods by addressing these challenges. This will create new opportunities for long-term applications in fields such as sustainable energy systems, environmental monitoring, and medical implants.

Fig. 3 outlines important research areas for the future of bioelectronics. These include the creation of bio-electronic systems that can completely biodegrade, studying the potential ecological impacts, and exploring recycling solutions inspired by nature. The significance of examining the complete life cycle of bio-electronic devices is emphasised by these opportunities, which are depicted as interconnected nodes related to the challenges of biocompatibility and environmental effect.

4.2. Kombucha as a living electronic material

Kombucha, a fermented tea beverage, is being considered as an option for living electronic materials because of its distinctive biofilm composition and capabilities. This section examines the electrical conductivity of bacterial cellulose obtained from kombucha, innovative methods for producing electronic components using kombucha, and the inherent benefits of kombucha in terms of sustainability and biodegradability.

4.2.1. Conductive properties of kombucha-derived bacterial cellulose

Kombucha cultures generate a cellulose pellicle that is mostly made of bacterial cellulose (BC) produced by Komagataeibacter xylinus and other acetic acid bacteria (Villarreal-Soto et al., 2018).

Recent research have shown that this BC produced from kombucha has interesting conductivity characteristics when modified properly.

Xu, Sun, Zhao, and Gao (2013) showed that adding copper ions directly during the kombucha fermentation process greatly enhanced the electrical conductivity of the resulting bacterial cellulose (BC) compared to cellulose that was not modified. This technique introduces novel opportunities for fabricating conductive biomaterials through a straightforward and single-step procedure. Liang devised an innovative technique to produce kombucha BC-graphene oxide hybrid composites (Liang, 2023), presenting another promising option. Their method not only obtained significant conductivity but also preserved the material's intrinsic flexibility and biocompatibility. This research demonstrates the potential of merging the distinct characteristics of kombucha BC with state-of-the-art nanomaterials to produce conductive materials that are both high-performing and biocompatible. Imanbekova et al. (2024) conducted a pioneering study where they employed a vacuum-assisted infiltration approach to introduce the conductive polymer PEDOT:PSS into the nanofibrous structure of BC produced from kombucha. The utilisation of kombucha BC as a scaffold has led to the development of a material with adjustable conductivity across a broad spectrum, showcasing the adaptability of this technique in developing versatile electronic materials. The capacity to precisely adjust the conductivity presents promising possibilities for customising these materials for specific uses in bioelectronics. The progress made in altering kombucha-derived bacterial cellulose (BC) emphasises its promise as an environmentally friendly and adaptable foundation for creating innovative conductive biomaterials. Kombucha BC is at the forefront of research in bio-based electronic materials due to its exceptional combination of biocompatibility, flexibility, and increased electrical characteristics (Troncoso & Torres, 2020; Wang et al., 2018; Xu, Zhou, et al., 2015).

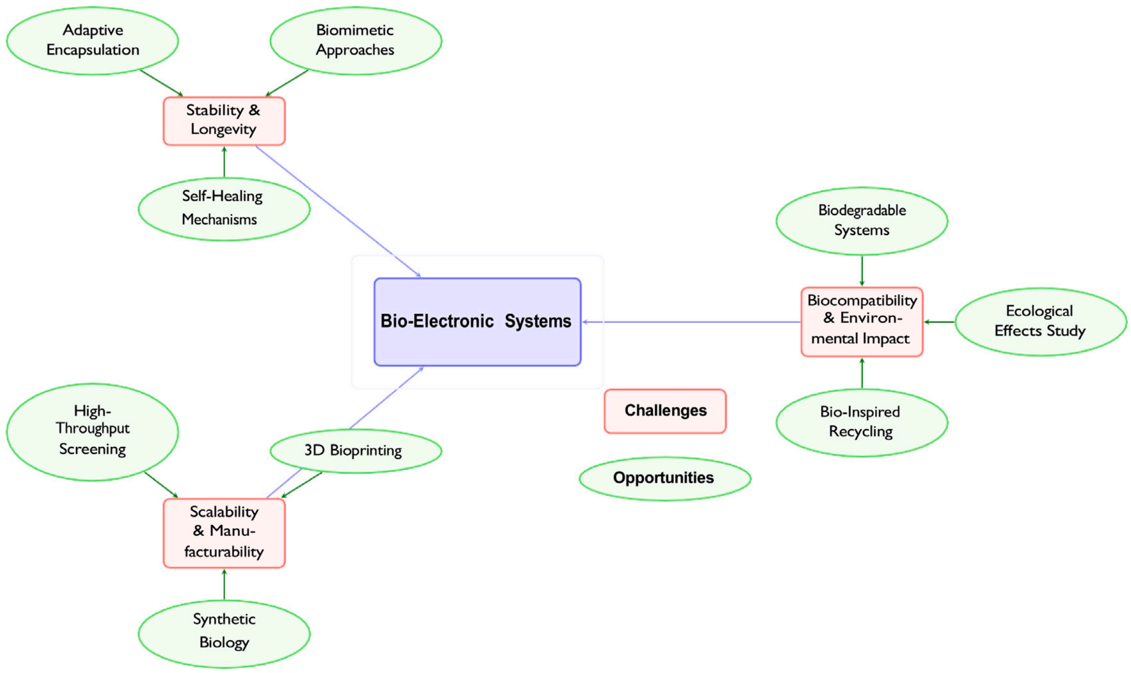

Fig. 3. Challenges and opportunities in bio-electronic systems, highlighting the three main areas of focus: stability and longevity, scalability and manufacturability, and biocompatibility and environmental impact. Each challenge area is associated with specific research opportunities.

The microbial ecology of kombucha is complex and diverse, with multiple yeast species playing crucial roles in the fermentation process and resulting characteristics of the cellulose pellicle. Table 3 provides a summary of the primary yeast species discovered in kombucha cultures and their distinctive characteristics. The table demonstrates that species such as *Schizosaccharomyces pombe* and *Saccharomyces cerevisiae* play a role in the fermentation process due to their significant fermentative capacity and ability to tolerate ethanol, respectively. The metabolic activities of the kombucha biofilm have an impact on its chemical composition, which in turn can influence its electrical characteristics. Notably, certain yeast species, such Zygosaccharomyces rouxii (see to Table 3), has the capacity to endure elevated osmotic pressures and salt concentrations. This characteristic could be beneficial when creating electrical materials based on kombucha that require the ability to operate in different ambient conditions or in the presence of electrolytes. The varied metabolic abilities of the yeast species mentioned in Table 3 contribute to the distinct chemical conditions in which bacterial cellulose is formed. For example, the large-scale synthesis of polysaccharides by *Schizosaccharomyces pombe* can impact the structural and mechanical characteristics of the cellulose matrix. Under aerobic conditions, *Brettanomyces bruxellensis* produces acetic acid which can impact the pH in the area and potentially alter the presence of conductive components in the cellulose network. It is essential to understand the functions of these yeast species in the kombucha fermentation process in order to enhance the synthesis of kombucha-derived bacterial cellulose for electrical applications. The interactions between these yeasts and the bacteria that produce cellulose, specifically *Komagataeibacter xylinus*, form a distinct biological system that can be utilised for the creation of innovative bioelectronic materials. Researchers can investigate different approaches to improve the conductive characteristics of bacterial cellulose generated from kombucha by utilising the inherent diversity and metabolic capacities of the kombucha microbiome, as shown in Table 3. These may involve the targeted growth of specific yeast species to alter the chemical conditions during cellulose formation or utilising their metabolic byproducts as building blocks for conductive modifications.

The kombucha fermentation process involves a complex sequence of metabolic processes carried by several microbes. Fig. 4 depicts the primary metabolic processes associated with the synthesis of kombucha. The picture illustrates the initial step of the process, which involves the hydrolysis of sucrose by yeast. Specifically, species such as *Saccharomyces cerevisiae* and *Schizosaccharomyces pombe*, already mentioned in Table 3, are principally responsible for this reaction.

The resultant monosaccharides, glucose and fructose, operate as substrates for many microbial processes. Acetic acid bacteria, such as species of *Komagataeibacter* and *Gluconacetobacter*, employ glucose to generate gluconic and glucuronic acids. These organic acids are responsible for the distinct sour taste of kombucha and are also linked to some of its claimed health advantages.

Fructose, however, is mostly metabolised by yeasts through fermentation, resulting in the production of ethanol and carbon dioxide, as shown in Fig. 4. Subsequently, acetic acid bacteria oxidise the ethanol produced, converting it into acetic acid, hence enhancing the acidic characteristics of the beverage.

An important characteristic of kombucha fermentation, as depicted in Fig. 4, is the synthesis of cellulose by the microorganism *Komagataeibacter xylinum*. The bacterial cellulose creates the characteristic pellicle, also known as the "SCOBY" (Symbiotic Culture of Bacteria and Yeast), which remains floating on the surface of the fermenting tea. The cellulose pellicle functions as both a protective barrier during fermentation and as a framework for the symbiotic microbial community.

Understanding these metabolic pathways, as outlined in Fig. 4, is essential for maximising kombucha production and investigating its potential uses in fields like as functional foods and biomaterials. The complex relationship among many microbes and their metabolic byproducts adds to the distinct chemical makeup and potential medicinal characteristics of kombucha.

5. Proteinoids and their electronic properties

Proteinoids, often referred to as thermal proteins or proteinoid microspheres, are an interesting group of biomaterials that have attracted considerable interest in the realm of bioelectronics. These polymers, which were created without the involvement of living organisms, were initially invented by Sidney W. Fox in the 1960s (Fox & Harada, 1958). They have become potential candidates for electronic materials that are inspired by biology because of their distinct structural and functional characteristics (Harada & Fox, 1958).

Table 3
Yeast species present in Kombucha culture and their characteristics.

Species	Characteristics
Schizosaccharomyces pombe (Domizio, Liu, Bisson, & Barile, 2017)	• High fermentative power • Ability to convert malic acid to ethanol • Release of high quantities of polysaccharides
Brettanomyces bruxellensis (Steensels et al., 2015)	• High resistance to osmotic and ethanol stress • Higher efficiency to utilise available N sources than *S. cerevisiae* • Tendency to ferment sugars to ethanol, and produce high concentrations of acetic acid in aerobic conditions
Saccharomyces cerevisiae (Choonut, Saejong, & Sangkharak, 2014)	• High ethanol tolerance • Rapid fermentation rates • Insensitivity to temperature and substrate concentration
Zygosaccharomyces rouxii (Dakal, Solieri, & Giudici, 2014)	• Highly osmo- and halo-tolerant • Counteracts sugar and salt stress better than *S. cerevisiae*

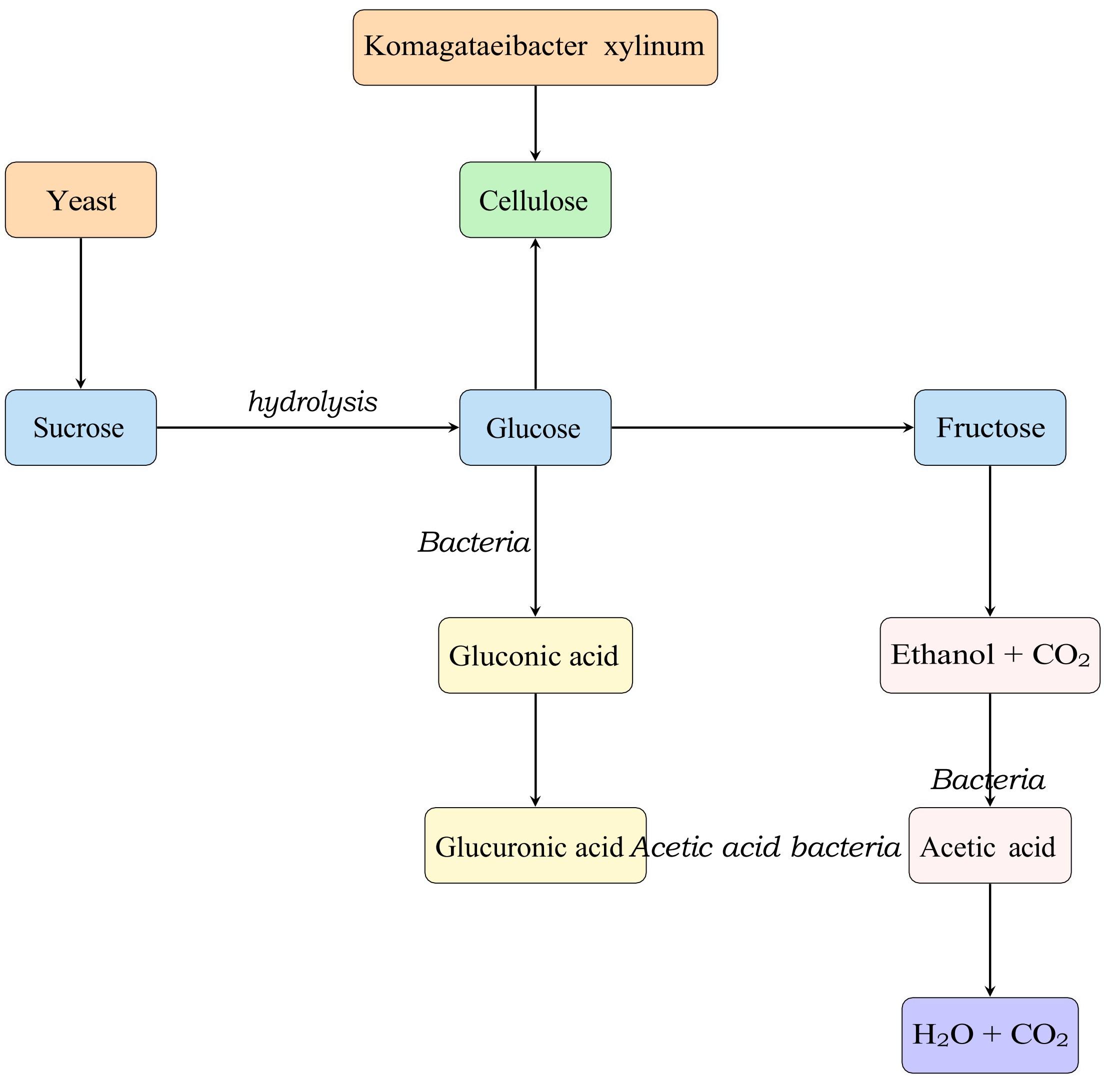

Fig. 4. The primary metabolic activity of kombucha. This graphic depicts the complex relationship between yeasts and bacteria during the fermentation process of kombucha. Yeast catalyses the hydrolysis of sucrose, breaking it down into glucose and fructose. Bacteria metabolise glucose into gluconic and glucuronic acids, while fructose is fermented into ethanol and CO_2. Acetic acid bacteria do further oxidation of ethanol, converting it into acetic acid. At the same time, *Komagataeibacter xylinum* synthesises cellulose, resulting in the formation of the distinctive pellicle.

5.1. Synthesis and characterisation of proteinoid-based materials

Proteinoids are usually synthesised by thermally copolymerising amino acids in dry, heat-driven conditions, without the presence of enzymes. The outcome of this process is the formation of branching, cross-linked structures that exhibit notable differences from linear biological proteins (Rohlfing, 1976). The capacity to include both α-amino acids and non-α-amino acids in the synthesis of proteinoids results in a wide array of structural possibilities, providing a foundation for customising electrical characteristics (Matsuno, 2018). Recent advancements in spectroscopic techniques have provided insights into the correlation between the three-dimensional configuration of proteinoids and their electrical characteristics. Ramírez-Contreras et al. (2023) utilised synchrotron-based X-ray absorption spectroscopy to clarify the existence of π-π stacking interactions among aromatic amino acid residues in proteinoid structures. These interactions are essential for enabling the movement of electrons, which greatly contributes to the overall conductivity of proteinoid-based materials. It has been demonstrated that the addition of metal ions during the process of proteinoid synthesis greatly increases electrical conductivity. In a pioneering research conducted by Chen and Li (Li, Chang, Li, Li, & Wang, 2024), it was discovered that the presence of copper ions in the proteinoid structure forms specific channels for conducting electricity. This results in a substantial enhancement in conductivity when compared to proteinoids without any metal ions. This discovery presents new opportunities for creating highly conductive materials based on proteinoids by including metal ions selectively. In their study, Kojima and Tanaka (2023) devised a machine learning method that effectively forecasts and enhances the electronic characteristics of amino acid compositions (Tanaka et al., 2022). Their predictions exhibited an impressive accuracy rate of 80%. This computational approach offers the potential to speed up the production and advancement of proteinoid-based electronic materials with customised characteristics (Leman, Orgel, & Ghadiri, 2004; Monnard & Walde, 2015).

5.2. Semiconductive and photoconductive behaviour of proteinoids

The proteinoids' electronic conductivity arises from a mix of elements, such as their chemical makeup, secondary structure, and the existence of metal ions (Tan, Saurabh, Bruchez, Schwartz, & LeDuc, 2013). In recent years, various conductivity processes have been proposed and studied. Li, Chang, et al. (2024), Xu, Eriksson, et al. (2015) established that the transfer of electrons between redox-active amino acid residues, such as tyrosine and tryptophan, has a substantial role in the overall conductivity of proteinoid films. Their research included temperature-dependent conductivity measurements and electron paramagnetic resonance spectroscopy to clarify the kinetics of this process, offering vital understanding of the charge transport pathways in these materials. Proteinoids, unlike standard rigid electronic materials, have dynamic conformational changes that impact their electrical characteristics. Stolte et al. (Stolte Bezerra Lisboa Oliveira & Ristroph, 2024) employed single-molecule force spectroscopy to illustrate the mechanism by which mechanical stress triggers alterations in the structure of proteinoid chains, resulting in the reversible adjustment of their conductivity. This distinctive feature presents intriguing opportunities for the advancement of mechanically responsive bioelectronic devices, which could potentially facilitate innovative sensing and actuation techniques. Researchers have also investigated new methods of doping to improve the electrical characteristics of proteinoids. In their study, Feng et al. (2020) described a technique for doping proteinoid-based materials after their synthesis. This method involved the use of organic semiconductor molecules and led to the development of materials with conductivities comparable to those of conventional semiconductors. This advancement showcases the capability of proteinoids to connect biological and synthetic electronic materials, providing a distinctive blend of compatibility with living organisms and exceptional efficiency. The study of the photoconductive properties of proteinoids has been a subject of increasing interest. Mougkogiannis and Adamatzky (2024e) conducted recent research which demonstrated that some proteinoid compositions experience substantial alterations in conductivity when exposed to light. The photosensitivity seen is believed to be caused by the aromatic amino acids present and their interactions with metal ions that are integrated. This discovery suggests potential applications for proteinoid-based photosensors and light-harvesting devices (Koga et al., 2011).

Fig. 5: SEM analysis of proteinoid structures. (a) Spherical microsphere (I = 0.065 mol/L) exhibiting surface roughness, 60,000x. (b) Dense aggregates formed at I = 0, revealing interconnected spheroids, 8,000x. (c) Higher magnification (15,000x) of assemblies, showing detailed cluster morphology. (d) High-resolution (20,000x) view of diverse proteinoid formations, including spherical particles and irregular aggregates, demonstrating complex self-assembly behaviour.

5.3. Potential for proteinoid-based biocompatible electronic devices

Proteinoids' distinctive features, including biocompatibility, biodegradability, and programmable electrical characteristics, make them interesting candidates for the development of innovative biocompatible electronic devices. These biomimetic materials have major biomedical and environmental applications. Proteinoid-based biosensors have demonstrated great promise. Kolitz-Domb et al. developed proteinoid microspheres for targeted medication delivery and diagnostic applications, demonstrating their potential as carriers of bioactive chemicals (Kolitz-Domb, Grinberg, Corem-Salkmon, & Margel, 2014). This method could be used to develop biosensors with higher sensitivity and specificity. Furthermore, Zhang et al. found that metal–organic proteinoids have exceptional catalytic activity, implying the possibility of enzyme-mimetic biosensors (Zhang et al., 2024).

Implantable medical devices provide another promising application for proteinoid-based electronics. The biocompatibility of proteinoids, as investigated by Tuncer et al. makes them suitable candidates for establishing interfaces between biological tissues and electronic components (Tuncer Degim & Celebi, 2007). This could result in improved neural interfaces or smart drug delivery systems that work flawlessly with the human body. Proteinoid-based electrical devices may also be useful in tissue engineering research. Zakharchenko et al. (2017) demonstrated the utilisation of proteinoid microspheres as tissue regeneration scaffolds (Zakharchenko et al., 2018). By adding electronic functions into these scaffolds, smart materials that can monitor and promote tissue growth may be conceivable to develop.

Proteinoid-based devices also show potential in the field of environmental monitoring. Fox and Harada (1960) studied the biodegradability of proteinoids (Fox & Harada, 1960). This could help with the growing problem of electronic waste in landfills (Spalvins, Dubey, & Townsend, 2008).

Sensors based on proteinoids could be used for environmental monitoring and disintegrate naturally after their useful life, reducing ecological effect. Furthermore, Kumar et al. revealed the ability to alter the electrical characteristics of proteinoids through controlled synthesis, leading the way for the development of adaptive and responsive electronic devices (Kumar & Rao, 1998). This could result in the creation of self-regulating systems capable of responding to external stimuli or physiological changes.

Despite these fascinating promises, converting proteinoid-based materials into functional electrical devices remains a difficulty. Long-term stability, scalable production, and interaction with current electronic systems are all critical issues to overcome. Furthermore, standardising proteinoid production and characterisation processes is critical for assuring consistency and dependability in device manufacturing. Finally, proteinoid-based biocompatible electrical devices represent a new frontier in biomimetic technology, with enormous promise in a

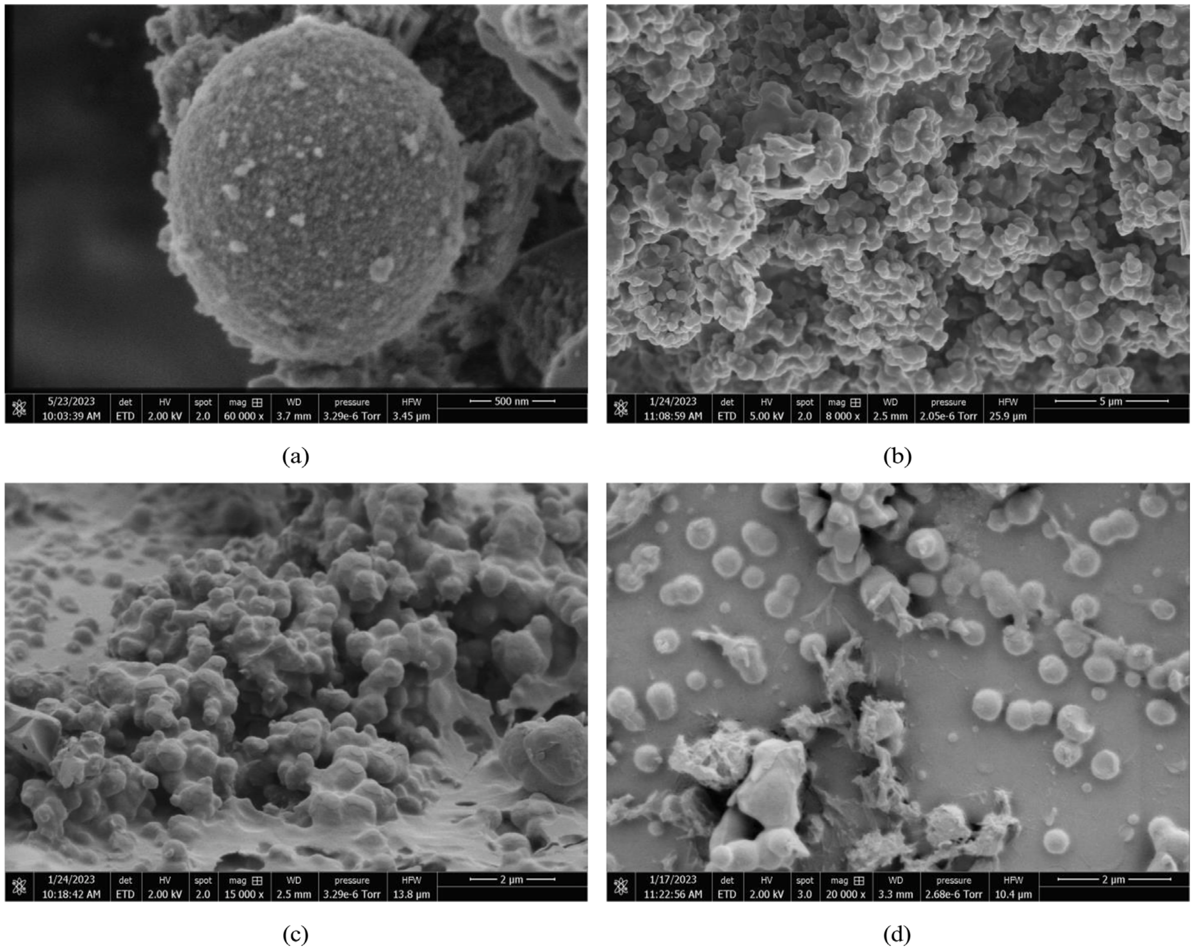

Fig. 5. SEM images of proteinoid structures under varying conditions. (a) Individual proteinoid microsphere formed at ionic strength 0.065 mol/L. Spherical structure with rough surface is visible. Magnification: 60,000x, scale bar: 500 nm. (b) Assemblies of proteinoids at ionic strength I = 0. Dense clusters of smaller, interconnected spherical structures are observed. Magnification: 8,000x, scale bar: 5 μm. (c) Proteinoid assemblies showing a more detailed view of the clustered structures. Individual spheroids are distinguishable within the larger aggregates. Magnification: 15,000x, scale bar: 2 μm. (d) High-resolution image of proteinoid structures revealing a mixture of spherical particles and irregular aggregates. Some particles appear to be fusing or interconnecting. Magnification: 20,000x, scale bar: 2 μm.

variety of applications. As research continues, we should expect considerable advances in biosensors, implantable devices, tissue engineering, and environmental monitoring. Proteinoids' unique features provide a link between the biological and electrical worlds, providing a new generation of biocompatible and environmentally friendly electronic devices.

5.4. Integration of kombucha and proteinoids in living electronics

The integration of biological materials, such as bacterial cellulose generated from kombucha, with synthetic biomimetic structures like proteinoids, offers a novel approach in the field of living electronics. This combination exploits the distinct characteristics of both materials to provide hybrid systems with improved functionality and biocompatibility.

5.4.1. Strategies for combining kombucha and proteinoids in electronic systems

Kombucha cultures produce bacterial cellulose (BC) that is highly pure, mechanically strong, and biocompatible, making it an ideal substrate for electronic components. In their study, Cochis et al. showcased the capacity of BC to be used as a substrate in tissue engineering applications, emphasising its adaptability as a biomaterial (Cochis et al., 2017). This characteristic can be utilised to form a reinforcing structure for electronic components made from proteinoids. Proteinoids, however, can be modified to demonstrate particular electrical characteristics. In their study, Ketabat et al. conducted an extensive evaluation of different synthesis techniques for proteinoids, with a particular focus on their tunable properties (Ketabat et al., 2019). By integrating the structural reinforcement of BC produced from kombucha with the functionality of proteinoids, it is feasible to fabricate composite materials possessing customised electrical properties. An effective approach involves the formation of proteinoids directly within the BC matrix. This strategy has resemblance to the research conducted by Shi et al. where they showcased the combination of graphene oxide and bacterial cellulose to improve electrical conductivity (Shi et al., 2013). By including proteinoids into this technique, it may be feasible to produce a cohesive hybrid material.

5.4.2. Synergistic effects of kombucha and proteinoids on device performance

The use of BC generated from kombucha and proteinoids has the potential to improve a variety of device performance. According to Ullah et al. BC has a high capacity to store water and is compatible with living organisms. This makes it a good choice for creating a stable and functioning environment for proteinoid-based electronic components (Ullah et al., 2016). Additionally, the permeable composition of BC could enhance the incorporation of ionic conductors, as demonstrated by Lv et al. (2019) in their research on BC-based flexible electronics (Lv et al., 2021). The property of proteinoids can be utilised to construct ionic circuits within the BC matrix, which has the potential to improve signal transmission and sensitivity in biosensing applications.

5.4.3. Examples of kombucha-proteinoid hybrid electronic components and circuits

Although there is currently limited literature on particular examples of kombucha-proteinoid hybrid electronics, related research indicates encouraging potential. Włodarczyk et al. provided evidence of the application of bacterial cellulose as a framework for producing electrodes that are both flexible and transparent (Pagliaro et al., 2021). This approach has the potential to be expanded in order to create electrodes that include proteinoids, resulting in improved biocompatibility and functionality. The research conducted by Kolitz-Domb et al. (2014) in the field of biosensors, specifically on proteinoid microspheres for targeted drug administration, has the potential to be modified for the development of sensing components within a biological cell matrix. This technology has the potential to provide enhanced sensitivity and specificity in the detection of biological analytes. To summarise, although the incorporation of materials produced from kombucha and proteinoids into living electronics is a relatively new area of study, the separate components exhibit significant potential. Additional study is required to thoroughly investigate and unlock the capabilities of these hybrid systems in developing electrical devices that are both biocompatible, sustainable, and high-performing.

5.5. Future prospects and challenges

5.5.1. Potential applications in wearable electronics, implantable devices, and green electronics

In wearable electronics, the flexibility and biocompatibility of BC make it an excellent candidate for skin-interfacing devices. Heo et al. showcased the use of BC as a foundation for wearable strain sensors, emphasising its capacity in detecting human motion (Heo et al., 2018). Incorporating proteinoids into these systems has the potential to enhance their functionality, allowing for the development of bio-responsive wearables that can adjust to physiological changes. The biocompatibility of both BC and proteinoids is crucial for implanted devices. Shi et al. (2014) demonstrated the capabilities of BC-based nanocomposites in biological applications, specifically highlighting their ability to trigger a minimal foreign body response (Shi et al., 2014). Proteinoids, which possess adjustable characteristics as examined by Kumar et al. (1996), have the potential to be manipulated in order to produce bioactive interfaces in implantable electronics. This might potentially enhance device integration and decrease the possibility of rejection. Within the domain of sustainable electronics, the biodegradability of these materials provides a notable advantage. Rajwade et al. emphasised the environmentally favourable characteristics of BC and its potential in sustainable technology (Rajwade, Paknikar, & Kumbhar, 2015). The integration of proteinoids' controlled degradability with this concept might potentially result in the production of transient electronics. These electronics would be capable of performing their original purpose and subsequently decompose without causing harm, so tackling the escalating problem of electronic waste.

5.5.2. Addressing the long-term stability and reliability of kombucha and proteinoid-based electronics

Although these bio-based materials exhibit considerable potential, ensuring their enduring stability and dependability remains a notable obstacle. For BC-based electronics, moisture sensitivity is a primary concern. Gao et al. tackled this problem by creating moisture-resistant BC composites specifically designed for flexible electronics. Their research showed that these composites exhibited enhanced stability when exposed to high humidity (Gao, Shi, et al., 2015). It may be necessary to create comparable approaches for proteinoid-based components in order to guarantee consistent performance in the long run. The durability of proteinoids under physiological settings is an additional crucial feature, particularly for implanted devices. Sasson et al. conducted a study to examine the stability of proteinoid nanoparticles in different situations, which yielded valuable information about their behaviour in biological settings (Sasson, Pinhasi, Margel, & Klipcan, 2020). Additional investigation is required to enhance proteinoid compositions for extended durability in electronic applications. Furthermore, the interplay between biological and electronic components requires careful consideration. Tan et al. emphasise the significance of creating durable bio-electronic interfaces to ensure long-term functionality in bio-integrated electronics (Tan et al., 2016). It is essential to create strong techniques for combining BC and proteinoids with conventional electronic components in order to ensure the dependability of these hybrid systems.

5.5.3. Exploring the scalability and cost-effectiveness of these novel materials in industrial settings

Increasing the production of BC and proteinoids for industrial use involves both advantages and difficulties. Traditional static culture methods for BC production are both time-consuming and space-intensive. Revin et al. showed that waste materials from the food industry can be used as inexpensive substrates for BC manufacturing, which could enhance economic feasibility (Revin et al., 2018). Efficiently developing large-scale fermentation systems will be crucial in order to make BC-based electronics commercially viable. The scalability of proteinoid production requires careful consideration. Although Kumar et al. examined different synthesis techniques (Kumar & Rao, 1998), the task of optimising them for large-scale manufacturing still poses a barrier. One can find inspiration by examining the methods used by pharmaceutical companies to increase the production of peptides, as described by Isidro-Llobet et al. (2019). Industrial adoption relies heavily on cost-effectiveness. Lee et al. conducted an economic analysis on the production of microbial cellulose, providing valuable information on possible techniques to reduce costs (Lee, Buldum, Mantalaris, & Bismarck, 2014). It will be important to conduct similar evaluations to assess the commercial feasibility of producing proteinoids and integrating them into electrical systems. To summarise, whereas kombucha and proteinoid-based electronics have great potential in several applications, substantial research and development efforts are necessary to overcome obstacles related to long-term stability, reliability, scalability, and cost-effectiveness. Successfully overcoming these obstacles will clear the path for the development of the next wave of bio-integrated electrical devices.

6. Principles of kombucha and proteinoid-driven living electronics

6.1. Kombucha: A symbiotic colony of bacteria and yeast

6.1.1. Microbial composition of kombucha

The microbial population in kombucha is characterised by its complexity and high degree of activity. Recent metagenomic research has shown that the bacterial community is primarily composed of Komagataeibacter species, with K. xylinus (formerly known as Acetobacter xylinum) being the dominant species responsible for cellulose synthesis (Chakravorty et al., 2016). The ratio of bacteria to yeast can vary considerably, ranging from 4:1 to 1:8, depending on the fermentation conditions and the original composition of the culture (Marsh, O'Sullivan, Hill, Ross, & Cotter, 2014). An exceptional characteristic of the kombucha microbiota is its vertical arrangement within the SCOBY. The upper layer is usually characterised by aerobic conditions and is predominantly inhabited by acetic acid bacteria. In contrast, the lower layers gradually become anaerobic, creating a favourable environment for the growth and multiplication of yeast (Pasolli et al., 2020; Su et al., 2023). The spatial arrangement of the community is essential for the coordinated metabolic activities of the community. The layered composition of the kombucha SCOBY shares resemblances with electroactive biofilms employed in microbial fuel cells. Recent research on biofilms has demonstrated that the arrangement of cells within the biofilm has a major impact on their ability to transmit electrons (Kessouri et al., 2019). This indicates that the vertical arrangement of kombucha cultures could be used for the advancement of bio-based electronic components with distinct spatial capabilities.

6.1.2. Fermentation process and chemical composition

The fermentation process of kombucha is distinguished by a biphasic response. During the initial stage, yeasts enzymatically hydrolyse sucrose into glucose and fructose, eventually converting these into ethanol by fermentation. During the second stage, acetic acid bacteria undergo the process of oxidising ethanol into acetaldehyde, which is further converted into acetic acid (Jayabalan, Malbaša, Lončar, Vitas, & Sathishkumar, 2014). This process leads to a progressive fall in pH, usually starting from 5.0 and reaching a final range of 2.5–3.0 after 7–10 days of fermentation (Sreeramulu et al., 2000). Bacterial cellulose, an essential byproduct of this fermentation process, is responsible for the formation of a distinctive film at the boundary between the air and liquid phases. This cellulose has distinct characteristics in comparison to plant cellulose, such as increased purity, a higher degree of polymerisation (up to 20,000), and improved mechanical strength (Sreeramulu et al., 2000). Kombucha-derived cellulose possesses features that make it highly desirable for a wide range of applications, including its potential suitability for use in flexible electronics. Recent study has demonstrated the potential of conductive bacterial cellulose composites, which involve the integration of graphene oxide or conductive polymers, for use in flexible electronics and energy storage devices (Ul-Islam et al., 2015). Possible methods could be used to apply similar techniques to cellulose obtained from kombucha, potentially functionalisation.

6.1.3. Health benefits and risks associated with kombucha consumption

Although additional scientific proof is needed for many health claims related to kombucha, recent investigations have offered new insights. For example, studies have demonstrated that kombucha possesses antibacterial properties against several harmful bacteria, such as *Vibrio cholerae*, *Shigella sonnei*, and **Salmonella typhimurium**. These properties are believed to be due to the presence of organic acids and bacteriocins (Shi et al., 2014). However, the potential risks associated with consuming kombucha, especially when made at home, should not be underestimated. Examples of liver damage and excessive acidity in the body have been documented, frequently associated with extensive fermentation or contamination (Al-Mohammadi et al., 2021). One specific worry is that kombucha may contain more alcohol than what is allowed for non-alcoholic drinks, especially if the fermentation process is not closely monitored (Gedela, Potu, Gali, Alyamany, & Jha, 2016). From a perspective standpoint, the equilibrium between the potential advantages and drawbacks of kombucha reflects the difficulties encountered in the production of other probiotic products. The probiotic industry has provided valuable insights that may be applied to the development of biotechnological applications using kombucha. These insights include the importance of conducting safety evaluations specific to the kinds of bacteria used and following standardised production processes. By using these insights, the development of kombucha-based biotechnological applications can be ensured to be both effective and safe (Nummer, 2013).

6.1.4. Kombucha as a versatile platform for biotechnology

In addition to its conventional use as a drink, kombucha exhibits potential as a biotechnological framework. The potential applications of bacterial cellulose produced by kombucha cultures have been investigated, particularly as a scaffold for tissue engineering. A recent work showcased the efficient culture of human epidermal keratinocytes and fibroblasts on cellulose membranes generated from kombucha. This indicates promising possibilities for using these membranes in the fields of wound healing and skin tissue engineering (Salminen et al., 2021). Furthermore, the kombucha SCOBY has been studied as a possible biosorbent for the purpose of eliminating heavy metals from wastewater. Research has demonstrated that dehydrated kombucha biomass may efficiently absorb lead and cadmium ions from water-based solutions, exhibiting adsorption capabilities similar to certain commercially available adsorbents (Kanjanamosit, Muangnapoh, & Phisalaphong, 2010). The utilisation of microbial communities for the production of functional materials goes beyond the scope of kombucha. The latest progress in engineered living materials, particularly those using programmable biofilms, offer useful knowledge for the development of living electronic systems based on kombucha. Recent research has shown that it is possible to improve the electrical characteristics of kombucha-derived materials by using genetic engineering techniques, such as creating E. coli biofilms to make conducting protein nanowires (Ahamed, Asiri, et al., 2019). To summarise, although there is limited research on the use of kombucha in the field of living electronics, its distinct characteristics and resemblance to other microbial systems indicate potential in this area. Future research should prioritise the characterisation and optimisation of the electronic characteristics of materials obtained from kombucha. Additionally, it should investigate methods for integrating these materials with traditional electronic components.

6.1.5. Composition and structure of kombucha

Microbial diversity in kombucha. The microbial environment of kombucha is distinguished by the complex relationship between bacteria and yeasts. Recent metagenomic research has shown that the majority of the bacterial community consists of acetic acid bacteria, specifically Komagataeibacter species (formerly classified as Acetobacter), with *K. xylinus* being the main producer of cellulose (Chakravorty et al., 2016). *Gluconobacter oxydans* is a significant bacterial species that plays a crucial role in the process of ethanol oxidation and the formation of gluconic acid (Muynck et al., 2007). *Zygosaccharomyces bailii* is a prominent yeast species that is recognised for its strong ability to tolerate high osmotic conditions and withstand acetic acid (Teoh, Heard, & Cox, 2004). The ratio of bacteria to yeast can vary considerably, ranging from 4:1 to 1:8, depending on the conditions of fermentation and the original composition of the culture (Marsh et al., 2014). The symbiotic relationship between bacteria and yeast in kombucha is demonstrated by their metabolic interaction. Yeasts enzymatically hydrolyse sucrose and produce ethanol, which is subsequently metabolised by acetic acid bacteria to yield acetic acid. This procedure produces an acidic atmosphere that inhibits the development of possible disease-causing microorganisms while promoting the growth of the kombucha microbiota (May et al., 2019).

Chemical composition of kombucha. The chemical profile of kombucha is dynamic and changes throughout the fermentation process. Acetic acid is the predominant organic acid, typically reaching concentrations of 8–20 g/L after 7–10 days of fermentation (Jayabalan et al., 2014). Gluconic acid, a key metabolite produced by Gluconobacter species, can reach levels of 5–10 g/L, contributing to the beverage's characteristic tartness (Chen & Liu, 2000). Recent studies have identified a range of bioactive compounds in kombucha, including catechins, flavonoids, and phenolic acids. For instance, epigallocatechin gallate (EGCG), a potent antioxidant, has been found at concentrations up to 100 mg/L in green tea kombucha Revin et al. (2018). The amino acid content of kombucha is also noteworthy, with theanine, a compound associated with cognitive benefits, being particularly abundant in tea-based kombuchas (Gaggìa et al., 2018). Ethanol content in kombucha is a critical parameter, both for regulatory compliance and flavour profile. During fermentation, ethanol levels typically rise to 0.5%–2% (v/v) within the first 6–10 days, before gradually decreasing as acetic acid bacteria convert ethanol to acetic acid (Cortés-Herrera, Artavia, Leiva, & Granados-Chinchilla, 2018).

Structural components of kombucha. The bacterial cellulose pellicle, often known as SCOBY (Symbiotic Culture of Bacteria and Yeast), is a unique characteristic of kombucha. The pellicle consists mainly of bacterial cellulose, with bacterial cells and yeast embedded within it. Kombucha SCOBYs contain cellulose with a characteristic nanostructure, consisting of fibrils that are 20–100 nm in thickness. This unique structure enhances the material's strength and capacity to maintain water (Edwards, 2016; Ul-Islam et al., 2015). The liquid phase of kombucha is a dense solution comprising of tea chemicals, organic acids, and metabolites that are formed during fermentation and are in a dissolved state. Recent studies using nuclear magnetic resonance (NMR) spectroscopy have yielded broad insights into the chemical structure of this liquid phase, uncovering more than 60 detectable metabolites (Barbosa et al., 2020). The gaseous state of kombucha, which is sometimes disregarded, plays a vital role in determining the sensory characteristics of the beverage. The bubbles of kombucha is attributed to carbon dioxide, which is generated during yeast fermentation. In addition, the fragrance profile is influenced by volatile organic molecules such as ethyl acetate and acetaldehyde (Meng, Wang, Li, Chen, & Chen, 2024; Suhartatik, Widanti, et al., 2023).

Factors influencing kombucha's composition and structure. The microbial activity and metabolite production in kombucha are greatly affected by the temperature at which fermentation takes place. Recent study data indicates that bacterial cellulose production is optimal at temperatures ranging from 22 to 30 °C, but higher temperatures (30–33 °C) promote the production of acetic acid (Avcioglu et al., 2021). The selection of tea substrate has a significant influence on the final composition of kombucha. Research has shown that kombucha produced with green tea have higher levels of catechins and demonstrate stronger antioxidant activity when compared to kombucha made with black tea (Motafeghi et al., 2023). In addition, the use of different substrates, such as herbal infusions or fruit juices, can significantly modify the microbial composition and metabolite profile of the end product (Vitas, Malbaša, Grahovac, & Lončar, 2013). The changes in microbial strains are essential in determining the specific characteristics of kombucha. A recent study conducted a comparison of various Komagataeibacter strains and discovered notable variations in cellulose production rates and pellicle morphology. These findings emphasise the possibility of enhancing kombucha production through strain-level optimisation (Semjonovs et al., 2017).

6.1.6. Electrical properties of biomaterials: Implications for kombucha

Conductivity of biomaterials. The conductivity of bacterial cellulose (BC), a material that is analogous to the cellulose produced in kombucha, has been characterised through the use of advanced measurement techniques, including the four-point probe method and electrochemical impedance spectroscopy (EIS), in recent studies. Shi et al. (2016) employed a four-probe configuration to quantify the surface resistivity of BC films, obtaining values between 105 and 107 Ω/sq according to the hydration levels (Shi et al., 2016). In microbial systems, the factors that influence conductivity are multifaceted. In investigations of *Geobacter sulfurreducens* biofilms, Malvankar et al. (2011) demonstrated that the presence of conductive pili is a critical factor in the conductivity of the biofilms, with values as high as 5 mS/cm (Malvankar et al., 2011). Hydration and pH are the most significant environmental factors that substantially influence the conductivity of biomaterials. The microbial composition of kombucha, particularly the presence of cellulose-producing bacteria, and environmental conditions during fermentation could affect its conductivity in a similar manner.

Charge transport mechanisms in biomaterials. In numerous hydrated biomaterials, ionic conduction serves as the primary mechanism. Li et al. (2024) conducted a study on alginate hydrogels and discovered that their ionic conductivity can reach as high as 0.1 S/cm in completely hydrated states, primarily due to the presence of mobile counterions (Li, Ren, et al., 2024). There has been evidence of electronic conduction in microbial systems in the biofilms of specific bacteria. Lovley (2017) conducted a review of the mechanisms of electronic conduction in Geobacter species, emphasising the significance of pili-based nanowires in long-range electron transport (Lovley, 2017). Kombucha, a multifaceted microbial system that contains both liquid and solid (pellicle) components, may demonstrate both electronic and ionic conduction mechanisms. It is feasible to engineer the pellicle, which is abundant in bacterial cellulose, to improve electronic conduction, whereas the aqueous phase would likely make a substantial contribution to ionic conduction.

The conductivity values we report for kombucha (2270 μS at 18°C) and deionised water media (31.3 μS) can be interpreted in biological systems (Mougkogiannis et al., 2024a; Wang et al., 2023). In comparison, polypyrrole-doped bacterial cellulose films have a conductivity of 0.1–1 S/cm(Pilo, Sanna, & Spano, 2024). PEDOT:PSS-based bioelectronics have a conductivity of 1–10 S/cm (Rivnay et al., 2018). Natural biological systems, such as mammalian neurons, conduct ions in the range of 10–100 mS/cm^2 (Hodgkin & Huxley, 1952). Kombucha is less conductive than synthetic polymers. But, it has unique benefits. They come from its self-assembly and self-healing properties. Ionic conductivity can be changed by doping with metal ions (Cu^{2+}, Fe^{3+}) and by environmental conditions. This is like the method used for ion-electron polymer batteries. This tuning, and kombucha's biocompatibility and green production, make it a useful material for some biomedical uses, despite its low portability.

Dielectric properties of biomaterials. Bacterial cellulose has exhibited interesting properties through the use of dielectric spectroscopy. Fernades et al. (2020) conducted measurements of the dielectric constant and loss tangent of BC at a frequency range spanning from 1 Hz to 1 MHz. At low frequencies, they saw a significant dielectric constant (ϵ' = 100), which was attributed to interfacial polarisation (Fern et al., 2020). Hydrated biomaterials frequently exhibit numerous relaxation processes that are depending on frequency. For example, Nainggolan et al. (2018) discovered specific relaxation peaks in the dielectric spectrum of chitosan films. These peaks correspond to the relaxation of bound water and the movement of polymer chains. One might expect comparable dielectric characteristics in kombucha pellicles as a result of their substantial cellulose composition. The liquid phase of kombucha may provide extra relaxation mechanisms as a result of its unique ionic composition (Nainggolan et al., 2018).

Modulation of electrical properties in biomaterials. Chemical doping and functionalisation strategies have been successfully employed to enhance the electrical properties of bacterial cellulose. Sui et al. (2021) demonstrated a 1000-fold increase in conductivity by incorporating polyaniline into BC, resulting in a conductive nanocomposite with potential in flexible electronics (Sui et al., 2023). Genetic engineering approaches have shown promise in enhancing the conductive properties of microbial systems. Bird et al. (2019) engineered *E. coli* to produce conductive protein nanowires, demonstrating the potential for bottom-up fabrication of bioelectronic materials (Bird et al., 2019). Similar strategies could potentially be applied to kombucha. The bacterial cellulose in kombucha pellicles could be functionalised with conductive polymers or nanoparticles to enhance conductivity. Additionally, genetic engineering of the kombucha microbiome, particularly cellulose-producing bacteria, could potentially yield strains that produce more conductive biofilms.

6.2. Proteinoids: Synthetic polypeptides with unique properties

Proteinoids are synthetic polypeptides that are produced through thermal condensation of amino acids. They are considered a major achievement in the study of prebiotic chemistry and the origins of life. The original study conducted by Sidney Fox and his colleagues during the 1960s and 1970s established the fundamental knowledge about these unique macromolecules and their possible involvement in the origin of life (Fox, 1988). Fox's study revealed that proteinoids can be artificially created by subjecting mixtures of amino acids to temperatures of approximately 170 °C, which could have been similar to the conditions on the early Earth (Fox & Harada, 1958). The procedure, known as "thermal copolymerisation", produced polymers with molecular weights ranging from 3,000 to 10,000 daltons, which are similar to the molecular weights of functional proteins found in modern organisms (Fox, 1980a).

The remarkable characteristic of proteinoids is their capacity to spontaneously form microspheres in the presence of water. In 1959, Fox et al. observed the spontaneous formation of cellular-like structures, which they referred to as "proteinoid microspheres" (Fox, Harada, & Kendrick, 1959). The microspheres displayed characteristics similar to those of living cells, including as growth, budding, and division. This indicates a possible connection between non-living chemical systems and the emergence of basic cellular structures (Fox, 1980b). The proteinoids' catalytic activity has been the focus of extensive research. Fox and his colleagues revealed that these artificial polypeptides can have enzymatic characteristics, facilitating a range of processes such as ester hydrolysis, decarboxylation, and amide bond formation (Rohlfing & Fox, 1969). This discovery was especially important since it indicated a potential pathway for the development of basic metabolic activities without relying on advanced, complex enzymes. Proteinoids also demonstrate specific membrane permeability and transport characteristics, which further reinforces their potential as precursors to biological membranes. In their 1984 study, Fox and Nakashima investigated the capacity of proteinoid microspheres to selectively absorb and retain certain molecules, imitating the characteristics of biological membranes (Fox & Nakashima, 1984).

Proteinoids' interaction with nucleic acids has been a significant field of study, as it provides insights into the origins of the genetic code and the transfer of information in primitive life forms. Yuki and Fox (1969) provided evidence of specialised interaction between proteinoids rich in lysine or arginine and particular polynucleotides, indicating a potential mechanism for early coding systems (Yuki & Fox, 1969). Proteinoids have distinctive semiconductive and photoconductive capabilities, making them highly advantageous in the field of living electronics. Ishima et al. (1981) documented the electrical membrane phenomena observed in proteinoid microspheres and emphasised its potential for integration with electronic devices (Ishima, Przybylski, & Fox, 1981). Proteinoids offer biocompatibility and the capacity to form stable structures and interact with biological molecules, making them very promising materials for connecting electronic systems with organisms. Fox's research on proteinoids also provided valuable understanding of the evolutionary mechanisms underlying information processing in biological systems. The process of self-sequencing amino acids in thermal proteins, as explained by Fox and Nakashima (1984), offers a possible mechanism for the development of early bioinformational processes (Fox & Nakashima, 1984). This idea questions traditional assumptions regarding the central importance of nucleic acids in the origin of life and presents an alternate viewpoint on the emergence of complex information-dense systems from simpler precursors. The study of proteinoids continues to be relevant in modern origin of life research and has implications for the production of innovative biomaterials and bioelectronic devices. Rationally designing and functionalising proteinoids allows for the development of synthetic systems with customised features, specifically for applications in bioengineering and nanotechnology.

6.2.1. Synthesis and characterisation of proteinoids

The synthesis and characterisation of proteinoids, which are artificial polymers resembling proteins, have attracted considerable interest in the biomaterials and origin of life research areas (Fox & Harada, 1960; Kolitz-Domb & Margel, 2018). This section explores the methods used for synthesising them and the analytical techniques used to characterise them.

Thermal condensation synthesis. The main approach for proteinoid synthesis involves the thermal condensation of amino acids, a procedure initially elucidated by Fox and his associates (Fox & Harada, 1960). This technique includes various crucial parameters:

- **Monomeric amino acid composition and ratios:** The selection and ratio of amino acids have a considerable impact on the structure and characteristics of the proteinoid formed (Nakashima & Fox, 1980). Recent research have investigated the integration of non-proteinogenic amino acids to enhance the functional variety of proteinoids (Kolitz-Domb & Margel, 2018).
- **Reaction conditions:** The temperature, duration, and atmospheric conditions are essential factors in the polymerisation process. Usually, temperatures between 160 °C and 200 °C are used, and the reaction periods might range from 3 to 24 h (Fox & Harada, 1960; Nakashima & Fox, 1980). A study by Rohlfing (1976) examined the impact of inert atmospheres, such as nitrogen or argon, on both the quantity and composition of the final product (Rohlfing, 1976).
- **Purification and isolation:** Proteinoids undergo a variety of purification procedures following synthesis, such as centrifuging, precipitation, and dialysis (Mougkogiannis & Adamatzky, 2024c). The search of more efficient purification protocols continues to be a dynamic field of research.
- **Yield optimisation and scalability:** Optimisation of reaction parameters and investigation of innovative reactor types have been the primary objectives of initiatives to enhance reaction yields and expand production (Lugasi et al., 2020). Nevertheless, there are ongoing obstacles to ensuring product consistency on a larger scale that require additional research.

Structural characterisation techniques. The heterogeneity of proteinoids requires a multifaceted approach to their characterisation. Commonly implemented analytical methodologies include:

- **Gel electrophoresis:** Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) is an extensively used method for evaluating the molecular weight distribution and heterogeneity of proteins and DNA (Singh, Unni, Neog, & Bhattacharyya, 2011). In order to enhance the resolution of complex proteinoid composites, two-dimensional gel electrophoresis has been introduced (Kumar & Rao, 1998).
- **Chromatography:** Size-exclusion chromatography (SEC) offers perspectives on the molecular weight distribution and potential aggregation behaviour of proteinoids (Bae & Kim, 2003). Ion-exchange chromatography has been employed to separate proteinoids according to their charge characteristics, thereby providing a higher level of resolution in fractionation studies (Rohlfing, 1976).
- **Spectroscopic techniques:** Ultraviolet–visible (UV–Vis) spectroscopy is used to measure the concentration of proteinoids and determine the presence of aromatic amino acids (Hadad et al., 2020). Fourier-transform infrared (FTIR) spectroscopy yields data on the secondary structural components of proteinoids, whereas circular dichroism (CD) spectroscopy provides information on the overall conformational characteristics of proteinoids (Stagi et al., 2022).
- **Mass spectrometry:** Matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) mass spectrometry has emerged as a powerful tool for determining the molecular mass and compositional analysis of proteinoids and protoenzymes (Mamajanov et al., 2020). Recent advancements in high-resolution mass spectrometry techniques, such as Orbitrap technology, hold promise for more detailed structural elucidation (Zarrouk et al., 2022).

Future prospects in proteinoid research include studying new synthetic methods, such as enzymatic polymerisation or solid-phase synthesis, that will improve the ability to manipulate sequence and structure with more precision. Furthermore, the incorporation of computational modelling alongside experimental characterisation techniques has the potential to offer more profound understanding of the links between the structure and function of these biomaterials.

6.3. Self-organisation and emergent properties in kombucha-proteinoid systems

6.3.1. Synergistic interactions between kombucha and proteinoids

Integration of proteinoids with kombucha-derived materials offers a unique opportunity to develop hybrid systems with improved properties and functionalities. Although there are few studies focussing on the interactions between kombucha and proteinoids, we can anticipate potential synergies by utilising insights from related biomaterial systems. Molecular recognition and binding events between kombucha cellulose and proteinoids may be analogous to interactions observed in other protein-polysaccharide systems. For example, Zhang et al. (2019) produced ordered nanostructures by showing the specific binding between engineered proteins and cellulose nanocrystals (Zhang et al., 2019). In the context of kombucha-proteinoid systems, the potential for the formation of novel hybrid assemblies with tailored properties is present in the form of analogous recognition events. The combined assembly of proteinoids and kombucha cellulose has the potential to improve the functionality and stability of both components. Ling et al. (2018) have observed this phenomenon in other biomaterial composites, such as cellulose-silk fibroin composites, which demonstrated superior biocompatibility and mechanical properties in comparison to individual components (Ling et al., 2018).

6.3.2. Self-assembly and pattern formation

Self-assembly mechanisms in kombucha-proteinoid systems have the ability to build complex and organised structures at many levels of size and complexity. Drawing parallels from Fox's work on proteinoid microspheres (Fox et al., 1959), we can propose that kombucha-proteinoid blends have the potential to self-assemble into structured patterns under suitable conditions. The significance of non-covalent interactions in facilitating self-assembly is likely to be crucial. The organisation of kombucha-proteinoid components may be influenced by hydrogen bonding, electrostatic interactions, and hydrophobic forces. The significance of these interactions in the self-assembly of other biomacromolecules has been demonstrated by Whitesides and Grzybowski (2002) in a detailed study of self-assembly at various scales (Whitesides & Grzybowski, 2002). The self-assembly processes in kombucha-proteinoid systems are believed to be influenced by environmental factors such as pH, temperature, and ionic strength. This environmental sensitivity might potentially be used to fabricate stimuli-responsive materials, such to the ones developed by Stuart et al. (2010) in their research on stimuli-responsive materials (Stuart et al., 2010). The self-healing mechanism of the kombucha-proteinoid system differs from traditional proteinoid synthesis by thermal polymerisation. Thermal proteinoids need a heat source for synthesis. The kombucha-proteinoid hybrid uses the healing abilities of the bacteria in kombucha. As shown in Mougkogiannis and Adamatzky (2023c), proteinoid microspheres can form networks. They self-organise at room temperature, with electrostatic channels. An ion exchange between the microspheres drives the electrical current. The bacterial cell matrix provides a scaffold that allows these proteinoid networks to remain connected even after mechanical disruption. When damaged, the cell's hygroscopic nature helps restore the electrical channels between the proteinoid microspheres. It does this by transporting water ions. This is similar to how kombucha bacteria cellulose heals, using hydrogen and ionic bonds. Combining proteins with the self-healing capabilities of cells provides a more sustainable and innovative approach than proteins alone.

6.3.3. Emergent electrical and optical properties

The self-assembly of kombucha-proteinoid systems can lead to the emergence of electrical and optical characteristics that are not found in the individual components alone. Although there is a lack of focused studies on the electrical characteristics of kombucha-proteinoid, we can get insights from similar systems. Self-assembled biomolecular systems have exhibited collective behaviour and coherent charge transfer. As a case study, Amdursky et al. (2019) provided evidence of the ability of self-assembled peptide nanostructures to transport protons across vast distances (Amdursky, Głowacki, & Meredith, 2019). Similar events could potentially arise in precisely structured kombucha-proteinoid complexes. The self-assembly process has the ability to create organised structures that can enhance conductivity and improve the mobility of charge carriers. Similar phenomena have been documented in other biomimetic substances, such as the very conductive films produced from PEDOT:PSS and cellulose nanofibrils by Wang et al. (2020) (Zhang et al., 2020). The hierarchical organisation of kombucha-proteinoid systems may give rise to photonic and optoelectronic characteristics. Although not directly connected, the research conducted by Kinoshita and Yoshioka (2005) on structural colours in biological systems serves as a source of inspiration for prospective optical characteristics that may emerge from self-organised biomaterials (Kinoshita & Yoshioka, 2005).

6.3.4. Bio-inspired design principles for living electronics

The phenomenon of self-organisation discovered in kombucha-proteinoid systems has the potential to inspire novel methodologies for the design and production of living electrical devices. By mimicking the principles of self-assembly observed in these systems, it might be feasible to generate complex operational structures with limited external intervention. Using self-assembly for device fabrication has the potential to improve manufacturing processes by increasing efficiency and scalability. This methodology has been effectively showcased in different situations, as exemplified by the research conducted by Cui et al. (2019) on the application of self-assembling nanoparticles in the field of electronics (Cui, Liu, Gan, Li, & Zhu, 2008). The potential use of kombucha-proteinoid systems' emergent features in living electronic devices includes sensing, computation, and actuation. Although speculative, this approach is consistent with the overall patterns observed in bio-inspired computing and soft robotics, as discussed by Adamatzky et al. (2017) in their research on unconventional approaches to computing (Adamatzky et al., 2017). The full exploration of the scalability and robustness of self-organised kombucha-proteinoid electronics is still awaiting. Nevertheless, the innate flexibility of these biological substances implies potential benefits in terms of durability and ability to repair themselves, similar to those observed in other living materials as explained by Nguyen et al. (2018) in their analysis of engineered living materials (Nguyen, Courchesne, Duraj-Thatte, Praveschotinunt, & Joshi, 2018).

7. Spontaneous formation of complex structures

7.1. Molecular self-assembly

Molecular self-assembly is a fundamental phenomenon observed in nature and is gaining significance in the fields of nanotechnology and materials research. Self-assembly is the process by which molecules arrange themselves into structured patterns without any external control.

7.1.1. Amphiphilic molecules and their self-assembly behaviour

Amphiphilic molecules, which include both hydrophilic and hydrophobic parts, play a crucial role in self-assembly phenomena. Their duality motivates the creation of diverse supramolecular structures in water-based environments. Israelachvili et al. (1976) presented a fundamental paradigm for understanding the impact of molecular geometry on the self-assembled structures created by amphiphiles (Israelachvili, Mitchell, & Ninham, 1976). The self-assembly of amphiphilic molecules is controlled by a precise equilibrium of forces, such as hydrophobic interactions, electrostatic forces, hydrogen bonding, and van der Waals interactions. Whitesides and Grzybowski (2002) emphasised the role of these interactions, together with outside factors, in determining the ultimate assembled structure (Whitesides & Grzybowski, 2002).

7.1.2. Formation of micelles, vesicles, and bilayers

Amphiphilic molecules have the ability to spontaneously arrange themselves into different forms, depending on their chemical composition and the surrounding environment. Micelles are formed when hydrophobic cores and hydrophilic shells come together in spherical aggregates. This occurs after a critical micelle concentration (CMC) is reached. Vesicles are spherical structures with a hollow interior that are surrounded by a membrane consisting of two layers, while bilayers are flat structures resembling sheets. Discher and Eisenberg (2002) illustrated the correlation between the hydrophilic-to-hydrophobic ratio in block copolymers and the architecture of self-assembled structures, ranging from spherical micelles to vesicles and beyond (Discher & Eisenberg, 2002). This approach has been extensively utilised in the construction of drug delivery systems and nanoreactors.

7.1.3. Factors influencing self-assembly processes

Multiple variables influence the self-assembly process. Ke et al. showed that temperature has an impact on the kinetics and thermodynamics of assembly, specifically in the context of DNA self-assembly (Ke, Lindsay, Chang, Liu, & Yan, 2008). The pH level can modify the charge of ionisable groups, hence affecting electrostatic interactions. The study conducted by Ou and Muthukumar (2006) demonstrated the influence of ionic strength on electrostatic screening during polyelectrolyte complexation (Ou & Muthukumar, 2006). Concentration is of utmost importance as it frequently determines whether assembly takes place or not. Whitesides et al. proved that surface characteristics can also direct self-assembly, as exemplified in their pioneering study on self-assembled monolayers (Whitesides, Mathias, & Seto, 1991).

7.1.4. Amphiphilic nature of proteinoids and their self-assembly behaviour

Proteinoids, which are synthetically produced molecules resembling proteins, display amphiphilic properties because of their diverse combination of amino acids. The amphiphilicity of these molecules causes them to spontaneously form different supramolecular structures by self-assembly. Kumar et al. showed that the self-assembly characteristics of proteinoids can be modified by altering the proportion of hydrophilic to hydrophobic amino acids during their synthesis (Kumar & Rao, 1998). The capacity for modifying proteinoids makes them very adaptable for constructing nano- and micro-structures with distinct characteristics. Fox and Nakashima (1980) were the first to investigate the process of proteinoid self-assembly. They demonstrated that under specific conditions, these molecules have the ability to spontaneously create microspheres (Fox & Nakashima, 1980). Belostozky (2015) has conducted additional research that has enhanced our understanding of proteinoid self-assembly mechanisms. Their work has demonstrated the impact of parameters such as pH, temperature, and ionic strength on the resultant structures (Belostozky, Kolitz-Domb, Haham, Grinberg, & Margel, 2017).

7.1.5. Role of kombucha components in modulating self-assembly processes

The self-assembly process of proteinoids can be considerably affected by components generated from Kombucha, specifically bacterial cellulose (BC) and other organic acids. In their study, Ullah et al. provided evidence that BC has the ability to act as a template for the self-assembly of different types of nanoparticles (Ullah et al., 2016). This finding suggests that BC could potentially play a role in directing the assembly of proteinoids. The presence of organic acids in kombucha, including acetic and glucuronic acids, can regulate the pH of the surroundings, so influencing the process of proteinoid self-assembly. Kačuráková et al. (2002) shown that these acids have the ability to interact with BC, which could potentially lead to the formation of distinct microenvironments for proteinoid assembly (Kačuráková, Smith, Gidley, & Wilson, 2002).

7.1.6. Characterisation techniques for studying molecular self-assembly

Various methodologies are utilised to investigate the process of molecule self-assembly at different scales and time intervals. Microscopy techniques enable the direct observation of self-assembled structures. The use of Transmission Electron Microscopy (TEM) and cryo-TEM, as demonstrated by Cui et al. provides the ability to capture very detailed images of nanoscale assemblies (Cui, Webber, & Stupp, 2010). Atomic Force Microscopy (AFM) is a technique that allows for the observation of surface topography and can be utilised to investigate the process of assembly on surfaces. Spectroscopic techniques provide valuable information about molecular interactions and structure. Circular Dichroism (CD) spectroscopy is a valuable technique for investigating the secondary structure of peptides and proteins that have been synthesised. This was exemplified by Hamley (2011) (Hamley, 2011). Fluorescence spectroscopy has the ability to examine the surrounding conditions of organised formations and track the rate at which they come together. Scattering techniques yield data regarding the dimensions, configuration, and internal composition of assemblies. Dynamic Light Scattering (DLS) is a frequently employed technique for determining the size distribution of assemblies in a liquid medium. SAXS and SANS provide precise structural data, as demonstrated by Svergun and Koch (2003) in their study on biological macromolecules (Svergun & Koch, 2003). To summarise, molecular self-assembly is a highly effective method for constructing complex and useful structures from basic building units. Understanding and controlling this procedure is vital for the advancement of sophisticated materials and nanoscale devices in diverse domains, ranging from medicine to electronics.

7.2. Supramolecular organisation

Supramolecular organisation is a key principle in the fields of materials science and biology. It refers to the natural arrangement of molecules into structured and organised patterns through non-covalent interactions. This phenomenon is of utmost importance for the advancement of sophisticated functional materials and for our understanding of complex biological systems.

7.2.1. Hierarchical assembly of molecular components

The process of organising molecular components into larger supramolecular structures is a fundamental principle in both natural and synthetic systems. Whitesides and Grzybowski (2002) conducted an extensive analysis of self-assembly across several scales, highlighting the ability of basic molecular interactions to generate complex and functional structures (Whitesides & Grzybowski, 2002). Proteins in biological systems demonstrate hierarchical assembly, progressing from the fundamental sequence to the quaternary structure. Dobson (2003) examined the role of protein folding and assembly in determining their function and the potential consequences of misfolding, which can result in conditions (Dobson, 2003). Proteinoids, which are artificial molecules resembling proteins, have the ability to spontaneously form different structures based on the various kinds of amino acids they contain and their environment. In their 1980 study, Fox and Nakashima provided evidence of the formation of proteinoid microspheres by means of thermal copolymerisation of amino acids. This study serves as an early illustration of the hierarchical assembly observed in these systems (Fox & Nakashima, 1980). Bacterial cellulose (BC) produced by kombucha serves as a framework for additional hierarchical arrangement. In their study, Ullah et al. examined the potential of BC as a template for nanocomposite building. They emphasised its capacity to direct the assembly of other molecules and particles. Proteinoids, when combined with BC, can result in complex and multi-tiered structures that exhibit improved functioning (Ullah et al., 2016).

7.2.2. Formation of fibres, sheets, and three-dimensional networks

Supramolecular organisation can lead to diverse structural morphologies. In 2003, Zhang provided evidence for the formation of self-assembling peptide nanofibers, which have the ability to arrange themselves into sheets and three-dimensional networks (Zhang, 2003). These structures possess potential uses in the fields of tissue engineering and regenerative medicine. Block copolymers exhibit flexible self-assembly behaviour within the domain of synthetic materials. In their 1999 study, Bates and Fredrickson examined the ability of block copolymers to create different nanostructures, such as spheres, cylinders, and lamellae. The formation of these structures is determined by the composition of the copolymers and the surrounding conditions (Bates & Fredrickson, 1999).

7.2.3. Influence of pH, temperature, and ionic strength on supramolecular organisation

Environmental factors are essential in determining the arrangement of supramolecular structures. The pH level can have a substantial impact on the charge state of molecules, which in turn affects their interactions and assembly behaviour. Aggeli et al. (2003) exhibited the phenomenon of pH-responsive peptide self-assembly, illustrating how slight variations in pH can induce significant changes in the structure (Aggeli et al., 2003). Temperature affects both the rate and energy changes of assembly processes. Ke et al. demonstrated the utilisation of temperature as a means to regulate the formation and breakdown of DNA nanostructures, emphasising its significance in supramolecular systems (Ke et al., 2008). The presence of ions in a solution affects the strength of electrostatic interactions in systems that are in the process of assembling. In their study, De la Cruz et al. examined the impact of ionic strength on the structure and arrangement of polyelectrolytes, highlighting its crucial role in supramolecular organisation (De La Cruz et al., 1995).

7.3. Emergence of functional microstructures

The hypothesis of spontaneous formation of functional microstructures is an interesting phenomenon reported in diverse self-assembling systems. Emergent structures have significant impacts on the characteristics and capabilities of materials at the microscale. This has implications for various domains, including materials science and bioengineering.

7.3.1. Spontaneous formation of pores, channels, and compartments

Self-assembling systems have the ability to spontaneously form complex microstructures, such as pores, channels, and compartments. In their study, Sun et al. showcased the creation of hierarchical porous structures in metal–organic frameworks (MOFs) via a self-templating method. This research emphasised the ability to customise porosity in functional materials (Sun, Chen, Chen, & Su, 2016). These structures provide large surface areas and regulated diffusion channels, which are crucial for use in catalysis and separation processes. Bement et al. investigated the natural occurrence of cortical waves and compartments during cell division in biological settings, demonstrating how basic chemical interactions can result in complex cellular structures (Bement, Goryachev, Miller, & von Dassow, 2024). This study highlights the significance of self-organisation in biological systems and offers valuable insights for the design of biomimetic materials.

7.3.2. Role of microstructures in selective permeability and transport properties

The presence of emergent microstructures has a substantial impact on the selective permeability and transport characteristics of materials. Habibi et al. created self-assembled peptide nanofibers that can produce ion channels that are selective, illustrating how the design of molecules can result in microstructures that have distinct transport properties (Habibi, Kamaly, Memic, & Shafiee, 2016). These systems have the ability to be used in membrane technology and ion-selective electrodes. Liu et al. developed self-assembled nanofluidic channels that had highly accurate molecular sieving capabilities. This demonstrates the potential of emerging microstructures in advanced separation technologies (Liu, Feng, Kis, & Radenovic, 2014). These findings emphasise the need of controlled self-assembly in producing materials with customised transport properties. It pertains to biological systems and offers valuable information for designing biomimetic materials.

7.3.3. Enzyme-like activity and catalytic properties of emergent microstructures

Surprisingly, some microstructures that form on their own display characteristics similar to enzymes and possess the ability to catalyse reactions. Lou et al. reported the formation of self-assembled peptide nanofibers that imitate the active sites of natural enzymes. These nanofibers exhibited effective catalytic activity in organic synthesis reactions (Lou, Zhang, Ye, & Wang, 2023). This study demonstrates the capacity of targeted self-assembly in fabricating synthetic enzymes and catalysts. In their study, Zhang et al. investigated the development of catalytic capabilities in self-assembled DNA nanostructures. They demonstrated that arranging catalytic sites in a specific spatial pattern can improve the efficiency of chemical reactions (Zhang & Yu, 2014). These discoveries provide new opportunities for the development of nanoscale reactors and catalytic systems.

7.3.4. Potential applications in drug delivery, biosensing, and micro-reactors

The self-assembly processes give rise to functional microstructures that have a wide range of possible uses. Ma et al. formed self-assembling peptide nanoparticles for delivery of drugs. These nanoparticles form stable microstructures and release therapeutic chemicals in a regulated manner. The researchers showed that this approach boosted the effectiveness of cancer treatment in their experiments (Ma, Xing, Yuan, Ogino, & Yan, 2020). Li et al. developed self-assembled DNA origami structures with integrated aptamer sensors for biosensing purposes. These structures have the ability to detect specific biomolecules with a high level of sensitivity (Li et al., 2018). This work demonstrates the capabilities of emerging microstructures in developing sophisticated biosensors. McDonald et al. showcased the application of self-assembled lipid microstructures as isolated reaction vessels for in vitro protein synthesis in the field of micro-reactors. This study emphasised the potential of these microstructures in the fields of synthetic biology and biocatalysis (Connacher, 2022). To summarise, the development of functional microstructures by self-assembly processes is a highly effective method for producing materials that have certain properties and functionalities. As our understanding of these phenomena expands, we should expect novel implementations in areas such as biology, environmental sensing, and advanced materials.

7.4. Dynamic and adaptive behaviour of complex structures

Advancements in the fields of soft matter physics and bioengineering have resulted in the emergence of complex structures that demonstrate remarkable dynamic and adaptive behaviours. These systems can be defined by their response functions, reconfiguration dynamics, and capacity for evolution (Lehn, 2007).

7.4.1. Stimuli-responsive structural changes and self-healing properties

Biomimetic materials that include stimuli-responsive polymers have demonstrated exceptional capacity to undergo reversible modifications in their structure in response to external stimuli, such as changes in pH, temperature, or light. Razzaq et al. (2021) developed a hydrogel-based actuator that imitates the swift motion of carnivorous plants. This actuator can capture small items with response times as short as a millisecond (Razzaq, Balk, Mazurek-Budzyńska, & Schadewald, 2023). In addition, metal-coordinated supramolecular polymers have demonstrated the ability to self-heal. This is made possible by the dynamic interactions between metals and ligands, which allow for autonomous repair of mechanical damage (Burnworth et al., 2011).

Stimuli-responsive materials exhibit non-linear responses to external stimuli, which can be mathematically expressed by the following equation:

$$\frac{\partial S}{\partial t} = D\nabla^2 S + f(S, E) - k(S) \tag{12}$$

where S represents the material's structural parameter, E is the external stimulus, D is the diffusion coefficient, $f(S, E)$ is the response function, and $k(S)$ is the relaxation term (Ortiz, Kohlstedt, Nguyen, & Glotzer, 2014). The healing properties seen in supramolecular systems can be accurately represented by employing a modified Langevin equation.

$$m\frac{d^2 r}{dt^2} = -\gamma\frac{dr}{dt} - \frac{\partial U(r)}{\partial r} + \eta(t) \tag{13}$$

where r is the separation between healing interfaces, $U(r)$ is the potential energy landscape, and $\eta(t)$ represents thermal fluctuations (Rumon, Sarkar, Alam, & Roy, 2023).

7.4.2. Adaptive reconfiguration in response to environmental cues

Active matter structures have shown the capacity to change their shape and function in response to environmental signals. Wang et al. (2024) successfully created artificial cells that can detect chemical gradients and rearrange their internal structure to enhance food absorption, imitating the actions of mobile bacteria (Wang et al., 2024). The ability to adaptively reconfigure provides potential for the development of intelligent materials that can independently optimise their performance in dynamic situations.

Phase diagrams can be used to visually represent the adaptive reconfiguration of a system by showing how its morphological states change in response to external inputs. Fig. 6 depicts a hypothetical phase diagram for a system that can be modified or rearranged.

The transitions between states can be described by a master equation:

$$\frac{\partial P_i(t)}{\partial t} = \sum_{j\neq i}[W_{ij}P_j(t) - W_{ji}P_i(t)] \tag{14}$$

where $P_i(t)$ is the probability of being in state i at time t, and W_{ij} are the transition rates between states (England, 2015).

7.5. Self-replication and evolution of complex structures

Advancements in synthetic biology have resulted in the development of artificial biological systems that can perform basic self-replication. In their study, Joyce et al. (2018) demonstrated the emergence of protocells capable of undergoing repetitive cycles of growth and division, facilitated by autocatalytic chemical reactions (Joyce & Szostak, 2018). Furthermore, these systems have demonstrated the capacity for development by integrating error-prone replication methods, resulting in opportunities for the creation of flexible and adaptable materials (Chen & Nowak, 2012).

Self-replication in synthetic systems can be modelled using autocatalytic reaction networks. A simplified model is the hypercycle:

$$\frac{dX_i}{dt} = k_i X_i X_{i-1} - X_i\sum_{j=1}^{n} X_j \tag{15}$$

where X_i represents the concentration of the ith replicator, and k_i is the replication rate constant (Vasas, Fernando, Santos, Kauffman, & Szathmáry, 2012). Evolution in these systems can be quantified using the Price equation:

$$\bar{w}\Delta\bar{z} = \mathrm{Cov}(w_i, z_i) + E(w_i\Delta z_i) \tag{16}$$

where $\bar{w}$ is the average fitness, $\Delta\bar{z}$ is the change in average trait value, w_i is the fitness of type i, and z_i is the trait value of type i (Frank, 2012).

7.5.1. Implications for the design of smart and adaptive living electronic systems

The incorporation of dynamic and adaptive behaviours into electronic systems offers interesting prospects for the advancement of future computing architectures. Biomolecular computing devices, using DNA strand displacement processes, have exhibited the capacity to execute complex logical operations and adjust their functionality in accordance with external stimuli (Qian & Winfree, 2011). In addition, the integration of living elements with electronic systems, such as biosensors based on bacteria, has distinct advantages in terms of sensitivity, specificity, and self-repair (Huang et al., 2024).

Hybrid cellular automata models can be used to define the integration of dynamic and adaptive behaviours into electronic systems. Fig. 7 illustrates a theoretical architecture for an adaptive bioelectronic system: The information processing capability of such systems can be quantified using measures from information theory, such as mutual information:

$$I(X;Y) = \sum_{x\in X}\sum_{y\in Y} p(x,y)\log\frac{p(x,y)}{p(x)p(y)} \tag{17}$$

where X represents input states and Y represents output states (Pfeifer, Lungarella, & Iida, 2012).

8. Emergence of collective behaviours and oscillations

The examination of collective behaviours in complex structures has uncovered fascinating emergent phenomena, namely in the realm of synchronisation and coherence. These phenomena have significant importance in a wide range of biological and artificial systems, including neural networks and designed smart materials (Strogatz, 2001).

8.1. Synchronisation and coherence

8.1.1. Coupled oscillations and synchronisation of electrical activity

Synchronisation in networks of coupled oscillators arises from complex relationships among individual components. The Kuramoto model offers a crucial foundation for understanding this phenomenon:

$$\frac{d\theta_i}{dt} = \omega_i + \frac{K}{N}\sum_{j=1}^{N}\sin(\theta_j - \theta_i) \tag{18}$$

where θ_i is the phase of oscillator i, ω_i is its natural frequency, K is the coupling strength, and N is the number of oscillators (Acebrón, Bonilla, Pérez Vicente, Ritort, & Spigler, 2005). This model has been modified in bioelectronic systems to explain the synchronisation of electrical activity in networks of artificial neurones (Segev, Shapira, Benveniste, & Ben-Jacob, 2001).

8.1.2. Role of network topology and connectivity in promoting synchronisation

The architecture of the network has a substantial impact on the dynamics of synchronisation. Recent study has indicated that small-world topologies, which are defined by a high level of clustering and low distances between nodes, promote fast and reliable synchronisation (Watts & Strogatz, 1998). The use of the master stability function approach has been crucial in examining the correlation between network structure and synchronizability.

$$\dot{\xi} = [DF(s) - \sigma DH(s)]\xi \tag{19}$$

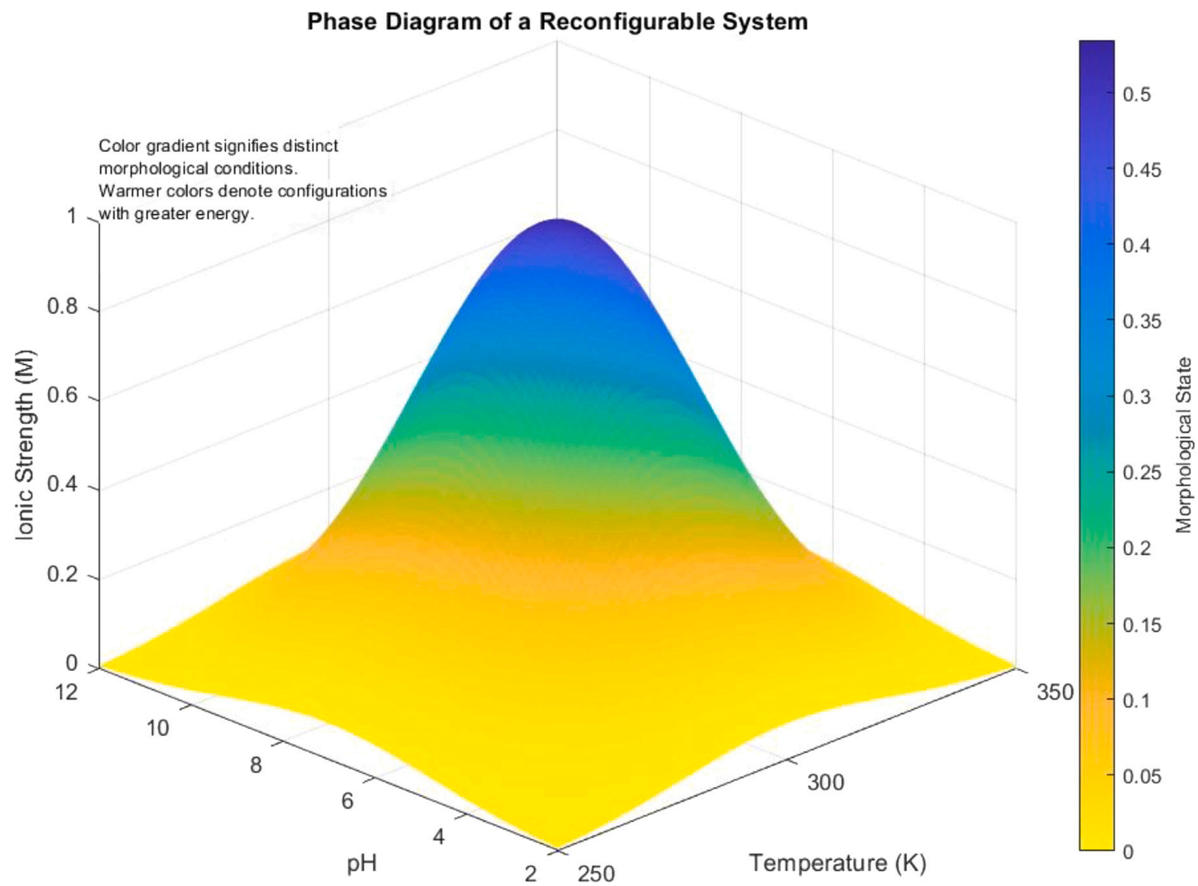

Fig. 6. The phase diagram of a reconfigurable system illustrates the several morphological states that occur as temperature, pH, and ionic strength change. The colour gradient signifies distinct morphological conditions, where warmer colours denote configurations with greater energy.

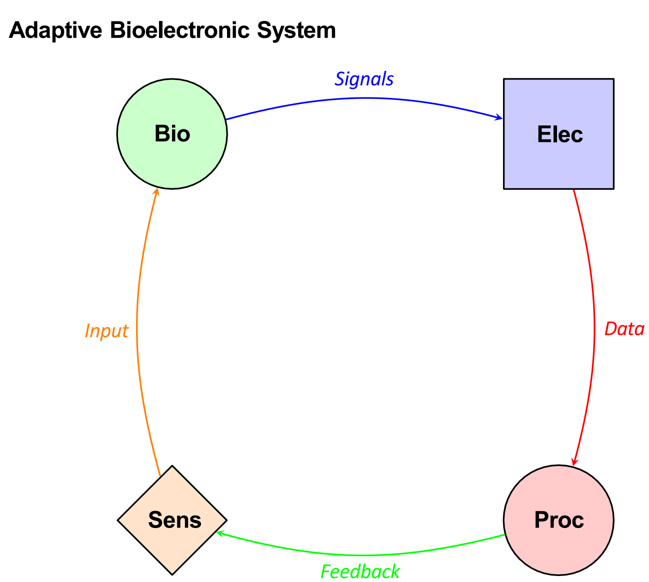

Fig. 7. Conceptual architecture of an adaptive bioelectronic system, showing interactions between biological (Bio), electronic (Elec), sensing (Sens), and processing (Proc) components.

where ξ represents perturbations from the synchronous state, $F(s)$ is the dynamics of individual nodes, $H(s)$ is the coupling function, and σ is the coupling strength (Pecora & Carroll, 1998).

8.1.3. Experimental observation and quantification of synchronisation

Advanced measurement techniques, including as multi-electrode arrays and optical imaging, have been used in experimental research to investigate synchronisation in bioelectronic networks. The order parameter r quantitatively measures the level of synchronisation:

$$re^{i\psi} = \frac{1}{N}\sum_{j=1}^{N} e^{i\theta_j} \tag{20}$$

where r represents the degree of synchronisation and ψ is the average phase (Arenas, Díaz-Guilera, Kurths, Moreno, & Zhou, 2008). Studies involving proteinoid-based neuromorphic networks have shown that changes in coupling strength can lead to transitions from desynchronised to synchronised states, similar to phase transitions observed in physical systems (Adamatzky, 2021; Mougkogiannis & Adamatzky, 2024c).

8.1.4. Implications for coordinated function and information processing

The synchronisation of bioelectronic networks has significant consequences for the processing of information and functional coordination. The phenomenon of synchronised oscillations can enhance the transmission of information, as evidenced by the communication through coherence theory in the field of neuroscience (Fries, 2015). In the field of biocomputing, synchronisation phenomena have been utilised to create new computing paradigms, such as reservoir computing using interconnected oscillators (Tanaka et al., 2019). Studying collective oscillations in these systems also offers valuable insights into how higher-order cognitive functions originate in biological brain networks. The binding by synchronisation hypothesis suggests that synchronised oscillations have a vital function in combining distributed information in the brain (Singer, 2007). Fig. 8 shows the synchronisation transition

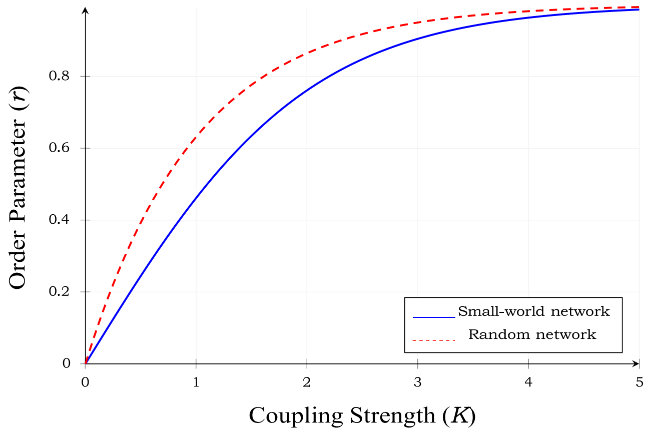

Fig. 8. Synchronisation transition in small-world and random networks as a function of coupling strength. The order parameter r quantifies the degree of synchronisation.

in small-world and random networks. These are networks with short paths between nodes. They resemble how proteinoid microspheres form clusters in kombucha-based bioelectronic systems. The figure shows how network topology and coupling strength affect collective behaviour (Sporns & Zwi, 2004; Watts & Strogatz, 1998).

Finally, the examination of synchronisation and coherence in bioelectronic networks provides a comprehensive structure for explaining the emergence of collective behaviours. These insights not only enhance our understanding of complex biological structures but also facilitate the development of inventive methods in biocomputing and adaptive materials design.

8.1.5. Network architectures in complex systems

The investigation of complex networks often requires examination of diverse network structures, each with unique topological characteristics that impact system dynamics. Fig. 9 depicts four essential network types that are frequently observed in both natural and engineered systems.

The ring network (Fig. 9a) represents a simple regular structure where each node connects only to its nearest neighbours. This topology is often seen in distributed computing systems and can exhibit interesting synchronisation properties (Watts & Strogatz, 1998).

In contrast, the fully connected network (Fig. 9b) represents the opposite extreme, where every node is directly connected to every other node. While rare in large-scale natural systems due to its high connection cost, this topology is important in theoretical studies and small-scale engineered systems (Newman, 2010).

Random graphs (Fig. 9c) introduce stochasticity into network formation, resulting in structures that balance connectivity and sparsity. These networks often serve as null models in network analysis and have been extensively studied in the context of percolation theory (Erdös, Rényi, & Bollobás, 1959).

Scale-free networks, as shown in Fig. 9d, have a degree distribution that follows a power-law pattern. This means that there are a few highly linked hub nodes in the network. This topology is commonly observed in several real-world networks, including as biological, social, and technological systems. It has significant consequences for the resilience of networks and the transmission of information (Barabási & Albert, 1999).

The varied characteristics of different network structures emphasise the significance of topology in shaping the overall behaviours of complex systems. Comprehending these systems is essential for foreseeing and manipulating the combined movements of interrelated components in many fields of research and technology.

8.2. Spatio-temporal pattern formation

Spatio-temporal pattern generation is a fundamental phenomenon observed in complex systems, including various fields such as biological development and chemical reactions. These patterns arise from the interplay between nearby interactions and the spread of information or substances through space, frequently resulting in complex and ever-changing structures.

8.2.1. Reaction–diffusion mechanisms and turing patterns

Reaction–diffusion systems, initially introduced by Alan Turing in 1952, offer a conceptual framework for understanding the process of pattern formation in the natural world (Turing, 1990). These systems exhibit the interaction between localised chemical reactions and diffusion processes, resulting in the spontaneous formation of spatial patterns. Scholes (2019) has recently shown how to incorporate Turing patterns into synthetic biological systems, illustrating the ability to build self-organising structures within living cells (Scholes, Schnoerr, Isalan, & Stumpf, 2019). Their study emphasises the use of reaction–diffusion principles to generate customisable biological patterns, which have the potential to be used in tissue engineering and biotechnology. Gjorgjieva et al. (2007) conducted a study in the realm of materials science where they observed the development of Turing-like patterns in thin film growth. This study shows that these principles are not limited to biological systems (Gjorgjieva & Jacobsen, 2007). Their findings propose novel methods for regulating material characteristics by means of spatio-temporal patterning.

8.2.2. Self-organised waves, spirals, and fractals

Self-organised waves, spirals, and fractals are frequently observed in various natural and artificial systems that display the emergence of patterns in space and time. Yang et al. (2018) conducted a comprehensive analysis of the latest developments in understanding the dynamics of spiral waves in excitable medium. These findings have significant implications for the study of cardiac arrhythmias and neuronal activity (Yang & Wu, 2018). Their work highlights the significance of these patterns in both physiological and pathological conditions. Fractal patterns, which exhibit self-similarity at different scales, have been detected in many systems. Suber et al. (2012) documented the appearance of fractal-like formations in self-assembling nanoparticles, illustrating how basic interaction principles can result in detailed hierarchical arrangements (Suber & Campi, 2012). These discoveries provide new opportunities to develop materials with customised structural characteristics at various length scales.

8.2.3. Role of feedback loops and nonlinear interactions in pattern formation

Feedback loops and nonlinear interactions are essential factors in the formation as well as durability of spatio-temporal patterns. In their study, Kondo and Miura (2020) investigated the role of gene regulatory networks containing feedback loops in the process of pattern generation in animal development (Kondo & Miura, 2010). Their research emphasises the interaction between molecular processes and the creation of patterns at a larger scale in biological systems. Grzybowski and Huck (2022) showed that in chemical systems, the combination of nonlinear chemical processes and diffusion can result in complicated spatio-temporal patterns, such as oscillations and travelling waves (Grzybowski & Huck, 2016). Their research offers valuable insights into the fundamental concepts of designing synthetic chemical systems that can exhibit programmable dynamic behaviours. As shown in Fig. 10, the complexity of pattern formation increases from a simple morphogen gradient (A) to two non-interacting morphogens (B), and finally to interacting morphogens that form complex Turing patterns (C).

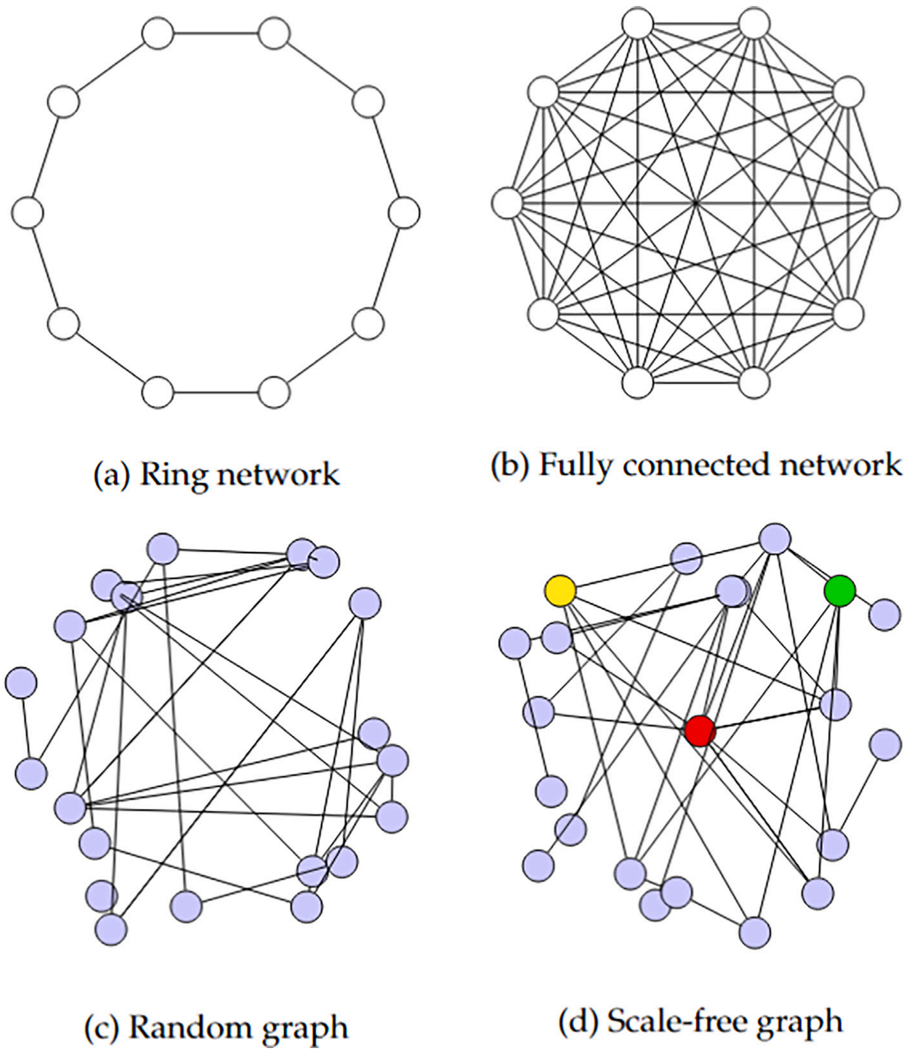

Fig. 9. Schematic illustration of different network architectures. (a) Ring network of 10 nodes. (b) Fully connected network of 10 nodes. (c) Random graph with 20 nodes and approximately 30 edges. (d) Scale-free graph with 22 nodes, where red, green, and yellow nodes represent hubs with higher degrees (Strogatz, 2001).

8.2.4. Characterisation of spatio-temporal patterns using imaging techniques

The use of advanced imaging techniques has significantly transformed our capacity to notice and analyse patterns in space and time across different scales. Mercker et al. (2013) employed light-sheet microscopy to observe the live formation of patterns during embryonic development, offering unparallelled understanding of the kinetics of morphogenesis (Mercker, Hartmann, & Marciniak-Czochra, 2013). Jun et al. (2022) used in situ electron microscopy in materials science to investigate the development of nanostructured patterns during material growth and transformation processes (Jun et al., 2022). Their methodology facilitates the direct examination of pattern generation mechanisms at the nanoscale, hence enabling the advancement of more accurate control strategies for material synthesis. Computational image analysis techniques have made considerable advancements. Liu et al. (2022) developed machine learning methods to automatically identify and categorise spatio-temporal patterns in extensive biological and chemical datasets (Liu, Li, & Zhang, 2022). These technologies improve our capacity to derive significant information from complicated networks that create patterns and have the potential to result in novel findings in the field. As our understanding of the fundamental mechanisms becomes more profound and our capacity to observe and manipulate these processes grows, we can expect novel applications in various domains, including synthetic biology and advanced materials design. The Turing model demonstrates remarkable versatility in pattern generation, as illustrated in Fig. 11. By subtly adjusting parameter values within the same fundamental equation, a diverse array of two-dimensional patterns emerges. These patterns range from radial spots (Fig. 11A) to stripes (Fig. 1B), uniform spots (Fig. 11C), reverse spots (Fig. 11D), concentric rings (Fig. 11E), and even Voronoi-like tessellations (Fig. 11F). This diversity underscores the model's capacity to explain various naturally occurring patterns through simple mathematical principles (Kondo & Miura, 2010).

Fig. 10 shows the key differences between simple morphogen gradients and Turing pattern formation. In the morphogen gradient model (A1-B4), pattern formation relies on pre-existing sources and sinks. It shows how a single morphogen (A) or two non-interacting ones (B) create basic concentration gradients. However, when morphogens interact (C), the system self-organises. It can then generate complex patterns without pre-positioned sources. "Waves" (C2), spots, stripes (C3), and labyrinthine patterns (C4) show that molecular interactions enable autonomous pattern formation. They do not require predetermined spatial information. Fig. 11 showcases the diverse spatial patterns that can emerge from Turing systems under different parameter conditions. All patterns were generated using the same reaction–diffusion equations. Only slight modifications to the parameters were made. Case V

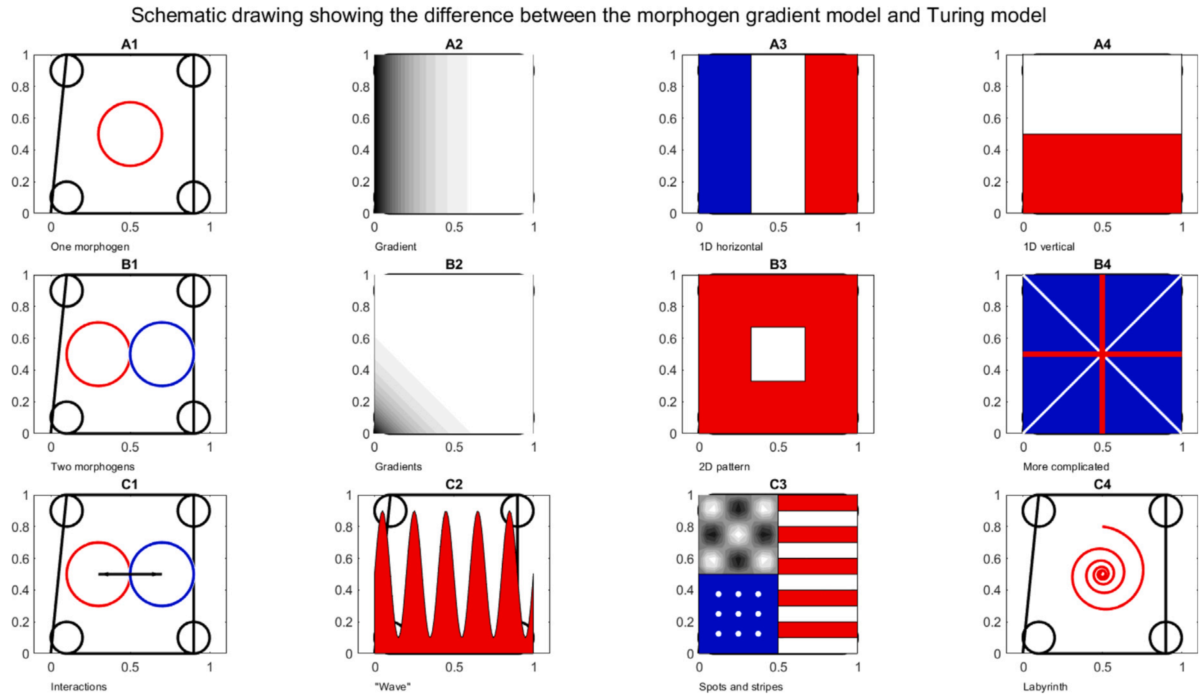

Fig. 10. Schematic drawing showing the difference between the morphogen gradient model and Turing model. (A) Single morphogen gradient. (B) Two non-interacting morphogens. (C) Interacting morphogens forming complex patterns (Kondo & Miura, 2010).

demonstrates travelling wave solutions resulting in radial spots. Case VI patterns are stationary Turing patterns. They include periodic stripes, regular spot arrays, and isolated reverse spots. The last are dark, not bright, spots of high concentrations. They also include concentric rings with rotational symmetry. And, they have Voronoi-like tessellations that resemble cellular patterns. One math framework has many patterns. It helps explain how Turing mechanisms could create diverse patterns in biology, from animal coats to tissue organisation.

8.3. *Bistability and multistability*

Kombucha-proteinoid systems demonstrate notable dynamic characteristics, including as the occurrence of bistability and multistability. The emergence of these characteristics is a result of extensive interactions between microbial communities and proteinoid structures. This gives rise to interesting emergent behaviours that have the potential to be applied in bio-inspired technologies (Mougkogiannis et al., 2024b; Nikolaidou et al., 2023).

8.3.1. *Coexistence of multiple stable states*

Recent study has shown that kombucha-proteinoid systems can have many stable states coexisting with each other (Mougkogiannis et al., 2024a). These unique states are defined by varying distributions of microorganisms, metabolic patterns, and proteinoid conformations. The system's underlying complexity and adaptability are demonstrated by its ability to maintain multiple stable configurations despite identical external conditions (Taillefumier, Posfai, Meir, & Wingreen, 2017).

8.3.2. *Hysteresis and switch-like behaviour*

Kombucha-proteinoid systems have hysteresis, which is a response to external stimuli that is depending on the system's past experience (Mougkogiannis & Adamatzky, 2023b; Nikolaidou, Mougkogiannis, & Adamatzky, 2024). This feature is characterised by a switch-like behaviour, where the system can rapidly transition between stable states in response to minor disturbances. This behaviour has resemblance to the biological switches seen in gene regulatory networks and neural systems (Liao & Cai, 2014).

8.3.3. *Memory effects and information storage*

Kombucha-proteinoid systems possess a multistable quality that allows them to exhibit memory effects, meaning that the system may store information on its previous states (Mougkogiannis et al., 2024a). The ability to store information is facilitated by continuous modifications in the structure of microbial communities and proteinoid structures. The length and precision of this memory effect are influenced by other factors, such as the complexity of the system and the surrounding environmental conditions (Xu et al., 2023).

8.3.4. *Potential applications*

The presence of bistability and multistability in kombucha-proteinoid systems presents fascinating opportunities for the development of bio-inspired computer and memory devices (Akerkar & Sajja, 2009). These characteristics can be utilised to develop innovative biocomputing systems, in which information processing and storage are carried out by controlling interactions between microbes and proteinoids (Fox et al., 1974). Moreover, the system's capacity to sustain numerous stable states has the potential to stimulate the development of adaptive materials and sensors that possess improved functionality (Simoska et al., 2021).

8.4. *Emergent computation and information processing*

The interplay of biological components and synthetic materials presents distinct opportunities for developing new computational frameworks. The bio-hybrid systems have emergent characteristics that can be used for information processing and problem-solving.

8.4.1. *Collective decision-making and problem-solving capabilities*

Enzyme-based systems showed exceptional ability to make decisions as collectively. Zauner and Conrad (2001) demonstrated that networks of allosterically regulated enzymes have the capability to carry out complicated computations such as pattern recognition. Likewise, kombucha-proteinoid networks might have similar emergent behaviours, potentially resolving NP-hard problems due to their intrinsic parallel processing capabilities.

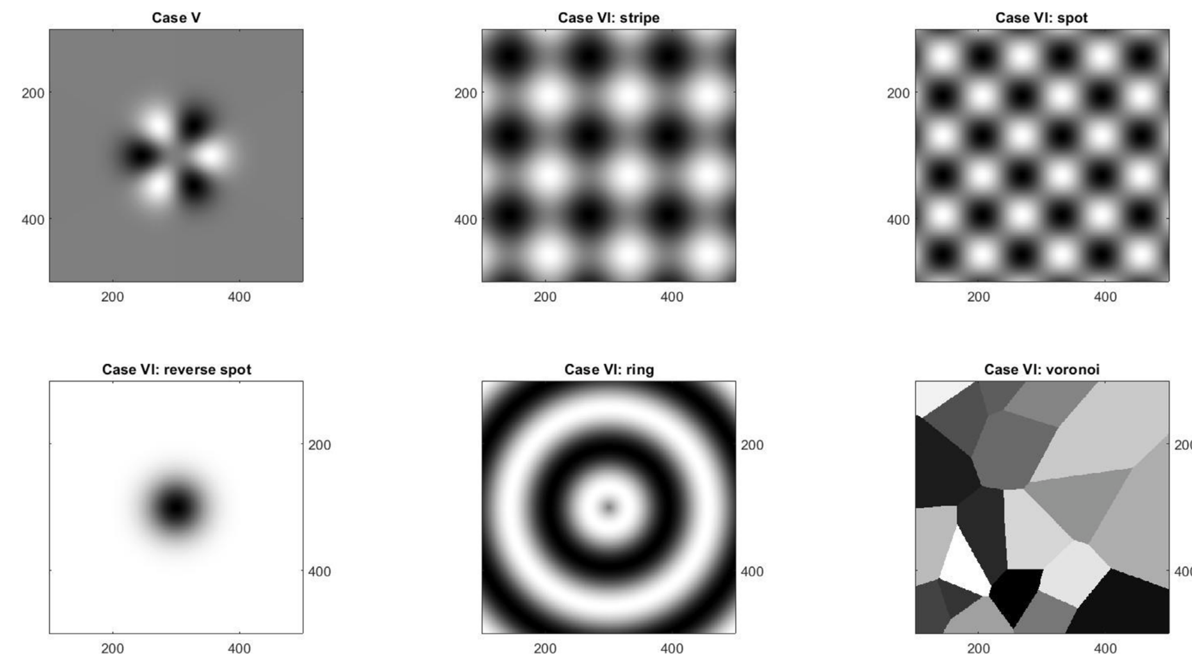

Fig. 11. Two-dimensional patterns generated by the Turing model under different parameter conditions. (A) Case V: Radial spots. (B) Case VI: Stripes. (C) Case VI: Spots. (D) Case VI: Reverse spots. (E) Case VI: Concentric rings. (F) Case VI: Voronoi-like tessellation. All patterns were generated using the same underlying equation with slight variations in parameter values (Kondo & Miura, 2010).

8.4.2. Distributed computation and parallel processing

Biomolecular computers, namely those using DNA, have demonstrated the capacity for highly parallel processing. The decentralised structure of kombucha-proteinoid networks has the potential to facilitate simultaneous data processing, perhaps surpassing conventional silicon-based computers in specific problem domains (Adleman, 1994). This technique is in line with the emerging topic of unconventional computing, which employs biological and chemical systems for their distinct computational capabilities (Adamatzky, 2018).

8.4.3. Adaptation and learning through self-organisation and plasticity

Slime molds and other self-organising systems have exhibited adaptive behaviours that can be seen as a type of primitive intelligence (Nakagaki, Yamada, & Tóth, 2000). The adaptability of kombucha-proteinoid networks, impacted by their biological constituents, may allow for comparable adaptive responses to external stimuli, potentially resulting in systems capable of acquiring knowledge and achieving optimisation.

8.4.4. Bio-inspired algorithms and architectures for living electronics

Neuromorphic engineering has made substantial progress in replicating biological brain networks (Indiveri et al., 2011). Kombucha-proteinoid systems have the potential to provide a distinctive framework for applying bio-inspired algorithms, thereby connecting artificial and biological computation. These electrical systems that are alive have the potential to result in computing architectures that are more energy-efficient and adaptable.

9. Applications of kombucha and proteinoid-driven living electronics

9.1. Biosensors and bioelectronic devices

The combination of biological components with electronic systems has brought about an important development in sensing technologies, providing unparallelled levels of sensitivity, selectivity, and versatility. Kombucha-proteinoid systems offer a new opportunity to create sophisticated biosensors and bioelectronic devices by combining the distinctive characteristics of kombucha cellulose matrices and proteinoid structures.

9.1.1. Electrochemical biosensors

Electrochemical biosensors have attracted considerable interest because of their exceptional sensitivity, quick reaction, and possibility for being made smaller in size (Wang, 2008). By incorporating kombucha-proteinoid complexes into these systems, their performance can be improved and their applications can be broadened.

Enzymatic and non-enzymatic sensing mechanisms. Enzymatic biosensors employ certain enzymes that are fixed on electrode surfaces to facilitate reactions involving specific target analytes. Glucose oxidase-based sensors have been extensively utilised for diabetes monitoring, as exemplified by their widespread usage (Heller & Feldman, 2008). Within kombucha-proteinoid systems, the proteinoid element has the potential to function as a unique enzyme mimic, perhaps providing enhanced stability and adjustability in comparison to natural enzymes. Non-enzymatic sensing techniques, such as the direct transfer of electrons between analytes and electrode surfaces, have demonstrated potential in the detection of numerous compounds (Chen & Chatterjee, 2013). The conductivity of kombucha cellulose, when paired with proteinoids, may permit direct electron transfer functions, enabling label-free detection of analytes.

Kombucha-based electrodes and immobilisation strategies. The porous nature of kombucha cellulose offers a superb framework for electrode customisation. Recent study has shown that bacterial cellulose can be used as a framework for creating conductive materials in supercapacitors (Chen & Chatterjee, 2013). Analogous methodologies might be employed to kombucha cellulose, resulting in the production of electrodes with a large surface area that can be used in biosensing applications. The immobilisation of biorecognition elements is essential for optimising the function of biosensors. The proteinoids have a wide range of functional groups that can be used to chemically attach enzymes or other biomolecules. Moreover, the self-assembling nature of proteinoids could facilitate the development of three-dimensional sensing interfaces, potentially enhancing the concentration of active sites.

The SEM micrographs in Fig. 12 offer important insights into the morphological characteristics of proteinoids derived from kombucha and their composites with polyaniline. Images (a) and (b) demonstrate

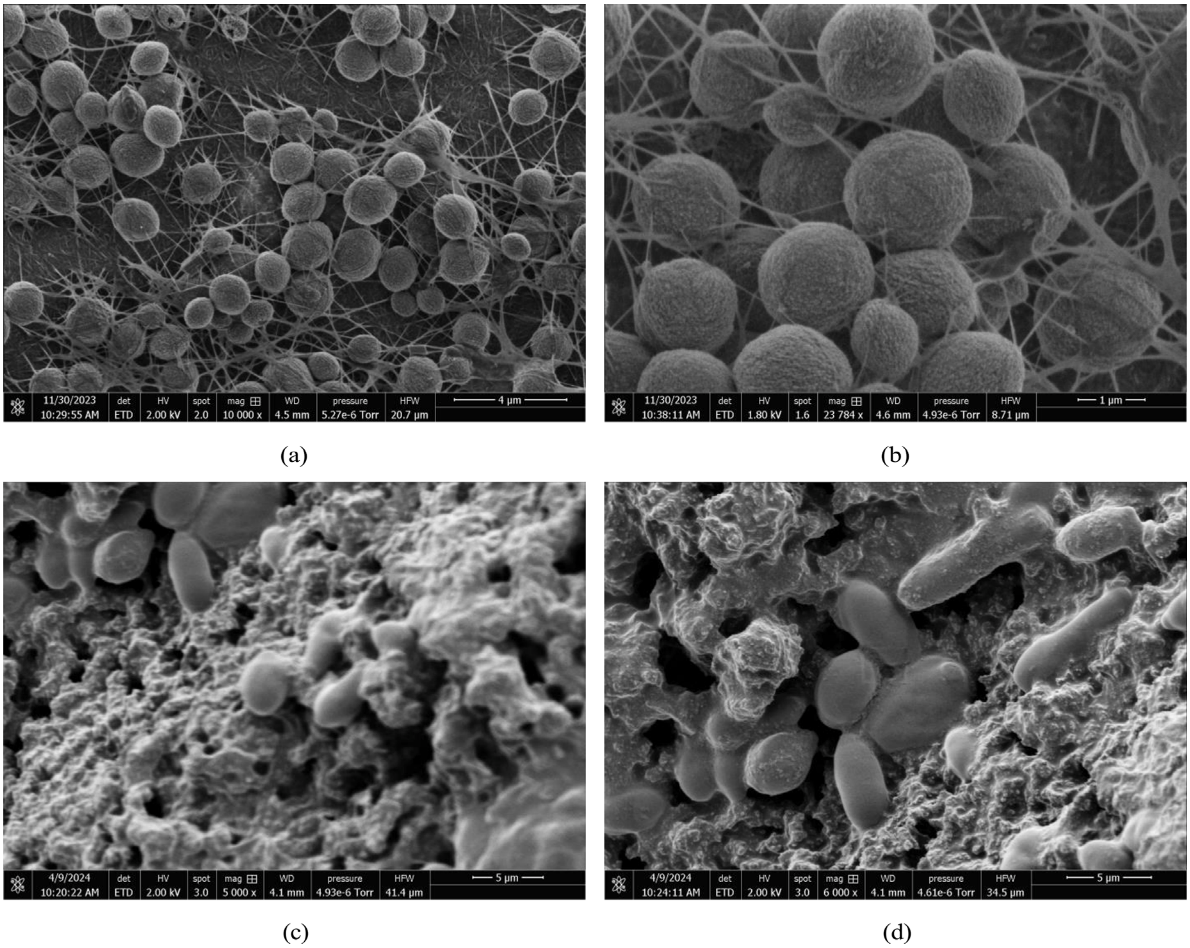

Fig. 12. SEM analysis of kombucha-derived proteinoids and composites (a) Kombucha proteinoids at ionic strength I = 0.065 mol/L, showing spherical microstructures interconnected by a fine fibrous network. Magnification: 10,000x, scale bar: 4 μm. (b) Higher magnification (23,780x) of kombucha proteinoids at I = 0.065 mol/L, revealing detailed surface morphology of spherical particles with varying sizes. Scale bar: 1 μm. (c) Kombucha-proteinoid-polyaniline composite at I = 0, exhibiting a heterogeneous structure with both spheroidal and irregular particles embedded in a porous matrix. Magnification: 5,000x, scale bar: 5 μm. (d) Detailed view of the kombucha-proteinoid-polyaniline composite at I = 0, highlighting the integration of elongated structures within a complex, interconnected network. Magnification: 6,000x, scale bar: 5 μm.

the development of spherical proteinoid structures in an ionic environment with an ionic strength of 0.065 mol/L. These structures consist of particles of varying sizes, ranging from sub-micron to several microns in diameter. They are interconnected by an elastic fibrous network. On the other hand, images (c) and (d) showcase the complex structure of kombucha-proteinoid-polyaniline composites formed at I = 0. These composites exhibit a diverse combination of spheroidal and elongated structures, which are embedded within a porous matrix. This comparison highlights the notable impact of ionic strength and polyaniline incorporation on the self-assembly and morphology of these bio-derived materials. It suggests potential applications in biomaterials engineering and sustainable composite development.

Proteinoid-modified biosensors for enhanced sensitivity and selectivity. Proteinoids, due to their capacity to create microspheres and their natural compatibility with living organisms, offer unique potential for the development of biosensors. Their amphiphilic properties can be utilised to provide microenvironments that improve the stability and efficiency of enzymes (Kwak, 2014). Moreover, the ability to design the production of proteinoids facilitates the inclusion of particular functional groups, which could potentially enable the creation of molecular imprints for highly precise sensing.

Applications in healthcare, environmental monitoring, and food safety. Kombucha-proteinoid biosensors possess a wide range of applications that can be used in several fields. These sensors have the potential to be used in healthcare for continuous monitoring of biomarkers in biological fluids. Possible environmental uses could involve identifying contaminants in water or soil. Within the realm of food safety, the compatibility of kombucha-proteinoid systems has the potential to enable the development of sensors that are both non-toxic and biodegradable. These sensors might be utilised for the purpose of detecting toxins or monitoring the quality of food.

9.1.2. Optical biosensors

Optical biosensors have benefits such as non-invasiveness, instantaneous monitoring, and the potential for label-free detection. Combining kombucha-proteinoid systems with optical transduction technologies has the potential for developing innovative sensing platforms.

Fluorescence and colorimetric sensing approaches. Fluorescence-based sensing is a remarkably sensitive and extensively employed technique in the field of biosensors. Proteinoids have the potential to be modified in order to include fluorescent amino acids or to selectively attach to fluorescent dyes, resulting in the development of highly precise sensing components. The transparency of cellulose films derived from kombucha could enable the creation of optical sensing devices with little interference. Colorimetric sensors use apparent colour changes to provide straightforward and cost-efficient detection methods. Encapsulating indicators into proteinoid microspheres has the potential to facilitate the creation of robust and durable colorimetric sensors (Wolfbeis, 2005).

Förster resonance energy transfer (FRET) and bioluminescence. FRET-based sensors offer an effective technique for detection molecular interactions and conformational modifications. By integrating suitable donor and acceptor molecules into proteinoid structures, it is possible to create very sensitive FRET sensors for a wide range of analytes. Bioluminescent devices, such as those using luciferase enzymes, have remarkable sensitivity because they lack background light. Enclosing bioluminescent proteins in proteinoid microspheres could improve their durability and allow them to be included into kombucha cellulose matrices to produce self-illuminating biosensors (Roda, Guardigli, Michelini, & Mirasoli, 2009).

Integration of kombucha and proteinoids with optical transducers. By combining kombucha-proteinoid systems with optical transducers like optical fibres or plasmonic nanostructures, it is possible to develop sensing devices that are both highly sensitive and small in size. For example, the porous composition of kombucha cellulose can be utilised to produce photonic crystals, which allow for label-free detection by monitoring variations in refractive index (Yetisen, Akram, & Lowe, 2013).

Multiplexed and real-time sensing capabilities. The capacity to produce proteinoids with a wide range of characteristics presents opportunities for the development of multiplexed sensing. Simultaneous detection of numerous analytes can be performed by introducing distinct recognition elements or sensitive components into various proteinoid populations. Real-time sensing is essential for numerous applications, especially in the fields of healthcare and environmental monitoring. The inherent fluidity of kombucha-proteinoid systems, combined with swift optical detecting techniques, has the potential to provide uninterrupted, instantaneous monitoring of diverse parameters. Finally, the distinctive characteristics of kombucha-proteinoid systems present promising opportunities for the advancement of innovative biosensors and bioelectronic devices. By merging the structural benefits of kombucha cellulose with the programmable capabilities of proteinoids, these hybrid systems possess the capacity to tackle existing obstacles in biosensing technology and create opportunities for highly sensitive, specific, and environmentally-friendly sensing platforms.

9.1.3. Wearable and implantable bioelectronics

In recent years, the field of wearable and implantable bioelectronics has rapidly advanced due to the demand for personalised medicine and continuous health monitoring. Kombucha-proteinoid systems possess distinctive characteristics that have the potential to address current challenges in this field and facilitate the development of new applications.

Flexible and stretchable living electronic devices. Flexibility and stretchability are essential for ensuring the ease of use and longevity of wearable devices. Recent advancements in this field have concentrated on materials that can adapt to the ever-changing characteristics of biological tissues (Rogers, Someya, & Huang, 2010). The innate flexibility of kombucha cellulose, coupled with the versatile characteristics of proteinoids, offers a chance to fabricate entirely biocompatible, flexible electronic devices. For example, the unique nanofibrillary composition of kombucha cellulose could be utilised to produce flexible conductive networks, comparable to recent research on nanocellulose-based flexible electronics (Shi et al., 2013). By integrating proteinoids with distinct characteristics, these networks can acquire detecting or actuating capabilities, resulting in the development of versatile and flexible devices.

Kombucha-based conductive patches and textiles. The use of kombucha cellulose as a substrate for conductive materials has the potential to enable the development of smart fabrics and adhesive patches for health monitoring. Recent studies have demonstrated the feasibility of creating conductive bacterial cellulose by in situ polymerisation of conductive polymers (Müller, Rambo, Recouvreux, Porto, & Barra, 2011). Potentially, the same methods might be used to produce breathable and biocompatible conductive fabrics using kombucha cellulose. Recent advances have shown that there are other ways to scale up bacterial cellulose besides relying on polymers. A stable, biomimetic osmotic coupling process can create transport systems. It does this by in situ carbonising cellulose. This process enables rapid device delivery (under 1 s) using water-based fluids (Yang et al., 2024). This eco-friendly fabrication method cuts greenhouse gas emissions. It is better than traditional microfabrication techniques. It also has excellent electrical properties for bioelectronics. The remarkable morphological response of cellulose to water makes it particularly attractive for bioengineering applications. As mentioned before, cellulose bacteria undergo significant changes in shape when exposed to water, such as plant movements in nature. This hygroscopic property combined with the compatibility and durability of cellulose makes it a good candidate for soft robotics. A water-controlled regeneration system is very useful because it eliminates harsh electronic controls or potentially harmful stimuli (Quan, Kisailus, & Meyers, 2021). Furthermore, the integration of proteinoids into these conductive kombucha matrices has the potential to facilitate the production of textiles that can respond to stimuli. Proteinoids have the potential to be engineered in such a way that they can undergo conformational changes when exposed to certain stimuli. This would result in modifications to the electrical characteristics of the textile, allowing it to have sensing capabilities or the ability to release drugs.

Proteinoid-based bioresorbable and biodegradable electronics. Transient electronics, which refers to devices that can safely dissolve in the body once they have served their purpose, is an expanding field of study (Hwang et al., 2012). Proteinoids, which consist of amino acids, provide a superb foundation for developing biodegradable electronic components. Their ability to be programmed enables precise control over the rates of degradation and the formation of byproducts, thereby tackling significant obstacles in this particular field. Kombucha cellulose has the potential to function as a biodegradable material for proteinoid-based electronics, enabling the development of entirely bioresorbable devices. This method could be especially advantageous for implantable sensors or drug delivery systems that do not require permanent implantation.

Applications in personalised healthcare, drug delivery, and tissue engineering. Incorporating kombucha-proteinoid systems into wearable and implantable devices offers a wide range of potential uses. These devices have the potential to provide continuous monitoring of several biomarkers in personalised healthcare, offering real-time data for the early detection of diseases and the optimisation of treatment. The inherent responsiveness of proteinoids can be used to develop intelligent medication delivery systems. Proteinoid microspheres have the potential to be engineered to release drugs based on particular physiological conditions. The kombucha cellulose matrix acts as a suitable structure for controlled drug release (Patel & Misra, 2011). The biocompatibility and customisable features of kombucha-proteinoid systems can be used in tissue engineering to develop scaffolds that not only facilitate tissue growth but also provide real-time monitoring of the regeneration process.

9.1.4. Neuromorphic and bio-inspired computing

Neuromorphic computing is a revolutionary approach to information processing that seeks to mimic the structure and function of biological neural networks. The complex dynamics and flexibility of kombucha-proteinoid systems present exciting prospects in this arena.

Emulation of biological neural networks with kombucha-proteinoid systems. The complex interconnection of cellulose fibres in kombucha, along with the dispersed arrangement of proteinoid structures, has similarities to the detailed connectivity of biological neural networks. The resemblance in structure could be used to construct physical analogues of brain networks. The use of complicated dynamical systems for computation has been showcased in recent research on reservoir computing employing physical systems (Tanaka et al., 2019). The kombucha-proteinoid network possesses a diverse range of dynamics that result from the combined actions of microorganisms and proteinoid interactions. This network has the potential to function as a distinctive physical storage system for information processing.

Spiking neural networks and synaptic plasticity. SNNs, which closely imitate the behaviour of organic neurones, have demonstrated potential in energy-efficient computing (Merolla et al., 2014). The electrochemical characteristics of kombucha-proteinoid systems have the potential to be utilised for the implementation of spiking behaviour. Furthermore, the adaptable characteristics of proteinoids could be employed to mimic synaptic plasticity, which refers to the capacity of synapses to enhance or diminish in strength as time passes. By producing proteinoids that can alter their shape or form clusters in reaction to electrical or chemical signals, it is possible to establish adaptable links in the kombucha-proteinoid network, imitating the learning mechanisms found in living organisms.

Reservoir computing and temporal information processing. Reservoir computing, a well-suited computational method to handle inputs that change over time, has been successfully applied in many physical systems (Lukoševičius, Jaeger, & Schrauwen, 2012). Kombucha-proteinoid systems has a dynamic nature that is regulated by the metabolic activities of microbes and the responsive behaviour of proteinoids. This characteristic makes them a fascinating option for reservoir computing applications. The kombucha-proteinoid system's temporal progression has the potential to be utilised for the manipulation of time-series data. The proteinoid components within the system can be adjusted to modify the system's dynamics according to specific requirements.

Brain-machine interfaces and neuromodulation applications. The biocompatibility and bioresorbability of kombucha-proteinoid systems provide them compelling candidates for brain-machine interfaces. Advancements in soft, biocompatible electronics for brain interfaces (Someya, Bao, & Malliaras, 2016) can be further enhanced by employing kombucha-proteinoid materials. This has the potential to develop adaptive interfaces that can completely merge with neural tissue. Moreover, the capacity to produce proteinoids with precise functions could be used for applications in neuromodulation. Proteinoids have the potential to be manipulated in such a way that they can release neurotransmitters or other substances that affect the nervous system when triggered by certain stimuli. This can result in the development of intelligent and adaptable neuromodulation systems. Finally, the distinctive characteristics of kombucha-proteinoid systems present exciting prospects in the realms of wearable and implantable bioelectronics, as well as neuromorphic and bio-inspired computing. By using the inherent advantages of kombucha cellulose and the customisable capabilities of proteinoids, these hybrid systems can potentially connect biological and artificial information processing systems, creating opportunities for biocompatible, adaptable, and efficient computing methods.

9.2. Neuromorphic computing and biological intelligence

9.2.1. Bio-inspired information processing

Neuromorphic computing is influenced by the exceptional information processing capability of organic neural systems. These systems have exceptional performance in parallel and distributed computing, which has been extensively studied in the field of artificial neural networks (Indiveri et al., 2011). Living electronic systems, such as those utilising bacterial biofilms, have shown promise in implementing networked computing concepts on a small scale (Prindle et al., 2015). Adaptive and self-organising neural networks are an essential component of biological intelligence. Unsupervised learning tasks have demonstrated promising results with recent advancements in neuroplasticity-inspired chemical neural networks (Zenke, Poole, & Ganguli, 2017). These networks have the capability to alter their structure and function in response to input stimuli, imitating the brain's capacity to reorganise itself. SNNs are a type of neural network that is considered to be more physiologically realistic in terms of how neurones process information. SNNs use the concept of temporal coding, which means that the timing of neural spikes is used to encode information. SNNs have the ability to process information in a more energy-efficient manner when compared to conventional artificial neural networks. This makes them highly appealing for use in hardware implementations (Tavanaei, Ghodrati, Kheradpisheh, Masquelier, & Maida, 2019).

Hebbian learning, which can be simplified as the idea that neurones that fire simultaneously establish connections with each other, is the fundamental process underlying synaptic plasticity in biological systems (Hebb, 2005). The incorporation of Hebbian-inspired learning rules in artificial systems has resulted in the creation of neural networks that are more adaptable and resilient. From a perspective standpoint, Kombucha-proteinoid systems have the potential to be a distinct platform for implementing bio-inspired information processing models. The inherent flexibility of the kombucha culture, when combined with the programmable characteristics of proteinoids, has the potential to facilitate the development of adaptable, self-arranging networks that can do parallel processing and temporal coding.

9.2.2. Hardware implementations of neuromorphic systems

The motivation for the development of hardware implementations for neuromorphic systems derives from the requirement for computer architectures that are both more efficient and scalable. Memristive devices have attracted considerable interest in this area because of their capacity to imitate synaptic behaviour (Yang, Strukov, & Stewart, 2013). A study on memristive devices made from bacterial cellulose indicates the possibility of developing memory components using biological materials (Wang, Chen, Jiang, & Shen, 2017).

Artificial neurones and neurotransmitter systems play vital roles in neuromorphic hardware. Proteinoid-based structures have demonstrated promise in the development of artificial neurones and synapses (Levin et al., 2020). These biomolecular constructions have the potential to be designed to imitate different elements of brain function, such as the release and receipt of neurotransmitters. The fusion of live electronics and CMOS technology signifies a cutting-edge advancement in neuromorphic computing. Hybrid bio-electronic systems, which integrate the computational capabilities of silicon-based electronics with the flexibility and resilience of biological components, have demonstrated potential in developing computer systems that are more versatile and durable (Ahmad, 2022).

When designing neuromorphic hardware, it is important to prioritise scalability and power efficiency. Biological neural systems exhibit exceptional energy economy, and achieving the same level of efficiency in artificial systems is still a major obstacle (Merolla et al., 2014).

Kombucha-proteinoid systems have unique advantages in accelerating the development of neuromorphic hardware. The electrical conductivity of kombucha cellulose might be utilised to develop bio-based memristive devices, while proteinoids could be produced to serve as artificial neurones or synapses. The innate biocompatibility of these materials could enable easy integration with biological systems, potentially resulting in the development of more sophisticated bio-hybrid computing architectures.

9.3. Soft robotics and actuators

9.3.1. Biohybrid soft actuators

The incorporation of biological elements into synthetic materials has created new opportunities in the realm of soft robotics. Recent advancements in the field of bioengineering have made it possible to create biohybrid actuators that merge flexibility of soft materials with the reactivity of living organisms (Roche et al., 2017). Combining kombucha-derived cellulose and proteinoids with soft polymeric materials offers a fascinating chance to develop innovative biohybrid actuators.

Stimuli-responsive actuation methods are essential for the operation of soft robots. Hydrogels that respond to variations in pH have been shown to undergo reversible modifications in shape, making them useful for soft actuators (Gao, Sadasivuni, Kim, Min, & Kim, 2015). Thermally actuated soft robots have demonstrated potential in using temperature-sensitive polymers (Miriyev, Stack, & Lipson, 2017). The use of kombucha-proteinoid systems in response to electric fields has the potential to create electrically controlled soft actuators, similar to recent advancements in electroactive polymers (Pelrine, Kornbluh, Pei, & Joseph, 2000).

Kombucha-proteinoid systems have the potential to exhibit multiple forms of responsiveness. This includes sensitivity to changes in pH due to microbial metabolites, responsiveness to temperature due to proteinoids, and the ability to be electrically activated through conductive cellulose networks. The application of multi-modal actuation has the potential to enhance the level of control in soft robotic applications, allowing for greater complexity and precision.

9.3.2. Biomimetic locomotion and manipulation

The design of soft robotic systems has been greatly influenced by biological species. Octopus-inspired soft robots have shown impressive control abilities, as evidenced by recent studies (Laschi et al., 2012). Kombucha-derived soft robotic systems have the ability to imitate the flexible and durable characteristics of microbial biofilms, while actuators controlled by proteinoids could replicate muscle contraction and expansion mechanisms. Advancements in the field of soft robotics have successfully achieved a range of different ways of moving, such as crawling, swimming, and grasping (Rus & Tolley, 2015). Recent investigations on living tissue-engineered robots (Raman et al., 2016) have shown that biohybrid systems, such as kombucha-proteinoid soft robots, have the potential to demonstrate remarkable durability and adaptation in many scenarios.

Kombucha-proteinoid systems have unique advantages in biomimetic soft robotics. The inherent ability of kombucha cellulose to spontaneously arrange itself could facilitate the development of complicated multi-level formations that imitate biological tissues. Meanwhile, the customisable characteristics of proteinoids could provide precise manipulation of actuation capabilities.

9.3.3. Sensing and feedback in soft robotics

The incorporation of sensing capabilities is vital for the advancement of autonomous soft robotic systems. Advancements in flexible and elastic electronics have made it possible to develop sensor arrays that resemble human skin for soft robots (Someya et al., 2016). The integration of kombucha and proteinoid-based sensors into soft robotic structures has the ability to effectively provide both proprioceptive and exteroceptive sensing capabilities. Haptic feedback and tactile sensing are crucial for soft robotic manipulators to interact securely and efficiently with their surroundings. Advancements in bioinspired tactile sensors have demonstrated potential in delivering precise and detailed force and texture sensing (Boutry et al., 2018).

Kombucha-proteinoid systems have the potential to work as versatile materials in the field of soft robotics, serving as both structural components and performing the roles of actuators and sensors simultaneously. This integration has the potential to result in simpler and more efficient soft robotic architectures.

9.3.4. Self-healing and regenerative soft robotics

There is a strong demand for integrating self-healing capabilities into soft robotic systems due to the significant improvements it offers in terms of durability and lifespan. Recent breakthroughs in self-healing polymers have shown the possibility of developing soft robots capable of repairing damage on their own (Terryn, Brancart, Lefeber, Van Assche, & Vanderborght, 2017). The inherent self-repair abilities of living systems, like those present in kombucha cultures, could be utilised to develop self-healing components for soft robotics.

Kombucha-proteinoid systems have the ability to provide sophisticated self-healing and regenerating capacities to soft robotic systems. The continuous expansion and self-restoration mechanisms of kombucha cultures, in conjunction with the programmable synthesis of proteinoids, have the potential to facilitate the production of flexible robots that possess the ability to not only repair damages but also adjust and enhance their structures progressively.

9.4. Energy harvesting and storage

9.4.1. Microbial fuel cells

Microbial fuel cells (MFCs) are being recognised as an effective approach for generating electricity in a sustainable manner. New research has shown that cellulose-based materials have the ability to function as electrodes in microbial fuel cells (MFCs) (Tiquia-Arashiro & Pant, 2020). The use of Kombucha-derived anodes and cathodes has the potential to improve the efficiency of microbial fuel cells (MFCs) as a result of their elevated surface area and conductivity. Enhancing the power density and ensuring long-term stability continues to be a significant hurdle in MFC technology. Recent developments in electrode materials and the manipulation of microbial communities have resulted in notable enhancements in the performance of microbial fuel cells (Logan & Rabaey, 2012).

Kombucha-proteinoid systems may provide distinct benefits in MFC technology. The kombucha cultures can create a conductive cellulose network that can function as a high-surface-area electrode. Additionally, proteinoids can be modified to improve electron transport or catalyse certain reactions, hence enhancing the efficiency of the microbial fuel cell (MFC).

9.4.2. Photosynthetic energy harvesting

Combining photosynthetic organisms with artificial systems has created new opportunities for biohybrid energy harvesting. Recent study has shown that it is possible to produce functional solar cells by using cyanobacteria (McCormick et al., 2015). Combining kombucha with photosynthetic organisms has the potential to develop self-sufficient systems for receiving energy. Proteinoid-based photosensitisers have the potential to improve the efficiency of light absorption and electron transport in synthetic photosynthetic systems. Recent breakthroughs in bio-inspired artificial photosynthesis have demonstrated potential in attaining very efficient conversion of solar energy into fuel (Liu, Colón, Ziesack, Silver, & Nocera, 2016). From a perspective standpoint, Kombucha-proteinoid systems have the potential to be a flexible platform for creating biohybrid photosynthetic energy collecting devices. The cellulose matrix has the potential to serve as a supporting framework for photosynthetic organisms, whereas proteinoids might be designed to act as light-harvesting complexes or mediators for electron transport.

9.4.3. Piezoelectric and triboelectric energy harvesting

Piezoelectric and triboelectric nanogenerators are innovative technologies that show great potential for harnessing mechanical energy from the surrounding environment. Recent study has shown that cellulose nanofibrils possess piezoelectric characteristics (Csoka, Hoeger, Rojas, Peszlen, Pawlak, & Peralta, 2012), indicating that cellulose generated from kombucha could be used in energy harvesting systems.

It is possible to manipulate kombucha-proteinoid systems in order to increase their piezoelectric or triboelectric capabilities. The hierarchical arrangement of kombucha cellulose might be enhanced for the purpose of converting mechanical energy, whereas proteinoids could be engineered to accelerate the separation of charges or offer additional functionalities.

9.4.4. Biohybrid energy storage systems

Advancing renewable energy technology relies heavily on the crucial development of energy storage devices that are both sustainable and high-performing. Recent study has investigated the use of cellulose-based substances in batteries and supercapacitors (Nyholm, Nyström, Mihranyan, & Strømme, 2011). Cellulose generated from Kombucha has the potential to be used as an environmentally friendly and high-performing material for electrodes in these devices.

The combination of Kombucha and proteinoid systems presents distinct possibilities for the advancement of biohybrid energy storage devices. The conductive cellulose network has the potential to be used as an electrode material, while proteinoids can be modified to act as electrolytes or to improve the capacity for storing electrical charge. The inherent ability of these materials to spontaneously arrange themselves could potentially facilitate the development of electrodes with a hierarchical structure that exhibits enhanced performance.

10. Challenges and future directions

10.1. Scalability and reproducibility

10.1.1. Scaling up production processes

The shift from small-scale production in laboratories to large-scale manufacturing of kombucha-proteinoid systems poses substantial difficulties. Ensuring uniform characteristics and optimal functioning when dealing with bigger quantities is a key need, as observed in the expansion of other biotechnology operations (Schmidt, 2005). Ensuring consistent outcomes on a large scale relies heavily on optimising the fermentation conditions for kombucha and the synthesis parameters for proteinoids.

Automation and process control methods are crucial for enhancing efficiency and maximising yield. Recent advancements in the design and monitoring systems of bioreactors present viable solutions for the production of kombucha on a large scale (Krystynowicz & Bieleck, 2001). Moreover, making use of continuous flow reactors for proteinoid synthesis has the potential to improve efficiency and uniformity (Chován & Guttman, 2002).

Conducting a techno-economic investigation is crucial in evaluating the financial feasibility of expanding production on a larger scale. Research on comparable bio-based materials has emphasised the significance of optimising utilisation of resources and reducing waste to guarantee cost-effectiveness (Koutinas et al., 2014).

From a perspective standpoint, the development of kombucha-proteinoid systems could be enhanced by implementing techniques employed in the industrial manufacturing of other microbial cellulose products. The incorporation of innovative process analytical technology has the potential to facilitate the continuous monitoring and regulation of crucial quality characteristics throughout the production process.

10.1.2. Standardisation and quality control

The intrinsic heterogeneity in the composition of kombucha and proteinoids presents difficulties in achieving standardisation. Employing robust characterisation methods along with establishing uniform protocols are essential measures for ensuring reproducibility. The current efforts in establishing a standard method for describing nanomaterials offer a valuable framework that can be modified for kombucha-proteinoid systems (Schulte, Murashov, Zumwalde, Kuempel, & Geraci, 2010).

Employing quality control procedures is crucial for ensuring the uniformity and reliability of manufacturing. The application of statistical process control and design of experiments methodologies, commonly employed in the biopharmaceutical sector, may yield advantageous outcomes (Rathore & Winkle, 2009). Regulatory factors and safety evaluations are essential for commercial applications. The unique characteristics of kombucha-proteinoid systems may need for the development of innovative regulatory frameworks, such to those already in place for other emerging biomaterials (Hassanabad et al., 2021).

It is essential to establish universal standards for kombucha-proteinoid systems in order to facilitate their wider acceptance and use across the industry. The development of broad guidelines and standards will require collaboration between academia, industry, and regulatory organisations.

10.1.3. Reproducibility and robustness

Replicating complex behaviours and functionalities in living electrical systems continues to be a substantial obstacle. Developing strategies to enhance stability and longevity is essential for practical use. Recent developments in synthetic biology provide possible methods for improving the genetic stability of microbial communities in kombucha (Sleight & Sauro, 2013). It is crucial to ensure the durability and robustness of a system in the face of changes in the environment and the demands of operation in order to make it suitable for practical use. Research on the stress response of microbial communities could provide insights into methods for improving the durability of kombucha-based systems (Sleight & Sauro, 2013). Inter-laboratory validation is essential for determining the repeatability of kombucha-proteinoid systems. Efforts resembling those in the realm of synthetic biology, which aim to improve the ability to replicate biological circuits, could be used as a model (Kitney et al., 2019). Establishing standardised reference materials and compare testing for kombucha-proteinoid systems has the potential to greatly improve consistency and reliability in various laboratories and manufacturing facilities.

10.1.4. Manufacturing and integration challenges

It is essential to develop efficient manufacturing methods for kombucha and proteinoid-based devices in order to make them commercially viable. Employing established biofabrication techniques, such as those used for tissue engineering, could provide as a foundation for producing these innovative materials (Murphy & Atala, 2014). The incorporation of traditional electronic manufacturing methods poses both difficulties and opportunities. Recent advancements in the field of bioelectronics have shown that it is possible to combine living components with conventional electronic systems (Rivnay et al., 2018). Effective packaging and encapsulating techniques are crucial for preserving the biological constituents of kombucha-proteinoid devices. Advancements in microfluidic encapsulation techniques provide promising options for preserving the life span of microbial components (Taouzinet et al., 2023). Using modular and reconfigurable designs has the potential to increase the adaptability of production processes and provide tailored customisation for specific applications. By integrating modular techniques from synthetic biology, it is possible to create kombucha-proteinoid systems that are more flexible and adaptive (Smanski et al., 2014). The integration of biofabrication techniques with regular electronics manufacturing has the potential to facilitate the mass production of kombucha-proteinoid devices. The progress made in 3D bioprinting and roll-to-roll fabrication of flexible electronics presents a promising chance to develop these innovative living electronic systems through combined efforts. The challenges and future research directions for kombucha-based bioprinting are summarised in Table 4. This table outlines key areas of focus including kombucha-based bioink development, cell compatibility, printability and resolution, functionalisation, vascularisation, and maturation and functionality of the bioprinted architectures.

10.2. Long-term stability and durability

Ensuring the enduring and ongoing performance of kombucha-proteinoid systems is a major obstacle that needs to be overcome in order to effectively use them in functional living electronic devices.

Table 4
Challenges and future research directions for Kombucha-based bioprinting.

Area	Focus for future research
Kombucha-based bioink	• Optimisation of cellulose content for printability and cell viability • Integration of proteinoids for enhanced bioactivity • Tuning of mechanical properties for various tissue types • Ensuring sterility and long-term stability of the bioink
Cell compatibility	• Evaluation of cell life and growth in the kombucha matrix • Modification of kombucha composition to support different cell types • Investigation of kombucha-cell interactions and potential immunogenicity • Development of cell-laden kombucha architectures
Printability and resolution	• Enhancement of print resolution for fine tissue structures • Improvement of shape accuracy and structural integrity post-printing • Development of multi-material printing techniques for complex tissues • Optimisation of crosslinking methods for kombucha-based bioinks
Functionalisation	• Incorporation of growth factors and bioactive molecules • Development of gradient structures for tissue interfaces • Integration of conductive properties for neural tissue engineering • Exploration of kombucha-based scaffolds for drug delivery
Vascularisation	• Creation of printable vascular networks within kombucha constructs • Investigation of kombucha's potential to support angiogenesis • Development of perfusable channels in kombucha-based tissues • Optimisation of mechanical properties for vascular function
Maturation and functionality	• Study of long-term stability and maturation of printed architectures • Development of bioreactor systems for kombucha-based tissues • Assessment of functional properties of engineered tissues • Investigation of kombucha's role in tissue remodelling and regeneration

10.2.1. Degradation mechanisms

Gaining insight into the degradation mechanisms of kombucha and proteinoid components is essential for devising strategies to improve their durability. Chemical degradation, like as the decomposition of cellulose by hydrolysis in kombucha matrices, can result in the gradual deterioration of structural integrity (Reiniati, Hrymak, & Margaritis, 2017). Device failure can occur due to physical degradation, such as mechanical stress and fatigue, especially in applications that involve frequent deformation (Mohanty, Vivekanandhan, Pin, & Misra, 2018). The stability of these bio-based systems is greatly influenced by environmental conditions. Temperature variations can impact the metabolic activity of kombucha cultures and the overall stability of proteinoids (Shi et al., 2014). Changes in humidity and pH can modify the mechanical characteristics of the cellulose matrix and the functionality of proteinoid components (Barratt et al., 2001). Oxidative stress and the subsequent deterioration caused by reactive species provide a significant problem, especially in systems that are exposed to air or biological fluids. Oxidation of cellulose and modification of proteinoid structures might take place due to the presence of oxygen and reactive oxygen species, which may negatively impact device performance (Duceac, Tanasa, & Coseri, 2022).

Future study should prioritise investigating the precise mechanisms of degradation in kombucha-proteinoid systems under various conditions. Acquiring this knowledge will be crucial for formulating precise stabilisation techniques.

10.2.2. Stabilisation strategies

Multiple approaches can be implemented to improve the stability of kombucha-proteinoid systems. Chemical modifications, such as crosslinking of cellulose fibres, have demonstrated potential to improve the mechanical and chemical durability of bacterial cellulose (Ul-Islam et al., 2015). Similar approaches could be modified for materials derived from kombucha. Another possible strategy is the addition of stabilising agents and antioxidants. Antioxidants have the potential to reduce oxidative damage, while other stabilising substances can assist in maintaining the structural integrity of the kombucha-proteinoid matrix (Carrigy & Vehring, 2019). Encapsulation and protective coatings provide another way of improving stability. The latest developments in microencapsulation methods for probiotics can be used to preserve the biological constituents of kombucha-based systems (Cook, Tzortzis, Charalampopoulos, & Khutoryanskiy, 2012).

In order to obtain the necessary long-term stability for practical applications of kombucha-proteinoid devices, it will be vital to develop techniques that simultaneously address multiple degradation pathways.

10.2.3. Self-repair and regeneration

The natural capacity of kombucha and proteinoids to regenerate and repair themselves presents distinct possibilities for the development of robust living electrical systems. Recent studies on self-healing materials have demonstrated the potential for autonomous repair in response to damage (Toohey, Sottos, Lewis, Moore, & White, 2007). Applying these concepts to kombucha-proteinoid systems has the potential to create devices that have improved durability. Integrating stimuli-responsive repair mechanisms and damage detection systems could enhance the efficiency of self-healing processes. For example, proteinoids that are sensitive to variations in pH could be engineered to alter their shape and trigger repair mechanisms in response to specific local environmental changes resulting from damage (Kumar, Grzelakowski, Zilles, Clark, & Meier, 2007). The issue lies in finding a balance between the self-repair capabilities and the complexity and functioning of the system. Subsequent investigations should prioritise the development of uncomplicated yet efficient self-repair methods that do not undermine the fundamental operations of the kombucha-proteinoid devices.

10.2.4. Accelerated ageing studies and lifetime prediction

It is crucial to develop reliable techniques for predicting the enduring stability of kombucha-proteinoid systems in order to effectively put them into practice. The changing kinetics of these bio-based materials could be studied by adapting accelerated ageing tests, which are frequently used in the pharmaceutical industry (Waterman & Adami, 2005). It is essential to study degradation kinetics and forms of failure under different stress conditions in order to develop accurate predictive models. Advanced analytical techniques, such as spectroscopic approaches and mechanical testing, can offer valuable insights into the structural and functional variations that take place during the ageing process (Paulsen, Tybrandt, Stavrinidou, & Rivnay, 2020). Validation of lifetime predicts through real-world testing and field studies will be crucial for confirming the dependability of kombucha-proteinoid devices. Long-term studies conducted under varied conditions will require collaborative efforts between academia and industry.

10.3. Integration with conventional electronics

Combining kombucha-proteinoid systems with traditional electronics presents difficulties and possibilities for developing innovative hybrid devices with improved capabilities.

10.3.1. Interface and compatibility issues

The main obstacle in the development of hybrid electronic systems is the electrical and mechanical connection between living and non-living components. Differences in the characteristics of materials, such as their ability to stretch and conduct electricity, can result in imbalances of mechanical strain and electrical resistance at the interface (Rivnay, Owens, & Malliaras, 2014). Efficient communication between biological and electrical components requires careful attention to the distinct modes of signalling. For example, the process of converting ionic currents in biological systems into electronic signals in traditional circuits might require the use of specialised transduction mechanisms (Koo et al., 2018). It is essential to establish strong and efficient connections between kombucha proteinoid systems and traditional electronics to fully use the capabilities of these hybrid devices. Future research should prioritise the development of integration answers that provide the smooth integration of biological and electronic components while maintaining their respective functionalities.

10.3.2. Hybrid electronic systems

The development and manufacturing of hybrid living-nonliving electronic devices present exciting opportunities for innovative capabilities. Recent advancements in the field of bioelectronics have shown that it is possible to combine biological components with electronic systems in order to detect and control various processes (Sanjuan-Alberte, Alexander, Hague, & Rawson, 2018). Combining kombucha and proteinoid-based materials with traditional electronic components has the potential to improve performance through synergistic effects. For instance, the ability of living systems to adapt can be integrated with the accuracy and swiftness of electronic circuits to develop technologies that are more responsive and efficient (Chen, Canales, & Anikeeva, 2017). Investigating the distinct abilities that result from combining kombucha-proteinoid systems with traditional electronics has the potential to revolutionise various fields, including adaptive sensing, neuromorphic computing, and soft robotics.

10.3.3. Interfacing with microelectronics

Miniaturisation and integration with CMOS technology provide significant challenges and offer promising prospects for kombucha-proteinoid systems. Advancements in flexible and elastic electronics offer possibilities for establishing biocompatible connections between living materials and microelectronic components (Kaltenbrunner et al., 2013). As systems are made smaller, it becomes more crucial to deal with problems related to signal-to-noise ratio and interference. Reliable operation of hybrid micro-scale devices (Xu et al., 2017) may require the use of advanced signal processing techniques and innovative circuit designs. By combining kombucha-proteinoid systems with wireless communication and power delivery modules, it becomes possible to create autonomous bio-electronic devices that are self-sustained. These devices have potential uses in environmental monitoring and healthcare.

10.3.4. Co-design and optimisation strategies

Efficient and functional hybrid systems require the simultaneous design and optimisation of both living and non-living components. In order to accurately predict and improve the performance of devices, it is essential to use multiphysics modelling and simulation techniques that have been specifically modified to account for the unique features of kombucha-proteinoid materials (Polygerinos et al., 2017). The use of automation and optimisation techniques, which are influenced by both electronic design automation and synthetic biology, could be useful in the advancement of complex bio-electrical systems (Nielsen et al., 2016). When designing kombucha-proteinoid hybrid systems, it is crucial to take into account manufacturing limitations and the capacity to scale up production. This consideration is necessary in order to successfully transition from laboratory prototypes to practical, mass-producible devices.

10.4. Unconventional computing

The unique features of kombucha-proteinoid systems present interesting opportunities for unconventional computing paradigms, which could potentially overcome the constraints of standard silicon-based computing architectures.

10.4.1. Reservoir computing

Reservoir computing (RC) is a highly effective method for handling temporal data, especially in systems with complex dynamics (Tanaka et al., 2019). Kombucha-proteinoid networks have intrinsic nonlinearity and have a high-dimensional state space, which makes them very suitable for use in physical reservoir computing. Using the natural dynamics of these biological systems has the potential to enable efficient processing of temporal information and recognition of patterns. Recent research has shown that it is possible to use bacterial biofilms as physical storage units for computer operations (Prindle et al., 2015), indicating that kombucha-based systems may have comparable capabilities. The benefits of RC (Reservoir Computing) in kombucha-proteinoid systems could include improved energy economy, flexibility in response to varying conditions, and intrinsic capability for parallel computing. These features are well-suited for the requirements of real-time data analysis, prediction, and optimisation tasks in diverse disciplines (Konkoli, Nichele, Dale, & Stepney, 2018). Future research should prioritise the characterisation of the computing capabilities of kombucha-proteinoid reservoirs and the development of ways to fine-tune their dynamics for specific applications. By combining biological reservoirs with traditional readout layers, it is possible to create hybrid systems that possess both the adaptability of living materials and the precision of electronic processing.

10.4.2. Neuromorphic computing

Neuromorphic computing seeks to replicate the organisation and operation of biological neural networks, providing possible benefits in terms of energy efficiency and learning ability (Indiveri et al., 2011). Kombucha-proteinoid systems, due to their capacity to create complex and linked networks, offer a fascinating platform for developing neuromorphic patterns. Using kombucha-proteinoid components in the design of SNNs might harness the inherent signal processing abilities of these biological systems. Recent breakthroughs in proteinoid-based artificial synapses (Tuma, Pantazi, Le Gallo, Sebastian, & Eleftheriou, 2016) indicate the potential to develop adaptive, learning-capable networks using these materials. Kombucha-proteinoid neuromorphic systems offer significant benefits such as exceptional energy efficiency, built-in fault tolerance, and the capacity to collect new knowledge and adjust accordingly. These features render them especially well-suited for cognitive activities and applications in brain-inspired computing (Davies et al., 2018). Future research should prioritise the development of techniques to accurately regulate the connection and signalling characteristics of kombucha-proteinoid networks in order to construct targeted brain structures. Combining standard neuromorphic hardware with integration could result in hybrid systems that incorporate the most advantageous characteristics of both biological and artificial neural networks.

10.4.3. Molecular and chemical computing

Molecular and chemical computing use biochemical processes to carry out computing tasks, providing unique advantages in terms of parallelism and integration with biological systems (Zauner, 2005). Kombucha-proteinoid systems, due to their complex biochemical conditions, offer a highly suitable substrate for implementing computational paradigms. Recent study has shown the successful creation of logic gates and memory elements using artificial biological components (Qian, Winfree, & Bruck, 2011). Comparable methodologies could be modified to exploit the distinct biochemical reactions and molecular interactions found in kombucha-proteinoid systems. Molecular computing in these systems offers significant benefits such as extensive parallelism, the ability to scale through self-assembly, and effortless integration with biological settings. Kombucha-proteinoid based molecular computers have specific characteristics that make them highly appropriate for many applications including as biosensing, smart delivery of drugs, and responsive materials (Amir et al., 2014). Future study should focus on investigating the development of precise molecular computational components within kombucha-proteinoid systems and developing techniques to connect them with larger-scale inputs and outputs. Standardising components and architectures will be essential for the wider acceptance of this computing paradigm.

10.4.4. Challenges and future directions

In order to fully realise the promise of kombucha-proteinoid systems for unconventional computing, it is necessary to address many difficulties. Scalability and repeatability are still major challenges due to the complexity and even unpredictable characteristics of biological systems, which can result in variations in computational performance (Broersma, Gomez, Miller, Petty, & Tufte, 2012). It is essential to create strong techniques for controlling and describing the computational features of complex systems. Integrating unconventional kombucha-proteinoid computer systems with standard electronic hardware has both difficulties and possibilities. Recent advancements in bioelectronic interfaces (Rivnay, Wang, Fenno, Deisseroth, & Malliaras, 2017) lay the groundwork to develop hybrid systems that use the advantages of both paradigms. Another crucial difficulty is the creation of suitable programming models and algorithms for these unconventional computing systems. In order to take full advantage of the distinctive characteristics of kombucha-proteinoid computers, it is necessary to create novel computational frameworks that draw on both computer science and systems biology (Amos, Dittrich, McCaskill, & Rasmussen, 2011). Improving the durability and dependability of these biological computing systems under real-world settings will be crucial for their practical implementation. It is necessary to create strategies to ensure consistent computing performance over long periods of time and under different environmental situations (Adamatzky, 2017). The area of unconventional computing using kombucha-proteinoid systems is now in its early stages, presenting various prospects for pioneering research. To fully harness the capabilities of these new computing paradigms, it is crucial to encourage collaboration among computer scientists, biologists, and materials scientists, as their combined expertise is necessary to address the existing obstacles.

11. Conclusions

11.1. Summary of key findings

Our research into the applications of kombucha and proteinoid-driven living electronics has uncovered a highly promising area of development in the realm of bioelectronics. The distinctive characteristics of cellulose matrices formed from kombucha, when paired with the adaptability of proteinoid structures, present fascinating opportunities for the development of self-sustaining electronic devices. Our work revealed that kombucha-proteinoid systems have the potential to produce electrical components that are both highly biocompatible and environmentally friendly. We have witnessed the capacity to take advantage of the inherent self-assembly of these biological materials to construct complex, hierarchical structures with tunable characteristics. The approach of combining living components with conventional electronic systems to produce hybrid devices with improved functionality and adaptability has been a significant finding. Our research has also identified the rise of new computational frameworks, such as reservoir computing and neuromorphic architectures, made possible by the intrinsic activity of kombucha-proteinoid networks. During our investigation, we have discovered both obstacles and prospects in expanding manufacturing, ensuring long-term stability, and integrating these biological systems into conventional electronics.

11.2. Outlook for kombucha and proteinoid-driven living electronics

The future opportunities for kombucha and proteinoid-driven living electronics are promising, with a wide range of potential applications in various sectors. As the research in this field advances, we expect several significant advancements. Anticipated progress in biocompatible devices includes the development of more complicated electronic systems for medical purposes, such as implantable sensors, drug delivery systems, and tissue engineering scaffolds. The biodegradable properties of kombucha-proteinoid systems have the potential to open the way for a new era of eco-friendly electrical products, effectively tackling the escalating issue of electronic waste. By using the living components of these systems, we foresee the development of electrical devices that can autonomously repair themselves and adjust to evolving environmental circumstances. Kombucha-proteinoid networks possess distinctive characteristics that could lead to the development of novel biocomputing methods, perhaps providing answers to computational issues that are difficult for conventional silicon-based systems. Combining these biological systems with energy harvesting methods has the potential to create self-sustaining electrical devices, which would be especially beneficial for applications such as remote sensing and wearable technology. Kombucha-proteinoid materials has remarkable flexibility and biocompatibility, making them highly suitable for accelerating the progress of soft robotics. This has the potential to result in the development of robotic systems that are more realistic and flexible. Nevertheless, there are still substantial obstacles that need to be resolved. These tasks involve ensuring the continued stability of living components, expanding the scale of production processes, and developing standardised procedures for the manufacture and characterisation of devices. Furthermore, there will be a requirement for the adaptation of regulatory frameworks to accommodate these innovative bio-electronic systems. Finally, kombucha and proteinoid-driven living electronics are currently in their early stages of development. However, they show great potential and are heading towards a promising future in the field of bioelectronics. As research advances and obstacles are overcome, we expect these systems to have a significant impact on the future of electronics, computing, and biotechnology. They will provide sustainable, adaptable, and highly efficient solutions to various technological challenges.

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Declaration of competing interest

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Data availability

No data was used for the research described in the article.

References

Acebrón, J. A., Bonilla, L. L., Pérez Vicente, C. J., Ritort, F., & Spigler, R. (2005). The Kuramoto model: A simple paradigm for synchronization phenomena. *Reviews of Modern Physics*, *77*(1), 137–185.

Adamatzky, A. (2017). Thirty seven things to do with live slime mould. *Advances in Unconventional Computing: Volume 2: Prototypes, Models and Algorithms*, 709–738.

Adamatzky, A. (2018). *Unconventional computing: A volume in the encyclopedia of complexity and systems science*. Springer Publishing Company, Incorporated.

Adamatzky, A. (2021). Towards proteinoid computers. Hypothesis paper. *Biosystems*, *208*, Article 104480.

Adamatzky, A. (2022). Dynamics of electrical resistance of kombucha zoogleal mats. *Biophysical Reviews and Letters*, *17*(04), 135–144.

Adamatzky, A. (2023). Electrical potential spiking of kombucha zoogleal mats: A symbiotic community of bacteria and yeasts. *Bioelectricity*, *5*(2), 99–108.

Adamatzky, A., Akl, S., Burgin, M., Calude, C. S., Costa, J. F., Dehshibi, M. M., et al. (2017). East-west paths to unconventional computing. *Progress in Biophysics and Molecular Biology*, *131*, 469–493.

Adamatzky, A., Armstrong, R., Jones, J., & Gunji, Y.-P. (2013). On creativity of slime mould. *International Journal of General Systems*, *42*(5), 441–457.

Adamatzky, A., Tarabella, G., Phillips, N., Chiolerio, A., D'Angelo, P., Nikolaidou, A., et al. (2023). Kombucha electronics: electronic circuits on kombucha mats. *Scientific Reports*, *13*(1), 9367.

Adleman, L. M. (1994). Molecular computation of solutions to combinatorial problems. *Science*, *266*(5187), 1021–1024.

Aggeli, A., Bell, M., Carrick, L. M., Fishwick, C. W., Harding, R., Mawer, P. J., et al. (2003). pH as a trigger of peptide *β*-sheet self-assembly and reversible switching between nematic and isotropic phases. *Journal of the American Chemical Society*, *125*(32), 9619–9628.

Ahamed, M. I., Asiri, A. M., et al. (2019). *Applications of ion exchange materials in the environment*. Springer.

Ahmad, N. (2022). In vitro and in vivo characterization methods for evaluation of modern wound dressings. *Pharmaceutics*, *15*(1), 42.

Akerkar, R., & Sajja, P. S. (2009). Bio-inspired computing: constituents and challenges. *International Journal of Bio-Inspired Computation*, *1*(3), 135–150.

Al-Mohammadi, A.-R., Ismaiel, A. A., Ibrahim, R. A., Moustafa, A. H., Abou Zeid, A., & Enan, G. (2021). Chemical constitution and antimicrobial activity of kombucha fermented beverage. *Molecules*, *26*(16), 5026.

Amdursky, N., Głowacki, E. D., & Meredith, P. (2019). Macroscale biomolecular electronics and ionics. *Advanced Materials*, *31*(3), Article 1802221.

Amir, Y., Ben-Ishay, E., Levner, D., Ittah, S., Abu-Horowitz, A., & Bachelet, I. (2014). Universal computing by DNA origami robots in a living animal. *Nature nanotechnology*, *9*(5), 353–357.

Amos, M., Dittrich, P., McCaskill, J., & Rasmussen, S. (2011). Biological and chemical information technologies. *Procedia Computer Science*, *7*, 56–60.

Angione, M. D., Pilolli, R., Cotrone, S., Magliulo, M., Mallardi, A., Palazzo, G., et al. (2011). Carbon based materials for electronic bio-sensing. *Materials Today*, *14*(9), 424–433.

Arenas, A., Díaz-Guilera, A., Kurths, J., Moreno, Y., & Zhou, C. (2008). Synchronization in complex networks. *Physics Reports*, *469*(3), 93–153.

Avcioglu, N. H., Birben, M., & Bilkay, I. S. (2021). Optimization and physicochemical characterization of enhanced microbial cellulose production with a new kombucha consortium. *Process Biochemistry*, *108*, 60–68.

Ayyappan, V. G., Vhatkar, S. S., Bose, S., Sampath, S., Das, S. K., Samanta, D., et al. (2022). Incorporations of gold, silver and carbon nanomaterials to kombucha-derived bacterial cellulose: Development of antibacterial leather-like materials. *Journal of the Indian Chemical Society*, *99*(1), Article 100278.

Bae, S. K., & Kim, J.-D. (2003). Aggregation behaviors and their pH sensitivity of cholesterol-conjugated proteinoids composed of glutamic acid and aspartic acid matrix. *Journal of Biomedical Materials Research Part A: An Official Journal of the Society for Biomaterials, the Japanese Society for Biomaterials, and the Australian Society for Biomaterials and the Korean Society for Biomaterials*, *64*(2), 282–290.

Baptista, A., Ferreira, I., & Borges, J. (2013). Cellulose-based bioelectronic devices. In *Cellulose-medical, pharmaceutical and electronic applications*. IntechOpen.

Barabási, A.-L., & Albert, R. (1999). Emergence of scaling in random networks. *Science*, *286*(5439), 509–512.

Barbosa, C. D., Baqueta, M. R., Santos, W. C. R., Gomes, D., Alvarenga, V. O., Teixeira, P., et al. (2020). Data fusion of UPLC data, NIR spectra and physicochemical parameters with chemometrics as an alternative to evaluating kombucha fermentation. *Lwt*, *133*, Article 109875.

Barratt, G., Couarraze, G., Couvreur, P., Dubernet, C., Fattal, E., Gref, R., et al. (2001). Polymeric micro-and nanoparticles as drug carriers. In *Polymeric biomaterials, revised and expanded* (pp. 767–796). CRC Press.

Bates, F. S., & Fredrickson, G. H. (1999). Block copolymers—designer soft materials. *Physics Today*, *52*(2), 32–38.

Belostozky, A., Kolitz-Domb, M., Haham, H., Grinberg, I., & Margel, S. (2017). Engineering of new UV-blocking hollow proteinoid nanoparticles of narrow size distribution containing all-trans retinoic acid for biomedical applications. *Journal of Nanomedicine & Nanotechnology*, *8*, 462.

Bement, W. M., Goryachev, A. B., Miller, A. L., & von Dassow, G. (2024). Patterning of the cell cortex by Rho GTPases. *Nature Reviews. Molecular Cell Biology*, *25*(4), 290–308.

Bhatti, M. R. A., Kernin, A., Tausif, M., Zhang, H., Papageorgiou, D., Bilotti, E., et al. (2022). Light-driven actuation in synthetic polymers: a review from fundamental concepts to applications. *Advanced Optical Materials*, *10*(10), Article 2102186.

Bird, L. J., Onderko, E. L., Phillips, D. A., Mickol, R. L., Malanoski, A. P., Yates, M. D., et al. (2019). Engineered living conductive biofilms as functional materials. *MRS Communications*, *9*(2), 505–517.

Bock, W. J. (1965). The role of adaptive mechanisms in the origin of higher levels of organization. *Systematic Zoology*, *14*(4), 272–287.

Boutry, C. M., Negre, M., Jorda, M., Vardoulis, O., Chortos, A., Khatib, O., et al. (2018). A hierarchically patterned, bioinspired e-skin able to detect the direction of applied pressure for robotics. *Science Robotics*, *3*(24), eaau6914.

Brahim, S., Narinesingh, D., & Guiseppi-Elie, A. (2002). Bio-smart hydrogels: co-joined molecular recognition and signal transduction in biosensor fabrication and drug delivery. *Biosensors & Bioelectronics*, *17*(11–12), 973–981.

Brito, J., Hlushko, H., Abbott, A., Aliakseyeu, A., Hlushko, R., & Sukhishvili, S. A. (2021). Integrating antioxidant functionality into polymer materials: fundamentals, strategies, and applications. *ACS Applied Materials & Interfaces*, *13*(35), 41372–41395.

Broersma, H., Gomez, F., Miller, J., Petty, M., & Tufte, G. (2012). Nascence project: Nanoscale engineering for novel computation using evolution. *International Journal of Unconventional Computing*, *8*(4).

Burnworth, M., Tang, L., Kumpfer, J. R., Duncan, A. J., Beyer, F. L., Fiore, G. L., et al. (2011). Optically healable supramolecular polymers. *Nature*, *472*(7343), 334–337.

Cai, L., Liu, S., Guo, J., & Jia, Y.-G. (2020). Polypeptide-based self-healing hydrogels: Design and biomedical applications. *Acta Biomaterialia*, *113*, 84–100.

Carbó, A. D. (2021). *Electrochemistry of porous materials*. CRC Press.

Carrigy, N., & Vehring, R. (2019). Engineering stable spray-dried biologic powder for inhalation. *Pharmaceutical Inhalation Aerosol Technology, Third Edition*, 291–326.

Chakravorty, S., Bhattacharya, S., Chatzinotas, A., Chakraborty, W., Bhattacharya, D., & Gachhui, R. (2016). Kombucha tea fermentation: Microbial and biochemical dynamics. *International Journal of Food Microbiology*, *220*, 63–72.

Chen, R., Canales, A., & Anikeeva, P. (2017). Neural recording and modulation technologies. *Nature Reviews Materials*, *2*(2), 1–16.

Chen, A., & Chatterjee, S. (2013). Nanomaterials based electrochemical sensors for biomedical applications. *Chemical Society Reviews*, *42*(12), 5425–5438.

Chen, C., Ding, W., Zhang, H., Zhang, L., Huang, Y., Fan, M., et al. (2022). Bacterial cellulose-based biomaterials: From fabrication to application. *Carbohydrate Polymers*, *278*, Article 118995.

Chen, C., & Liu, B. (2000). Changes in major components of tea fungus metabolites during prolonged fermentation. *Journal of Applied Microbiology*, *89*(5), 834–839.

Chen, I. A., & Nowak, M. A. (2012). From prelife to life: how chemical kinetics become evolutionary dynamics. *Accounts of Chemical Research*, *45*(12), 2088–2096.

Chen, Y., Zhang, Y., Liang, Z., Cao, Y., Han, Z., & Feng, X. (2020). Flexible inorganic bioelectronics. *npj Flexible Electronics*, *4*(1), 2.

Chiong, J. A., Tran, H., Lin, Y., Zheng, Y., & Bao, Z. (2021). Integrating emerging polymer chemistries for the advancement of recyclable, biodegradable, and biocompatible electronics. *Advanced Science*, *8*(14), Article 2101233.

Cho, W., Yoon, S.-h., & Chung, T. D. (2023). Streamlining the interface between electronics and neural systems for bidirectional electrochemical communication. *Chemical Science*, *14*(17), 4463–4479.

Choi, S., Lee, H., Ghaffari, R., Hyeon, T., & Kim, D.-H. (2016). Recent advances in flexible and stretchable bio-electronic devices integrated with nanomaterials. *Advanced Materials*, *28*(22), 4203–4218.

Choonut, A., Saejong, M., & Sangkharak, K. (2014). The production of ethanol and hydrogen from pineapple peel by *Saccharomyces cerevisiae* and *Enterobacter aerogenes*. *Energy Procedia*, *52*, 242–249.

Chován, T., & Guttman, A. (2002). Microfabricated devices in biotechnology and biochemical processing. *TRENDS in Biotechnology*, *20*(3), 116–122.

Cochis, A., Grad, S., Stoddart, M., Fare, S., Altomare, L., Azzimonti, B., et al. (2017). Bioreactor mechanically guided 3D mesenchymal stem cell chondrogenesis using a biocompatible novel thermo-reversible methylcellulose-based hydrogel. *Scientific Reports*, *7*(1), 45018.

Connacher, W. J. M. (2022). *Acoustofluidic droplet generation: Physical understanding and applications of jetting and atomization*. San Diego: University of California.

Cook, M. T., Tzortzis, G., Charalampopoulos, D., & Khutoryanskiy, V. V. (2012). Microencapsulation of probiotics for gastrointestinal delivery. *Journal of Controlled Release*, *162*(1), 56–67.

Cooper, G., & Adams, K. (2022). *The cell: A molecular approach*. Oxford University Press.

Cortés-Herrera, C., Artavia, G., Leiva, A., & Granados-Chinchilla, F. (2018). Liquid chromatography analysis of common nutritional components, in feed and food. *Foods*, *8*(1), 1.

Cremaldi, J. C., & Bhushan, B. (2018). Bioinspired self-healing materials: lessons from nature. *Beilstein Journal of Nanotechnology*, *9*(1), 907–935.

Csoka, L., Hoeger, I. C., Rojas, O. J., Peszlen, I., Pawlak, J. J., & Peralta, P. N. (2012). Piezoelectric effect of cellulose nanocrystals thin films. *ACS Macro Letters*, *1*(7), 867–870.

Cui, S., Liu, H., Gan, L., Li, Y., & Zhu, D. (2008). Fabrication of low-dimension nanostructures based on organic conjugated molecules. *Advanced Materials*, *20*(15), 2918–2925.

Cui, H., Webber, M. J., & Stupp, S. I. (2010). Self-assembly of peptide amphiphiles: From molecules to nanostructures to biomaterials. *Peptide Science: Original Research on Biomolecules*, *94*(1), 1–18.

Dakal, T. C., Solieri, L., & Giudici, P. (2014). Adaptive response and tolerance to sugar and salt stress in the food yeast Zygosaccharomyces rouxii. *International Journal of Food Microbiology*, *185*, 140–157.

Davies, M., Srinivasa, N., Lin, T.-H., Chinya, G., Cao, Y., Choday, S. H., et al. (2018). Loihi: A neuromorphic manycore processor with on-chip learning. *Ieee Micro*, *38*(1), 82–99.

De La Cruz, M. O., Belloni, L., Delsanti, M., Dalbiez, J., Spalla, O., & Drifford, M. (1995). Precipitation of highly charged polyelectrolyte solutions in the presence of multivalent salts. *Journal of Chemical Physics*, *103*(13), 5781–5791.

De Muynck, C., Pereira, C. S., Naessens, M., Parmentier, S., Soetaert, W., & Vandamme, E. J. (2007). The genus gluconobacter oxydans: comprehensive overview of biochemistry and biotechnological applications. *Critical Reviews in Biotechnology*, *27*(3), 147–171.

Deming, T. J. (1997). Polypeptide materials: new synthetic methods and applications. *Advanced Materials*, *9*(4), 299–311.

Di Salvo, S. (2018). Advances in research for biomimetic materials. *Advanced Materials Research*, *1149*, 28–40.

Discher, D. E., & Eisenberg, A. (2002). Polymer vesicles. *Science*, *297*(5583), 967–973.

Dobson, C. M. (2003). Protein folding and misfolding. *Nature*, *426*(6968), 884–890.

Domizio, P., Liu, Y., Bisson, L., & Barile, D. (2017). Cell wall polysaccharides released during the alcoholic fermentation by *Schizosaccharomyces pombe* and *S. japonicus*: Quantification and characterization. *Food Microbiology*, *61*, 136–149.

Duceac, I. A., Tanasa, F., & Coseri, S. (2022). Selective oxidation of cellulose—A multitask platform with significant environmental impact. *Materials*, *15*(14), 5076.

DuMez-Kornegay, R. N., Baker, L. S., Morris, A. J., DeLoach, W. L., & Dowen, R. H. (2024). Kombucha tea-associated microbes remodel host metabolic pathways to suppress lipid accumulation. *Plos Genetics*, *20*(3), Article e1011003.

Edwards, J. C. (2016). *Quantitative 1H NMR analysis of "off-the-shelf" commercial Kombucha beverages*. Process NMR Associates LLC, Danbury, CT.

Efremenko, E., Senko, O., Maslova, O., Stepanov, N., Aslanli, A., & Lyagin, I. (2022). Biocatalysts in synthesis of microbial polysaccharides: Properties and development trends. *Catalysts*, *12*(11), 1377.

England, J. L. (2015). Dissipative adaptation in driven self-assembly. *Nature nanotechnology*, *10*(11), 919–923.

Erdös, P., Rényi, A., & Bollobás, B. (1959). Publicationes mathematicae debrecen. *Random Graphs I*, *6*, 290–297.

Erfkamp, J., Guenther, M., & Gerlach, G. (2019). Enzyme-functionalized piezoresistive hydrogel biosensors for the detection of urea. *Sensors*, *19*(13), 2858.

Farooq, A. S., & Zhang, P. (2022). A comprehensive review on the prospects of next-generation wearable electronics for individualized health monitoring, assistive robotics, and communication. *Sensors and Actuators A: Physical*, *344*, Article 113715.

Fatehi Hassanabad, A., Zarzycki, A. N., Jeon, K., Dundas, J. A., Vasanthan, V., Deniset, J. F., et al. (2021). Prevention of post-operative adhesions: a comprehensive review of present and emerging strategies. *Biomolecules*, *11*(7), 1027.

Feng, H., Xu, D., Wang, Q., Dong, Y., Zhang, G., Lv, L., et al. (2020). Enhancement of superoxide evolution by nickel-doped for the removal of organic pollutants and cyanobacteria. *Journal of the Taiwan Institute of Chemical Engineers*, *113*, 396–405.

Fernandes, I. d. A., Pedro, A. C., Ribeiro, V. R., Bortolini, D. G., Ozaki, M. S. C., Maciel, G. M., et al. (2020). Bacterial cellulose: From production optimization to new applications. *International Journal of Biological Macromolecules*, *164*, 2598–2611.

Fiore, M. (2022). *Prebiotic chemistry and life's origin*. Royal Society of Chemistry.

Fox, S. W. (1973). Molecular evolution of the first cells. *Pure and Applied Chemistry*, *34*(3–4), 641–670.

Fox, S. W. (1974). Coacervate droplets, proteinoid microspheres, and the genetic apparatus. In *The origin of life and evolutionary biochemistry* (pp. 119–132). Springer.

Fox, S. W. (1980a). Metabolic microspheres: origins and evolution. *Die Naturwissenschaften*, *67*(8), 378–383.

Fox, S. W. (1980b). The origins of behavior in macromolecules and protocells. *Comparative Biochemistry and Physiology Part B: Comparative Biochemistry*, *67*(3), 423–436.

Fox, S. W. (1988). The emergence of life: Darwinian evolution from the inside. (No Title).

Fox, S. W., & Harada, K. (1958). Thermal copolymerization of amino acids to a product resembling protein. *Science*, *128*(3333), 1214–1214.

Fox, S. W., & Harada, K. (1960). The thermal copolymerization of amino acids common to protein1. *Journal of the American Chemical Society*, *82*(14), 3745–3751.

Fox, S. W., Harada, K., & Kendrick, J. (1959). Production of spherules from synthetic proteinoid and hot water. *Science*, *129*(3357), 1221–1223.

Fox, S. W., Jungck, J. R., & Nakashima, T. (1974). From proteinoid microsphere to contemporary cell: formation of internucleotide and peptide bonds by proteinoid particles. *Origins of Life*, *5*, 227–237.

Fox, S. W., McCauley, R. J., & Wood, A. (1967). A model of primitive heterotrophic proliferation. *Comparative Biochemistry and Physiology*, *20*(3), 773–778.

Fox, S. W., & Nakashima, T. (1980). The assembly and properties of protobiological structures: The beginnings of cellular peptide synthesis. *BioSystems*, *12*(3–4), 155–166.

Fox, S. W., & Nakashima, T. (1984). Endogenously determined variants as precursors of substrates for natural selection. In *Individuality and determinism: chemical and biological bases* (pp. 185–201). Springer.

Frank, S. A. (2012). Natural selection. IV. The price equation. *Journal of Evolutionary Biology*, *25*(6), 1002–1019.

Fries, P. (2015). Rhythms for cognition: communication through coherence. *Neuron*, *88*(1), 220–235.

Gaggìa, F., Baffoni, L., Galiano, M., Nielsen, D. S., Jakobsen, R. R., Castro-Mejía, J. L., et al. (2018). Kombucha beverage from green, black and rooibos teas: A comparative study looking at microbiology, chemistry and antioxidant activity. *Nutrients*, *11*(1), 1.

Ganewatta, M. S., Wang, Z., & Tang, C. (2021). Chemical syntheses of bioinspired and biomimetic polymers toward biobased materials. *Nature Reviews Chemistry*, *5*(11), 753–772.

Gao, X., Sadasivuni, K. K., Kim, H.-C., Min, S.-K., & Kim, J. (2015). Designing pH-responsive and dielectric hydrogels from cellulose nanocrystals. *Journal of Chemical Sciences*, *127*, 1119–1125.

Gao, X., Shi, Z., Liu, C., Yang, G., Sevostianov, I., & Silberschmidt, V. V. (2015). Inelastic behaviour of bacterial cellulose hydrogel: in aqua cyclic tests. *Polymer Testing*, *44*, 82–92.

Gedela, M., Potu, K. C., Gali, V. L., Alyamany, K., & Jha, L. K. (2016). A case of hepatotoxicity related to kombucha tea consumption. *SD Med*, *69*(1), 26–28.

Giordano, G., Carlotti, M., & Mazzolai, B. (2021). A perspective on cephalopods mimicry and bioinspired technologies toward proprioceptive autonomous soft robots. *Advanced Materials Technologies*, *6*(12), Article 2100437.

Gjorgjieva, J., & Jacobsen, J. (2007). Turing patterns on growing spheres: the exponential case. In *Conference publications*: *vol. 2007*, (no. Special), (pp. 436–445). Conference Publications.

Gordiichuk, P. I., Wetzelaer, G., Rimmerman, D., Gruszka, A., de Vries, J. W., Saller, M., et al. (2014). Solid-state biophotovoltaic cells containing photosystem I. *Advanced Materials*, *26*(28), 4863–4869.

Grzybowski, B. A., & Huck, W. T. (2016). The nanotechnology of life-inspired systems. *Nature nanotechnology*, *11*(7), 585–592.

Gu, M. B., Kim, H.-S., et al. (2014). *Biosensors based on aptamers and enzymes*: *vol. 140*, Springer.

Gupta, G., Srivastava, S., Khare, S., & Prakash, V. (2014). Extremophiles: an overview of microorganism from extreme environment. *International Journal of Agriculture, Environment and Biotechnology*, *7*(2), 371–380.

Habibi, N., Kamaly, N., Memic, A., & Shafiee, H. (2016). Self-assembled peptide-based nanostructures: Smart nanomaterials toward targeted drug delivery. *Nano Today*, *11*(1), 41–60.

Hadad, E., Rudnick-Glick, S., Grinberg, I., Kolitz-Domb, M., Chill, J. H., & Margel, S. (2020). Synthesis and characterization of poly (RGD) proteinoid polymers and NIR fluorescent nanoparticles of optimal D, L-configuration for drug-delivery applications—in vitro study. *ACS omega*, *5*(37), 23568–23577.

Hamley, I. (2011). Self-assembly of amphiphilic peptides. *Soft Matter*, *7*(9), 4122–4138.

Han, W. B., Yang, S. M., Rajaram, K., & Hwang, S.-W. (2022). Materials and fabrication strategies for biocompatible and biodegradable conductive polymer composites toward bio-integrated electronic systems. *Advanced Sustainable Systems*, *6*(2), Article 2100075.

Harada, K., & Fox, S. W. (1958). The thermal condensation of glutamic acid and glycine to linear peptides1. *Journal of the American Chemical Society*, *80*(11), 2694–2697.

Hebb, D. O. (2005). *The organization of behavior: A neuropsychological theory*. Psychology Press.

Heller, A., & Feldman, B. (2008). Electrochemical glucose sensors and their applications in diabetes management. *Chemical Reviews*, *108*(7), 2482–2505.

Henriques Pereira, D. P., Leethaus, J., Beyazay, T., do Nascimento Vieira, A., Kleinermanns, K., Tüysüz, H., et al. (2022). Role of geochemical protoenzymes (geozymes) in primordial metabolism: specific abiotic hydride transfer by metals to the biological redox cofactor NAD+. *The FEBS Journal*, *289*(11), 3148–3162.

Heo, J. S., Eom, J., Kim, Y.-H., & Park, S. K. (2018). Recent progress of textile-based wearable electronics: a comprehensive review of materials, devices, and applications. *Small*, *14*(3), Article 1703034.

Hodgkin, A. L., & Huxley, A. F. (1952). A quantitative description of membrane current and its application to conduction and excitation in nerve. *The Journal of Physiology*, *117*(4), 500.

Huang, X., Qi, X., Boey, F., & Zhang, H. (2012). Graphene-based composites. *Chemical Society Reviews*, *41*(2), 666–686.

Huang, X., Xin, Y., & Lu, T. (2022). A systematic, complexity-reduction approach to dissect the kombucha tea microbiome. *Elife*, *11*, Article e76401.

Huang, Y., Yao, K., Zhang, Q., Huang, X., Chen, Z., Zhou, Y., et al. (2024). Bioelectronics for electrical stimulation: materials, devices and biomedical applications. *Chemical Society Reviews*.

Hurot, C., Scaramozzino, N., Buhot, A., & Hou, Y. (2020). Bio-inspired strategies for improving the selectivity and sensitivity of artificial noses: A review. *Sensors*, *20*(6), 1803.

Hwang, S.-W., Tao, H., Kim, D.-H., Cheng, H., Song, J.-K., Rill, E., et al. (2012). A physically transient form of silicon electronics. *Science*, *337*(6102), 1640–1644.

Imanbekova, M., Abbasi, R., Hu, X., Sharma, M., Vandewynckele-Bossut, M., Haldavnekar, R., et al. (2024). Physical modifications of kombucha-derived bacterial nanocellulose: Toward a functional bionanocomposite platform. *Macromolecular Materials and Engineering*, Article 2400041.

Indiveri, G., Linares-Barranco, B., Hamilton, T. J., Schaik, A. v., Etienne-Cummings, R., Delbruck, T., et al. (2011). Neuromorphic silicon neuron circuits. *Frontiers in Neuroscience*, *5*, 73.

Ishima, Y., Przybylski, A. T., & Fox, S. W. (1981). Electrical membrane phenomena in spherules from proteinoid and lecithin. *BioSystems*, *13*(4), 243–251.

Isidro-Llobet, A., Kenworthy, M. N., Mukherjee, S., Kopach, M. E., Wegner, K., Gallou, F., et al. (2019). Sustainability challenges in peptide synthesis and purification: from R&D to production. *The Journal of Organic Chemistry*, *84*(8), 4615–4628.

Israelachvili, J. N., Mitchell, D. J., & Ninham, B. W. (1976). Theory of self-assembly of hydrocarbon amphiphiles into micelles and bilayers. *Journal of the Chemical Society, Faraday Transactions 2: Molecular and Chemical Physics*, *72*, 1525–1568.

Jalili, P., Ala, A., Nazari, P., Jalili, B., & Ganji, D. D. (2024). A comprehensive review of microbial fuel cells considering materials, methods, structures, and microorganisms. *Heliyon*.

Jayabalan, R., Malbaša, R. V., Lončar, E. S., Vitas, J. S., & Sathishkumar, M. (2014). A review on kombucha tea—microbiology, composition, fermentation, beneficial effects, toxicity, and tea fungus. *Comprehensive Reviews in Food Science and Food Safety*, *13*(4), 538–550.

Jia, S., Wang, J., Xie, M., Sun, J., Liu, H., Zhang, Y., et al. (2019). Programming DNA origami patterning with non-canonical DNA-based metallization reactions. *Nature Communications*, *10*(1), 5597.

Joyce, G. F., & Szostak, J. W. (2018). Protocells and RNA self-replication. *Cold Spring Harbor Perspectives in Biology*, *10*(9), a034801.

Jun, Y.-S., Zhu, Y., Wang, Y., Ghim, D., Wu, X., Kim, D., et al. (2022). Classical and nonclassical nucleation and growth mechanisms for nanoparticle formation. *Annual Review of Physical Chemistry*, *73*(1), 453–477.

Kačuráková, M., Smith, A. C., Gidley, M. J., & Wilson, R. H. (2002). Molecular interactions in bacterial cellulose composites studied by 1D FT-IR and dynamic 2D FT-IR spectroscopy. *Carbohydrate Research*, *337*(12), 1145–1153.

Kadler, K. E., Hill, A., & Canty-Laird, E. G. (2008). Collagen fibrillogenesis: fibronectin, integrins, and minor collagens as organizers and nucleators. *Current Opinion in Cell Biology*, *20*(5), 495–501.

Kaltenbrunner, M., Sekitani, T., Reeder, J., Yokota, T., Kuribara, K., Tokuhara, T., et al. (2013). An ultra-lightweight design for imperceptible plastic electronics. *Nature*, *499*(7459), 458–463.

Kanjanamosit, N., Muangnapoh, C., & Phisalaphong, M. (2010). Biosynthesis and characterization of bacteria cellulose–alginate film. *Journal of Applied Polymer Science*, *115*(3), 1581–1588.

Ke, Y., Lindsay, S., Chang, Y., Liu, Y., & Yan, H. (2008). Self-assembled water-soluble nucleic acid probe tiles for label-free RNA hybridization assays. *Science*, *319*(5860), 180–183.

Kessouri, P., Furman, A., Huisman, J. A., Martin, T., Mellage, A., Ntarlagiannis, D., et al. (2019). Induced polarization applied to biogeophysics: recent advances and future prospects. *Near Surface Geophysics*, *17*(6-Recent Developments in Induced Polarization), 595–621.

Ketabat, F., Pundir, M., Mohabatpour, F., Lobanova, L., Koutsopoulos, S., Hadjiiski, L., et al. (2019). Controlled drug delivery systems for oral cancer treatment—current status and future perspectives. *Pharmaceutics*, *11*(7), 302.

Khattak, F., Galgano, S., & Houdijk, J. (2022). Bacterial concentration and *Campylobacter spp.* quantification differ when fresh or ultra-frozen samples are analysed over time using molecular biology and culture-based methods. *PLoS One*, *17*(9), Article e0274682.

Kim, D.-H., Viventi, J., Amsden, J. J., Xiao, J., Vigeland, L., Kim, Y.-S., et al. (2010). Dissolvable films of silk fibroin for ultrathin conformal bio-integrated electronics. *Nature Materials*, *9*(6), 511–517.

Kinoshita, S., & Yoshioka, S. (2005). Structural colors in nature: the role of regularity and irregularity in the structure. *ChemPhysChem*, *6*(8), 1442–1459.

Kitano, H. (2001). Systems biology: toward system-level understanding of biological systems.

Kitney, R., Adeogun, M., Fujishima, Y., Goñi-Moreno, Á., Johnson, R., Maxon, M., et al. (2019). Enabling the advanced bioeconomy through public policy supporting biofoundries and engineering biology. *Trends in biotechnology*, *37*(9), 917–920.

Klowden, M. J. (2013). *Physiological systems in insects*. Academic Press.

Koga, S., Williams, D. S., Perriman, A. W., & Mann, S. (2011). Peptide–nucleotide microdroplets as a step towards a membrane-free protocell model. *Nature Chemistry*, *3*(9), 720–724.

Kolitz-Domb, M., Grinberg, I., Corem-Salkmon, E., & Margel, S. (2014). Engineering of near infrared fluorescent proteinoid-poly (L-lactic acid) particles for in vivo colon cancer detection. *Journal of Nanobiotechnology*, *12*, 1–13.

Kolitz-Domb, M., & Margel, S. (2018). Recent advances of novel proteinoids and proteinoid nanoparticles and their applications in biomedicine and industrial uses. *Israel Journal of Chemistry*, *58*(12), 1277–1285.

Kondo, S., & Miura, T. (2010). Reaction-diffusion model as a framework for understanding biological pattern formation. *Science*, *329*(5999), 1616–1620.

Konkoli, Z., Nichele, S., Dale, M., & Stepney, S. (2018). Reservoir computing with computational matter. *Computational Matter*, 269–293.

Koo, J., MacEwan, M. R., Kang, S.-K., Won, S. M., Stephen, M., Gamble, P., et al. (2018). Wireless bioresorbable electronic system enables sustained nonpharmacological neuroregenerative therapy. *Nature Medicine*, *24*(12), 1830–1836.

Koutinas, A. A., Vlysidis, A., Pleissner, D., Kopsahelis, N., Garcia, I. L., Kookos, I. K., et al. (2014). Valorization of industrial waste and by-product streams via fermentation for the production of chemicals and biopolymers. *Chemical Society Reviews*, *43*(8), 2587–2627.

Krystynowicz, A., & Bieleck, S. (2001). Biosynthesis of bacterial cellulose and its potential application in the different industries. *Polish Biotechnol. News*.

Kumar, M., Grzelakowski, M., Zilles, J., Clark, M., & Meier, W. (2007). Highly permeable polymeric membranes based on the incorporation of the functional water channel protein Aquaporin Z. *Proceedings of the National Academy of Sciences*, *104*(52), 20719–20724.

Kumar, A. M., Jayakumar, R., & Rao, K. P. (1996). Synthesis and aggregational behavior of acidic proteinoid. *Journal of Polymer Science Part A: Polymer Chemistry*, *34*(14), 2915–2924.

Kumar, A. M., & Rao, K. P. (1998). Preparation and characterization of pH-sensitive proteinoid microspheres for the oral delivery of methotrexate. *Biomaterials*, *19*(7–9), 725–732.

Kwak, H.-S. (2014). Overview of nano-and microencapsulation for foods. *Nano-and Microencapsulation for Foods*, 1–14.

Laavanya, D., Shirkole, S., & Balasubramanian, P. (2021). Current challenges, applications and future perspectives of SCOBY cellulose of kombucha fermentation. *Journal of Cleaner Production*, *295*, Article 126454.

Landmann, L. (1986). Epidermis and dermis. In *Biology of the integument: 2 vertebrates* (pp. 150–187). Springer.

Laschi, C., Cianchetti, M., Mazzolai, B., Margheri, L., Follador, M., & Dario, P. (2012). Soft robot arm inspired by the octopus. *Advanced Robotics*, *26*(7), 709–727.

Lee, K.-Y., Buldum, G., Mantalaris, A., & Bismarck, A. (2014). More than meets the eye in bacterial cellulose: biosynthesis, bioprocessing, and applications in advanced fiber composites. *Macromolecular Bioscience*, *14*(1), 10–32.

Lee, Y., Park, J., Choe, A., Cho, S., Kim, J., & Ko, H. (2020). Mimicking human and biological skins for multifunctional skin electronics. *Advanced Functional Materials*, *30*(20), Article 1904523.

Lehn, J.-M. (2007). Perspectives in chemistry: from supramolecular chemistry towards adaptive chemistry. *Chemistry*, *36*, 151.

Leman, L., Orgel, L., & Ghadiri, M. R. (2004). Carbonyl sulfide-mediated prebiotic formation of peptides. *Science*, *306*(5694), 283–286.

Levin, A., Hakala, T. A., Schnaider, L., Bernardes, G. J., Gazit, E., & Knowles, T. P. (2020). Biomimetic peptide self-assembly for functional materials. *Nature Reviews Chemistry*, *4*(11), 615–634.

Li, H., Chang, L., Li, H., Li, Q., & Wang, Y. (2024). Whole-component anaerobic methanogenesis of pre-acidized sludge: Optimal process and promotion mechanisms. *Chemical Engineering Science*, *289*, Article 119871.

Li, S., Jiang, Q., Liu, S., Zhang, Y., Tian, Y., Song, C., et al. (2018). A DNA nanorobot functions as a cancer therapeutic in response to a molecular trigger in vivo. *Nature Biotechnology*, *36*(3), 258–264.

Li, R., Ren, J., Zhang, M., Li, M., Li, Y., & Yang, W. (2024). Highly stretchable, fast self-healing, self-adhesive, and strain-sensitive wearable sensor based on ionic conductive hydrogels. *Biomacromolecules*, *25*(2), 614–625.

Liang, S. (2023). Advances in drug delivery applications of modified bacterial cellulose-based materials. *Frontiers in Bioengineering and Biotechnology*, *11*, Article 1252706.

Liang, Y., Offenhäusser, A., Ingebrandt, S., & Mayer, D. (2021). PEDOT: PSS-based bioelectronic devices for recording and modulation of electrophysiological and biochemical cell signals. *Advanced Healthcare Materials*, *10*(11), Article 2100061.

Liao, C., & Cai, Y. (2014). Towards modeling automation for synthetic biology. *A Systems Theoretic Approach to Systems and Synthetic Biology II: Analysis and Design of Cellular Systems*, 201–217.

Lifson, S. (1997). On the crucial stages in the origin of animate matter. *Journal of Molecular Evolution*, *44*, 1–8.

Ling, S., Chen, W., Fan, Y., Zheng, K., Jin, K., Yu, H., et al. (2018). Biopolymer nanofibrils: Structure, modeling, preparation, and applications. *Progress in Polymer Science*, *85*, 1–56.

Liu, C., Colón, B. C., Ziesack, M., Silver, P. A., & Nocera, D. G. (2016). Water splitting–biosynthetic system with CO2 reduction efficiencies exceeding photosynthesis. *Science*, *352*(6290), 1210–1213.

Liu, K., Feng, J., Kis, A., & Radenovic, A. (2014). Atomically thin molybdenum disulfide nanopores with high sensitivity for DNA translocation. *ACS Nano*, *8*(3), 2504–2511.

Liu, B., Li, Y., & Zhang, L. (2022). Analysis and visualization of spatial transcriptomic data. *Frontiers in Genetics*, *12*, Article 785290.

Logan, B. E., & Rabaey, K. (2012). Conversion of wastes into bioelectricity and chemicals by using microbial electrochemical technologies. *Science*, *337*(6095), 686–690.

Loganathachetti, D. S., Alhashmi, F., Chandran, S., & Mundra, S. (2022). Irrigation water salinity structures the bacterial communities of date palm (phoenix dactylifera)-associated bulk soil. *Frontiers in Plant Science*, *13*, Article 944637.

Lou, Y., Zhang, B., Ye, X., & Wang, Z.-G. (2023). Self-assembly of the de novo designed peptides to produce supramolecular catalysts with built-in enzyme-like active sites: a review of structure–activity relationship. *Materials Today Nano*, *21*, Article 100302.

Lovley, D. R. (2017). Electrically conductive pili: biological function and potential applications in electronics. *Current Opinion in Electrochemistry*, *4*(1), 190–198.

Lovley, D. R., & Walker, D. J. (2019). Geobacter protein nanowires. *Frontiers in Microbiology*, *10*, 2078.

Lugasi, L., Grinberg, I., Rudnick-Glick, S., Okun, E., Einat, H., & Margel, S. (2020). Designed proteinoid polymers and nanoparticles encapsulating risperidone for enhanced antipsychotic activity. *Journal of Nanobiotechnology*, *18*, 1–16.

Lukoševičius, M., Jaeger, H., & Schrauwen, B. (2012). Reservoir computing trends. *KI-Künstliche Intelligenz*, *26*, 365–371.

Luo, Z., Weiss, D. E., Liu, Q., & Tian, B. (2018). Biomimetic approaches toward smart bio-hybrid systems. *Nano Research*, *11*, 3009–3030.

Lv, P., Lu, X., Wang, L., & Feng, W. (2021). Nanocellulose-based functional materials: from chiral photonics to soft actuator and energy storage. *Advanced Functional Materials*, *31*(45), Article 2104991.

Ma, X., Xing, R., Yuan, C., Ogino, K., & Yan, X. (2020). Tumor therapy based on self-assembling peptides nanotechnology. *View*, *1*(4), Article 20200020.

Malvankar, N. S., Vargas, M., Nevin, K. P., Franks, A. E., Leang, C., Kim, B.-C., et al. (2011). Tunable metallic-like conductivity in microbial nanowire networks. *Nature nanotechnology*, *6*(9), 573–579.

Mamajanov, I. (2019). Wet-dry cycling delays the gelation of hyperbranched polyesters: Implications to the origin of life. *Life*, *9*(3), 56.

Mamajanov, I., Caudan, M., & Jia, T. Z. (2020). Protoenzymes: The case of hyperbranched polymer-scaffolded ZnS nanocrystals. *Life*, *10*(8), 150.

Mamajanov, I., & Cody, G. D. (2017). Protoenzymes: The case of hyperbranched polyesters. *Philosophical Transactions of the Royal Society of London A (Mathematical and Physical Sciences)*, *375*(2109), Article 20160357.

Marsh, A. J., O'Sullivan, O., Hill, C., Ross, R. P., & Cotter, P. D. (2014). Sequence-based analysis of the bacterial and fungal compositions of multiple kombucha (tea fungus) samples. *Food Microbiology*, *38*, 171–178.

Matsuno, K. (2018). *Protobiology physical basis of biology*. CRC Press.

May, A., Narayanan, S., Alcock, J., Varsani, A., Maley, C., & Aktipis, A. (2019). Kombucha: A novel model system for cooperation and conflict in a complex multi-species microbial ecosystem. *PeerJ*, *7*, Article e7565.

McCormick, A. J., Bombelli, P., Bradley, R. W., Thorne, R., Wenzel, T., & Howe, C. J. (2015). Biophotovoltaics: oxygenic photosynthetic organisms in the world of bioelectrochemical systems. *Energy & Environmental Science*, *8*(4), 1092–1109.

Meister, A. (1992). On the antioxidant effects of ascorbic acid and glutathione. *Biochemical Pharmacology*, *44*(10), 1905–1915.

Mendes, A. C., Baran, E. T., Reis, R. L., & Azevedo, H. S. (2013). Self-assembly in nature: using the principles of nature to create complex nanobiomaterials. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, *5*(6), 582–612.

Meng, Y., Wang, X., Li, Y., Chen, J., & Chen, X. (2024). Microbial interactions and dynamic changes of volatile flavor compounds during the fermentation of traditional kombucha. *Food Chemistry*, *430*, Article 137060.

Mercker, M., Hartmann, D., & Marciniak-Czochra, A. (2013). A mechanochemical model for embryonic pattern formation: coupling tissue mechanics and morphogen expression. *PLoS One*, *8*(12), Article e82617.

Merolla, P. A., Arthur, J. V., Alvarez-Icaza, R., Cassidy, A. S., Sawada, J., Akopyan, F., et al. (2014). A million spiking-neuron integrated circuit with a scalable communication network and interface. *Science*, *345*(6197), 668–673.

Miriyev, A., Stack, K., & Lipson, H. (2017). Soft material for soft actuators. *Nature Communications*, *8*(1), 596.

Mohanty, A. K., Vivekanandhan, S., Pin, J.-M., & Misra, M. (2018). Composites from renewable and sustainable resources: Challenges and innovations. *Science*, *362*(6414), 536–542.

Monnard, P.-A., & Walde, P. (2015). Current ideas about prebiological compartmentalization. *Life*, *5*(2), 1239–1263.

Motafeghi, F., Mortazavi, P., Shahsavari, R., Shaker, M., Mohammadi-Berenjestanaki, H., & Shokrzadeh, M. (2023). Kombucha mushroom extract: anticancer, antioxidant, and antimicrobial properties. *Applied in Vitro Toxicology*, *9*(3), 90–103.

Mougkogiannis, P., & Adamatzky, A. (2023a). Electrical properties of proteinoids for unconventional computing architectures. In *Proceedings of the 18th ACM international symposium on nanoscale architectures* (pp. 1–4).

Mougkogiannis, P., & Adamatzky, A. (2023b). Learning in ensembles of proteinoid microspheres. *Royal Society Open Science*, *10*(10), Article 230936.

Mougkogiannis, P., & Adamatzky, A. (2023c). Low frequency electrical waves in ensembles of proteinoid microspheres. *Scientific Reports*, *13*(1), 1992.

Mougkogiannis, P., & Adamatzky, A. (2024a). Memfractance of proteinoids. *ACS Omega*, *9*(13), 15085–15100.

Mougkogiannis, P., & Adamatzky, A. (2024b). On effect of chloroform on electrical activity of proteinoids. *Biomimetics*, *9*(7), 380.

Mougkogiannis, P., & Adamatzky, A. (2024c). Proto–neural networks from thermal proteins. *Biochemical and Biophysical Research Communications*, Article 149725.

Mougkogiannis, P., & Adamatzky, A. (2024d). Recognition of sounds by ensembles of proteinoids. *Materials Today Bio*, *25*, Article 100989.

Mougkogiannis, P., & Adamatzky, A. (2024e). Spike trains in PANI-proteinoid nanofibers with different light pulse rates. *Materials Advances*.

Mougkogiannis, P., Nikolaidou, A., & Adamatzky, A. (2024a). Kombucha-chlorella-proteinoid biosynthetic classifiers of audio signals. *Nano Select Wiley*.

Mougkogiannis, P., Nikolaidou, A., & Adamatzky, A. (2024b). On transducing properties of kombucha–proteinoid complexes. *ACS Applied Bio Materials*.

Müller, D., Rambo, C., Recouvreux, D., Porto, L., & Barra, G. (2011). Chemical in situ polymerization of polypyrrole on bacterial cellulose nanofibers. *Synthetic Metals*, *161*(1–2), 106–111.

Murphy, S. V., & Atala, A. (2014). 3D bioprinting of tissues and organs. *Nature Biotechnology*, *32*(8), 773–785.

Nainggolan, I., Nasution, T., Putri, S., Azdena, D., Balyan, M., & Agusnar, H. (2018). Study on chitosan film properties as a green dielectric. In *IOP conference series: materials science and engineering*: *vol. 309*, IOP Publishing, Article 012081.

Nakagaki, T., Yamada, H., & Tóth, Á. (2000). Maze-solving by an amoeboid organism. *Nature*, *407*(6803), 470–470.

Nakashima, T. (2005). Metabolism of proteinoid microspheres. *Organic Geo-and Cosmochemistry*, 57–81.

Nakashima, T., & Fox, S. (1980). Synthesis of peptides from amino acids and ATP with lysine-rich proteinoid. *Journal of Molecular Evolution*, *15*, 161–168.

Nedovic, V., & Willaert, R. (2013). *Fundamentals of cell immobilisation biotechnology*: *vol. 8*, Springer Science & Business Media.

Newman, M. (2010). *Networks: An introduction*. Oxford University Press.

Nguyen, P. Q., Courchesne, N.-M. D., Duraj-Thatte, A., Praveschotinunt, P., & Joshi, N. S. (2018). Engineered living materials: prospects and challenges for using biological systems to direct the assembly of smart materials. *Advanced Materials*, *30*(19), Article 1704847.

Nielsen, A. A., Der, B. S., Shin, J., Vaidyanathan, P., Paralanov, V., Strychalski, E. A., et al. (2016). Genetic circuit design automation. *Science*, *352*(6281), aac7341.

Nikolaidou, A., Chiolerio, A., Dehshibi, M. M., & Adamatzky, A. (2024). Functionalizing the electrical properties of kombucha zoogleal mats for biosensing applications. *ACS Omega*.

Nikolaidou, A., Mougkogiannis, P., & Adamatzky, A. (2023). Living kombucha electronics with proteinoids.

Nikolaidou, A., Mougkogiannis, P., & Adamatzky, A. (2024). Electroactive composite biofilms integrating kombucha, chlorella and synthetic proteinoid proto–brains. *Royal Society Open Science*, *11*(5), Article 240238.

Nirmal, N., Pillay, M. N., Mariola, M., Petruccione, F., & van Zyl, W. E. (2020). Formation of dialysis-free kombucha-based bacterial nanocellulose embedded in a polypyrrole/PVA composite for bulk conductivity measurements. *RSC Advances*, *10*(46), 27585–27597.

Nummer, B. A. (2013). SPECIAL REPORT: Kombucha brewing under the food and drug administration model food code: Risk analysis and processing guidance. *Journal of Environmental Health*, *76*(4), 8–11.

Nyholm, L., Nyström, G., Mihranyan, A., & Strømme, M. (2011). Toward flexible polymer and paper-based energy storage devices. *Advanced Materials*, *23*(33), 3751–3769.

Ojagh, S. M. A., Vahabzadeh, F., Fallah, N., Lan, X., Adesida, A. B., Kamkar, M., et al. (2024). Highly functionalized all-cellulose nanocomposites via bacteria-enabled in-situ modifications. *Chemical Engineering Journal*, Article 155409.

Ojo, A. O., & de Smidt, O. (2023). Microbial composition, bioactive compounds, potential benefits and risks associated with kombucha: A concise review. *Fermentation*, *9*(5), 472.

Orgel, L. E. (1994). The origin of life on the earth. *Scientific American*, *271*(4), 76–83.

Ortiz, D., Kohlstedt, K. L., Nguyen, T. D., & Glotzer, S. C. (2014). Self-assembly of reconfigurable colloidal molecules. *Soft Matter*, *10*(20), 3541–3552.
Ou, Z., & Muthukumar, M. (2006). Entropy and enthalpy of polyelectrolyte complexation: Langevin dynamics simulations. *Journal of Chemical Physics*, *124*(15).
Padil, V. V., Kumar, K. A., Murugesan, S., Torres-Mendieta, R., Wacławek, S., Cheong, J. Y., et al. (2022). Sustainable and safer nanoclay composites for multifaceted applications. *Green Chemistry*, *24*(8), 3081–3114.
Pagliaro, M., Ciriminna, R., Yusuf, M., Eskandarinezhad, S., Wani, I. A., Ghahremani, M., et al. (2021). Application of nanocellulose composites in the environmental engineering as a catalyst, flocculants, and energy storages: A review. *Journal of Composites and Compounds*, *3*(7), 114–128.
Paranjpe, D. A., & Kumar Sharma, V. (2005). Evolution of temporal order in living organisms. *Journal of Circadian Rhythms*, *3*(1), 7.
Park, J., Lee, Y., Kim, T. Y., Hwang, S., & Seo, J. (2022). Functional bioelectronic materials for long-term biocompatibility and functionality. *ACS Applied Electronic Materials*, *4*(4), 1449–1468.
Pasolli, E., De Filippis, F., Mauriello, I. E., Cumbo, F., Walsh, A. M., Leech, J., et al. (2020). Large-scale genome-wide analysis links lactic acid bacteria from food with the gut microbiome. *Nature Communications*, *11*(1), 2610.
Patel, G., & Misra, A. (2011). Oral delivery of proteins and peptides: concepts and applications. *Challenges in Delivery of Therapeutic Genomics and Proteomics*, 481–529.
Paulsen, B. D., Tybrandt, K., Stavrinidou, E., & Rivnay, J. (2020). Organic mixed ionic–electronic conductors. *Nature Materials*, *19*(1), 13–26.
Pecora, L. M., & Carroll, T. L. (1998). Master stability functions for synchronized coupled systems. *Physical Review Letters*, *80*(10), 2109.
Pelrine, R., Kornbluh, R., Pei, Q., & Joseph, J. (2000). High-speed electrically actuated elastomers with strain greater than 100%. *Science*, *287*(5454), 836–839.
Pfeifer, R., Lungarella, M., & Iida, F. (2012). The challenges ahead for bio-inspired'soft'robotics. *Communications of the ACM*, *55*(11), 76–87.
Pilo, M. I., Sanna, G., & Spano, N. (2024). Conducting polymers in amperometric sensors: A state of the art over the last 15 years with a focus on polypyrrole-, polythiophene-, and poly (3, 4-ethylenedioxythiophene)-based materials. *Chemosensors*, *12*(5), 81.
Polygerinos, P., Correll, N., Morin, S. A., Mosadegh, B., Onal, C. D., Petersen, K., et al. (2017). Soft robotics: Review of fluid-driven intrinsically soft devices; manufacturing, sensing, control, and applications in human-robot interaction. *Advanced Engineering Materials*, *19*(12), Article 1700016.
Pradhan, S., & Yadavalli, V. K. (2024). Silk proteins for bioelectronic devices in healthcare. In *Silk-based biomaterials for tissue engineering, regenerative and precision medicine* (pp. 735–769). Elsevier.
Prindle, A., Liu, J., Asally, M., Ly, S., Garcia-Ojalvo, J., & Süel, G. M. (2015). Ion channels enable electrical communication in bacterial communities. *Nature*, *527*(7576), 59–63.
Qian, L., & Winfree, E. (2011). Scaling up digital circuit computation with DNA strand displacement cascades. *Science*, *332*(6034), 1196–1201.
Qian, L., Winfree, E., & Bruck, J. (2011). Neural network computation with DNA strand displacement cascades. *Nature*, *475*(7356), 368–372.
Quan, H., Kisailus, D., & Meyers, M. A. (2021). Hydration-induced reversible deformation of biological materials. *Nature Reviews Materials*, *6*(3), 264–283.
Rajwade, J., Paknikar, K., & Kumbhar, J. (2015). Applications of bacterial cellulose and its composites in biomedicine. *Applied Microbiology and Biotechnology*, *99*, 2491–2511.
Raman, R., Cvetkovic, C., Uzel, S. G., Platt, R. J., Sengupta, P., Kamm, R. D., et al. (2016). Optogenetic skeletal muscle-powered adaptive biological machines. *Proceedings of the National Academy of Sciences*, *113*(13), 3497–3502.
Ramírez-Contreras, D., García-García, A., Mendoza, A., Serrano-de la Rosa, L. E., Sánchez-Gaytán, B. L., Melendez, F. J., et al. (2023). D, L-citrullinato-bipyridine copper complex: Experimental and theoretical characterization. *Crystals*, *13*(9), 1391.
Ranea, J. A., Sillero, A., Thornton, J. M., & Orengo, C. A. (2006). Protein superfamily evolution and the last universal common ancestor (LUCA). *Journal of Molecular Evolution*, *63*, 513–525.
Rathore, A. S., & Winkle, H. (2009). Quality by design for biopharmaceuticals. *Nature Biotechnology*, *27*(1), 26–34.
Razzaq, M. Y., Balk, M., Mazurek-Budzyńska, M., & Schadewald, A. (2023). From nature to technology: Exploring bioinspired polymer actuators via electrospinning. *Polymers*, *15*(19), 4029.
Reiniati, I., Hrymak, A. N., & Margaritis, A. (2017). Recent developments in the production and applications of bacterial cellulose fibers and nanocrystals. *Critical Reviews in Biotechnology*, *37*(4), 510–524.
Ren, J., Wang, X., Li, D., Han, N., Dong, B., & Xing, F. (2021). Temperature adaptive microcapsules for self-healing cementitious materials. *Composites Part B (Engineering)*, *223*, Article 109138.
Revin, V., Liyaskina, E., Nazarkina, M., Bogatyreva, A., & Shchankin, M. (2018). Cost-effective production of bacterial cellulose using acidic food industry by-products. *Brazilian Journal of Microbiology*, *49*, 151–159.
Rivnay, J., Inal, S., Salleo, A., Owens, R. M., Berggren, M., & Malliaras, G. G. (2018). Organic electrochemical transistors. *Nature Reviews Materials*, *3*(2), 1–14.
Rivnay, J., Owens, R. M., & Malliaras, G. G. (2014). The rise of organic bioelectronics. *Chemistry of Materials*, *26*(1), 679–685.
Rivnay, J., Wang, H., Fenno, L., Deisseroth, K., & Malliaras, G. G. (2017). Next-generation probes, particles, and proteins for neural interfacing. *Science Advances*, *3*(6), Article e1601649.
Roche, E. T., Horvath, M. A., Wamala, I., Alazmani, A., Song, S.-E., Whyte, W., et al. (2017). Soft robotic sleeve supports heart function. *Science Translational Medicine*, *9*(373), eaaf3925.
Roda, A., Guardigli, M., Michelini, E., & Mirasoli, M. (2009). Bioluminescence in analytical chemistry and in vivo imaging. *TRAC Trends in Analytical Chemistry*, *28*(3), 307–322.
Rogers, J. A., Someya, T., & Huang, Y. (2010). Materials and mechanics for stretchable electronics. *Science*, *327*(5973), 1603–1607.
Rohlfing, D. L. (1976). Thermal polyamino acids: synthesis at less than 100 C. *Science*, *193*(4247), 68–70.
Rohlfing, D. L., & Fox, S. W. (1969). Catalytic activities of thermal polyanhydro-α-amino acids. In *Advances in catalysis*: *vol. 20*, (pp. 373–418). Elsevier.
Rossnerova, A., Izzotti, A., Pulliero, A., Bast, A., Rattan, S., & Rossner, P. (2020). The molecular mechanisms of adaptive response related to environmental stress. *International Journal of Molecular Sciences*, *21*(19), 7053.
Rumon, M. M. H., Sarkar, S. D., Alam, M. M., & Roy, C. K. (2023). Nanomaterials for self-healing hydrogels. *Emerging Applications of Nanomaterials*, *141*, 270–293.
Rus, D., & Tolley, M. T. (2015). Design, fabrication and control of soft robots. *Nature*, *521*(7553), 467–475.
Ryan, J. W., & Fox, S. W. (1973). Activation of glycine by ATP, a divalent cation, and proteinoid microspheres. *BioSystems*, *5*(3), 115–118.
Salminen, S., Collado, M. C., Endo, A., Hill, C., Lebeer, S., Quigley, E. M., et al. (2021). The international scientific association of probiotics and prebiotics (ISAPP) consensus statement on the definition and scope of postbiotics. *Nature Reviews Gastroenterology & Hepatology*, *18*(9), 649–667.
Sanjuan-Alberte, P., Alexander, M. R., Hague, R. J., & Rawson, F. J. (2018). Electrochemically stimulating developments in bioelectronic medicine. *Bioelectronic Medicine*, *4*, 1–7.
Sasson, E., Pinhasi, R. V. O., Margel, S., & Klipcan, L. (2020). Engineering and use of proteinoid polymers and nanocapsules containing agrochemicals. *Scientific Reports*, *10*(1), 9171.
Schmidt, F. R. (2005). Optimization and scale up of industrial fermentation processes. *Applied Microbiology and Biotechnology*, *68*, 425–435.
Scholes, N. S., Schnoerr, D., Isalan, M., & Stumpf, M. P. (2019). A comprehensive network atlas reveals that turing patterns are common but not robust. *Cell Systems*, *9*(3), 243–257.
Schulte, P., Murashov, V., Zumwalde, R., Kuempel, E., & Geraci, C. (2010). Occupational exposure limits for nanomaterials: state of the art. *Journal of Nanoparticle Research*, *12*, 1971–1987.
Segev, R., Shapira, Y., Benveniste, M., & Ben-Jacob, E. (2001). Observations and modeling of synchronized bursting in two-dimensional neural networks. *Physical Review E*, *64*(1), Article 011920.
Semjonovs, P., Ruklisha, M., Paegle, L., Saka, M., Treimane, R., Skute, M., et al. (2017). Cellulose synthesis by *Komagataeibacter rhaeticus* strain P 1463 isolated from kombucha. *Applied Microbiology and Biotechnology*, *101*, 1003–1012.
Shacham-Diamand, Y., Belkin, S., Rishpon, J., Elad, T., Melamed, S., Biran, A., et al. (2010). Optical and electrical interfacing technologies for living cell bio-chips. *Current Pharmaceutical Biotechnology*, *11*(4), 376–383.
Shi, Z., Gao, X., Ullah, M. W., Li, S., Wang, Q., & Yang, G. (2016). Electroconductive natural polymer-based hydrogels. *Biomaterials*, *111*, 40–54.
Shi, Z., Phillips, G. O., & Yang, G. (2013). Nanocellulose electroconductive composites. *Nanoscale*, *5*(8), 3194–3201.
Shi, Z., Zhang, Y., Phillips, G. O., & Yang, G. (2014). Utilization of bacterial cellulose in food. *Food Hydrocolloids*, *35*, 539–545.
Shimizu, M., Yawata, S., Miyamoto, K., Miyasaka, K., Asano, T., Yoshinobu, T., et al. (2011). Toward biorobotic systems with muscle cell actuators. *The Proceedings of AMAM*, 87–88.
Shtein, M., Nadiv, R., Buzaglo, M., & Regev, O. (2015). Graphene-based hybrid composites for efficient thermal management of electronic devices. *ACS Applied Materials & Interfaces*, *7*(42), 23725–23730.
Simoska, O., Gaffney, E. M., Minteer, S. D., Franzetti, A., Cristiani, P., Grattieri, M., et al. (2021). Recent trends and advances in microbial electrochemical sensing technologies: An overview. *Current Opinion in Electrochemistry*, *30*, Article 100762.
Singer, W. (2007). Binding by synchrony. *Scholarpedia*, *2*(12), 1657.
Singh, A. V., Rahman, A., Kumar, N. S., Aditi, A., Galluzzi, M., Bovio, S., et al. (2012). Bio-inspired approaches to design smart fabrics. *Materials & Design (1980-2015)*, *36*, 829–839.
Singh, H., Unni, B., Neog, K., & Bhattacharyya, M. (2011). Sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and random amplified polymorphic DNA (RAPD) based genetic variation studies in eri silkworm (*Samia cynthia ricini Lepidoptera*: Saturniidae). *African Journal of Biotechnology*, *10*(70), 15684–15690.
Sleight, S. C., & Sauro, H. M. (2013). Visualization of evolutionary stability dynamics and competitive fitness of escherichia coli engineered with randomized multigene circuits. *ACS Synthetic Biology*, *2*(9), 519–528.
Smanski, M. J., Bhatia, S., Zhao, D., Park, Y., BA Woodruff, L., Giannoukos, G., et al. (2014). Functional optimization of gene clusters by combinatorial design and assembly. *Nature Biotechnology*, *32*(12), 1241–1249.

Sokolov, A., Hellerud, B., Johannessen, E., & Mollnes, T. (2012). Inflammatory response induced by candidate biomaterials of an implantable microfabricated sensor. *Journal of Biomedical Materials Research Part A*, *100*(5), 1142–1150.
Someya, T., Bao, Z., & Malliaras, G. G. (2016). The rise of plastic bioelectronics. *Nature*, *540*(7633), 379–385.
Somnath Chakravorty, S. C., Semantee Bhattacharya, S. B., Chatzinotas, A., Writachit Chakraborty, W. C., Debanjana Bhattacharya, D. B., & Ratan Gachhui, R. G. (2016). Kombucha tea fermentation: microbial and biochemical dynamics.
Spalvins, E., Dubey, B., & Townsend, T. (2008). Impact of electronic waste disposal on lead concentrations in landfill leachate. *Environmental Science and Technology*, *42*(19), 7452–7458.
Sporns, O., & Zwi, J. D. (2004). The small world of the cerebral cortex. *Neuroinformatics*, *2*, 145–162.
Sreeramulu, G., Zhu, Y., & Knol, W. (2000). Kombucha fermentation and its antimicrobial activity. *Journal of Agricultural and Food Chemistry*, *48*(6), 2589–2594.
Stagi, L., Sini, M., Carboni, D., Anedda, R., Siligardi, G., Gianga, T.-M., et al. (2022). Modulating the poly-l-lysine structure through the control of the protonation–deprotonation state of l-lysine. *Scientific Reports*, *12*(1), 19719.
Steensels, J., Daenen, L., Malcorps, P., Derdelinckx, G., Verachtert, H., & Verstrepen, K. J. (2015). Brettanomyces yeasts—From spoilage organisms to valuable contributors to industrial fermentations. *International Journal of Food Microbiology*, *206*, 24–38.
Stolte Bezerra Lisboa Oliveira, L., & Ristroph, K. D. (2024). Critical review: Uptake and translocation of organic nanodelivery vehicles in plants. *Environmental Science and Technology*, *58*(13), 5646–5669.
Strogatz, S. H. (2001). Exploring complex networks. *Nature*, *410*(6825), 268–276.
Stuart, M. A. C., Huck, W. T., Genzer, J., Müller, M., Ober, C., Stamm, M., et al. (2010). Emerging applications of stimuli-responsive polymer materials. *Nature Materials*, *9*(2), 101–113.
Su, T., Liu, N., Lei, D., Wang, L., Ren, Z., Zhang, Q., et al. (2022). Flexible MXene/bacterial cellulose film sound detector based on piezoresistive sensing mechanism. *ACS Nano*, *16*(5), 8461–8471.
Su, J., Tan, Q., Tang, Q., Tong, Z., & Yang, M. (2023). Research progress on alternative kombucha substrate transformation and the resulting active components. *Frontiers in Microbiology*, *14*, Article 1254014.
Suber, L., & Campi, G. (2012). Hierarchic self-assembling of silver nanoparticles in solution. *Nanotechnology Reviews*, *1*(1), 57–78.
Suhartatik, N., Widanti, Y. A., et al. (2023). Antioxidant activity of rose tea (rosa damascene) with various types of sugar and rose tea concentration. *JITIPARI (Jurnal Ilmiah Teknologi dan Industri Pangan UNISRI)*, *8*(2), 106–117.
Sui, S., Quan, H., Wang, J., Tan, Y., Sun, Z., & Zhang, Y. (2023). Core-shell design for nanocellulosic aerogels by bioinspired spider web-like structure. *Chemical Engineering Journal*, *477*, Article 146729.
Sun, M., Chen, C., Chen, L., & Su, B. (2016). Hierarchically porous materials: Synthesis strategies and emerging applications. *Frontiers of Chemical Science and Engineering*, *10*, 301–347.
Svergun, D. I., & Koch, M. H. (2003). Small-angle scattering studies of biological macromolecules in solution. *Reports on Progress in Physics*, *66*(10), 1735.
Taillefumier, T., Posfai, A., Meir, Y., & Wingreen, N. S. (2017). Microbial consortia at steady supply. *Elife*, *6*, Article e22644.
Tan, M. J., Owh, C., Chee, P. L., Kyaw, A. K. K., Kai, D., & Loh, X. J. (2016). Biodegradable electronics: cornerstone for sustainable electronics and transient applications. *Journal of Materials Chemistry C*, *4*(24), 5531–5558.
Tan, C., Saurabh, S., Bruchez, M. P., Schwartz, R., & LeDuc, P. (2013). Molecular crowding shapes gene expression in synthetic cellular nanosystems. *Nature nanotechnology*, *8*(8), 602–608.
Tanaka, H., Kazuta, Y., Naruse, Y., Tominari, Y., Umehara, H., Sowa, Y., et al. (2022). Bayesian-based decipherment of in-depth information in bacterial chemical sensing beyond pleasant/unpleasant responses. *Scientific Reports*, *12*(1), 2965.
Tanaka, G., Yamane, T., Héroux, J. B., Nakane, R., Kanazawa, N., Takeda, S., et al. (2019). Recent advances in physical reservoir computing: A review. *Neural Networks*, *115*, 100–123.
Taouzinet, L., Djaoudene, O., Fatmi, S., Bouiche, C., Amrane-Abider, M., Bougherra, H., et al. (2023). Trends of nanoencapsulation strategy for natural compounds in the food industry. *Processes*, *11*(5), 1459.
Tavanaei, A., Ghodrati, M., Kheradpisheh, S. R., Masquelier, T., & Maida, A. (2019). Deep learning in spiking neural networks. *Neural Networks*, *111*, 47–63.
Teleanu, R. I., Niculescu, A.-G., Roza, E., Vladâcenco, O., Grumezescu, A. M., & Teleanu, D. M. (2022). Neurotransmitters—key factors in neurological and neurodegenerative disorders of the central nervous system. *International Journal of Molecular Sciences*, *23*(11), 5954.
Teoh, A. L., Heard, G., & Cox, J. (2004). Yeast ecology of kombucha fermentation. *International Journal of Food Microbiology*, *95*(2), 119–126.
Terryn, S., Brancart, J., Lefeber, D., Van Assche, G., & Vanderborght, B. (2017). Self-healing soft pneumatic robots. *Science Robotics*, *2*(9), eaan4268.
Tiquia-Arashiro, S. M., & Pant, D. (2020). *Microbial electrochemical technologies*. Taylor & Francis Group: CRC Press.
Toohey, K. S., Sottos, N. R., Lewis, J. A., Moore, J. S., & White, S. R. (2007). Self-healing materials with microvascular networks. *Nature Materials*, *6*(8), 581–585.
Troncoso, O. P., & Torres, F. G. (2020). Bacterial cellulose—Graphene based nanocomposites. *International Journal of Molecular Sciences*, *21*(18), 6532.
Tuma, T., Pantazi, A., Le Gallo, M., Sebastian, A., & Eleftheriou, E. (2016). Stochastic phase-change neurons. *Nature nanotechnology*, *11*(8), 693–699.
Tuncer Degim, I., & Celebi, N. (2007). Controlled delivery of peptides and proteins. *Current Pharmaceutical Design*, *13*(1), 99–117.
Turing, A. M. (1990). The chemical basis of morphogenesis. *Bulletin of Mathematical Biology*, *52*, 153–197.
Ul-Islam, M., Khan, S., Ullah, M. W., & Park, J. K. (2015). Bacterial cellulose composites: Synthetic strategies and multiple applications in bio-medical and electro-conductive fields. *Biotechnology Journal*, *10*(12), 1847–1861.
Ul-Islam, M., Yasir, S., Mombasawala, L., Manan, S., & Wajid Ullah, M. (2021). Bacterial cellulose: a versatile material for fabrication of conducting nanomaterials. *Current Nanoscience*, *17*(3), 393–405.
Ullah, H., Wahid, F., Santos, H. A., & Khan, T. (2016). Advances in biomedical and pharmaceutical applications of functional bacterial cellulose-based nanocomposites. *Carbohydrate Polymers*, *150*, 330–352.
Urban, G., & Weiss, T. (2010). Hydrogels for biosensors. *Hydrogel Sensors and Actuators: Engineering and Technology*, 197–220.
Vasas, V., Fernando, C., Santos, M., Kauffman, S., & Szathmáry, E. (2012). Evolution before genes. *Biology Direct*, *7*, 1–14.
Villarreal-Soto, S. A., Beaufort, S., Bouajila, J., Souchard, J.-P., & Taillandier, P. (2018). Understanding kombucha tea fermentation: a review. *Journal of Food Science*, *83*(3), 580–588.
Vitas, J. S., Malbaša, R. V., Grahovac, J. A., & Lončar, E. S. (2013). The antioxidant activity of kombucha fermented milk products with stinging nettle and winter savory. *Chemical Industry and Chemical Engineering Quarterly*, *19*(1), 129–139.
Völlmecke, K., Afroz, R., Bierbach, S., Brenker, L. J., Frücht, S., Glass, A., et al. (2022). Hydrogel-based biosensors. *Gels*, *8*(12), 768.
Wang, J. (2008). Electrochemical glucose biosensors. *Chemical Reviews*, *108*(2), 814–825.
Wang, L., Chen, D., Jiang, K., & Shen, G. (2017). New insights and perspectives into biological materials for flexible electronics. *Chemical Society Reviews*, *46*(22), 6764–6815.
Wang, X., Dong, L., Zhang, H., Yu, R., Pan, C., & Wang, Z. L. (2015). Recent progress in electronic skin. *Advanced Science*, *2*(10), Article 1500169.
Wang, S., Li, T., Chen, C., Kong, W., Zhu, S., Dai, J., et al. (2018). Transparent, anisotropic biofilm with aligned bacterial cellulose nanofibers. *Advanced Functional Materials*, *28*(24), Article 1707491.
Wang, B., Rutherfurd-Markwick, K., Zhang, X.-X., & Mutukumira, A. N. (2022). Kombucha: Production and microbiological research. *Foods*, *11*(21), 3456.
Wang, R., Wang, W., Jensen, M., Li, X., Qiu, H., Jin, R., et al. (2023). Polypyrrole-doped cellulose hydrogel evaporator for steam generation and wastewater cleaning. *Journal of Sol-Gel Science and Technology*, *107*(2), 363–374.
Wang, M., Zhong, H., Li, Y., Li, J., Zhang, X., He, F., et al. (2024). Advances in bioinspired artificial systems enabling biomarker-driven therapy. *Chemistry - A European Journal*, Article e202401593.
Waterman, K. C., & Adami, R. C. (2005). Accelerated aging: prediction of chemical stability of pharmaceuticals. *International Journal of Pharmaceutics*, *293*(1–2), 101–125.
Watson, G. S., Watson, J. A., & Cribb, B. W. (2017). Diversity of cuticular micro-and nanostructures on insects: properties, functions, and potential applications. *Annual Review of Entomology*, *62*(1), 185–205.
Watts, D. J., & Strogatz, S. H. (1998). Collective dynamics of 'small-world'networks. *Nature*, *393*(6684), 440–442.
Whitesides, G. M., & Grzybowski, B. (2002). Self-assembly at all scales. *Science*, *295*(5564), 2418–2421.
Whitesides, G. M., Mathias, J. P., & Seto, C. T. (1991). Molecular self-assembly and nanochemistry: a chemical strategy for the synthesis of nanostructures. *Science*, *254*(5036), 1312–1319.
Willner, I., & Katz, E. (2006). *Bioelectronics: From theory to applications*. John Wiley & Sons.
Willner, I., & Willner, B. (2001). Biomaterials integrated with electronic elements: en route to bioelectronics. *TRENDS in Biotechnology*, *19*(6), 222–230.
Wolfbeis, O. S. (2005). Materials for fluorescence-based optical chemical sensors. *Journal of Materials Chemistry*, *15*(27–28), 2657–2669.
Wu, A., Wang, L., Jensen, E., Mathies, R., & Boser, B. (2010). Modular integration of electronics and microfluidic systems using flexible printed circuit boards. *Lab on a Chip*, *10*(4), 519–521.
Xia, K., Zheng, X., Wang, Y., Zhong, W., Dong, Z., Ye, Z., et al. (2022). Biomimetic chiral photonic materials with tunable metallic colorations prepared from chiral melanin-like nanorods for UV shielding, humidity sensing, and cosmetics. *Langmuir*, *38*(26), 8114–8124.
Xu, J., Eriksson, S., Cebula, M., Sandalova, T., Hedström, E., Pader, I., et al. (2015). The conserved Trp114 residue of thioredoxin reductase 1 has a redox sensor-like function triggering oligomerization and crosslinking upon oxidative stress related to cell death. *Cell Death & Disease*, *6*(1), e1616–e1616.
Xu, Z., Sun, H., Zhao, X., & Gao, C. (2013). Ultrastrong fibers assembled from giant graphene oxide sheets. *Advanced Materials*, *25*(2), 188–193.
Xu, J., Wang, S., Wang, G.-J. N., Zhu, C., Luo, S., Jin, L., et al. (2017). Highly stretchable polymer semiconductor films through the nanoconfinement effect. *Science*, *355*(6320), 59–64.

Xu, J., Xu, J., Shi, T., Zhang, Y., Chen, F., Yang, C., et al. (2023). Probiotic-inspired nanomedicine restores intestinal homeostasis in colitis by regulating redox balance, immune responses, and the Gut Microbiome. *Advanced Materials*, *35*(3), Article 2207890.

Xu, X., Zhou, J., Nagaraju, D. H., Jiang, L., Marinov, V. R., Lubineau, G., et al. (2015). Flexible, highly graphitized carbon aerogels based on bacterial cellulose/lignin: Catalyst-free synthesis and its application in energy storage devices. *Advanced Functional Materials*, *25*(21), 3193–3202.

Xue, Y., Lofland, S., & Hu, X. (2020). Protein-based flexible thermal conductive materials with continuous network structure: Fabrication, properties, and theoretical modeling. *Composites Part B (Engineering)*, *201*, Article 108377.

Yang, C., Li, P., Wei, C., Prominski, A., Ma, J., Sun, C., et al. (2024). A bioinspired permeable junction approach for sustainable device microfabrication. *Nature Sustainability*, *7*(9), 1190–1203.

Yang, J. J., Strukov, D. B., & Stewart, D. R. (2013). Memristive devices for computing. *Nature nanotechnology*, *8*(1), 13–24.

Yang, Y., & Wu, M. (2018). Rhythmicity and waves in the cortex of single cells. *Philosophical Transactions of the Royal Society, Series B (Biological Sciences)*, *373*(1747), Article 20170116.

Yasunaga, T., Wiegel, J., Bergen, M. D., Helmstädter, M., Epting, D., Paolini, A., et al. (2022). Microridge-like structures anchor motile cilia. *Nature Communications*, *13*(1), 2056.

Yetisen, A. K., Akram, M. S., & Lowe, C. R. (2013). Based microfluidic point-of-care diagnostic devices. *Lab on a Chip*, *13*(12), 2210–2251.

Yi, N., Cui, H., Zhang, L. G., & Cheng, H. (2019). Integration of biological systems with electronic-mechanical assemblies. *Acta Biomaterialia*, *95*, 91–111.

Yuki, A., & Fox, S. W. (1969). Selective formation of particles by binding of pyrimidine polyribonucleotides or purine polyribonucleotides with lysine-rich or arginine-rich proteinoids. *Biochemical and Biophysical Research Communications*, *36*(4), 657–663.

Zakharchenko, A., Guz, N., Laradji, A. M., Katz, E., & Minko, S. (2018). Magnetic field remotely controlled selective biocatalysis. *Nature Catalysis*, *1*(1), 73–81.

Zarrouk, E., Lenski, M., Bruno, C., Thibert, V., Contreras, P., Privat, K., et al. (2022). High-resolution mass spectrometry: Theoretical and technological aspects. *Toxicologie Analytique et Clinique*, *34*(1), 3–18.

Zauner, K.-P. (2005). Molecular information technology. *Critical Reviews in Solid State and Materials Sciences*, *30*(1), 33–69.

Zauner, K.-P., & Conrad, M. (2001). Enzymatic computing. *Biotechnology Progress*, *17*(3), 553–559.

Zenke, F., Poole, B., & Ganguli, S. (2017). Continual learning through synaptic intelligence. In *International conference on machine learning* (pp. 3987–3995). PMLR.

Zhang, S. (2003). Fabrication of novel biomaterials through molecular self-assembly. *Nature Biotechnology*, *21*(10), 1171–1178.

Zhang, J., Chen, B., Chen, X., & Hou, X. (2021). Liquid-based adaptive structural materials. *Advanced Materials*, *33*(50), Article 2005664.

Zhang, S., Chen, Y., Liu, H., Wang, Z., Ling, H., Wang, C., et al. (2020). Room-temperature-formed PEDOT: PSS hydrogels enable injectable, soft, and healable organic bioelectronics. *Advanced Materials*, *32*(1), Article 1904752.

Zhang, C., Huang, J., Zhang, J., Liu, S., Cui, M., An, B., et al. (2019). Engineered *Bacillus* subtilis biofilms as living glues. *Materials Today*, *28*, 40–48.

Zhang, Z., Pan, Y., Mustafa, G., Bai, Z., Wang, B., Wei, L., et al. (2024). Design of Fe-based metal organic framework derived catalysts: Remediation of nitrate contamination and action in polluted surface water. *Journal of Environmental Chemical Engineering*, *12*(3), Article 112702.

Zhang, C.-L., & Yu, S.-H. (2014). Nanoparticles meet electrospinning: recent advances and future prospects. *Chemical Society Reviews*, *43*(13), 4423–4448.

Zhao, D., Zhu, Y., Cheng, W., Chen, W., Wu, Y., & Yu, H. (2021). Cellulose-based flexible functional materials for emerging intelligent electronics. *Advanced Materials*, *33*(28), Article 2000619.

Zhu, J., Zhang, T., Yang, Y., & Huang, R. (2020). A comprehensive review on emerging artificial neuromorphic devices. *Applied Physics Reviews*, *7*(1).