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Proto–neural networks from thermal proteins

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A B S T R A C T

Proteinoids are synthetic polymers that have structural similarities to natural proteins, and their formation is achieved through the application of heat to amino acid combinations in a dehydrated environment. The thermal proteins, initially synthesised by Sidney Fox during the 1960s, has the ability to undergo self–assembly, resulting in the formation of microspheres that resemble cells. These microspheres have fascinating biomimetic characteristics. In recent studies, substantial advancements have been made in elucidating the electrical signalling phenomena shown by proteinoids, hence showcasing their promising prospects in the field of neuro–inspired computing. This study demonstrates the advancement of experimental prototypes that employ proteinoids in the construction of fundamental neural network structures. The article provides an overview of significant achievements in proteinoid systems, such as the demonstration of electrical excitability, emulation of synaptic functions, capabilities in pattern recognition, and adaptability of network structures. This study examines the similarities and differences between proteinoid networks and spontaneous neural computation. We examine the persistent challenges associated with deciphering the underlying mechanisms of emergent proteinoid–based intelligence. Additionally, we explore the potential for developing bio–inspired computing systems using synthetic thermal proteins in forthcoming times. The results of this study offer a theoretical foundation for the advancement of adaptive, self–assembling electronic systems that operate using artificial bio–neural principles.

1. Introduction

1.1. From vital forces to chemical evolution: foundations for proteinoids

Theories on the emergence of life have developed and changed over hundreds of years, providing the basis for Sidney Fox's groundbreaking research on thermal proteinoids [1]. For centuries, the most common theory about the beginning of life was "spontaneous generation" – the idea that live beings may emerge from inanimate components [2]. This viewpoint was developed by Ancient Greek philosophers such as Aristotle, who wrote circa 350 BCE that "some [animals] spring from parent animals according to their kind, whereas others grow spontaneously and not from kindred stock." Aristotle's belief that life might spontaneously develop from non–living substances persisted well into the Renaissance. This belief in innate "vital forces" distinguishing life from non–living things gave way to more modern mechanistic ideas. However, integrated models that reconcile physical-chemical, biological, and cognitive phenomena are still sought to properly explain the origins of life [3–5].

During the early 20th century, Alexander Oparin played a significant role in reintroducing the concept of abiogenesis [6]. He proposed a theoretical framework suggesting that coacervates, which are colloidal aggregates, may potentially function as rudimentary structures resembling cells. Oparin's concept of the "primordial soup" was a crucial shift towards the investigation of biochemical beginnings [7–9].

In 1929, biologist J.B.S. Haldane provided the "primordial soup" idea for the origin of life in a small article titled "The Origin of Life" [10]. Haldane proposed that the early Earth had a decreasing atmosphere deficient in oxygen. He proposed that the Sun's ultraviolet radiation produced reactions in a marine soup of water, carbon dioxide, and ammonia [11]. This soup collected organic compounds synthesised abiotically, such as sugars and amino acids. The primaeval oceans eventually became hot and dilute, containing a wide range of organic chemicals [12]. Haldane claimed that the first replicating organisms emerged from this rich prebiotic broth. Though specifics have been revised, the primordial soup notion — that life arose from complex organics spontaneously synthesised in the early oceans — has had an impact on origin of life research and is a forerunner of present prebiotic chemistry models [13–15].

The primordial soup idea received critical scientific corroboration in

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1953, when Stanley Miller and Harold Urey replicated early Earth conditions in the lab [16]. They used sparks to create a methane, ammonia, and hydrogen gas combination to simulate Haldane's predicted decreasing environment. The now–famous Miller–Urey experiment was successful in synthesising basic amino acids, providing the first experimental proof that chemical compounds arise spontaneously under primordial conditions [17]. Joan Oró's subsequent study demonstrated that nucleic acid bases like adenine originate from ammonium cyanide solutions, demonstrating potential prebiotic routes to both protein and genetic polymer building blocks [18]. These fundamental investigations provided critical support for the primordial soup paradigm, which proposed that life evolved from complex organics naturally generated in the early oceans. Subsequent research is also being conducted to investigate prebiotic synthesis processes in various postulated early Earth conditions [19–21].

These suggestions provide a foundation for conducting empirical studies on the abiogenic synthesis of biological molecules. During the 1960s, Sidney Fox conducted groundbreaking experiments in polymerization by heating mixtures of amino acids to produce proteinoids [22]. Fox demonstrated that these thermal proteins have the ability to self–organize into microspheres that resemble cells [23]. These microspheres exhibit lifelike behaviours that are not present in the individual amino acids [24].

The concept of proteinoids offers a plausible model for the spontaneous formation of polypeptides and protocell structures from basic prebiotic chemistry. Fox's research clarified the pathways that connect non–living substances to organised biological systems. This research aligns with the conceptual shifts in theories about the origin of life, moving away from the idea of vital forces and towards the understanding of biochemical evolution [25].

2. Building Proto–Cells from thermal proteins

The groundbreaking research conducted by Sidney Fox in the field of proteinoid synthesis has established a fundamental framework and experimental plan for the construction of artificial protocells using basic biomolecular building blocks [26]. The application of heat to mixtures containing amino acids results in the formation of proteinoids, which possess the ability to spontaneously assemble into structures resembling cells when exposed to water [27]. The strategy of producing primitive biomimetic compartments from the bottom–up differs from top–down strategies aimed at simplifying current cells to a minimal extent [28].

Proteinoids present an avenue for investigating the emergence of primitive living forms through non–directed chemical and physical processes, rather than simplifying existing biology [29]. The thermal conditions might replicate the heating conditions that existed on the early Earth. The polymerization process, which is energetically favourable, leads to the formation of polypeptide chains, so forming a favourable environment for further self–structuring [30].

After they are formed, proteinoids form vesicles that are bound by proteinoid membranes and have specialised microenvironments [31]. These protocells demonstrate indications on their potential ability to have selective permeability, harvest energy, metabolise nutrients, growth dynamics, and mechanisms for propagation [32]. The architecture of the membrane plays a crucial role in localising reactions and compartmentalising the earliest protobiochemistry [33].

Proteinoids serve as a conceptual link between prebiotic molecules and organised protocell assemblies, enabling them to exhibit quasicellular functions [34]. The biomimetic capabilities of this system offer a flexible opportunity to investigate the origins of microscale biological order [35]. The use of thermal proteinoids facilitates the advancement of research on the transition from individual molecular components to organised populations that exhibit collective dynamics similar to those found in primitive cells [36].

3. Neuromorphic computing: Brain–Inspired intelligence

Neuromorphic computing seeks to simulate neural processing by emulating the brain's architecture and dynamics [37]. Important characteristics include massively parallel processing, the co–location of computation and memory, and adaptive learning mechanisms [38]. Memristive devices, which function as artificial synapses, and spiking neural networks make this possible [39]. They employ parallelism and adaptation to implement bio–inspired algorithms [40]. Neuromorphic computing offers significant advantages such as enhanced pattern recognition features, reduced power consumption, increased scalability, and improved fault tolerance [41]. By employing a distributed processing approach, similar to the functioning of the human brain, the need for high–power central processors is circumvented [42]. Local learning rules enable the capacity for real–time adaptation and the ability to withstand setbacks [43]. Neuromorphic systems exhibit favourable characteristics that render them very suitable for machine learning applications [44]. Neuromorphic computing demonstrates exceptional proficiency in perception tasks such as image and voice recognition, owing to its highly parallel and adaptable characteristics [45,46]. The direct integration of sensor input into neural nodes facilitates rapid and dynamic classification [47,48]. Edge computing devices have the capability to execute these inferences locally, independent of cloud access. Neuromorphic circuits are making significant progress in enhancing autonomous robots by facilitating precise sensation–action loops [49].

The field of medical diagnostics [50] has the potential to realise advantages from the use of neuromorphic computing, specifically due to its pattern recognition capabilities [51]. The identification of irregularities in intricate sensor data, such as MRI scans, necessitates the ability to perceive and differentiate tiny characteristics. Neuromorphic artificial intelligence (NAI) [52] has the potential to undergo training using huge amounts of medical data, thereby providing valuable assistance to physicians in their diagnosis operations. Additionally, it has the potential to facilitate the development of novel brain–interfaced assistive technologies [53].

The brain's impressive computational capabilities arise from the use of distributed processing, the presence of co–located memory, and its inherent plasticity [54]. Neuromorphic systems strive to attain comparable efficiency while consuming significantly lower power by replicating these characteristics [55]. The use of bio–inspired methodologies is facilitating the integration of natural intelligence into artificial systems, hence exhibiting potential applications in the domains of sensing, control, and autonomy [56].

4. Electrical signaling in proteinoids

Proteinoids are capable of electrical excitation and signalling [1,57–60]. Low frequency waves can propagate along chains of proteinoid microspheres that have been synthesised. Potentially, protons hopping between microspheres are responsible for these pulses. The frequency of the waves depends on the composition of the proteinoids and their surrounding environment. This observation provides evidence that proteinoid networks can transmit information via electrical signals. The waves resemble action potentials utilised for long–distance communication in the axons of biological neurons. Although considerably slower, proton hopping replicates the regenerative propagation of spikes [61].

The identification of electrical excitability inside proteinoids represents a significant advancement in the pursuit of constructing protocells that possess the capacity for integrated sensory perception, inter-cellular communication, and adaptive behaviour [62]. The development of effective communication among constituent proteins is crucial for the purpose of achieving coordination and control. When electrically active proteinoids are combined with selective permeability and metabolic activity, they exhibit enhanced lifelike characteristics [63]. As proteinoids gradually acquire the characteristics of living cells, they reveal how these functions may have evolved in early life forms. Electrical signalling is essential for the survival of complex multicellular organisms [64,65]. Its emergence spontaneously in protein networks suggests possible routes to primitive cognition [66].

As depicted in Fig. 1, chains of proteinoids can exhibit propagating electrical spiking activity. As protons hop between microspheres, small amplitude spikes occur at regular intervals, generating a slow travelling wave. This emergent electrical signalling, which is considerably simpler than neuron potentials, suggests how early proteins may have self–organized to transmit information. Extending this capacity for excitation and transmission could allow proteinoids to form interconnected networks of sensors, computers, and actuators. By combining proteinoids with other biomolecules, synthetic cells may one day replicate essential electrical characteristics of living cells.

5. Transfer functions and plasticity in proteinoids

Recenty we demonstrated that proteinoids are able to perform fundamental information processing via electrical inputs and outputs [67]. We identified transfer functions resembling neural computations by applying electric pulses to networks of proteinoid microspheres and measuring the resulting signals. Proteinoids demonstrated dynamic signal amplification, thresholding, and integration. The reconfiguration of the microspheres into different morphologies in response to applied voltages enables these processes. The input–output output can be modified by altering the proteinoids' chemical composition.

The find of transfer functions inside self–assembled proteinoids implies that they feature innate characteristics that are advantageous for information processing [68]. Through additional engineering efforts, it is conceivable that proteinoids might be intentionally engineered to possess synthetic logic and processing capabilities [69], akin to a rudimentary artificial nervous system [70].

The signal processing capabilities offer indications that pre–cellular living forms potentially engaged in information processing prior to the development of cells possessing distinct genomes. The collective electrical excitability exhibited by proteinoids provides insights into the potential mechanisms underlying sensation and responsiveness in prebiotic assemblies [71].

Proteinoids have characteristics that bear resemblance to living organisms, and these characteristics have recently been observed to include basic capacities in information transfer and computation [72]. Their rich potential is guiding efforts to construct lifelike systems from the bottom up. The integration of synthetic biomaterials into bioinspired computing holds great promise for advancements in both engineering and origins of life research [73].

Fig. 2 highlights the selective signal processing capability of proteinoids across many frequencies. As seen, the parameters of impedance, capacitance, and gain exhibit variations in relation to the input frequency. At lower frequencies, the rate of proton hopping between microspheres is restricted, as indicated by the significant resistance and limited capacitance. Nevertheless, as the frequencies increase, the impedance and capacitance of proteinoids decrease due to the enhancement in proton mobility. In addition, it is seen that the proteinoids demonstrate optimal amplification at frequencies that are within an intermediate range, indicating that the transmission of energy within the network is maximally effective at these specific frequencies. The observed frequency–dependent responses illustrate the inherent ability of proteinoids to selectively process inputs and dynamically adjust their behaviour, which are essential attributes for effective information processing.

6. Light–activated oscillations in proteinoids networks

Recent research has demonstrated that proteinoids have the capability to display oscillatory reactions upon exposure to cold white light [74]. The oscillation in amplitude of the proteinoids was noticed at initial exposure. Nevertheless, when subjected to uninterrupted illumination, the strength of oscillation gradually decreased. Interestingly, the act of pulsating the light by turning it on and off resulted in more pronounced oscillations when compared to the continuous illumination.

The proteinoids exhibit a response to alterations in illumination conditions, rather than solely being influenced by variations in brightness. The intermittent activation and deactivation of pulses could potentially stimulate an intrinsic oscillator embedded within the network of proteinoids. Under conditions of continuous illumination, the amplitude of the oscillations diminishes while the frequency of the oscillations actually increases. This suggests that the oscillations survive at a higher rate of tempo.

The incorporation of light–induced oscillations contributes to the realistic characteristics of proteinoids, hence enabling the manifestation of primitive sensory capabilities and adaptability [75]. The capacity to adjust dynamics in reaction to external signals bears resemblance to habitat tracking behaviours observed in natural systems [76]. Additional research on photosensitivity could potentially reveal underlying systems involved in the efficient utilisation of light energy.

The inherent oscillatory mechanisms and light–sensing capabilities of early protocells provide potential explanations for the emergence of circadian rhythms that are synchronised with the diurnal cycle [77]. The presence of photo–sensitive proto–clocks, when integrated with metabolic pathways, could potentially have provided certain benefits [78]. The investigation of emergent response in proteinoids is a valuable avenue for gaining insights into the fundamental mechanisms underlying cellular behaviour [79].

Proteinoids once again demonstrate biomimetic characteristics, specifically by displaying oscillatory reactions that are triggered by light stimulation. The intricate dynamics observed in these relatively uncomplicated protein systems provide indications of potential mechanisms through which responsiveness and regulation may have developed throughout the early stages of life. The sensitivity of proteinoids to external stimuli presents novel opportunities for the development of engineered biomimetic materials.

Fig. 3 demonstrates the notable capacity of proteinoids to display light–sensitive oscillations. When subjected to continuous illumination, the electrical potential exhibits oscillatory behaviour with a decreasing amplitude as time progresses. Nevertheless, the act of switching the light on and off induces strong oscillations that are synchronised with the pulses. This observation underscores the inherent responsiveness of proteinoids to alterations in illumination conditions, encompassing factors beyond mere intensity. According to the principles of adaptive dynamics [81], proteinoid networks are believed to possess oscillators that have the ability to be activated by external stimuli. Additional investigation into these photosensitive reactions could potentially reveal underlying mechanisms that could be utilised for the purpose of capturing light energy in artificial protocells [82]. The emerging receptive behaviours observed in proteinoids offer valuable insights into the potential mechanisms by which early living forms could have evolved basic sensory capabilities.

7. Building logic with proteinoids

Recently we demonstrated the ability of proteinoid microspheres to perform fundamental Boolean logic operations [83], potentially functioning as unconventional biomolecular computer components [84]. Proteinoids have successfully implemented AND, OR, and NOT gates by accepting electrical pulses as inputs and spike patterns as outputs.

The presence or absence of output spikes within specific temporal periods can be attributed to combinations of input pulses. The temporal arrangement of the spikes conveys the logical output function. Through making use of proteinoids' capacity for excitability and integration of signals, it becomes possible to establish input–output logic linkages.

This proof–of–concept serves as an illustration of how the computational potential of proteinoid networks might be effectively leveraged.

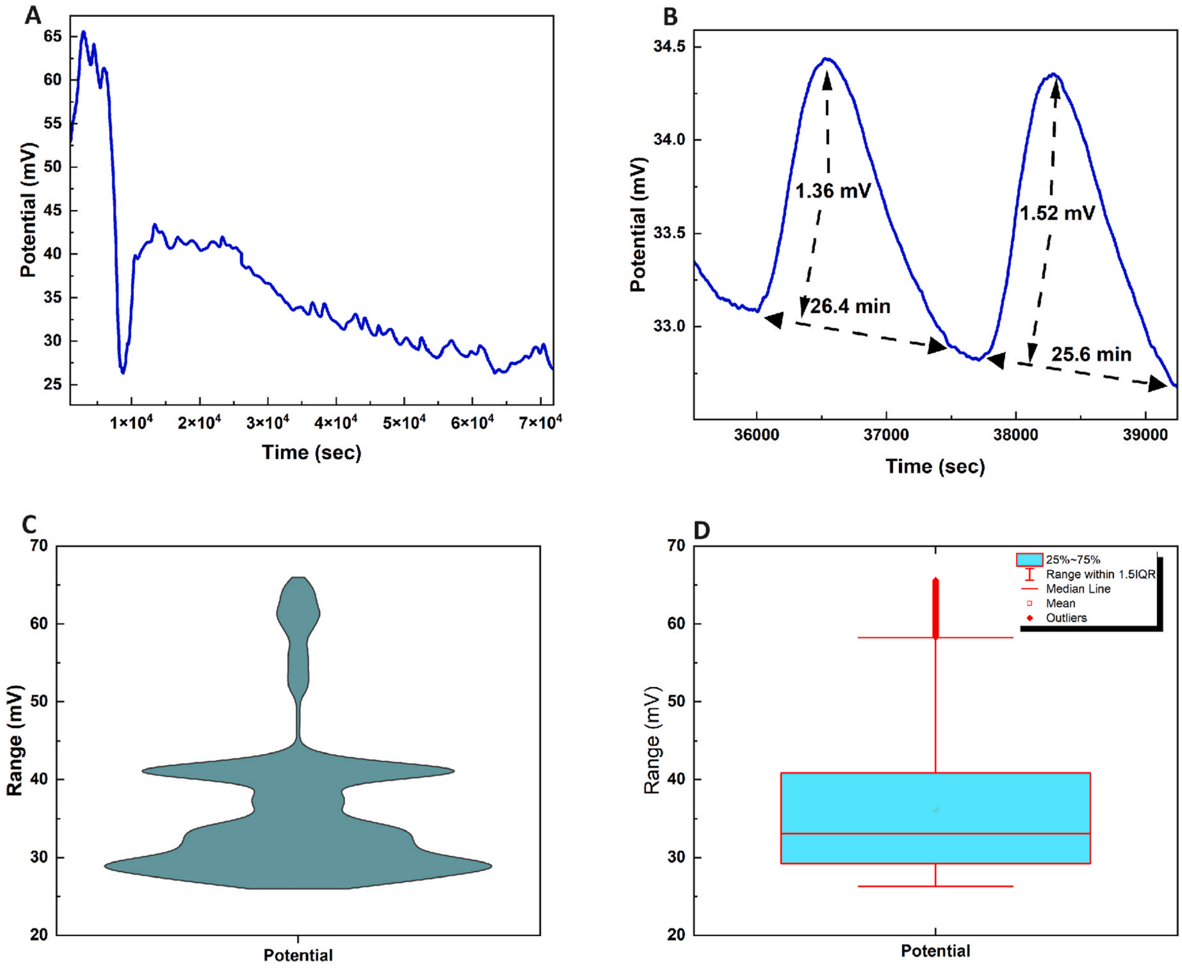

Fig. 1. A,B) Electrical transmission within proteinoids. This graph illustrates electrical potential surges measured across a chain of L–glutamic acid and L–phenylalanine proteinoid microspheres. The pulses have a period of 26 minutes and an amplitude of approximately 1 mV. This low frequency propagating wave is attributed to protons moving between nearby proteinoids, demonstrating primitive information propagation comparable to action potentials in neurons. C) D) The provided plot illustrates the occurrence of temporary electrical potential spikes observed in a chain of L–glutamic acid and L– phenylalanine (L–Glu:L–Phe) proteinoid microspheres. The proteinoid ensemble architecture allows for bursts of signalling activity transmission, which can be measured by rapid variations in potential. The spiking shapes exhibit distinct characteristics that closely match the action potentials observed in brain systems, thus enhancing the biomimetic similarities. Statistical analysis allows for the identification of signalling behaviours based on their composition, which can be used to design materials that closely resemble biological systems. (D) Quantile plots provide a statistical representation of the distribution of signals, allowing for a comparison of the patterns of electrical potential displayed by various proteinoid formulations. By comparing quartile spreads, we can identify differences in the range of values, the degree of asymmetry, and the prevalence of extreme values among different samples. The median values of the aggregate proteinoids are consistently centred around zero. However, the quantiles that deviate from the median reveal both positive and negative spikes, indicating the presence of conveyed information. By utilising common statistical abbreviations, the electrical potential fluctuations may be categorised, enabling quick characterization of signalling phenotypes. This is crucial for transforming the versatile proteinoid computational capabilities towards specific applications by targeted cross–linking and doping [60]

Materials that display intricate patterns in both space and time could potentially serve as substitutes for logic gates based on silicon [85]. The emergent logic functions emphasise proteinoids as possible bioinspired computer substrates [86].

The capacity to arrange proteinoids as logical operators establishes a foundation for the development of advanced biomolecular information processing and signal manipulation techniques. The establishment of proteinoid networks has the potential to facilitate the development of programmable chemical controllers [87]. The incorporation of other protocell features would enable the implementation of logic–based processes like as metabolism, movement, and division [88].

Proteinoids continue exhibiting their enormous potential as primitive synthetic biomaterials. Proteinoids possesses the ability to perform fundamental computational tasks, in addition to their structural, excitable, and oscillatory characteristics. The ongoing development of intelligent proteinoid systems has the potential for more insights into the origins of life and the use of these systems in unconventional computing [89].

Fig. 4 demonstrates the capacity to execute fundamental logical processes utilising proteinoids. AND, OR, and NOT gates can be implemented by employing particular input pulse combinations and observing the resulting output spike activity within predetermined time intervals. The occurrence or non–occurrence of spikes subsequent to stimulations signifies distinct logical outputs. The spike timing encoding approach presented in this study showcases the usage of proteinoids' excitable dynamics for the purpose of mapping input patterns to desired output functions. The robust implementation of Boolean logic employing unconventional biomolecular computing elements can be achieved by further optimising the latency and spike characteristics for each function.

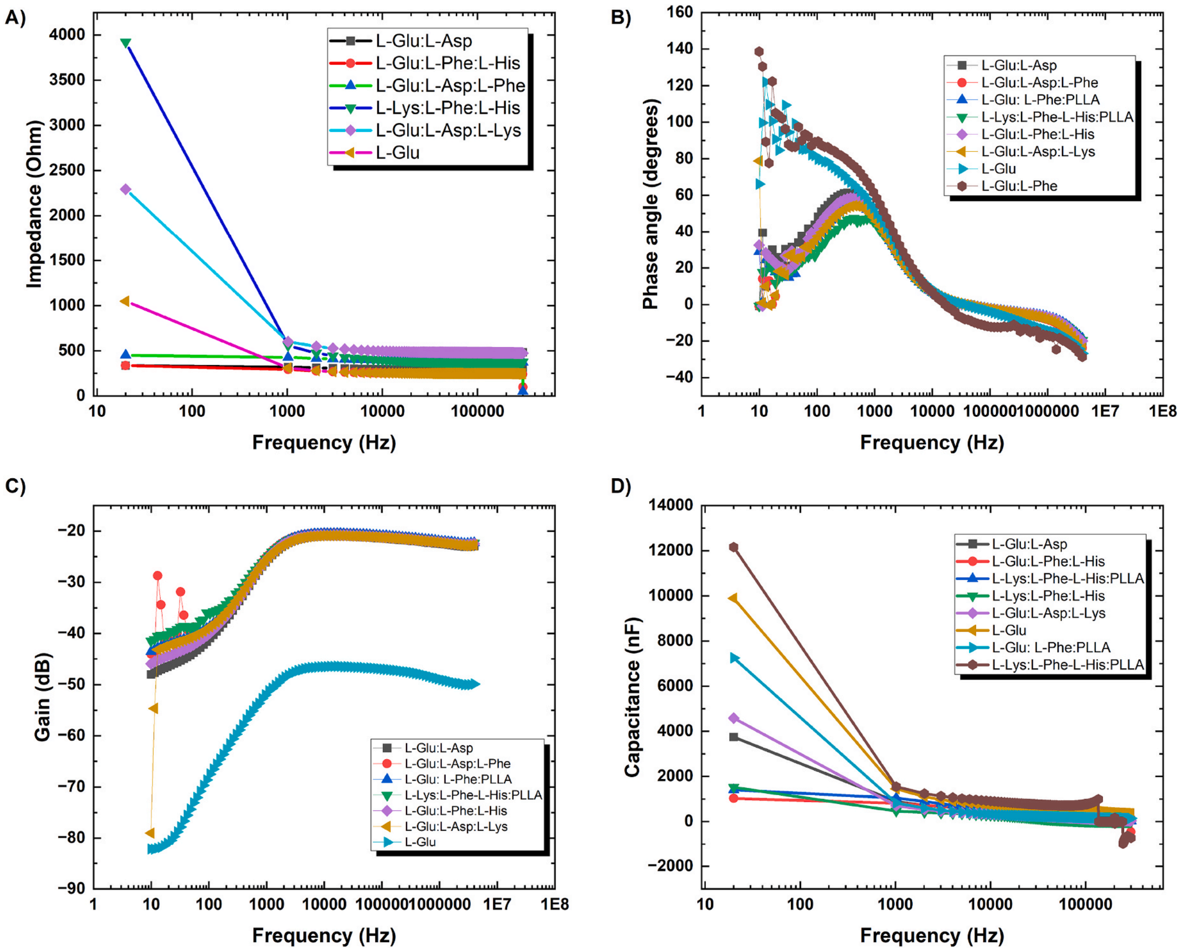

Fig. 2. Frequency response of proteinoids microspheres. Electrical measurements of impedance (resistance), capacitance, and gain in networks of proteinoid microspheres reveal frequency–dependent responses. At lower frequencies, the impedance and capacitance exhibit large values, suggesting that the movement of protons between microspheres is constrained by the rate at which it occurs. The proteinoids exhibit maximum gain at middle frequencies, indicating that energy transfer inside the proteinoids is most efficient at these frequencies. The frequency–selective electrical properties exhibited by proteinoids illustrate their capacity to effectively filter inputs and adjust response dynamics [67].

8. Proteinoids as Bio–Inspired speech recognizers

The proteinoids possess the ability to manifest electrical reactions that are specifically attuned to distinct phonetic units [90]. A sort of speech recognition was accomplished by recording and analysing the signals of proteinoids when subjected to auditory stimuli in the form of letter sounds.

Although the letter waveforms in the input were characterised by a high degree of regularity, the outputs of the proteinoids exhibited a greater level of variability. The main frequencies shown by the inputs were found to be lower, accompanied by a broader range of amplitudes. This observation suggests that proteinoids do not merely replicate or passively convert the auditory impulses.

Proteinoids, on the other hand, have an active role in the conversion of inputs into unique electrical patterns that effectively reflect the distinctive characteristics associated with each individual letter. The inherent ability of individuals to manipulate signals in a dynamic manner allows for a natural connection between auditory stimuli and corresponding reactions. With other advancements, it is possible to build proteinoids that are more refined and responsive to speech.

The capacity to recognise letters contributes to the repertoire of information processing and computational capabilities exhibited by proteinoids. The ability of bioinspired auditory technology to effectively process complicated audio inputs is underscored by its remarkable sensitivity. Proteinoid networks have the potential to interpret multidimensional data when combined with their present light–responsive properties.

Proteinoids continue to manifest emergent biomimetic phenomena, as evidenced by their capacity to undergo differentiation and respond to diverse environmental stimuli. The foundational basis for sensory processing and pattern recognition offers insights into the beginnings of perception and cognition in early organisms [91].

Fig. 5 highlights the capacity of proteinoids to respond selectively to spoken letters. When stimulated by audio recordings of various letters, the proteinoids produce distinct electrical patterns, which may be seen in the voltage time series. Cross–correlation analysis indicates that proteinoids' signal peaks correspond to distinct aspects of each input letter sound. While the answers are not exact replicas, they do capture critical timing and shape clues that allow the letters to be distinguished. This demonstrates the feasibility of constructing proteinoids networks with customisable bioinspired voice recognition functions. The inherent ability of proteinoids to translate complicated audio inputs to dynamic electrical outputs underscores the promise of proteinoids in the development of novel auditory processing systems [92].

9. Modeling Inter–Proteinoid signaling

Neuronal communication occurs through synapses, where

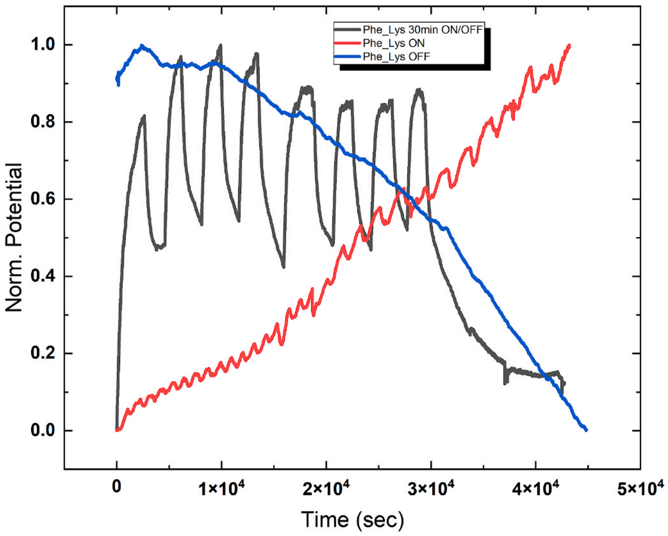

Fig. 3. The above graph illustrates variations in electrical potential (measured in millivolts)over a certain time period for a sample of proteinoids, when subjected to varied lighting conditions. Under conditions of uninterrupted illumination, early oscillations are induced, but their amplitude subsequently diminishes. The act of alternating the illumination state of a light source at regular intervals of 30 minutes has been observed to elicit more pronounced and enduring oscillatory patterns. Under conditions of low light intensity, the baseline voltage remains constant without any fluctuations. The diverse oscillatory responses observed indicate that proteinoids possess an inherent ability to respond to alterations in illumination conditions, hence displaying a basic form of photosensitivity and adaptive dynamics[80].

neurotransmitters can be utilised to regulate the firing of postsynaptic neurons [93–95]. Although proteinoids have been observed to display spiking electrical activity [57], their ability to engage in synaptic–like signalling requires further explanation. As a preliminary framework, computer modelling has been employed to simulate hypothesised presynaptic (PSI) and postsynaptic (PPI) proteinoids [75].

This research [75] investigates the potential formation of transitory connections via the diffusion of molecules generated by the presynaptic interneuron (PSI), which subsequently modulate the excitability of postsynaptic interneurons (PPIs). The simulations investigate the impact of spike timing on neuronal activity and explore potential applications in logical operations. Nevertheless, there is a requirement for empirical information regarding the production and distribution of proteinoids, as well as their ability to mimic neurotransmitters and the potential interactions that may occur between them.

The present modelling approach offers an abstract representation of putative inter–proteinoid communication, which should be noted as speculative rather than verified pathways. Further biochemical investigation and dynamic measurements are required in order to ascertain whether proteinoids are capable of exhibiting synaptic activities. The validity of comparing neurons to proteinoids is currently hypothetical unless empirical evidence is provided to support the existence of directed and responsive signalling amongst proteinoids.

Nonetheless, developing a theoretical architecture is a good place to start when trying to understand inter–proteinoid interactions. The supposed synaptic–like connectivity could help researchers better understand the intricate subcellular processes that underlie transmission. Coordination of proteinoids networks could allow for distributed sensing, logic, and actuation [96].

Further research into the emergent functions of proteinoids promises to shed light on both realistic steps in proto–life evolution and the fabrication of complex biomaterials [97]. At this point, it is important to avoid associating primitive protein dynamics with integrated brain networks. A specific investigation of proteinoids as communication elements remains an unresolved challenge.

Fig. 6 illustrates a theoretical transmission mechanism among proteinoids by simulating the firing of a presynaptic proteinoid in response to external stimuli. It appears that the temporal pattern of the pulses propagates to a postsynaptic proteinoid that is associated with them. As it processes the spike signal, the postsynaptic response is conceptually represented by dynamic variations in initial weight and synaptic indices over time. This establishes a theoretical foundation for examining the possibility that proteinoids could exchange information through chemical diffusion and pulse timing [99], in a manner similar to synaptic transmission. Nevertheless, experimental confirmation through directed signalling and response between proteinoid networks remains necessary. The modelling establishes a foundation for subsequent research that investigates the ability of proteinoids to function as interconnected information processing units [100].

10. Harnessing proteinoids for unconventional neural engineering: capacities and next steps

The functional resemblances between proteinoids and biological systems extend far beyond mere physical resemblance. Proteinoid microspheres, self–organized aggregates of protein–like polymers, have surprising neuronal parallels in biophysical properties [101]. Proteinoid architectures exhibit a membrane potential generating electrical spikes when stimulated, emulating nerve cell action potentials [102]. These synthesised spheres further form interconnections capable of transmitting signals along chains in a neuron–like manner. Most impressively, proteinoids display learning behaviors [103], adapting electrical outputs to varied inputs rather than following fixed templates. Such dynamic microspheres may remodel conductive properties over time through intrinsic plasticity mechanisms [104]. Additionally, nonlinear bioelectric elements enable logical computations–from voltage pulses, proteinoids can recreate basic Boolean logic gates like AND, OR, XOR and NAND [69]. Though far simpler than cortical structures, this prototype wetware platform powered by an adaptable microgel lattice already replicates fundamentals of signaling, information processing, and adaptive responses seen in biological nervous systems. Moving forward, harnessing the platform towards spontaneously self–assembled biological neural nets and unpacking abiotic analogues of complex neuro–evolutionary processes remain active research frontiers [105].

In 1994, Leonard Adleman introduced a groundbreaking idea that involved the manipulation of genetic code fragments through splicing and recombination [106]. Proteinoid systems function similarly to other unconventional computational methods that make use of programmable

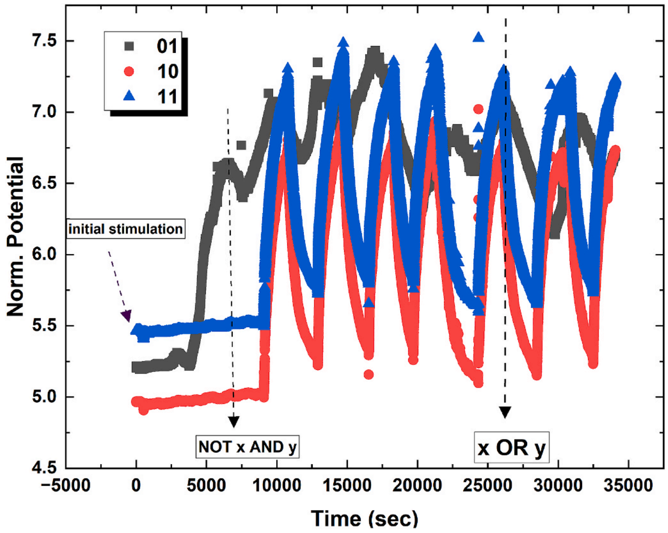

Fig. 4. The incorporation of logical operations utilising proteinoid spikes. The presented graphic demonstrates how to use of timed spikes for encoding Boolean logic operations within proteinoids. The input pulse patterns (01, 10, 11) are correspondingly associated with output spike trains, which serve as representations of AND, OR, and NOT gates. The logic output is represented by the presence or absence of spikes within certain time intervals following stimulation. The ability to manipulate the dynamics of proteinoids in order to carry out computations is exemplified by the presence of fluctuating latency and varying number of spikes per output function [74].

biological substrates. Early concepts about DNA computing envisioned the use of combinatorial mixing and matching of base–pair sequence codes to enable massively parallel decision–tree search algorithms within nucleic acids. By utilising randomly mixed ribonucleic components, such as heat proteins, genetic mechanisms optimise biocomputation. Diverse peptide microstructures self–assemble via the polymerization of early threading monomers, demonstrating natural diversity in signalling across dynamic molecular networks produced from bottom-up variances rather than top–down instructions. The electrical responses of proteinoid membranes and junctions, like DNA hybridization processes, can reveal minor changes in the surrounding environment. As a result, real–time monitoring of early proteinoid soup allows for the observation of information orchestration at the origin stage, during which unsupervised structures permanently encode high-–dimensional data.

11. Conclusions

Proteinoids possess remarkable biomimetic properties, serving as synthetic analogues of proteins and early cells. The thermal proteins, initially synthesised by Sidney Fox, have the ability to self–assemble into microspheres that display lifelike behaviour. Proteinoids' inherent ability to generate electrical activity and transmit signals has been discovered in recent breakthroughs, allowing for the development of simulated neural networks. The experiments exhibit spiking dynamics, synaptic–like functions, pattern recognition, and network adaptivity that resemble the natural computation of neural systems. Nevertheless, there are still numerous unresolved inquiries concerning the molecular basis of the cognitive–like phenomena exhibited by proteinoids. This study lays the groundwork for developing flexible, bio–inspired electronics that utilise artificial biomaterials to achieve realistic autonomy. Proteinoids, while not as advanced as biological systems, provide insight into the initial development of collective dynamics and rudimentary intelligence through the self–organization of early non–living polymers. Understanding the underlying physical mechanisms behind the dynamic behaviours exhibited by proteinoids remains a fascinating scientific endeavour that holds significant potential for advancements in both artificial and natural cognition.

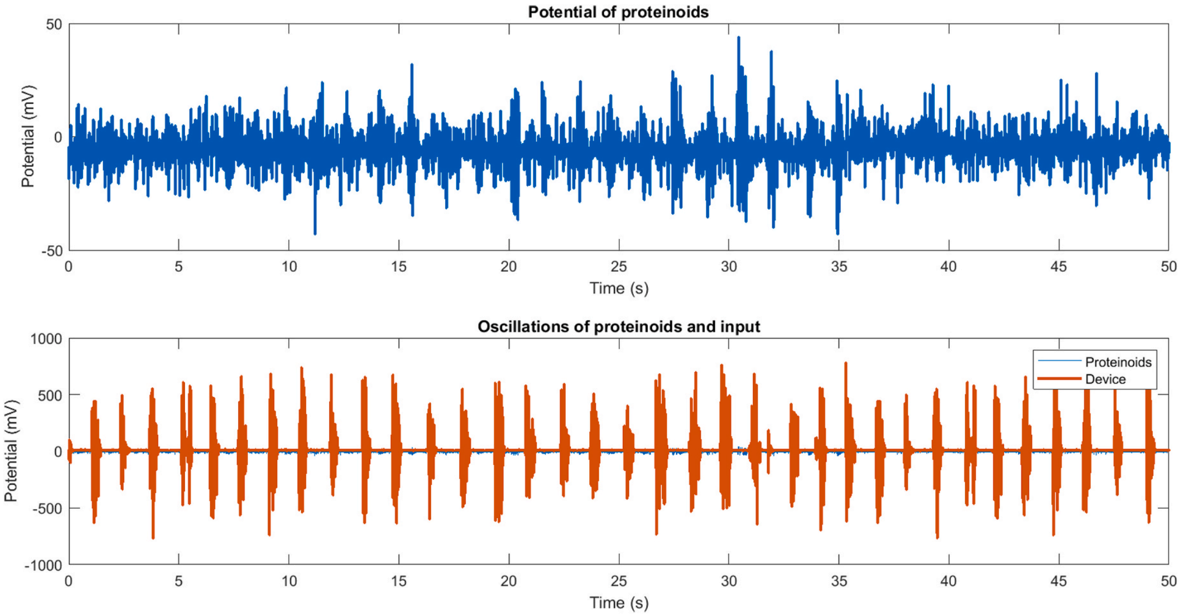

Fig. 5. The proteinoids exhibit detectable reactions in response to auditory stimuli in the form of spoken letters. The upper panel displays illustrative voltage time series pertaining to proteinoids that have been subjected to auditory stimuli in the form of diverse letter audio recordings. The lower panel exhibits the correlation between the input waveforms and the proteinoids' responses for each letter. The audio waves possess discernible waveforms, which are then converted by the proteinoids into distinctive electrical patterns. The observed temporal and morphological patterns of the response peaks provide evidence for the capacity of proteinoids to acquire the ability to discern and react specifically to intricate stimuli. This study establishes a fundamental basis for the application of proteinoid networks in the field of engineering speech recognition [90].

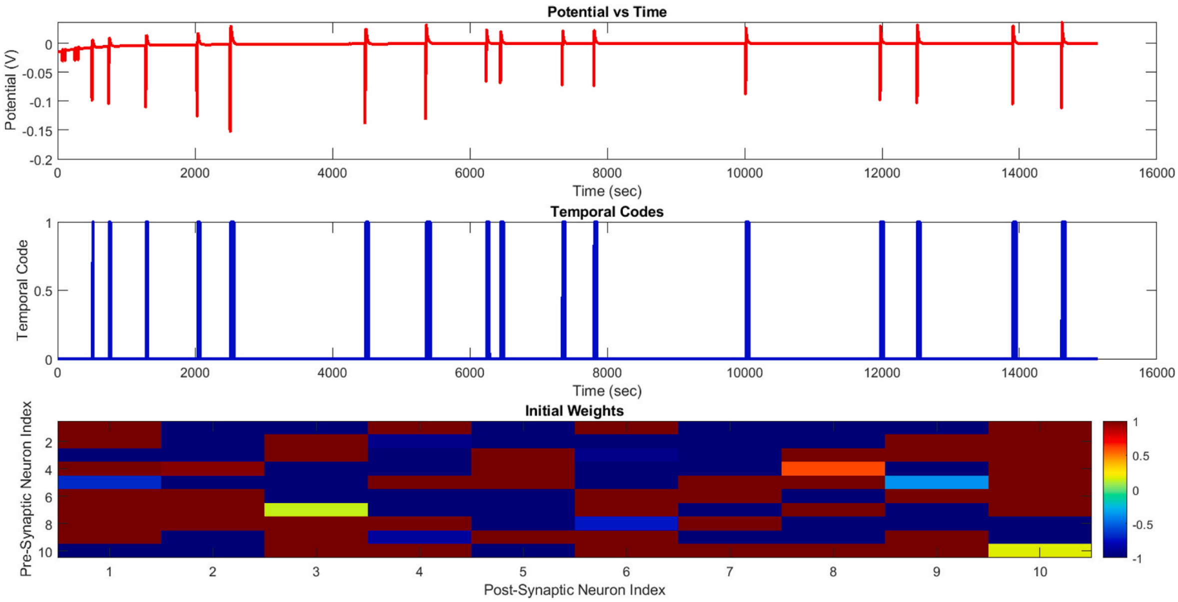

Fig. 6. Signalling between model proteinoids was simulated. Plots illustrate the potential response of a fictitious presynaptic proteinoid (PSI) to electrical stimulation. Communication with an associated postsynaptic proteinoid (PPI) is facilitated by the temporal arrangement of pulses. Alterations in the initial weight and presynaptic and postsynaptic indices over time symbolise the dynamic response of the simulated PPI during spike processing. This establishes a preliminary computational framework for examining the possibility that proteinoids could exchange information through spike timing, in a manner similar to synaptic transmission between neurons. Additional biochemical analysis is required to substantiate the directed signalling capability of proteinoids [98].

CRediT authorship contribution statement

Panagiotis Mougkogiannis: Conceptualization, Data curation, Methodology, Software, Writing – original draft. **Andrew Adamatzky:** Conceptualization, Funding acquisition, Methodology, Supervision, Validation, Writing – review & editing.

Declaration of competing interest

We, the authors Panagiotis Mougkogiannis and Andy Adamatzky, declare that we don't have conflicts of interest associated with the article. We confirm that the content of the article is the result of our research and that we have received support from the EPSRC Grant EP/W010887/1 "Computing with proteinoids".

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