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Review Article

Closed-Loop Neuronal-Computational Systems: Potentials and Problems

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Abstract

Microelectrode arrays can organize cultivated neurons on various scales for closed feedback loops to measurably enhance their computational capacity. A significant step toward advancing computational interfacing of neural networks employs the use of organoid-computing integration (OCI). The use of OCIs can expand capabilities for bio-electronic assimilation via "encoding" cultured neurons (and neuronal systems of multi-scalar organoids) by developing interconnected computerized signaling on surfaces of multielectrode array contacts. It may be that OCIs could afford a valid simulacrum for the functional computational capabilities of neural networks of a living brain, and in so doing may enable insights to both the "hard question" of neuroscience (viz. how conscious and cognitive processes arise in/from a material (biological) system, and if, how and to what extent OCIs impart sentient characteristics to hybrid and/or synthetic systems (*in silico*). The potential emergence of high-functioning organic-computational intelligence gives rise to a number of neuroethico-legal and social issues, which require address in ways that are herein proposed.

Keywords: *Neuro-Computational Interface (NCI); Brain Organoids; Organoid-Computing Integration (OCI); Ethical Considerations; Neurorights; Neuroethics*

Introduction

Current advances in biocomputing promise extraordinary capabilities and efficiencies. Computational interfacings with living brains, (i.e. brain-computer interfaces, BCIs; or neural-computational interfaces, NCIs) have gained recent attention in light of commercial developments, such as those of Neuralink. However, despite iterative developments in the field, recording and "decoding" brain activity remains challenging. Conversely, neuromorphic computing (viz. the engagement of neural-like systems architectures and functions to enable rapid hierarchical processing of multimodal information) has made significant progress, primarily via the engagement of machine learning and artificial intelligence (AI) models and programs. Yet, AI encoding and actual utility is no less challenging. To overcome such challenges, it has been proposed that neuronal-computational systems, colloquially referred to as "brain-on-a-chip" approaches, may be viable and of increasing value [1,2].

One neuronal-computational model employs the conjoinment of silicon-based computational architectures and cerebral organoids. Still, recording and utilizing internal neural activity of larger-scale organoids remains nascent. A significant step toward advancing computational interfacing of cerebral organoids may involve the use of organoid-computing integration (OCI), which affords capabilities for bio-electronic assimilation via “encoding” of cultured neurons (and neuronal systems of multi-scalar organoids) by developing interconnected computerized signaling on surfaces of multielectrode array contacts. Encoding and decoding are simultaneously unified, and further networking (utilizing “downstream” robotics or prosthetics, for example) may interface directly with processed neuronal-computational information [3].

The computational power of entrained organoid neurons, functioning within closed feedback loops may be accelerated from unsupervised general learning to more task-oriented foci. Ideally, the metrics of and for such learning processes should be based upon organoid behavior(s), since, we posit, reproducible signaling feedback serves to manage and manipulate the system’s overall activity over time. It also appears plausible to us that the establishment of collaborative NCIs of this sort, which employ a common reinforcement language, could allow multiple closed-loop NCIs to perform complex tasks through connection to a central “synthesizer” system/device. In this light, we are particularly interested in the viability of 2-D OCI for parallelized unsupervised development and some level of instantiated “intelligence”, which may display efficient capabilities not yet evidenced from 3-D brain organoids or AI alone.

Neuro-computational power and possibilities

The pioneering work of DeMarse some twenty years ago was notable for demonstrating the potential of closed-loop OCI “wet devices”, with emergent properties capable of exercising extrinsic control of computationally linked vectors [4]. Subsequent projects have involved the use of cultured neurons in NCIs. Cultured neurons are arranged upon micro-electrode arrays (MEAs) that contain multiple loci for biological and neural signals to be obtained and organized, thereby facilitating direct neuronal-computational connectivity. MEAs also can serve as workable substrates for facilitating 2-D closed-loop neural-computational systems, inclusive of OCIs. The implications of closed-loop OCIs extend many of those of traditional AI. As Rouleau notes: “Applied to cultured neural networks, embodiment begins with the measurement of activity from both individual and groups of cells” [5].

Despite increasing research and development of closed-loop OCI technology, there has been little investigation to date toward quantifying the computational power of different scalar arrays of neuronal platforms. DeMarse’s evaluation of the potential of neural-computational technology was limited to systems containing a relatively small number (i.e. around 25,000) neurons, which is significantly less than the neuronal population - and resultant dynamics - of a larger 3-D brain organoid [6]. By expanding the scale of cultured neurons that are incorporated into these systems, it becomes ever more possible to quantify the computational power of individual, as well as various network dimensions of neurons in an organized and controlled environment. As Rouleau has acknowledged, “Applied to investigations of embodied cognition, 3D NCIs are likely to provide increased physiological relevance and additional dimensions of complexity, control, tunability, and programmability” [5].

Pro Rouleau, we posit that such advances will soon make it feasible to quantifiably identify the point at which a defined number of neurons can function in ways that are similar to a 3D brain organoid. Thus it will be possible to gain insights to the actual computational capabilities of individual and networks of neurons, organoids, and by extension, neuronal/neural systems in particular organisms (inclusive of neuro-analogous and/or hybrid or chimeric neuro-integrative networked systems *in silico*) [7,8]. Other models under development, such as cell culture plates, bioreactors, extracellular matrix (ECM) scaffolding, 3D bioprinting, and microfluidic electrospray techniques, tend to employ some iteration of an “organoid-on-a-chip” [9]. Such “organoid-on-a-chip” designs permit reliable measurements of the computational power of controlled quantities of cultured neurons, and thereby make it possible to utilize vectors to assess spike train patterns to quantify the computational power of singular neurons. These techniques have prompted the question of whether, and to what extent, complex neuro-computational ensembles could be created. Additionally, we propose that multiple independent closed-loop NCIs sharing a common language (e.g. via use of positive and negative reinforcement) could be connected via a CPU, and thus enable cooperative engagement in performing complex proto-cognitive tasks. Combining multiple interfaces would allow for parallel processing to decrease time and increase responsivity within the closed-loop system, and could allow neurons to respond to simultaneous stimuli.

Demonstrated learning through a multi-NCI system would allow quantification of key, involved (or substrate) neuronal processes that are learning on a variety of scales. This would also allow for learning capabilities to be enhanced through applications of mathematically-based, physics' dynamics [10]. For example, an increased number of vectors in the inter-neuronal space, and the relative alignment of activity frequency patterns would allow for more rapid and fortified informational transmission within the system, and, by extension, to those external elements to which it is coupled (e.g. for interpretation, communication, and feed-forward task execution).

Reduced computational processing time would be instrumental to significant improvement of neuro-computer integrations, which could be employed for ""reciprocal investigation(s)" of the (1) computational power of neurons (and neural units in networked arrays of differing configurations and scales), and (2) computational capabilities to generate neural-like (i.e. neuro-analogous) properties, which, when taken together could provide insights to both the "hard questions" of brain science, and de-limiting computational power [11,12].

Opportunities, potential and problems

The opportunities offered by 2-D and 3-D NCI systems also increase technological issues inherent to their use. The emergent properties demonstrated in DeMarse's work and subsequent exploratory projects present significant implications for creating more adaptable and near-autonomous neural-computational AI. Integrating biocomputing systems with AI may result in dramatic improvements in information processing, not for further "general intelligence," but for greater domain-specific complexity and capability than deep-learning computational technology alone, and the potential for OCI-coupled AI to develop "Organoid Intelligence" represents a clear and current consideration [13-15].

The potentials for advanced NCIs do appear impressive, but it is important to consider that the cultivated neurons in OCIs may not develop many of the advanced functions attributable to full 3-D organoids and/or living brains [16,17]. Although it is theoretically possible - and perhaps intentionally ideal - that the neurons of an OCI would obtain such properties, the lack of evidence to date poses an interesting conundrum. Namely, if and to what extent organoids (and OCIs) would actually afford a valid simulacrum for the functional computational capabilities of neural networks of a living brain and in that way, perhaps allow a viable address of the "hard question" of how conscious and cognitive processes arise in/from a material system, whether biological, or *in silico*.

For argument's' sake, let us assume that such properties would be obtained. Herein lies the possibility that humans might become iteratively less involved with, and aware of, the attainment of certain developmental milestones of such "closed looped "systems, and thus might be excluded from the "closed room" of independent bio-AI hybrid intelligence. Such technology may become increasingly autonomous, perhaps by design (so as to investigate "how" these neuronal arrays develop the structural basis for particular functional capacities). Therein, human input might be considered a liability, rather than an advantage. But what of the liability of so-called runaway effects (i.e. if/when the properties of a system progress to a point at which problematic issues arise, and may be extreme)? And what if these types of OCIs actually do enable insight to, if not elucidation of the efficient causal basis of consciousness? Are societies prepared for the implications, and possible manifestations of such discovery relative to the regard and treatment of conscious non-human "others" - including perhaps organoids, OCIs, and/or certain forms of AI? [7,8,18,19].

Might "runaway OCIs", or even OCIs per se therefore represent some sort of Golem (viz. a mythical entity that arises from human labor, only to threaten its creator in some way)? We opine that research in these directions would be best served by heeding philosopher

Hannah Arendt's warnings about the nature of human enterprise: not to simply slave away blindly in what she referred to as "*animal laborens*" but rather to endeavor with prudence and foresight at each and every step of effort (i.e. in accordance with Arendt's construct of *Homo faber*) [20].

Ethical, legal, and social issues

The aforementioned questions, issues and problems bring into stark relief those ways that emerging science and technology affect, and are affected by social attitudes, values, and norms. For instance, at what point might organoids, OCIs (and perhaps even neurons, and/or an AI entity) begin to obtain "subjective experience", or perhaps some construct of an identifiable "self"? A significant concern in this discourse centers upon the potential for such systems becoming ever more advanced and thereby capable of the emergence of valency [21]. An "inner" transition from 'negative' feedback into induced 'negativity' introduces a moral dimension, and questions of moral obligation as based upon responsibilities borne of painience [22,23].

Here, we urge caution against anthropomorphic traps. What humanity creates, needn't be "just like us" to engender moral responsibility. As neurally-based computation evolves (both directly via human engagement, and indirectly as subsequent consequences of initial human fabrications) there may be iteratively greater moral obligation(s) to at least regard, if not attend to its welfare, if not perhaps rights [24,25]. Are we "there" yet? Likely not; however, pro Kagan., *et al.* [26], we argue that it is not too hasty to propose specific guidelines toward evaluation of both the level of cognition at which developments in neural computation operate and the extent to which the rights of this technology must be afforded.

A precautionary approach would seek to afford protections to any neural-computational technology that demonstrates high-level cognitive functions and behaviors [27]. One way in which this could be implemented for high-functioning organic-computational intelligence is by continuously assessing if it operates at a level approaching that of a recognized sentient being. But given the expanding view of non-human organisms' sentience, which being? Here too, a working caveat would extend any considerations and protections of the OCI-system to its referential comparator. Thus, if we move from "model-object" to referential subject (i.e. from considerations about OCI-consciousness, to issues of consciousness in entire organisms) then we must ponder whether human society (within and beyond confines of certain religions' practices) can be prepared to afford such protections to (1) humans whose consciousness may not be apparent; and/or (2) non-human organisms [7,28].

Summary

The field and practices of neuroethics are situated to address such issues [29]. Indeed, neuroethics has been regarded as "an ethics of neurotechnology" [28], and in this light, is surely tasked with monitoring and assessing advances made in neuroscience and neurotechnology (neuroS/T) for the merits of their impacts on human beings at every level from the synaptic to the social [30]. This descriptive aspect of neuroethics is foundational for forming judgments about the meaning, value, and morality of neuroS/T research and application. The arrival of debates over the need for neurorights signals yet again the need for robust discourse about the rightful goals of neurotechnologies [31]. Neural computation, while presenting unusual challenges about ontologically classifying its nature(s), cannot be permitted to foster exceptions to important norms and rules respecting sentience and protecting personhood. Two of this article's authors (Shook and Giordano) situate neuroethics at the nexus of core ethical principles capable of bearing the burden of setting reasonable and seasonable expectations for novel neurotechnologies [32]. While approaches to the dilemma of protecting the rights of advanced organic technology are unprecedented and arguably complex, there remains a general expectation that ethical guidelines must be established and adhered to with transparency in order to ensure that both advanced neuro-computational technology, and any sentient organisms are responsibly and ethically regarded and treated.

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Conflict of Interest Statement

No financial interest or conflict of interest exists for any of the authors.

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