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Letter

A response to claims of emergent intelligence and sentience in a dish

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The article "*In vitro* neurons learn and exhibit sentience when embodied in a simulated game-world" by Kagan et al.[1] triggered a wave of positive mainstream and scientific media coverage as well as a widespread negative reaction from the scientific community. Here, we discuss why this negative reaction is legitimate and must be taken seriously. We raise concerns about the key claim of the article: that it demonstrates that "a single layer of *in vitro* cortical neurons can self-organize activity to display intelligent and sentient behavior when embodied in a simulated game-world."

Our concerns go beyond the appropriateness of the methodology, quantification, and controls used in the study and the lack of details with which they were presented. These concerns include the unsupported use of terms and concepts that misrepresent the findings of this study, the lack of acknowledgment of previous literature, and the ensuing overselling of translational and societal relevance.

The first concern regards the unsupported use of terms and concepts to describe properties of biological and/or artificial neural networks, such as "sentience," "goal-directed behavior," "embodiment," tackling "uncertainty," and "intelligence." Assessing whether animals, and their neural networks, display these properties is indeed an important topic in neurobiology and computer science, as well as in philosophy, psychology, and ethology. This effort has led to a progressive refinement of these concepts, and the development of benchmarking for such cognitive capacities has recently become a crucial aim of machine learning and artificial intelligence research. Considering this large-scale effort, we believe Kagan et al. made strong claims for the application of these terms to neural networks with relatively weak evidence.

By associating elements of cognition with the properties of cultured neurons, Kagan et al. inevitably created a media buzz. This paper also attracted a lot of attention in the scientific community in part because of concerns about "concept hijacking" or at least their misleading usage. Although there are indeed legitimate discussions in the field about how to benchmark and test the abilities of agents and networks to display cognitive or goal-directed behaviors (and about how to precisely define such behaviors), the current report does not evaluate the outcome of their experimental observations on those

grounds and, in addition, makes claims well beyond the acquired data and effect sizes.

For example, attributing intelligence to a network that displays short-term plasticity is not supported by relevant scientific fields such as machine learning, neurobiology, and psychology. Similar arguments apply to the yet more provocative use of the term sentience. This application to neurons *in vitro* is in our view even more inappropriate and is not justified by the data presented in the paper. The term sentience is notoriously hard to define but refers to a process that encompasses feeling, sensing, and subjective evaluation.[2] The application of intelligence and sentience to neurons-in-a-dish in this paper is not based on any established or robust consensus on the definitions of these very important terms.[3] Instead, it is based on the authors' own recent theoretical propositions,[4] which are general enough to allow the term to be applied to nearly any interactive computational system of even modest complexity.

Beyond provoking a controversy, it is unclear how the use of terms such as sentience and intelligence adds to the understanding of neural network properties in this paper. Because it is currently challenging for mechanistic or reductionist neurobiological studies to link these concepts to biological phenomena, we suggest that the terms ought to be used with more caution. Moreover, the concept of sentience has a key role in the philosophical and sociological issues surrounding animal welfare and for that reason should not be used loosely or in unconventional manners in the context of this or any other scientific study.

To be clear, we are not arguing that research in isolated neural networks is problematic. Unquestionably, these approaches can provide crucial knowledge of neural network dynamics, plasticity, and computational and organizational principles and processing capacities. In fact, beyond the unnecessary or unfounded use of terminology, further concerning are limitations of results and failures of scholarship. Strong conclusions are compromised by weak results, some of which fail to adequately match control and experimental conditions. Also, Kagan et al. do not acknowledge previous use of biological neural networks embedded in closed-loop systems that has helped, for example, to assess the potential application of plasticity to drive external artifacts, e.g., robots.[5,6]

We conclude our opinion with a discussion of why this paper and the media coverage of it illustrate the importance of scientific communication to the general population. Media tend to directly republish information included in abstracts and significance statements, and interviews of scientists by media tend to amplify these statements. Overselling scientific results directly impacts the evaluation of scientific reliability and credibility.[7] In the present specific case, claiming that a cell culture embedded in a closed-loop system demonstrates sentience and intelligence might impact the public perception of what in nature is sentient and intelligent and could trigger ethical debates fueled by misunderstanding. It puts an unnecessary risk on the whole community of systems neuroscience that tries to understand higher brain functions and dysfunctions by fueling an argument, albeit invalid, to extreme animal rights movements that lobby daily to stop animal research, while also creating potential future financial benefits for the possible usage of the methods in this paper.

Studies related to nervous systems and their computational abilities represent a huge area of research for the advancement of our knowledge of what we are and what we are capable of and accordingly pose several scientific, ethical, and societal challenges. Therefore, the questions and challenges we raise regarding definitions of intelligent behavior and sentience in neuroscience in general, and in the work by Kagan et al. specifically, are of fundamental importance to fulfill the high expectations that neuroscience has created for understanding brain functions, curing brain diseases, and conducting responsible research in developing machines capable of performing complex behavior.

DECLARATION OF INTERESTS

The writers and key corresponding authors of this document, I.E.M. and E.P., do not have any patents or interests related to our work to declare. The rest of the authors are "signers" and gave comments to improve the manuscript, therefore they were not polled on this issue.

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Letter

Scientific communication and the semantics of sentience

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The use of language to describe specific phenomena has always been, and will likely remain, a contentious aspect of scientific discourse. Effective scientific communication must be considered in the context of the field in which the given signifiers are used. While the response by Balci et al. may be described as polemic and contains reasoning subject to equivocation and other fallacies, we do appreciate the core concerns. Here, we address these concerns and suggest some constructive pathways that might help improve scientific communication in the future.

Firstly, the assumption that we acted to internationally "oversell" and create "media buzz" or "controversy" should be addressed. Contrary to this furtive fallacy, our intention in using "sentience" and related terminology was to be deflationary and principled—in line with the recent literature in theoretical biology in general and in the free energy principle (FEP) in particular. The FEP is a first principles account of biotic self-organization, namely, active inference or sentient behavior.[1] In this setting, many terms acquire a straightforward and technical meaning; for example, "surprise" refers to self-information, "uncertainty" to information entropy, and Bayesian "beliefs" to posterior probability distributions[1]—in the sense of Bayesian belief updating and propagation. This reflects a recent trend in treatments of self-organization that tries to find the common ground in physics, biology, and psychology, e.g., basal cognition.[2] The intent is to concretize concepts in testable and falsifiable ways[3]—and in a way that underwrites current collaborations testing theories of consciousness, e.g., https://www.templetonworldcharity.org/projects-database/0646.

The core results that were presented[4] have been publicly available via a preprint on bioRxiv since 2021, allowing widespread, careful consideration, collegiate communication, and outreach to the wider scientific community. The overwhelmingly helpful and supportive comments received led to significant refinement, including a clear definition—in the peer-reviewed version—of "sentience." This definition reflects current philosophical accounts of sentience in predictive processing (e.g., https://www.penguinrandomhouse.com/books/608016/the-experience-machine-by-andy-clark/). Furthermore, the suggestion by Balci et al. that our use of terms is "unsupported" is inaccurate. Journal requirements for these letters (limited to seven references) precludes a detailed inclusion of the supporting literature. Yet, as an example, recent rigorous endeavors to study the biological basis of sentience have found our formal definitions useful.[3] More generally, at least 71 distinct definitions of "intelligence" have been previously identified, and our usage accords with many of these definitions.[5] However, leaving aside the above-mentioned concerns, we now focus on common ground and constructive pathways forward.

Foremost, we agree with the concluding sentiment by Balci et al. that the questions and challenges around definitions of intelligent behavior and sentience are important. The widespread positive (sentiment analysis shows only <9% to be negative, which includes outlandish concerns such as the creation of "zombies") response to our work highlights the importance of establishing a shared nomenclature to communicate results clearly. In the short term, we propose that future work should include (and we would encourage journals to allow) glossaries. Glossaries provide clarity for the reader, in terms of understanding what a particular term is meant to convey. This approach has been adopted in an upcoming work on which some of our authors collaborated.[6] In the longer term, it would be beneficial to establish a generally accepted nomenclature for standard definitions. We have made open invitations to the scientific community for collaboration and take this opportunity to again welcome collaborative interest. Especially as, poignantly, the current exchange highlights the importance of good-faith discussions in formulating nomenclature standards.

Secondly, we agree with Balci et al. that accurate scientific communication is important. For our work, we took care not to oversell the research and minimize hype often seen in related fields. We made no claims about treatments or cures

for disease. We circulated the media release to experienced science reporters via EurekAlert and carefully briefed experienced science reporters to promote responsible reporting. A primary motive for creating *DishBrain* is to study how genetic alterations and pharmacological agents influence the real-time behavior of neurons—to elucidate underlying mechanisms of interest. Any discussions of more complex applications were carefully positioned as future work, requiring further research and development. Likewise, we do acknowledge that citations identified by Balci et al. were not present in our introduction. As with most research articles, due to space constraints our review of the literature was not intended to be exhaustive and required highlighting only a subset of previous work in this field. However, we do acknowledge the need for future work to focus on consolidating the cross-disciplinary work in this field.

Finally, we also agree with Balci et al. around the importance of making sure that ethical debates are not fueled by misunderstandings. To that extent, we have engaged with independent ethicists, discussing terms such as ''sentience'' in this context[7] and aiming to further explore these issues more in the future. While it is reasonable to note that improvements to this technology could, for some applications, offer an alternative to behavioral research using animals, at no point do we imply animal research can be completely replaced. Yet this does not mean the possibility of advancements should be discounted or that discussions about future applications of scientific work are inherently ''overselling.'' New technologies, such as synthetic biological intelligence, have the potential to offer significant gains to both society and science if we can work collaboratively to realize the potential benefits. Explaining this potential is an important part of scientific communication to frame where future work may lead. Ultimately, as much as signifiers in scientific communication must be understood in context, the scientific outcomes must also be considered in their own context—in this case, as *in vitro* work. Fundamental exhibitions of any phenomena in a dish may be hard to define, especially without consistent definitions within and across fields, as we see here. Multidisciplinary work seeking to advance research is seldom likely to be perfect initially due to difficulties integrating across fields. Nomenclature may differ, and approaches diverge. Yet, if these differences are recognized not only as an opportunity to criticize but to improve and innovate, our scientific community and scientific progress can hopefully continue to benefit.

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Letter

Conceptual conundrums for neuroscience

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In their recently published work, Kagan and colleagues argue that cultures of human and mouse neurons can exhibit goal-directed activity adaptations and are thus "sentient." In their commentary to this piece, Balci and colleagues[1] offer a critical review of the work. In addition to discussing the value of the research and the soundness of the methodology, they question the appropriateness of using language such as "sentience" in the context of the study. Research in isolated neural networks provides crucial knowledge, Balci and colleagues note, but the terms that Kagan et al. use to interpret the findings risk confusion, particularly as they enter the public domain. Kagan et al., in their response,[2] push back, emphasizing that the notion of "sentience" in the original paper was clearly and scientifically circumscribed. Furthermore, they claim that the "scientific community's" response to the research and its claims has been largely positive.

Calls for clear language and concepts in scientific practice and communication are not new within the field of neuroethics. We and others have argued that conceptual clarity leads to improving science, to enhancing its understanding, and to a more nuanced and productive discussion of the ethical issues it raises.[3,4] But, in this case, the call for conceptual clarity comes directly from those doing the science itself, giving further support to the idea that this is not a mere terminological issue to be debated amongst philosophers, but one that might impact scientific practice, the interpretation of its products, and their societal acceptability. It also points to the responsibilities that scientists and publishers might have when disseminating neuroscience discoveries.

Indeed, although Kagan et al. and Balci et al. challenge each other, both agree on the importance of conceptual clarity: Kagan et al. by referencing Friston's article, which circumscribes how "sentience" is to be understood in the context of the study, and Balci et al. by insisting that the choice of language plays a key role in how diverse publics conceptualize the research and emerging technologies. Therefore, Balci et al. state that terms such as "intelligence" and "sentience" should not be used "loosely" or in an "unconventional" manner, given the possibility for a plurality of possible negative interpretations by a wider public. In short, clearly, neither party thinks that conceptual clarity is unimportant or that terms can be arbitrarily used. Still, they disagree, and their disagreement suggests conflicting underlying views regarding two points. The first is whether science's impact can be fully captured by the rigor of scientific methodological considerations. The second is about *who* the relevant reader and media audience are.

To address the first conflict: indeed, in general, science has enjoyed a kind of moral authority in society because of a dedicated systematic methodology that is intended to create generalizable knowledge and strives to be free of social, cultural, and ethical considerations.[5] This promotes the use of circumscribed definitions that are clear to peers and thus useful within the scientific community, a point emphasized in Kagan et al.'s justification of the use of "sentience." An enduring frame of science is that by reflecting epistemic values demonstrated by the scientific method—i.e., by adhering to the scientific process—one is able to obtain knowledge that is truthful, consistent, and accurate, for example. Further, in so doing, the process should avoid the non-epistemic values (ethical, social, cultural) that usually creep into it and can lead to unintended biases.

Yet, the repercussions of believing that the scientific methodology might somehow cleanly translate into deeply ingrained cultural assumptions about certain terms are nontrivial: such assumptions miss the social and ethical impact that the choice of some "scientific" terms might have. Neuroscience is particularly inherently fraught with ideas and attitudes that are culturally and historically ingrained.[6] Ultimately, this is Balci et al.'s concern: it is unlikely that non-expert publics would circumscribe the term "sentience" to mean merely "responsive to sensory perceptions" as intended by Kagan et al. Even further, when the terms in question have anthropomorphic connotations, they might lead to fears and unjustified worries in specific audiences.

Kagan et al. and Balci et al. agree on the importance of communication. However, the divergence seems to rest on for whom that communication matters and to whom it should be directed. This is a topic of contention for many scientists. To that extent, communication methods, and the ecosystem of science communication, cannot be fully separated from the scientific enterprise. This point brings us to the second issue suggested by the Kagan et al. and Balci et al. disagreement. Balci et al. point to concerns arising from hyped descriptions of the research in popular media reporting of the findings that might lead to fear and mistrust in science. Kagan et al. rebut that the reactions of their scientific peers were largely positive. Scientists, like many users, take for granted the idea that social media and online social networking platforms might be a viable place for knowledge dissemination and scientific assessment without fully appreciating the divisive echo chamber successful platforms often depend upon.[7]

Insofar as science is considered a public good, it must leave the lab and the

academic journal pages and, once it does, it is naturally and unavoidably subject to public interpretation and dissemination. The science of the laboratory will continue to intersect with other mainstream products of popular consumption, like social media, and scientists remain largely untrained to navigate these evolving spaces for public communication and public engagement with science. To help fill this gap, the field of public engagement with science has been systematically focusing on methodologies to facilitate multi-directional and inclusive dialog and exchange that are richer than those enabled by platforms like social media and popular media pieces.

Indeed, the suggested divergence in Kagan et al.'s and Balci et al.'s opinions on who the relevant audience is for science invites us to consider whether diverse publics *should* have a role in the development of responsible science and applications.

The recognition that needs and values of diverse publics can inform the scientific agenda has led to several high-level calls for public engagement, such as from the Organisation for Economic Co-operation and Development, the UNESCO International Bioethics Committee, and the US National Academies of Sciences and Medicine, and for the creation of intentional spaces for social and ethical reflection about science and innovation. However, some scientists are still either reluctant—often because of disinterest or lack of incentivization—to acknowledge the importance of public engagement and the value of including the views of different publics in the scientific agenda or have a limited understanding of what meaningful engagement means and entails.[8,9] In practice, public engagement is often misunderstood as the transfer of information from scientists to the general public. Instead, robust public engagement as a rich and dialogical interaction adapted to different publics is intended to promote the type of conceptual clarity that Kagan, Balci, and colleagues appear to seek. Public engagement, along with multidisciplinary conversation, would be key for developing glossaries, as Kagan et al. suggest in their response letter, as well as creating generally accepted nomenclatures, as both parties recommend.

Offering conceptual clarity can be a difficult task when scientists are increasingly called to keep up with the broader ecosystem of science communication such as social media and trends to incorporate persuasive writing in federally funded grants.[10] We applaud Balci and Kagan's shared enthusiasm for clarifying the language. We hope Kagan et al.'s invitation to further discussion and collaboration on clear nomenclature also acknowledges the importance of addressing core underlying divergent assumptions of whether scientific impact can be fully captured by scientific methodologies and who the relevant reader and audience of science are. We offer that the inclusion of diverse stakeholder voices and collaborative input that extends beyond the lab would better support the connections between science and society's challenges and opportunities and maximize the potential of science to do good.

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DECLARATION OF INTERESTS

K.S.R. is a member of the California Stem Cell Agency Standards Working Group and is a member of *Neuron*'s advisory board.

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