Check for updates

OPEN ACCESS

APPROVED BY Frontiers in Science Editorial Office, Frontiers Media SA, Switzerland

*CORRESPONDENCE Thomas Hartung THartung@jhu.edu

RECEIVED 12 October 2022 ACCEPTED 23 November 2022 PUBLISHED 28 February 2023

CITATION

Hartung T, Smirnova L, Morales Pantoja IE, Akwaboah A, Alam El Din D-M, Berlinicke CA, Boyd JL, Caffo BS, Cappiello B, Cohen-Karni T, Curley JL, Etienne-Cummings R, Dastgheyb R, Gracias DH, Gilbert F, Habela CW, Han F, Harris TD, Herrmann K, Hill EJ, Huang Q, Jabbour RE, Johnson EC, Kagan BJ, Krall C, Levchenko A, Locke P, Maertens A, Metea M, Muotri AR, Parri R, Paulhamus BL, Plotkin JD, Roach P, Romero JC, Schwamborn JC, Sillé F, Szalay AS, Tsaioun K, Tornero D, Vogelstein JT, Wahlin KJ and Zack DJ. The Baltimore declaration toward the exploration of organoid intelligence. Front Sci (2023) 1:1068159. doi: 10.3389/fsci.2023.1068159

COPYRIGHT

© 2023 Hartung, Smirnova, Morales Pantoja, Akwaboah, Alam El Din, Berlinicke, Boyd, Caffo, Cappiello, Cohen-Karni, Curley, Etienne-Cummings, Dastgheyb, Gracias, Gilbert, Habela, Han, Harris, Herrmann, Hill, Huang, Jabbour, Johnson, Kagan, Krall, Levchenko, Locke, Maertens, Metea, Muotri, Parri, Paulhamus, Plotkin, Roach, Romero, Schwamborn, Sillé, Szalay, Tsaioun, Tornero, Vogelstein, Wahlin and Zack. This is an open-access article distributed under the terms of the Creative Commons Attribution License (CC BY). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

The Baltimore declaration toward the exploration of organoid intelligence

Thomas Hartung^{1,2*}, Lena Smirnova¹, Itzy E. Morales Pantoja¹, Akwasi Akwaboah³, Dowlette-Mary Alam El Din¹, Cynthia A. Berlinicke⁴, J. Lomax Boyd⁵, Brian S. Caffo⁶, Ben Cappiello⁷, Tzahi Cohen-Karni^{8,9}, J. Lowry Curley⁷, Ralph Etienne-Cummings³, Raha Dastgheyb¹⁰, David H. Gracias^{11,12,13,14,15,16}, Frederic Gilbert¹⁷, Christa Whelan Habela¹⁰, Fang Han¹⁸, Timothy D. Harris^{19,20}, Kathrin Herrmann¹, Eric J. Hill²¹, Qi Huang¹¹, Rabih E. Jabbour²², Erik C. Johnson²⁰, Brett J. Kagan²³, Caroline Krall¹, Andre Levchenko²⁴, Paul Locke¹, Alexandra Maertens¹, Monica Metea²⁵, Alysson R. Muotri^{26,27}, Rheinallt Parri²⁸, Barton L. Paulhamus²⁰, Jesse D. Plotkin¹, Paul Roach²⁹, July Carolina Romero¹, Jens C. Schwamborn³⁰, Fenna Sillé¹, Alexander S. Szalay^{31,32,33}, Katva Tsaioun¹. Daniel Tornero^{34,35}, Joshua T. Vogelstein³⁶, Karl J. Wahlin³⁷ and Donald J. Zack^{38,39,40,41}

¹Center for Alternatives to Animal Testing (CAAT), Department of Environmental Health and Engineering, Bloomberg School of Public Health and Whiting School of Engineering, Johns Hopkins University, Baltimore, MD, United States, ²Center for Alternatives to Animal Testing (CAAT)-Europe, University of Konstanz, Konstanz, Germany, ³Department of Electrical and Computer Engineering, Johns Hopkins University, Baltimore, MD, United States, ⁴Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ⁵Berman Institute of Bioethics, Johns Hopkins University, Baltimore, MD, United States, ⁶Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States, ⁷AxoSim Inc., New Orleans, LA, United States, ⁸Department of Biomedical Engineering in Carnegie Mellon University, Pittsburgh, PA, United States, ⁹Department of Materials Science and Engineering in Carnegie Mellon University, Pittsburgh, PA, United States, ¹⁰Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ¹¹Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, MD, United States, ¹²Department of Chemistry, Johns Hopkins University, Baltimore, MD, United States, ¹³Department of Materials Science and Engineering, Johns Hopkins University, Baltimore, MD, United States, ¹⁴Laboratory for Computational Sensing and Robotics (LCSR), Johns Hopkins University, Baltimore, MD, United States, ¹⁵Center for Microphysiological Systems (MPS), Johns Hopkins University School of Medicine, Baltimore, MD, United States, ¹⁶Oncology and Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ¹⁷Philosophy Program, School of Humanities, University of Tasmania, Hobart, TAS, Australia, ¹⁸Department of Statistics and Economics, University of Washington, Seattle, WA, United States, ¹⁹Janelia Research Campus, Howard Hughes Medical Institute, Ashburn, VA, United States, ²⁰Research and Exploratory Development Department, Johns Hopkins University Applied Physics Laboratory, Laurel, MD, United States, ²¹School of Biosciences, College of Health and Life Sciences, Aston University, Birmingham, United Kingdom, ²²Bioscience and Biotechnology Department, University of Maryland, Rockville, MD, United States, ²³Cortical Labs, Melbourne, VIC, Australia, ²⁴Biomedical Engineering Department, Yale Systems Biology Institute, Yale University, New Haven, CT, United States, ²⁵Preclinical Electrophysiology Consulting, LLC, Mattapoisett, MA, United States, ²⁶Departments of Pediatrics and Cellular & Molecular Medicine, School of Medicine, University of California, San Diego, La Jolla, CA, United States, ²⁷Center for Academic Research and Training in Anthropogeny (CARTA), Kavli Institute for Brain and Mind, Archealization Center (ArchC), University of California, San Diego, La Jolla, CA, United States, ²⁸Aston Pharmacy School, College of Health and Life Sciences, Aston University, Birmingham, United Kingdom, ²⁹Department of Chemistry, School of Science,

Loughborough University, Leicestershire, United Kingdom, ³⁰Luxembourg Centre for Systems Biomedicine (LCSB), University of Luxembourg, Belvaux, Luxembourg, ³¹Department of Computer Science, Whiting School of Engineering, Johns Hopkins University, Baltimore, MD, United States, ³²Department of Physics and Astronomy, Krieger School of Arts and Sciences, Johns Hopkins University, Baltimore, MD, United States, ³³Mark Foundation Center for Advanced Genomics and Imaging, Johns Hopkins University, Baltimore, MD, United States, ³⁴Department of Biomedical Sciences, Institute of Neuroscience, University of Barcelona, Barcelona, Spain, ³⁵Clinic Hospital, August Pi i Sunyer Biomedical Research Institute (IDIBAPS), Barcelona, Spain, ³⁵Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD, United States, ³⁷Viterbi Family Department of Ophthalmology & the Shiley Eye Institute, University of California, San Diego, La Jolla, CA, United States, ³⁶Department of Ophthalmology, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ³⁹Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ⁴¹Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ⁴¹Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, United States, ⁴¹Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD, United States

KEYWORDS

manifesto, organoid, artificial intelligence, microphysiological systems, learning, synthetic biology, bioengineering, biocomputing

An Editorial on the Frontiers in Science Lead Article Organoid intelligence (OI): the new frontier in biocomputing and intelligence-in-a-dish

We, the participants of the First Organoid Intelligence Workshop – "Forming an OI Community" (22–24 February 2022), call on the international scientific community to explore the potential of human brain-based organoid cell cultures to advance our understanding of the brain and unleash new forms of biocomputing while recognizing and addressing the associated ethical implications.

The term "organoid intelligence" (OI) has been coined to describe this research and development approach (1) in a manner consistent with the term "artificial intelligence" (AI) – used to describe the enablement of computers to perform tasks normally requiring human intelligence.

OI has the potential for diverse and far-reaching applications that could benefit humankind and our planet, and which urge the strategic development of OI as a collaborative scientific discipline. OI holds promise to elucidate the physiology of human cognitive functions such as memory and learning. It presents game-changing opportunities in biological and hybrid computing that could overcome significant limitations in silicon-based computing. It offers the prospect of unparalleled advances in interfaces between brains and machines. Finally, OI could allow breakthroughs in modeling and treating dementias and other neurogenerative disorders that cause an immense and growing disease burden globally.

Realizing the world-changing potential of OI will require scientific breakthroughs (1). We need advances in human stem cell technology and bioengineering to recreate brain architectures and to model their potential for pseudo-cognitive capabilities. We need interface breakthroughs to allow us to deliver input signals to organoids, measure output signals, and employ feedback mechanisms to model learning processes. We also need novel machine learning, big data, and AI technologies to allow us to understand brain organoids. In addition to confronting these scientific and technical challenges, we also need to anticipate (as far as possible) and address the significant and largely unexplored ethical challenges associated with this research. We must be alert to any possibility that organoids could develop forms or aspects of consciousness and mitigate and safeguard against this. The cell donor's personal rights and interests are among other important considerations. These issues warrant stringent, ongoing discussions throughout the development of OI toward an accepted ethical framework. Such discussions should include all relevant stakeholders and take due account of public values.

We are only just beginning this multidisciplinary and multistakeholder endeavor. The potential benefits are worldchanging, but the challenges are daunting. We call on the scientific community to join us on this journey. Only by collaborating will we be able to realize the full potential of OI to advance science, technology, and medicine.

Author contributions

TH, LS, and IMP drafted the Declaration. All authors reviewed and approved the final version.

Acknowledgments

The First Organoid Intelligence Workshop – "Forming an OI Community" took place online on 22–24 February 2022 with financial support from the Johns Hopkins University Center for Alternatives to Animal Testing, the Johns Hopkins University Whiting School of Engineering, the Transatlantic Think-Tank for Toxicology (t^4), and Frontiers. The authors would like to thank Lee

Baker for editing it on behalf of the Frontiers in Science Editorial Office.

Conflict of interest

TH is employed by, and inventor on a patent by Johns Hopkins University on the production of brain organoids, which is licensed to AxoSim, New Orleans, LA, USA, and receives royalty shares. TH also consults for AxoSim. LS is employed by Johns Hopkins University and consults for AxoSim, New Orleans, LA, USA. BC and JLC are employed by AxoSim. JS is employed by, and inventor on a patent by the University of Luxembourg on the production of midbrain organoids, which is licensed to OrganoTherapeutics SARL, Esch-sur-Alzette, Luxembourg. JS is also co-founder and shareholder of OrganoTherapeutics SARL.

ARM is employed by the University of California, San Diego and is co-founder and has equity interest in TISMOO, a company dedicated to genetic analysis and human brain organogenesis, focusing on therapeutic applications customized for autism spectrum disorders and other neurological disorders origin genetics. The terms of this arrangement have been reviewed and

Reference

1. Smirnova L, Caffo BS, Gracias D, Huang Q, Morales Pantoja IE, Tang B, et al. Organoid intelligence (OI): the new frontier in biocomputing and intelligence in-adish. *Front Sci* (2023) 1:1017235. doi: 10.3389/fsci.2023.1017235 approved by the University of California, San Diego, in accordance with its conflict of interest policies. BK is employed by Cortical Labs Pty Ltd, Melbourne, Australia, and is an inventor on patents for technology related to this article, and holds shares in Cortical Labs Pty Ltd, Melbourne, Australia. MM is employed by and owner of Preclinical Electrophysiology Consulting, LLC. Preclinical Electrophysiology Consulting, LLC does not have any commercial or financial relationships that could be construed as a potential conflict of interest.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.