Applications and ethics of computer-designed organisms

Levin, M.; Bongard, J.; Lunshof, J. E.

Published in:
Nature Reviews Molecular Cell Biology

DOI:
10.1038/s41580-020-00284-z

Publication date:
2020

Applications and ethics of computer-designed organisms

M. Levin[1,2✉], J. Bongard[3] and J. E. Lunshof[2,4,5]

Computer-designed organisms — biobots, such as xenobots — are at the intersection of synthetic developmental biology and machine learning. This technology, which enables the evolution of real, living forms to take place in a virtual world, is part of an emerging new research field with applications in biomedicine and engineering, and raises profound philosophical questions.

[1]Allen Discovery Center at Tufts University, Medford, MA, USA.
[2]Wyss Institute for Biologically Inspired Engineering, Harvard University, Boston, MA, USA.
[3]Department of Computer Science, University of Vermont, Burlington, VT, USA.
[4]Department of Global Health and Social Medicine, Harvard Center for Bioethics, Harvard Medical School, Boston, MA, USA.
[5]Department of Genetics, University Medical Center Groningen, University of Groningen, Groningen, Netherlands.
✉e-mail: michael.levin@tufts.edu

https://doi.org/10.1038/s41580-020-00284-z

Synthetic biology is moving from rewiring the metabolic activity of single cells to synthetic morphology[1] — living machines created via guided self-assembly of multicellular forms[2]. The programming of such 'biobots' for novel structure and behaviour will greatly advance our understanding of the relationship between genome, multicellular morphology and the evolution of basal cognition. Moreover, it has the potential for a deeper consilience between computer science and biology. Here, we summarize key questions of science and philosophy raised by this new model system through the lens of a recent study that produced 'xenobots', whose evolutionary history took place entirely within a computer, but was subsequently realized using frog cells.

From biobots to xenobots

Bioengineering employs highly predictable 3D constructs (moulds, 3D matrices and so forth) seeded with cells[3–5]. A key future goal is 'guided self-assembly', where multicellular dynamics are guided towards desired structures, functions and computational capacity. Advances in evolutionary developmental biology, regenerative medicine and robotics depend on cracking this morphogenetic code.

A recent study[6] has revealed a remarkable degree of plasticity in cells, as wild-type *Xenopus laevis* skin and cardiac cells were able to aggregate and self-assemble into a novel motile 'living entity' of ~0.1–0.5 mm in diameter, without genomic editing and without an inorganic scaffold to dictate the final shape. Instead, specific cells were removed, as determined by an algorithm that simulates their evolution. Devoid of nerves or a brain, these synthetic living machines move, regenerate after damage and cooperate with each other to redistribute smaller particles in their environment. The creation of such novel living entities with highly unexpected behaviours and whose multicellular evolutionary history and selection pressures took place entirely in a virtual world, rather than in the biosphere, presents fundamental philosophical and biological questions.

Biobots as organisms: ethical aspects

Biobots are made of living cells and meet most reasonable definitions of being 'alive'. But, are they animals? Are they organisms? Such philosophical questions and the regulations on research with biobots are comparable to those covering research with classical animal model systems. Current biobots do not have a nervous system, but future versions probably will. The mere presence or absence of a nervous system is not a criterion for moral considerability, as is being discussed for research using human brain organoids[7]. Biobots are in a similar position as organisms with aspects of basal cognition: pre-neural life forms that can exhibit preferences, intrinsic motivation in behaviour, decision-making and learning[8,9]. Given the growing knowledge of complex behavioural repertoires of aneural forms, the existence of biobots drives discussion of fundamental philosophical questions concerning the status of artificial intelligences, putative exobiological entities and other systems whose embodiment is radically different from the familiar animals we encounter in daily life.

Potential applications: use and misuse

In vivo applications include context-sensitive delivery of specific biomolecules, abrasion of unwanted material deposits (for example, in arthritic joints) or inactivation of cancer cells in lymph nodes. They might also be used to clean up waterways (collecting toxins) and as biosensors. Current xenobots cannot reproduce, are difficult to make in quantity, are limited to a life of <14 days and are fully biodegradable. However, lifespan, reproductive and mutagenic potential, and possible interactions with other organisms must be considered when introducing synthetic living machines into the environment. Future biobots will probably be capable of metabolic pathways that increase lifespan (necessitating tractable kill-switch technology). The use of self-propagating biobots would introduce novel inhabitants in unprepared food chains and ecosystems. Ethics and policies will resemble those of ecosystem engineering; for example, they will include unresolved issues related to gene drives.

Novel synthetic living machines, like new viruses, bacteria and genetically modified metazoan organisms, could be generated by malevolent actors. Oversight and possibly scientific crowdsourcing will reduce potential risks, but malicious efforts might be very hard to detect and likely outside the regulations aimed at scientists. But concerns about misuse should be placed into context. The risk is far lower than that of naturally evolved and engineered viruses, bacteria and genetic elements such as gene drives, already optimized for reproduction in the biosphere. As with deadly infectious diseases, rather than stifling research in the hope of preventing hypothetical hazards, the way forwards is via a vigorous research programme to fully understanding the technology and its risks.

The potential benefits of biobots are far-reaching. Construction and customization efforts will drive increased quantitative, multi-scale understanding of how cell collectives orchestrate morphogenesis. This would revolutionize biomedicine — birth defect repair, regeneration after traumatic injury, reversal of ageing and tumour reprogramming. Many unsolved problems in biomedicine hinge on the ability to control the 3D structures that cells build, which cannot be overcome by gene editing and directed stem cell differentiation alone. Beyond biomedicine, biobots advance our understanding of the evolution and scaling of cognition[10], by building diverse organisms from scratch. Studying the ability of single cells and collectives to process information will potentiate technology through enhanced understanding of the dynamics by which resilient, plastic, functional systems can be created out of smaller competent agents.

Evolutionary origins and opportunities

Xenobots[6] were designed by an evolutionary algorithm, which scored the quality of each simulated biobot for its capacity to move in specific ways. However, this automated scoring introduces an AI control problem: a problem might be solved but not in the way that the user wished. Biobots provide an opportunity to understand how complex structures emerge from simple interacting parts, enabling better control of system-level behaviours. However, it is also important to limit the emergence of new unpredictable features. Unforeseen outcomes could be limited by closely monitoring small incremental changes in a highly controlled setting to improve our understanding of opportunity/risk tradeoffs.

The biobot field provides a further crucial opportunity: to mitigate technological risk more broadly. Learning to program biobots represents an ideal platform in which to advance our ability to predict and mitigate the consequences of large numbers of units acting in parallel. From the internet of things to communications networks, financial markers, traffic and so forth, major knowledge gaps hinder our ability to anticipate what swarm intelligence systems (natural or artificial self-organizing systems) are capable of and, most crucially, what they will try to do. Minimizing unpredictability, during the inevitable advances of increasingly powerful technologies, is an essential ingredient for thriving now and for surviving into the next century.

Conclusions and perspectives

This powerful enabling technology, with additional sensory capacities and effectors, will reveal how neural and non-neural tissue networks process information for multicellularity, scaling of basal cognition, biological computation and evolution of body plans. One way in which philosophy will drive scientific progress is by clarifying how biobots stretch current categories and require the development of more useful, non-binary definitions of commonly used but deeply contentious terms (such as machine, robot, animal, living, evolved, welfare, software, genetic and physiological programming and so forth).

Biobots are an important complement to natural model species, giving scientists and engineers the opportunity to develop new ways to understand the rules of biology, physics and computation. Importantly, this new model system is not only the living machine itself, but actually includes the computer that evolves it and the human (or robot) scientist that constructs and evaluates the biobots. The study of the cycle comprising computer evolution of functional forms, their cellular implementation in a real-world environment and the inference of the rules of morphogenesis will transform areas of science and technology well beyond direct applications of useful synthetic living machines smaller than any inorganic robot. The lessons about control of morphological and behavioural plasticity will transform regenerative medicine, robotics, communication technology and machine learning. Understanding how units such as cells cooperate in novel circumstances to lead to new forms and functions will be important in the context of a future rife with potential for unintended consequences of technology. Understanding biological self-organization opens new avenues for overcoming the challenges of ecosystem and species survival in the coming century.

1. Levin, M. & Martinez Arias, A. Reverse-engineering growth and form in Heidelberg. *Development* **146**, dev177261 (2019).
2. Kamm, R. D. et al. Perspective: the promise of multi-cellular engineered living systems. *Apl. Bioeng.* **2**, 040901 (2018).
3. Chan, V. et al. Development of miniaturized walking biological machines. *Sci. Rep.* **2**, 857 (2012).
4. Park, S. J. et al. Phototactic guidance of a tissue-engineered soft-robotic ray. *Science* **353**, 158–162 (2016).
5. Nawroth, J. C. et al. A tissue-engineered jellyfish with biomimetic propulsion. *Nat. Biotechnol.* **30**, 792–797 (2012).
6. Kriegman, S., Blackiston, D., Levin, M. & Bongard, J. A scalable pipeline for designing reconfigurable organisms. *Proc. Natl Acad. Sci. USA* **117**, 1853–1859 (2020).
7. Hyun, I., Scharf-Deering, J. C. & Lunshof, J. E. Ethical issues related to brain organoid research. *Brain Res.* **1732**, 146653 (2020).
8. Cook, N. D., Carvalho, G. B. & Damasio, A. From membrane excitability to metazoan psychology. *Trends Neurosci.* **37**, 698–705 (2014).
9. Baluska, F. & Reber, A. Sentience and consciousness in single cells: how the first minds emerged in unicellular species. *BioEssays* **41**, e1800229 (2019).
10. Levin, M. The computational boundary of a “self”: developmental bioelectricity drives multicellularity and scale-free cognition. *Front. Psychol.* **10**, 2688 (2019).

Acknowledgements

M.L. gratefully acknowledges support (via grant TWCF0315) from the Templeton World Charity Foundation and from the Defense Advanced Research Projects Agency (DARPA) under Cooperative Agreement Number HR0011-18-2-0022. J.E.L. is supported by a grant from the Greenwall Foundation.

Competing interests

The authors declare no competing interests.