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№ 5827

The Edge of the Organic: Philosophical Issues of Synthetic Morphology

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June 16, 2021

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Abstract

Bioengineering is progressing vigorously, with biomedical applications already within our grasp and many more on the horizon. More profoundly, and perhaps unexpectedly, are the deep philosophical and conceptual implications raised by bioengineering, particularly synthetic morphology - the subdiscipline concerned with the creation of novel living forms. Advancement in this field is necessitating a radical reconsideration of some of our commonplace assumptions, as well as providing a unique opportunity for discovery, creativity, and consilience between biology, engineering, and computer science.

1 Introduction

How do we define an organism? It's a question that would concede some fairly ubiquitous answers. Perhaps we might say: it makes decisions, it grows, it metabolizes, it's motile, it evolved, it's made of organic material, it self-organises. The list of what defines an organism would be quite extensive, with the few attributes listed surely to be agreed upon by many.

However, recent advancements in synthetic biology call for a reexamination of these seemingly common-sense notions. The most pertinent concepts that we are being forced to question are the theory of evolution, the distinction between living and non-living, and what it means to be an individual.

2 The Role and Development of Bioelectricity

Somewhere between untrue and incomplete lies the assumption that the genome – often inaccurately referred to as the "software of the cell" – is responsible and sufficient for producing a biological body. The Central Dogma of Molecular Biology describes how the genome encodes for the production of particular proteins, which are subsequently utilised by cells for various functions (Crick, 1970). Thus, the genome is akin to a 'parts list' – it does not specify how the proteins will be used, only which ones are to be made. It therefore follows that most genetic engineering techniques are aimed at micromanaging individual biochemical parts bottom-up (Hsu et al., 2014), at the 'hardware' level of the organism.

Another approach is via the utilization of the biophysics of electricity. This understudied field is beginning to provide valuable insight as to how organisms can be efficiently manipulated top-down by taking advantage of the bioelectric patterns inherent to bodies that store informational anatomic memories separate from the genome (Whited and Levin, 2019).

Most people are aware of how neurons communicate via electrical signaling; much of artificial intelligence research is based on mimicking the brain. But it is little-known that bioelectricity is an ancient cellular communication medium, pre-dating nervous systems, and a driving force behind the evolution of multicellularity (Levin and Martyniuk, 2019).

Endogenous bioelectric networks operate such that information is shared between cells through the conductance of ions across cell membranes and, downstream, in the propagation of signals for control of cell behaviour in larger systems-level spaces, i.e., organs and tissues (Levin, 2012). Manipulation and control are achieved by pharmacological or optogenetic stimulation, triggering a cascade of signals between cells (Nanos and Levin, 2021), analogous to a subroutine in computer programming.

In the early days of computer science, programming was done by physically rewiring hardware. This is where current mainstream bioengineering is, which is not to dismiss its achievements. The next step is manipulation at the level of biological 'software,' i.e., bioelectricity, which has seen significant progress in recent years, in cancer suppression (Payne et al., 2019), regenerative medicine (McLaughlin and Levin, 2018; Pezzulo and Levin, 2015), the mechanisms underlying memory encoding (Blackiston et al., 2015; Pezzulo et al., 2021), and cognitive science (Levin, 2019). Furthermore, bioelectricity, in conjunction with computer science, is now being harnessed for the creation of novel morphologies, the focus of the next section.

3 Biobots: The Computer-Aided Design of Biology

'Biobots' is the name given to organisms designed in silico. In 2019, a type of biobot called a 'xenobot' was created, which led to an influx of media attention (Heaven, 2020; Weisberger, 2020; Yasinski, 2020), and even a nomination for a prestigious art and design award (Keats, 2021).

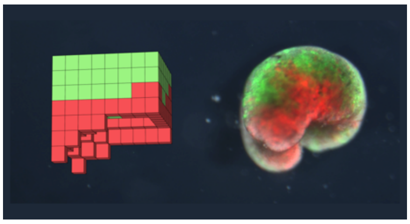

Fig. Xenobot designed by Doug Blackiston, Sam Kriegman, Josh Bongard, and Michael Levin (Kriegman, et al., 2020)

Xenobots are a little less than a millimeter wide and are composed of cells harvested from pluripotent African clawed frog (*Xenopus laevis,* hence the name) embryos (Ball, 2020).

The approach to designing xenobots consists in using an evolutionary algorithm (EA) to realise a morphology best suited to the given constraints: a behavioural goal, and the type of building blocks (Kriegman et al., 2020).

In the case of xenobots, the building blocks were passive skin cells and contractile heart muscle cells. The behavioural goal fed into the EA was "maximise displacement," i.e., move as much as possible. The EA sought to devise the best ratio of passive to contractile cells, and the best configuration, given the behavioural goal (Ibid.).

This approach was successful due to the compatibility of the building blocks and behavioural goal. For example, if only skin cells were used, no displacement could have been achieved because they do not possess the contractile ability that muscle cells do. On the other hand, if only muscle cells were used, the organism would have too much movement capability, unable to stay in control of its overall form.

The EA first evolved an initial random population from which was returned the best configuration. It was rerun 99 times with different starting populations. The highest performing designs were developed in vitro – coaxed, via bioelectric stimulation, to self-assemble into the given configuration – on the surface of a Petri dish, where their behaviour was observed, compared to the in silico behaviour, and fed back into to the EA. Eventually, a configuration was produced that provided optimally matching in silico and in vitro behaviours (Ibid.).

Unlike the brittleness of current technologies made from glass, metal, plastic, etc., these "technologies" are biocompatible and self-regenerative, providing exciting opportunities in the delivery of biomolecules, removal of unwanted material deposits, whether in other organisms or environments such as waterways, or inactivation of cancer cells (Levin et al., 2020).

4 The Philosophy of Xenobots

Aside from practical applications, there are also a variety of conceptual issues that arise with the instantiation of human-created, computer-designed, bioelectrically self-assembled organisms. This section will seek to expose some of these issues, not with the intention of solving them – as we are only now beginning to see the possibilities of this technology – but simply to bring these not-so-obvious implications to the attention of the reader.

Cells are incredibly plastic. In one experiment, an eye was induced on the tail of a tadpole (Pai et al., 2012). Remarkably, the ectopic eye was fully functional and provided perfectly normal vision despite being attached to the spinal cord and not directly to the brain, as is typical. This incredible plasticity is one of the primary factors enabling the creation of novel forms.

Herein lies the first problem: What does it mean for the theory of evolution if the evolutionary history of organisms, and eventual lineages of organisms, takes place, or at least begins, within a computer? 'Traditional' evolutionary processes take many thousands to millions of years for new phenotypic expressions to emerge. How might the theory itself be in need of revision if, within days, never before seen morphologies are brought into existence? Must we incorporate technological evolution into the theory of evolution, in a more all-encompassing theory?

Even classical taxonomic concepts may be in need of revision. The xenobots self-assembled from frog cells. Thus, the xenobot's genotype is identical to that of the frog from which the cells came, despite not resembling, nor behaving like a frog. Neither did it evolve or develop like one. What, therefore, even is a 'frog,' or more generally, an individual, in biological terms? It is often overlooked that, due to being more like a parts list, a genomic mapping will not allow for prediction of anatomical outcome unless a comparison is made with a genome of which the animal it belongs to is known prior. Surely, then, the definition of an individual cannot rely, in a reductionist manner, solely on genetics – an assumption often held by the general public.

What, finally, do xenobots mean for the future of organic-mechanic interfaces and the fuzzy boundary between them? Creating hybrid agents with parts both biologically and virtually evolved is now a possibility, with confronting implications for the distinction between living and non-living, and the multitudinous middle cases.

In all probability, we will see hybridisation take place first in relatively trivial ways, such as in household appliances. We already have robot vacuum cleaners; soon enough we will see vacuum cleaners bioelectrically embedded with neural cells optimised for sensing or control.

This idea is, though incredible, not unfathomable. What becomes difficult to wrestle with are the inherent potentialities. Most people would likely be comfortable in denoting a household appliance a 'machine' when, say, only 2% of it is composed of organic material. What about 10, 20, 50, 80%? It is the classic "When does a pile of sand become a pile?" conundrum. Where in the continuum could, or should, we delineate machine from animal? Living from non-living? This also poses ethical dilemmas: How should we treat a vacuum cleaner composed of 80% neurons, 20% *Xenopus* cells, and 10% electronics?

Conclusion

As stated in the previous section, the aim of this paper has been only to elucidate some of the looming conceptual difficulties of bioengineering, specifically synthetic morphology. These difficulties are due foremost to the novelty of computationally designed organisms, which are engineered in vitro via bioelectric stimulation; biological engineering at the level of the organism's 'software,' as opposed to the painstaking process of manipulation at the level of genetic 'hardware.'

Though it is evident that vocabularies will need redefining as the field progresses, it will be exciting, and at times bewildering, to uncover the state space of, as Darwin said, "endless forms most beautiful and most wonderful" (Darwin, 2009).

References

Ball, P. (2020). "Living robots." Nature Materials **19**(3): 265-265.

Blackiston, D. J., et al. (2015). "The stability of memories during brain remodeling: A perspective." Communicative & Integrative Biology **8**(5): e1073424.

Crick, F. (1970). "Central Dogma of Molecular Biology." Nature **227**(5258): 561-563.

Darwin, C. (2009). On the Origin of Species, Penguin Classics.

Heaven, W. D. (2020). "These "xenobots" are living machines designed by an evolutionary algorithm." From https://www.technologyreview.com/2020/01/14/238128/these-xenobots-are-living-machines-designed-by-an-evolutionary-algorithm/.

Hsu, P. D., et al. (2014). "Development and applications of CRISPR-Cas9 for genome engineering." Cell **157**(6): 1262-1278.

Keats, J. (2021). "Nominated For A Prestigious Design Award, This Living Organism Is Poised To Redesign Life Itself." from https://www.forbes.com/sites/jonathonkeats/2021/01/15/nominated-for-a-prestigious-design-award-this-living-organism-is-poised-to-redesign-life-itself/?sh=4d394b8e666d.

Kriegman, S., et al. (2020). "A scalable pipeline for designing reconfigurable organisms." Proceedings of the National Academy of Sciences **117**(4): 1853-1859.

Levin, M. (2012). "Morphogenetic fields in embryogenesis, regeneration, and cancer: non-local control of complex patterning." Biosystems **109**(3): 243-261.

Levin, M. (2019). "The Computational Boundary of a "Self": Developmental Bioelectricity Drives Multicellularity and Scale-Free Cognition." Frontiers in Psychology **10**(2688).

Levin, M., et al. (2020). "Applications and ethics of computer-designed organisms." Nature Reviews Molecular Cell Biology **21**(11): 655-656.

Levin, M. and C. J. Martyniuk (2018). "The bioelectric code: An ancient computational medium for dynamic control of growth and form." Biosystems **164**: 76-93.

McLaughlin, K. A. and M. Levin (2018). "Bioelectric signaling in regeneration: Mechanisms of ionic controls of growth and form." Developmental Biology **433**(2): 177-189.

Nanos, V. and M. Levin (2021). "Rewiring Endogenous Bioelectric Circuits in the Xenopus laevis Embryo Model." Methods Mol Biol **2258**: 93-103.

Pai, V. P., et al. (2012). "Transmembrane voltage potential controls embryonic eye patterning in Xenopus laevis." Development **139**(2): 313.

Payne, S. L., et al. (2019). "Bioelectric Control of Metastasis in Solid Tumors." Bioelectricity **1**(3): 114-130.

Pezzulo, G., et al. (2021). "Bistability of somatic pattern memories: stochastic outcomes in bioelectric circuits underlying regeneration." Philosophical Transactions of the Royal Society B: Biological Sciences **376**(1821): 20190765.

Pezzulo, G. and M. Levin (2015). "Re-membering the body: applications of computational neuroscience to the top-down control of regeneration of limbs and other complex organs." Integr Biol (Camb) **7**(12): 1487-1517.

Weisberger, M. (2020). "World's First "Living Machine" Created Using Frog Cells and Artificial Intelligence." from https://www.scientificamerican.com/article/worlds-first-living-machine-created-using-frog-cells-and-artificial-intelligence/.

Whited, J. L. and M. Levin (2019). "Bioelectrical controls of morphogenesis: from ancient mechanisms of cell coordination to biomedical opportunities." Curr Opin Genet Dev **57**: 61-69.

Yasinski, E. (2020). "Algorithm Designs Robots Using Frog Cells." from https://www.the-scientist.com/news-opinion/algorithm-designs-robots-using-frog-cells-66961.