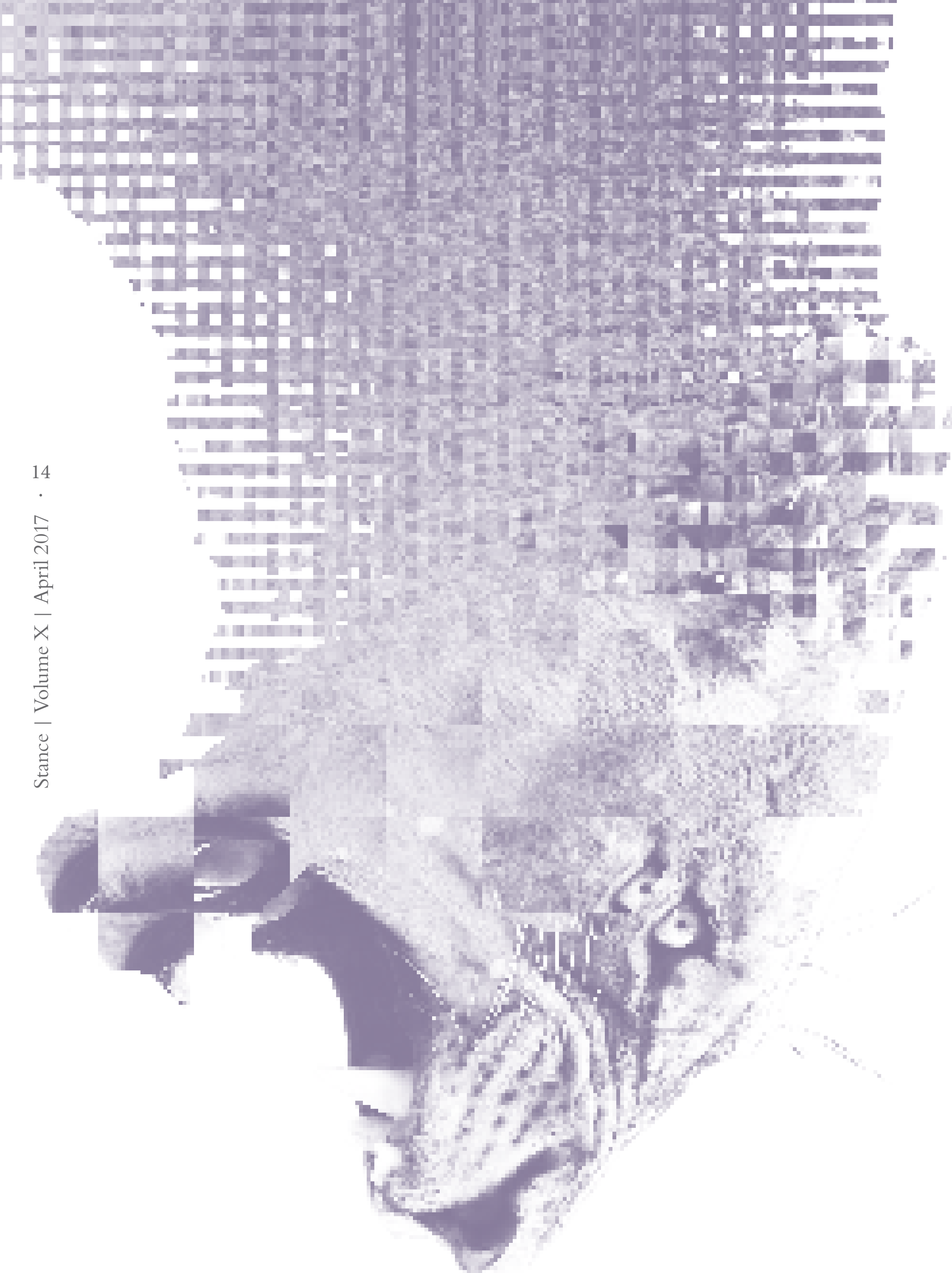

Synthetic Biology and Natural Kinds:

Homeostatic Property Cluster Theory in the Post-Genomic Era

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Abstract: *In the life sciences, biologists and philosophers lack a unifying concept of species—one that will reconcile intuitive demarcations of taxa with the fluidity of phenotypes found in nature. One such attempt at solving this "species problem" is known as Homeostatic Property Cluster theory (HPC), which suggests that species are not defined by singular essences, but by clusters of properties that a species tends to possess. I contend that the arbitrary nature of HPC's kind criteria would permit a biological brand of functionalism to inform species boundaries, thereby validating synthetic organisms as members of a species that do not belong.*

Introduction

"This paper's account of natural kinds pursues a challenging question, attacking the problems of the budding world of modern technology. It focuses on our fundamental notion of 'life' as we know it."

-Quintin Thompson
Associate Editor

In an ongoing pursuit to effectively carve nature at its joints, the philosophical consensus has more or less abandoned kind essentialism as a viable solution to the question of natural kinds in search of something more empirically sound.[1] A popular alternative is Richard Boyd's Homeostatic Property Cluster theory (HPC),[2] which holds that natural kinds are defined by self-maintaining clusters of properties with no one property being sufficient for kind membership. This element of HPC allows us to navigate away from a strict essentialist account of natural kinds, but it also invites a subjective discrepancy by placing the onus of kind membership on a cluster of properties that a kind *tends* to have. I contend that, if this is a viable theory of natural kinds, it allows for a biological brand of functionalism whereby synthetic organisms are classified as proper species members if they demonstrate an arbitrary collection of proper-

[1] Marc Ereshefsky, "Species," in *The Stanford Encyclopedia of Philosophy* (Summer 2016), ed. Edward N. Zalta, https://plato.stanford.edu/archives/sum2016/entries/species/.

[2] Richard Boyd, "Homeostasis, Species, and Higher Taxa," in *Species: New Interdisciplinary Essays*, ed. R. A. Wilson (MIT Press, 1999), 141–85.

ties the species tends to possess. If, for example, we were to model a cellular version of Alan Turing's "Imitation Game"[3] that could successfully bar a scientist from distinguishing between a natural and artificial cell, it can be argued that, according to HPC, the artificial cell possesses enough properties in common with its natural counterpart for both cells to be considered members of the same species. With no essential requirements, HPC allows the theorist to select whichever properties they so choose as the arbiters of species membership. Therefore, as the ingredients of life become more widespread in the midst of a biotechnological revolution, I contend that the lenient nature of HPC's kind criteria would permit a biological brand of functionalism to inform species boundaries, thus producing an undesired consequence: validating synthetic organisms as members of a species to which they do not belong.

I. Problems and Solutions: A Brief History of Natural Kinds

From Linnaean binomial classification and taxonomic realism to chemical elements and psychological states, scientists and philosophers have wrapped themselves in contention over the place of natural kinds in scientific practice, as well as their extensions in reality.[4] Among the special sciences, however, we lose the clarity of kind criteria that is present in lower levels, i.e., chemical and physical sciences. In the case of biological systems, for example, "the species problem" is a question of the nature of species, whether they exist, and if they exist as natural kinds independently of our classifications. Furthermore, while we have struggled to reach an understanding of species of natural organisms with ancestral lineages and fleshy, organic material substance, the debate becomes even more complex with the introduction of synthetic biological systems. As we move forward in thinking about natural kinds in scientific practice and elsewhere, we are encouraged by a widely accepted view to orient our "kinding"[5] in such a way that reflects technological advances and empirical evidence in contemporary research. After all, the more we learn about the vastly interwoven roots and branches of our Great Tree,[6] the less clear are our classificatory merits. Moreover, the kind thinker must now tend to two demanding, albeit abbreviated agendas, viz., a descriptive notion of kinds that satisfies a natural historical account—which remains largely unsolved—as well as a prescriptive notion that satisfies a relentless mass of empirical research in synthetic biology. Recent advances in bioengineering have afforded researchers the ability to do everything from eliminate the genes for carrying malaria in populations of mosquitoes to build completely functioning synthetic cells from minimal, unexpected ingredients, as we will explore later. The unprecedented and exponential progress in synthetic biology and bioengineering calls us not only to consider the nature of presently existing life in the universe, but the life that we have yet to create.

From Aristotle all the way to the pre-Darwinian backdrop to philosophical naturalism, essentialism was most widely favored in considering demarcations of biological taxa.[7] It is an intuitive assumption that every kind of thing has a distinct property that makes it so. The chemical elements, for example, are seemingly paradigmatic natural kinds based on an essential property that offers inductive value. Every hydrogen atom has a single proton, and we can predict that every hydrogen atom hereafter will have a single proton.

What of species, then? As Darwin postulated, species are mutable and dynamic.[8] Their essence, should they possess any at all, is fluid. A species' fitness is determined by its ability to adapt to exogenous pressures, which is informed by the richness in diversity among the phenotypes of its constituents. Biologists and philosophers needed a revitalized way of thinking about natural kinds—one that could reconcile the intuitive boundaries between species with the vast body of genetic and phenotypic variability within them. Enter Richard Boyd and his Homeostatic Property Cluster theory, otherwise referred to as HPC.[9] According to his proposal, natural kinds are not defined by single essences at all, but rather by a *cluster* of properties. The cluster acts as a nexus of a kind's identifying characteristics.

Perhaps one of the more appealing theoretical components of the largely problematic kind essentialism is its rigid demarcation in the kinding process, bound by notions of necessity. Something is either X or not X, either this kind of thing or not this kind of thing, based on whether it possesses the essential property in question. This, however, has generally proven difficult in practice. Even the genome, the code of life divided amongst four nucleotides in innumerable combinations, does not provide us with a cut-and-dried essentialist criterion of species, as any amount of mutation, recombination, and drift would compromise the integrity of a genetic essence. As Marc Ereshefsky puts it, "The universality of a biological trait in a species is fragile."[10] Boyd and subsequent proponents of HPC have therefore championed property clusters as a way around difficult essence claims.[11] Biological kinds, they argue, are defined by

3 Alan Turing, "Computing Machinery and Intelligence," *Mind* 59, no. 236 (October 1950): 433-60.

4 Alexander Bird and Emma Tobin, "Natural Kinds," in *The Stanford Encyclopedia of Philosophy*, (Summer 2016), ed. Edward N. Zalta, https://plato.stanford.edu/archives/win2016/entries/natural-kinds/.

5 Catherine Kendig, ed. *Natural Kinds and Classification in Scientific Practice* (Abingdon, Oxon: Routledge, 2016).

6 A reference to an image laid out by Charles Darwin, *On the Origin of Species* (London: J. Murray, 1859), 129.

7 Ereshefsky, "Species."

8 Darwin, *On the Origin*.

9 Boyd, "Homeostasis, Species, and Higher Taxa."

10 Ereshefsky, "Species."

11 Robert A. Wilson, Matthew J. Barker, and Ingo Brigandt, "When Traditional Essentialism Fails: Biological Natural Kinds," *Philosophical Topics* 35, no. 1/2 (2007): 189-215, http://www.jstor.org/stable/43154503.

clusters of properties that collectively serve to maintain the kind's identity. Most importantly, no single property or particular subset of properties is necessary or sufficient for kind membership. It is important to mention that advocates of Boyd's cluster kind concept find the argument most compelling due to its "natural flexibility" and "explanatory integrity."[12] The latter refers to Boyd's "accommodation thesis," the inductive, predictive value of biological kinds in scientific practice.[13] The former, however, is the crux of the debate. This is how HPC aims to circumvent the problem of kind essentialism—by appealing to the intuitive desideratum of classifying nature while observing its contents as they are, ever in flux. Its apparent success as a biological kinding method is in its consideration of "intrinsic heterogeneity," the very intraspecific variety that endows a species with evolutionary vitality. It recognizes *typical* properties that a kind *tends* to have but by no means requires that kind members exhibit them. Furthermore, it recognizes that individual kind members possess their own physiological and behavioral variants that collectively reinforce the species' fitness with myriad adaptations. The contrast with kind essentialism is quite clear: whereas essentialism may be palatable in the physical or chemical sciences, it does not do well in categorizing nature's "endless forms most beautiful."[14] As Wilson, Barker, and Brigandt put it, if you see one electron, you have seen them all.[15] There may be a difference of numerical identity between two individual electron tokens but no difference in type or function. The same cannot be said of tigers or coral reefs. If you see one, there are still thousands of others to be seen, each with its own significant uniqueness.

Thus, in the absence of essential properties or subsets of properties, HPC's fluid boundaries and mutable clusters leave us with a subjectivity problem. Thomas Reydon outlines this problem extensively in his critique and proposed solutions for HPC.[16] Whereas essentialism offers cut-and-dried criteria for kind membership, HPC fails to provide such guidelines. According to Reydon, even if we have comprehensively identified all members of a family of properties, as well as the underwritten causal foundations of a kind, we still have no means of determining its extension. This is due to the fact that HPC kinds, their properties, and their causal mechanisms are entirely open-ended. This is both HPC's strength and its vulnerability. As Reydon puts it, "On this view, kind membership is decided more by us than by nature."[17] Furthermore, commentators have noted that drawing kind boundaries around clusters with no clear necessity or sufficiency allows for a disciplinary bias.[18] That is, as opposed to being carved at its joints, HPC allows nature to be carved at arbitrary, potentially artificial places. As Catherine Kendig says,

> Despite widespread acceptance of the HPC theory, if the kinds it claims are successful kinds in science are actually not, or if it fails to account for kinds that are, then its promise of providing an alternative approach to natural kinds that is responsive to scientific practice may be wanting.[19]

These appear to be legitimate concerns about HPC as a means of illuminating natural kinds with ontological extensions in scientific practice.

II. Evaluating Homeostatic Property Cluster Theory

The question therefore surfaces: with the capabilities endowed to us by synthetic biology and genome editing technologies in the post-genomic era, to what extent may we push the intuitive genetic and phenotypic boundaries of a species before it is no longer *that* species according to HPC?

To pursue this question further, let us consider Alan Turing's Imitation Game from his "Computing Machinery and Intelligence."[20] At first glance, importing the Turing Test may seem problematic, but a rehearsal of his thought experiment may assist us in conceptualizing a method for testing HPC's flexibility. In concealing both a human and a computing machine from an interrogator, Turing conceals the presence or absence of some *typical,* often privileged properties associated with a conscious agent (i.e., fleshy body that contains a brain, neurons, axons, etc.). He then asks the interrogator to decide, based on responses from both subjects, which responder is the computing machine and which is the human (i.e., the conscious agent). If the computing machine is capable of fooling the interrogator into believing its responses were generated by a human mind, Turing sees no quibble in concluding that the machine is capable of possessing intelligence. This is the functionalist criterion that the Turing Test puts forth. Simply put, "Functionalism in the philosophy of mind is the doctrine that what makes something a mental state of a particular type does not depend on its internal constitution, but rather on the way it functions, or the role it plays, in the system of which it is a part."[21] If we follow this line of thought, but instead frame it within the context of kind membership, the functionalist may invoke HPC in their defense. If an HPC definition is centered on the properties a kind *tends* to have but lays no essentialist framework for such properties, then in considering "intel-

12 Ibid.

13 Boyd, "Homeostasis, Species, and Higher Taxa."

14 Darwin, *On the Origin*, 491.

15 Wilson, Barker, and Brigandt, "When Traditional Essentialism Fails."

16 Thomas Reydon, "How to Fix Kind Membership: A Problem for HPC Theory and a Solution," *Philosophy of Science* 76, no. 5 (2009): 724-36, doi: 10.1086/605814

17 Ibid.

18 Catherine Kendig, "Editor's Introduction: Activities of Kinding in Scientific Practice," *History and Philosophy of Biology: Natural Kinds and Classification in Scientific Practice* (New York: Taylor and Francis, 2015), 1-13.

19 Ibid.

20 Alan Turing, "Computing Machinery And Intelligence," 433-60.

21 Janet Levin, "Functionalism," in *The Stanford Encyclopedia of Philosophy*, ed. Edward N. Zalta (Summer 2016), https://plato.stanford.edu/archives/win2016/entries/functionalism/.

ligence," the naturalist might say that its tendency as a kind is instantiated in a brain within a skull, surrounded by a fleshy, organic exterior, whereas the functionalist may argue that the goings on *within* and functions *of* that brain are what the kind tends toward. Thus, we have reintroduced the subjectivity problem, i.e., the arbitrary disciplinary bias.

III. Biological Imitation Games

Imagine then, if you will, a sort of cellular Turing Test to evaluate a brand of *biological* functionalism.[22] If we were to follow the method of The Imitation Game, we would set up a system including an interrogator scientist, a natural cell, and an artificial cell. We would construct a completely synthetic cell capable of responding to signaling stimuli with the correct outputs—i.e., central dogma, protein expression, cell division, etc. If a diagnostic record of the synthetic cell's functions could "fool" a scientist, the interrogator, into believing it were the natural cell, then the artificial cell may as well be alive. That is, it may as well be alive according to the standards of a homeostatic property cluster. Taking this one step further, we may also use such a test to "fool" a scientist into thinking a certain species is something that it is not. For example, an undergraduate genetics lab can take a common chassis organism, such as *E. coli* or baker's yeast, and genetically modify it to produce a proteome that is considerably different from that of its immediate natural ancestors. Extrapolating this, and assuming we were able to have the cell replicate and carry out all of its necessary functions for life, if our microbiologist interrogator misnames our model organism by looking at its diagnostic record, we will have fooled him with a different functionalist account—one that has demonstrated the function of a different species altogether.

One does not need an impressive imagination to conceive of such a test. Whereas Turing's test seemed wildly hypothetical in 1950, we have witnessed recent booms in bioengineering that put a cellular Turing Test within reach of reality. Consider, for example, current research at the Kavli Institute for Nanoscale Science at Cornell University. Researchers are making significant inroads in the pursuit of discovering cellular origins and have recently concocted "cell-free" hydrogels from nothing but clay, saltwater and DNA.[23] The hydrogels act to confine the biochemical processes of the system and, astoundingly, transcription and translation is enhanced within them. Then, of course, there were the J. Craig Venter Institute researchers who successfully created a proliferating synthetic cell.[24] The cell was transcribed with a genome built entirely of human-made chemical parts and was designed using a computer program. The cell

22 I am grateful to Dr. Todd Eckdahl of the Missouri Western State University biology department for helping develop this concept.

23 Dayong Yang et al., "Enhanced Transcription and Translation in Clay Hydrogel and Implications for Early Life Evolution," *Scientific Reports* 3 (2013).

24 D. Gibson et al., "Creation of a Bacterial Cell Controlled by a Chemically Synthesized Genome," *Science* 329, no. 5987 (2010): 52-56.

went on to undergo mitosis several times afterward. To reiterate, it is not difficult to conceive of the test proposed above with breakthroughs such as these behind us. If researchers can bolster protein production within a solution-phase system made entirely of sea and dirt, then we are surely not far from completely artificial, fully functioning cells capable of cohesion and cooperation with their natural counterparts.

It seems clear, then, how a cellular Turing Test would be consistent with a notion of biological functionalism—that is, an entity's classification is not based on internal constitution (i.e., physical makeup) but its role, its exchanges, and its interactions with other entities. As I have just argued, HPC may then invite the same conclusion. The salient properties of cells are deeply entrenched within the lens of a discipline, and as no specific properties are necessary for property cluster kind membership, a biological functionalist may consider properties such as "ancestral lineage" or "phospholipid bilayer membrane" to be expendable. Furthermore, a functionalist may draw species boundaries as natural kinds, or, at the very least, functional kinds legitimized by HPC, that subsume both natural and synthetic entities.

IV. Objections in Defense of HPC

One reasonable rebuttal is that, if anything, the Turing Test puts forth an *essentialist* criterion for intelligence, and not one that is compatible with HPC's fluid boundaries. If the computing machine is able to fool an interrogator into thinking it is a human, it is displaying artificial intelligence. Therefore, the essential property for something to be "intelligent" is its ability to outwardly mimic understanding and thought. Conflating HPC with this reading of the Turing Test would doubtless complicate an assertion that HPC allows for functionalism, as HPC has no essentialist criterion whatsoever. In fact, HPC aims to provide the exact opposite of an essentialist criterion as a method of kinding. However, a slight reframing of Turing's criterion ought to help illuminate my intended use of Imitation Games. The salient point is not that an outward display of understanding is necessary and sufficient for something to possess intelligence, but that this is what Turing insists an intelligent being tends to demonstrate. John Searle, among others, would come to fundamentally disagree with the criterion Turing put forth.[25] If we follow this analogy in the philosophy of mind, the functionalist may agree with Turing's expectations whereas the naturalist will not. The naturalist may reply, "No, intelligence is a property of the mind, and minds are byproducts of organic material. The capacity for intelligence invariably tends toward brains housed in skulls." The naturalist, like Turing, has set forth their expectations of what properties an intelligent being tends to possess. They focus on physical composition of the agent instead of the function, i.e., the output, of the agent. The point here is that both the functionalist and the naturalist use their understandings of tendency to put forth their expectations of the

25 John Searle, "Minds, Brains and Programs," *Behavioral and Brain Sciences* 3 (1980): 417–57.

kind member. This translates quite well to our cellular Turing Test, and helps to clarify what is meant by an arbitrary disciplinary bias. The biological naturalist may deem a cell a species member by virtue of its physical composition when determining what properties the kind most frequently tends toward. Microbiology students practice this with diagnostic methods, such as Gram stains, quite frequently. However, the biological functionalist will deem a cell a species member by virtue of its function and the way it interacts with its environment. Thus, should the naturalist and the functionalist both play our biological Imitation Game, they would likely report different findings. Whether Turing had chosen his criterion as an essence or as a tendency is a semantic debate. It is certainly a debate worth having, but its outcome is irrelevant to the potency of the claim of this paper. What is most important is that Turing selectively chose a property that he found most pertinent to an agent that possesses intelligence and created a rubric from it. In a possible world where Turing had used his Imitation Game to defend a naturalist account to argue against artificial intelligence, the model would be just as effective in disputing species membership of synthetic organisms, as it rests upon the selective expectations of the interrogator.

Conclusion

To reiterate, the aim here is to ultimately force the hand of Homeostatic Property Cluster theory as a means of classifying biological taxa by using it to push a species' boundaries to the extent that it is no longer intuitively considered that species. If HPC's epistemic reliability is to be maintained in light of its subjectivity problem, it must confront the fact that a functionalist interpretation of its fluid boundaries allows it to validate individuals as species members, and therefore natural kind members, when they are intuitively not so. Its lenience does allow an escape from the strict, impractical demands of kind essentialism. In doing so, however, it allows the theorist to neglect properties such as genealogy that are otherwise seen as paramount to species membership. In a season of biological renaissance, a species' natural tendencies are nothing more than glass ceilings waiting to be shattered in research laboratories. Thus, in order to remain a viable species concept in the post-genomic era, HPC must draw clearer lines in the sand around species membership. Otherwise, to paraphrase Kendig, it has potential to claim that kinds are successful when they really are not, thus proving insufficient to meet the demands of kinding in scientific practice.

About Caleb Hazelwood

Caleb Hazelwood studies biology and philosophy at Missouri Western State University in Saint Joseph, Missouri. His research takes place at the intersection of these two disciplines, focusing on the ethical, legal, and social implications of advancements in genome editing. Caleb will attend a graduate program for philosophy in fall 2018.