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ORIGINAL RESEARCH

# Scientific progress, normative discussions, and the pragmatic account of definitions of life

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## Abstract

Discussions on the status of definitions of life have long been dominated by a position known as definitional pessimism. Per the definitional pessimist, there is no point in trying to define life. This claim is defended in different ways, but one of the shared assumptions of all definitional pessimists is that our attempts to define life are attempts to provide a list of all necessary and sufficient conditions for something to count as alive. In other words, a definition of life is a strict, descriptive definition. Against this, several pragmatic alternatives have been put forward. On these pragmatic accounts, definitions of life are not strictly, but rather loosely descriptive. Their purpose is not to be true, but to be useful to scientists by guiding scientific practice. More recently, this position has come under attack for not being able to explain how our attempts to define life are connected to scientific progress within the biological sciences. Here, I argue to the contrary by showing how pragmatic definitions of life can be, and in fact are, conducive to scientific progress. Additionally, I show how the pragmatic account of definitions of life can be brought to bear upon our normative discussions involving definitions of life.

**Keywords** Definition of life · Scientific progress · Synthetic biology · Science and democracy · Risk · Pragmatism

## 1 Introduction

There exist numerous definitions of life. Depending on our tastes, these definitions may be straightforwardly scientific (Schejter & Agassi, 1994), they may be focused on the metaphysics of properties and kinds (Diéguez, 2013), they may reinvoke vital

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categories (Mulder, 2016), and so on and so forth. This wide variety in available definitions, and particularly the absence of consensus on which definition is correct, has caused some philosophers and scientists to question our very attempt to formulate the definition of life. These 'definitional pessimists' have argued that our attempts to define life are premature, arbitrary, useless, impossible in principle, or even potentially harmful to scientific progress.[1] As a consequence, we are better off not formulating definitions of life at all.

There has been significant pushback against this claim. Various authors have argued that definitions of life should not be understood as strict, singular definitions, but are instead to be understood as loose, pluralist definitions that are at their core pragmatic (Bich & Green, 2018; Dupré & O'Malley, 2009; Knuuttila & Loettgers, 2017; Pennock, 2012). Understood in this way, there is no need for definitional pessimism because the point of our attempts to define life is not to converge onto the universal, final definition. Instead, definitions of life guide scientific practice in some important way. Recently, however, Alba Amilburu, Álvaro Moreno, and Kepa Ruiz-Mirazo (2021) have argued against such a pragmatic understanding of definitions of life. Although they present a variety of problems, their primary complaint is that a pragmatic account cannot help us to explain how these definitions contribute to scientific progress in the biological sciences.

In this paper, I do two things: First, I argue that the pragmatic account of definitions of life *can* be meaningfully connected to scientific progress in substantial parts of the biological sciences. Second, I argue that the pragmatic account of definitions of life shows a particularly good fit with our normative questions about life and its status. This is something that has not yet been put forward explicitly and which has been overlooked in the critique of the pragmatic approach by Amilburu and co-authors.

The structure of this paper is as follows: In Sects. 2 and 3, I present the template argument for definitional pessimism, the arguments of its various proponents, and the pragmatically optimistic alternative. In Sect. 4, I examine the recent critique by Amilburu and coauthors that the pragmatic approach is insufficient to explain or safeguard scientific progress. In Sect. 5, I show how the pragmatic approach can be meaningfully connected to scientific progress and I show several examples of this connection from our current, best science. Moreover, in Sect. 6, I show how the pragmatic account of definitions of life can be fruitfully extended to our normative discussions. Finally, in Sect. 7, I briefly summarize the case in favor of the pragmatic approach to defining life and I argue that the current discussion runs the risk of becoming repetitive if the focus remains on what definitions life should or should not be, instead of what they can or cannot do.

[1] Smith (2016) was the first to view those denying the possibility of defining life as a group: the definitional pessimists.

## 2 Definitional pessimism

While the arguments brought forward against definitions of life vary both in their premises and their conclusions, they share a common form. Usually, the argument runs as follows: definitions of life are either useless, arbitrary, impossible (in principle), harmful to progress in the natural sciences, premature, or some combination of these. If some human activity is either of these things, then it cannot or should not be pursued. Thus, scientists and philosophers cannot or should not try to define life. Call this the argument for *general definitional pessimism*:[2]

*The Template Argument for General Definitional Pessimism*

(1) All definitions of life have at least one of the following characteristics, they are:

a. *arbitrary*
b. *useless*
c. *impossible in principle*
d. *harmful*
e. *premature*

(2) If definitions of life have at least one of the characteristics (a) through (e), then we cannot or should not (yet) define life.

(C) We cannot or should not (yet) define life.

Let us look at how these characteristics have been understood by various definitional pessimists. Edouard Machery (2012) has argued that trying to define life is either arbitrary or impossible. Per Machery, anyone intent of defining life is confronted with a dilemma. When discussing life, we are either discussing the folk concept or the scientific concept. If we are discussing the folk concept, then we run into a dead end because folk concepts are not formal definitions and folk concepts have no place in science. If instead we are discussing the scientific concept, then definitions of life are either impossible or arbitrary. Machery's primary reason for claiming that definitions of life are impossible is that the various disciplines studying life come up with seemingly irreconcilable definitions. This means, in turn, that we can only define life if we allow our definitions to be discipline specific. However, on a discipline specific view,

[2] *General definitional pessimism* can be contrasted with *historical definitional pessimism*. Historical definitional pessimism departs from the observation that there has been a tremendous effort to formulate the definition of life, with over a hundred possible candidates having been proposed, so far without success (cf. Popa, 2004). When this historical observation is combined with pessimistic induction, the historical definitional pessimist arrives at the conclusion that, given our complete lack of success, our future chances of success are small at best. Agnosticism may seem to be a way out of this situation, but the historical definitional pessimist could argue that the burden of proof for the claim that we *can*, at least in principle, define life lies squarely with those attempting to formulate such a definition. On the historical approach, in absence of a convincing definition, we may well resort to pessimism.

we would no longer be talking about 'The Definition of Life' but merely about one possible definition amongst many. Hence, every definition of life would be arbitrary.

Taking a more linguistic approach, Jiri Benovsky (2017) has argued that formulating the definition of life is impossible in principle. Per Benovsky, the only way for a phrase such as 'is alive' to be predicable of some object is for this phrase to refer to a genuine property. Benovsky does not provide an explicit definition of what constitutes a 'genuine property', but he does provide examples of what he believes to be genuine properties such as 'having a positive charge' or 'being round', but also 'being able to talk' or 'being able to play the violin' (2017: pp. 4–5). We can gleam three important characteristics of genuine properties from Benovsky's text: (i) they are independent of our thinking, i.e. *x* is a property of some object in the world; (ii) they are straightforward and non-controversial, i.e. there is a test we can do to show that some object has property *x*; (iii) they are not vague, i.e. property *x* is a definite metaphysical property of some object. However, according to Benovsky, and in reverse order, 'is alive' is (iii) a linguistically vague concept that is extremely sensitive to extant borderline cases; (ii) it is not straightforward and non-controversial in the sense that there is no test we can do that clearly shows that something is alive; and (i) it is not independent of us in the sense that 'is alive' is a linguistic property and not a metaphysical one. The upshot, according to Benovsky, is that 'is alive' is a human fiction that is misapplied to a range of different objects. This leads Benovsky to defend an eliminativist view of life. Rather than trying to define life, we should be looking at the much more specific and scientifically interesting genuine properties of living things.[3]

Scientists have also expressed their pessimism when it comes to defining life. According to biologist and Nobel laureate Jack Szostak (2012), defining the boundary between life and non-life is an arbitrary endeavor. In the end, scientists are only interested in understanding the physical and chemical processes of life. As Bich and Green have argued, Szostak develops his view of definitions of life specifically within the context of the transition of chemical processes to biological life, leaving some room for scientists to use definitions as tools (Bich and Green, 2018: footnote 13). Nevertheless, Szostak does maintain that he has "not seen that efforts to define life have contributed at all to [our understanding of the transition of chemistry to biology]" (Szostak, 2012: p. 600). Thus, the space he leaves for a pragmatic understanding of definitions of life in terms of their usefulness seems limited at best.

Rob Hengeveld (2011) has expressed a similar view: "When, as a beginning ecologist, I was studying ground beetles, and later as a biogeographer, I never felt any need for a definition of life." (2011: p. 324). He supports this view with an argument from analogy: we do not need a definition of the Moon to understand its origin, hence we do not need a definition of life to understand the origins of life either. Moreover, Hengeveld thinks a focus on definitions of life may be harmful to our understanding of life as it constrains our scientific thinking. By focusing on some fixed, eternal definition we might miss important observations or new avenues of research.

[3] There is a lot to be said against Benovsky's account, as he involves several complicated and hotly debated issues into a dense argument. However, discussing these issues in detail falls outside the scope of this paper.

This last point has also been voiced by Carol Cleland, who has argued that definitions of life are potentially harmful but certainly premature (Cleland, 2012, 2013; Cleland & Chyba, 2002, 2010). Our current attempts to define life are premature because we lack an adequate scientific theory of life, much as we once lacked the molecular theory needed to define 'water' as '$H_2O$'. If we have no scientific theory of life with which we can adequately identify living things, then there is no sense in trying to answer the question 'What is life?' in any definitive way, just as there was no sense in answering the question 'What is water?' before the development of molecular theory. This problem is exacerbated by the nature of the sort of definition that a definition of life needs to be. Our search for a definition of life is a search for an 'ideal definition' (2010). This is a list of necessary and sufficient conditions for something to qualify as alive. But ideal definitions are not well-suited for identifying categories carved out by nature without backup from a scientific theory. An ideal definition of life is only useful if there is an actual scientific concept behind the term 'life'. Currently, such a concept embedded in a theory is lacking because the only examples of life that we know of are carbon-based and Earth-bound. We know nothing about life in the rest of the universe, which might be completely different from life on Earth. Together, these issues prevent us from formulating a proper definition of life. What is more, our attempts to define life might even harm our scientific understanding of what life is, as they might prevent us from keeping an open mind when scouring the Earth and other planets for weird signs of life (2012: pp. 140–143).[4]

## 3 From definitional pessimism to pragmatic optimism

Although each of the accounts presented above has plenty of individual points to object to, there is a general objection that can be brought against all of them. In each case, it is assumed that the only definition of life that could satisfy scientists and philosophers is a *strict descriptive definition*.[5] A strict descriptive definition of life is a list of the necessary and sufficient conditions for something to count as alive – or one that demarcates all cases of life from all cases of non-life. Given how elusive this list has proven to be, it is not surprising that a fair few philosophers and scientists have embraced some form of definitional pessimism. But there is an alternative. Instead of our definitional efforts being aimed at finding the universal, strictly demarcational definition of life, attempts to define life should be understood as a means to reach the scientific goals that are deemed relevant by a community of scientists (cf. Dupré

[4] In more recent work, Cleland has suggested that, although definitions of life are out of bounds, we can formulate tentative criteria for describing life (2019). Crucially, tentative criteria for life might help us identify anomalies that do not sufficiently resemble Earth life and would otherwise be misunderstood to be abiotic. In this way, tentative criteria can help us to find and identify weird signs of life on other planets. The distinction between tentative criteria and definitions of life has also been discussed briefly in Bich and Green (2018) and Bains (2014). For a more extensive discussion, see Griesemer's (2015) suggestion of a heuristic, engineering-inspired approach, where models of life are proposed in terms of tentative criteria that can have a theoretical or empirical basis.

[5] In Cleland and Chyba (2010: p. 329–330), these are called 'ideal definitions', while Bich and Green (2018, p. 3941–3943) call these 'strong definitions'.

& O'Malley, 2009). Definitions of life are *loose descriptive definitions*. This attitude leads us to a pluralist view of definitions of life (Pennock, 2012). Definitions serve a functional purpose, for instance by guiding scientific practice (Bich & Green, 2018), or by facilitating communication between the various disciplines studying life (Knuuttila & Loettgers, 2017). Accounts such as these show that definitions of life can have a function in scientific practice and, consequently, that general definitional pessimism is not as warranted as it might seem.

Robert Pennock has offered one of the earlier defenses of such a pragmatic, pluralist approach to defining life (2012). Pennock argues that life is complex phenomenon that defies straightforward definition. Rather, our continued discussions about the nature and definition of life are a consequence of the causal and pragmatic considerations that are relevant to these discussions. To arrive at this conclusion, Pennock makes use of an insight from Darwin that there is no definite difference maker between biological 'species' and 'varieties', combined with the Wittgensteinian notion that our language is an instrument not aimed at ultimate description but at understanding relative to the game that is being played. Taken together, Pennock contends these considerations lead us to a kind of realist pluralism, where our definitions of life are guided by empirical and theoretical scientific considerations, but where multiple definitions are possible and their content depends on our theoretical interests.

More recently, Leonardo Bich and Sara Green (2018) have observed that definitions of life are usually derived from a particular experimental context and that these definitions are connected to specific theoretical models. This is particularly clear in biological subdisciplines such as synthetic biology and astrobiology. They propose an operational account of definitions of life where these "coherently combine, or integrate into a theoretical model, a set of mutually dependent *necessary and satisficing criteria* for life that imply observable operations, and that are considered pertinent and relevant for research." (2018: pp. 3934–3935) Here, 'necessary criteria' do their usual job of specifying the minimal requirements for class-membership, while 'satisficing criteria' represent "the minimum requirements necessary to achieve a certain goal." (2018: p. 3934) In other words, a satisficing condition is a sufficient condition given a certain perspective that suits the scientists' aim and approach. Thus, the value of definitions of life can be found in their role in scientific practice.

In a similar vein, Tarja Knuuttila and Andrea Loettgers (2017) have provided a detailed account of the various functions definitions of life can serve in scientific research. While they do not fully deny the value of strictly classificatory approaches, they argue that definitions of life can serve many different purposes, most notably as transdisciplinary and diagnostic definitions.[6] Each of these has a different function. Transdisciplinary definitions are interest-dependent definitions formulated by communities of scientists coming from different disciplines. An example would be the (unofficial) NASA definition of life: "Life is a self-sustaining chemical system capable of Darwinian evolution." (2017: p. 1194) This is a vague and general definition,

[6] Knuuttila and Loettgers also consider theoretical definitions, which "seek to align theories and theoretical concepts from different disciplines" in a way that is different from transdisciplinary definitions by taking a (disciplinary) concept as their point of departure (2017: p. 1187). But these are less relevant to my current argument.

but that is precisely what allows scientists with different backgrounds and different understandings of key notions such as ‘self-sustaining’ and ‘evolution’ to communicate effectively.[7] Diagnostic definitions, on the other hand, are not about effective communication but about providing instruction. Looking at the case of biosignatures on exoplanets, a diagnostic definition is one based in part on what data can be acquired from actual measurements on exoplanets. This is mostly spectral data, and a minimal, diagnostic definition of life accommodates this fact by focusing on gaseous molecules that we would expect to be produced by any form of carbon-based life.

We might suspect at this point that the debate on the status of definitions of life is in reality a debate on the status of definitions. After all, if we agree with the definitional pessimists that definitions of life should be strict descriptive definitions, then we would believe that the final definition of life can never be obtained. However, the definitional pessimists are not merely arguing or assuming that definitions of life are strictly descriptive. Ultimately, they argue that attempts to define life are premature, arbitrary, useless, impossible, and potentially harmful *tout court*. There is very little room, if any, in scientific debate for attempts to define life. This claim is far from trivial and moves far beyond the claims that a definition of life only makes sense if it is a strict definition and if strict definitions are possible.

## 4 Problems with the pragmatic account

The accounts of Bich and Green and Knuuttila and Loettgers have an explicitly pragmatic character. They show successfully that general definitional pessimism is unwarranted because definitions of life are relevant to the practice of biological research.[8] In a recent publication, Amilburu, Moreno, and Ruiz-Mirazo (2021) argue that pragmatic accounts do not go far enough in showing the value of definitions of life to the biological sciences. They claim that definitions of life are not merely helpful tools in scientific practice, but necessary for progress. Crucially, a pragmatic definition of life cannot lead to demarcation – of life from non-life, or biology from non-biology – nor to further unification of biology and, as such, it cannot help us in “our understanding of what life actually is”, nor can it “foster the global advance of the biological sciences” or a route towards “asymptotic targets in the scientific horizon of the life sciences” (2021: pp. 10580–10581). One of the assumptions behind this critique is that the biological sciences must be unified and must revolve around demarcation. But it is unclear why this has to be the case. Biologists have been very successful in explaining all manner of things about living creatures without a unified theory of biology. Moreover, demarcational issues have not prevented biologists,

[7] Bich and Green make a similar point when discussing the work of Szostak and Luisi, as “Definitions not only specify individual research trajectories, but also facilitate collaborations and intersections between different perspectives” (2018: p. 3928).

[8] The pragmatic account of definitions of life is not only capable of assuaging the worries of the general definitional pessimist, but also of the historical definitional pessimist. Formulating definitions of life is not a matter of success, but a matter of usefulness. Or, alternatively, it is a matter of success only in terms of usefulness.

chemists, and physicists from fruitful collaboration and great discoveries about the inner workings of life.[9]

Two further problems of the pragmatic account, per Amilburu and co-authors, relate to comparisons between different research programs and to the question why definitions of life are as controversial as they are.[10] Regarding the comparison of different research programs, they argue that pragmatic definitions of life hinder the comparative analysis of different research programs because they lead us to regard each research program in isolation. However, as has been shown by Knuuttila and Loettgers (2017), the pragmatic approach to definitions of life actually allows us to transcend research programs and disciplinary boundaries by facilitating communication between scientists. Regarding the meta-question, Amilburu and co-authors claim that the pragmatic account of definitions of life cannot help us explain why attempts to define life are difficult and controversial. But as I have argued above, the difficultly of defining life comes only when we insist on definitions of life being strict descriptive definitions, and thus when we misunderstand their function. This also neatly explains the controversy, as definitions of life are controversial only if we mistakenly believe that there is a strict descriptive definition of life to be had. But such a definition cannot be had and so (virtuous rather than vicious) controversy goes on indefinitely.

Nevertheless, Amilburu, Moreno, and Ruiz-Mirazo are correct in noting that there is currently no direct theoretical connection between the pragmatic account of definitions of life and the notion of scientific progress in the biological sciences. In the next section, I show how a pragmatic understanding of definitions of life can be meaningfully connected to progress in a substantial part of the biological sciences. I submit that attempting to define life, understood pragmatically, is a worthwhile endeavor because it is directly or indirectly conducive to scientific progress in the biological sciences.

## 5 The pragmatic account and scientific progress

The central aim of science is generally taken to be something along the lines of 'generating new knowledge about the (material, natural) world', or 'improving our explanations of why things happen the way they do in the world', or more broadly 'fostering understanding of the world'.[11] Whatever purposes individual scientists might have for doing research, as a whole science is supposed to increase our understanding of things such as circadian rhythms, the elementary particles of the Standard Model, cloud formation, and the effects of pesticides on microbial ecology. When-

[9] How one looks at demarcation also has implications for the evaluation of results in relation to definitions of life and scientific progress. For an account that seeks to develop this relation along the pragmatic account presented in Bich and Green (2018), see Bich (2020).

[10] The latter of which has been called the 'meta-question' in Bedau (2012).

[11] See, for instance, Khalifa (2017) and De Regt (2017, 2020). I am here invoking something similar to Popper in his *Objective Knowledge*: "it is the aim of science to find *satisfactory explanations*, of whatever strikes us as being in need of explanation", as quoted in De Regt (2020: p. 922).

ever our understanding of these sorts of phenomena or entities increases, there is progress in science.

Generally speaking, there are two broad perspectives on scientific progress, which we may call *convergent realism* and *scientific pragmatism*.[12] For the convergent realist, scientific progress primarily consists in our theories and explanations becoming more and more true (Niiniluoto, 1987, 2011), or it consists in our knowledge becoming more and more complete (Bird, 2007, 2010). When some event or action is conducive to scientific progress, it is so by directly or indirectly leading to a theory or explanation with a higher verisimilitude, or by improving our knowledge of some part of the natural world. For the scientific pragmatist, scientific progress primarily consists in our scientific theories and models improving our abilities for prediction and control, or more broadly our ability to intervene in the world (Chang, 2007; Douglas, 2014). Thus, when something leads to scientific progress, it does so by directly or indirectly leading to a theory or model which has a higher predictive power or permits us more control over this or that part of the universe. None of this is to say that on a convergent realist perspective there is no place for prediction and control, nor that on a pragmatist perspective there is no place for truth and knowledge. Rather, these perspectives each place different concepts at the nexus of our understanding of scientific progress.

On my view, definitions of life ultimately do not derive their value from *counting as* scientific progress, but from being *conducive to* scientific progress. On the strict account, for some generation of definitions $D_n$, the next generation $D_{n+1}$ adds or removes definite properties of life to or from our list, thereby capturing progress in our understanding of life in a definite and direct way. That we have made progress in understanding life is captured – although not necessarily exclusively so – in each improved generation of definitions. On the pragmatic view, however, progress is captured not by definitions themselves being more correct, but by the extent to which they can aid in prediction and control.

This view is in principle compatible with both convergent realism and scientific pragmatism, albeit in different ways. If a pragmatic definition of life leads to more knowledge of bacterial infections, or the biophysics of the cytoplasm, or aquatic ecology, then it has a role to play in a realistic account of scientific progress. This is possible so long as the effect is entirely indirect, where it does not matter whether a definition of life is itself true or false. Alternatively, if a pragmatic definition of life leads to a better treatment of bacterial infections, or increased productivity in a bioreactor, or better capabilities to remove pollutants from aquatic environments, then it has a role to play in a pragmatic account of scientific progress. Of course, here the effect would be direct.

While pragmatic definitions of life fit both a realist and a pragmatist perspective on scientific progress, from a conceptual point of view they fit more naturally with the pragmatist perspective. Those who favor a pragmatist perspective usually want

[12] I want to avoid using the label 'anti-realism' for the view presented here, because this implies that realism – or the centrality of the concept of truth to science – is the standard view. That might be true from a historical point of view, but I reject this from a normative one. The point of the non-realist and the authors mentioned here – at least as I read them – is not the rejection of truth but the elevation of practice.

to stay away from convergent realism because they see all sorts of problems regarding the theory-ladenness of observation (Chang, 2007; Regt, 2017), the nature of objectivity (Douglas, 2004), and the myriad of roles played by epistemic and non-epistemic values in science (Douglas, 2007; Hicks, 2014). Science is not ultimately about truth or final knowledge, but about the use of scientific theories and models in societies.

Here, the account presented by Heather Douglas (2014) is a particularly good fit with my own. Douglas argues that it is difficult to see that science is overall a progressive undertaking if we make a sharp distinction between the truth-and-knowledge-*producing* pure sciences and truth-and-knowledge-*using* applied sciences. According to Douglas, on such a view, any Kuhnian-type revolution – such as the transition from the classical physics of the 19th century to the modern physics of the 20th century – destroys the purely scientific foundation that applied science is built upon, as well as our teleological hopes for progress. But with this distinction removed, Douglas argues that:

> …scientific progress can be defined in terms of the increased capacity to predict, control, manipulate, and intervene in various contexts. This is the kind of success that translates well across paradigms, that is rarely lost with theoretical change, and which matters greatly to both scientists and the public. […] Theories or paradigms may come and go, but the ability to intervene in the world, or at least predict it, has staying power (Douglas, 2014: p. 62).

When we apply this view to pragmatic definitions of life, these can be understood as promoting scientific progress by improving our capabilities for prediction and control.

For a detailed example, we can look at the role played by loose definitions of life in state-of-the-art research in top-down synthetic biology. Over the past twenty years, scientists at the J. Craig Venter Institute (JCVI) have managed to construct a series of minimal cells with a minimal genome, which can nevertheless grow and divide (Gibson et al., 2010; Glass, 2012; Hutchison et al., 2016). In the construct JCVIsyn3.0, they have reduced the genome of *Mycoplasma mycoides* from 985 protein encoding genes to a mere 473 protein encoding genes and inserted it into a genome-less *Mycoplasma capricolum* shell without losing the capacity for growth and division.[13] Many of the genes present in the 473-gene minimal genome are involved in crucial cellular processes such as metabolism (17%), cell membrane structure and function (18%), and expression and preservation of genomic information (48%). Interestingly, 79 genes (17%) of the minimal construct had an unknown function at the time of publication.[14]

[13] For comparison, the ubiquitous model organism *Escherichia coli* has about 4100 protein encoding genes, compared to roughly 20.000 in humans and chimpanzees (cf. Milo & Phillips, 2016).

[14] This example of research at the JCVI constitutes a clear case of scientific progress. We now know that the minimal lower limit of protein encoding genes necessary for viable life – loosely defined in terms of growth and division – is 473 genes. Moreover, we also know which genes these are and that some of these genes have unknown functions while still being essential. Finally, the ability to manipulate genome-sized fragments of DNA can find applications in top-down and bottom-up synthetic biology, as well as biotech-

The spectacular reduction in the number of genes required for life-like behaviour has been an explicit aim of the scientists working at the JCVI. As senior scientist John Glass wrote in an account detailing the history of creating JCVIsyn1.0: "[now that JCVIsyn1.0 has been constructed] we will start trying to figure out exactly how this minimal organism free from all redundancies is capable of life." (Glass, 2012: p. 485) Thus, the aim of the JCVI project is twofold. On the one hand, it is a technical challenge aimed at efficient and effective chemical synthesis and transplantation of large genomes. On the other hand, it is about finding the lower boundary of life through the identification and removal of non-essential genes.

It is the second aim that is important for present purposes. It raises the question 'When are genes essential?' The answer to this question betrays the importance of definitions of life in top-down synthetic biology. Essential genes are those genes that are necessary for autonomous self-replication by growth and division (Gibson et al., 2010; Hutchison et al., 2016). Although the focus on growth and division is an explicit choice made by the authors, they do not put this description forward as an explicit, strict descriptive definition of life. Instead, it functions as what I have described as a loose descriptive definition, namely as a means to reach at least two worthwhile scientific goals, that of genome reduction and manipulation. This guides their choice of which genes might be good candidate genes for deletion from the genome without growth and division being threatened. Thus, the conception of life of Gibson, Hutchison, Glass, and their many co-workers directly guides their research. Genes that would otherwise be crucial in the evolutionary and environmental context of *M. mycoides*, but that are not important within the laboratory environment, are not considered essential. There are no temperature fluctuations, droughts, substrate shortages, bacteriophages, and a host of other variables and general threats for bacteria to worry about inside the safety of the scientist's incubator. This means any gene involved in those processes is a potential candidate for elimination.

One Cleland-style worry we could have about this example is that, rather than leading to scientific progress, a definition-specific distinction between essential and inessential genes could actually lead to bias, entrench misconceptions, and thereby cause us to miss potentially dangerous synthetic cell-environment interactions. This would indeed be the case if the loose definition employed at the JCVI was adopted by the synthetic cell community at large, but the point of the pragmatic account is precisely that no definition should be adopted by the entire community.[15] Different, smaller research communities within synthetic biology will take different loose definitions of life as their starting point. It is precisely this diversity in views that should prevent a monist view of synthetic cell-environment interactions from becoming entrenched. For instance, contrary to the JCVI approach, part of the bottom-up synthetic biology community takes evolution to be the foremost feature of life around

nology more broadly (cf. Olivi et al., 2021). This should satisfy both the realist's and pragmatist's view of scientific progress.

[15] Moreover, the fact that 17% of the genes that turned out to be essential for growth and division had an unknown function is a *prima facie* reason to believe that definitions do not make us blind to the unknown. In this case, it very much revealed unknown but important genes for growth and division.

which a research strategy should be formulated (cf. Abil & Danelon, 2020).[16] These sorts of differences should ensure a broad spectrum of approaches to understanding synthetic cell-environment interactions, as I argue more extensively in Sect. 6.

Another possible point of critique would be that any example from synthetic biology falls short of proving how definitions of life can be conducive to scientific progress in biology in general, simply because synthetic biology is too far removed from biology proper. At its broadest, biology includes fields as diverse as virology, ethology, evolutionary biology, molecular cell biology, and marine biology. Definitions of life are not equally important in each of these fields. The ethologist studying breeding behavior in arctic foxes will have little need to consider whether these foxes are alive, and what that means (cf. Hengeveld, 2011). However, the fact that definitions of life are not equally important in all of biology does not entail that these definitions are not important in a significant part of biology. As a biological subfield becomes more focused on the molecular workings of life at the smallest scale – and its object of study moves closer to boundary cases of life – definitions of life become more important. This applies to a wide range of (often more interdisciplinary) biological subfields including synthetic biology, origins of life (OoL) research, astrobiology, and molecular evolutionary biology.[17] It should not surprise us that definitions of life are most important in those parts of biology where we are least sure about whether we are talking about life, and what that means.

To add further weight to the proposed relationship between pragmatic definitions of life and scientific progress, we can look at an additional example from origins of life research. The key question in origins of life field is how abiotic chemistry could have given rise to biological cells. Similar to the JCVI case, the definition of life that a group of scientists adopts has a great influence on the kind of research that will be pursued. For instance, the work of Jack Szostak and Sheref Mansy revolves around the following two conceptual requirements for life: life requires (i) a definite unit of selection and (ii) a method of information transmission. Their research explores the likely molecular instantiations of these requirements, namely lipid compartments and a RNA-based storage and replication system (Joyce & Szostak, 2018; Mansy, 2010). In one of the early, landmark papers, Mansy and Szostak have created lipid compartments that can take up and incorporate individual ribonucleotides into an encapsulated RNA molecule (Mansy et al., 2008). These initial results have helped initiate a bourgeoning field investigating the biochemistry of lipid vesicles and catalytic RNA.[18] Crucially, what counts as progress in this field is not ultimately dependent on

[16] Recent years have seen the inception of multiple different programs aimed at bottom-up synthetic cell construction. Examples are the ‘Building a Synthetic Cell’ (BaSyC) program based in the Netherlands, as well as Max Planck Research Network in Synthetic Biology (MaxSynBio) based in Germany. Generally, these programs are aimed at concrete synthesis of a synthetic cell from smaller part – e.g. proteins, fatty acids, synthetic genomes, or cell extracts – that resemble bacterial cells. As with the top-down synthetic approach, attempts at bottom-up construction raise a similar question: When does a synthetic cell construct resemble a natural cell – i.e., one that is the direct product of natural evolution – closely enough? The answer to this question has great influence on what research path is pursued.

[17] Recent examples used in discussions on the definition of life tend to come from one of these fields (Bich & Green, 2018; Cleland, 2019; Knuuttila & Loettgers, 2017).

[18] For examples, see (Strulson et al., 2012), (Lai et al., 2021), (Peng et al., 2022), and others.

whether the loose definition of life that can be found in the work of Szostak, Sheref, and others is correct. Rather, from a pragmatic perspective, it is enough that this loose definition leads to scientific progress, i.e. a tangible increase in our understanding of and control over the biological world.[19]

## 6 Pragmatic definitions of life and normative discussions

The discussion on the status of definitions of life has mostly been focused on the metaphysical possibility of these definitions on the one hand, and on the epistemic value of these definitions to a scientific understanding of life on the other. This focus is easy enough to understand but it does obscure the fact that definitions of life do not only have epistemic and metaphysical roles to play, but also societal, political, and ethical ones. In what follows, I present two examples of how a pragmatic, pluralist understanding of definitions of life leads to a more fruitful understanding of the roles these definitions can play. One such discussion is on embedding synthetic biology in modern democratic societies, and the other is on the risks involved in this type of research. Through these examples, I want to call attention to a possibility Amilburu and co-authors (2021) do not seem to consider, namely, that the value of the pragmatic approach does not rest with scientific progress alone, but also with a kind of moral progress.

(1) *Pragmatic definitions in democratic societies*: One of the more influential and extensive accounts of the relationship between science and society has been presented by Philip Kitcher (2011). Kitcher's account departs from the observation that modern science is facing a legitimacy problem. Well-established scientific theories are doubted by a significant and vocal portion of the population of Western societies. His own examples are the acceptance of climate science and evolutionary biology, but a more recent example would be COVID and vaccine skepticism. While Kitcher investigates multiple sources of this legitimacy problem, he traces an important source back to the tension between the division of epistemic labor that is required for modern science to function and the democratic promise inherent in any widely democratic society that every perspective is taken along, in some relevant sense, in our shared decision making. Once a complicated albeit well-established scientific theory clashes with the broad value system of part of the population, but is nevertheless adopted as the primary support for policy, conflict arises. In Rawlsian fashion, Kitcher argues that these conflicts can be resolved through the pursuit of what he calls "*well ordered science*: [where] science is well ordered if its specification of the problems to be pursued would be endorsed by an ideal conversation, embodying all human points of view, under conditions of mutual engagement". (Kitcher, 2011: p.

[19] Interestingly enough, although Szostak is one of the scientists who is skeptical about the use of definitions of life (see Sect. 2), his own work shows how these definitions can have pragmatic value. As a side note, various prominent members of the OoL field have recently put forward a position paper in which they argue that divisions in the field due to differing theories about the origins of life are beginning to disappear, allowing space for new perspectives on, and approaches to, origins of life research (Preiner et al., 2020). This more general trend fits with the pragmatic view defended here, where definitions serve to offer new perspectives and approaches as needed by a scientific community.

42) If every group involved is willing to give up on their respective claims to objective truth at least temporarily – whether this objective truth is scientific, religiously revealed, or of some other sort – then we have the best chance of coming to a shared understanding and a shared basis for decision-making.

Although Kitcher's account is far richer and more detailed then has been explained here, and although I do not agree with all of the specifics, his approach of putting democracy in the role of mediator between specialist science and wider society seems to me the right one. The strength of this approach lies in how it deals with the kind of science that is well-established, complicated, and what we might call 'conflict-bearing', where a scientific theory is conflict-bearing if it is perceived by some group to conflict with their broad value system, leading to the rejection of the scientific theory in favor of that broad value system. By not rejecting or excluding either a scientific theory or a broad value system *a priori*, nor for that matter, any other methodology or perspective, well ordered science creates the space for different groups to find common ground.

But the above does not just apply to *well-established*, complicated, conflict-bearing scientific theories. I contend that it can also be applied to *unestablished*, complicated, conflict-bearing scientific concepts and definitions – that may or may not be part of a wider theory – such as a definition of life. Definitions of life are unestablished in the sense that there is no single, commonly accepted definition, they are certainly complicated, and they are conflict-bearing in much the same way as evolutionary biology. Even in Western societies, there are several actual and potential conflicts we can identify. For instance, there is a conflict with revealed knowledge about the creation of life. Definitions of life tend to be formulated in natural scientific terms and without any mention of intelligent design. Similarly, they are difficult to unify with the notion that certain living beings have souls, where 'soul' should be understood along broader spiritual lines. Typically, definitions of life are consistent with a kind of methodological naturalism that leaves no room for non-natural, spiritual entities such as souls. For a more down-to-Earth example, naturalist definitions of life conflict with the assumption that life is somehow a special phenomenon which resists reduction of the naturalist or physicalist sort. In each of these cases, insistence on a single, true definition of life is bound to clash with broad value systems in line with the three examples above.

If we adopt Kitcher's account, then it seems that insistence on finding *the* definition of life, as well as denying that defining life is worthwhile at all, are both out of place. The former insistence is out of place because it is apt to worsen the legitimacy problem of modern science. Insisting that there is only one, true definition of life takes away the possibility of finding common ground with those who hold radically different value systems that clash with this definition. Viewing definitions of life as worthless is equally detrimental, because conceptions of what makes something alive, and what that means, are central to discussions on the value of life and living beings (Boldt, 2013; Persson, 2021). Rather, what counts as an adequate definition of life depends on what we take to be relevant for that definition, which is primarily informed by practical and discipline-specific considerations. This pluralist perspective meshes well with the notion of well-ordered science. It allows for embedding both scientific and value considerations in our discussions about or involving biological life. Leaving such issues unresolved is not an option, nor can we resolve them purely scientifically, as if there were epistemic deficits in the general population that simply need correction. Opting for a pluralist view of definitions of life provides the clearest path to the resolution of these issues.[20]

(2) *Pragmatic definitions, synthetic life, and risk*: One of the chief risks of scientific research is unpredictability. This applies in particular to research in biotechnology and synthetic biology. It is not just unpredictable how synthetic life forms and the knowledge that is required to create them are going to be used, but it is also unpredictable how a particular synthetic construct itself is going to behave. Synthetic cells of sufficient complexity would have, quite literally, a life of their own, one that is characterized by a myriad of complex cell-cell and cell-environment interactions that are difficult if not impossible to map exhaustively. Part of the problem is that synthetic life would lack much of the natural evolutionary history that normally results in a stable fit between an organism and its biotic environment, making accurate predictions about behavior difficult (Bedau & Larson, 2013). Moreover, a reductive view of life could constrain how we think about the synthetic cell-environment interaction. Because of life's complexity and unpredictability, research in synthetic biology carries the risk of unforeseen consequences.

These risks can be partly anticipated by being as specific as possible about the molecular make-up of whatever synthetic cell we have created. However, I contend that a singular definition of life increases the risk of missing synthetic cell-environment interactions. My argument is somewhat analogous to Cleland's (2012) argument that insisting on a singular definition of life decreases our chances of finding alternative forms of life. Cleland argues that so long as a unifying, scientific theory of life is absent – as she believes is currently the case – we should not search for alternative life forms based on its resemblance to our favorite Earth-life characteristics alone, but also based on how they might "deviate from it in provocative ways" (Cleland, 2012: p. 141). Similarly, if we take some conceptual characteristic of life as the defining feature of a synthetic life form, we are more likely to miss potential synthetic cell-environment interactions that are not seemingly a direct consequence of whatever set of characteristics we have taken to be central to our synthetic cell. A pragmatic, pluralist attitude towards definitions of life can reduce this risk by not forcing our thinking down a particular path.[21]

For an example of how a monist approach within the life sciences may constrain our thinking, we can look at the history of virology. The first effective antidote to a viral infection, cow pox, was confirmed by Edward Jenner by the end of the 18th century (Jenner, 1802). Strikingly, Jenner was able to confirm the efficacy of his

[20] Of course, all of this is on the assumption that Kitcher's account of the relationship between science and democratic society is by and large correct. Also, to the hard-line realist or rationalist, I may be putting the proverbial cart before the horse: religious or vitalist or other forms of non-natural thinking have no place in discussions on the definition of life anyway, so that cannot be a reason why pragmatic definitions of life are sensible or useful. Nevertheless, where science and values clash, as is the case with defining life, I contend that pragmatic definitions are more likely to help us find solutions to the clash.

[21] See Sect. 5. Also, where Cleland believes that our open attitude is temporary, at least provided that we manage to formulate an adequate scientific theory of life, I believe that this attitude may well be permanent.

vaccination approach long before even the germ theory of disease was formulated. When it comes to viruses, it would take until the early 20th century before a comprehensive scientific theory of viral infections could be formulated and treatments could (slowly) be developed (Burrell et al., 2017). One important reason for this is that viruses are too small (~30 nm) to observe using conventional light microscopy and thus – unlike the much larger bacteria (~1–2 μm) – it was more difficult to confirm their existence and causal relationship to disease. Proof of this difficulty can be found in the formulation of the famous and influential Henle-Koch's postulates at the end of the 19th century (Ross & Woodward, 2016). One of the postulates specifies that the causative agent of disease must be isolated as a pure culture, which works well for bacteria, but it does not work for viruses as these require host cells to replicate.[22] The discovery of bacteria as the causal agent of infection had locked in the idea that infectious microbes must be able to self-replicate autonomously. While physicians and biologists at the time were aware that diseases existed that did not fit the Henle-Koch's postulates, and while effectively invisible microbial causes were proposed, it is likely that the slow progress in virology since Jenner can be attributed in part to the dominance of much more autonomous bacteria in thinking about infectious disease.

This example is not so much an example of risk that was overlooked, but instead of an opportunity for understanding disease and preventing harm that was missed due to a monist approach to microbial life. A microbial cause of disease became synonymous with being an autonomous, single-cell bacterium. In the case of synthetic cells, if we insist upon a particular set of characteristics as the defining feature of such cells, we are equally liable to miss important interactions, thereby increasing the risk of unforeseen consequences. Here, it helps to have a wide understanding of what makes a particular synthetic cell alive in order to gain a deeper understanding of its potential capabilities and the potential risks involved.

## 7 Concluding remarks

When it comes to definitions of life, much of the recent literature has turned on the notion that there is something fundamentally mistaken with our efforts to define life. However, as I have argued, pragmatic definitions of life have a clear function in contemporary biological research both scientifically and normatively. From a scientific perspective, pragmatic definitions of life serve to guide scientific practice and can be indirectly conducive to scientific progress in a realist sense, and directly conducive to scientific progress in a pragmatist sense. From a normative perspective, pragmatic definitions of life fit much more naturally with ongoing debates surrounding the acceptance of synthetic biology and the risks involved in this field. This is yet another way in which the pragmatic, pluralist account of definitions of life defended here is conducive to a kind of progress.

However, an important problem for the pragmatic account remains. The pragmatic account of definitions of life cannot bring the monist realist what they want (cf. Pen-

[22] Although Ross and Woodward (2016) make the point that Koch does not formulate his postulates as explicitly or generally as they are represented in contemporary literature.

nock, 2012). After all, if value of these definitions is entirely derived from their function in guiding scientific and normative practice, then there is nothing more for a definition of life to do and there is nothing more it should be. Of course, the monist realist about definitions of life believes that, in principle and hopefully in practice, we can arrive at the final, universal definition of life. To them, the opposition between living matter and lifeless matter stands out so clearly that life must be something with sufficient metaphysical heft, such as a proper natural kind. But, on a pragmatic account, the opposition between life and lifelessness, and its supposed metaphysical heft, are rejected because these are not relevant dimensions when talking about, developing, and using definitions. To see the value and use of definitions of life, we need to look no further than present and historical scientific and normative practice.

Nevertheless, as a fallback position, pragmatism about definitions of life provides an explanation for the existence of definitions of life and our continued interest in these definitions, which is something that the monist realist should be able to accept without abandoning their hopes. Moreover, the pragmatic account also offers some protection against a repetitive discussion. When Cleland and Chyba revitalized the modern discussion about the status of definitions of life, they argued that in order to properly define life we require a scientific theory of biology to set the relevant boundaries (2002). This generated substantial debate, where multiple pessimistic accounts were proposed, followed by a series of pragmatic alternatives, which have subsequently been rejected again. Central to the rejection of the pragmatic account by Amilburu, Moreno, and Ruiz-Mirazo is that, although definitional pessimism is not the solution to the plurality of definitions of life that we encounter, a pragmatic account cannot be the solution either because it cannot provide us with an asymptotic progression of increasingly correct definitions of life. That is, it cannot lead to scientific progress in a way they think is relevant (2021). Of course, this is where the definitional pessimists can renew their previous objection: there is no final definition of life and so attempts to find this final definition, asymptotically or otherwise, should be abandoned.

Alternatively, if we let go of these realist, monist intuitions, we can focus on what definitions of life can provide, namely guidance to scientific practice and normative discussions. On the pragmatic account, this is all there is to be understood about definitions of life. There is no doubt that those who keep their options open and hope for ever more convergent definitions of life will continue to do so. Yet, equally, there is no doubt that our current attempts to define life are wholly benevolent, without any need for monist realism about definitions of life, nor for the definitional pessimism that this attitude engenders.

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