# **The Diversity of Engineering in Synthetic Biology**

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**Abstract**: A recurrent theme in the characterization of synthetic biology is the role of engineering. This theme is widespread in the accounts of scholars studying this field and the biologists working in it, in those of the biologists themselves, as well as in policy documents. The aim of this article is to open this black-box of engineering that is supposed to influence and change contemporary life sciences. Too often, both synthetic biologists and their critics assume a very narrow understanding of what engineering is about, resulting in an unfruitful debate about whether synthetic biology possesses genuine engineering methodologies or not. By looking in more detail to the diversity of engineering conceptions in debates concerning synthetic biology, a richer perspective can be developed. In this article, I will examine five influential ways in which engineering is understood in these debates, namely engineering as applied science, as rational methodology, context-sensitive practice, cunning activity or design. The claim is first of all thus to argue that engineering must not be seen as something stable or characterized by a fixed essence. It rather has multiple meanings and interpretations. Secondly, the claim is that most of the debates on synthetic biology cannot be indifferent towards the question which conception of engineering is at play, since the specific questions and concerns that pop up depend to a great extent on the precise conception of engineering one has in account. Many of the existing debates around synthetic biology can thus be reinterpreted and readdressed once one is aware of which conception of engineering is at play.

1. **Introduction**

A recurrent theme in the characterization of synthetic biology is the role of engineering. This theme is widespread in the accounts of scholars studying these biologists, in those of the biologists themselves, as well as in policy documents. The anthropologist Paul Rabinow, for instance, characterizes synthetic biology as the continuation of the “engineering ideal in American culture” [1, p. 36]. Similarly, Sophia Roosth, starts her book on synthetic biology by arguing that

[i]n the final years of the twentieth century, émigrés from mechanical and electrical engineering and computer science resolved that if the aim of biology was to understand life, then *making* life would yield better theories than would experimentation. [2, p. 1]

For Roosth, the clearest example is Drew Endy. She records how, “when I first asked Endy what drove synthetic biology, he gave me a lesson, not in biology, but in mechanical engineering” [2, p. 180]. Quite similarly, Giese and colleagues conclude that despite the heterogeneity of the field, synthetic biology “advocates a common denominator that seems to define this field: the principles of rational engineering” [3, p. 324].

Endy himself makes the same point in his own work, starting from the question why it has remained unsuccessful in the past to apply engineering techniques to biology. Two options come to mind for Endy. Either biology is (still) too complex for our understanding or “the engineering of biology remains a research problem because we have never invented and implemented foundational technologies that would make it an engineering problem” [4, p. 499]. Synthetic biology is identified with the aim to implement the correct and mature methods of engineering centering around the question “How do we make biology easy to engineer?” [5, p. 340].

This idea is not restricted to the work of Endy, but is present in the majority of synthetic biology publications [6-7]. George Church, another famous synthetic biologist, records his start as follows:

By emulating the engineering practices that made silicon chip technology so successful, we hoped to make biological engineering into an equally revolutionary enterprise. What had hitherto been called genetic engineering, we were convinced, was not engineering in the true sense of the word. [8, p. 160]

Synthetic biologists thus define their own field as “the rational engineering of biology” [9, p. 8] or “the interface between molecular biology and hard-core engineering” [10, p. 822].[[1]](#footnote-1)

This focus is finally shared by policy documents concerning synthetic biology, such as the European Commission, who similarly defines synthetic biology “as the engineering of biology” [12, p. 5] or the roadmap for synthetic biology in the UK, which demarcates synthetic biology as “the design and engineering of biologically based parts, novel devices and systems as well as the redesign of existing, natural biological systems” [13, p. 4].

The prominence of the engineering theme has not escaped commentators, and forms the basis not only for the definition of the field, but also for many criticisms. Synthetic biologists have been criticized for being misled by one-sided engineering metaphors [14-15] or that there is a huge gap between engineering rhetoric and the actual practice of synthetic biologists [3, 16-17]. However, the validity of these claims depends on what engineering actually is about. Therefore one would expect a vivid debate among these scholars on the nature and history of engineering. Nonetheless, with a few notable exceptions [18-20], most scholars take a certain common sense notion of engineering for granted.

The aim of this article is to open this black-box of engineering that is supposed to influence and change contemporary biology. Too often both synthetic biologists and their critics assume a very narrow and stable concept of engineering, resulting in unfruitful debates about whether synthetic biology possesses genuine engineering methodologies or not. I argue instead that engineering can and does mean multiple things and that this diversity must be recognized. Moreover, the claim is that many debates about synthetic biology are the product of these different conceptions of engineering and their potential mutual contradictions.

This article will elaborate on five possible conceptions of engineering relevant for synthetic biology, either because they are endorsed by synthetic biologists or by their critics. The first conception of engineering is that of engineering as ‘applied science’. As philosophers and historians of engineering have noted [21-22], this often remains the standard interpretation of engineering. This is also the case in synthetic biology, as will be illustrated by the case of cell-free synthetic biology. It moreover plays a role in a number of criticisms of synthetic biology, such as that of the ‘instrumentalisation’ of nature.

The second conception is related, but different and particular to synthetic biology: engineering is itself seen as an abstract and rational methodology that can be applied to different fields, such as biology. Prominent in synthetic biology discourses, it has repercussions concerning the question whether synthetic biology is a viable project, what differentiates the field and whether biology can be standardized and automatized.

The third and fourth conception are more inspired by reflections of philosophers and historians than by the accounts of synthetic biologists themselves. The third conceptions sees engineering as a context-sensitive practice. This idea plays a prominent role in the work of critics of synthetic biology and in the debate over the differentiation between synthetic biology and genetic engineering. The fourth conception understands the engineer rather as a trickster and engineering as characterized by a cunning reason. This view comes forward in some self-descriptions of synthetic biologists and in concerns about whether synthetic biology is ‘natural’.

Finally, there is the conception of engineering as design. This again is a prominent theme in synthetic biology. Yet, design itself, like engineering, is an ambiguous notion. By an examination of the recent history of engineering, the argument will be made that what constitutes design is up for debate. This recontextualizes a number of debates about synthetic biology, such as whether it is a ‘genuine’ form of engineering or not. This will be illustrated by the debate surrounding the question whether ‘directed evolution’ is a genuine form of synthetic biology and engineering. The claim is that this debate can be reinterpreted as a recurrent theme within the history of engineering: to what extent can engineering methods be formalized or not?

Five different conceptions of engineering are thus discussed. The claim is not that this is an exhaustive list, but rather that at least each of them play a prominent role in synthetic biology discourses and have affected debates surrounding it. Secondly, my claims limit themselves also to the level of discourse. Whether this diversity in discourse also reflect a diversity in practice is a question that falls out of the scope of this article. It rather concerns the claim that one cannot understand, let alone solve, many debates about synthetic biology if one does not cease to essentialize what engineering is and instead recognize the diversity of the conceptions of engineering.

1. **Engineering as applied science**

The first conception of engineering that I wish to discuss is that of engineering as applied science. This is a popular account of what engineering is about, found in many textbooks and discussions. Philosophically, it is perhaps most elaborately grounded in an article by Mario Bunge [23]. More broadly, it is associated with the ‘linear model of innovation’, according to which innovation stems from basic science which is then subsequently translated in applied science, leading eventually to the development of new products and new markets. Whereas sciences such as physics play the central role in the first stage, engineering and design are typically located in ‘applied science’ part [24].

* 1. Examples from synthetic biology

Although problematized as a useful notion ([24], see below), it is still influential in many discussions about synthetic biology. Its influence is, for instance, found in policy reports on synthetic biology, such as recent reports of the European Commission, which defines synthetic biology as “the application of science, technology and engineering to facilitate and accelerate the design, manufacture and/or modification of genetic materials in living organisms” [25, p. 5]. Secondly, it still plays a role in the discourse of synthetic biologists themselves, namely when they define their own work as the application of insights from biology or chemistry in order to create useful applications and technology. Such discourses are found in popular accounts of synthetic biology [8, 26], but one of the clearest examples is cell-free synthetic biology.

Cell-Free Synthetic Biology (CF-synbio) or Cell-Free Protein Synthesis (CFPS) is a subdiscipline that aims to synthesize proteins and other useful biomaterials through in-vitro translation, thus using cell mechanisms and parts to do the work, but without whole cell integrity:

Based on in vitro transcription and translation systems, this application-focused domain builds on decades of cell-free biochemistry and protein expression to operate synthetic gene networks outside of cellular environments. [27, p. 91]

Synthetic biologists see it as a way to “overcome the inherent limitations of using a living organism” [28, p. 2755], which, “[b]ypassing all walls, […] can access and manipulate biology directly” [29, p. 672). Or as Odgman and Jewett put it:

Rather than attempt to balance the tug-of-war between the cell’s objectives and the engineer’s objectives, cell-free synthetic biology activates, integrates, and focuses cellular resources towards an exclusive user-defined objective. Physical removal of the cell wall enables direct access to inner workings of the cell. […] In short, a decreased dependence on cells leads to an increase in engineering flexibility [30, p. 262]

These synthetic biologists portray themselves as applying the technology of CFPS to a number of new fields and problems. Revealing in this regard is the historical narrative found in many articles: although originally developed for basic science purposes (and used in deciphering the genetic code [31]), this piece of basic science is now ready to be applied to practical problems in synthetic biology:

Today, thanks to significant progress made to the miniaturization, automation and optimization of fed-batch and semicontinous reactions, *in* *vitro* synthesis of proteins has found a large variety of low- and high-throughput applications suitable for functional and structural proteomics. [32, p. 152]

The main concern of the field is overcoming the “several obstacles” of CFPS that “have previously limited their use as a protein production technology” [33, p. 1186]. Nonetheless, these synthetic biologists are optimistic that these obstacles can be overcome, since CFPS is already “an effective tool for the applications of antibody production, vaccine assembly, gene circuit development, biocatalyst production, and uAA incorporation” [28, p. 2750]. Therefore, according to them, “[t]he ability to manipulate the reaction conditions and to generate novel applications will probably only be limited by our creativity” [32, p. 155].

* 1. Ethical and epistemological concerns about applied science

There are a number of discussions to which this idea of engineering typically leads. One, for instance, is the concern that synthetic biology leads “towards a reconstruction of nature which is instrumentalizable and utilizable for our purposes” [34, p. 95]. If one sees engineering as all about reducing a studied phenomenon to useful applications, then the concern about instrumentalization and commodification becomes central [35].

Related to this is the concern that if synthetic biology is merely engineering, understood in this narrow sense as applying science, no new knowledge can or will come from it. This concern is formulated as one that stresses that new breakthroughs tend to come from fundamental and basic research, rather than largescale investments in applied science [36].

A good example is CRISPR, of which one of the co-discoverers, Jennifer Doudna, states that it illustrates how an application-driven science policy would be problematic:

such an approach would not have produced the CRISPR-based gene-editing technology, which was inspired by curiosity-driven research into natural phenomena. The technology we ended up creating did not take anywhere near ten to twenty million dollars to develop, but it *did*  require a thorough understanding of the chemistry and biology of bacterial adaptive immunity, a topic that may seem wholly unrelated to gene editing. This is but one example of the importance of fundamental research – the pursuit of science for the sake of understanding our natural world – and its relevance to developing new technologies. Nature, after all, has had a lot more time than humans to conduct experiments! [37, p. 245]

At the same time, there are a number of criticisms of this notion of engineering to be made, as already hinted at above. First of all, as we will see below, from the 1980s on, this view was heavily criticized, stating that “engineering is not applied science” [22, p. 5], “is not so much the *application* of knowledge as a *form* of knowledge, one persistently dependent on technical skill” [38, p. 203] and, “though it may *apply* science, [it] is not the same as or entirely *applied* science” [21, p. 4].

Secondly, this position is problematic because the basic/applied science distinction is one which is hard to draw and historically its meaning has changed in function of shifts in science policy [39-40]. As the concept of engineering itself, ‘applied science’ is actually a very ambiguous concept with a specific history and when mobilized often reveals a specific political agenda. Historically, the concept of applied science was shaped through the creation of its counterpart, namely that of fundamental or basis science. This, in its turn, was inspired by a number of tensions in the 20th-century history of science and science policy, namely (a) devastating effects that science could have (e.g. the atomic bomb), (b) the increasing need for science to justify itself and the question whether it should be submitted to democratic or state control; and (c) the ideological antagonism during the Cold War, related to the question whether science was (in)compatible with capitalism or communism. Therefore, “the dissociation of the natural sciences from applied research” was “a strategy of individual, professional, and institutional relief” [40, p. 312]:

Firstly, a strategy that avoids assuming ethical responsibility for the changes caused by scientific knowledge. Secondly, a sort of self-protecting strategy that sought to avoid the direct line of political fire in a society entirely concerned with national security, the latter which produced an atmosphere of suspicion. And thirdly, a strategy of political neutrality and independence from any self-serving interests as a means of guaranteeing the institutional freedom of academic science and a selfregulating scientific community which, from a scientific point of view, was best capable of dealing with the open and often unpredictable process of epistemic progress. [40, p. 312]

The image of such a neutral and independent basic science has been strongly criticized and it is therefore equally questionable whether the notion of ‘applied science’ is insightful to understand synthetic biology. Nevertheless, as Calvert notes, “[d]espite this ambiguity, and despite long-standing dissatisfaction and debate over the definition of the term, crucially important decisions are made on the basis of this concept. Money is allocated, power is gained, and status is achieved.” [39, p. 199] What first might look like a neutral tool of analysis, is in fact a political object of boundary work [41].

1. **Engineering as abstract methodology**

A related, but distinguished conception of engineering present in debates concerning synthetic biology is that of engineering as an abstract and rational methodology which itself can be applied to novel fields. Engineering is thus about application, but not application of science but of engineering itself to a field such as biology. Although a very prominent way of framing synthetic biology, it should surprise us, since seeing engineering as applicable itself, for instance, is not self-evident and comes into conflict with the previous conception of engineering as applied science.

This conception of engineering is perhaps most famously endorsed by Drew Endy. As stated before, Endy claims that “the engineering of biology remains a research problem because we have never invented and implemented foundational technologies that would make it an engineering problem” [4, p. 449]. He proposes a number of foundational engineering technologies, such as standardization, decoupling and abstraction in order to “best enable the routine design and construction of useful synthetic biological systems” [4, p. 450]. Manipulating biological systems would become easy if one divided them into biological parts that are well-described and defined (standardisation), separated in simple problems that can be dealt with (decoupling) and must be so arranged that separate levels, dealing with parts, devices or systems, can be dealt with without intervention from the other levels (abstraction). The development of a strict rational methodology would thereby enable us to produce biological applications and gain knowledge about biological nature during the process.

Another good example is François Képès, who similarly claims that “synthetic biology is the rational engineering of biology” [9, p. 8]. According to Képès, synthetic biology differentiates itself through the fact that it wants to “rationally conceive new systems inspired by biology, or grounded on its components, and construct them in a standardized manner” [9, p. 8]. Although biotechnology has a long artisanal history dating back to brewing wine, synthetic biology is the first to become a real engineering discipline by “liberating itself from that artisanal method to transform biotechnology in a mature engineering” [9, p. 23]. In this sense, synthetic biology constitutes for the actors “a new paradigm” ‘[42, p. 704] within molecular biology, a “biotechnology 2.0” [43].

* 1. Synthetic biology and genetic engineering

This second definition of engineering inspires a famous debate about synthetic biology, namely how to differentiate between the latter and earlier forms of genetic engineering. In this context, the (narrower) history of genetic engineering has been stressed, which, although present earlier, really took off in the 1970s, with the discovery of recombinant DNA and the Asilomar conference in 1975. A year later, in 1976, there was already the first genetic engineering company, Genentech. The notion of ‘biotechnology’ has an even longer history, going back to the beginning of the twentieth century [44]. In this sense, the question is often framed as: is engineering biology new at all or is synthetic biology just a new name for something that was already there?

One the one hand, you have someone as Joachim Boldt, who claims that compared to “genetic engineering, synthetic biology constitutes a shift from the paradigm of manipulating exiting organisms to creating novel entities” [45, p. 37]. Synthetic biologists seem to be the “Newtons of the leaves of grass”, something that Kant himself predicated to be impossible:

if we look at nature through the glasses of genetic engineering, we see a world filled with entities that are already useful to us in many respects and that just need some reshaping here and there to perfectly match our interests. […] Seen from the perspective of synthetic biology, nature is a blank space to be filled with whatever we wish. [46, p. 388]

One the other hand, Luis Campos stresses how claims that ‘finally we are able to engineering life’ have been made numerous times in the history of biology, often in vain [47]. Michel Morange, similarly, points out how “experiments done in synthetic biology appear no different from those previously performed by genetic engineering” [48, p. 544]. Tim Lewens therefore concludes that one should replace metaphors of discontinuity by that of a continuum ranging from having no control to having full control over the design. Synthetic biology is then just one further step towards one end of this continuum, namely that of rational design [17, p. 643].

A major problem within this debate is that engineering is assumed to be a stable entity which is either present or not. It is equally possible, for instance, to argue that different forms or discourses of engineering are at play. From a perspective that recognizes the diversity of engineering discourses, synthetic biology can also be interpreted not as engineering finally or better being applied to biology, but as a different engineering being applied to it. Again, a look at the diversity of the conceptions of engineering is warranted.

* 1. Is a genuine engineering methodology possible?

Another debate inspired by this definition of engineering is the accusation that there is a huge gap between the promises and rhetoric of synthetic biology and the actual practice. Maureen O’Malley, most famously, captures this gap by opposing ‘rational design’ and ‘kludge’:

Rational design is clearly taken seriously by advocates of engineering approaches in biology. Such design is usually taken to be the opposite of the kludge - a colloquial term for a workaround solution that is *k*lumsy, *l*ame, *u*gly, *d*umb, but *g*ood *e*nough […]. Kludging emphasizes the achievement of a particular function rather than the rational pathway to that function. It does not matter how inelegant the process is to get there, or how inefficient […]. If the system works, that is the ultimate vindication of construction. [16, p. 382]

This notion of kludging is linked with concepts such as ‘tinkering’ or ‘bricolage’. Tinkering is a concept introduced by François Jacob, to describe the trial-and-error method of natural selection at work in biological nature [49]. Tinkering, similarly to kludging, refers to a creative but not necessarily efficient process of making something work by using the means at hand, rather than starting from a preconceived plan or blueprint. Jacob opposed tinkering categorically to engineering. But, synthetic biologists, according to some authors, are better described as tinkerers, starting from the idea that “[t]he sharp and illuminating distinction between engineers and tinkerers holds only as far as one has an ideal view of the behavior of engineers” [50, p. 371].

O’Malley and others argue that, in practice, many of the methods of synthetic biologists are more akin to kludging, tinkering or bricolage than to the abstract methodologies described above. But important for her is that kludging is not a failure to engineer, but rather an alternative to it – just like tinkering is an alternative to the intelligent design of God in the case of Jacob. The diagnosis of synthetic biology as kludge is thus no argument against the practice, since “[k]ludging should not be interpreted as a failure of synthetic biology, but as a highly creative and effective process” [16, p. 382]. Rather the claim is that it points to a difference in what synthetic biologists say they do and what they actually do. In fact, as we will see in the next session, they mobilize an alternative conception of engineering to criticize the idea of engineering as an abstract methodology.

Similar distinctions can be found in the work of Bernadette Bensaude-Vincent or Jane Calvert. Distinguishing between the discourse of rational design and that of trial-and-error, Bensaude-Vincent argues that “[t]he first discourse appears to be better suited for propaganda purposes to attract public attention or to capture the interest of investors. The second seems to better reflect the daily laboratory practices” [51, p. 109]. Calvert similarly notes how there is often an “idealisation of electrical engineering” [52, p. 412] at work within synthetic biology. She argues that by giving up “on the idealised understanding of rational engineering we can perhaps get a better grip of interdisciplinary activities that go under the heading of synthetic biology” [52, p. 415].

But what is missing, again, is a historical perspective on engineering versus kludging. Where do both ideas come from? And how are they related? Moreover, it is an open question whether the idea of engineering as a rational methodology should be dismissed as a false ideology of the real practice of kludging. While Calvert or O’Malley seem to suggest it is a false picture that holds us captive, Bensaude-Vincent is more hesitant and states that both discourses respectively serve specific normative projects [51]. And as we will see in the part about engineering as design, it is also possible to argue that there has certainly been a tension between both, but in the form of an internal tension within the history of engineering, rather than between engineering and its other.

Stressing the diversity can thus help us avoid a number of pitfalls in these debates, mainly related to a too rigid idea of engineering, that would be radically opposed to activities such as tinkering. Alfred Nordmann correctly argues that “[t]he hierarchical conception that places rational engineering above tinkering is blind to the possibility of rational tinkering” [53, p. 36]. In a similar vein, Brett Calcott *et al.* noted that too many of these discussions “operate with idealized views of engineering that tend to overemphasize the conscious, planned capacities of designers, and neglect the iterative, error-prone process that actually takes place” [54, p. 53]. They themselves draw inspiration from software engineering, which more often than not is more rational when “the design process […] is explicitly iterative with testing and feedback, in view of imprecise and shifting goals” [54, p. 53]. Such a perspective is also found in the work of synthetic biologists themselves. Ernesto Andrianantoandro *et al.* are quite explicit about this in their review of the ‘new engineering rules for an emerging discipline’:

The success of synthetic biology will depend on its capacity to surpass traditional engineering, blending the best features of natural systems with artificial designs that are extensible, comprehensible, user-friendly, and most importantly implement stated specifications to fulfill user goals. [6, p. 13]

Engineering is thus not stable. Several discussions about synthetic biology might benefit from looking more closely at the diversity of engineering conceptions. Many relevant questions simply are not asked, because it is assumed that engineering is a stable resource waiting out there to be (un)succesfully used by biology or not. Instead, one could also argue that not only the goals of biology have changed, allowing engineering to enter the scene, but engineering also has a history, one that has allowed it to influence a field like synthetic biology.

* 1. Can biology be automatized?

A final debate inspired by this conception of engineering is that of automation. For if synthetic biology, through its abstract methodologies, is able to reduce the “basic laboratory routines of molecular biology […] to recipes that everyone can follow” [26, p. 63], what stops industry and academia from replacing biologists with machines or at least impose a top-down control? Sophia Roosth, in her ethnographical studies on synthetic biology, observes

the deskilling of PhD benchwork in favour of undergraduate labor in one company and short-term manual laborers operating robots in the other. […] I show how engineers have imported not only technical principles of manufacture (such as standardisation and abstraction) into biology but also the labor relations and forms of alientation that underwrite mass production in late capitalism. As a result, synthetic biological work is fragmented, divided between the high-prestige work of biological design and the automated tasks of biological manufacture. [2, p. 12]

Standardisation in synthetic biology is not just a matter of standardising cells, but also of people. Indeed, the first is sometimes simply pursued in function of the latter, as is evident in claims such as that “[v]ast computational power is at our fingertips, but its use is constrained by the paucity of our knowledge of many of the biological processes that we wish to engineer” [43, p. 18]. While some applaud these developments as necessary progress, others fear “that ‘deskilling’ biology could render PhDs obsolete” [2, p. 102].

A transformation that Roosth sees at work is one where biological research facilities and companies, such as Ginkgo Bioworks, are being reorganized into a “biological assembly line” [2, p. 104]. In a similar manner to how the assembly line brought forth fundamental societal shifts in the nature of work, these transformations in the life sciences might alter biological research in analogously radical ways. One such element that Roosth highlights is the physical separation between the staff devoted to designing the cells and those building or testing them. As a consequence, “when biological design and biological manufacture are decoupled, the ‘site of intelligence’ is reticulated among designers and automated robotic systems, while manufacture is limited to managing automated robotic assembly” [2, p. 111]. The power and knowledge to decide what biological phenomena to take into account and what it means to do research are thus redistributed in specific ways. “Little biological knowledge is required to perform these pro forma recipes for synthetic microbes, as all that ‘thinking’ is already programmed into the system” [2, p. 111].

Roosth is not the first to express such concerns. Analogous worries existed in physics where “opponents of an increased use of computation contended that computers would make experimentation automatic, and so block discovery” [55, p. 497]. Similarly, in the history of engineering this has been a common theme, especially in its recent phases of professionalization which Kathryn Henderson describes “as a series of attempts to codify the nonverbal knowledge base of master craftsmen and machine shop culture” [56, p. 15]. She links these shifts particularly to the introduction of the CAD/CAM system, which “destroyed traditional boundaries between design engineers and the shop floor, thereby restructuring social relations and generating responses to that restructuring” [57, p. 449]. As a consequence, feedback between design and manufacture became more problematic and both sides felt a certain loss of control.

A good example of this anxiety is Mike Cooley, who in 1980 worried that “we are beginning to repeat in the field of intellectual work, most of the mistakes already made in the field of skilled manual work at an earlier historical stage when it was subjected to the use of high capital equipment” [58, p. 1]. The introduction of CAD/CAM, for Cooley, “is a tool for silencing the common sense and creativity of the skilled worker on the shop floor” [58, p. 6]. The computer is not celebrated, but rather seen as “a Trojan Horse for Taylorism in the fields of management and scientific work” [58, p. 37]. Such worries gain new momentum in current science, where machine learning, simulation and data-driven research become prominent, but depend on the question whether one sees engineering as something that can be formalized or standardised. As we will see in the next two candidates, not all engineering conceptions are compatible with that idea.

1. **Engineering as a practice**

So far we have seen two candidates for what engineering is about, namely applied science and a rational methodology. Both share a common assumption, namely that engineering can be grasped through a well-defined and standardized methodology, either in the form of a linear model of innovation or in a number of methodological principles. As we have already seen in the previous sections, there has been a strong resistance against such abstract conceptions of engineering. Therefore some propose an alternative definition of engineering, which can be grasped under the banner of engineering as a *practice*, i.e. as something that must be defined through a context-sensitive activity, often associated with things such as practical knowhow, tacit knowledge or nonverbal learning. This understanding of engineering is not as strongly present in the rhetoric of synthetic biologists, but as we will see, plays a role in a number of debates about synthetic biology.

* 1. Historical and philosophical reflections on engineering

Let me discuss a number of possible ways in which scholars have understood engineering as a practice. The first one is to state that engineering differentiates itself by having a different *goal*, namely that science is focused on *what is* and engineering is focused on *what can or might be*. The engineer Carl Rogers, for instance, argues that a “scientist looks at the world and tries to explain what he sees; an engineer looks at the world and tries to supply what he sees is missing” [59, p. 3].

Others are unsatisfied with such a definition, since it is rather shallow or at least ambiguous. It is shallow in the sense that a different aim does not necessarily entail any other differences: science and engineering can still have the same methods, results, knowledge, etc. This is exactly what the notion of ‘applied science’ suggests: engineering starts from the same methods, but applied to practical problems. Wybo Houkes has formulated a similar critique on what he calls the ambiguous ‘truth vs usefulness’ intuition [60, p. 312]. He suggests that it often obscures a second and stronger demarcation candidate. While the weak claim states that science and engineering are irreducible to one another due to their different goals, the strong claim endorses that this is due to the existence of two autonomous and even different types of knowledge. While the weak claim is defensible but somewhat trivial, the strong claim is promising but hard to defend.

An example is Vincenti, who argues that “the inseparability of knowledge and its practical application is in fact a distinguishing characteristic of engineering” [21, p. 207]. Thus even though these scholars recognise that engineering needs mathematics and scientific theories, they add that it distinguishes itself by the fact that its practice, “like art, involves important levels of nonverbal communication” [61, p. 174]. In this context two specific notions often pop up. First, one often finds a reference to a distinction going back to Gilbert Ryle, between ‘knowing that’ and ‘knowing how’ [62, 21, p. 13]. A second notion is that of ‘tacit knowledge’, referring to forms of knowledge that remain implicit and are not or even can’t be made explicit and transmitted through words [63].

This has been applied to engineering by authors like Kathryn Henderson [56-57]. Another clear example is the work of the engineer Eugene Ferguson, who stresses how “[v]isual thinking is necessary in engineering. A major portion of engineering information is recorded and transmitted in a visual language that is in effect the *lingua franca* of engineers in the modern world” [64, p. 41]. Engineering, from this perspective, differentiates itself by another type of knowledge: while science consist in knowledge best grasped through the notion of *episteme,* in engineering knowledge is of a different type, namely that of *techne*.

* 1. Is synthetic biology something new and feasible?

As stated above, this conception of engineering is not really present within the discourse of synthetic biologists themselves. A reason for this absence might be the discussion mentioned above, namely that of the demarcation between genetic engineering and synthetic biology. For if engineering is always this practical activity, it becomes hard to distinguish between genetic engineering and synthetic biology. If engineering is such a practice, at best it could be argued that the difference between the two is merely gradual.

This is a claim occasionally found in more modest accounts of synthetic biology, namely that the difference with genetic engineering is merely one of scale: instead of editing a few genes, synthetic biology synthesize a whole genome or metabolic pathway [65, p. 4]. A similar argument is endorsed by the philosopher Tim Lewens, who claims that synthetic biology does not constitute a break, but is rather to be situated on a continuum, merely bringing genetic engineering one step closer to a more standardized approach [17]. Most synthetic biologists, however, argue for a more substantial difference between the two.

One the other hand, a number of critics and commentators have argued that while synthetic biology might portray itself as a rational methodology that can be abstractly applied to biology, in reality it is closer to a practice. This seems indeed the rationale between the debate about kludging vs. rational design, mentioned above, but it is also found in the work of Jane Calvert and colleagues of her, such as Pablo Schyfter [18-20]. “If we give up on the idealised understanding of rational engineering we can perhaps get a better grip of interdisciplinary activities that go under the heading of synthetic biology” [52, p. 415] Their work starts from the following question: are not the *methods of engineering being transformed by biology* at the moment of their introduction in fields such as synthetic biology? “We will perhaps see a new type of engineer/biologist emerging who will be particularly well suited to working with the contingencies and unpredictabilities of the biological substrate” [52, p. 416]

This is certainly an interesting claim, one that testifies to the fact that engineering is not a fixed concept, but can mean many things. Interestingly, the alternative that Calvert and colleagues propose, namely to understand the engineering of synthetic biology as ‘heterogeneous engineering’ [66], comes remarkably close to the account given above: one that is context-sensitive, rather than standardized, and relies on forms of tacit knowledge and practical knowhow, rather than formal principles.

Taking this alternative idea of engineering as a starting point also leads to a certain skepticism concerning the claim that the automation of biology is a genuine possibility. For those who see engineering as a practice, it is unlikely that the dream of creating a fully standardized and context-independent biology is possible, since engineering itself cannot be standardized. Similar to engineering, synthetic biology will remain a practice characterized by practical knowhow and tacit knowledge.

It can even lead to the stronger claim that the real engineering is precisely occurring the traditional field of genetic engineering, rather than in synthetic biology. Such a perspective seems to be the inspiration, for instance, of Kogge and Richter, who argue that all what makes biological systems superior to their artificial counterparts reside in their context-dependency and complexity, precisely the elements that synthetic biologists aim to delete from the picture. But remarkably, they equate this automation dream with engineering *tout court*, rather than only with one conception of it: “Must we not, therefore, say that the plausibility of an engineering approach decreases in line with the increasing expectations placed in the capabilities of biotechnological artefacts?” [67, p. 186] It certainly decreases the plausibility of engineering as an abstract methodology, but not necessarily the engineering of the earlier context-sensitive genetic engineering.

* 1. A number of internal tensions

This alternative conception of engineering thus has a number of deviating consequences and additionally has a certain appeal, especially since it succeeds in linking it with the above remarks on synthetic biology as kludging. Nonetheless, it is at the same time not free from its own internal tensions. A first problem, for example, is that many other engineers and even historians of engineering resist against identifying engineering with practical *techne*. Ferguson, for instance, already notes how “engineers today are happy to be called scientist but resist being called artists” [64, p. 22]. Auyang similarly distinguishes this practical knowledge, identified with craftsmen or artisans, from engineering:

Craft inventions rely mostly on tinkering, varying slightly existing solutions but not venturing far, for those efforts would require too many resources, both intellectual and material. In contrast, engineers are kin to natural scientists, who are not content to be stuck to immediate tasks, although they never forget utility. Individually, an engineer may have to conform to a production schedule that prohibits comprehensive investigation. Collectively in a discipline, engineers are willing to spend additional resources for a broader perspective [68, pp. 15-16].

One option is to claim that engineering is the same as craftsmanship, but that there is a certain political ideology that prevents them from being honest about it. They need the prestige of being a science to gain higher status and funding. And although there is some truth in such a claim, it brings us dangerously close to the Hegelian story: Engineering has always been practical knowledge, but we have simply forgotten this.

Of course, a *reductio ad Hegelum* is not a definitive argument, but it does point to a problem. Seeing engineering as *techne* might be seen as problematic, not only because there would be no demarcation with artisans and artists, but because things such as tacit knowledge are found in scientific practices as well. In scientific practices you will equally encounter the necessity of practical skills, tacit knowledge and visualisation. Many authors have in fact argued that there are enormous amounts of *techne* presentin scientific practices. In the line of this, Houkes argues that, if *techne* play a crucial role, this cannot be restricted to engineering. “If the arguments of Ryle and Polanyi are sound, they would show that all knowledge contains a tacit component.” [61, p. 334] In that sense, what it specific to engineering, in contrast to science or art, remains unclear. The often implicit assumption by many critics and commentators, thus, that engineering as practice mirrors the *real* essence of engineering is thus problematic. Rather it should be seen as merely one conceptions among the others.

1. **Engineering as a ruse**

These tensions have moreover led some scholars to understand engineering in a different manner. According to this alternative, engineering does not consist in merely having a different objective nor in being based on practical knowledge, but rather in a different *attitude* or *rationality* at work. The historian Antoine Picon, for example, argues that the only “common denominator” of engineers throughout their history “is perhaps the idea of a specific kind of a reason at work in their endeavour” [69, p. 429]. More specifically, the argument is that engineering differentiates itself by a *trickster* element or a cunning reason: an engineer is one who tricks nature into doing things.

Similar to the previous conception of engineering, this account is not as explicitly articulated by the synthetic biologists themselves, but rather by philosophers and historians. One does, however, find indications of this account in some remarks by biologists. A good example is again the work of Jennifer Doudna, when she describes the work of genetic engineers:

By tricking a cell into thinking that the recombinant DNA was simply an extra chromosome that needed to be paired with a matching gene already in its genome, scientists could ensure that the new DNA was combined with the existing, native genetic code through homologous recombination.” [37, p. 24]

This trickster element is present in several of her descriptions of the work of engineers, who “trick the cell into thinking it had suffered a natural source of DNA damage and supply it with a new piece of DNA, disguised as a second chromosome, that could use to fix the broken site” [37, p. 28]. As a consequence, the “cells would practically do the work for you” [37, p. 28]. But more prominently, this conception of engineering has been theorized by philosophers and historians, though it does again play a role in a number of debates and problems concerning synthetic biology and its nature.

* 1. The etymology of engineering

To flesh out this alternative conception of engineering, a number of historians and philosophers of engineering have looked at the etymology of the word of engineering, which leads us neither to that of *episteme* nor that of *techne* (or even *praxis*). In this they divert from a very popular etymological candidate, namely stating that engineering is derived from the Latin *ingenero*, meaning ‘to implant’, ‘to generate’, ‘to produce’ [38, p. 71]. For authors such as Hélène Vérin or Vilém Flusser, a different etymological angle is more revealing [71-72].

For these authors engineering is derived not from *ingenero*, but from *ingenium*, coming close to something as ‘ingenuity’. In Latin, the term *geno* had in fact the connotation of ‘cunning reason’ or ‘trickster’. A term such as *geno* could both refer to what we would grasp with the term of genius, but also that of a djinn: a cunning and fooling spirit, that tricks us into doing things [71, p. 19]. In a similar vein the term *Enghinhart* referred to the devil and the *Malin Génie* of Descartes might be better translated by that of an ‘evil engineer’ instead of ‘evil demon’, if such a distinction is even meaningful [71, p. 27]. Flusser, in his work, points to related etymologies of words such as design and machine. Both these notions refer to that of cunning or deceit, where a “designer is a cunning plotter laying his traps” and “a machine is a device designed to deceive; a lever, for example, cheats gravity, and ‘mechanics’ is the trick of fooling heavy bodies” [72, p. 17].

Terms such as *ingeniator, ingeniorius* or *ingeniosus* originally referred in the 12th or 13th century to builders of war machines, i.e. those who tricked enemy defences by making holes, using ladders, etc. [71, p. 21]. They did not negate the defences nor completely destroyed them, but went around them, made small holes in them, tricked them. In a similar vein the word *engine* in old French and English still had the connotation of being a ruse or trickery, referring to the ingenuity of its builder rather than the product itself.

Thus, when an engineer solves a problem he is not merely ‘applying’ theoretical knowledge, nor does he uses mere practical knowledge, but he is first and foremost trying to do something different, namely tricking nature into doing things. For this reason there was throughout the whole Medieval period a debate surrounding the figure of the engineer, concerned with the ambiguous morality of this tricking ingenuity. “Does he increase the power of human organs, or does he orchestrate bodies for suspicious purposes?” [71, p. 77]

Engineering, thus, consists not in *episteme* or *techne*, but rather in this cunning reason, of tricking nature into doing things. A helpful concept in this regard has been saved from oblivion by Marcel Detienne and Jean-Pierre Vernant, namely that of *mētis*. In their book they argue that within Greek society there was another category of intelligence, that has been forgotten nowadays, precisely linked with this cunning reason:

There is no doubt that *mētis* is a type of intelligence and of thought, a way of knowing; it implies a complex but very coherent body of mental attitudes and intellectual behaviour which combine flair, wisdom, forethought, subtlety of mind, deception, resourcefulness, vigilance, opportunism, various skills, and experience acquired over the years. It is applied to situations which are transient, shifting, disconcerting and ambiguous, situations which do not lend themselves to precise measurement, exact calculation or rigorous logic. [73, pp. 3-4]

Famous examples of *mētis* are Daedalus, father of Icarus, and creator of many engines such as the Labyrinth for the Minotaur on Crete, or Prometheus, who tricked Zeus and stole the fire from the gods and gave it to mankind. But perhaps the clearest example is that of Odysseus, the Greek king and hero, often known by the epithet Odysseus the cunning (*mētis*). Similarly, Flusser notes how he is also called Odysseus the *polymechanikos*, meaning not only the man of many machines, but most of all the man of many tricks [72, p. 17]. Not only is his Trojan Horse a clear example of such an engine, a trick to get through the gates of Troy, but also his many adventures on his *nostos* or ‘homecoming’ are clear examples of *mētis.*

Odysseus has also been taken up in a very telling way by Max Horkheimer and Theodor Adorno [74]. They use Odysseus as an example of the instrumental reason, a reason that tricks everything into becomes means. In this context they speak of a ‘cunning reason’, for instance in relation to the story of the Sirens. While sailors who hear the songs of the Sirens normally are drawn towards them and lost forever, Odysseus uses his *mētis* to trick this natural law: he put wax in the ears of his crew and chains himself to the mast of the ship. In this sense he can both listen to and escape from the Sirens.

Cunning, however, is defiance made rational. Odysseus does not try to steer a different course to the one past the Sirens' island. Nor does he try to insist on the superiority of his knowledge and listen freely to the temptresses, believing his freedom protection enough. […]. But he has found a loophole in the agreement, through which he eludes it while fulfilling its terms. [74, p. 46]

Precisely this last remark seems crucial to our analysis of *mētis*. Odysseus never breaks the ‘natural laws’ of the gods, but instead he finds a loophole. By his cunning reason he does not break, but bends the laws to his own advantage. He controls nature by tricking it. Nature is seen as a rival, even a stronger one, but *mētis* allows the engineer to “manipulate hostile forces too powerful to be controlled directly but which can be exploited despite themselves, without ever being confronted head on, to implement the plan in mind by some unexpected, devious means” [74, p. 47]. Although this category was still recognised in ancient myths and authors like Homer, around the time of Socrates it had been reduced to the “level of mere routine, chancey inspiration, changeable opinion or even charlatanerie, pure and simple” [74, p. 4].

* 1. Is engineering merely an unnatural trick?

This idea of engineering plays a role in a number of discussions about synthetic biology, mainly centering around the ambiguities of engineering on the epistemological and ethical level. First of all there is the concern whether synthetic biology can produce genuine scientific results that can really help us to understand life. Someone as Evelyn Fox Keller, for examples, argues “that even though synthetic organisms in physical space-time are no longer computer simulations, they are still simulations, albeit in a different medium” [75, p. 288]. Although synthetic biology can produce nice tricks in the laboratory, it should not be confused with life out-there, in the outside world.

We thus encounter the same ambiguities that plagued engineering throughout its whole history, for instance in the so called *Theatres de machines*. Clear examples are the ‘Defecating Duck’ by Jacques Vaucanson, an automaton displayed in 1738 that was able to digest food and produce faeces. Another famous example is ‘The Turk’, created around 1770 by Wolfgang von Kempelen, an automaton claimed to be able to play chess. Both cases turned out the be hoaxes and that seemed to be an intrinsic part of engineering. In fact, it can be argued that balancing this thin line between a truly ingenious invention and a forgery seems to be central to the engineering attitude. It is very telling that both Vaucanson and von Kempelen, for example, also created automata such as the Flute Player and the Speaking Machine that are not considered hoaxes.

Synthetic biology is not free from similar ambiguities. The clearest example is the debate surrounding Craig Venter’s alleged creation of ‘artificial life’ and a ‘synthetic cell’ [76]. Here too, the reactions oscillated between intense praise of his accomplishments on the one hand and accusations of overselling his work or even of producing nothing but a neat trick or ruse [77-78]. It was simply unclear for many whether Venter produced genuine knowledge or simply tricked nature into mimicking life.

Such ambiguities are even more clearly present on the ethical domain. Synthetic biology is typically linked with concerns about the ‘unnaturalness’ of its creations. “For many, human nature as well as the integrity of nature more generally seemed threatened.” [1, p. 2] One aspect of this discussion is the previously mentioned concern about the instrumentalisation of nature [34-35], where the worry is expressed that synthetic biologists reduce nature to a mere resource that they can manipulate in any way they want.

But there is more at stake, since precisely the attitude of synthetic biologists themselves on how ‘natural’ their work is, is unclear. As Roosth, for example, shows in her ethnographical work:

[Synthetic biologists] simultaneously saw themselves as *unnatural,* building artificial organisms that are ‘fit’ to thrive only in the artificial environment of the laboratory; as *natural* doing the work that comes to them ‘naturally’; and as *supernatural*, effecting feats of biological engineering that renders them divine. [2, p. 24]

In their own accounts, there is indeed a double attitude towards nature within synthetic biology: (a) either synthetic biologists start from the idea that they are going to transcend the limits of nature, gaining full control of it and even improving it. Synthetic biology is then described as aimed “to overcome the limits of natural evolution” [50, p. 368]. From this perspective, “synthetic biology has the potential, not yet realized, to create objects or organisms performing better than their natural counterparts, at least in a given niche. […] Can synthetic biology be stronger that Nature?” [9, p. 53, p. 57].

(b) A second attitude recognizes nature as a formidable opponent which we should take into account and trick its forces to use them for our own purposes. The goal is to “harness the power of natural selection to produce new types of biomaterials and o[f] natural building blocks particularly suitable for these approaches” [80, p. 1762]. Synthetic biologists, from this perspective, marvel at the forces of nature:

Biology’s remarkable ability to execute precision growth of highly complex structures dwarfs ours. Myriad opportunities exist in harnessing the power of biology for the programmed manufacture of human artifacts that possess precise functions. The seemingly wild speculation that a pinecone could instead be programmed to differentiate into a stack of microchips is worthy of exploration. [43, p. 6]

They immediately add, however, the question whether “we could move biology’s capacity forward? Having learned its tricks, can we teach it new ones?” [43, p. 6] Or whether we could “harness the same DNA-repair mechanisms to build a synthetic genome” [81, p. 125]?

Seeing engineering as a cunning reason can shed light on these debates, for instance by stressing how it is not a matter of being ‘unnatural’, in the sense of clearly breaking the laws of nature or creating something that clearly does not occur in nature. Rather it is precisely this element of ambiguity that, for several of synthetic biologists’ critics, plays a crucial role. The ethical question thus remains, but becomes more complex:

Biologists indeed are making new things. And while this may not violate any sacrosanct ontology of nature, it does not mean that anything goes. It is precisely because we do not think that nature is by essence immutable that these practices and the objects they produce must be carefully examined. [1, p. 4]

Despite its appeals, this account of engineering is again not free from its internal tensions and ambiguities. One open question, for instance, is whether this cunning element is really something particular to engineering. One could argue that is has been present in scientific practices as well, exemplified by Francis Bacon’s famous dictum that science can only learn by ‘twisting the lion’s tail’. And secondly, if it is indeed present in engineering, or more strongly so, one could still be skeptical whether examples from centuries or even millennia ago are still so helpful to understand contemporary engineering. Has engineering not changed since the time of Odysseus or Descartes? It is indeed towards that more recent history of engineering that I wish to turn in the final conception of engineering I wish to discuss.

1. **Engineering as design**

A final candidate to define engineering is that of engineering defined as design. Engineering is then defined as the activity to *design* parts, devices or systems. This is a common theme in the definitions of synthetic biologists. Bryksin *et al.*, for example, defines synthetic biology as “the design and construction of biological systems” [80, p. 1766]. And Guillaume Cambray *et al* open their article “Toward rational design of bacterial genomes” by arguing that to solve our current societal problems, we “require the development of a true science of biological design, which could both control and harness the idiosyncratic capacity of biological systems to evolve” [82, p. 624]. This science is of course that of synthetic biology which provide us with the tools to finally solve these problems. “Equipped with such tools, genetic engineers can begin to truly design” [82, p. 628].

The notion of design is indeed omnipresent, not only in the titles of their articles, such as “biology by design”, “designing de novo” or “designing biological systems” [83-85], but also in the name and descriptions of their tools, for instance the software programs they use for computer-aided design (CAD), such as TinkerCell, BioJADE, CellDesigner and GenoCAD.

As a result many sociologists and philosophers have picked up the term, for instance by defining synthetic biology by “the overarching aim of designing and creating new forms of life” [86, p. 432], “the design and construction of new biological systems not found in nature” [87, p. 3] or the “the intentional design of artificial biological systems, rather than on the understanding of natural biology” [88, p. 302]. Finally, it is also present in recent synthetic biology policy documents, for instance in the UK, where there is a “shift towards ‘Biodesign’ capabilities” which promises to be the “key to unlocking the commercialization of applications” in synthetic biology [89, p. 1]. The result is that nowadays BioDesign institutes are being created (such as BBI in Bristol) and it is possible to get a Master in Biodesign.

* 1. Elements of the history of design

It is therefore remarkable how little attention have been paid to this notion of design in debates on synthetic biology, despite the interesting existing literature on the topic [90-91]. Rather it is often taken for granted and unreflexively equated with the idea of rational design, as advocated by Drew Endy and other synthetic biologists [4-7]. This then typically inspires the debates, described above, whether synthetic biology is really rational design and not just a form of kludge [16-17]. However, the idea of design is richer than that of rational design. It is therefore useful to briefly look at the history of design to fully understand what role it plays in synthetic biology.

Design however has its own history. To fully grasp this, it is fruitful to go back to the middle of the 20th century. From the 1940s to the 1960s engineering disciplines witnessed a shift is often called the *rise of engineering sciences*. Throughout all engineering curricula, a new category of *engineering sciences* pops up as a novel way to organize engineering curricula where the scientific basis and method of engineering is stressed at the cost of traditional practical courses. What occurred was that “academic researchers increasingly attacked, not practical problems, but theoretical questions related to materials or engineering principles. And as theory attracted more attention, many engineering research projects became difficult to distinguish from ‘pure’ scientific studies” [92, p. 345]. Specifically, traditional courses focusing on very practical subjects, such as ‘bridge structures’ or ‘roads and pavements’ started to disappear and new academic programs were created, allowing college degrees in ‘engineering science’. Courses related “to practical skills such as drafting, surveying, and other traditional features of engineering curricula” were replaced by “courses in fundamental sciences, mathematics, and engineering science” [93, p. 285].

This shift is reflected in influential policy reports, such as the Grinter Report in 1955 or the preliminary Goals Report of 1965. They advised that engineering should become more scientific and that the graduate and postgraduate programs for engineering must be more fully developed. Why this took place only from the 1950s and 1960s has mainly to do with a crucial shift and increase in federal funding. Bruce Seely in particular has stressed this factor, claiming that the most important factor for “the adoption of the new style of engineering by academia was a massive volume of federal funding” [92, p. 367].

Very soon after the engineering sciences became dominant, several critics from within the field of engineering arose and started to criticize the overemphasis on engineering sciences. For these critics, the ever increasing scientific and theoretical courses in engineering curricula “would guarantee that students learned everything except engineering” [94, p. 18]. Too much stress on engineering sciences was worrisome, since “to educate engineering students along these principles may well have a lasting and detrimental effect on their approach to engineering practice” [95, p. 113]. Ferguson’s work, which we already encountered, is a clear example of this criticism. In fact, he started to write about engineering precisely to warn against this false ideal of reducing engineering to science. As he says in the preface to his book:

The art of engineering has been pushed aside in favour of the analytical ‘engineering sciences,’ which are higher in status and easier to teach. The underlying argument of this book is that an engineering education that ignores its rich heritage of nonverbal learning will produce graduates who are dangerously ignorant of the myriad subtle ways in which the real world differs from the mathematical world their professors teach them. [64, p. xii]

The result has been that in the US “since the late 1980s there has been a national movement to increase undergraduate engineering students’ exposure to design” [94, p. 97]. In a sense, one could even say that the ideal of ‘engineering science’ was being replaced (or at least complemented) with that of ‘design’. In this context, design was not understood as the simple allocation of a number of additional modules, but often was claimed to be required to “permeate the entire curriculum, to the extent that the student is made aware of its importance at every opportunity” [96, p. 75].

To grasp this shift, Nigel Cross introduces a helpful distinction between *scientific design, design science,* and a *science of design* [97, p. 51]. *Scientific design* refers to a practice of design which relies on scientific findings in terms of content, but methodologically still follows a practical or intuitive approach. Attempts to formalize this process of ‘doing design’ in a scientific manner is what *design science* is about: design is then not just using scientific ideas, but is seen as a (distinct) scientific activity on its own. Design is then a scientific practice using scientific data. The *science of design*, finally, is the study of attempting to make our understanding of design into a scientific one (so the people studying the designers become scientists).

Perhaps the clearest case of such an attempt to produce a ‘design method’ was Herbert Simon’s *Science of the Artificial* (1968; revised in 1981). In this book Simon aims to lay down the foundations for a science of the artificial or a design science, i.e. a scientific method for fields such as engineering, computer science and even economics. It is, however, interesting to note that he stresses several times that “a science of the artificial will be closely akin to a science of engineering – but very different, as we shall see in my fifth chapter, from what goes currently by the name of ‘engineering science’” [98, p. 7]. Indeed, his aim is to correct this misdirection “toward natural science and away from the sciences of the artificial” due to the “hunker after academic respectability” [98, p. 130]. This alternative, Simon finds in design. Design forms the central difference between disciplines such as engineering and traditional sciences. “Design, so construed, is the core of all professional training; it is the principal mark that distinguishes the professions from the sciences” [98, p. 129].

Such a focus on design as novel methodologies for engineering is also reflected in policy documents from that time. Government reports, such as the Moulton Report of 1976 and the Finniston Report of 1979 resulted in the institutional incorporation of design in engineering curricula. While Moulton clearly defined engineers as designers, the Finniston Report resulted in the creation of the Engineering Council in 1981, which issued the Standards and Routes to Registration (SARTOR) in 1984 that made design content obligatory in accredited engineering courses in the UK. This focus on design was similarly present in the United States, for instance through the Accreditation Board for Engineering and Technology, Inc. (ABET), which started to increase the requirements of design in engineering curricula.

The open question is, of course, what precisely is meant with this notion of design. My ambition is not to give a definition of the term, since its meaning is exactly what is contested in these debates. Attempts to correct the ideal of engineering sciences in favour of strict design methods have, as a consequence, resulted in mixed successes. Many engineers kept stressing how such a design science cannot be formalized, but must be based on case studies to allow room for unpredictability ungraspable through abstract, analytic methods [99-100]. For them, design was inherently linked with creativity and unpredictability. The “design methods movement”, as Nigel Cross calls it, received “a backlash against design methodology and a rejection of its underlying values, notably by some of the early pioneers of the movement” [97, p. 50]. But it was a testimony to the fact that there has been clear resistance to the idea that engineering could become a science are a completely formalized methodology.

This ambiguity also has to do with the fact that engineering did not simply shift from engineering science to design because some reformers wanted it to. Again, it was linked with broader societal shifts. A crucial factor was that “concerns about economic competitiveness replaced Cold War emphasis. The dual oil shocks and U.S. economic stagnation during the 1970s contributed to [a shift where …] U.S. engineering schools began to focus upon bolstering U.S. industrial capacity” [101, p. 25]. Science and engineering were no longer a means to prove one’s ideological superiority, but became linked with the rise of neoliberalism and the growing competition first with Japan and later with China. Or in the words of Rosalind Williams, “the back-to-practice movement could also be called a back-to-the-market movement, in the sense of renewed and direct attention to profitability” [102, p. 50].

The implication is that the claim that engineering is design is thus open for multiple interpretations, as is clear from this brief historical sketch. These ambiguities are still present in synthetic biology, as I want to illustrate by looking at the debate about rational design versus directed evolution. Rather than, once again, seeing this as a clash between a well-defined idea of engineering and alternative methods, it can be interpreted as a clash between different conceptions of engineering and design.

* 1. Directed evolution as design

Let me first be clear about terminology. ‘Rational design’ refers in this connection to the practice where biologists (aim to) develop a full blueprint of the organism they want to construct (e.g. which genes to include, which parts to exclude, etc.). ‘Directed evolution’, in contrast, refers to the method by which biologists create a ‘library’ with high genetic diversity and subsequently screen the library for the desired traits, or introduce a mechanism of Darwinian selection: a stress or selection effect is introduced that makes only the cells with the desired traits survive.

Within synthetic biology, a discussion exists to which extent directed evolution can still be seen as genuine engineering, since in that case the biologists lose control and oversight over the solution path and the solution itself: is it still engineering or mere kludging? [16-17] They do not know why the organism works the way it does, only that it does work. But it is misleading to see this tension as one between engineering and its other.

Tero Ijäs, for examples, has pointed out that “engineering as a discipline and a practice is not uniform in its design methodology” [103, p. 154]. In his own work, Ijäs stresses how rational design and directed evolution can both be seen as legitimate methodologies in synthetic biology and even engineering. Based on previous discussion about the history of design, this claim can be substantiated. The debate can be reinterpreted as a tension within the field of engineering itself, precisely about what engineering is and whether a standardized ‘design method’ is possible.

Nevertheless, the debate is often framed as an opposition between engineering as rational design and other approaches as ‘merely’ tinkering. For instance, Giese et al. argue in a quantitative study of the field of synthetic biology that only roughly 50% actually talks about and implies ‘rational engineering methods’. They therefore conclude that, “[d]espite its prominent role among the claims of synthetic biology, rational engineering has not yet entirely replaced biotechnological methods based on ‘tinkering’ and non-rational principles” [3, p. 324]. The conclusion that engineering therefore plays no real role in synthetic biology would only hold if engineering was strictly identified with this narrow conception. For in fact, Giese et al. claim that this ‘stagnation’ of the influence of rational design principles is partly due to the increased importance of other methods, inspired by evolution or based on novel DNA-synthesis techniques [3, p. 331].

Thus, rather than asking whether or not engineering is present, the question becomes: what kind of engineering is at play? One traditional candidate is indeed associated with Endy and his principles of rational design [4-7]. Their perspective clearly echoes the ambition to develop a rational design method. Such a perspective is also found in policy documents, such as the UK roadmap for synthetic biology mentioned above, which stresses how “engineering concepts of modularisation, characterisation and standardisation are central to the field” [13, p. 13].

But alternative conceptions of design are present as well, for example in the George Church group. Church and his colleagues have in the last decade developed a method called Multiplex Automated Genome Engineering (MAGE), aimed to improve directed evolution methods in synthetic biology, which aims to let nature solve problems for them by constructing novel biological systems which they can use. With their technique, Church and his colleagues are able to introduce genetic modifications by first disabling the DNA repair mechanisms of the cell, then introducing new single-stranded pieces of DNA (by electroporation). These pieces of DNA are similar at both ends to the DNA of the cell in question, but have a novel sequence of up to 90 bases in the middle. Specific Beta Proteins bind these novel pieces of DNA with complementary parts, but are unable to ‘repair’ the mismatch in the middle with the novel bases. The consequence is that when the cell multiplies the novel part is transmitted to (half of) the next generation, which will possess the introduced mutation.

This process is iteratively repeated at multiple cells, at multiple sites of their genomes in an automated MAGE device. ‘Multiplexing’ thus refers to the possibility to simultaneously target multiple chromosomal sites, which is one of the advantages of this system in comparison with earlier techniques of directed evolution. A second advantage is that it is highly automated, making “the intermediate step of colony isolation for genotyping or phenotyping” [104, p. 411] redundant. This is possible due to so-called ‘sensory proteins’, which are made “responsive to a number of target chemicals to couple the concentration of the target chemical in each cell to individual cell fitness. This coupling of chemical production to fitness allows us to harness evolution to progressively enrich superior pathway designs” [105, p. 17803]. Such coupling with genetically encoded biosensors makes cells with the desired traits either resistant to antibiotics or fluorescent, allowing for an automated selection procedure.

The Church group is quite explicit in considering their own approach as a form of ‘design’, one which is superior to earlier design approaches. They identify “[t]he engineering process in which these designs are evaluated and iterated on [a]s the design–build–test cycle” [106, p. 198]. Their approach is claimed to cope better with biological complexity and to solve some ‘bottlenecks’ present in the design cycle.

This is in fact the case, since to individually analyze each design solution for a specific desired trait is time-consuming work, while “a fully multiplexed design cycle can shift the mindset of bioengineers such that they can think in terms of whole design spaces rather than single design instances” [106, p. 199]. Their method allows for a faster, automated exploration of the ‘design space’, the whole realm of possible designs that would take too long to consider individually ‘by hand’. It is claimed to be superior in exploring biological possibilities.

The Church group also sees this as a step beyond the traditional engineering approach associated with Endy. “In the initial stages of synthetic biology, design has been closely linked to physical assembly. For example with BioBricks—the first major standard implemented—assembly is kept general and independent of specific parts through the use of a restriction-ligation scheme” [107, p. 1154]. According to Church and his colleagues, we are witnessing a greater flexibility, which allows synthetic biologists to cope with and incorporate biological complexity. There is thus a recognition that a purely top-down rational design is unfeasible, and they advocate a more open-minded form of design.

They plead for a form of design that incorporates “a form of directed evolution in which an engineer monitors the flow of designs and intervenes as necessary” [106, p. 200]. “Our multiplex approach embraces engineering in the context of evolution by expediting the design and evolution of organisms with new and improved properties.” [108, p. 894]. Or differently put: “This rapid chromosomal engineering method offers the opportunity to construct both highly modified genomes and explore large sequence landscapes by directed evolution in a semirational fashion.” [104, p. 411] The power of evolution is thus harnessed as a strategy to synthesize biological possibilities. If the goal is indeed to explore a design space, evolution is “a powerful tool for resolving the complexity of biology. Using evolution to guide rational design should ultimately lead to a better understanding of the genotypic basis of biological function” [105, p. 17808].

In the work of the Church group we thus find a specific form of design, one that quite explicitly distances itself from ‘rational design’ understood in a narrow sense, linked with authors such as Drew Endy. It is rather a form of engineering based on creating a setting in which directed evolution is used to solve and purify design choices. One might ask: Is this still engineering? My claim is that from the history of engineering and design sketched above, directed evolution can surely be seen as part of engineering.

Tensions about whether this form of ‘directed evolution’ still has anything to do with design must thus be seen in a historical light, namely as a continuation of earlier debates about the possibility and nature of design methods in engineering. A struggle between different understandings of engineering is thus continued in synthetic biology in the shape of the tension between directed evolution and rational design. But these are discussions to be considered within engineering, rather than between engineering and its other.

The way how engineering and design were understood has thus shifted in the 20th century and this can shed light on a number of the debates mentioned above. While the first two definitions stress the formal and scientific aspects of science, seeing engineering as applied science or a formal methodology, the third and fourth, seeing engineering as a practice or a ruse, tend to stress this other side of engineering, that evades all formalization.

1. **Conclusion**

In this article I have shown how the concept of engineering, central to synthetic biology, is far from unambiguous, but can mean multiple different things. In this article five different candidates were discussed. As stated in the introduction, the claim is not that this list is exhaustive, but merely serves to illustrate that there are more than one interpretation of what engineering is. It thus remains an open question whether other conceptions of engineering play a role in synthetic biology and its debates. Future research has to show whether important alternative conceptions were overlooked here or whether, in the line of the argument found in the work of Calvert and others [18-20], synthetic biology is perhaps developing a novel form of engineering. If such a novel form of engineering exists, it would be wise to analyze it in its own terms, instead of reducing it to one of the above conceptions of engineering. It links to the related question whether different conceptions about engineering also result in different practices. To repeat, the argument presented here mainly played at the level of discourse, but one can wonder how these different discourses not only reflect different philosophical debates or policies, but also different engineering practices.

Another open question is whether the these conceptions of engineering similarly play a role in discussions in related disciplines, such as systems biology. Joan Fujimura notes how “[m]any systems biological metaphors and languages are taken from engineering models of the complex of systems of automobiles, airplanes, and robots and then applied to complex living systems.” [109, p. 196] In fact, many systems biologists themselves have a background in engineering [110 p. 9]. It remains to be studied how these different conceptions play out in different ways in systems biology and whether other conceptions of engineering might be more prominent there.

In that sense, the first take-home message is precisely the diversity of conceptions of engineering that are present in synthetic biology. Engineering can be understood in many ways, namely as applied science, as rational methodology, context-sensitive practice, cunning activity or design. Hardly any debate on synthetic biology can be indifferent towards the question which conception of engineering is at play.

Each of these conceptions has different connotations, consequences and tensions, each leading to specific debates, concerns and ideas. Recognizing this diversity thus helps us to understand and perhaps even dismantle some of the debates about synthetic biology. More specifically, four broader debates about synthetic biology have been discussed. The first one concerned the question whether synthetic biology is really engineering or something else, such as tinkering or kludging. Once it is recognized that engineering means multiple things, this discussion can be reinterpreted as one, not about engineering versus its other, but rather as an internal debate within engineering about its nature.

Secondly, and related, there is the debate about the relation between synthetic biology and genetic engineering which can be interpreted as a conflict between different ideas about engineering and even about the question of what kind of engineering synthetic biology is or aspires to be. This diversity of engineering conceptions, thirdly, sets the worry about whether biology is falling prey to automation in a new light. Whether the automation of biology is possible and what it would mean depends on what kind of engineering, and more particularly what kind of formalization, is possible and to what extent.

Finally, also ethical debates are affected by the conception of engineering one has in mind. How we must understand and evaluate the discontent about the ‘naturalness’ of genetic engineering and synthetic biology depends on what kind of engineering one is dealing with: is synthetic biology imposing its will on nature through abstract principles, thereby ignoring its own tendencies or habits? Or is the engineering of synthetic biologists rather one of a practical nature, with room for the particularities of nature? Or are synthetic biologists mainly in the business of tricking nature into doing things it was not ‘supposed’ to do, not in the sense of breaking the laws of nature, but rather of using nature’s tendencies against itself? The answers to these questions depend, first of all, one how one understands the practice of engineering.

1. **Bibliography**

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1. Synthetic biologists also rewrite the history of biology in light of the ideal of ‘engineering life’ [11]. [↑](#footnote-ref-1)