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opinion

Perfect time or perfect crime?

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Imagine the situation: "One day, you notice an old country woman crossing a downtown street, just about to put one foot down on the rails of the streetcar line. […] Suppose, now, that at the very moment she puts her foot on the rail a streetcar comes rushing down the tracks toward her. If the old woman does not notice the car and continues across the tracks nothing will happen. But if someone should happen to shout 'Look out, old woman!' what would be her natural reaction? […] she would suddenly become flustered and would pause to decide whether to go on or step back […] the mere words 'Look out, old woman!' would be as dangerous a weapon as any knife or firearm. […] the man who sounds the warning actually becomes a murderer!" (Ranpo, 1956).

In the same way, the Asilomar conference on genetic engineering in 1975 was the perfect crime in using cautionary exclamations as a weapon that had far-reaching consequences for the emerging field of molecular biology and its applications: a moratorium stopped research in some places, while others proceeded and took the lead.

The same fate may lie in store for synthetic biology (SB). The usual crooners have understood the importance of appealing to ethics and playing on people's fears to make themselves known and have begun a discussion of the purported dangers of creating organisms *à la carte*. Such clamouring for attention may yet end up being a shot to our own feet. Moreover, does minimization of a bacterial genome really pose ethical questions? Should we worry, and if so, why? After all, what is the purpose of SB? We must first explore the knowledge that we are required to master to (re)construct life before we can start asking the economic and ethical questions.

Humans are driven by a combination of pragmatism and curiosity and SB is the perfect illustration of this. The idea is to construct cellular factories that do our bidding, whether the goal is to produce fuel or fine chemicals, trap carbon dioxide or break down toxic chemicals. However, to do so, we must understand what life is—and the best current strategy to understand something is to reconstruct it. SB, with this goal in mind, combines historical biology—phylogeny and evolution—and experimental biology. In parallel, it is based on the belief that some functions of life are computable. The popular view of SB is that its nuts and bolts are simply pieces of DNA: algorithms of the general software of life. However, even if we ignore the hardware—proteins, nucleic acids and metabolites—the process of life differs from computers, as it spans many generations; biology has a historical component. This implies a subtle but essential feature: the hardware—the cell or the organism—reproduces a similar copy of itself, while the genetic programme replicates an exact copy of itself.

We immediately see that reproduction is more or less absent from the technological goals of SB. Could we accept factories that deliver products that are similar, but not identical to each other? Quality control in biology does not have the same meaning as for ISO manufacturing standards. For example, the final result of protein synthesis is a collection of proteins with similar, not the same, sequences and shapes. Progeny are *not* a replica of their parents: they are young, not old. This is not a trivial observation; it means there must be processes and genes that ensure children are born young.

A tentative identification of the essential genes from various bacterial species leads to some 250 genes. Yet, twice that number and more persist in bacterial genomes, with many persistent and non-essential genes coding for energy-dependent degradation processes. This suggests that their proteins use energy to perform some kind of measurement, similar to Maxwell's demon. In the same way, a biological demon, making a young organism from an old one, must eliminate aged objects and erase the genetic memory of past events, using energy to make such choices. This is exactly the role of the non-essential persistent genes coding for energy-intensive degradation enzymes: to *preserve* entities that have some particular feature, such as a young age or a required catalytic activity.

Coming back to SB, we see that this degrading function, if it exists, is not readily compatible with the aims of SB, the purpose of which is to design living cells that will follow specific goals. If the conjecture discussed previously has some validity, then living cells manipulate information, recovering, trapping and accumulating it by using Maxwell's demon-like devices—enzymes that use energy to prevent the degradation of context-dependent information-rich entities. This will inevitably go against the engineering goal of SB. Indeed, being 'myopic', these demons only see their immediate environment and cannot readily adapt to human design. A remedy might be to omit these genes in SB constructs, but the corresponding cells will inevitably age and die and loose their capacity to generate rejuvenated progeny. Yet, it will be extremely rewarding for the purpose of understanding what life is.

Do we need to be afraid of SB? Probably not at this time, and it is difficult to predict when the question will become relevant. Life itself is far less predictable than SB, and this is where the danger resides.

REFERENCE

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