The 'atom-splitting' moment of synthetic biology

Nuclear physics and synthetic biology share common features

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On 16 July 1945, in the desert of New Mexico, the first nuclear bomb was exploded. It was a crucial moment in the history of the physical sciences—proof positive of the immense forces at work in the heart of atoms—and inevitably changed the world. In 2010, a team at the J. Craig Venter Research Institute in the USA first created artificial life by inserting a synthetic 1.08 megabase pair genome into a mycoplasma cell that lacked its own. They demonstrated that this new cell with its man-made genome was capable of surviving and reproducing [1]. It was a colossal achievement for biology, and its significance might well rank alongside the detonation of the first atomic bomb in terms of scientific advance.

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There are several similarities between twentieth century physics, and twentieth and twenty-first century biology. The nuclear explosion in New Mexico was the result of decades of research and the first splitting of an atom in Otto Hahn's laboratory in 1938. It ushered in an era of new ideas and hopes for a brighter future built on the power of the atom, but the terrible potential of nuclear weapons and the threat of nuclear warfare ultimately overshadowed these hopes and changed the course of science and politics. The crucial achievement of synthetic life is a strikingly similar event; the culmination of decades of research that started with its

own atom-splitting moment: recombinant DNA technology. It promises to bring forth a new era for biology and enable a huge variety of applications for industry, medicine and the military. However, as with post-war physics, synthetic biology's promises of a brighter future might not all materialize and could have far-reaching effects on society, science and politics. Biology should therefore take note of the consequences of nuclear physics' iconic event in 1945 for science, politics and society.

To appreciate the similarities of these breakthroughs and their consequences for society, it is necessary to understand the historical perspective. The pivotal discoveries for both disciplines were related to fundamental elements of nature. The rise of nuclear physics can be traced back to the discovery of neutrons by James Chadwick in 1932 [2]. Neutrons are essential to the stability of atoms as they insulate the nucleus against the repulsive forces of its positively charged protons. However, the addition of an extra neutron can destabilize the nucleus and cause it to split, releasing more neutrons and a tremendous amount of energy. This nuclear fission reaction was first described by Otto Hahn and Fritz Strassmann in 1938. Leo Szilard realized the possibility of using the neutrons released from the fission of heavy atoms to trigger a nuclear chain reaction to release huge quantities of energy. The first successful chain reactions took place in 1942 in Germany at Leipzig University in the laboratory of Robert Döpel, and in the USA at the University of Chicago in the so-called Chicago Pile-1 reactor, developed by Enrico Fermi. These first nuclear reactors provided the proof of concept for using a nuclear chain reaction as a source of energy. However, even before that,

Albert Einstein and Leo Szilard wrote to US President Franklin D. Roosevelt in 1939, suggesting that the US government should develop a new powerful bomb based on nuclear fission. President Roosevelt created the Manhattan Project, which developed the first atomic bomb in 1945.

The Cold War and the mutually assured nuclear destruction between the USA and the USSR fanned widespread fears about a nuclear Third World War that could wipe out human civilization; Robert Oppenheimer, one of the physicists who developed the atomic bomb, was actually among the first to warn of the spectre of nuclear war. By contrast, the civilian use of nuclear physics, mainly in the form of nuclear reactors, promised a brave new future based on harnessing the power of the atom, but it also generated increasing concerns about the harmful effects of radioactivity, the festering problems of nuclear waste and the safety of nuclear power plants. The nuclear disasters at the Chernobyl reactor in 1986 and the Fukushima power plant in 2011 heightened these concerns to the point that several nations might now abandon nuclear energy altogether.

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The fundamental discovery in biology, crucial to the creation of synthetic organisms was the double helix structure of DNA in 1953 by Francis Crick and James Watson [3]. The realization that DNA molecules have a universal chemical structure to store and pass on genetic information was the intellectual basis for the development of recombinant DNA (rDNA) technology and

genetic engineering. Twenty years after this discovery, Stanley Cohen and Herbert Boyer first transferred DNA from one organism into another by using endonucleases and DNA ligases [4]. This early toolkit was later expanded to include DNA sequencing and synthesizing technologies as well as PCR, which culminated in the creation of the first artificial organism in 2010. Craig Venter's team synthesized a complete bacterial chromosome from scratch and transferred it into a bacterial cell lacking a genome: the resulting cell was able to synthesize a new set of proteins and to replicate. This proof of concept experiment now enables scientists to pursue further challenges, such as creating organisms with fully designed genomes to achieve agro-biotechnological, commercial, medical and military goals.

Similarly to nuclear physics, the advent of rDNA technology has concerned the public, as many fear that genetically modified bacteria could escape the laboratory and wreak havoc, or that the technology could be abused to create biological weapons. Unlike with nuclear physics, the scientists working on rDNA technology anticipated

these concerns very early on. In 1974, a group of scientists led by Paul Berg decided to suspend research into rDNA technology to discuss possible hazards and regulation. This discussion took place at a meeting in Asilomar, California, in 1975 [5].

A pertinent similarity between these two areas of science is the confluence of several disciplines to create a hybrid technoscience, in which the boundaries between science and technology have become transient [6]. This convergence was vital for the success of both nuclear physics and later synthetic biology, which combines biotechnology, nanotechnology, information technologies and other new fields that have been created along the way [7]. In physics, technoscience received massive support from the government when the military potential of nuclear fission was realized. Although the splitting of the atom took place before the Manhattan Project, the Second World War served as a catalyst to combine research in nuclear physics with organized and goal-directed funding. As most of this funding came from the government, it

changed the relationship between politics and research, as scientists were employed to meet specific goals. In the wake of the detonation of the first atomic bombs, the post-war period was another watershed moment for politics, technoscience, industry and society as it generated new and more intimate relationships between science and governments. These included the appointment of a scientific advisor to the President of the USA, the creation of funding organizations such as the National Science Foundation, or research organizations such as the National Aeronautics and Space Administration, and large amounts of federal funding for technoscience research at private and public universities. It also led to the formation of international organizations such as the civilian-controlled International Atomic Energy Agency [6].

There is no global war to serve as a catalyst for government spending on synthetic biology. Although the research has benefited tremendously from government agencies and research infrastructure, the funding for Venter's team largely came from the private sector. In this regard, the relationship

between biological techno-science and industry might already be more advanced than with the public sector given the enormous potential of synthetic life for industrial, medical and environmental applications.

Research and innovation at universities has always played a vital role in the success of industry-based capitalism [8]; technoscience is now the major determinant of a knowledge-based economy or 'technocapitalism' [9]. At the heart of technocapitalism are private and public organizations, driven by research and innovation, which are in sharp contrast to industrial capitalism, where the factories were production-driven and research was of less importance [10]. Furthermore, synthetic biology might provide valuable resources to the scientific community and thereby generate new research opportunities and directions for many biological fields [11].

However, given the far-reaching implications of creating synthetic life and the risk of abuse, it is probable that the future relationship between synthetic biology and government will include issues of national security. In the light of potential misuse of synthetic biology for bioterrorism, and the safety risks involved in commercial applications, synthetic biology will eventually require some government regulation and oversight. In contrast to nuclear physics, in which the International Atomic Energy Commission was established only after the atomic bomb, the synthetic biology community should hold a new Asilomar meeting to address concerns and formulate guidelines and management protocols, rather than waiting for politicians or commercial enterprises to regulate the field.

So far, synthetic biology differs from nuclear physics in terms of handling information. The Manhattan Project inevitably created a need for secrecy as it was created at the height of the Second World War, but the research maintained this shroud of secrecy after the war. After the bombing of Hiroshima and Nagasaki in August 1945, the US government released carefully compiled documents to the American public. The existence of useable nuclear power had been secret until then, and the control of information ensured that the public further supported or tolerated

the technology of nuclear fission and the subsequent use of atomic bombs [12]. This initially positive view changed in the ensuing decades with the threat of a global nuclear war.

Information management in synthetic biology differs from nuclear physics, in that most of the crucial breakthroughs are immediately published in peer-reviewed journals and covered by the media. The value of early public discourse on science issues is evident from the reaction towards genetically modified crops and stem cell research. In this regard, synthetic biology has side-stepped the mistakes of nuclear physics and might well achieve a more balanced public integration of future developments.

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The main issues that might threaten to dampen public support for synthetic biology and favourable public perception are ethics and biosecurity concerns. Ethical concerns have already been addressed in several forums between scientists and public interest groups; this early engagement between science and society and their continuing dialogue might help to address the public's ethical objections. In terms of biosecurity, biology might learn from nuclear physics' intimate entanglement with politics and the military. Synthetic biologists should maintain control and regulation of their research and avoid the fate of nuclear physicists, who were recruited to fight the Cold War and were not free to pursue their own research. For synthetic biology to stay independent of government, industry and society, it must capitalize on its public engagement and heed the lessons and mistakes of nuclear physics' atom-splitting moment. It should not just evaluate, discuss and address the risks for human or environmental health or biosafety concerns, but should also evaluate potential risks to synthetic biology research itself that could either come from falling public acceptance or government intrusion.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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