

# **Recombinant DNA and Self-replicating Molecular Manufacturing: Parallels and Lessons**

## **Editor's Note**

*This article was adapted from a written presentation by James B. Lewis, Ph.D. for Terasem Movement, Inc.'s 5th Annual Workshop on Geoethical Nanotechnology on July 20, 2009 at the Terasem Island Amphitheatre in the virtual meeting environment of "Second Life".*

*Dr. Lewis expounds on why an Asilomar-like conference, as well as other venues involving relevant members of the scientific and technical communities, should be explored to identify and avoid immediate threats to public safety at such time when self-replicating nanotechnology is imminent.*

Several papers published in 1972 showed that it was possible to cleave virtually any DNA molecule so that the pieces could be spliced together in the test tube to create a new biologically active DNA molecule—a recombinant DNA molecule that joined together genes from very different organisms to form a molecule that could self-replicate in bacteria to produce huge numbers of copies. It was immediately recognized that this capability offered great potential to advance fundamental knowledge of biology and possibly to alleviate human health problems, but some concerned scientists objected that it also might produce hybrid molecules that could prove hazardous to laboratory workers and to the public (for example by multiplying genes from a cancer-causing virus inside bacteria living in the human gut, perhaps leading to more cancer) [1]. The crux of the concern was the potential that artificial self-replicating molecules might have unknown properties that would cause nasty surprises. As a result of these concerns, a high-level committee of prominent scientists proposed voluntarily deferring certain experiments until further evaluation of potential hazards had been done, and appropriate procedures and guidelines to minimize risk had been developed. They declared, "[A]n international

meeting of involved scientists from all over the world should be convened early in the coming year to review scientific progress in this area and to further discuss appropriate ways to deal with the potential biohazards of recombinant DNA molecules." [2]

As a result of the Asilomar Conference [3], the three-day meeting held in February 1975 to consider the moratorium on recombinant DNA experiments, strict procedures were spelled out for working with recombinant DNA. Various methods of physical containment (specially equipped laboratories, special procedures and training) and biological containment (fastidious bacteria that could only survive under laboratory conditions and vectors that could only multiply in certain hosts) were specified, with the most stringent containment methods matched to what were considered the most hazardous experiments. Most of the scientists involved felt that there was little risk involved in most of the experiments that were to be regulated, but there was little hard data available on which to base rational risk analysis, and few wanted to chance being catastrophically wrong.

The meeting had been called by scientists in response to concerns about threats to public safety that had been raised by scientists themselves, and members of the press were invited to attend and report the proceedings. As a result, the "meeting was widely hailed as a landmark of social responsibility and self-governance by scientists" [4]. The immediate effect of the meeting was to end the moratorium so that research could proceed under the new guidelines, and to help convince the US Congress that no further restrictions were needed because the scientists could govern themselves. As a consequence, recombinant DNA technology became the basis for a profound explosion of knowledge. Genes and genomes were no longer abstract entities, but instead segments of

DNA that could be manipulated and studied in detail. Numerous therapies and diagnostics were developed, and within 30 years the human genome and many other genomes had been sequenced. The technologies that grew from the recombinant DNA technology of the 1970s have brought us to the verge of deep knowledge of biology and of the ability to manipulate genes and cells to cure diseases and improve human health.

Over the years as experience and knowledge of the real risks accumulated, the guidelines were substantially loosened or eliminated so that experiments could legally be done in open laboratories, or eventually even in someone's basement. We now know that organisms have exchanged DNA for millions of years as a common feature of evolution. Indeed, in the 34 years since Asilomar, there have been no documented hazards to public health attributed to recombinant DNA. Those scientists who, at the time, thought that the new recombinant DNA technology posed no significant risk turned out to have been correct. (For perspectives on Asilomar 25-30 years later, see [4], [5], [6] and [7].)

Asilomar succeeded because the organizers made a deliberate choice to only address the immediate issue of how to prevent recombinant DNA technology from threatening public health. This was the one issue that had raised the concern that necessitated the meeting, and in principle (although not all the important information was yet available at the time of the meeting) it was a question that could be answered by science: [what types of containment could reduce the risk to acceptable levels?](#) Further, this was the one crucial issue that had to be resolved for research to go forward and for the myriad benefits of biotechnology to be realized.

The Asilomar participants chose not to consider various ethical issues that could be linked to recombinant DNA research, and which were associated with a general

uneasiness felt in many quarters about the prospects for genetic engineering [8]. Would recombinant DNA technology make biological warfare more lethal? What were the implications of gene therapy, germ line modifications, or the patenting of organisms and genes? Who bore the risks and who collected the profits? What were the implications of genetically modified foods for health, for the environment, and for farmers? Genetically modified food (especially in Europe), embryonic stem cell research, and human enhancement and cloning have proven to be particularly controversial topics. These various social, economic, political, religious, and ethical issues remain controversial because they reflect deep divisions of interests and values within society, and fundamental differences of opinion on the nature of human dignity and human value. Further, biotechnology has become an important component of international economic competition.

A related issue that developed in the years following Asilomar is that, although initially the scientific community was praised for being socially responsible and self-governing for first addressing and then resolving the issue of the safety of recombinant DNA technology, it was later criticized for self-regulating an emerging technology (genetic engineering) that was seen to have significant public policy aspects without including non-scientists in the discussions and decision-making. In retrospect, the scientists were certainly correct to do it the way they did—had they opened Asilomar to a wider community and addressed the other, underlying issues they never would have dealt with the crucial safety question that had occasioned the moratorium, the experiments would probably have been greatly delayed, and biotechnology might have been stillborn. One cannot help wonder, however, whether some of the later controversy would have

been ameliorated had a parallel series of discussions been initiated in which a wider community had been invited to consider a wider range of issues.

In sum, Asilomar provided what was needed to launch a new field of science, a new technology, and a new industry. It dealt very well with the perceived problem with the new biotechnology, but the perceived problem was not really a problem after all, and the perceived problem had very little to do with the real problems that underlay societal unease with respect to the new technology, and which formed the basis for continuing controversy. Perhaps the legacy of Asilomar is best summed up by Berg and Singer, two organizers of the Asilomar conference, writing in 1995 (when the human genome project was launched) [5]:



[http://www.ornl.gov/sci/techresources/Human\\_Genome/elsi/elsi.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/elsi/elsi.shtml) September 14, 2009 9:29AM EST

"Inferring evil intent and calling for bans on genetic research denies the value of such research in fulfilling human dreams for improved health and the sustenance of a growing human population. Vigorous, informed public debate on all these issues should be fostered, as it is by the Ethical, Legal, and Social Implications (ELSI) Program of the Human Genome Project. The need for this debate is one reason to encourage widespread improvement in science education in American schools.

“In retrospect, very few of those attending the Asilomar Conference foresaw the pervasive, complex, robust, and rich ramifications of recombinant DNA technology. Nor could most have predicted the pace at which fundamental understanding of biology has deepened. As with all changes in human thought and technological developments, we are left with new and unanticipated issues. And, as so often in the past, science, which itself is a uniquely human endeavor, is challenging traditional ideas and values.”

What lessons does Asilomar have to teach us about “reconciling conflicts, apprehensions, and scientific ambitions regarding self-replicating nanotechnology”?

Comparisons of self-replicating DNA molecules and self-replicating nanotechnology are clouded by the fundamental differences between evolved biological replicators and designed self-replicating nanotechnology, and by the history of how visionary ideas of self-replicating nanotechnology were introduced. In particular, the fact that the initial treatment of nanotechnology (in 1986) envisioned self-replicating, microscopic assemblers [9] has caused a confusion of issues by making self-replicating nanotechnology seem more similar to a self-replicating DNA molecule in a bacterium living in a gut than is in fact the case. Further confusing discussion of the safety of nanotechnology is the notorious "gray goo" scenario [10], in which the biosphere is consumed by out-of-control assembler-like machines.

Superficially, the threat of out-of-control replicators destroying the biosphere seems similar to the threat of a biological replicator with unexpected properties spreading disease. However, there is no real similarity because the idea of accidentally out-of-

control assemblers was almost immediately (1988) recognized to be a red herring [11]. Furthermore, it soon (1992-1999) became apparent that universal self-replicating assemblers formed an extremely inefficient self-replicating molecular manufacturing system compared to more complex macroscopic nanofactories composed of large numbers of molecular mills and parts assemblers [12, 13, 14]. The risks of self-replicating nanotechnology were succinctly summarized by Phoenix and Drexler writing in 2004:

"It has since become clear that all risk of accidental runaway replication can be avoided, since efficient manufacturing systems can be designed, built, and used without ever making a device with the complex additional capabilities that a hypothetical 'grey goo robot' would require. However, this does not mean that molecular nanotechnology is without risks. Problems including weapon systems, radical shifts of economic and political power, and aggregate environmental risks from novel products and large-scale production will require close attention and careful policymaking."

Despite the early recognition that the issue of feral self-replicating assemblers is a red herring, early attempts (in 2000) [15] to develop guidelines for advanced molecular nanotechnology, which explicitly reference the precedent of Asilomar for self-regulation of a powerful emerging technology, were heavily focused on restricting self-replicating nanotechnology. Even the current version of those guidelines [16], written in 2006, retains a prohibition against autonomous replicators. Commenting on the guidelines in 2006, Rothblatt [17] notes the disproportionate emphasis on prohibiting autonomous replication of nanotechnology systems:

"The guidelines seem to take the position that self-replication is unnecessary, uneconomic, and therefore unlikely. Yet they are overwhelmingly consumed with the issue of self-replication to the point that nearly half of the guidelines deal either explicitly or implicitly with self-replication."

Instead of prohibiting self-replicating nanotechnology, Rothblatt proposes establishing (via treaty), an international organization that would have "exclusive worldwide rights to self-replicator production rights." In responding to Rothblatt's proposal, Kurzweil adds the thought that self-replicating nanotechnology will be a necessary component of any immune-type system to protect the world from pathological (or malicious) self-replication.



Photo after 9/11 attack on NYC



It might also be noted that in some situations self-replicating molecular manufacturing systems might need to do something similar to what would be done by gray goo: turn the surrounding environment into feedstocks and molecular building blocks for molecular manufacturing, but under controlled conditions. Examples could include vast rubble fields left after some disaster, hydrocarbon oceans on some frozen moon, asteroids awaiting conversion to space habitats, or virgin solar systems to be made suitable for human intelligence. In such cases the relevant question becomes not low-level controls



on the replication machinery, but the behavior of the intelligence controlling the systems. These might be much more difficult questions, but focusing on the low-level controls on the replication machinery distracts attention from the important problems.

So, to return to the question: What lessons does Asilomar have to teach us about “reconciling conflicts, apprehensions, and scientific ambitions regarding self-replicating nanotechnology”? The set of problems facing self-replicating molecular manufacturing today is very different from the situation with recombinant DNA technology in 1975.

*1. Asilomar was needed to demonstrate that an existing technology could be safely implemented, and that the community of practitioners could be trusted to regulate themselves.*

Unlike recombinant DNA in 1975, self-replicating nanotechnology is not an existing technology. It is a visionary proposal about which the scientific mainstream remains largely skeptical, and the implementation of self-replicating molecular systems is still decades away. None of the work that needs to be done in the next decade or so to develop the basic technology is awaiting guidelines on how to prevent autonomous self-replicating manufacturing systems from escaping into the environment.

The relevant comparison today to recombinant DNA in 1975 is the widespread environmental, health, and safety concerns with various types of nanomaterials that have already entered into widespread commercial use. A number of studies have provided evidence that there are indeed concerns about the effects of some nanomaterials on the environment and on human health, and some groups have advocated a moratorium on work with nanomaterials. It is imperative that all those involved in current day nanoscience and nanotechnology follow the example of Asilomar with respect to

openness, sufficient scientific study to understand the problem, and adoption of regulations that evolve in step with evolving scientific understanding. Consideration of the EHS issues with current and next generation nanomaterials is beyond the scope of this presentation, but current activity in this area is intense [18]. At least superficially, it looks like this activity is following the lessons learned from Asilomar, although the size and complexity of the problem, the number of international stakeholders, and the immediate economic interests at stake, are far larger than was true with recombinant DNA in 1975, so [it is too soon to predict outcomes](#).

*2. Asilomar avoided considering those broader issues underlying public attitudes about genetic engineering that were not immediately related to the safety of recombinant DNA technology.*

Because no parallel process was established to involve those outside the scientific community to consider the broader issues, these issues were dealt with on an *ad hoc* basis as the technology advanced—with variable success. As each technological advance arose, it was dealt with in the context of the current social and political issues. Genetically modified food ran afoul of the European Green movement; embryonic stem cells became entangled in anti-abortion politics and the general revulsion against human cloning. Asilomar thus provides no guidance on how to deal with complex issues in advance of the technological progress that places the issue in the public spotlight.

Attempts to deal with the consequences and ethical implications of self-replicating nanotechnology are thus in uncharted waters. Initial attempts [15, 16] to specify guidelines for the development of self-replicating nanotechnology focused on restricting autonomous replicating manufacturing systems. An alternative [17] proposes an

international treaty under which such systems could be safely developed, especially noting that they may be an essential part of a protective system against malicious autonomous replicating manufacturing systems.

However, autonomous replicating manufacturing systems, whether accidentally out-of-control or maliciously unleashed, are not the only—and perhaps not the major—consequence of self-replicating molecular manufacturing needing attention. One list of such consequences has been compiled by the Center for Responsible Nanotechnology [19]. Some serious issues might arise directly from the successful deployment of a surveillance/immune system to detect malicious replicators or dangerous products of molecular manufacturing. Eric Drexler [20] is concerned that surveillance/immune systems will suppress terrorism so effectively that governments will use them to suppress other dissent:



<http://e-drexler.com/p/idx04/00/0404drexlerBioCV.html> September 14, 2009 9:35AM EST

"It's often said that we face an unending struggle against terrorism. This is nonsense. Advancing technologies will eventually make it easy to suppress terrorism. The great struggle will be to keep this power from suppressing too much more."

In another attempt to address the impact of improved surveillance on privacy and freedom, the Foresight Institute is exploring an open source project [21] to bring "the benefits of a bottom-up, decentralized approach to sensing for security and environmental

purposes. The intent of the project is to take advantage of advances in sensing to improve both security and the environment, while preserving — even strengthening — privacy, freedom, and civil liberties."

Among the many issues that will be raised by the development of self-replicating molecular manufacturing technology, perhaps the greatest and most immediate impact will be on the ability of most people to earn a living. If artificial general intelligence takes over the jobs of scientists, engineers, and other professionals, and molecular manufacturing systems and robots make all necessary goods and perform all necessary services, how will humans earn a living? Will all wealth accrue to those who own the various technologies? Will it be possible for humans to own AI systems that are millions of times more intelligent and capable than they are? Among the few proposals that address this problem, my favorite was made by Eric Drexler in 1986 [22]:

"...distributing ownership of the resources of space (genuine, permanent, transferable ownership) equally among all people — but doing so only once, then letting people provide for their progeny (or others') from their own vast share of the wealth of space. This will allow different groups to pursue different futures, and it will reward the frugal rather than the profligate. It can provide the foundation for a future of unlimited diversity for the indefinite future, if active shields are used to protect people from aggression and theft. No one has yet voiced a plausible alternative."

However, the date suggested by Drexler for doing this distribution (April 12, 2011) is far too imminent for any such agreement to be in place by then.

If we are to improve upon the results of Asilomar and prepare in advance for the issues that are associated with a technology that does not yet exist—self-replicating

nanotechnology—then we first have to prepare the ground for discussing and resolving the most fundamental and pressing issues that will arise with respect to that technology (which probably do not include “gray goo”). The lessons of Asilomar suggest that serious discussion of those issues will not occur until there is a consensus that the technology at issue, if not already existing, is at least very likely to develop soon. Therefore, we can expect that “reconciling conflicts, apprehensions, and scientific ambitions regarding self-replicating nanotechnology” will be a long, drawn-out process stretching through the decades until the imminent advent of the technology becomes obvious—perhaps paralleling the efforts to get society to come to grips with the effects of human activities upon climate change. What might advance such a reconciliation?

1. Use EHS issues with respect to current and near-term nanomaterials technology to establish the precedent of open and rational discussion, support for conclusive research, and a consensus process for appropriate regulations regarding nanotechnology, paralleling the historical regulation of recombinant DNA technology.
2. To render self-replicating nanotechnology more credible, publicize progress toward that goal, and lobby for more support for similar research. For example, recent results [23] with structural DNA nanotechnology and protein design indicate acceleration of progress along the modular molecular composite nanosystems path toward atomically precise productive nanosystems [24].
3. Promote films, books, and other media that depict self-replicating nanotechnology and other “Singularity”-associated technologies to foster awareness of and discussion of impacts.

4. Promote conferences to develop consensus positions on dealing with impacts. As progress towards the technology becomes more credible, more specific Asilomar-like conferences to deal with specific issues will become appropriate.
5. Follow and encourage development of open source 3D printers capable of making some or most of their own parts [25] as a prototype of self-replicating nanotechnology. At what point in their development do these projects raise issues comparable to the issues that will be raised by self-replicating nanotechnology? Can possible solutions be tested with these projects?

The above suggestions are made in the belief that the more people who can be convinced that a goal is worthwhile and doable, the more people will work to uncover and solve the whole spectrum of problems that could be associated with the goal, and thus the more likely that the outcome will be both successful and ethical.

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[7] "Asilomar and Recombinant DNA," Paul Berg (2004) [http://nobelprize.org/nobel\\_prizes/chemistry/articles/berg/index.html](http://nobelprize.org/nobel_prizes/chemistry/articles/berg/index.html)

[8] In addition to the above perspectives on Asilomar, the issues involved in the public mind with respect to genetic engineering over the past several decades are examined, especially with respect to European attitudes toward genetically modified food, in this article. "Ethics in the societal debate on genetically modified organisms: A (re)quest for sense and sensibility," Yann Devos, Pieter Maesele, Dirk Reheul, Linda Van Speybroeck, And Danny De Waele, *Journal of Agricultural and Environmental Ethics* **21**, 29–61 (2008). <http://dx.doi.org/10.1007/s10806-007-9057-6>

[9] *Engines of Creation: The Coming Era of Nanotechnology*, K. Eric Drexler, Anchor Books, New York, 1986. See Chapter 1, section 6 "Universal Assemblers" [http://e-drexler.com/d/06/00/EOC/EOC\\_Chapter\\_1.html-section06of10](http://e-drexler.com/d/06/00/EOC/EOC_Chapter_1.html-section06of10)

[10] *Engines of Creation: The Coming Era of Nanotechnology*, K. Eric Drexler, Anchor Books, New York, 1986. See Chapter 11, section 1 "The Threat from the Machines" [http://e-drexler.com/d/06/00/EOC/EOC\\_Chapter\\_11.html-section01of05](http://e-drexler.com/d/06/00/EOC/EOC_Chapter_11.html-section01of05)

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[14] "Safe exponential manufacturing," Chris Phoenix and Eric Drexler, *Nanotechnology* **15**, 869-872 (2004). <http://dx.doi.org/10.1088/0957-4484/15/8/001>

[15] Draft Version 3.7 of June 2000 of the "Foresight Guidelines on Molecular Nanotechnology," available at <http://www.foresight.org/guidelines/2000june.html> includes among other restrictions the statement:

"Development Principles

1. Artificial replicators must not be capable of replication in a natural, uncontrolled environment.”

[16] Draft Version 6: April, 2006 of the “Foresight Guidelines for Responsible Nanotechnology Development,” Neil Jacobstein, available at <http://www.foresight.org/guidelines/current.html> includes the statement: "Productive nanosystem based manufacturing makes use of inherently safe system designs requiring no autonomous replication."

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[18] Much information about nanomaterials EHS issues can be found on the web site of the Project on Emerging Nanotechnologies of the PEW Charitable Trusts and the Woodrow Wilson International Center for Scholars <http://www.nanotechproject.org/> For example, see their report *Oversight of Next Generation Nanotechnology*, J. Clarence Davies (April 2009).

<http://www.nanotechproject.org/publications/archive/pen18/> Europe has also been very active in this field. From the Swiss-based Innovation Society FramingNano project, the report "Mapping Study on Regulation and Governance of Nanotechnology" (January 2009) [http://www.innovationsgesellschaft.ch/media/archive2/publikationen/FramingNano\\_MappingStudy.pdf](http://www.innovationsgesellschaft.ch/media/archive2/publikationen/FramingNano_MappingStudy.pdf) "The report gives an insight on the international debate on risks and concerns related to nanotechnologies (EHS issues and ELSI), and provides an ample overview of the different regulatory approaches proposed or already developed to deal with these issues ..."

<http://www.innovationsgesellschaft.ch/index.php?section=news&cmd=details&newsid=157&teaserId=7>

[19] <http://crnano.org/dangers.htm>

[20] "The stealth threat: An interview with K. Eric Drexler" *Bulletin of the Atomic Scientists* **63**, 55-58 (2007) <http://dx.doi.org/10.2968/063001018>

"Technological innovations might help fight terrorism and prevent wars, but some may become the tiny engines that rule our lives."

[21] <http://www.opensourcesensing.org/>

[22] [http://e-drexler.com/d/06/00/EOC/EOC\\_References.html#Ch\\_15](http://e-drexler.com/d/06/00/EOC/EOC_References.html#Ch_15)

[23] "Protein design revolution points toward advanced nanotechnology," posted by Jim Lewis on April 9th, 2009 <http://www.foresight.org/nanodot/?p=3007>

"DNA nanorobot walks without intervention along rigid track," posted by Jim Lewis on April 10th, 2009 <http://www.foresight.org/nanodot/?p=3008>



"Modular DNA nanotubes provide programmable scaffolds for nanotechnology," posted by Jim Lewis on April 27th, 2009 <http://www.foresight.org/nanodot/?p=3019>

"Advancing nanotechnology by organizing functional components on addressable DNA scaffolds," posted by Jim Lewis on April 29th, 2009  
<http://www.foresight.org/nanodot/?p=3023>

[24] See <http://metamodern.com/2008/11/10/modular-molecular-composite-nanosystems/> and <http://www.foresight.org/roadmaps/index.html>

[25] See, for example, the RepRap project started in 2004 by Adrian Bowyer. <http://www.reprap.org/> "RepRap is short for Replicating Rapid-prototyper. It is the practical self-copying 3D printer shown on the right - a self-replicating machine. This 3D printer builds the parts up in layers of plastic."

"A fundamental principle of the RepRap project is that anyone who has a RepRap machine will always be able to use it to build the next generation improvement. That way even if you start with the very bootstrap machine, you can always build your way back up to the full technology." <http://reprap.org/bin/view/Main/FuturePlans>

For a discussion of ReRap and nanotechnology, see "The other half of nanotech" by J. Storrs Hall, posted on April 28th, 2009 <http://www.foresight.org/nanodot/?p=3020>

## **Bio**



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Dr. Lewis holds a Ph.D. in the field of biochemistry from Harvard University. His interests include the convergence of biotechnology, artificial intelligence, information science, and cognitive science. Fascinated by current and advanced nanotechnologies, Dr. Lewis applies his knowledge to the writing and editing of works associated with nanotechnologies in hopes of solving the world's most pressing human problems.