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Build a Synthetic Self-Replicator
Focus Group Summary

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Summary:

Focus Group 2 met to discuss how scientists might develop synthetic self-replicators, devices that can make copies of themselves. These devices could have many valuable applications. Substances made of microscopic self-replicators could heal themselves by producing replacements for damaged parts. For example, molecular scale self-replicators could combine to form self-maintaining paint or spacecraft skins that can repair damage caused by space debris. In addition to replacing damaged parts, self-replicators can scale up production exponentially, as each new product is at the same time a new factory for more products. This could be a solution for accurately and inexpensively producing useful quantities of novel nanoscale materials.

While technological applications have caught the attention of many, including science fiction writers, researchers are also excited about potential non-technological payoffs for research into self-replicators. Building our own self-replicators could give us insight into the origins and mechanisms of existing self-replicators, ranging from bacteria to balboa trees, all of life, in fact, including ourselves.

Life serves as proof that self-replication is in fact possible. Other, non-living self-replicators also exist. Because a range of self-replicators exist in the world, the members of the focus group had to first define the parameters for designing a model self-replicating system.

The group discussed several types of existing self-replicators. First, several examples of simple replicators were named. Fire, in the right environment, produces more fire. Crystal seeding leads to more crystal. Autocatalytic reactions produce chemicals that in turn increase the reaction. For example, if hit with a source of energy, like gamma rays, formaldehyde makes glycoaldehyde. Once glycoaldehyde is present, it can couple with formaldehyde and break it apart, making two glycoaldehyde molecules where there had been one. These in turn can convert more formaldehyde to glycoaldehyde. As long as formaldehyde is available, this reaction causes more of itself to occur.

Viruses fall into another category of self-replicators. They are more complex than fire, but to make copies of themselves they have to depend upon the machinery inside biological cells. One of the things that make viruses interesting is that, like life, they carry instructions for copying themselves. They inject either DNA or RNA into a cell, where cellular machinery follows the directions and produces more viruses.

The last category of self-replicators the group considered was biological cells. In part because many in the group hoped to use the pursuit of a synthetic self-replicator to throw light on the origins of life, the group decided to specify a self-replicator much like a cell. Like fire and crystals, its self-replicator would make copies of itself. Like viruses, it would contain instructions for self-replication. It would be like a cell in many ways. First, unlike viruses, the replicator would include the machinery for carrying out the instructions. Also, it would take simple environmental materials, as cells use amino acids, and create something more complex, such as a cell's proteins. The group wanted to make clear it was not looking for a self-replicator that made copies of itself by, for example, breaking off parts of a more complex material in the environment.

In addition to these basic requirements, the group hoped its self-replicator would have other things in common with a cell. The instructions in a cell can be changed, and as a result the cell can produce different kinds of products and perform various functions. Muscle cells can contract. Nerve cells can process and send signals. Likewise, an ideal synthetic self-replicator would be programmable so that it could serve multiple functions.

The group decided its self-replicator could be different than a cell in one important way: it would not necessarily have to have a physical barrier like the cell's membrane. The group's self-replicator still would need to be distinct from its environment, if only to confirm that it is indeed making a copy of itself. Rather than using a physical barrier, however, this distinction could be made by defining the parts or functions of the self-replicator.

By agreeing not to include a requirement for a cell membrane-like physical boundary, the group significantly reduced the complexity of the design task. At the same time, the group increased the requirement for researchers to control the environment for the self-replicator. In a cell, the membrane, including its embedded proteins, control what comes into the cell. By doing this it creates a special environment within the cell that allows the reactions necessary for the cell to function and eventually copy itself. For the group's self-replicator, the researchers in effect take the place of the membrane, carefully preparing and maintaining the environment. They would keep out things that might damage the machine, and they would include an energy source and all the required raw materials. The need for this specified environment makes it much less likely that this self-replicator could survive and reproduce outside of the lab.

In summary, the group defined as its goal a self-replicator that

- produces a copy of itself
- carries information for replication
- is distinct from its environment
- uses raw materials that are simpler than the final product
- ideally would be programmable and multifunctional

The group's defined goal will not be easy to accomplish. As a first step, however, the group outlined a research direction building on current work with RNA. David Bartel of the Massachusetts Institute of Technology has developed an RNA-based RNA polymerase, that is, a form of RNA that can copy RNA. If this polymerase could make a copy of its own RNA sequence, it would be a self-replicator.

For this to happen, key obstacles need to be overcome. For one thing, so far the polymerase is slow and as a result cannot copy long strands of RNA such as itself. Another main problem is the fact that once the RNA is copied and folds into a non-linear structure, like a helix, its parts are no longer available to be copied again. What is needed is another enzyme, a helicase, that will unfold the structure so it can be copied.

In spite of these obstacles, working with RNA seems promising because, in addition to possibly fulfilling the group's basic requirements, it might even lead to a device that can be programmed to perform a variety of functions. Nucleic acids have been used for a variety of surprising things. Researchers have made DNA that folds into an octahedron, opens and closes like a pair of tweezers, or walks on a substrate much as the protein molecular motor kinesin walks along microtubules. They have also used RNA for a variety of catalytic roles. Even more functions may be found if the so-called RNA world hypothesis is correct. According to Nobel Prize for Chemistry winner Sidney Altman, in the primitive earth RNA both stored genetic information and performed, "the full range of catalytic roles necessary in a very primitive self-replicating system." If scientists are able to synthesize an RNA-based self-replicator, it may confirm this hypothesis and give us a better understanding of how life could have begun and evolved.

The proposed self-replicator might work something like this: RNA polymerase would be added to a solution containing all the raw materials it needs, including fuel in the form of rNTP. The helicase would unfold some of them, making them available for copying by other, still folded, molecules of RNA polymerase. These copies would fold into new RNA polymerase molecules. These could be fed other strands of RNA that code for RNA-based structures like tweezers and catalysts, or more polymerase.

After offering the RNA example, the group went on to suggest that non-biological heteropolymers might be used to make self-replicating machines that could survive within extreme environments like space, where the vacuum, cold, and radiation would keep biological self-replicators from functioning or even maintaining integrity. Such non-biological self-replicators would depend upon a supply of raw materials that do not occur naturally, suggesting that they would not be able to replicate outside of a carefully prepared environment. While the theoretical advantages of non-biological heteropolymers make them desirable, the group noted that building them would present an array of new obstacles.

Public concerns about self-replicators have been heightened by books like Michael Crichton's *Prey*. Although the replicators proposed by the group would likely have trouble surviving outside of narrow environments, the group proposed that attempts to make self-replicators should be accompanied by critical assessments of safety issues, including consideration of ways to recognize and respond to unforeseen problems. These assessments from the beginning should include discussions between scientists and nonscientists with the goal of self-regulation.