

2<sup>nd</sup> Annual National Academies Keck *Futures Initiative* Conference  
*Designing Nanostructures at the Interface  
between Biomedical and Physical Systems*  
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**Build a Synthetic Self-Replicator**  
**Focus Group Description**

**Background**

Long a fascination of science fiction writers and space exploration visionaries, nanomachines that can replicate themselves are already here: we have an existence proof on Earth in complex living systems such as one celled ( and even more complex many- celled ) organisms. Other “bionanomachines” - viruses - are able to reproduce themselves through the use of cell machinery external to themselves. Creating synthetic self-replicators would greatly scale up production of nanomachines from the atomic and molecular scale to the macroworld, as the process of self-replication allows for exponential growth. Your task is to propose a scientific plan for the design and creation of a simplified synthetic self-replicating nano-machine, using a replication method either completely self-contained as in a cell, or requiring the use of external machinery such as by a virus.

**The Problem**

All cells on earth appear to be built according to the same molecular plan, using evolved molecular self-replication –

- Ribosomes are molecular assemblers working from stored information
- DNA is the information storage medium, directing the assembly of other parts
- DNA polymerase duplicates the information storage medium
- Thousands of enzymes convert available raw materials to building blocks required for the assembler and duplicator
- The cell provides the required infrastructure:
  - The lipid cell membrane serves to define the body of the cell
  - The membrane signaling and transport proteins serve to allow for communication, energy and raw material transport to and from the external environment
  - Complex machinery exists to allow for reproduction by binary fission
  - Various enzymes exist for regulation and error correction of cell processes
- Current estimates (Ref 1) of the minimal number of DNA genes needed to create a living organism modeled after the modern cell machinery above are in the range of 250-350, however this design is limited by the process of evolution – Can we design a more efficient and simpler self-replicator? For example, it is believed (Ref 2) that primordial life was based on RNA, and there are attempts to create RNA ribozymes in the lab (Refs 1, 2) as well as a major advance in understanding of ancient RNA processes that still exist in modern organisms (Ref 3). Another possibility would be to create stable alternatives to DNA and RNA such as synthetic short peptide chains that can be more robust (Ref 1) for information storage and control. Yet another possibility is to create self-replicating DNA objects using synthetic DNA structures as engineering materials akin to viruses, requiring access to external machinery for replication (Ref 4).
- Current cell machinery is limited to water environments and thus a limited temperature range, in which thermal statistical motion and a diffusion-to-capture paradigm occurs for most functional tasks. Larger and more specialized tasks are carried out by machine-phase assemblies. - Could we design self-replicators that evolve and grow in environments without water?
- DNA, RNA and most proteins have limited lifetimes in cells due to degradation by nucleases and denaturation (Ref 5) - Is it possible to create more robust and longer lived replicators? What are the trade-offs?
- The measured mutation rate in bacterial cells is 1 nucleotide in 10<sup>9</sup> nucleotide polymerization events. What level and kinds of transcription and replication error rate and error correction processes are needed to sustain self-replicating nanomachines? (Ref 6) Although transcription errors can be fatal,

some types of transcription errors along with gene duplication and complex gene networks can help an organism evolve in a changing environment (Ref 7).

- Self-replicating nanomachines would have many positive uses for society, but their possible existence in the near future also raises many concerns of “gray goo” either inadvertently or purposefully being unleashed on the environment with unforeseen possible grave consequences. What kind of ethical controls should be put in place over their creation and use?

### Initial References

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- 7 - Bergman, A., Siegal, M., Evolutionary capacitance as a general feature of complex gene networks. Nature, July 2003. 424 pp. 549-552. Also for a discussion of ageing mechanisms in Eukaryotic cells, damage due to ATP and oxidants, DNA mutation and repair mechanisms see Dying Before Their Time – Studies of prematurely old mice hint that DNA mutations underlie aging, J. Travis, Science News, July 10, 2004 166 pp. 26-28.