Quick guide

Self-replication

Natasha Paul and Gerald F. Joyce

What is it? Self-replication is a means by which an individual can duplicate itself. Such molecular photocopying occurs when a reaction product directs its own formation from component parts. This has been hypothesized to be a route by which primitive life may have sustained itself.

How does it work? It involves product-directed assembly of components to form a new product. The simplest self-replicating system entails the joining of only two components (see Figure 1). The product acts as a template to position the components correctly for the joining reaction, allowing for more efficient joining in the presence compared to the absence of the product. The newly-formed product then dissociates from the template to provide a new copy of the template with the potential to enter another cycle of replication.

What happens if it works well? In an efficient self-replicating system, all product molecules contribute to the formation of new product by binding available components. After the reaction, the product–product complex comes apart readily so that additional component molecules can be assembled. If the product molecules can participate in multiple replication cycles, sustained exponential growth can occur — autocatalytic self-replication.

What usually goes wrong? Self-replicating systems usually are limited in their ability to undergo efficient autocatalytic self-replication. If the product molecules bind the component molecules too tightly, then the product–product complex may be slow to dissociate, reducing the number of available product molecules. If the product–product complex dissociates too readily, then the product may not bind the components very well. Either case reduces the number of functional products that can serve as a template: a delicate balance has to be achieved between strong binding of the components and facile release of the newly-formed products.

What was the first example? In 1986, Günter von Kiedrowski provided the first working example of a chemical self-replicating system, based on oligonucleotides. Watson–Crick base pairing brought together a template and two component oligonucleotides, leading to the formation of a reaction product that was both complementary and identical to the template. Several other examples of self-replication have since been described, showing that assembly of the components can involve various forms of molecular recognition, including hydrogen bonding, salt-bridge formation and hydrophobic interactions. These self-replicating systems use oligonucleotides, small organic compounds, short peptides and, most recently, catalytic RNAs (ribozymes).

Does it have to be molecular? Self-replication has been carried out *in silico* using cellular automata. These are computer programs, whose code can be regarded as 'genotype' and operation as 'phenotype.' For an automaton to be self-replicating, its operation must include copying of both the computer code and the code-operating machinery. The first example of a self-replicating automaton was described by the mathematician John von Neumann in 1953, the same year that Watson and Crick reported the structure of DNA.

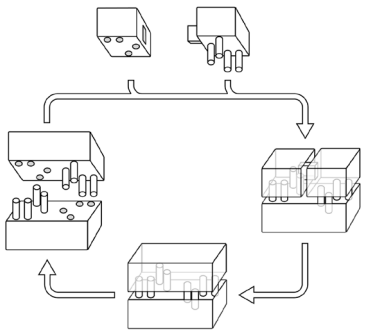

Figure 1. Self-replication cycle. Each cycle involves positioning the components on a template, joining the components to form a product, and dissociation of the template and product to provide a new copy of the template that can enter another replication cycle.

Did life start this way? Self-replication is only part of the story; it also is necessary for the system to adapt in response to a changing environment. This requires a chemical basis for information storage to preserve genetic instructions that have proven advantageous to survival. Although the instructions necessary for survival may evolve in response to environmental pressures, the self-replication process must continue to copy the revised instructions faithfully.

Will we be taken over by self-replicating nanobots? Probably not in our lifetimes. Based on current understanding, it will be difficult to build artificial self-replicators that do not suffer from the limitations described above. It is much easier to modify evolving systems from biology than to build one from scratch. On the off chance that someone does succeed in rearing a self-replicating entity that can survive on its own, would they let it go?

Where can I find out more?

Orgel, L.E. (1992). Molecular replication. Nature *358*, 203–209.

Rebek, J. (1994). Synthetic self-replicating molecules. Sci. Am. *271*, 48–55.

Bag, B.G. and von Kiedrowski, G. (1996). Templates, autocatalysis and molecular replication. Pure Appl. Chem. *68*, 2145–2152.

Sipper, M. and Reggia, J.A. (2001). Go forth and replicate. Sci. Am. *285*, 35–43.

Departments of Chemistry and Molecular Biology and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037, USA. E-mail: npaul@scripps.edu, gjoyce@scripps.edu