11

Self-reproducing Machines and Manufacturing Processes

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11.1 Introduction

Anyone who has ever made a machine can see how it *ought* to be done: all they have to do is to look up from their workbench and out of the window. There they will see a riot of manufacturing excess that has created a knee-deep layer of machines covering the entire planet; indeed our very knees are made from those machines.

This chapter is about harnessing the planet-transforming power of self-reproduction to make products that are useful to people. Of course, in one sense, doing this is our oldest technology—we call it farming. But for farming, we took naturally evolved reproducers, genetically engineered them by selective breeding to make them more to our liking, and set them to work to feed and to clothe us. Farming is still our most important technology—we could live without engineering, but not without food; however, in this chapter, I will look at attempts to create artificial reproducers to make the goods normally manufactured by industrial production.

The first question is obviously, why bother? Since the industrial revolution,* humanity has created a global system of production and distribution using conventional engineering that has given every nation that has adopted it wealth beyond the imaginings of our pre-industrial ancestors. Why would we alter that?

The answer lies in the difference between an arithmetic and a geometric progression. Suppose you run a factory that has an injection molding machine making 200,000 door handles a day. Tomorrow the machine will make another 200,000, and another 200,000 the day after. The number of door handles made grows arithmetically, as—consequently—do your profits.

Now suppose that you had a self-reproducing machine that took a whole day to copy itself, and—in that day—it had just enough time left over to make one, single, pathetic door handle. That is 0.000005 times the production rate of the injection molding machine. But the number of self-reproducing machines will grow geometrically (2, 4, 8, 16, 32, …), and so will the number of door handles. In just 18 days, the self-reproducing machines will be making door handles faster than the injection molding machine. After a month, there will be a self-reproducing machine (and a door handle) for every man, woman, and child on Earth.

Of course, that apparently inexorable growth would be checked by resource limitations well before then. That is the same reason that we are not up to our necks in rabbits. But the ability of self-reproduction to produce goods geometrically, in contrast to the arithmetic production of conventional industrial processes, is what makes it so economically very attractive.

There is another, even better, reason why we should bother: because it would be interesting.

11.2 A Historical Perspective

How far back does the idea that a human-engineered machine might be made to reproduce itself go?

In their excellent book *Kinematic Self-Replicating Machines*, Robert Freitas and Ralph Merkle (2004) recount an anecdote: when Descartes told Queen Christina of Sweden his opinion that the human body was a machine, she asked, "How can machines reproduce themselves?" Descartes was visiting the queen in the winter of 1649,† and that is the most probable date for the conversation, although they had previously corresponded.

In another version of the anecdote, the queen is reported to have pointed at her clock and said imperiously, "See to it that it reproduces offspring,"—a less perceptive response, and less likely; she was noted for her gifted and inquiring mind.

Moving forward 200 years, in Chapter 23 of his simultaneously utopian and dystopian novel *Erewhon*, Samuel Butler's first-person narrator gives a translation of an Erewhonian "Book of the Machines." This recounts philosophical speculations on what

* Rather appropriately, I write these words while on holiday in Ironbridge in Shropshire, popularly—if naively—known as the birthplace of the Industrial Revolution.

† The Swedish winter of 1649, incidentally, was what did for poor Descartes; he died of pneumonia on February 11, 1650. The queen was distraught—she had warned him against visiting in the winter, suggesting spring or summer instead.

we, today, would call artificial intelligence and artificial life. It contains the following passage:

> "Surely if a machine is able to reproduce another machine systematically, we may say that it has a reproductive system. What is a reproductive system, if it be not a system for reproduction? And how few of the machines are there which have not been produced systematically by other machines? But it is man that makes them do so. Yes; but is it not insects that make many of the plants reproductive, and would not whole families of plants die out if their fertilisation was not effected by a class of agents utterly foreign to themselves? Does anyone say that the red clover has no reproductive system because the humble bee (and the humble bee only) must aid and abet it before it can reproduce? No one. The humble bee is a part of the reproductive system of the clover. Each one of ourselves has sprung from minute animalcules whose entity was entirely distinct from our own, and which acted after their kind with no thought or heed of what we might think about it. These little creatures are part of our own reproductive system; then why not we part of that of the machines?" (Butler, 1872)

Erewhon was published in 1872, just 13 years after *The Origin of Species* (Darwin, 1859). Butler can reasonably be credited with the idea that self-reproducing machines would be useful for industrial production and with the idea that they would be inescapably subject to Darwinian evolution. At the time, some thought that he was attempting to disprove Darwin by *reductio ad absurdum.* To disabuse people of this opinion Butler later wrote, "I regret that reviewers have in some cases been inclined to treat the chapters on Machines as an attempt to reduce Mr. Darwin's theory to an absurdity. Nothing could be further from my intention, and few things would be more distasteful to me than any attempt to laugh at Mr. Darwin."

Moving forward another 140 years, our own age is more accommodating of the conceit that machines might both reproduce and evolve, in large part because we now make machines more subtle and fabulous than any seen in even the most opiate Victorian Limehouse pipe dream, and also because we are starting to achieve solid, reproducible (in every sense) research results in artificial machine reproduction.

11.3 Scope and Some Definitions of Terms

It is not possible in a single book chapter to do justice to the considerable research into artificial self-reproducing machines that has been carried out in the last fifty years. The reader wanting detail at a more profound level is guided to Freitas and Merkle's (2004) previously mentioned book. Here I have attempted to use examples to adumbrate the breadth of the field, rather than to present parts of it in depth while (then necessarily) ignoring other areas completely.

Also, this is a book on biomimetics, and so the reader might expect many of the examples presented here to have been biologically inspired. But aside from the central idea of reproduction itself, few of them have been. Biology is the study of things that copy themselves, and so has formed a general background to this work. But the detail of most artificial reproducers comes from engineering thought. In the main, it is only after the devices have succeeded that biological *analogies* have been noticed. These will be pointed out as we go along.

Historically, the terminology used in the field of self-reproducing machines has sometimes been unclear, with different meanings being ascribed to the same words. In an attempt to bring some systematization to this, I will define key terms for use in this chapter at least:

Kinematic machine—a physical machine that is composed of fixed and moveable parts. These parts may be such that you could hold them in your hand, or they may be microscopic, or even atomic. Kinematic machine makes a distinction between real machines and software models (which are frequently used for simulation). The words kinematic machine encompass both artificial mechanisms and evolved living organisms (including, of course, people).

Self-replication—to define this, let us start with the idea that self-replication could mean an imaginary Platonic process by which a kinematic machine was able to create an exact copy of itself. The Second Law of Thermodynamics and Shannon's (1948) theorem shows that information cannot be copied without loss or error indefinitely, implying that the idea of an exact replicator is an impossibility. (It is the errors, of course, that drive Darwinian evolution.) Although it is philosophically and poetically useful to have words for impossible ideas, here the strength of the word replication is reduced to give it an engineering meaning: a copy within specified tolerances that will work as well as the original.

Self-reproduction—a process by which a kinematic machine is able to create an approximate copy of itself, perhaps with either insignificant or significant errors. All living organisms are self-reproducers. The specified-tolerances-and-works-as-well distinction between replication and reproduction follows through the definitions below, and the rest of this chapter. Replicators are a subset of reproducers.*

Self-manufacturing—the ability of a kinematic machine to make some or all of its own parts from raw materials. This clearly prompts a requirement for a definition of "raw": is an etched printed-circuit board a raw material? Or a uniform sheet of copper-clad fiberglass and a bottle of ferric chloride etchant? Or some copper, some glass, and some epoxy resin? Forensically, many Gordian Knots of this sort are cut by asking, "Would a reasonable person say it is so?" and leaving it at that. Here the same approach as that of the law is adopted.

Self-assembly—this refers to the ability of a kinematic machine to manipulate a series of parts into an assembled copy of itself.

Autotrophic self-reproduction or self-replication—the ability of a system to make a direct copy of itself from raw materials without assistance. As yet, no artificial autotrophic self-reproducing kinematic machine has been made. However, examples exist in biology. For a kinematic machine to achieve autotrophic self-reproduction, it must contain a number of critical subsystems. One attempt to identify these subsystems was undertaken in Freitas and Merkle's (2004) "Map of the Kinematic Replicator Design Space" in their book referred to above. This identified 137 design properties in order for autotrophic self-reproduction to be possible.

Assisted self-reproduction or self-replication—a kinematic machine that includes at least one, but not all, of the critical subsystems required for autotrophic self-reproduction or replication and so needs human (or other) intervention to reproduce.

11.4 Simulation and Analysis

When people cannot make something they want, they often make a model of it instead. This is sometimes mere superstitious sympathetic magic. But other times a model is a step on

* Many researchers in the field consider it ethical to make only fragile reproducers. That is, reproducers that become sterile when virtually any mutation occurs in their makeup.

the path to having the real object that the model represents. These days no one would build an aeroplane speculatively and then test-fly it to see if it would stay up. They would spend many hundreds of hours of computer time using finite-element models to find out if the wings were likely to fall off and many more hundreds of hours using computational fluid dynamics models to find out if those wings were able to suspend the aeroplane in the air.

Before engineering had reached the point where kinematic artificial self-reproducing machines could even begin to be made,* computers were powerful enough to model how they might, in the future, work. And before computers were that powerful, the theory of computation (another model) had progressed to the point where it was obvious that future computers would be able to process such models of self-reproducing machines. Much of this early modeling of self-reproducers was done by John von Neumann toward the end of his life in the middle of the last century.

11.4.1 Cellular Automata

Imagine that you have in front of you a sheet of graph paper, a pencil, and an eraser. Further imagine that someone has already shaded in a few squares on the graph paper and has given you a set of rules. These rules say:

1. If a shaded square has two or three shaded neighbors, it stays shaded.
2. If a shaded square has less than two, or more than three, shaded neighbors rub it out.
3. If an unshaded square has three shaded neighbors, shade it in.

You could follow these rules, and the consequent patterns of squares would grow and shrink across your sheet of paper.†

The graph paper squares (together the rules and you to execute them) are cellular automata. The moving patterns that such cellular automata can generate are extraordinarily rich. For example, it is possible to make a pattern that acts like a factory, producing smaller identical patterns that repeatedly split off and drift across the paper forever. Wikipedia has an animation of this happening that you can watch; it is rather hypnotic (*Wikipedia: Conway's Game of Life*, http://en.wikipedia.org/wiki/Conway's_Game_of_Life). Stephen Wolfram (2002) has even maintained that cellular automata are the best (or maybe even the only) way to study very complicated systems in nature.

Cellular automata were invented by Stanislaw Ulam, followed by his collaborator von Neumann, in the 1940s. Ulam wanted to use cellular automata to study crystal growth, and von Neumann wanted to use them to study self-reproducing machines.

A cellular automaton's neighbor-rules are analogous to cell-cell communication during morphogenesis, which helps to define tissue boundaries and cause cells to differentiate into different phenotypes (Bray, 2006), although this was only noticed long after they were invented.

11.4.2 von Neumann Reproduction

von Neumann started with the idea that there was a strong similarity between the then-nascent digital computer and an animal's brain (von Neumann et al., 1963) and went on

* Although see the work of the Penroses, *père et fils*, below.

† This particular set of three cellular automaton rules were devised by John Conway and are called "Life" (Gardner 1970).

to study the idea of a robot making another identical robot—a kinematic self-reproducing machine (von Neumann, 1966).

He very quickly ran up against two difficulties that can be summarized as size and containment.

Today, the size problem that he identified seems the less difficult of the two to surmount. He compared the size of a neuron with that of an electronic valve, arriving at a factor of a billion, and pointed out that their energy requirements differed by a similar factor. Following this through to build an artificial self-reproducing machine of a similar complexity to—say—a beetle one centimeter long would require the entire mass of the Earth. Once the researchers had finished building their earth-beetle, lack of further material would make demonstrating its reproductive ability difficult.

However, just the nucleus of a neuron is about 10 μm across,* whereas we can now easily make transistors under 1 μm across. What we cannot (yet) do is to connect a transistor to very many others. Typically a single transistor in a microprocessor might drive 20 more. One of the neurons in your brain, in contrast, might well act as input to 10,000 other neurons. But it is certainly the case that modern electronics is processing information at about the same length scales as natural biological systems, if not smaller.

(In passing, it is perhaps worth observing that von Neumann was concerned with the limits of computation in the context of reproducing machines and other things. But most self-reproducing entities in nature have no brain at all—they are microbes. However, they do all still process information. A bacterium dividing is, of course, copying the information in its DNA, and that information is then used to make the proteins that form the two new bacteria—see below.)

von Neumann's second problem—containment—is at once both more obvious and more subtle. You can get together with someone else and have a baby; all you both need for that is food. You two parents and your baby form a closed reproduced system that requires nothing from outside itself except raw-materials to eat.

But it is extraordinarily difficult to have a robot driven by a computer make all the parts for another identical robot from a supply of raw materials such as steel and plastic. It is a little bit easier if the raw materials are steel gears and plastic pipe, and—revisiting the brief discourse on the meaning of the word "raw" in "raw materials" above—this is how you eat: you cannot eat carbon, hydrogen, nitrogen and oxygen, but you can eat amino acids made from those elements. However, going back to the robot, even if it could make itself from gears and pipe, it would not have copied the computer that is driving it—it is not a closed reproducing system like you, your partner and your baby. This requirement also to copy the computer adds another—and very daunting—layer of complexity to the artificial self-reproduction problem.

Stumped by these difficulties, von Neumann turned to his friend Ulam and, at Ulam's suggestion, decided to concentrate on simulating reproducing machines using their just-invented cellular automata to build a model. von Neumann gave an existence proof that a particular pattern would make endless copies of itself within his cellular universe. His cells only considered their four orthogonal cells to be neighbors (that is, he used rook's—and ignored bishop's—one-square moves). His cells had 29 possible different states (as opposed to the two—shaded and unshaded—in Conway's Life).

von Neumann did all this without the distraction of having access to an actual computer. In the 1940s they were too rudimentary for the task. He thus demonstrated the

* So a whole neuron is bigger. It is hard to be specific because a neuron's dendrites can be very long—of the order of one meter.

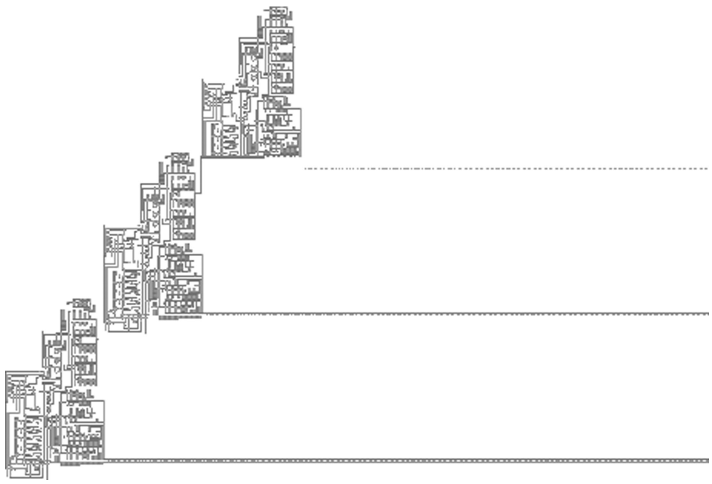

FIGURE 11.1
Pesavento's implementation of von Neumann's cellular automaton model of a reproducing machine. A parent (bottom) and its child (middle) are complete. The child is making a grandchild (top). (Image courtesy of Wikipedia.)

possibility of artificial mechanical replication (the digital copies really are identical*) by making *a model of a model* of a reproducing machine.

It was not until 1995 that his work was implemented in a computer program and run. Figure 11.1 shows the program working. The implementation was done by Umberto Pesavento (1995).

Pesavento's von Neumann implementation is, *in its own cellular universe*, an autotrophic self-reproducing kinematic machine by the definitions above. But it is not even a kinematic machine in our Universe; it is a simulation.

On May 18, 2010, Andrew Wade posted the first ever self-replicating pattern in Conway's Life (the automata of which have much simpler rules than those of von Neumann) on the Web. (Wade, 2010).

11.4.3 Moving from Mathematics toward physics

In 2010, William Stevens published a PhD thesis in which he presented a three-dimensional simulation of a reproducing machine (Stevens, 2010). This did not merely use three-dimensional cellular automata: given Pesavento's work that would be trivial (the two-dimensional automata could easily be made to work in a plane slice through a three-dimensional cellular universe, for example).

Stevens's universe consisted of an array of boxes that could be moved about by the actions of other boxes as if they were real material objects in a three-dimensional rectangular lattice. There was no friction and no gravity, but the boxes had different types such as logic gates, wires, and—necessarily—a type that caused any box next-door to it to move. He then designed a self-reproducing machine that would operate in the universe that he had defined. It is shown working in Figure 11.2. Interestingly, the first child produced by his designed parent was not identical to that parent, but the first grandchild—and all

* This is not strictly true. What I said above about the impossibility of perfect replication still holds. A stray alpha particle can flip a bit in a computer's memory, for example. Such events are almost preternaturally rare, but – given long enough – they are inevitable.

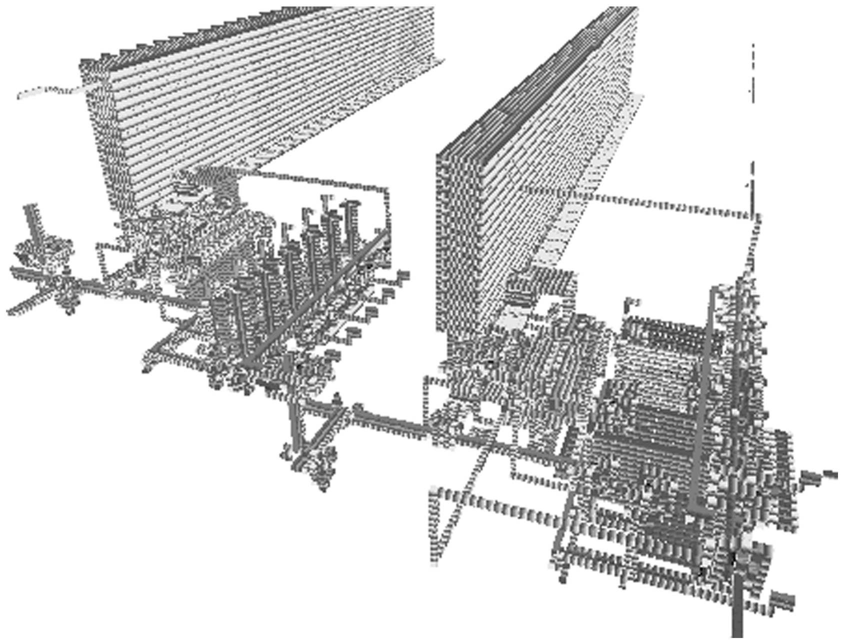

FIGURE 11.2
(See color insert following page xxx.) William Stevens's three-dimensional physical self-reproducer simulation. The parent is on the right; the child it is constructing is on the left. The big yellow blocks are the "computer memory" of each. (Image courtesy of William Stevens, Open University.)

subsequent generations—was identical to the first child. The original machine had reproduced approximately, and then converged on exact replication.

11.5 Electromechanical Self-reproduction

This simulation work is all very interesting, but obviously it's not going to make an aeroplane, or even a door handle, for us any time soon. If we are going to use self-reproducing machines to do industrial production, then we are going to have to move from simulation to the world of nuts and bolts or to the world of chemistry. This section is about making real kinematic self-reproducers as macroscopic machines—things that can initially be built with a screwdriver and a soldering iron.

11.5.1 Self-assembling Kinematic Machines

A self-assembling kinematic machine is a robot that can make a copy of itself when provided with a kit of parts. You are a self-assembling kinematic machine, and your kit of parts consists of those amino acids mentioned above, together with a lot of other complicated premanufactured* kit parts that are all in the soya beans, beef, lettuce, sea bass, walnuts, and so on that you eat.

* Premanufactured, ultimately, by plants and microbes. In fact, you can also make some, although not all, amino acids for yourself.

This brings us back to the definition of raw materials. A robot that can merely take another identical robot off a shelf and present it to you as its offspring cannot reasonably be said to have reproduced. But—as observed above—even you and a partner cannot make a baby from a collection of uncombined chemical elements. Most reasonable people would consider a machine working halfway between these extremes—say a robot made of Lego that could take a box of Lego bricks and make a copy of itself—to be legitimately capable of self-reproduction.

It is also legitimate to consider the manufacture of the kit to be something that assists the reproducer.* That manufacture provides the reproducer with a competence that it itself does not have. Thus, our notional Lego robot is an assisted self-assembling kinematic machines.

The first such kit-part kinematic self-reproducers were made by the father-and-son team of Lionel and Roger Penrose† just a few years after von Neumann's work. They made a collection of cleverly shaped wooden cutouts that were placed on a one-dimensional slide (Penrose, 1958). If the slide were randomly shaken (cf. Brownian motion), then the cutouts would move about, but nothing special would happen. But if the cutouts were first hooked together (as they were intended to be) in a pattern, then shaking the slide would recruit further cutouts into copies of that original pattern (Figure 11.3 shows the device).

The way that the Penrose's patterns reproduce has been compared with the way that prion proteins misfold when in contact with an already misfolded one, although—once again—the similarity was only noticed long after the blocks were invented (prions were unknown at the time).

More recently, there have been other self-assembling kinematic self-reproducing machines that have taken advantage of microelectronics to allow kit parts that exhibit more subtle behaviors. One of the most elegant is the machine designed by Victor Zykov and his colleagues at Cornell (Zykov et al., 2005) (see Figure 11.4). It consists of a collection of identical cubes, each split by a diagonal plane. The two halves are motorized and can thus rotate relative to each other about an axis at right angles to the splitting plane. Each face of each cube is equipped with electromagnets that can be turned on or off, allowing one cube to pick up and to release another. An initial tower of cubes held together magnetically is constructed by hand. This tower can then automatically bend and flex like a

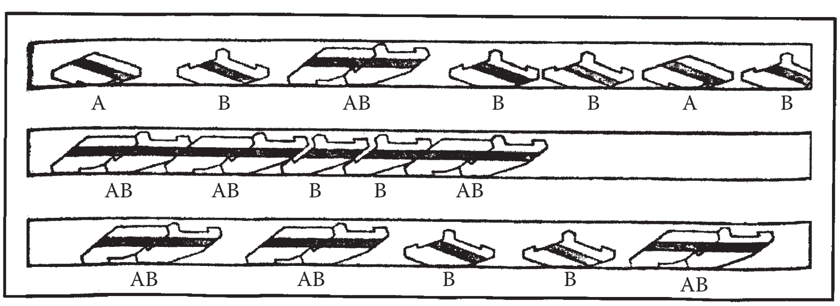

FIGURE 11.3
The Penroses' one-dimensional block reproducer. They also made a more complicated two-dimensional one. (Image courtesy of Sir Roger Penrose, Oxford.)

* Whether by photosynthesis in the leaf of a soya plant, or by injection moulding in a Lego factory.
† Now Sir Roger Penrose, one of the world's most preeminent mathematical physicists.

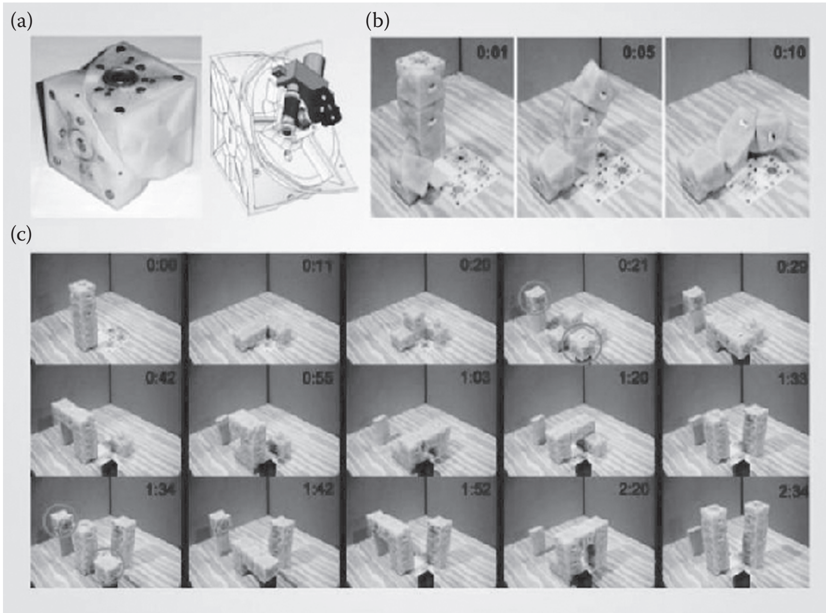

FIGURE 11.4
Zykov's self-reproducing tower of cubes. (From Zykov, V., E. Mytilinaios, B. Adams, and H. Lipson, "Self-reproducing machines," *Nature*, Vol. 435, (2005) p163, http://tinyurl.com/ygozg37.) One cube is shown top left (a). The sequence (c) shows the tower copying itself using a supply (red circles) of more identical cubes. (Image courtesy of Hod Lipson, Cornell.)

robot arm, picking up extra cubes with its magnets and assembling them into an identical tower.

11.5.2 Self-manufacturing Kinematic Machines

A self-manufacturing kinematic machine is one that can make its own kit of parts from raw materials. If, in addition, it could also then assemble the kit into a copy of itself like the devices in the last section, it would be a fully autotrophic self-reproducing kinematic machine. So far, no artificial fully autotrophic self-reproducing kinematic machines have been made, but most bacteria, archaea, protists, and plants are autotrophic self-reproducing kinematic machines.

As Butler, and then von Neumann, observed: any sufficiently well-equipped workshop could be considered to be an assisted self-manufacturing kinematic machine if it was capable of making the parts for all the tools it contained. People would have to assemble the tools, and then the workshop would have reproduced using the people as its assistants.

The problem lies in that "sufficiently well-equipped" phrase. Adding different equipment gives more manufacturing versatility and so gives more complete potential for reproduction, but it often also requires even more manufacturing versatility to make the new extra equipment. We end up chasing a receding target, although human engineering considered as a whole is obviously an assisted self-manufacturing kinematic machine.

Fab Lab, which was created by Neil Gershenfeld at Massachusetts Institute of Technology, is an example of a workshop that is currently one of those closest to being a reproducing workshop. It is also extremely useful in its own right.

A Fab Lab (Figure 11.5) consists of a carefully selected group of digitally controlled manufacturing machines.

This group usually contains computers, a laser cutter, a small three-axis numerically controlled mill, and a vinyl cutter. In addition, Fab Labs have the materials and tools necessary for soft tool casting in a variety of substances such as polydimethyl siloxane, waxes, and plasters. Finally, they have hand tools, especially those needed to make electronic circuits. The mill and the vinyl cutter are used for making printed circuit boards (conventional and flexible, respectively) as opposed to making those traditionally by ferric-chloride etching. Some Fab Labs also have three-dimensional printers (see below) and other more powerful tools.

That tool-group does not form a Butler/von-Neumann self-manufacturing kinematic machine. It cannot, for example, make the integrated circuits and the storage discs in its computers. But advances in such technologies as the printing of integrated circuits using ink-jet technology will move Fab Labs further along that road to becoming true reproducing workshops.

By the definitions above, a Fab Lab is an assisted self-manufacturing kinematic machine.

Another assisted self-manufacturing kinematic machine is RepRap (Sells et al., 2009). RepRap is short for replicating rapid prototyper.* It is an attempt to get a single machine to make a kit of parts for a copy of itself. One is shown in Figure 11.6.

RepRap is a three-dimensional printer that uses fused filament fabrication† to build parts. Fused filament fabrication is rather like a computer-controlled glue gun: an extrusion head emitting a fine filament of molten plastic scribbles on a flat bed to form the bottom layer of a three-dimensional part that is to be made. The head then moves upwards a small amount and scribbles the next layer. This, because it is molten, welds to the first. The process is repeated until the part is finished.

FIGURE 11.5
A Fab Lab. Neil Gershenfeld is the one with the beard. (Image courtesy of Neil Gershenfeld, Massachusetts Institute of Technology.)

* "Rapid Prototyper" is engineer-speak for three-dimensional printer. I invented RepRap. That is the reason that I was invited to write this.

† Sometimes called "fused deposition modeling," although that phrase is trademarked (unlike fused filament fabrication), and so is not in free use.

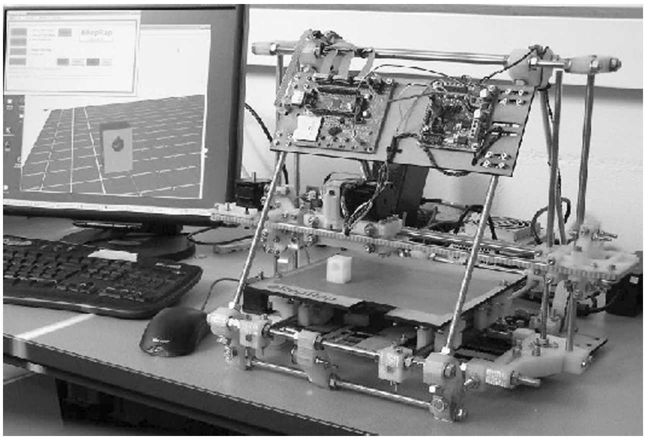

FIGURE 11.6
A RepRap machine. It has just made the white part that is on the blue build-base (the computer model of the part is also shown on the screen of the computer driving the RepRap machine). That part is a component of the RepRap machine itself. (Image courtesy of The RepRap Project, http://reprap.org.)

Not counting nuts and bolts,* RepRap can print about 50% of its own parts. The remainder are deliberately chosen to be low cost and very widely available worldwide. Because all the designs, software, and documentation for RepRap are released free under the GNU General Public Licence, anyone who wants to make one can do so. They can then print another and give that RepRap to a friend.

11.5.3 Self-assembling versus Self-manufacturing Kinematic Machines

As was mentioned at the start of the last section, an unassisted combination of self-assembling and self-manufacturing technologies would be a fully autotrophic self-reproducing kinematic machine. These have been extant on Earth for three and a half billion years, but have yet to be made artificially.

Assisted self-assembling kinematic machines tend to be more impressive to watch than assisted self-manufacturing kinematic machines, but the latter tend to be more useful.

Self-assembling kinematic machines are hard enough to make work on their own, without requiring from them the additional capacity to make useful goods from their kit parts. Also, for most such machines that have been developed, the parts tend to be quite big (of the order of several centimeters across), optimized for operation in the self-assembling machine, and of more or less uniform size, which all again limits what can be made from them.

In contrast, an assisted self-manufacturing kinematic machine can make a wide variety of other goods in addition to the parts of itself because of the manufacturing versatility that it has to have anyway. Both Fab Lab and RepRap are intended to manufacture many other items that will be useful to people. In the case of RepRap, this is a deliberate designed-in reproductive strategy: people getting goods from RepRap machines will have an incentive to help RepRaps to reproduce, just as the bee getting nectar from the clover has an incentive to help the clover to reproduce.

* The nuts and bolts could be replaced by printed cylinders plus glue, and the machine would work just as well. But it would then be more difficult to experiment with and to modify.

11.6 Physicochemical Self-assembly and Reproduction

Life is chemistry, dancing. Many people have made self-assembling systems using the toolbox provided by chemistry. Their early days attempts are, perhaps, a mosh pit compared with the *Ballets Russes* of a clover or a bee, but living organisms give a clear existence proof that this approach can be made to work.

11.6.1 Mesoscale Self-assembly

We know that self-assembled collections of atoms—molecules—make up everything in the world including everything that reproduces, but we cannot take those collections apart by hand, or even forceps, to turn their parts about and see how they are shaped and how they work.

George Whitesides and his colleagues at Harvard have been modeling molecules with artificial atoms a millimeter or so across (Bowden et al., 2001).

They make a set of very small plastic squares, hexagons, or other polygons that will float at the interface between two immiscible fluids, usually perfluorodecalin and water (see Figure 11.7). They treat the edges of the shapes so that they have matching patterns of hydrophobic and hydrophilic sections. Capillary forces cause the tiles tend to stick together selectively depending on the patterns, allowing complicated structures to self-assemble.

This technique can be extended to tiles that are active. Figure 11.8 shows a pattern of LEDs that have self-assembled into an array on the surface of a cylinder using similar

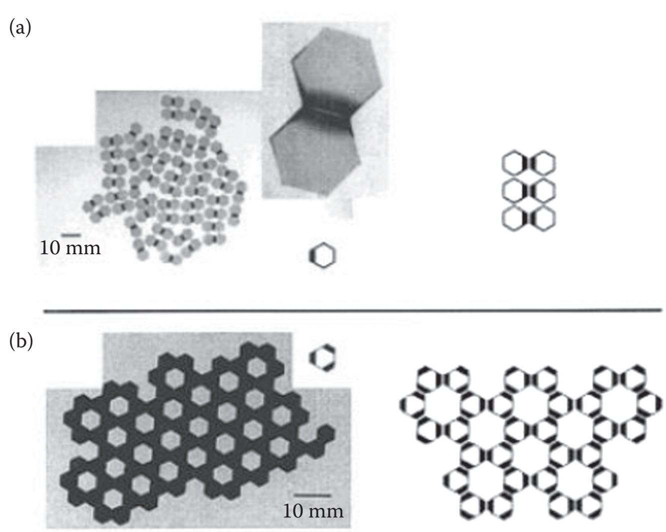

FIGURE 11.7
Two-dimensional self-assembling structures at a fluid interface, taken from (Bowden et al., 2001). (a) Hexagonal tiles with one active edge forming "dimers." (b) Hexagons with three active edges forming a reticulated pattern of larger hexagons. Left: photographs of the experiments; right: diagrams of what's going on. (Image courtesy of George Whitesides, Harvard.)

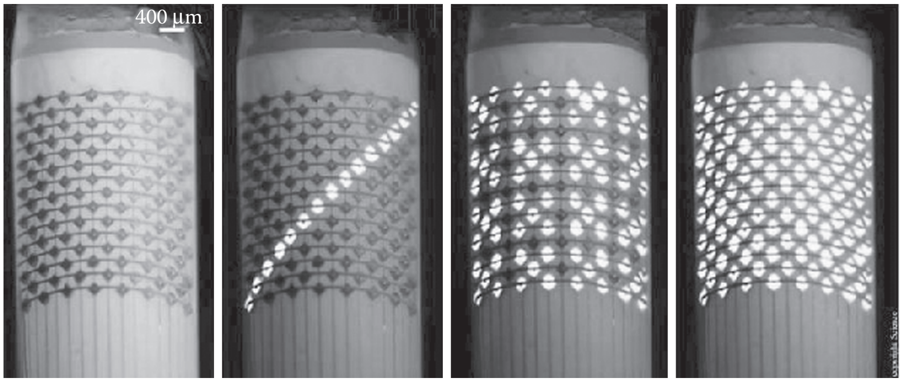

FIGURE 11.8
An array of LEDs self-assembled on the surface of a cylinder. (Image courtesy of George Whitesides, Harvard.)

methods. It is straightforward to use conventional chip-manufacturing techniques to make an LED array on a flat surface, but those conventional techniques (which use image projection) do not extend well, or at all, to curved surfaces.

11.6.2 Synthetic Biology

Moving back down among the molecules, we finally arrive at the research that is where all these other projects are heading: research that is trying to make a real living organism, or at least parts of one, from scratch. I, and all the others who did the work above, are synthetic-biologists manqué. Like the manufacturing engineer looking out of their window at the riot of life in the shrubbery, we know that that is the right way to do it, really.

The fundamental machine that is life is quite simple to describe and, superficially, quite easy to understand. A length of DNA is a list that describes the order of amino acids that needs to go together to make a protein. That length of DNA is copied to a length of RNA, which is then fed end-on into an assembly called a ribosome. The ribosome reads the RNA like an old-fashioned computer reading a punched paper tape and stitches together the right amino acids in the right sequence to make the protein.

Some of those proteins help to copy that DNA when the cell in which all this is happening reproduces. Other proteins (together with some RNA) make up more ribosomes. The rest build bones, give people food poisoning, put all the oxygen into the air, compose Chopin's Nocturne in B-flat minor Opus 9, turn a flower to face the sun, and write about all these things.

The RNA list consists of triples called codons, each one of which corresponds to an amino acid. There are 64 (4^3) possible codons, and they are all used. However, there are only 20 natural amino acids that codons define,* so most amino acids have several different codons that can be used to call them up. For example, the codons AUU,† AUC, and AUA all mean tack-an-isoleucine‡-onto-the-protein-being-made.

* There are two more, selenocysteine and pyrrolysine, that are incorporated by different mechanisms.

† Nucleotides: A = adenine: $C_5H_5N_5$; C = cytosine: $C_4H_5N_3O$; G = guanine: $C_5H_5N_5O$; U = uracil: $C_4H_4N_2O_2$.

‡ $HO_2CCH(NH_2)CH(CH_3)CH_2CH_3$—an essential amino acid, that is to say one of the ones that we cannot make ourselves.

However, it is possible to make many artificial amino acids that do not occur in nature, and—if we could build those into proteins too—we could greatly expand the sorts of chemistry that could be carried out in living things. ~~However,~~ all the 64 possible three-nucleotide codons are already used (if redundantly), and so there are no spare ones left to use to tell a ribosome to build the artificial amino acids into a protein.

Jason Chin and his colleagues in Cambridge have, in a piece of genetic engineering that is a *tour de force*, solved this problem (Newman et al., 2010). They redesigned the ribosome so that it works with codons consisting of four nucleotides as well as three. This gives 256 (4^4) new codons. Together with the existing 64 natural codons that code for 20 amino acids, that means that 276 amino acids can be used in proteins. They inserted all their new bits of machinery into *Escherichia coli* bacteria and got them to make a modified conventional protein that incorporated two new artificial amino acids. Those artificial amino acids were designed to hold the protein's folds together in a different, more stable, way to that used by all the natural amino acids. This could mean proteins that work at higher temperatures, in more acidic or alkali environments, or a host of other possible improvements over what has evolved biologically.

It is hard to overstate how important and revolutionary all this is. The exponential-growth advantages of self-reproducing manufacture that were described in the introduction to this chapter kick-in immediately you start to use bacteria (or any other living thing) to make products, just as they do with artificial reproducers. If we can use bacteria to make new materials that cannot exist in nature or in the output of our conventional chemical engineering industry, then truly extraordinary possibilities open up.

Hence, if we can reengineer that core and fundamental part of all living things, can we build an entire living organism from scratch?

Just, if you count viruses as living. Eckard Wimmer and his colleagues have made a polio virus from its components (Cello et al., 2002).

Mycoplasma mycoides has one of the smallest genomes of any organism that can be grown in pure culture. Craig Venter and his colleagues have identified which parts of its genetic material can be removed without affecting how it lives (all genomes contain DNA that does nothing useful and that just hitches a ride when the useful stuff copies itself). They have then built the resulting edited genome from scratch. They have put that genome into a bacterium that has had its own genetic material removed and had it reproduce (Gibson et al., 2010).

Other people are assembling toolkits of genes for specific behaviors and characteristics that can then be included in synthetic organisms to give them those characteristics. The ultimate aim is to end up with a toolkit analogous to an electronic engineer's catalogue of integrated circuits. People would decide what they want to make and, with assistance from a computer controlling a genetic engineering robot, take a minimal synthetic bacterium and add the appropriate tools from the kit to it. The bacteria would then start churning out exponentially expanding amounts of conducting polymers for battery electrodes, drugs to break down the *amyloid plaques* in the brains of Alzheimer's sufferers, or diamond fibers for making aircraft wings.

At least, that is the vision.

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