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Organic Production Systems: What the Biological Cell Can Teach Us About Manufacturing

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Biological cells run complicated and sophisticated production systems. The study of the cell's production technology provides us with insights that are potentially useful in industrial manufacturing. When comparing cell metabolism with manufacturing techniques in industry, we find some striking commonalities, but also some important differences. Like today's well-run factories, the cell operates a very lean production system, assures quality at the source, and uses component commonality to simplify production. While we can certainly learn from how the cell accomplishes these parallels, it is even more interesting to look at how the cell operates differently. In biological cells, all products and machines are built from a small set of common building blocks that circulate in local recycling loops. Production equipment is added, removed, or renewed instantly when needed. The cell's manufacturing unit is highly autonomous and reacts quickly to a wide range of changes in the local environment. Although this "organic production system" is very different from existing manufacturing systems, some of its principles are applicable to manufacturing, and indeed, a few can even be seen emerging today. Thus, the organic production system can be viewed as a possible scenario for the future of manufacturing.

Key words: organic production; bionics; manufacturing strategy; local production; part commonality; volume flexibility; recycling
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1. Introduction

Division of labor and interchangeable parts led to the emergence of the mass production systems of the nineteenth and twentieth centuries. These systems were able to produce highly complex products in high volumes, making them affordable to a large number of people. In the second half of the twentieth century, flexible manufacturing equipment, information technology, and employee involvement led to emergence of the lean production systems that provided consumers with a larger variety of sophisticated products, exhibiting previously unseen levels of quality and reliability. Currently, at the start of the twenty-first century, new manufacturing technologies are once again forcing manufacturing companies to change. Manufacturing managers need to make sense of the impact of rapid manufacturing, recycling, bioengineering, and, perhaps, even nanotechnology.

Faced with these many new trends, can we say anything about possible directions that the changes in manufacturing might take? We try to do so in this paper by studying a high-performance manufacturing system that is two billion years old—namely, the biological cell. A careful examination of the production principles used by the biological cell reveals that cells are extremely good at making products with high robustness, flexibility, and efficiency. Using the biological cell as an analogy, we describe an alternative

manufacturing system that we call the "organic production system," and we argue that it holds useful ideas for possible future trends in manufacturing.

Our argument is organized as follows. Section 2 provides a review of related literature and introduces the methodology of learning from analogies. Section 3 describes the basic metaphor of this article, the biological cell as a production system, and shows that the cell is subject to similar performance pressures. Section 4 further deepens the metaphor by pointing out the similarities between the biological cell and a modern manufacturing system. We then point to the limits of the metaphor in §5 before we identify, in §6, four important production principles that are sources of efficiency and responsiveness for the biological cell, but that we currently do not widely observe in industrial production. Analogical reasoning then leads to §7, in which we formulate and illustrate the principles of an "organic production system," based on those four distinctive principles. We also show that partial examples of its application already exist. In the final section, we discuss the relevance of this innovative production system for possible future trends in manufacturing.

2. Learning from Comparable Systems

Metaphors and analogies are known to be powerful tools used to think and learn about organizations and systems (e.g., Beer 1984, Morgan 1986, Tsoukas 1991). Biological metaphors have long been used in the study of organizations (e.g., Hannan and Freeman 1977, McKelvey and Aldrich 1983) and have enhanced the understanding of organizational growth, decay, and variety by explaining them in terms of the evolutionary principles of variation, selection, and retention (e.g., Campbell 1970).

In engineering also, the study of comparable biological systems has been a source of innovative thinking. Labeled bionics, this branch of engineering science has been concerned with the technical realization of construction, process, and development principles of biological systems (Neumann 1993, Nachtigall 2002). Two examples of bionics are a freshwater production system based on the reverse osmosis processes employed by the mangrove (Lieckfeld 1993), and a self-cleaning façade paint based on the water- and dust-repellent properties of the lotus leaf (Neinhuis and Barthlott 1997).[1]

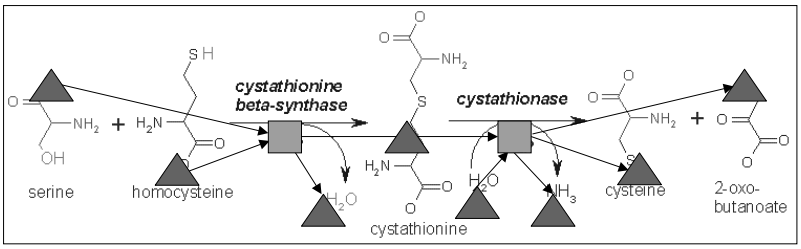
Earlier studies in flexible manufacturing systems have also suggested taking a bionic approach (Engel 1990). The concept of biological manufacturing systems (BMS), in which principles of biology are applied to manufacturing problems, was initially developed and tested in Japan (Ueda 1992). Vaario (1996), for example, suggests exploiting the principles of self-organization and evolution for the design of assembly lines. This approach allowed him to model dynamic reconfiguration of assembly lines in the case of malfunction or changes in demand. The aim was to develop a flexible system for a dynamic environment instead of an optimal configuration for a static environment.

With a stronger emphasis on exploring the isomorphic relations, Bozinovski carried out some groundbreaking work in linking manufacturing sciences and protein biosynthesis (Bozinovski and Bozinovska 2001). He recognized, in biosynthesis, the just-in-time principle for the making of products and machines (enzymes) in the cell. In addition, he pinpointed the cell's autonomy and its information and regulation efficiency, which is sometimes referred to as self-assembly. He convincingly suggested that these features were worth studying and worth replicating in a new generation of autonomous manufacturing systems.

Another example of the use of biology as a metaphor for industrial production is the widely cited book *Biomimicry* (Benyus 1997). The author draws from material science research to compare nature's way of making things with the "heat, beat and treat" philosophy of industrial production. Benyus identifies four principles for nature's way of producing. One, nature manufactures its materials under life-friendly conditions (e.g., no chemical baths or high pressure or high temperature). Two, nature makes materials in an orderly hierarchical structure (e.g., self-similar fractals across dimensions, which arise from growing structures from the ground up). Three, nature

[1] Biologists, in turn, are now discovering that they can learn something from engineering in analyzing complex biological systems, for example, in understanding for robustness and modularity (see, e.g., Alon 2003).

Figure 1 Analogy Between a Biochemical Pathway and a Flow Diagram from Manufacturing: A Sequence from the Biosynthetic Pathway for Cysteine, 1 of 20 Amino Acids



Note. The enzymes catalyzing the two reactions can be depicted as work centers or machines (squares). The different intermediates and products represent work-in-process inventory (triangles).

relies on self-assembly—no central logic, but decentralized growth according to local rules. Four, nature customizes materials through the use of templates; the genes are templates for proteins, which become templates for material growth. The templates can be varied, so materials are made as needed and required by the environmental challenge, with little waste.

Similarly to this previous work, our paper applies methods of analogical reasoning in order to learn about manufacturing systems. The methodology for extracting insights from the study of comparable systems is well described and has many different levels, each of which bring their own contribution (e.g. Beer 1984, Gentner 1989, Tsoukas 1991). In this paper, we attempt to establish a metaphor ("A biological cell is like a production system") by demonstrating that similar behaviors are driven by similar causal mechanisms. Then, using similar conceptualizations of the two systems, we attempt to derive insights from comparing them. We find that interesting insights can be gained from studying the dissimilarities in the systems that are being compared (Oswick et al. 2002). More than the above-cited previous work, we emphasize the interactions of many elements in a system.

3. The Cell Metabolism as a Manufacturing System

The cell is quite clearly a manufacturing system. It uses a small set of inputs to "manufacture" a wide range of compounds that help it to interact appropriately with its environment, and eventually allow it to reproduce itself (see the Appendix). The cell manages this production in a complex network of several thousands of biochemical reactions. For example, the intestinal bacterium, *Escherichia coli*,[2] runs 1,000–1,500 biochemical reactions in parallel. Just as in manufacturing, cell metabolism can be represented by flow diagrams in which raw materials are transformed into final products in a series of operations. Figure 1, for example, shows part of a biochemical pathway, which is the equivalent of a production line, in which enzymes, which are the cell's machines, perform operations on the different types of work-in-process inventory. As in manufacturing, each of these operations has a certain capacity, and the amount of production at each step is controlled directly by signals or indirectly by limiting the material flow. With its thousands of biochemical reactions and high number of flow connections, the complexity of the cell's production flow matches even the most complex industrial production networks we can observe today.

The performance pressures operating on the cell's production system also exhibit clear parallels with manufacturing. Both production systems need to be fast, efficient, and responsive to environmental change. Speed and range of response, as well as efficiency of its production systems, are clearly critical to the biological cell. Biologists have made the argument that the evolution of the basic structure of modern cells has largely been driven by "alimentary efficiency," or the input-output efficiency of turning available nutrients into energy and basic building blocks (Rizzotti 2000). In addition, it is clear that in dynamic environments, the ability of the cell to react quickly and decisively is vital to ensure survival and reproduction. An important type of response, indeed,

[2] *Escherichia coli* is one of the best-studied microorganisms—It is a preferred organism for experiments.

is the cell's biosynthetic response, i.e., the response of its production systems (Bozinovski et al. 2000). Over the course of evolution, the cell has had to develop competencies that allow for efficiency through energy and building block conservation, while maximizing responsiveness to environmental changes.

As it is for the cell in biology, a lack of operational efficiency or responsiveness can lead to a company's demise in industry. As has been argued by the Business Process Reengineering movement (e.g., Hammer and Champy 1993, Hammer 2002), the fate of a company may be decided by the quality of its operations rather than by its strategy. Examples abound of companies that struggled or went bankrupt because of poor operations management: Harley Davidson was on the brink of bankruptcy in 1981 because of poor product quality, high inventories, and high manufacturing costs. Boeing lost market share to Airbus in 1998 because of its inability to manufacture its backlog of ordered planes on time. Kmart filed for bankruptcy in 2000 because of poor logistics and inefficient supply chain management. And so on.

Given the "manufacturing" nature of cell biochemistry and the comparable performance pressures on it, one should not be surprised to find interesting solutions developed by the cell that are applicable in manufacturing—especially since "cell technology" is much older and more mature than any human technology.

4. Commonalities Between the Cell and Manufacturing

Although a cell and a manufacturing plant are, of course, very different organisms (we further discuss differences below), we have argued that at least some of the pressures for efficiency and responsiveness that act on the biological cell's production systems are similar to those acting upon industrial production systems. In this section, we show that, indeed, many solutions that these two systems have developed are similar as well, suggesting that we can look at them as an example of convergent evolution[3] (Dawkins 1996). We may, therefore, expect that the biological cell holds some useful lessons for manufacturing systems, in spite of the differences.

Historically, the cell[4] came first—Its production principles precede human industrial activity by two billion years,[5] a very long time even in evolution terms. The cell has not served as a role model in the historical development of manufacturing, so we should not expect to find similarities as a result of imitation or copying. However, the cell applies many of the mechanisms that can also be observed in modern manufacturing: lean production, quality at the source, and postponement. The cell carries out a very lean[6] operation: By using pull systems and excess capacity, the storage of intermediates is kept to a minimum within the pathways.[7] The cell also assures quality at the source, avoiding rework loops for the repair of "broken" molecules.[8] Finally, the cell takes advantage of modularity, component commonality,

[3] The evolutionary acquisition of similar features (analogies) in genetically unrelated organisms as the result of adaptation to similar selective pressures from their environments (e.g., whales and fish).

[4] There are two major versions of "cells," eukaryotic and prokaryotic cells. Prokaryotic cells (represented by bacteria) arose before eukaryotic cells, and they are generally smaller and simpler in their construction. Bacteria nevertheless exhibit all the same basic characteristics of life and share the same biochemistry with their eukaryotic cousins. Eukaryotic cells are more complex, exhibiting organelles (such as nucleus, mitochondria, endoplasmatic reticulum, golgi apparatus), and only they have developed multicellularity. In this article, we have eukaryotic cells in mind, but will often refer to bacteria because certain principles are easier to demonstrate with them.

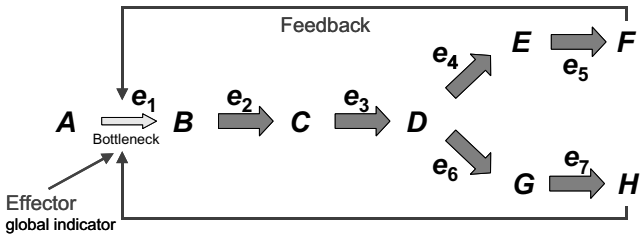
[5] Eukaryotic cells evolved around two billion years ago. Bacteria, prokaryotic cells, are much older. Fossil records date their first appearance to around 3.5 billion years ago.

[6] The term "lean production" was coined by John Krafcik and popularized in Womack et al. (1991). While involving a range of management principles, it is mostly associated with waste minimization, low levels of work-in-process inventories and just-in-time production.

[7] See, for example, Voet and Voet (1994). The cell is, however, capable of storing raw materials for bad times, e.g., glycogen in roots or fat tissue. In addition, many organisms store nutrients for their offspring, e.g., in seeds or eggs. These different types of storage represent a "strategic reserve," not intermediates.

[8] Repair mechanisms for DNA can be regarded as the only exception to this principle. The genetic material of the cell can be damaged by external factors such as chemicals, UV-light, or radioactivity. To ensure the integrity of vital information, all have developed various organisms mechanisms to reverse such damage, e.g., yeast possesses about 50 different ones.

Figure 2 Schematic Representation of a Biochemical Pathway



Note. The capital letters *A* to *H* represent precursors, intermediates, and final products of the pathway. The letters e_1 to e_7 stand for the enzymes, i.e. the machines, involved in the pathway. The first step catalyzed by e_1 is the bottleneck, regulated by feedback inhibition from the final products, *F* and *H*. Furthermore, global effectors might control the bottleneck, which allows for general regulation according to specific physiological conditions triggered by, for instance, external stimuli. Starting at intermediate *D*, the pathway splits into to subpathways, which allow the cell to use a platform strategy to synthesize *F* and *H*, thus employing fewer enzymes than in the case of independent synthesis, as well as postponing the decision to make either *F* or *H*.

and postponement in its biochemical pathways. We will explain each of these similarities below.

Using Pull Systems to Avoid Overproduction

In biochemical pathways, production occurs only when triggered by a downstream shortage. Or, inversely, any build-up of downstream product will immediately halt further production. As long as there is still final product available, the first enzyme or "machine" of the pathway is physically blocked by an interaction between the final product and the enzyme, a mechanism called "feedback inhibition" (Figure 2).

When the final product of a pathway is depleted by high "demand," the first enzyme is unblocked. As it opens up for production, it gets hold of a piece of raw material and starts processing it. The cell never forecasts demand; it achieves responsiveness through speed, not through inventories. The limits to responsiveness depend only on the capacity limits of the enzymes in a particular pathway. The corresponding mechanism in manufacturing is referred to as a pull system. It produces only in response to actual demand, not in anticipation of forecast demand, thus preventing overproduction.[9]

Minimizing Work in Process by Using Bottlenecks to Control the Release Rate

In virtually all biochemical pathways, the first enzyme is the bottleneck that limits the entry rate (Voet and Voet 1994), as illustrated in Figure 2. The enzymes within the pathway can process products much faster than the entry rate and, as a result, the level of intermediate products is kept to a minimum (Holms 1996). In manufacturing, the principle of using the bottleneck to control the release of jobs into a production line is also well known.[10]

As both the pull mechanism and the upfront bottleneck are known to simplify production control in manufacturing, it is interesting to check the amount of control and regulation overhead in the two analogous systems. *Escherichia coli*, for instance, is known to dedicate about 11% of its genes to regulation and control (Mulder et al. 2000). While it is difficult to make direct comparisons with manufacturing plants, some case examples illustrate that the cell operates with little waste, even in regulating its pathways. In a U.S. electric-connectors factory in the early 1990s, 28.6% of plant labor was devoted to control and materials handling, while the figure was 14.9% in a simpler and leaner Japanese plant (Pisano 1992, Exhibit 5). In a house-care products plant, a cost analysis revealed that at least 14% of production costs were incurred by production planning and quality assurance (Hayes 1995, Exhibit 2).[11] With its 11% of regulatory genes, the cell seems to set a pretty tight benchmark for regulation efficiency.

Using Excess Capacity to Simplify Control and Lower Work in Process

It is important for the cell to keep intermediates at a low level in order to save energy and building blocks. Work in process, in the form of intermediates, is costly—first, because space comes at a

[9] If we look at higher multicellular organisms, the only form of forecasting that we might find is the preparation for seasonal environmental changes by storing food, e.g., for hibernation in animals. Some plants have developed the ability to anticipate sunrise and open their leaves just before this event (Davis and Millar 2001). These behaviors are imprinted genetically, rather than an act of rational forecasting in a human sense.

[10] See, for example, Goldratt and Cox (1986).

[11] Costs for production planning and quality assurance were compared with the costs of direct labor and all direct labor production overheads.

premium in the cell,[12] and second, because inventory may degrade and represents unproductive use of material. The question is whether the cell pays a price for keeping the level of intermediates at such a low level. It does have excess capacity for all but the first enzyme in its pathways, and one may wonder whether this is efficient. In manufacturing, such excess capacity may be too costly. However, if capacity becomes more flexible and more affordable, and responsiveness more important, one may see more factories in which some safety capacity, in all operations but the first, is used to lower work in process, simplify control, and increase responsiveness to sudden market changes. The clothing retailer Zara, for example, known for its quick response capabilities, is seen to use excess capacity in its distribution systems to ensure short leadtimes and to avoid costly build-up of inventories in its warehouses (Ferdows et al. 2003; see also Goldratt and Cox 1986).

Managing Quality at the Source

The cell also uses quality-management techniques used in manufacturing today. The cell invests in defect prevention at various stages of its replication process, using 100% inspection processes, quality assurance procedures, and foolproofing techniques. An example of the cell inspecting each and every part of a product is DNA proofreading. As the DNA gets replicated, the enzyme DNA polymerase adds new nucleotides to the growing DNA strand, limiting the number of errors by removing incorrectly incorporated nucleotides with a proofreading function.[13]

An example of quality assurance can be found in the use of helper proteins, also called "chaperones." These make sure that newly produced proteins fold themselves correctly, which is critical to their proper functioning. Finally, as an example of foolproofing, the cell applies the key-lock principle to guarantee a proper fit between substrate and enzyme, i.e., product and machine. The substrate fits into a pocket of the enzyme like a key into a lock, ensuring that only one particular substrate can be processed.[14] This is comparable with poka-yoke systems in manufacturing (Shingo 1986). An everyday example of poka-yoke is the narrow opening for an unleaded gasoline tank in a car. It prevents you from inserting the larger leaded-fuel nozzle.

Exploiting Postponement and Platform Strategies

The cell's pathways are designed in such a way that different end products often share a set of initial common steps (as is shown in Figure 2). For example, in the biosynthesis of aromatic amino acids,[15] a number of common precursors are synthesized before the pathway splits into different final products.[16] This commonality reduces the number of enzymes needed to synthesize amino acids, thus conserving energy and building blocks. It postpones the decision of which amino acid, and how much of it, to synthesize.

Another striking example of commonality is steroids, a class of common molecules in microorganisms, plants, and animals.[17] Steroids help in performing various biological functions, such as regulation (hormones) or solubilization of fat (bile acids). Their basic structure is a sterane skeleton, which is modified by side chains and functional groups that give the particular molecule its specific biological activity. Steroids perfectly match the industrial definition

[12] The internal space of a cell is limited: With an increase in size, the volume grows much faster than the available surface for exchanging energy and substances with the environment. The ratio of volume that must be fed and supported over surface area available for exchange with the environment sets a cap on the maximal cell size.

[13] DNA is a double helix of two intertwined DNA strands, where the nucleotide adenine pairs with tymidine, and cytosine with guanine. DNA is replicated when a new DNA strand is synthesized using one strand of the double helix as a "negative." DNA polymerase is one of the enzymes responsible for the replication of DNA. DNA polymerase synthesizes the new strand by adding new nucleotides that are complementary to the nucleotide sequence of the matrix strand. When a wrong nucleotide is added, DNA polymerase possesses an exonuclease activity that removes the wrong nucleotide, thus ensuring correct replication.

[14] The pocket is an indentation of the protein into which the substrate fits like a key in a lock.

[15] An amino acid is an organic compound containing an amino group ($-NH_2$) and a carboxyl group ($-COOH$). There are 20 naturally occurring amino acids that form the building blocks for all proteins including DNA.

[16] Aromatic amino acids, phenylalanine, tyrosine, and tryptophane are all synthesized from phosphoenolpyruvate and D-erythrose-4-phosphate. The pathway branches late at the intermediate chorismate.

[17] Currently, about 20,000 steroids are known. About 2% have significance in medicine.

of a platform—a set of subsystems and interfaces that form a common structure from which a stream of derivative products can be efficiently developed (Meyer and Seliger 1998).

5. Limits of the Metaphor Between the Cell and Manufacturing

In the previous section, we described a set of similarities between the cell's production principles and modern manufacturing, providing evidence of convergent evolution for both systems. We now examine what insights and lessons we can derive from examining some of the differences between biochemical pathways and current manufacturing systems. Before turning to insight-generating differences (§6), we must first recognize the limits of the metaphor, or fundamental differences that could invalidate parts of it or prevent the transfer of the cell's production principles to manufacturing.

First, many differences between a cell and industrial manufacturing fall outside the scope of the metaphor—many simply reflect differences in size or materials used and cannot be clearly linked with performance, or are not meaningful within the context of industrial production. For example, the enzymatic reactions in cells all exploit basic chemical equilibria and are, in principle, reversible. This is not true in manufacturing, but since the cell does not really employ this feature in a way that makes it more efficient or more responsive,[18] we did not explore this characteristic further. For other characteristics of cell production, the difference is real and perhaps significant, but their implications would be difficult to imagine or analyze. For example, in biological cells, the basic form of energy, the ATP molecule, is so prevalent that one is tempted to attach meaning to the lack of a clear analogous element, a "currency," in industrial production. While noteworthy, we did not include an analysis of this difference because it did not lead to clear implications.

Second, the cell faces important constraints that limit the usefulness of some otherwise clear analogies. First, as mentioned in the previous section, there are physical constraints on the maximum size of the biological cell, so we have to be careful not to draw any direct conclusions about the right scale of a manufacturing unit. A second constraint faced by one-cellular organisms is that they cannot rely on contract law or memory-enabled reciprocity to establish cooperation among multiple individuals or units. Cells may, therefore, have a stronger need to be autonomous than factories or plants.[19] We take both of these constraints into account when proposing lessons for manufacturing in §7.

A final concern is that the biological cell is the result of evolution, not design. This could raise questions about the usefulness of the cell's production principles for manufacturing. Consider the cell's technology, which stabilized about two billion years ago. Before that time, many technologies competed for survival: for example, RNA molecules instead of DNA for the storage of genetic information, ribozymes instead of proteins for biocatalysis, and chemosynthesis as the primary mode of energy production versus photosynthesis today. However, around two billion years ago, the fundamental "cell technology," with its production system, reached a mature design—i.e., a stable configuration of system components and their interactions (Utterback and Abernathy 1978, Anderson and Tushman 1990). This mature design gained a dominant "market share" of biomass on the planet and has not fundamentally changed since, as it has not been outcompeted by any other technology (although countless numbers of mutations arose). This does not mean this design is perfect; on the contrary, it is known in biology that many basic elements of cells and organisms are evolutionary relics and could

[18] As a matter of fact, the cell uses certain "biochemical tricks" to make the flow of many reactions irreversible in order to keep the process going in the right direction.

[19] In multiorganism cooperation, the analogy between the cell and manufacturing is less direct. A useful analogy does hold between alliances, or supply chain coordination, and the biology of social animals, where reciprocity and the equivalent of contracts are widely used and analyzed with similar tools as in business (e.g., see Maynard Smith 1982, de Waal 1996). This is true even for nonconscious single-cell organisms, among which reciprocity has been found. It is enforced not between individuals (who have no means by which to keep track and enforce), but statistically between populations (e.g., Velicer et al. 2000). Exploring this analogy to organizational populations is beyond the scope of this article.

be improved upon, but they are stable because they are part of the system.[20]

The quirks of evolution may indeed put some limits on the applicability of the cell's production principles. However, these limits should not be overstated. First, even if evolution comes with some constraints, it does not mean that its solutions should be disregarded. Second, human technologies also display characteristics of evolutionary systems. Take the recent evolution of software as an example. There are still some "Stone Age" routines hidden deep down in modern software (commonly referred to as legacy code) that were written 40 years ago on card punchers, were embedded in large systems, ported to new languages, cross-linked with interfaces, and made invisible to users with layers of user interfaces. These modules may no longer be optimal or efficient; system performance could be improved if they were reengineered. The reason for retention is that reengineering has been infeasible because either the improvements would have to be implemented everywhere (impossible), or the improved versions would lose compatibility and cross-sharing (debilitating). The same is true for manufacturing systems,[21] which contain ancient relics as well (see, for example, the discussion of today's railway-track-width standard, which may stem ultimately from the Roman warrior chariots, Fine 1998, pp. 40–41). Thus, it seems that manufacturing systems are also constrained by evolution, which should only increase the relevance of the biological cell as a useful template.

6. Revealing Differences Between the Cell and Manufacturing

We now turn to those differences that most clearly contribute to the cell's ability to be efficient and responsive and have a meaningful interpretation for industrial production systems. There are likely to be more differences whose relevance we have not yet grasped.

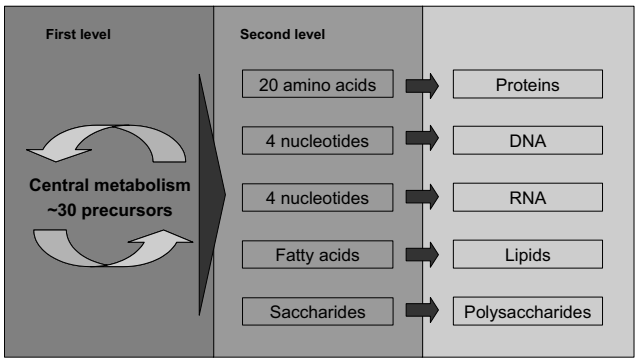
Products and Machines Are Built from a Small Set of Common Building Blocks

The cell uses a small set of basic materials to produce an extremely wide variety of tools and products. As production technologies become more advanced, manufacturing may see a similar convergence around a common set of versatile materials.

Four nucleotides, twenty amino acids, some saccharides, and fatty acids are the basic building blocks that are used for the synthesis of major cell molecules: DNA, proteins, polysaccharides, and lipids, respectively. These ingredients of life are so universal that nucleotides, amino acids, saccharides, and fatty acids can easily be exchanged across species, usually when they devour one another.

A second, lower level of commonality is found in the central metabolism. Here, a limited number of about 30 intermediates can be identified, which serve as precursors for the abovementioned nucleotides, amino acids, saccharides, fatty acids, and many other biomolecules (Holms 1996). Figure 3 shows a schematic representation of the cell's component commonality. Interestingly, the intermediates used for "products" and "machines" (enzymes) are identical. In other words, the cell can easily degrade an enzyme into its component amino acids and use these amino acids to synthesize a new enzyme (a "machine"),

Figure 3 Different Levels of Component Commonality in the Cell



Note. The first level represents the central metabolism with approximately 30 different precursors. These 30 precursors are converted into amino acids, nucleotides, etc., which are the building blocks for macromolecules such as proteins and DNA.

[20] While mutations still happen at the "component" level (for cells as well as organisms), the cell and organism architectures have remained extremely stable over evolutionary time because any change is negative (Dawkins 1996, p. 255).

[21] Although managers plan, they often do so with insufficient and/or wrong information. Thus, manufacturing systems as a whole may also evolve "blindly," subject to selection pressure (Mokyr 1990, 1996; Silverberg et al. 1990).

replenish the central metabolism, or make another molecule (a "product"), e.g., a biogenic amine.

It seems an amazing achievement by the cell to build the complexity and variety of life with such a small number of components. Imagine that all industrial machines were made of only 20 different modules, corresponding to the 20 amino acids from which all proteins are made. As we further explain below, this modular approach allows the cell to be remarkably efficient and responsive at the same time. Basically, with both products and machines being built from just a few recyclable components, the cell can efficiently produce an enormous variety of products in the appropriate quantities when they are needed.

In industry, parts commonality and material versatility are on the rise, but at a very rudimentary level. For example, supply chains are designed with common processes upfront and the differentiating operations at the end (Feitzinger and Lee 1997). The Franco-German company, SEW, produces small and medium-size electric motors for a wide range of industrial applications. For a certain line of motors, there are 50 million customer-specific variants, but by clever localization of the customized parts in a few modules of the motor, fewer than a thousand different parts suffice to yield this amount of variety.

Another widely discussed industrial example is HP's design of a "universal printer" with a generic power supply and locally added manuals. Similarly, today's high-end cars contain complex local area networks that perform hundreds of control functions and coordinate as many sensors. In the past, dedicated ASICs[22] were used to perform the logic functions, which were cheap to manufacture but had to be custom designed for each function. Carmakers have begun to use freely programmable logic chips, which can be used for all functions, reprogrammed by the sales force, and reused. The higher costs of these chips are offset by the increased flexibility and speed in development. Other examples are 2×4 lumber or standardized thread sizes.

Generally, standardization does not cut across product categories, although a few production materials are gaining in versatility. For example, the use of aluminum, polypropylene, and polyethylene is on the rise across multiple industries (such as automotive and construction) as a result of improved methods for conversion and handling. Despite such advances, it is still too early to determine if common building blocks will ever meet all the engineering and economic requirements of industrial production, and if so, of what materials they will be made. However, it is conceivable that once a set of materials is sufficiently versatile for a wide enough range of applications, a chain reaction of research and investment could widen their use even more, to a level seen in biological cells.

[22] Application Specific Integrated Circuits.

Production Equipment Is Added, Removed, or Renewed Instantly

The capacity of the cell's pathways can be adjusted almost immediately if the demand for its products changes. If the current capacity of a pathway is insufficient to meet demand, additional enzymes are "expressed" to generate more capacity within a certain range. Once the demand goes down, these enzymes are broken down again into their basic amino acids. This avoids waste as the released amino acids are then used for the synthesis of new proteins. At any moment, synthesis and breakdown for each enzyme happen in the cell. The constant renewal eliminates the need for other types of "machine maintenance." Assembly and disassembly of the cell's machines are so fast and frictionless that they allow a scheme of constant machine renewal.

In some industrial manufacturing settings, we are also witnessing signs of the emergence of flexible capacity. Some of these companies do not repair their manufacturing equipment, but have it replaced. Take, for example, a contract manufacturer in Singapore that provides semiconductor assembly and test services for INTEL, AMD, and others. Its manufacturing equipment includes die bonders, wire bonders, and encapsulation and test equipment, all organized in pools.[23] As soon as one machine goes down, the

[23] In this process, the circuit dies are first bonded to the package frame using a die bonder. Then, with the wire bonder, each pad on the die is connected to a corresponding pin on the package frame via a thin gold or aluminum wire. The encapsulation equipment is then used to seal the package with a lid. In the final step, the test equipment is used to test the chip's functionality under different temperatures.

managers work with the equipment supplier to make a one-to-one replacement. All this goes very rapidly indeed. This policy makes sense because the low cost of a machine compared to the cost of downtime makes it economically feasible to have a couple of machines idle in the somewhat longer repair cycle. One can imagine this practice spreading as manufacturing equipment becomes more standardized and less expensive, and as the cost of a capacity shortage increases.

In this scenario, machines are still repaired, although at the supplier site rather than on the manufacturing floor. The cell has pushed this principle even further. First, it does not even wait until the machine fails, but replaces it long before it has a chance to break down. And second, it completely recycles the machine that is taken out of production. The components derived from this recycling process can be used not only to create other machines of the same type, but also to create different machines if that is what is needed in the "plant."

This way of handling its machines has some clear advantages for the cell. New capacity can be installed quickly to meet current demand. At the same time, there are never idle machines around taking up space or hogging important building blocks. Maintenance is a positive "side effect" of the continuous machine renewal process, thereby guaranteeing the quality of output. Finally, the ability to quickly build new production lines from scratch has allowed the cell to take advantage of a big library of contingency plans in its DNA that allow it to quickly react to a wide range of circumstances, as we will describe next.

Manufacturing Units Are Highly Autonomous and React Quickly to External Change

The cell is highly responsive to change. Its production system can quickly adapt to a wide range of changing conditions and, thus, operate with a high degree of autonomy. This ability is so prominent that one could say that learning from the cell is learning how to quickly respond to change. A fast response to environmental change, such as a change in temperature, a change in the nutrient supply, or the approach of a predator, enables the cell to ensure its survival. This is true for manufacturing organizations too. The response time to changing conditions in the market, the regulatory environment, or the inquiry of a potential customer has a major impact on the survival of the organization.

A single-cell organism, such as the bacterium *Escherichia coli*, has encoded in its genes a large potential to adapt to very different environmental conditions. Not all of these genes are constantly expressed; the cell selectively switches them on, depending on the environment, thus changing the associated pathways. In this way, the cell has a number of "backup plans" in its genetic material. These backup plans are based on the historical experience of the species. They are biologically stored in the genetic material, enabling the organism to react effectively in circumstances "memorized" by the species' gene pool (from which the individual organism draws; see Plotkin 1993).

It has been shown in laboratory experiments that bacteria are able to do even more: They can rearrange their chromosomes by multiple recombinations in response to persistent unfavorable environmental conditions, in a way different from the genetic backup information (Papadopoulus et al. 1999, Nass et al. 1994). The recombinations allow the cell population to create *new* beneficial gene combinations, and thus new knowledge, out of preexisting chromosome combinations. Of course, lots of individual cells die (those that had the ex post "wrong" recombinations), while the lucky ones survive, and the population as a whole gains.

Manufacturing plants apply something analogous when engaging in continuous local experimentation. We have seen innovative plants that are hardly recognizable after five years, without any major technology shift or new, major products. They achieve this by constantly experimenting with small changes in layouts, processes, and machines. However, even in the most innovative plants, change seems much slower than in cells. For cells, experimentation is not so costly, and it can truly make the difference between survival and extinction for the genes involved. For plants, however, extensive experimentation much above normal TQM quality circles invites reluctance. It disrupts the efficiency of current operations, it is expensive (most experiments *do* fail), and it places a burden of failure on those who conduct those experiments that fail, an experience for which

few people have the stomach and few managers the patience.[24]

A technology on the horizon (still far from commercialization) that could achieve levels of experimentation similar to a cell is nanotechnology. Its concept of self-assembly grew out of chemists' attempts to make molecules that aggregated spontaneously into specific configurations, in the same way that biological molecules form complex cell membranes. Nanotechnology aims to use self-assembly for the "automated" manufacture[25] of many compound objects simultaneously and in parallel, rather than sequentially. Once self-assembly becomes feasible, it may allow levels of experimentation and evolutionary change at a level observed in cells, because of lower costs of failure than in today's manufacturing systems.

The second aspect of bacteria's high responsiveness lies in their high degree of autonomy, carrying with them all the information to reproduce. Because they use locally found materials for reproduction, bacteria do not require any supply chains to deliver goods to them. This complete localization of production, along with flexibility and component commonality, provides the cell with the robustness and adaptability that make it such a strong survivor.

Here too, we see a few analogous trends in manufacturing. Fuel cells, although still in an early development state, have the potential to allow for local energy supply, thereby increasing the autonomy of production units and making them potentially mobile. An increase in the service component of manufactured goods will push for local production, or at least assembly, as practiced, for example, by the electrical motor producer, SEW, that we mentioned above. A progressive move from hardware features to software (for example, via intelligent machine control, and especially the commercialization of rapid manufacturing) will reduce economies of scale, thus allowing local production with generic tools, or the renting and moving around of such tools. This vision of generic reconfigurable tools exists in manufacturing labs, but has not yet been put into practice. Visible on the horizon, perhaps five to ten years from now, is the migration of rapid prototyping technologies into manufacturing. When freely programmable rapid machines can spray-produce any three-dimensional shape in layers not only in plastic, but also in high-strength sinter metal,[26] machines may indeed become generic, able to produce any product rather than only specialized, high-volume series. Moreover, as these machines produce arbitrary shapes, they may become capable of reproducing at least parts of themselves.

Modern high-performance factories also seem to exhibit a trend toward more flexibility and autonomy by a setup called "the plant within the plant." Lines take on the responsibility for their entire process, from supplies, quality control, and planning, to delivery. In the extreme case, the only thing that is shared is common knowledge and expertise (Loch et al. 2003).

Building Materials Circulate in Local Recycling Loops

The cell's production system obtains part of its efficiency from closed cycles both within the cell and within the ecosystem of which it is part. The cell recycles building blocks such as nucleotides and amino acids.[27] This saves energy and time for the resynthesis of amino acids, facilitated by the limited number of building blocks and the commonality of biomolecules.

A higher degree of parts commonality and product modularity could also facilitate closed cycles in future manufacturing systems. The current lack thereof might be the reason why current recycling attempts are often not economically viable. For example, recyclers reconvert plastic waste into a petroleum-like substance, which is a low-level raw material, whereas the cell's recycling occurs at the level of commonly used intermediate products.

Closed loops exist not only in the cell, but also across the entirety of the living world. Interestingly, the players in the closed cycles in nature are all selfish organisms that perform degradation or synthesis

[24] Moreover, there is evolutionary experimentation, including the death of unsuccessful "organisms" or firms, at the industry level (e.g., Nelson and Winter 1982).

[25] www.landesbioscience.com/nanomedicine/2.3.html.

[26] Alternatively, the rapid manufacturing machines may layer-produce metal tools for stamping or extrusion that last only for a few hundred units, but are very fast and cheap to make.

[27] A so-called scavenger pathway prevents further degradation of nucleotides after the breakdown of DNA and RNA. Proteins are also constantly renewed. Broken-down amino acids are reused to build new proteins.

only for their own benefit. Value is created at each step of the cycle in the form of biologically available energy or scarce resources, as in the carbon cycle or the nitrogen cycle. In the carbon cycle, for example, plants form saccharides from airborne carbon dioxide using photosynthesis. As a waste product, oxygen is released. The saccharides serve as a source of energy and building blocks to the plant, representing its profit from this process. Animals eat plants and thus capture the saccharides produced by photosynthesis. They gain energy and building blocks for their metabolism from the plant material they eat, which is their profit from the process. The animals, in turn, use respiration to release a maximum of energy from their nutrition, using oxygen to degrade saccharides to water and carbon dioxide. The carbon dioxide is a waste product for the animal but an input for the plant, whereas the oxygen is waste from photosynthesis but essential for respiration. Each participant in the carbon cycle has its benefit. Each makes a living in the niche it occupies.

While these biological recycling participants cohabitate locally, making recycling available at low transportation costs, current industrial recycling loops stretch over large distances; waste is collected and then transferred to central/regional locations where partial recycling takes place. This increases costs and compromises responsiveness, making it more difficult for recycling to become a win-win proposition.

Thus, while manufacturing industries are also composed of selfish participants, the cycles are not closed, and even in the rare closed cycles, value is not added at every step, and transportation is a major barrier. In some countries, governments intervene to close the cycles—for example, with the introduction of disposable cans and bottles in Germany. Although commendable in its objectives, this type of government intervention may not be necessary in the long run. Nature's production cycles show that it is possible to create material cycles in which value is obtained at every step.

However, government regulation is likely to increase, and it may indeed jumpstart the recycling loop. In 2000, the European Union passed "end-of-life" legislation, requiring car manufacturers to recycle or reuse at least 80% of their old cars by 2006. Car recycling is just the beginning—The regulatory trend will expand to computers and electronic products.[28] Enterprises are responding. The U.S. company MBDC,[29] for example, has specialized in redesigning manufacturing processes in order to eliminate toxic products and enhance recyclability. The founders of MBDC, in discussing the paper industry, argue strongly that paper could be recycled indefinitely (McDonough and Braungart 2002). Such efforts mark a beginning of increased recycling in manufacturing, and the cell may serve as a model of how far this might be able to go.

7. Lessons: The Organic Production System

We try to consolidate the potential lessons from the differences between the cell and manufacturing by hypothesizing a possible industrial production system that leverages the same production principles that the cell uses so successfully. We call the proposed system an *Organic Production System*. Its distinguishing principles, which are contrasted with the features of a more traditional production system in Table 1, are the following:

(1) *Customized Local Production.* Products are custom built locally, with a very short delivery time and minimal inventory.

(2) *Universal Components.* Products are made to a large degree from standard universal components or common raw materials that are bought in local markets.

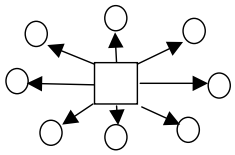
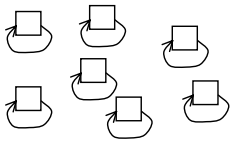
(3) *Just-In-Time Tools.* Desired production capacity is met with small-volume production machine tools that are easy to configure for universal application; these tools can easily be added, dismantled, or rearranged.

(4) *Local Closed Recycling Loops.* All parts, generic and customized, are part of an efficient closed-loop cycle in which they are used again in local markets (as parts or raw materials), without having to be moved over long distances.

[28] PC recycling currently has negative value—PC makers currently offer customers an arrangement in which they will dispose of old PCs for a small fee, often even leaving the customer to pay the transportation costs.

[29] McDonough Braungart Design Chemistry Charlottesville, www.mbdc.com.

Table 1 Characteristics of the Organic Production System

	Mass production (and distribution) systems	Organic production systems	
Geographical structure		1. Customized local production	
Scale	• Large—to reduce production costs		• Small—low transportation and inventory costs; close to customers
Response capabilities	• Restricted due to distance of large centralized plants from customers • Limited response knowledge		• Unrestricted, facilitated by small decentralized units close to the customer • Extensive response knowledge
Production materials	• Many different materials • "Best" material for each part or function	2. Universal components	• A few basic materials that can be "combined" to serve many purposes • Materials are modular, don't need to be broken down to basic components to be recycled
Capital equipment	• Large, costly equipment • Difficult to add, remove, or replace • Limited volume flexibility	3. JIT tools	• Small, inexpensive tools • Easy to add, remove or replace • High volume flexibility
Material reuse	• Very low	4. Local recycling loops	• High—sometimes close to 100% (sometimes within a facility, sometimes materials from one product become input to other products)

The reader should notice that the four principles form a system, complementing and reinforcing one another, so the system is more than the sum of the parts. For example, universal components represent sufficient mass to allow local recycling. Flexible just-in-time tools and local recycling make local production more attractive. With local production and recycling ability in place, it will pay off to further invest in versatility of components.

The four principles were derived by using analogical reasoning to "translate" what is useful and different in the cell into something that is potentially useful in manufacturing. We remained mindful, in this reasoning, of the limits of the metaphor identified in §5. For example, we did not push analogies for mechanisms that give cells their autonomy and, while we do pose small scale as a feature of organic production systems, it does not derive from a direct analogy with the biological cell. In the proposed organic production system, small-scale manufacturing is concerned with volumes, not physical size, and it is driven by small-volume, just-in-time tools in an economic environment with significant transportation and inventory costs.

Current Partial Examples

While a fully developed organic production system does not yet exist in manufacturing, we can identify a few precursors today, one in the aluminum industry and one in the packaging industry.

Recycled aluminum is less expensive to produce than the primary material because it takes 90% less energy to process. Compared to primary aluminum, the production of recycled aluminum is more geographically distributed and smaller in scale: 50 aluminum recyclers operate in the United States alone, while only three sites refine bauxite into alumina (the raw material).

Hydro Norsk (the largest public company in Norway) developed innovative new processes enabling the production of high-quality aluminum from scrap. This allowed the company to build a network of small

aluminum (re)processing plants throughout Europe and the United States. Hydro Norsk is "closing the loop" with its customers by offering remelting as a service, converting their process scrap in local plants into high-value cast-house products. Aluminum producers are entering into long-term contracts with the aluminum users, who produce cans and other products, and their customers; scrap is returned, remelted, and then sold back to the users. The quantities of post-consumed scrap as a raw material source (e.g., for the automotive industry) are steadily increasing. Thus, an improvement in recycling technology has created a manufacturing system in which the principles of organic production are beginning to emerge. The products are made and recycled locally in relatively small-scale, inexpensive plants that are responsive to their local environments.

The second example is Regale, a Californian producer of molded-fiber packaging. These packages are made entirely from postconsumer waste paper and are best known in the form of egg cartons. Currently, molded-fiber packages are being used for packing wine bottles, ink cartridges, shoes, and several other products. Because its technology is small scale and flexible, Regale has a vision of building one packaging plant per "township."

Regale's technology contains several innovations that allow for flexibility and fast response. The molds used to press the packages are no longer made of metal. Regale uses a three-dimensional printing technology to build molds from a mixture of nylon and plastic. These new molds cost 90% less than metal molds, and the time required to design and "print" a new mold is 40 hours compared with weeks or even months for a metal mold. This rapid-tooling technology allows Regale to respond quickly to customer requests for new packaging designs. Interesting also is the ease with which Regale can adapt its product mix by replacing one or more molds in its presses. The setup times are in the order of minutes. With the largest cost component being the variable energy cost for drying, a Regale plant can also maintain high volume flexibility. Regale reckons that the optimal size for their plants is about 10,000 tons per year, requiring less than 10 million U.S. dollars investment and fewer than 10 full-time workers. Each plant could economically serve a small geographical area, hence the name township model.

In their own words: "Any increase in scale will not significantly improve operating efficiency, since increased raw material and product shipping costs offset scale economies. A typical Regale plant would source its raw material and deliver its product within about a 100-mile radius range. [...] It is important to understand that the township model for a Regale plant is not only a strong vision, but also an economic optimum." As another illustration of an organic production system, it is not difficult to imagine every reasonable-size town to have a Regale-type plant, using local waste paper as the only material input and quickly responding to the many packaging needs of local manufacturers.

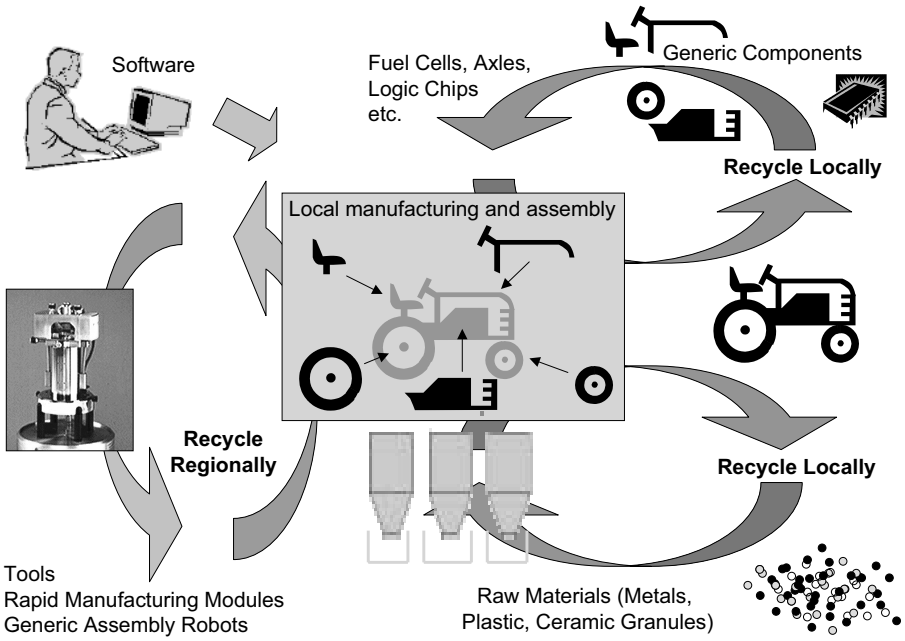
8. Discussion and Conclusion

We have compared the oldest production system on earth, that of the biological cell, with current industrial production systems. Using analogical reasoning, we have identified a set of four production principles that offer the biological cell efficiency and responsiveness and that could offer similar benefits to industrial production. The four principles are customized local production, universal components, just-in-time configurable tools, and local recycling loops. Combined, they form a system that we have labeled an organic production system, in which the individual principles reinforce and complement one another. While it is clear that current manufacturing technology cannot deliver an organic production system yet, we have pointed to the emergence of some industrial systems that move in the direction of organic production. Before we discuss where and how organic production systems might be relevant in the future, we first provide a detailed, speculative scenario of what a fully developed organic production system might look like (summarized in Figure 4).

Imagine it is the year 2020. A local farmer collaborative in Southern Arizona wants to buy 50 medium-size tractors, tailor made for the local soil conditions and mountainous terrain. The customer wants the customized tractors delivered within one week.

The local utility-vehicle dealer, Rio Grande Inc., takes the order and adapts a standard design to the local conditions. For each tractor, seven standard fuel cells are stacked together, exactly fulfilling the power requirements of the unit. The fuel cells are obtained

Figure 4 **A Local Arizona Manufacturer Fulfills a Custom Order of 50 Tractors by Relying on Locally Recycled Generic Materials and Components and on Universal Machines**



locally, on the spot market. An electric motor with the right power and torque range that will be driven by the fuel cells, along with generic cockpit displays, is bought from an electrical equipment supplier in Tucson and shipped to Rio Grande Inc. by truck. The wheels and axles, including shock absorbers and brakes, as well as the connection rods to pull a trailer, are bought locally.

For the frame, body, and cockpit, rapid manufacturing machines are rented from a special equipment-rentals company and shipped in via UPS from the Phoenix storehouse. One machine produces a tractor frame from sintered metal, which is deposited, layer by layer, with a spray nozzle, controlled by a computer that works from a CAD file of the tractor's dimensions. The second machine builds the tractor's outer shell and cockpit in a similar fashion, direct-depositing carbon plastics, layer by layer, according to a CAD file of the dimensions. Rio Grande Inc.'s engineer programs the engine control and driver electronics directly onto generic chips, with a program downloaded from a website of a Detroit software company that specializes in engine control. The engineer then parameterizes the software to fit the local operating conditions. The only thing left to do is download the assembly program into the generic assembly robots, also rented from a Phoenix rental agency. After five days, the tractors are delivered to the farmer collaborative. The two direct-deposit rapid-manufacturing machines and the assembly robots are trucked back to Phoenix.

A few years later, when the tractors are no longer needed, they will be disassembled, and all their generic components, including the fuel cells, axles, and wheels, instruments, and chips, will be sold back to the local suppliers where they were bought. The suppliers will inspect, and possibly repair them, and incorporate them into other equipment. Mechanically worn-out parts, including body and frame, are ground to metallic or carbon plastic granules and sold locally on the market of raw materials for direct-deposit production machines.

This example embodies all four principles of organic production. The tractor is custom built locally, leveraging knowledge of local conditions, with minimal inventory and transportation costs. It is made to a large degree from locally bought standard components or locally available raw materials. The manufacturing tools are delivered and configured for this application just in time and are sent back when no

longer needed. All parts are part of an efficient and local closed-loop cycle.

We are definitely not claiming that organic production systems will appear in all manufacturing industries in the foreseeable future. However, we do believe that the organic production principles may have an impact in several industries, perhaps as soon as in two generations. Most likely, these are industries that carry a wide variety of products for which the potential economies of scale are small compared to the benefits of fast response and low inventories. One can think of wearable consumer products that come in different sizes, shapes, and colors or, for example, simple spare parts for consumer appliances.

Also, any product that contains some fashion element with an otherwise simple functionality would be a candidate for organic production. Travel goods, tableware, and even small home furnishings come to mind as potential candidates. If transportation costs are a major component in the cost of a product, this will speed up a potential transformation.

A major acceleration can be expected when engineered materials become available that are versatile in color, elasticity, and texture; that come with their own rapid manufacturing technology; and that are easily recyclable. As soon as a critical mass develops around such a material, the range of products that can be manufactured based on it could expand rapidly.

For uniform mass-produced goods, the organic production system is less relevant. For such products, a large investment in small cost reductions is efficient, and thus, significant economies of scale exist. For example, diapers are uniform products (no tailoring to local needs necessary), the demand for which can be precisely planned, so mass production has advantages over local production. Here, the tendency of large-scale plants to overproduce, and thus waste resources, is the least relevant.

There are also product categories for which we still lack fundamental technological progress in basic materials and product physics. For example, manufacturers of television screens, computers, and displays have not yet settled on a common technology, so universal components cannot emerge. Another example is the move from copper to optical cables in telecommunications. The knowledge of making the basic components belongs to a small number of firms. Thus, the components cannot be widely shared and reused in local recycling loops.

While organic production is not applicable everywhere, our comparative analysis suggests that *some* form or combination of local production cycles with universal components and just-in-time tools will increase in importance in the near-to-medium term. Once set in motion, the application of the organic production principles could lead to scenarios as radical as the one described above. Understanding the organic production system and its potential scenarios will help manufacturing firms to monitor the likelihood of its appearance and to develop the strategic options needed to adapt to it if needed.

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Appendix. Some Basics of Biochemistry[30]

This appendix contains some background information on the basic functionalities and processes of a biological cell. It provides additional context for interested readers. The smallest organized form of life is the cell. It can be defined in a physicochemical sense as a reaction room separated from the environment by a barrier, which allows for selective inflows and outflows of energy, material, and information. It is an open system in a steady state that strives for thermodynamic efficiency. The cell possesses the unique property of being able to replicate itself, often arbitrarily. In order to ensure survival, the cell economizes the consumption of energy and building blocks, while ensuring a fast response to environmental changes. During evolution, the cell has acquired a high level of robustness, while constantly evolving further.

The cell is based on a number of key molecules that perform the "process of life": DNA (deoxyribonucleic acid), RNA (ribonucleic acid), proteins, lipids, and polysaccharides. These molecules are all built from a limited number of smaller building blocks. For instance, DNA is composed of four alternating nucleotide bases (forming a code) that are connected by a backbone of sugar and phosphate groups. A wide variety of proteins are combinations of 20 amino acids. Many lipids are formed from the combination of three fatty acids with glycerol.

The roles of these key molecules are as follows. A double-layered lipid membrane forms the barrier between the cell and its environment. Within this isolated room, the infor-

[30] See, for example, Voet and Voet (1994).

mation of the composition and function of a cell is stored in the DNA, organized into genes (the blueprints for proteins). DNA is transcribed into messenger RNA, which is, in turn, translated into proteins with the help of ribosomes. Ribosomes are the "cellular tool works." The proteins, finally, execute the "process of life" in the cell, taking on structural, regulatory, and catalytic functions.

For the maintenance of the "process of life," the cell employs a specialized machinery of catalytically active proteins called enzymes. Enzymes are (bio)catalysts that are able to facilitate chemical reactions, thus transforming a substrate into a product:

$$E + S \leftrightarrows [ES] \leftrightarrows [EP] \leftrightarrows E + P.$$

Enzyme (E) and substrate (S) form an enzyme substrate complex (ES), which is an unstable intermediate that reacts to become the enzyme product complex (EP). The EP-complex is unstable as well, and separates into enzyme and product (P). The enzyme facilitates the process, but it itself exits the process unchanged, and can immediately engage in further reactions. Enzymes are the workhorses that perform the "production process" of most molecules required for life. Although a biochemical reaction is quite different from the types of transformation occurring in most manufacturing processes, one can easily draw parallels between the enzymes in the cell and the machines in a manufacturing environment.

Biochemical reactions are carried out in a living organism under particularly mild conditions, e.g., 37°C, watery environment, and normal atmospheric pressure. A specific characteristic is the chemical equilibrium, a natural constant, which describes the ratio between the concentrations of the substrate(s) and the product(s) under certain conditions. In principle, a biochemical reaction is reversible, which means that the equilibrium between substrate and product can be reached from either side.

Several enzymatic reactions related to one another and organized in a sequence form a *biochemical pathway*. Pathways are governed by the following principles:

(1) Every pathway has a determining initial step. Most reactions involved in a pathway are working close to the chemical equilibrium. The cell commits an intermediate early on in a pathway to a strong exothermic (heat-producing) reaction. Under the mild conditions in the cell, this makes the direction of the reaction for the pathway irreversible (there is not enough energy to reverse the initial step). Still, most isolated enzymes are able to catalyze forward and backward reactions; a number of physiologically important reactions, such as transaminase reactions, work unlimited in both directions.

(2) Several catabolic and anabolic pathways share a number of common steps.

(3) All pathways are regulated. The first reaction in a pathway is usually the regulated step that controls the flow of carbon into the pathway.

(4) The flow through a biochemical pathway is controlled by a pull mechanism. The consumption of the product by the next step shifts the equilibrium of the first reaction towards a further conversion of substrate to product.

Within the cell, a large number of enzymatic reactions occur in parallel, forming an intricately regulated network of reactions. Once completely switched off, it can no longer be re-animated.

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