Developing Molecular Manufacturing

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Introduction

Any of several diverse pathways might be used to develop molecular manufacturing. There are many strategies, techniques, and tools that may contribute to its development. Further study will be needed to decide which approach is best. Questions to be answered for each approach include the effort required to develop it, the performance (throughput and cost) of the manufacturing system, and the performance of the products.

Three milestones can be identified for molecular manufacturing.

1**Basic molecular manufacturing**: Digital control of precise molecular assembly.

2**Exponential molecular manufacturing**: The ability to use molecular manufacturing systems to build additional usable molecular manufacturing systems, making it possible to produce large quantities of product.

3**Integrated molecular manufacturing**: The ability to combine the outputs of molecular manufacturing into large products.

The first milestone has almost been achieved already; the principle has been demonstrated in the laboratory. This level of technology may be used to make sensors, as well as a variety of research tools, and possibly to make limited but useful quantities of pharmaceuticals.

The requirements to move from the first to the second milestone can be identified and preliminary design work can be started today. The ability to build large quantities of individually constructed molecularly precise products would be extremely valuable. Potential products include computers, pharmaceuticals, medical tools, and advanced materials.

Moving from the second to the third milestone would greatly increase the range of possible products. It has been argued elsewhere that this step might not be prohibitively difficult[1]. However, the engineering details will depend on the molecular manufacturing technology being used, which could vary widely.

After exploration of the range of options for developing these capabilities, several specific areas for study are suggested. These studies, which could be initiated today, would help to quantify the potential of the technology and the effort required to develop that potential.

Basic molecular manufacturing

The individual control of molecular composition and placement is often cited as a goal of nanotechnology. To date, many nanotechnology efforts have been content to achieve

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[1]   Phoenix, C. (2003). "Design of a Primitive Nanofactory", *Journal of Evolution and Technology* 13. http://www.jetpress.org/volume13/Nanofactory.htm

nanoscale—but not atomic—precision, or to build large quantities of small identical molecules. However, there are some technologies that are on the verge of achieving the goal.

Liao and Seeman have built a nanomachine out of DNA[2] that can guide the construction of any of several different strands of DNA; the product sequence can be chosen by "programming" the machine with other DNA strands. This is a demonstration of programmable molecular fabrication. A planned extension to the machine would allow it to build longer and more interesting strands. Although this machine does not select from among multiple sites for the reaction, it does select from among multiple potential reactants, and its product has a precise and programmable molecular structure.

Aono[3] developed the ability to transport individual silicon atoms from one place to another in a covalent crystal, and was even able to automate this to make two-dimensional patterns. Several other researchers have also used electricity (fields and/or currents) with scanning probe microscopes to implement reactions at sites chosen with atomic precision. Hersam[4] has removed single selected hydrogen atoms from silicon at room temperature. Oyabu[5] has removed and replaced single silicon atoms with purely mechanical force, but has not yet reported the ability to build multi-atom patterns.

A strategy for easier atomically precise positioning is to separate the possible deposition sites. For example, a self-assembled repetitive grid could be used to create widely separated sites that might even be individually accessed optically for higher throughput. A related strategy is to deposit large molecules into large receptors that are designed not to bond if misaligned.

There are several possible ways to increase the throughput of molecular manufacturing without requiring it to build its own tools. If the manufacturing operation is done with a scanning probe microscope, then an array of MEMS microscopes like IBM's "millipede"[6] could be used. If it is done with molecular tools similar to Liao and Seeman's, many tools could be created and used in parallel.

Exponential molecular manufacturing

The productivity of individual control of molecules is limited by the small size of the molecules. A typical scanning probe microscope might weigh two kilograms, have a size of about 10 cm, and carry out ten automated operations per second. If each operation

[2] Liao S, Seeman NC. (2004). "Translation of DNA signals into polymer assembly instructions." *Science* 306(5704):2072-4

[3] See the group's website at http://www.jst.go.jp/erato/project/agsh_P/agsh_P.html

[4] R. Basu, N. P. Guisinger, M. E. Greene, and M. C. Hersam, "Room temperature nanofabrication of atomically registered heteromolecular organosilicon nanostructures using multistep feedback controlled lithography," *Appl. Phys. Lett.*, **85**, 2619 (2004). See http://www.northwestern.edu/univ-relations/media_relations/releases/2004/09/molecular.html

[5] Noriaki Oyabu, Óscar Custance, Insook Yi, Yasuhiro Sugawara, and Seizo Morita. (2003). "Mechanical vertical manipulation of selected single atoms by soft nanoindentation using a near contact atomic force microscope" Phys. Rev. Lett. 90, 176102. See http://link.aps.org/abstract/PRL/v90/e176102 and http://focus.aps.org/story/v11/st19

[6] See http://www.zurich.ibm.com/st/storage/results.html

deposits one carbon atom, which masses about 2×10^{-26} kg, then it would take 10^{26} seconds or six billion billion years for that scanning probe microscope to fabricate its own mass!

The speed with which a molecular manufacturing tool can create its own mass of product may be called "relative productivity." This depends on several factors: the mass of the tool, its frequency of operation, and the mass deposited per operation. Roughly speaking, an object's mass will be about the cube of its size; hence for each factor of ten shrinkage, the mass of the tool will decrease by 1,000. In addition, small things move faster than large things, and the relationship is roughly linear. Taken together, each factor of ten shrinkage of the tool will increase its relative productivity by about 10,000 times; relative productivity increases as the inverse fourth power of the size.

If a tool could be shrunk by a factor of a million, from 10 cm to 100 nm, then its relative throughput could increase by 10^{24}, in which case it would take only 100 seconds to fabricate its own mass. This assumes an operation speed of 10 million per second (which requires a linear speed of only 2 m/s over a 100 nm range). This is about ten times faster than the fastest known enzymes (carbonic anhydrase and superoxide dismutase). But a relative productivity of 1,000 or even 10,000 seconds would be sufficient for a very worthwhile manufacturing technology. (An inkjet printer takes about 10,000 seconds to print its weight in ink.)

The following techniques all share a goal of controlling molecular joining and/or placement in order to build intricate, engineerable, functional, nanoscale, kinematic systems that are capable of building more of the same. In general, it is not required that every covalent bond in the final product be formed under direct mechanical control, or even at the time of the deposition process. For example, useful molecular building blocks can be pre-built by bulk chemistry. Also, crosslinking can be triggered optically or chemically after the manufacturing is completed to increase strength and stiffness.

The goal of building functional manufacturing systems implies that the newly built systems must be controllable. Many types of control can be broadcast, including chemicals, photons, pressure, and electric or magnetic fields. Electric current is harder to broadcast, but systems too small to be contacted via micromanipulation could self-assemble to electrodes. Electrical control may ultimately be the fastest and most flexible approach.

Although the techniques can be conveniently divided into groups according to the working conditions and bonding structure, the divisions between the groups are not absolute. For example, a system that used liquid xenon as a solvent would fall halfway between solution-phase and machine-phase. This reinforces the point that none of these approaches is entirely distinct from the rest; there is a continuum from today's well-established techniques to the most extreme machine-phase proposals.

Polymer techniques

Ribosomes, which are made of RNA and protein, show that polymers can fold into functional shapes that carry out manufacturing operations. Polymer sequences can be controlled digitally by selecting the building blocks in the right sequence, as ribosomes

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do, or by flushing different building blocks past while controlling whether or not they stick, as DNA synthesizers do. Some polymers including DNA and RNA fold predictably, so their shapes can be engineered. Seeman's machine selects short sequences to join rather than individual monomers, but a variant that could select monomers or could be constructed out of a few short repeated sequences would be able to build a copy of itself.

Polymer chemistry is known to be quite versatile, and it should be possible to incorporate molecular actuators to select the polymer sequence; this would be faster and probably more reliable than using DNA strands to program the device. Molecular actuators can be controlled and powered by light, electricity, or changes in the composition of the solution.[7]

Bulk controlled polymerization techniques, such as DNA synthesis, often use two repeated steps: first they make the end of the polymer reactive by "deprotecting" it, then add a monomer that is protected from further deposition. Nanoscale controlled polymerization could control either the timing of the deprotection step or the monomer selection for the polymerization step. Or the system could protect the addition site by steric hindrance. Alternatively, it could use a polymerization reaction that is exothermic but has a high barrier, and accelerate the desired reaction—possibly by many orders of magnitude[8]—by holding the monomer in place. The ratio of reaction rates of confined and unconfined monomers will approximate the error rate.

Because there is only one reaction site and one choice—to add a monomer or not— extreme stiffness should not be required in polymer-based molecular manufacturing systems. Even minimally crosslinked polymers (as shown by the ribosome) can implement a controllable, low-error system.

Implementing polymer exponential molecular manufacturing systems appears to be a fairly small step from existing and currently feasible non-exponential polymer-based polymer-building systems.

Solids built in solution

Instead of building a linear chain that then folds into a shape, it may be possible to build the desired shape directly by depositing small molecular building blocks. These building blocks could either form covalent bonds during deposition, or be held by hydrogen bonds (similar to self-assembly) and perhaps joined later by crosslinking.

Making an atomically precise product does not require atomic precision in block positioning—only enough precision to select between adjacent block deposition sites. Branched molecules, possibly including dendrimers, may be of interest as building blocks.

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7   "Depending on the type of rotaxane setup, the stimuli can be chemical, electrochemical, or photochemical." C. Mavroidis, A. Dubey, and M.L. Yarmush. (2004). Annu. Rev. Biomed. Eng. 2004. 6:10.1–10.33. http://www.bionano.neu.edu/AR220-BE06-10_001-033_.pdf

8   Creighton, T. E. (1984) *Proteins*. New York: W. H. Freeman and Company. Creighton lists one intramolecular reaction with an effective concentration of 3.3×10^9. See discussion in *Nanosystems* 8.3.3a. (Drexler, 1992, *Nanosystems*, Wiley)

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This approach has not been much studied yet. It may be worth pursuing because exotic environments would not be needed, but 3D shapes and structures might be built directly rather than needing to be formed by folding. Actuator molecules could either be placed individually or added by self-assembly once the structure was built.

Any useful moving system needs to have parts moving relative to other parts. This has not been explored in systems of this class. As in MEMS, springs might be useful instead of sliding-surface bearings. A wider palette of materials might allow the spring designs to be more compact. Precise covalent structures with nanoscale width might be able to bend more sharply without fatigue or plastic deformation. Another option might be to have monolayer bearings self-assemble in spaces left during construction. The techniques used in low-friction biological molecular moving parts (e.g. ATP synthase) might be useful once they are better understood.

This approach might make use of relatively large molecular building blocks. It would probably be possible to place large blocks with a relatively crude scanning probe microscope in order to build the first manufacturing system. Silicatein, an enzyme that builds silica, may be useful (see below under "Engineered molecules"). Also, a polymer-based molecular machine system might be used if one had been developed previously.

Solids built in machine-phase

"Machine-phase" means that all reactive molecules are controlled and moved mechanically rather than diffusing randomly, and reactions take place under mechanical control. Deposition of atoms and inducing of reactions in vacuum has already been accomplished. A complete set of reactions for vacuum deposition of arbitrary shapes in a covalent solid has not yet been worked out and verified, but there are quite a few covalent solids that would be useful to build due to their excellent material properties, including diamond, silica, alumina (sapphire), and cubic boron nitride.

This approach to building nanoscale tools may be unfamiliar to chemists and molecular biologists, but may be a better fit than most nanoscale techniques for today's mechanical engineering disciplines.[9] If cleanliness can be maintained, it may be possible to take advantage of superlubricity between stiff surfaces.[10] Mechanical transport may be faster and more predictable than diffusive transport. Absence of fluids could reduce drag, increasing efficiency and improving performance through higher speeds. High density of strong covalent bonds in some materials implies superior material properties. Although it is too early to say with confidence which of these theoretical benefits will be practically useful, they are certainly attractive targets. (Some of these benefits may be available to systems built in solution and then dried.)

Investigation to date on machine-phase synthesis of covalent solids has focused on reactions that deposit just one or a few atoms per operation. This would require many

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[9]   Although the lower size limits of mechanical engineering (the point where classical approximations give way to quantum effects) are not known, preliminary analysis indicates that structures smaller than 10 nm and perhaps approaching 1 nm may be usefully analyzed classically. See *Nanosystems* Ch. 5.

[10]   See http://focus.aps.org/story/v13/st14 for survey and links to papers. See also http://www.berkeley.edu/news/media/releases/2000/07/27_nano.html for mention of near-frictionless sliding nanotubes.

operations to build a complete nanoscale manufacturing tool, and this could be difficult to achieve with macro-scale scanning probe microscopes—especially given the ultra-clean conditions needed to prevent some of the proposed highly reactive "tool tips" from being spoiled by contact with random molecules. MEMS scanning probes, or even specially-built NEMS systems (perhaps made with ion etching), could reduce this problem. An intermediate tool also might be built using one of the solution-phase methods. The smaller the tool, the faster it could work, and the less volume would have to be kept clean. Also, if actuators can be made on the same size scale as the tool tip, then more actuators may be included to make a more flexible and functional tool.

Integrated molecular manufacturing

A far-term goal of molecular manufacturing research is to build not just a large mass of products, but large integrated products. Sufficiently large products would create the possibility of manufacture for direct human use, without further expensive manufacturing steps, and the integration of familiar user interfaces. Several problems would have to be solved in order to achieve this. A preliminary high-level description of possible solutions for some of these problems for a single hypothetical technology filled an eighty-page paper[11]. This section very briefly summarizes that work.

In any system containing huge numbers of nanoscale components, some will be defective. It appears that, at least for simple hierarchical designs, the use of simple redundancy at multiple levels can result in excellent aggregate reliability. For example, if a device has less than a 3% chance of failing in a certain time period, then a group of eight devices plus one spare will have higher reliability than a single device. Multiple levels of such redundancy can make the aggregate failure rate negligible at a modest cost in extra mass.

To produce an integrated product, it helps to have the production stations fastened into a framework so that the position of each nanoscale partial product is known. The framework can also be used to deliver power and control, and separate the workspace from the feedstock and cooling channels. (Waste heat appears to be a significant but not insurmountable problem, which will presumably improve in less primitive designs.) With strong materials, the mass of the framework may be a fraction of the mass of the active components.

To produce a heterogeneous product, the manufacturing systems must be individually controlled. The instructions may be delivered through a simple hierarchical network, but probably must be processed locally. This would require nanoscale computers, which would be responsible for significant portions of the mass and power budget. (Commonly used molecular pieces could be built by special-purpose high-speed systems—mills—substantially reducing the required control inputs.)

Nanoscale subproducts must be joinable to make a large product. With the high speed implied by small size, each workstation could fabricate millions of mechanical features. This should make it possible to build mechanical fastening systems into each subproduct, facilitating the task of joining them. (In some systems, chemical reactions may be used

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[11] "Design of a Primitive Nanofactory", *ibid.*

for joining subproducts.)

The reference technology was diamond deposition and diamondoid materials. The nanoscale fabricator was adapted from Merkle's work, which itself was intentionally primitive and simple[12]. The mechanical positioning/reaction system was assumed to be actuated by ratchets, requiring many control inputs for each motion. Despite the handicaps imposed by primitive design, it was calculated that the proposed nanofactory might be able to build another nanofactory—even a version twice as big—in less than a day.

Enabling technologies

Several existing and projected technologies may be useful for development of the various approaches and stages of molecular manufacturing. The following is only a partial list. The technologies listed are useful for imaging, fabrication of nanoscale shapes and tools, and basic research into relevant nanoscale phenomena. Because many technologies can perform more than one function, they are not grouped into categories.

Computers

Computers have become quite powerful and will continue to improve. Computational chemistry is becoming increasingly trusted. Estimates can be determined of physical properties of molecular structures. Eventually, multilevel integrated simulations might be useful in planning and evaluating larger systems.

Computers can also be useful for some design processes. For example, recent work on protein folding to a desired shape used a repeated simulate-and-modify process to arrive at appropriate sequences. Appropriate DNA sequences for optimum folding to a desired shape also have been generated by computer. As more extensive mechanosynthetic capabilities are developed, the ability to automate them will become crucial to carrying out repeated operations without excess labor.

Scanning probe microscopes

Scanning probe microscopes (SPMs) can image areas with atomic resolution, and also manipulate molecules and do chemistry. Most SPMs have only a single probe with three degrees of freedom, but Xidex Corp. is developing two-probe, six-degree-of-freedom systems that will be able to touch the tips together[13]. This may be useful for research into mechanosynthetic reactions: A tip with an active molecule could be brought together with another tip acting as a receptive surface, at various repeatable angles and offsets, to test the effects of displacement and angle on the reaction. SPMs can work in air, water, or vacuum, at room temperature or cryogenic temperature. A deposition system that can create 15-nm lines of molecules has been developed, called dip-pen nanolithography (DPN).

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[12] Merkle, R. (1999). "Casing an assembler." *Nanotechnology* 10 (1999) 315-322. See
      http://www.foresight.org/Conferences/MNT6/Papers/Merkle/
[13] http://www.xidex.com/Xidex%20Caliper%20CD%20AFM%20SPIE%202002.pdf

Electron microscopes

Electron microscopes can image with near-atomic resolution. They can be used to cut carbon nanotubes, even to trim outer tubes from multiwalled tubes[14]. They can also deposit a variety of materials from gas feedstock (electron beam induced deposition, EBID). These deposits have a feature size as small as 10 nm and can form three-dimensional structures.[15]

Sub-wavelength imaging

FRET (fluorescence resonance energy transfer, which is very sensitive to nanoscale distance) can be used to determine relative positions[16]. NanoSight has developed an imaging system that can be placed in an existing optical microscope and image 20 nm particles[17]. AngstroVision has claimed to be developing 3D nm-scale imaging using visible light.[18] A paper at NASATech claims that imaging below the diffraction limit should be possible with incoherent light.[19]

Ion etching

Ion etching systems can achieve single-atom accuracy and can use tiltable workpieces.[20] This may enable production of freestanding (undercut) kinematic structures from high-performance materials that might be useful for research into nanoscale machinery or even as nanoscale molecular manufacturing systems.

Engineered molecules and molecular composites

DNA structures have been used to position carbon nanotubes to make a working transistor. Protein folding prediction is still problematic, but the inverse problem—design of sequences that will fold into a desired shape—is becoming reliable.[21]

Silica can be deposited from water; this deposition can be mediated in shirtsleeve conditions by the enzyme silicatein.[22] A silicatein molecule attached to a positioning system might be useful in building silica structures to specified shapes.

Levins and Schafmeister have developed a new polymer that uses two bonds between each monomer for significantly increased stiffness and well-defined shape even without folding[23]. This may make it easier to design and build desired molecular shapes.

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[14] http://www.berkeley.edu/news/media/releases/2000/07/27_nano.html
[15] http://www.nims.go.jp/hvems/nano_char/facilities/facility6/NanofabSEM_e.html
[16] http://www.iscid.org/encyclopedia/Fluorescense_Resonance_Energy_Transfer
[17] http://www.nanosight.ukideas.com/
[18] http://www.parc.com/cms/get_article.php?id=223
[19] "Parallel-Beam Interferometry With Incoherent Light"
http://www.nasatech.com/Briefs/Sept00/NPO20687.html
[20] Personal communication, Sakhrat Khizroev, December 2004
[21] See http://www.biochem.duke.edu/Hellinga/hellinga.html#Recent%20Publications for some examples.
[22] Shimizu, K., Cha, J., Stucky, G. D., Morse, D. E. (1998). "Silicatein ?: Cathepsin L-like protein in sponge biosilica" *Proc Natl Acad Sci U S A.* May 26; 95(11): 6234–6238. See http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=27641
[23] Levins, C. G., Schafmeister, C. E. "The Synthesis of Functionalized Nanoscale Molecular Rods of Defined Length" *Journal of the American Chemical Society*, **125**, (2003), 4703-4704. See

Schafmeister states[24] that conventional amino acids can be incorporated into the polymer chain; this increases chemical flexibility at the expense of local stiffness.

A vast number of other molecules may be suitable for forming nanoscale engineered structures.

Recommendations for study

The essence of molecular manufacturing is very simple: the formation of precise molecular structures under direct mechanical guidance. Artificial examples of this are close to being demonstrated, and a set of fairly short steps may lead from there to the achievement of a useful manufacturing technology.

The mechanical component of molecular manufacturing does not require a classical mechanical engineering approach, but such an approach seems to be a good fit for the method—especially since the creation of designed molecules will make it relatively easy to specify their shape. Nanoscale structures are often assumed to be inherently floppy and unstable, but this will be less true for strongly crosslinked polymers or covalent solids than for weakly crosslinked biological molecules. It is worth investigating how small a mechanical structure implemented in various materials can be made before thermal noise or quantum effects spoil its applicability as a mechanical design element. A related question, which has not yet been studied[25], is how to design nanoscale mechanical elements to be reliable machines in the face of thermal noise and surface forces, and how small such designs can be made. A major and underappreciated potential advantage of molecular manufacturing products over MEMS is that the use of atomically precise surfaces may eliminate wear and greatly reduce friction.

There are many possible approaches to molecular manufacturing: many materials in at least four basic processes (polymer, covalent in solvent, noncovalent in solvent, covalent in machine-phase). Most of the possibilities have received little study. A study of the merits and potentials of a range of approaches and materials would be very useful. Once the potential capabilities and products were better understood, a more detailed roadmap to their development could be produced.

Although low friction and low wear have been demonstrated in a few cases, the mechanisms of nanoscale friction are not well understood.[26] The study of low-friction sliding interfaces would help in determining the performance limits of nanoscale machinery. The study should include wet as well as superclean interfaces, and stiff materials and surfaces as well as biological-style non-stiff, wetted, or bushy surfaces.

Nanoscale and molecular actuators are being studied, but many of these studies are not

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http://www.foresight.org/Conferences/AdvNano2004/Abstracts/Schafmeister/
[24] personal communication, 10/24/04
[25] A few studies have been made of individual machines, such as a planetary gear; there is room for guarded optimism.
[26] M Dienwiebel et al. 2004 Superlubricity of graphite Phys. Rev. Lett. 92 126101. Also various work by Zettl with rotating and sliding nested carbon nanotubes. "Friction at the nano-scale" is a recent Physics World article by a nano-tribologist explaining how much is still unknown. http://physicsweb.org/articles/world/18/2/9/1

directed at large-scale integration of the actuators into nanoscale machines. The complex construction promised by even basic molecular manufacturing indicates that multi-actuator systems soon may be desirable. It would be useful to do studies emphasizing actuators that can be integrated with a variety of structures and that can be controlled via rapid, small, and independent channels.

The binding and positioning of molecules will be a key competency for molecular manufacturing. Antibodies seemingly can be developed to bind almost anything. Binding pockets for individual molecules have been made by taking "molds" of the molecules in plastic. It would be useful to further explore how to bind and transport molecules, especially how to design binding sites based mainly on steric properties (shape) that will be flexibly engineerable in molecular manufacturing approaches.

Reliability will be an important factor in the ability to make complicated automated manufacturing systems. The mechanosynthetic operations have not yet been selected, but it may be possible to estimate upper and lower bounds on classes of operation, or at least begin to understand what factors affect reliability. Preliminary arguments indicate that reliabilities between 10^9 and 10^{15} may be achievable.[27] If and when massively parallel systems are built, fault tolerance will be required. More detailed study of fault tolerant systems would help.

As results from the above studies become available, it will be possible to form preliminary estimates of the manufacturing throughput and product capabilities of a particular molecular manufacturing technology. It would be useful to start such studies today, for two reasons. First, preliminary answers to many of the above questions are already available for at least one technology. Second, attempts to quantify performance will show what other questions need to be studied.

Any estimate of the time and resources that would be required to develop any particular approach to any given level will necessarily be preliminary. However, it seems important to develop such estimates as soon as possible. Exponential molecular manufacturing may significantly impact the semiconductor and pharmaceutical industries, among others; and integrated molecular manufacturing may even be competitive as a general-purpose manufacturing technology. This implies that development of molecular manufacturing may have a very high payoff. The basic ideas have been in the literature for over two decades[28] and a quantitative analysis of the extremely high potential performance of one approach was published in 1992.[29] The continuing development of enabling technologies, as well as the rapidly advancing theory of molecular manufacturing, increase the possibility that an all-out Manhattan Project-like effort will be launched by some government or large corporation.[30] The likelihood of this cannot be estimated without an

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[27] See *Nanosystems* chapter 6. Note that high reliability is possible even in simple non-machine-phase systems; a solution-phase system that simply increases effective concentration by many orders of magnitude at chosen reaction sites may have a comparably low rate of unwanted reactions if reaction energy barriers are well-chosen.

[28] Drexler, K. E. (1981). "Molecular engineering: An approach to the development of general capabilities for molecular manipulation." *Proc. Natl. Acad. Sci. USA* Vol. 78, No. 9, pp. 5275-5278.

[29] Drexler, K. E. (1992) *Nanosystems*, Wiley Interscience, New York.

[30] IBM's effort to build the System 360 cost $5 billion and required developing and integrating a number of

improved understanding of what will be required to develop a given capability.

Conclusion

Molecular manufacturing relies on two counterintuitive ideas: first, that mechanical operations can reliably be carried out at the nanoscale; second, that handling of individual molecules can be scaled up to produce useful quantities of product. On closer examination, these ideas appear to be supportable; this indicates that molecular manufacturing may have been underappreciated and may deserve more focused attention.

The development of molecular manufacturing can be an incremental process from today's capabilities. Although the most exciting results rely on the most advanced and integrated capabilities, even the earliest products of basic molecular manufacturing could be useful for basic research and for components such as sensors.

There are several specific areas of study that can advance our understanding of the potential of the approach. These studies can and should be initiated today.

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innovations.