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POINT ↔ COUNTERPOINT

# NANOTECHNOLOGY

Drexler and Smalley make the case for and against 'molecular assemblers'

RUDY BAUM

## DREXLER OPEN LETTER

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Prof. Smalley:

I have written this open letter to correct your public misrepresentation of my work.

**Drexler** PHOTO BY LINDA CICERO

As you know, I introduced the term "nanotechnology" in the mid-1980s to describe advanced capabilities based on molecular assemblers: proposed devices able to guide chemical reactions by positioning reactive molecules with atomic precision. Since "nanotechnology" is now used to label diverse current activities, I have attempted to minimize confusion by relabeling the longer term goal "molecular manufacturing." The consequences of molecular manufacturing are widely understood to be enormous, posing opportunities and dangers of first-rank importance to the long-term security of the U.S. and the world. Theoretical studies of its implementation and capabilities are therefore of more than academic interest and are akin to pre-*Sputnik* studies of spaceflight or to pre-Manhattan Project calculations regarding nuclear chain reactions.

You have attempted to dismiss my work in this field by misrepresenting it. From what I hear of a press conference at the recent National Nanotechnology Initiative (NNI) conference, you continue to do so. In particular, you have described molecular assemblers as having multiple "fingers" that manipulate individual atoms and suffer from so-called fat finger and sticky finger problems, and you have dismissed their feasibility on this basis. I find this puzzling because, like enzymes and ribosomes, proposed assemblers neither have nor need these "Smalley fingers." The task of positioning reactive molecules simply doesn't require them.

I have a 20 year history of technical publications in this area and consistently describe systems quite unlike the straw man you attack [*Annu. Rev. Biophys. Biomol. Struct.*, **23**, 337 (1994); *Phil. Trans. R. Soc. London A*, **353**, 323 (1995)]. My proposal is, and always has been [*Proc. Natl. Acad. Sci. USA*, **78**, 5275 (1981)] to guide the chemical synthesis of complex structures by mechanically positioning reactive molecules, not by manipulating individual atoms. This proposal has been defended successfully again and again, in journal articles, in my MIT doctoral thesis [the basis of "Nanosystems: Molecular Machinery, Manufacturing, and Computation," John Wiley & Sons (1992)]. And before scientific audiences around the world. It rests on well-established physical principles.

The impossibility of Smalley fingers has raised no concern in the research community because these fingers solve no problems and thus appear in no proposals. Your reliance on this straw-man attack might lead a thoughtful observer to suspect that no one has identified a valid criticism of my work. For this I should, perhaps, thank you.

You apparently fear that my warnings of long-term dangers will hinder funding of current research, stating: "We should not let this fuzzy-minded nightmare dream scare us away from nanotechnology. ... NNI should go forward." However, I have from the beginning argued that the potential for abuse of advanced nanotechnologies makes vigorous research by the U.S. and its allies imperative. Many have found these arguments persuasive. In an open discussion, I believe they will prevail. In contrast, your attempt to calm the public through false claims of impossibility will inevitably fail, placing your colleagues at risk of a destructive backlash.

Your misdirected arguments have needlessly confused public discussion of genuine long-term security concerns. If you value the accuracy of information used in decisions of importance to national and global security, I urge you to seek some way to help set the record straight. Endorsing calls for an independent scientific review of molecular manufacturing concepts would be constructive.

A scientist whose research I respect has observed that "when a scientist says something is possible, they're probably underestimating how long it will take. But if they say it's impossible, they're probably wrong." The scientist quoted is, of course, Richard Smalley.

K. Eric Drexler
Chairman, Foresight Institute

## SMALLEY RESPONDS

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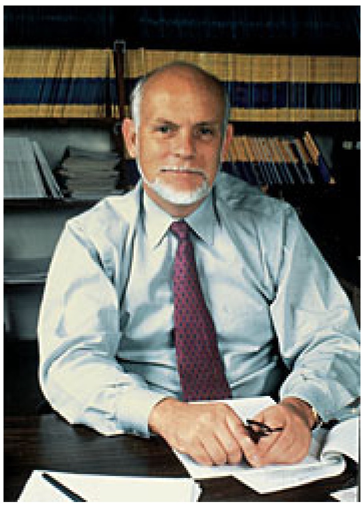
Dear Eric,

I apologize if I have offended or misrepresented you in my 2001 article in *Scientific American*. That was not my intention. I was fascinated by your book "Engines of Creation" when I first read it in 1991. Reading it was the trigger event that started my own journey in nanotechnology, and I believe the Foresight Institute you founded with Christine Peterson has made, and continues to make, very positive contributions to the advancement of technology on the nanometer scale. You have my respect and thanks.



**Smalley** PHOTO BY RUDY BAUM

I am gratified that you appear to agree that the precision picking and placing of individual atoms through the use of "Smalley fingers" is an impossibility. If in fact you do agree with this statement, that is progress. In the infinity of all conceivable ideas for self-assemblers, we agree that at least this computer-controlled "Smalley finger" type of assembler tool will never work.

I hope you will further agree that the same argument I used to show the infeasibility of tiny fingers placing one atom at a time applies also to placing larger, more complex building blocks. Since each incoming "reactive molecule" building block has multiple atoms to control during the reaction, even more fingers will be needed to make sure they do not go astray. Computer-controlled fingers will be too fat and too sticky to permit the requisite control. Fingers just can't do chemistry with the necessary finesse. Do you agree?

So if the assembler doesn't use fingers, what does it use? In your letter you write that the assembler will use something "like enzymes and ribosomes." Fine, then I agree that at least now it can do precise chemistry.

But where does the enzyme or ribosome entity come from in your vision of a self-replicating nanobot? Is there a living cell somewhere inside the nanobot that churns these out? There then must be liquid water present somewhere inside, and all the nutrients necessary for life. And now that we're thinking about it, how is it that the nanobot picks just the enzyme molecule it needs out of this cell, and how does it know just how to hold it and make sure it joins with the local region where the assembly is being done, in just the right fashion? How does the nanobot know when the enzyme is damaged and needs to be replaced? How does the nanobot do error detection and error correction?

And what kind of chemistry can it do? Enzymes and ribosomes can only work in water, and therefore cannot build anything that is chemically unstable in water. Biology is wonderous in the vast diversity of what it can build, but it can't make a crystal of silicon, or steel, or copper, or aluminum, or titanium, or virtually any of the key materials on which modern technology is built. Without such materials, how is this self-replicating nanobot ever going to make a radio, or a laser, or an ultrafast memory, or virtually any other key component of modern technological society that isn't made of rock, wood, flesh, and bone?

I can only guess that you imagine it is possible to make a molecular entity that has the superb, selective chemical-construction ability of an enzyme without the necessity of liquid water. If so, it would be helpful to all of us who take the nanobot assembler idea of "Engines of Creation" seriously if you would tell us more about this nonaqueous enzymelike chemistry. What liquid medium will you use? How are you going to replace the loss of the hydrophobic/hydrophilic, ion-solvating, hydrogen-bonding genius of water in orchestrating precise three-dimensional structures and membranes? Or do you really think it is possible to do enzymelike chemistry of arbitrary complexity with only dry surfaces and a vacuum?

The central problem I see with the nanobot self-assembler then is primarily chemistry. If the nanobot is restricted to be a water-based life-form, since this is the only way its molecular assembly tools will work, then there is a long list of vulnerabilities and limitations to what it can do. If it is a non-water-based life-form, then there is a vast area of chemistry that has eluded us for centuries.

Please tell us about this new chemistry.

With best wishes,

Rick Smalley

## DREXLER COUNTERS

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Dear Prof. Smalley,

I'm glad you found my early work stimulating, and applaud your goal of debunking nonsense in nanotechnology. I hope that our exchange will result in broader discussion within the community, and in better understanding of molecular manufacturing as a strategic objective.

In light of the nature of your questions and of misperceptions frequently articulated in the press, I should first sketch the fundamental concepts of molecular manufacturing. These spring from Richard Feynman's famous 1959 talk, "There's Plenty of Room at the Bottom," which envisioned using productive machinery--factories--to build smaller factories, leading ultimately to nanomachines building atomically precise products.

Although inspired by biology (where nanomachines regularly build more nanomachines despite quantum uncertainty and thermal motion), Feynman's vision of nanotechnology is fundamentally mechanical, not biological. Molecular manufacturing concepts follow this lead.

Hence, to visualize how a nanofactory system works, it helps to consider a conventional factory system. The technical questions you raise reach beyond chemistry to systems engineering. Problems of control, transport, error rates, and component failure have answers involving computers, conveyors, noise margins, and failure-tolerant redundancy. These issues are explored in technical depth in my book "Nanosystems: Molecular Machinery, Manufacturing, and Computation" (Wiley/Interscience, 1992), which describes the physical basis for desktop-scale nanofactories able to build atomically precise macroscopic products, including more nanofactories.

These nanofactories contain no enzymes, no living cells, no swarms of roaming, replicating nanobots. Instead, they use computers for digitally precise control, conveyors for parts transport, and positioning devices of assorted sizes to assemble small parts into larger parts, building macroscopic products. The smallest devices position molecular parts to assemble structures through mechanosynthesis--'machine-phase' chemistry.

Machine- and solution-phase chemistry share fundamental physical principles, yet differ greatly. In machine-phase chemistry, conveyors and positioners (not solvents and thermal motion) bring reactants together. The resulting positional control (not positional differences in reactivity) enables reliable site-specific reactions. Bound groups adjacent to reactive groups can provide tailored environments that reproduce familiar effects of solvation and catalysis. Positional control itself enables a strong catalytic effect: It can align reactants for repeated collisions in optimal geometries at vibrational (greater than terahertz) frequencies.

Further, positional control naturally avoids most side reactions by preventing unwanted encounters between potential reactants. Transition-state theory indicates that, for suitably chosen reactants, positional control will enable synthetic steps at megahertz frequencies with the reliability of digital switching operations in a computer. The supporting analysis for this conclusion appears in "Nanosystems" and has withstood a decade of scientific scrutiny.

It should be clear that chemical reactions (whether machine-phase or conventional) need no impossible fingers to control the motion of individual atoms within reactants. As molecules come together and react, their atoms (being "sticky") stay bonded to neighbors, and thus need no separate fingers to hold them. If particular conditions will yield the wrong product, one must either choose different conditions (different positions, reactants, adjacent groups) or choose another synthetic target. Direct positional control of reactants is both achievable and revolutionary; talk of additional, impossible control has been a distraction.

What can be made using mechanosynthesis? Organic and organometallic reactions in solution-phase and chemical vapor deposition systems can, in the hands of skilled chemists, produce a vast diversity of structures. These include all the products of organic synthesis, as well as metals, semiconductors, diamond, and nanotubes. Augmenting such chemistries with positional control of reactants will enable the fabrication of macroscale products containing chemically diverse structures in complex, precise, functional arrangements. Nanofactories based on mechanosynthesis thus will be powerful enablers for a wide range of other nanotechnologies.

Synthetic reactions and molecular machinery of the sort required for nanofactories have parallels in known systems, and have been explored using computational chemistry by Georgia Institute of Technology professor Ralph Merkle and others. The physical realization of nanofactories, however, will require a multistage systems engineering effort. In 1959, Feynman suggested scaling down macroscopic machines. In 2003, the flourishing of nanotechnologies suggests a bottom-up strategy: using self-assembly (and perhaps scanning probes) to build solution-phase molecular machines, using these to gain limited positional control of synthesis, and then leveraging this ability to build systems enabling greater control. Thus, multiple areas of current research (in computational chemistry, organic synthesis, protein engineering, supramolecular chemistry, and scanning-probe manipulation of atoms and molecules) constitute progress toward molecular manufacturing.

However, because it is a systems engineering goal, molecular manufacturing cannot be achieved by a collection of uncoordinated science projects. Like any major engineering goal, it will require the design and analysis of desired systems, and a coordinated effort to develop parts that work together as an integrated whole.

Why does this goal matter? Elementary physical principles indicate that molecular manufacturing will be enormously productive. Scaling down moving parts by a factor of a million multiplies their frequency of operation--and in a factory, their productivity per unit mass--by the same factor. Building with atomic precision will dramatically extend the range of potential products and decrease environmental impact as well. The resulting abilities will be so powerful that, in a competitive world, failure to develop molecular manufacturing would be equivalent to unilateral disarmament.

U.S. progress in molecular manufacturing has been impeded by the dangerous illusion that it is infeasible. I hope you will agree that the actual physical principles of molecular manufacturing are sound and quite unlike the various notions, many widespread in the press, that you have correctly rejected. I invite you to join me and others in the call to augment today's nanoscale research with a systems engineering effort aimed at achieving the grand vision articulated by Richard Feynman. In this effort, an independent scientific review of molecular manufacturing concepts will be a necessary and long-overdue first step.

Best wishes,

K. Eric Drexler

## SMALLEY CONCLUDES

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Dear Eric,

I see you have now walked out of the room where I had led you to talk about real chemistry, and you are now back in your mechanical world. I am sorry we have ended up like this. For a moment I thought we were making progress.

You still do not appear to understand the impact of my short piece in *Scientific American*. Much like you can't make a boy and a girl fall in love with each other simply by pushing them together, you cannot make precise chemistry occur as desired between two molecular objects with simple mechanical motion along a few degrees of freedom in the assembler-fixed frame of reference. Chemistry, like love, is more subtle than that. You need to guide the reactants down a particular reaction coordinate, and this coordinate treads through a many-dimensional hyperspace.

I agree you will get a reaction when a robot arm pushes the molecules together, but most of the time it won't be the reaction you want. You argue that "if particular conditions will yield the wrong product, one must either choose different conditions (different positions, reactants, adjacent groups) or choose another synthetic target." But in all of your writings, I have never seen a convincing argument that this list of conditions and synthetic targets that will actually work reliably with mechanosynthesis can be anything but a very, very short list.

Chemistry of the complexity, richness, and precision needed to come anywhere close to making a molecular assembler--let alone a self-replicating assembler--cannot be done simply by mushing two molecular objects together. You need more control. There are too many atoms involved to handle in such a clumsy way. To control these atoms you need some sort of molecular chaperone that can also serve as a catalyst. You need a fairly large group of other atoms arranged in a complex, articulated, three-dimensional way to activate the substrate and bring in the reactant, and massage the two until they react in just the desired way. You need something very much like an enzyme.

In your open letter to me you wrote, "Like enzymes and ribosomes, proposed assemblers neither have nor need these 'Smalley fingers.'" I thought for a while that you really did get it, and you realized that on the end of your robotic assembler arm you need an enzymelike tool. That is why I led you in my reply into a room to talk about real chemistry with real enzymes, trying to get you to realize the limitations of this approach. Any such system will need a liquid medium. For the enzymes we know about, that liquid will have to be water, and the types of things that can be synthesized with water around cannot be much broader than the meat and bone of biology.

But, no, you don't get it. You are still in a pretend world where atoms go where you want because your computer program directs them to go there. You assume there is a way a robotic manipulator arm can do that in a vacuum, and somehow we will work out a way to have this whole thing actually be able to make another copy of itself. I have given you reasons why such an assembler cannot be built, and will not operate, using the principles you suggest. I consider that your failure to provide a working strategy indicates that you implicitly concur--even as you explicitly deny--that the idea cannot work.

A few weeks ago I gave a talk on nanotechnology and energy titled "Be a Scientist, Save the World" to about 700 middle and high school students in the Spring Branch ISD, a large public school system here in the Houston area. Leading up to my visit, the students were asked to write an essay on "Why I Am a Nanogeek." Hundreds responded, and I had the privilege of reading the top 30 essays, picking my favorite five. Of the essays I read, nearly half assumed that self-replicating nanobots were possible, and most were deeply worried about what would happen in their future as these nanobots spread around the world. I did what I could to allay their fears, but there is no question that many of these youngsters have been told a bedtime story that is deeply troubling.

You and people around you have scared our children. I don't expect you to stop, but I hope others in the chemical community will join with me in turning on the light, and showing our children that, while our future in the real world will be challenging and there are real risks, there will be no such monster as the self-replicating mechanical nanobot of your dreams.

Sincerely,

Rick Smalley