Molecular Nanotechnology – the best tech on offer if only we could find the assembly manual

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Abstract

I here solve one of the most significant problems in the technological development of humanity: how to make the transition to full control of the molecular structures of materials, in particular crystalline carbon and silicon. I ask if technological progress has an end state, and argue that this can only be the attainment of the ability to make any viable material. I give a very brief account of the characterization of this ability as molecular nanotechnology (MNT) and mention one particular debate which illustrated both the fundamental difference between conventional technology and MNT and a potential barrier to the development of MNT if we adhere to conventional approaches. **I then describe a non-conventional approach that solves this problem: the directed evolution of nanomineral isomers. The six stages of this are described: crystal growth, antibody conglomeration, antibody separation, antibody/nanomineral separation, nanomineral characterization and selection, and repetition.** I then discuss the near and longer term applications of MNT (in particular nanomineral catalysis), the augmentation of nanominerals with functional groups, some aspects of the design of nanomineral components, and the implications for robotics. In conclusion I argue that the development of MNT is essential if we are to fulfil our potential as a species, and that we needlessly limit ourselves if we do not do that.

Introduction – an overview of technology

Technology, perhaps the defining feature of humanity, has long shaped how we live our lives. We name historical ages after the dominant material of the time: the stone, bronze, and iron ages (the age we currently live in could be called the carbon/silicon age). Our technology evolved for millennia, but the process sped up in the seventeenth century due, in part, to the emergence of modern science. Our tools had allowed us to study natural and artificial phenomena more carefully, which led to theories explaining how the physical world works, which often inspired and enabled the development of even better technology. An obvious question is – how will this process end? Is there an ultimate technological capability which, if acquired, would enable us to do anything that is physically and economically possible? Currently, the capabilities of our non-molecular technologies are determined by the skill with

which we can shape and blend matter. The capabilities of our molecular technologies (chemistry and biochemistry) are determined by how effectively we, or the micro-organisms we control, can synthesize organic molecules.

But these latter disciplines leave an enormous range of potential molecular technologies unexplored and undeveloped – those are technologies that could exist if we had control over the molecular structure of hard materials (minerals, crystalline solids etc). This is the realm of inorganic chemistry and materials science. Each mineral crystal is defined by its 'unit cell' – an irreducible arrangement of atoms conceptually similar to a chemical compound (these could be called *mineral isomers*). When geological conditions are right a lattice of these can form which results in the crystal itself. (This can be contrasted with metals and alloys where a species is defined by its constituents, but the actual composition and arrangement of atoms in a given volume is only known probabilistically.) We can emulate geological processes in the laboratory with the right equipment, but beyond what that allows us to do we cannot synthesize chemically arbitrary mineral unit cells. This matters because we know that mechanical engineering, in the broadest sense of the term, is best done with hard materials. **A truly vast range of materials and molecular devices are therefore unobtainable to us.** Speaking figuratively, half of the technological possibilities that molecular science promises (i.e. those based on minerals not organic chemicals) are simply unavailable.

Molecular Nanotechnology – what technology could become

Molecular nanotechnology is the recognition of this fact, the study of those technological possibilities, and the development of the capability to synthesize chemically tailored minerals. MNT was inspired to a certain extent by the emergence of biochemistry in the first half of the twentieth century and the realization that certain classes of macromolecule within the cell *are* actually molecular machines. The most famous exposition of this realization was Richard Feynman's speech There's Plenty of Room at the Bottom in 1959[1]; however, many people seem to have independently concluded that the general idea of molecular machines may also be applicable outside the realm of biochemistry. Computer simulations have since confirmed that this is the case, the mineral most often simulated being diamond, but other minerals may make more convenient candidates to start with. Since minerals are, in some ways, similar to metals many of the techniques of mechanical engineering could be used with nanominerals – that is, molecular-scale mineral components could be combined to form devices and machines (thus completing the trend of miniturization that has, among other things, massively

increased computing power since the 1950s). Since such molecular devices could interact with other molecules with atomic precision, and since an understanding of their structure would depend on chemistry and quantum mechanics, this development would signify the unification of molecular science and engineering (which is even today largely explained by classical physics). Molecular nanotechnology *is* the ultimate technological capability, because if acquired it could be used to develop any other viable technology. But how could such a breakthrough occur? Could it happen incrementally? Or are there any practical or conceptual barriers that would need to be overcome?

There may well be one conceptual barrier to overcome, which dates back to the early 2000s, and concerns how we envisage MNT and to what extent normal macroscopic engineering can inform us about how MNT would work. The best engineering tool we have ever possessed is our own hands, and it would be nice to be able to manipulate atoms and molecules freely and bond them together exactly as we wished (as if playing with building blocks). But it is not that simple. Everything at the molecular level is structured to the same (atomic) level of detail. Therefore for any given molecular structure there is one and only one spatially complementary structure that can hold a given part of it perfectly and thus manipulate it with perfect control (enzymes are a good example of this – each is tailored to a particular reaction). MNT researchers could not therefore make one 'molecular assembler' that could make anything else, because that would entail the manipulator changing *its own* structure. This point was made by the chemist Richard Smalley in a debate with the main advocate of MNT, Eric Drexler, from 2001-03.

There is however a very simple answer to this critique – multitasking. A common design solution within engineering is to have a set of tools each attached to the same type of grip. One machine can then pick up and use all of the tools with one gripping mechanism. This remedy is found in machine tool multitaskers, multi-bit screwdriver sets, and ribosomes – although ribosomes do not 'pick up' tRNA molecules, they select them from solution using complementary hydrogen bond patterns, and the workpiece (i.e. the protein) folds into shape by itself so the ribosome does not have to move around it. Molecular multitaskers will certainly play a large role in the final form of MNT but it is difficult to see how that possibility can help to create MNT in the first place, since the simplest way to make one would be with the help of another molecular multitasker! (This 'chicken or egg' dilemma could be seen as Smalley's underlying critique.[2]) It is also worth noting that anything that can be made with a multitasker (either macroscopic or molecular) can also be made with single purpose methods (currently most manufacturing methods *are* single purpose). However, to state the obvious,

we do not have molecular scale nanomineral production lines either, so the problem remains. To solve it we need to stop thinking about final forms and instead think about what incremental steps we can take to eventually attain them.

Directed evolution – a remedy for the intractable

An obvious parallel to this exists in nature where species evolve through small incremental changes in their anatomy and physiology. A nanomineral species can be imagined as a single atom onto which other atoms have been added in the right order and location so that a novel nanomineral isomer has been formed, indeed this is how we would construct a model of such a mineral cell in a computer simulation. (Note that the word 'isomer' is used to emphasize the fact that different nanomineral species could have the same chemical composition but different structures.) In the simulation *we* are causing the changes that we want, but in the physical world we cannot do this by fiat, so our only option is to emulate biological evolution and mutate a growing mineral crystal while repeatedly selecting those species that are intermediaries on a synthetic path to the *desired* nanomineral isomer. (The selection would be done using a technique called *affinity chromatography* which employs antibody proteins to latch on to specific molecular shapes.) Artificial selection, like its natural counterpart, works cumulatively (but is thankfully quicker) – exactly the sort of strategy we need to overcome the daunting challenges of creating MNT. And this particular strategy would also be useful in the long term – any future molecular multitasker would not be able to make every conceivable nanomineral, so a completely general purpose (albeit inefficient) evolutionary method will be needed to fill in the gaps of our multitasking abilities. Here is how the method would work in more detail:

1. **Crystal growth:** A sample of identical seed crystals would be exposed to growth conditions for a short period – these would typically be a high temperature, a high pressure, or perhaps laser radiation. (The short duration of the growth period would ensure that crystal variants are limited in size.)
2. **Antibody conglomeration:** The mixture would be exposed to a range of antibodies as in normal affinity chromatography. Particular antibody species would, by their nature, selectively bond to particular crystal variants. This obviates the need to simulate how a given antibody bonds with a given crystal variant.

3. **Antibody separation:** The antibody/crystal complexes would be separated according to differences in *their* mass or charge e.g. using conventional chromatography. This obviates the problem of how to separate crystal variants with different structures but the same mass and charge i.e. different isomers (and would be more effective than alternatives like high performance liquid chromatography).
4. **Antibody/nanomineral separation:** Each antibody sample would be separated from its crystal variant using conventional chemical methods. To work properly each antibody species would have to bond with only one nanomineral isomer and vice versa, but if this did not happen, different antibody combinations could be tried until that *was* the case.
5. **Nanomineral characterization and selection:** Each crystal variant would be analyzed using X-ray diffraction or micro-electron diffraction.[3] Apparently the latter would not only identify the variant but would also tell us if there were any impurities i.e. it would tell us if a given antibody is absolutely selective. We would then select the isomer which was the best intermediary nanomineral for obtaining the desired product.
6. **Repetition:** The chosen variant would then be put through the procedure again to obtain the next desired variant, a mutation of the first, starting at step one. (Note that we would soon know exactly which antibody species to use for each iteration in order to extract the desired variant.) This process could be repeated as many times as necessary to obtain almost any structure.

Note that the choice of mineral to use is not specified. The ideal material for MNT is diamond but this is also the hardest mineral, and it is therefore difficult to synthesize, so it might be best to start with another one – there is a range of inorganic solids to choose from that can also bond with carbon, which would be important for augmenting the isomers with functional groups. (We would have to avoid pure metals and alloys simply because they suffer from ware, and for a molecular scale device the ware of even one atom could cause failure.) The most important criterion is that the mineral can be used to build molecular machines – those machines would themselves provide a more direct method for making mineral components. This sort of thinking, similar to retrosynthetic analysis in organic chemistry, is what we will require to reach meaningful goals in nanotechnology; whereas much of current research can be characterized as attempts to extend existing experimental methods without much of a clear end goal. Purely speculative research can offer some modest achievements, but the time is now right to take a step back and work out what strategies are most likely to eventually result in the really valuable breakthroughs.

Near and longer term applications of MNT

So far I have assessed current technology and described a research and development strategy for acquiring MNT, but it is also worth thinking about the applications it promises. Tailored nanomineral isomers could theoretically be used to catalyze reactions in conventional organic chemistry, and this capability would improve if we not only used the shapes of their surfaces for interactions but if the nanominerals contained moving parts, which could 'grab' molecules and pull them apart or immobilize reagents and force them together. This is how enzymes work, although for them the reaction is often coupled with the burning of a fuel molecule (e.g. ATP). So how could an inorganic crystal incorporate moving parts? (Diamond is considered inorganic even though it is made of carbon.) In many devices the moving parts hold themselves in place, but it would be difficult to assemble that kind of structure in the early stages of MNT. Instead, nanominerals could be augmented with functional groups bonded to their surfaces at particular places which would give them chemical properties in aqueous solution. Different nanominerals functionalized in this way would react together in solution according to normal chemical rules. This would allow for the connection of rigid crystals with covalent bonds so that the final structure could move in pre-determined ways, perhaps in response to an electric charge (in a similar way to electroactive polymers). This is conceptually similar to disulphide bridges in proteins.

Some chemical reactions, such as the Haber process, would benefit greatly from having nanomineral catalysts to speed up the reaction; other reactions might become feasible for the first time. In time the catalysts could be arranged in production lines with the workpiece molecule being passed between them – this could be very efficient but would also require specialized devices for transporting the workpiece and supplying the supplementary reagents. All of these nanomineral devices would of course have to be designed on computer so that we could be sure they would fulfil their intended functions – fortunately the simulations would be easier than those of proteins because of the natural rigidity of minerals. The design process could also be facilitated by the use of virtual reality – this would allow designers to 'get a feel' for the nanominerals and would make their development more similar to how we develop new technologies at our level. Three other obvious applications of MNT are the ultimate miniturization of computer circuitry, seamless brain/computer interfacing, and much more efficient solar panels – current commercial panels can have a conversion efficiency of 23% but panels have been developed with an efficiency of 39% (for natural light). These latter panels are too expensive for mass production because of the

different layers of minerals they contain – a technology specifically intended for the manufacture of minerals could make them much more affordable.

Clearly the development of MNT would have profound technological and social consequences. We would be able to create new types of material for a variety of different purposes – they could even be 'smart' materials programmed to form certain shapes or behave in certain ways when experiencing particular environmental conditions. We could build nanometre scale robots (nanobots) that could move through the bloodstream or link together to form structures like organs – neuron-like nanobots could possibly form an equivalent to the brain. Existing technologies would be able to continue improving with the help of MNT e.g. it could lead to the development of small scale robotics. We could build 'insects' of our own fitted with sensors and able to follow instructions and report back their findings (with obvious applications in farming). The end result would be a technology that could emulate and improve on the plants and animals we see in nature – artificial machines that could grow, move, use materials they find, and respond intelligently to new situations. They could also be designed to withstand and operate in harsher conditions than we are able to endure.

Conclusion

Developing full molecular nanotechnology is essential if we want to fulfil our potential as an intelligent species – and computer simulations, which are done using conservative physical assumptions, attest to it being physically viable. In addition to the applications given above it will be essential for the successful exploration of space – arguably any so-called universal constructor (these arise in discussions of the Fermi Paradox) would have to possess a full MNT capability. If we do not develop molecular nanotechnology, technology itself will cease improving and at some point no new useful materials or chemicals will be developed. But why *would* we limit our technological capabilities before we are forced to by physical law? It would be contrary to human nature to realize that something is possible and desirable but not go out and make it happen. The first step in this endeavour will be to conduct a basic demonstration of the above procedure as a ‘proof of concept’ test, and then to create mineral catalysts and so prove the benefit of having much more general synthetic capabilities at the molecular level. Our current capabilities at that level are badly and unnecessarily constrained to the standard forms of organic chemistry – rings, polymers and the like.

References

(1) To quote Feynman's speech:

But I am not afraid to consider the final question as to whether, ultimately – in the great future – we can arrange the atoms the way we want; the very atoms, all the way down! What would happen if we could arrange the atoms one by one the way we want them (within reason, of course – you can't put them so that they are chemically unstable, for example). Up to now, we have been content to dig in the ground to find minerals. We heat them and we do things on a large scale with them, and we hope to get a pure substance with just so much impurity, and so on. But we must always accept some atomic arrangement that nature gives us. We haven't got anything, say, with a "checkerboard" arrangement, with the impurity atoms exactly arranged 1,000 angstroms apart, or in some other particular pattern. What could we do with layered structures with just the right layers? What would the properties of materials be if we could really arrange the atoms the way we want them? They would be very interesting to investigate theoretically. I can't see exactly what would happen, but I can hardly doubt that when we have some control of the arrangement of things on a small scale we will get an enormously greater range of possible properties that substances can have, and of different things that we can do.

Richard Feynman, 1959, https://www.zyvex.com/nanotech/feynman.html**; p2.**

(2) In the debate Smalley said:

Because the fingers of a manipulator arm must themselves be made out of atoms, they have a certain irreducible size. There just isn't enough room in the nanometer-size reaction region to accommodate all the fingers of all the manipulators necessary to have complete control of the chemistry... [Also] the atoms of the manipulator hands will adhere to the atom that is being moved. So it will often be impossible to release this minuscule building block in precisely the right spot. Both these problems are fundamental, and neither can be avoided. Self-replicating, mechanical nanobots are simply not possible in our world.

To which Drexler replied:

This ubiquitous biological molecular assembler [the ribosome] suffers from neither the "fat finger" nor the "sticky finger" problem. If, as Smalley argues, both problems are "fundamental", then why would they prevent the development of mechanical assemblers and not biological assemblers? If the class of molecular structures known as proteins can be synthesized using positional techniques, then why would we expect there to be no other classes of molecular structures that can be synthesized using positional techniques?

And later:

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.

Of course, it is possible that Smalley never owned a multi-bit screwdriver set and so lacked the experience necessary to appreciate Drexler's point. But apart from that, the possibility that Smalley was inadvertently alluding to

problems inherent in actually creating MNT in the first place does not seem to have been appreciated at the time.

Richard Smalley and Eric Drexler, 2001-03, https://en.wikipedia.org/wiki/Drexler%E2%80%93Smalley_debate_on_molecular_nanotechnology**; p3.**

(3) From an online article:

In chemistry, structure rules because it determines how a molecule behaves. But the two standard ways to map the structure of small organic molecules... have drawbacks. This week, two research teams report they've adapted a third technique, commonly used to chart much larger proteins, to determine the precise shape of small organic molecules. The new technique works with vanishingly small samples, is blazing [sic] fast, and is surprisingly easy... Instead of firing their electron beam from one direction at a static crystal, they rotated the crystal and tracked how the diffraction pattern changed. Instead of a single image, they got what was more like [a] molecular computerized tomography scan. That enabled them to get structures from crystals one-billionth the size of those needed for x-ray crystallography.

'A new day for chemistry': Molecular CT scan could dramatically speed drug discovery, Robert F. Service, 2018, https://www.sciencemag.org/news/2018/10/new-day-chemistry-molecular-ct-scan-could-dramatically-speed-drug-discovery**; p5.**

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