

In the beginning there were nanoparticles

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Nanoparticles have been around since the beginning of man's time on Earth, so what is all the fuss about? The earliest stone masons, Iron Age smelters and cave painters either worked with, or produced crushed ores and minerals which, on a random basis, contained nanoparticles. In some cases this was purely an accidental by-product of the process, whereas in others, such as painting, the shape and refractive index of the material provided the colour desired by the artist. The early stained-glass craftsman understood the value of finely crushed mineral ores added to molten glass in order to produce the plethora of rich colours found in the windows of so many churches. There is also evidence that the early sword makers understood the value of carbon nanoparticles in order to produce the finest blades.¹

Nanoparticles have thus been around for a long time but they were randomly distributed in the process of producing the materials used as the building blocks of finished products. What has changed is that the last 20 years have seen two revolutions. The first was the ability to see and measure particles down to the size of a single atom, partly instigated by knowledge from theoretical physics (that the particles and their properties existed), and the second was the ability to understand the processes of production so that nanoparticles could be made to order.

A nanoparticle itself is now fairly well defined,² and is anything from a large molecule in size to a small bacterium. Nanotechnology is perhaps less well defined, since it represents a liaison between the traditional natural sciences of mathematics, physics, chemistry and biology together with engineering and manufacturing. Indeed, the ability to visualize nanoparticles with atomic force microscopes, scanning electron microscopes and scanning tunnelling microscopes is a product of physics and the advances in the electronics industry, which has only become possible with the advent of the microprocessor. There is still some confusion in the academic literature in terms of where "nano" scientific development and discovery really belongs. Much of the nano-physics, chemistry and biology still appears in the traditional single-discipline journals. However the growth in papers citing nanotechnology as a keyword over the last 20 years is following an exponential growth curve, and in more recent years the number of nanotechnology-

¹ M. Reibold et al., Materials: carbon nanotubes in an ancient Damascus sabre, *Nature (Lond.)*, Vol. 444 (2006) p. 286.

² NanoDictionary, Basel: Collegium Basilea (2005); Vocabulary—Nanoparticles, Publicly Available Specification 71 (London: British Standards Institute, 2005).

specific academic journals is also growing.³ What is certainly happening is that the nanotechnology label has focused attention onto the interdisciplinary sciences to the extent that public research funding is available and nanotechnology products are regarded as one of the major growth markets.⁴

Nowadays, nanoparticles and nanotechnology feature almost daily in the popular media, and apart from the marketing hyperbole associated with the use of the word “nanotechnology” in product descriptions,⁵ one might be forgiven for asking, “what is a nanoparticle? how is it made? how does it work? where are they in everyday use? and, should I be concerned?” All of these questions have been asked and, to some extent, many have been answered,⁶ but what this article seeks to do, is to provide a few examples of nanoparticles, and to explain why these questions are asked. There is no doubt that more and more nanomaterials will appear in the market place. A recent study⁷ identified 381 products incorporating nanoparticles, including hard drives, memory devices, processors, light emitting diodes (LEDs), bandages, sports goods, scratch-resistant car paint, cosmetics, lubricants etc.

Currently topical is the question of what long-term effects the addition of nanoparticles into cosmetic products might be having. An ancient example of a possibly harmful cosmetic concerns the use of lead. Roman fashion in the 2nd century AD dictated that noble women should use lead-based face creams.⁸ Soon after, the toxic effects of lead began to be understood and the practice was discouraged. However, after an attack of smallpox, Queen Elizabeth I was still using lead-based face creams to hide the ravages of the disease. The cosmetic in question was a paste made from white lead and vinegar, which in later years gave Elizabeth her iconic white face. White lead is lead carbonate or cerussite and its relevant characteristic is its high refractive index (2.07). Growing awareness of the toxicity of lead meant that by the late 16th century it was already being replaced by tin and zinc, which anyway were more abundant in Britain.

Nowadays lead is no longer used in these products and has been completely replaced by zinc oxide and titanium dioxide nanoparticles. Particularly prolific is titanium dioxide, which has a refractive index of 2.4 and when used in the form of particles less than 100 nm in diameter is transparent to visible light, while absorbing much ultraviolet. This has resulted in sun creams combining very high sun protection factors and a clear transparent appearance, which are now ubiquitous on holiday beaches in the summer months.

The picture in Figure 1 shows a titanium dioxide nanoparticle of typical size 60 nm produced by hot aerosol deposition. Each particle contains about 200 molecules. At these sizes there is some evidence⁹ that the nanoparticles will enter the epithelial layers under the skin and may even penetrate cell nuclei. So far the evidence suggests that the body is able to cope with a

³ R.N. Kostoff, R.G. Koytcheff & C.G.Y. Lau, The growth of nanotechnology literature, *Nanotechnology Perceptions*, Vol. 2 (2006) pp. 229–248.

⁴ [http://www.nanotecni.com/images/market_summary.pdf-search=%22global nanotechnology sales%22](http://www.nanotecni.com/images/market_summary.pdf-search=%22global%20nanotechnology%20sales%22)

⁵ D.M. Berube, The magic of nano, *Nanotechnology Perceptions*, Vol. 2 (2006) pp. 249–256.

⁶ *Nanotechnology Perceptions*, Vol. 2, No 1a (2006) and Vol. 2, No 1b (2006).

⁷ Project on Emerging Nanotechnologies, established in April 2005 as a partnership between the Woodrow Wilson International Center for Scholars and the Pew Charitable Trust (<http://www.nanotechproject.org/index.php?id=44&action=view>).

⁸ http://www.eurekalert.org/pub_releases/2004-11/uob-rfc110304.php

⁹ P.A. Revell, The biological effects of nanoparticles, *Nanotechnology Perceptions*, Vol. 2, (2006) pp. 283–298.

limited invasion of such particles. Macrophages in the epithelial layer capture the nanoparticles, coat them in antigen so that the T-cells attack the particle, which is transferred to the bloodstream for eventual removal via the liver.

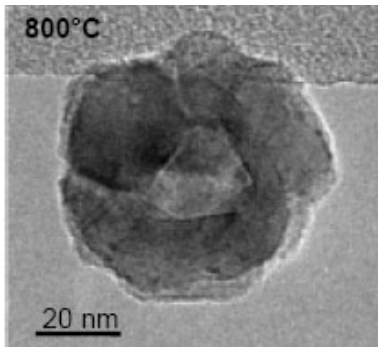


Figure 1. TEM image of a 60 nm TiO₂ nanoparticle.¹⁰

Another cosmetic application with the “nano” label, used to imply that the product benefits from the latest technology, is in anti-ageing or anti-wrinkle creams. These creams, containing so-called nanosomes, are used as a means of delivering drugs directly into the cells beneath the skin. The nanosome is a liposome some 200 nm in diameter (Figure 2), consisting of a lipid membrane encapsulating an aqueous solution. The lipid bilayer is able to fuse with the bilayer of the cell membrane, thereby delivering the nanosome’s contents directly into the cell.

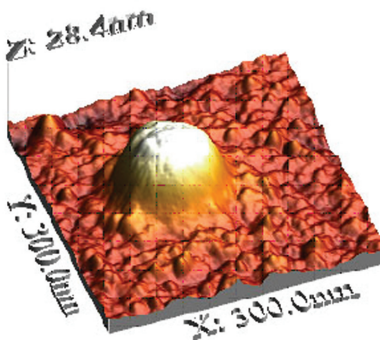


Figure 2. Atomic force microscopy (AFM) image of a nanosome.¹¹

One popular anti-ageing product delivers vitamin A (retinol, C₂₀H₃₀O) in this manner, because of the vitamin’s anti-ageing capabilities, which were demonstrated in the skin of mice as early as 1998.¹² Oxidatively damaged DNA is one of the main causes of ageing and at present it is a little difficult to understand exactly how this vitamin aids the repair process. Vitamin A is

¹⁰ P. Ahonen, Aerosol production and crystallization of titanium dioxide from metal alkoxide droplets, Helsinki University of Technology PhD thesis, (2001).

¹¹ http://www.phantomsnet.net/files/abstracts/TNT2005/TNT05_Casuso.pdf

¹² Tiansen Li et al, Effect of vitamin A supplementation on rhodopsin mutants threonine-17 methionine and proline-347 serine in transgenic mice and in cell cultures, Proc. Natl Acad. Sci., Vol. 95 (1998) pp. 11933–11938.

a known antioxidant and one can only assume that it is this benefit in preventing further damage that is being promoted, rather than actual repair of damaged DNA.

These nanoparticle cosmetic products are causing some concern that is spreading to the area of regulation. Friends of the Earth have raised the question as to whether such cosmetics are really delivering a drug,¹³ in which case the full rigours of health and safety testing would have to be applied. Currently, cosmetic manufacturers are claiming that their vitamin constituents are all tried, tested and trusted substances. However, growth peptides operating as protein messengers instructing cells to regenerate are being contemplated as future anti-aging cosmetics,¹⁴ since by age 50 or more natural growth peptides are considerably reduced in quantity in most human beings. Delivery of these peptides into the deeper layers of the skin would doubtless make them be considered to be a drug, and thus the cost of bringing them to the market would be considerably increased. This is an area to watch, judging by the estimated size of the market for anti-ageing skin care treatments, which continues to grow from the \$9.9 billion (US) of 2004.¹⁵ L'Oréal is one of the leaders in cosmetic nanotechnology research and last year alone invested US\$600 million in it.

Carbon, the very foundation of life, is an element that has been used for a long time in many applications, e.g. iron manufacture and gunpowder, and in the form of soot contains many nanoparticles. It is only comparatively recently that the true properties of carbon nanoparticles have really been understood. Carbon fibre composites have been used for some time because of their structural strength, but the real benefits of carbon on the nanoscale were only realized with the published discovery of the fullerene in 1985,¹⁶ and the carbon nanotube in 1991.¹⁷ The 60 atom football-like structure of the fullerene gives it many unusual properties that are only apparent at the nanoscale. For instance, the C₆₀ molecule is violet in colour and about 1 nm in size. In fact fullerenes may be produced in several different sizes, eg. C₇₆, C₈₀ and C₈₂, which enable them when illuminated in solution to have varied colours of the visible spectrum. Fullerenes and carbon nanotubes are still produced in much the same way as soot: a hydrocarbon is burned at high temperature in a sophisticatedly controlled environment to produce carbon nanoparticles of the required size.¹⁸ Carbon nanotubes can be anything from a few nanometres in diameter to many hundreds of nanometres or even micrometres in length and may be either an electrical conductor or a semiconductor depending on the orientation of the vertices (the carbon atoms) in the rolled-up graphene sheet constituting the tube. The hexagonal lattice structure of the sheet may be deformed by squashing the hexagons in one direction, thus changing the conductivity.

¹³ http://www.icta.org/doc/Nano_PP_final_May_16,_2006.pdf

¹⁴ <http://www.organicconsumers.org/bodycare/nanoparticles.cfm>

¹⁵ http://www.businessweek.com/magazine/content/05_50/b3963100.htm

¹⁶ The existence of C₆₀ was predicted by Oosawa of Toyohashi University of Technology (E. Oosawa, *Superaromaticity*, Kagaku, Vol. 25 (1970) pp. 854–863).

¹⁷ Although the discovery is usually ascribed to Iijima of NEC, Radushkevich and Lukyanovich of the Institute of Physical Chemistry of the USSR Academy of Sciences published an account of what appear to have been carbon nanotubes almost 20 years earlier (L.V. Radushkevich and V.M. Lukyanovich, *On carbon structures formed by the thermal decomposition of carbon monoxide on an iron substrate*, Zh. Fiz. Khim., Vol. 26 (1952) pp. 89–95).

¹⁸ A. Mineyuki, *Fullerenes—an attractive nano carbon material and its production technology*, *Nanotechnology Perceptions*, Vol. 2 (2006) pp. 221–228.

At present nanoparticulate carbon has not found its way into commercial use in the mass production market, rather carbon nanotubes and fullerenes are essentially still produced for the research market, where they find numerous applications such as atomic force microscope tips, electron microscopy electron sources, nanoscale transistors, capsules for drug delivery, antioxidants and as the basis of prototypical high-strength composites. It is only in this last form, typically carbon-reinforced plastics, that the general public will have any contact with them.

Considerable research is underway, as part of the drive to reduce the world dependence on fossil fuels, to use carbon-based nanostructures to contain hydrogen without the need for either expensive cooling or pressure vessels. The contained hydrogen might then be released for use in fuel cells or combustion engines to produce energy without carbon dioxide.

This is a good example of the triumph of hope over experience where nanotechnology is concerned. Hydrogen is twice as efficient in extracting energy from combustion as petrol, but in containment, either by pressure vessel or by cooling to near absolute zero, can only achieve about 15% of total stored mass as energy compared to 70% for petrol. This means that nearly 4 times as much stored mass including hydrogen compared to petrol must be carried to achieve the same kilometres per kilogram of fuel in an automobile.¹⁹ The hope was that nanotechnology would be able to match the storage of hydrogen using cooling or pressure vessels with carbon nanotubes, but without the expense of constructing the containment. Early results were promising, predicting that 14% by weight could be contained in large single-walled carbon nanotubes, which would overcome some of the repulsion of the free hydrogen molecules. This was well above the threshold of 8% by weight that was regarded as the lower economic limit. On the other hand, processes developed so far, in fact using doped carbon nanotubes employing chemical absorption of hydrogen near room temperature and at atmospheric pressure, have barely achieved storage of 1% of hydrogen by weight, see Figures 3 and 4. Figure 4 shows a model of three graphene sheets with potassium atoms attached to contain deuterium (heavy hydrogen) molecules.

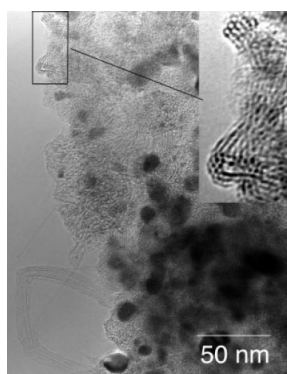


Figure 3. Scanning electron micrograph of single walled carbon nanotube.²⁰

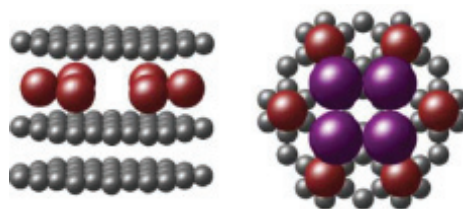


Figure 4. Stacking model with potassium. The left figure shows the stacking sequence for KC_{24} . The grey spheres represent carbon and the larger red spheres show the dodecahedral arrangement of the potassium atoms. The right figure shows a view down the basal direction of the dodecahedral K (red atoms) structure atop a single graphene layer. In addition, a possible arrangement for four larger deuterium molecules is depicted in purple. The optimal packing of hydrogen or deuterium into this structure would result in $KC_{24} \cdot 2H_2$, or 1.2 wt%.¹⁸

¹⁹ W. Peschka, The status of handling and storage techniques for liquid hydrogen in motor vehicles, *International Journal of Hydrogen Energy*, Vol. 12 (1987) pp.753–764.

²⁰ C. Channing et al., Hydrogen storage in metal-modified single-walled carbon nanotubes, *Proceedings of the 2002 U.S. DOE Hydrogen Program Review*, NREL/CP-610-32405.

Recent studies²¹ are more optimistic, achieving 7% by weight, but the graphene sheets with potassium are hydrogenated at 2000 °C, and are stable at room temperature and pressure, while the hydrogen is released by heating to 250–450 °C.

An area where Moore's law is certainly on track and nanotechnology is playing a key role is in the next generation of electronic data storage. Manganese and cobalt are ferromagnetic, and using a magnetic field it is possible to control the electron spin of the molecule. By sandwiching the ferromagnetic manganese or cobalt between thin layers of non-magnetic material, the spin orientation may be detected by the giant magnetoresistance (GMR) effect discovered in 1988.²² This phenomenon (the basis of spintronics) has potential for memory devices in which one bit is stored in a single molecule, with the consequent possibility of terabits of data contained on a chip only a few μm square. Single magnetic nanoparticles, see Figure 5, may be used for quantum computing, in which the electron spin is simultaneously both up and down in orientation until probed.²³

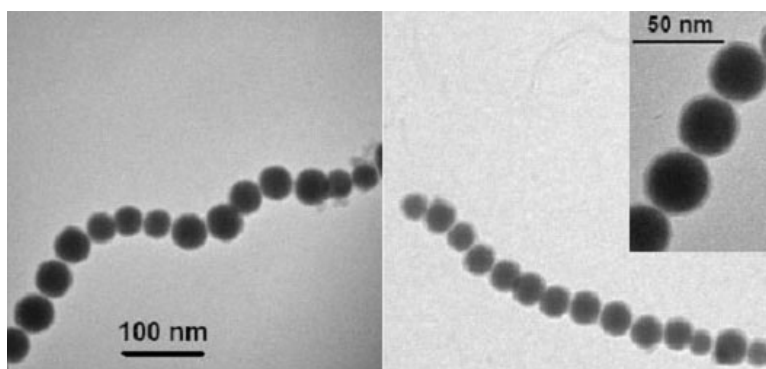


Figure 5. Cobalt nanoparticles assembling into a necklace (spins aligned) under the influence of a magnetic field (transmission electron microscope (TEM) images of silica-coated cobalt).²⁴

Another area showing rapid development and already yielding interesting research results, especially in biology and medicine, is quantum “dots”. These are nanoparticle semiconductors, typically chalcogenides such as cadmium selenide, see Figure 6.²⁵ Usually they are contained in a shell of zinc sulfide and operate as a quantum potential well: stimulation by ultraviolet light or electrical current excites electrons into the conduction band, which then fall back into the valence band releasing a quantum of energy. The size of this band gap is determined by the size of the dot. Consequently, it may be made to fluoresce precisely at any desired colour of the visible spectrum. The conversion of stimulating energy to emitted light is very high and hence they are attractive both as markers and as light sources (semiconductor lasers).

²¹ http://gcep.stanford.edu/pdfs/QeJ5maLQrugiSYMF3ATDA/2.1.4.4.nilsson_06.pdf

²² P.J. Kervalishvili, *Semiconducting nanostructures—materials for spintronics*, *Nanotechnology Perceptions*, Vol. 1 (2005) pp. 161–168.

²³ P.A.M. Dirac, *The Principles of Quantum Mechanics*, 4th edn. Oxford: Clarendon Press, 1958.

²⁴ <http://www.uni-duisburg-essen.de/physik/fbphysik/Experiment/Jan06/Article.pdf>

²⁵ The extreme biotoxicity of cadmium is usually blithely overlooked by the promoters of these materials.

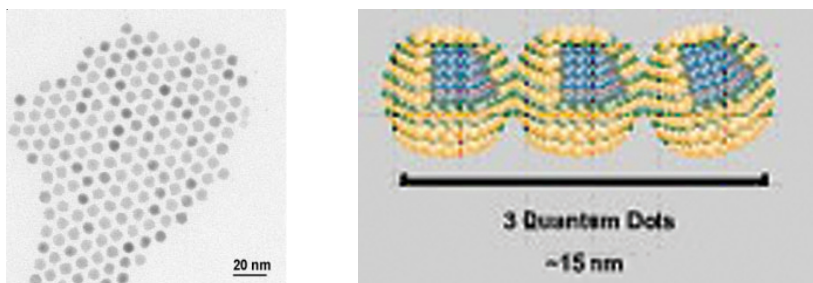


Figure 6. TEM image of a large PbSe quantum dot, and a model of three ZnS-coated quantum dots.²⁶

The next generation of quantum dots will have multiple shells, the outermost being a ligand coating, in order to protect living cells from the toxic cadmium, lead or selenium. Considerable progress has been made in biology and medicine by attaching these quantum dots to cells, bacteria or DNA. The manufacture of quantum dots is probably close to mass production using microreactors to mix the starting materials in solution. Another promising technology for the production of an array of quantum dots, useful for semiconductor lasers, is self-assembly. For example, deposition of a thin layer of indium arsenide on gallium arsenide generates elastic energy, causing the atoms to partly break free with the formation of three-dimensional islets of InAs. Partly covering these islets with gallium arsenide or another higher melting point material and allowing large islets to evaporate produces a uniform array of quantum dots.²⁷

Gold and silver have long been known for their medicinal properties. The Romans used silver nitrate therapeutically and Paracelsus wrote of the virtues of silver as a healing agent in the 16th century. In the 18th century, silver-coated bandages were advocated but the difficulty and cost of production meant that the concept was never more than hypothetical. Now the ability to produce nanoparticles, see Figure 7, of silver and gold and the possibility to use them

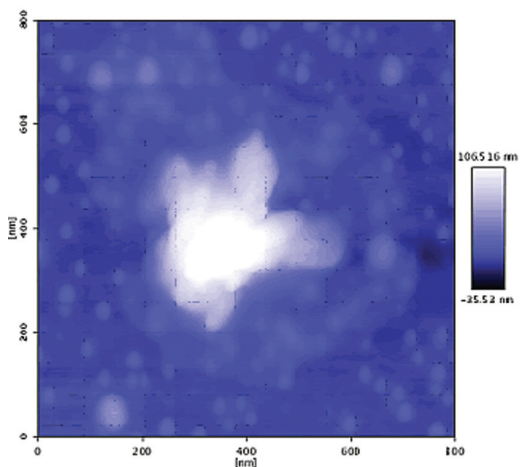


Figure 7. Atomic force microscope (AFM) image of gold nanoparticles (courtesy of JPK Instruments AG).

²⁶ <http://www.evidenttech.com/qdot-definition/quantum-dot-introduction.php>

²⁷ Nikolai N. Ledentsov, Nanostructures, how nature does it (http://web.edu.ioffe.ru/lectures/leden/index_en.html)

in coatings where the mass of the nanoparticles in total is still very small, has led to a resurgence of silver as an antibacterial agent. In fact the Hong Kong mass transit authority is investing in a silver-decorated titanium dioxide coating for all surfaces passengers commonly touch on their underground railway.²⁸

Gold nanoparticles on the other hand are particularly finding use as biological markers since they can easily be attached to DNA. These nanoparticles enable the surface-enhanced Raman spectroscopy effect to be exploited. Plasmon resonance of the electrons in the metallic nanoparticles enhances the Raman effect in molecular assemblies to which the nanoparticles are attached. The Raman spectrum, characteristic of the molecular structure, results from photonic stimulation of interatomic bond vibrations. This gives a characteristic spectrum of absorbed energies, which is normally very weak. The plasmon enhancement greatly increases the signal-to-noise ratio, and for example enables structures to be identified *in vivo*.

The earliest metal used for fabricating artefacts is copper. Apart from early tools and jewellery, copper sheathing was used as an antifouling treatment for some of the earliest ships. In the 20th century it was replaced by tributyltin as the main constituent of antifouling paint. In 1987 this was banned because of its deleterious effect on other marine life, and as a consequence copper oxide microparticles are now to be found in antifouling paints. Copper is essential to many life forms, and is carried in minute quantities in our bloodstream, but at larger concentrations it is toxic, hence its use as a biocide. Because this toxicity discourages not only the fouling organisms but also higher life forms, the European Union is contemplating banning the use of copper in antifouling paints. There is evidence that copper on the nanoscale is even more toxic than in the bulk since it penetrates tissue and is very reactive with many enzymes.²⁹ This could be exploited beneficially by enabling the use of the copper in a more focused way, hence eliminating the need to have vast quantities of toxic material exposed to the environment, as is the case with the non-nano use of copper.

It would be a Herculean task to describe every element and material that is now being investigated for their characteristics in nanoparticle form. The increase in surface area to volume afforded by nanoscale comminution exposes all the weak forces normally hidden by the strong bonding between atoms prevalent at the microscale. Nanoparticles have indeed properties never before seen, for instance gold appears red as a nanoparticle, carbon is mostly black (but transparent as diamond) while as a nanoparticle (“soluble carbon”) it can be almost any colour. Weak interactions such as those of van der Waals, and hydrophobicity and hydrophilicity, enable molecules to self-assemble into larger structures merely by directing the energy provided by Brownian motion.

The minute size of these particles also enables them to penetrate living tissue, but this is both a benefit and a scourge. Therapeutic drugs carried by nanoparticles may be introduced to diseased cells and even toxic materials targeted at cancer cells, however care must be taken to ensure that healthy cells are not affected. On the global scale, the focused use of toxic nanoparticles

²⁸ http://www.nanotechbuzz.com/50226711/hong_kong_testing_antibacterial_nanocoating_in_subways.php

²⁹ Zhen Chen et al., Acute toxicological effects of copper nanoparticles *in vivo*, *Toxicology Letters*, Vol. 163 (2006) pp. 109–120.

as biocides and pesticides will reduce the need to have vast quantities of these hazardous substances polluting the environment as happens in traditional nonfocused modes of application.

The materials of nanoparticles on the whole are not new, but combinations of existing elements and exploration of their properties looks as though it will produce new and exciting structures at a rate never before seen. Certainly electronic memory and possibly, with the advent of quantum computing, electronic processing appear robustly to follow Moore's law. Biological discovery is also rapidly advancing, but whether, as Kurzweil suggests,³⁰ all the sciences will advance at the same rate following the advent of nanotechnology, is still perhaps debatable.

There is still a long way to go before quantum computing is a reality and before the most complex structure of all, the human brain, is understood. The cynic might be forgiven for thinking that what comes around goes around, especially since nanoparticles have been around, albeit unseen, since the earth was formed, but in reality the last 20 years have seen an almost exponential growth in understanding. The question is perhaps whether this rate is sustainable and whether Kurzweil's singularity will come to pass approximately when predicted, i.e. in 2045.

³⁰ R. Kurzweil, *The Singularity is Near*, New York: Viking (2005).

