Nanotechnology in Dentistry: Reduction to Practice

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Abstract: **The speed at which advances are being made in science has catapulted nanotechnology from its theoretical foundations straight into the real world. There are now many examples of commercially available products demonstrating that, in given situations, the technology really does work and that its scope for further application is wide. Healthcare, along with society as a whole, is facing a major revolution in the wake of ongoing technological developments in the field of nanotechnology. Dentistry as an individual healthcare discipline is not exempt, having already been targeted directly with novel 'nano-materials' at the same time as indirectly enjoying the benefits of nano-related advances in the electronics industry through the ongoing computerization of the modern practice. This article examines current practical applications of nanotechnology alongside proposed applications in the future and aims to demonstrate that, as well as a good deal of science fiction, there is some tangible science fact emerging from this novel multi-disciplinary science.**

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Clinical Relevance: **Newly developed dental nanocomposites are expanding the armoury of restorative materials available to the general dental practitioner. It is likely that the reader has already interacted with the fruits of this technology without realizing it. Current applications are discussed and potential future developments relevant to dental practice are hypothesized.**

Nanotechnology has been entering the vocabulary of most scientific communities with increasing vigour over the last 5–10 years. (A search of the *Science Citation Index* [Web of Science] using the keyword 'nanotechnology' reveals 27 articles published in 1995 and 266 articles in 2000). Many speculations have been made regarding its future impact, ranging from improved drug delivery systems[1] to replication devices or morphable nano-bots,[2] which sound like something from science fiction. But what does 'nanotechnology' really mean? What will its impact be? And why should you care?

WHAT IS NANOTECHNOLOGY?

Defining nanotechnology is not a simple task. Many definitions describe an emergent science formed from the convergence of chemistry (classically restricted to atomic interactions) and molecular-scale physics and biology (previously restricted to the micron scale). However, this definition lacks precision and often results in the use of the 'nano' prefix to bolster interest in enterprises involved in research with any link to the molecular scale. As one source put it recently: "A bartender mixes molecules of vermouth and gin. Is he a nanotechnologist?"[3] The recent hype centred upon nanotechnology has seen the birth of many companies utilizing the 'nano' prefix whilst freely admitting no link to the technology itself.

A more accurate definition of nanotechnology, and the one we will adhere to in this article, relates to the deliberate placement, manipulation and measurement of sub-100 nanometre scale matter. A nanometre is a billionth (10^{-9}) of a metre, several orders of magnitude smaller than the scale with which most scientists work. The relative scales, with reference to scientific advances over time, are illustrated in Figure 1.

FUNDING FOR NANOTECHNOLOGY RESEARCH

At the time of writing, the scientific community (fuelled by significant funding from both government and industry) is engaged in a cornucopia of nano-related research areas, arising from the approximately exponential increase in global funding over the last six years (see Figure 2).

- In the USA, the National Nanotech Initiative (NNI) has pledged $710 million in 2003 for nanotech research,[1] and significant levels of funding are coming from NASA and the American energy and defence departments.
- A total spend for all of Western Europe of around US$400 million was achieved in 2002, and the EC has proposed ¸1.2 billion to establish nanotech research networks throughout Europe over the next 4 years.[1]

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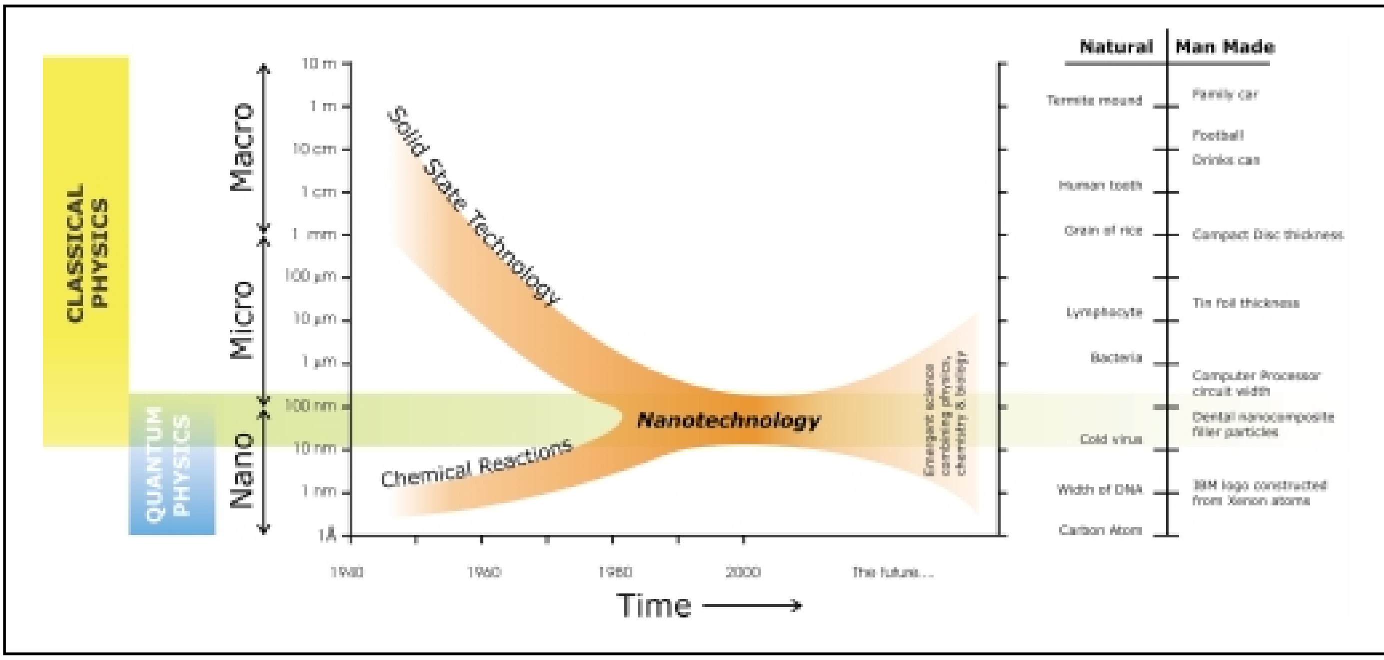

Figure 1. *Nanotechnology exists at a scale where the sciences of classical physics and quantum physics overlap, both of which are underpinned by distinctly different mathematical rules. The figure illustrates the overlap of these two theories in relation to the scale and convergence of solid-state technology and traditional chemistry. In future the principles and theories of nanotechnology will gradually be incorporated into both small- and large-scale systems. An approximate comparison of the scale to more familiar objects is provided for reference.*

With these levels of funding available, the future for this new technology looks bright.

APPLICATIONS OF NANOTECHNOLOGY

The generic basis of nanotechnology means that the range of research areas and potential applications is vast. Although it is very much a man-made science, many of the major areas of research utilize natural biological systems as their templates. Such systems naturally combine supramolecular chemistry with molecular biology and physics, and as our understanding of these areas increases, biological systems will provide crucial insights into how these previously distinct technologies interface. For example, the human body contains nanosystems that include motors, memory, sensors, signal processing, catalysis, synthesis, circuitry and delivery systems, many of these occurring simultaneously within individual cells – during, for instance, the replication and repair of DNA.

The parallels between natural systems operating at the nanoscale and the devices produced by humans seeking to harness the potential of such technology are startling. For each example cited in the paragraph above, the race is on to develop a corresponding artificial system at the nano level, and in certain areas (such as memory) this has already been achieved. Anyone who uses a computer has nanotechnology to thank for the fact that the amounts of data they can store on their hard disk are becoming larger and larger at a surprising rate. These increases in storage potential can be attributed in part to the discovery of giant magnetoresistance (GMR) in 1988,[4] which has allowed production of extremely sensitive magnetic sensors that can be used within the reading/recording heads of hard disk drives.[5] As these heads become smaller, corresponding reductions are made in the size of the magnetic domains (in effect the data-storage positions) that cover the surface of a hard disk, and hence greater data densities may be achieved. At present, the size increases are approximately following Moore's Law, which (broadly speaking) predicts that computer technologies will double in capacity approximately every 12 months. In the case of microchips, Moore's Law applies to the number of transistors that can be incorporated into a single chip. However, classical methods of chip fabrication are beginning to face their limit and scientists are turning to nanotechnology to solve their problems, which should allow Moore's Law to hold true well into the future. Ultimately, nanotechnology may be used directly in the fabrication of electronic components, with circuitry becoming possibly no wider than a few electrons.

The application of nanoscale particles is a recurrent theme when existing commercial applications of nanotechnology, or those close to the marketplace, are considered. The ability to create and use nano-sized particles of material has led to the optimization of many materials and individual material characteristics, with a strong likelihood of many more following suit. Here are a few examples:

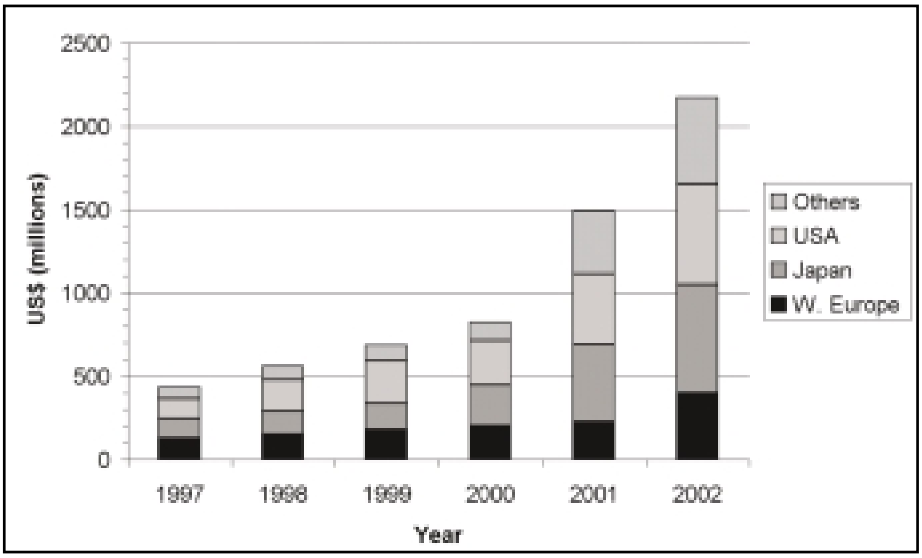

Figure 2. *A histogram illustrating global expenditure on research and development in nanotechnology over recent years. Each bar is subdivided to represent the proportions contributed by major individual economies.[1]*

- Currently under scrutiny in biomedical research labs around the world are nano-structured ceramics and metals resulting from nanoscale powder particle precursors. These offer mechanical characteristics superior to those of conventional materials and may find application in the articulation of biomedical implants used in total joint replacements.[6]
- Nanoparticles capable of absorbing UV radiation have found application in sun-block.
- Solid lipid nanoparticles have been suggested as carriers for vitamin E in cosmetic skin creams,[7] and more recently as drug delivery systems that could be produced on a commercial scale.[8]
- Nanoparticles have also been researched as additives to liquid-based lubricants[9] and as solid-state lubricants in their own right[10] for demanding applications where liquid lubricants would not be appropriate.
- In the field of clinical dentistry, a nanocomposite restorative material has been claimed by 3M ESPE, the developers, to combine the features of previous hybrid and microfilled composites. The material is offered as a universal restorative, suitable for both anterior and posterior restorations and incorporates reinforcing spherical particles of 20 nm and 70 nm in diameter. Rather than all particles in the system being independent entities dispersed through the resin matrix, some are loosely agglomerated to form micron-sized clusters that reportedly act as a conventional filler particle, but which are intended to break down gradually during a wear process and avoid problems arising from particle pull-out and weakening of the surrounding material. The nanocomposite, branded 'Filtek Supreme', has been around for such a short period that no independent research data is yet available, so we may have to wait for verification of the various claims by 3M ESPE regarding superior wear and strength properties[11] and polish retention.[12]

PROGRESS BEYOND PARTICLES

It is apparent that the present-day particulate applications of nanotechnology are inherently passive – the particles are added to something to improve a certain characteristic. Thus, although they may actively do clever things in their own right, they do so in a way that essentially enhances something we already know about. No external monitoring is required to reap the benefits of their presence and no input is required to make them work once they are in place. However, many proposed applications of nanotechnology, rather than being passive in the way that additive particles are, rely on active monitoring of a process or function and are hence dependent on the human's ability to interface with objects operating at the nanometre level.

It should come as no surprise therefore that the recent surge in interest in nanotechnology is largely due to the advancement of the tools enabling humans to interact with objects at this previously restricted scale.The ongoing development of Scanning Probe Microscopy (SPM)

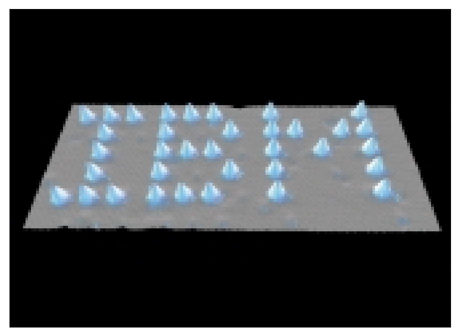

Figure 3. *I-B-M in Xeon Atoms. In 1990 a Scanning Tunnelling Microscope was used to manipulate individually Xenon atoms upon a nickel substrate to create a very well known company logo. Courtesy: IBM Research, Almaden Research Center. Unauthorized use not permitted.*

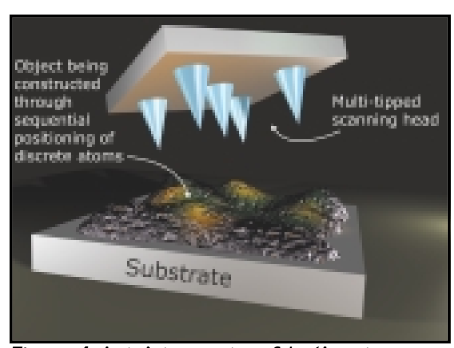

Figure 4. *Artist's impression of the 'Atomic Toothbrush' being employed (multi-probe Scanning Tunnelling Microscope).*

and Micro Electro Mechanical Machines (MEMS) allows scientists to observe atoms directly and molecules as discrete components. Scanning Tunnelling Microscopy (STM) and Atomic Force Microscopy (AFM), although primarily observational techniques, also allow for positional self-assembly on a small scale, as famously shown by IBM in 1990 when they formed the IBM logo from 35 Xenon atoms using an STM (Figure 3).[13] Amongst other ongoing developments of STM technology, a multiple probe design consisting of several static silicon tips has been proposed by scientists at the University of Birmingham's Nanoscale Physics Research Lab.[14] This will potentially provide another significant improvement to general nanoscale interaction and would be another step on the road to the Holy Grail of efficient atomic assembly. Coincidentally, this new device has been nicknamed the 'Atomic Toothbrush' (Figure 4). Of course, this particular reference has no direct link with dentistry (the atomic toothbrush would be highly unsuitable for cleaning teeth); however, research is ongoing into many areas that will have a direct impact on the dental industry.

In a recent edition of the Forbes/Wolfe Nanotech Report[15] an interviewer reported a conversation with Harold Craighead, Director of Cornell's Nanobiotechnology Centre, who indicated that single-molecule detection represented a very exciting application for point-of-care diagnostic devices. When later asked whether anyone had already expressed interest in the idea the reply was "You'd be surprised but ... dentists." The suggestion was that it would be possible to compare a full analysis of all the compounds present in saliva with healthy saliva to obtain a disease signature. This, combined with the fact that people tend to visit their dentist more frequently than their GP, led to the suggestion that point-of-care testing in the general dental practice could revolutionize healthcare as a whole. A sensor for a wide range of problems could be placed in the patient's mouth at the start of a dental check-up and, by the end, the dentist would be able to advise the patient as to whether he/she was in good general health or not, recommending specialist opinion if appropriate. Early warning systems such as these could greatly increase ease of treatment and hence healthcare could be revolutionized without requiring GDPs to stray far from what they do best.

MONITORING THE NANO-SCALE

To illustrate the point we can take the example of a single substance that can be detected in saliva: C-reactive protein (CRP). The measured levels of CRP in blood plasma increase in response to injury and infection during the early inflammatory response:[16]

- elevated CRP levels have been shown to correlate with patients presenting symptoms of carotid artery disease;[17]
- in apparently healthy male subjects high levels of CRP are associated with the risk of future cataract formation;[18]
- CRP is also an indicator of the risk of future myocardial infarction and stroke.[19]

This molecule therefore has tremendous diagnostic potential. CRP is detectable in saliva at levels analogous to those in plasma and has additionally been suggested as one of a collection of factors that provide an indication of an individual's periodontal health status.[20]

In theory, detection of CRP in saliva could provide the basis for a sensor application designed to give early warning of a range of impending systemic illnesses. However, a test for a single substance would not yield information sufficiently specific about any particular condition. In order to be able to generate a specific diagnosis from a sensor application, the sensor should be capable of detecting and quantifying many other compounds at the same time, which is where things become complicated. Nanotechnology is realistically the only avenue by which an enormous number of individual sensors for the detection of the full range of organic molecules in saliva could be incorporated onto a substrate small enough to avoid impeding the dentist's work.

However, it is important not to lose sight of the fact that the nanoscale world must interface with the macroscopic world – a sensor is no good unless it can inform its user what it is sensing. This requires that somewhere along the line the 'nanosensor' must interface with a form of technology that humans can interpret, clearly no simple task. Zamborini *et al*.[21] have demonstrated that their sensor system, designed to monitor organic vapours, is capable of presenting feedback in the form of a change in mass, optical properties and conductivity, each factor being measurable (albeit using highly advanced equipment). It appears therefore that a diagnostic sensor capable of reacting measurably to a wide range of compounds may be practicable, assuming the measuring devices connected to them become increasingly more sophisticated, user friendly and, crucially, affordable.

The likelihood that such enhancements will take place within a relatively short period of time is extremely high, given the wide range of disciplines in which the field is being researched and applied. Technological advancement in nanotechnology can be regarded almost as a self-fuelling process where challenges that arise in one area are overcome by developments in another. For example, the large pieces of complex equipment required to interface with nanoscale sensors will inevitably become smaller as computer technologies and manufacturing processes are optimized, and hence will be more suited to real-world application by non-specialists. Indeed, a list generated by the DTI in their June 2002 report on nanotechnology[1] suggested seven applications that might appear within the next decade, including two directly related to electronic devices. Interestingly, from the remaining suggestions a total of four applications were solely related to healthcare and included retinal implants, drug delivery, and patient monitoring. Healthcare is therefore standing right in the path of some potentially exciting applications of this emergent science.

CONCLUSIONS

It may have come as a surprise to find aspects of nanotechnology already having an impact on the dental industry. However, whilst this technology may be making its presence felt throughout most industry sectors, there is still a long way to go before the family dental practice undergoes a significant change. Even when that change occurs, it will probably not be a sudden, spectacular event. Instead, benefits from advances in nanotechnology will gradually accrue and it will only be when dentistry at some point in time is clearly distinguishable from dentistry today that we will fully appreciate any impact that has occurred.

Nanotechnology is still very much a science and, whilst our understanding of certain aspects of this science may already be leading to practical applications, there is much to learn and understand, not least of which are the fundamental properties of nanoscale materials and their predictability under variable conditions. In addition to the understanding of the raw science, more sophisticated computer aided design (CAD) tools are required for use at the nanoscale, alongside improved and more efficient observation and manipulation techniques.

Fortunately, owing to the increased publicity, awareness and interest from government, public and private organizations, along with the associated increased funding levels and steady flow of talented researchers turning their attentions towards this revolutionary technology, you may not have to wait too long before the first practical applications of this technology begin entering your workplace. Of course, there's always the possibility that this has already happened. The science fiction of today has never looked so achievable. The future is indeed bright, it may not be orange, but it will be small.

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DECEMBER CPD Answers

1. A, B	6. B, C,
2. B, C, D	7. B, C
3. A, B, D	8. A, C, D
4. C	9. A, B, D
5. D	10. B, C, D