Delivering nanotechnology to the healthcare, IT and environmental sectors — a perspective from the 'London Centre for Nanotechnology'

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Nanotechnology research is booming worldwide, having an impact on multiple sectors and with a general belief that medical and biological applications will form the greatest area of expansion over the next decade, driven by an attempt to bring radical solutions to areas of unmet medical need. What is true in the USA is also being fulfilled in Europe, though generally at a significantly lower investment level, even for 'large' capital infrastructure and interdisciplinary centres. Against this, the UK and its European partners are following the maxim 'small is beautiful' and are attempting to identify and grow academic research and commercial businesses in areas that traditional nanotechnology developments out of engineering or physics find challenging. Thus, University College London and Imperial College, in a major joint project linked to other centres of excellence both in the UK and in the rest of Europe, are building upon their internationally competitive medical and hard-matter research activities to focus on and develop nanotechnology as a major sector of research activity. The two universities together form one of the largest centres of biomedical research outside the USA. A novel approach to commercialisation has been taken, exemplified by the establishment with government and private equity funds of a 'Bio-nanotechnology Centre' — this will act as a portal for UK industry to access specialist skills to solve issues relating to developing nanotechnology-based medical applications, for example, for environmental screening, diagnostics and therapy. This paper reviews our academic and business strategy with examples from our current research portfolio, biased towards medicine as the London Centre for Nanotechnology's most rapidly growing area.

1. Nanotechnology — the new driver of academic and commercial success

Nanotechnology is a fundamental 'enabling technology' that gives us the capacity to see, manipulate and manufacture on the smallest of scales. It is widely accepted that nanotechnology is developing into a major driver for commercial success in the 21st century, and, in some applications, it is expected to become a 'disruptive technology', promising massive change [1, 2].

The technology has excellent prospects for exploitation across the medical, pharmaceutical, biotechnology, engineering, manufacturing, telecommunications, IT and environmental markets. Its impact in these areas will be broad and far reaching, providing not only cost and performance improvements to current products and processes but, in the longer term, yielding new approaches to health and societal problems [3].

Nanotechnology involves the precise manipulation and control of atoms and molecules, the building blocks of all matter, to create novel materials with properties controlled at the nanoscale, billionths of a metre. Broadly, two production approaches exist — the bottom-up and the top-down. The first, bottom-up, approach involves physically manipulating small numbers of the basic building blocks, either individual atoms or more complex molecules, into structures typically using minute probes. For example, it is possible to 'push' atoms into a desired location using atomically fine force-microscope tips, intricately carve material using beams of electrons or heavy metal ions, or write molecules directly on to surfaces using tools, both from the physics laboratory or the home office, with inks made of various materials. At present this technology is limited to low-volume, high-value applications such as high-performance chip manufacture, but the range of bottom-up techniques and their areas of application are growing rapidly. The second, top-down, approach involves controlling physical processes, e.g. the conditions under which materials are grown, to coerce atoms and molecules to move themselves *en masse* to a desired location or structure. This approach is already used to create nanoparticles for various industrial applications, with high-volume lower-cost applications being readily in reach. However, the technique is generally limited to producing less complex structures than the bottom-up approach. Here, too, new processes are being discovered or existing processes modified to increase the level of complexity. More importantly, both approaches can work together within both biological and non-biological systems, bridging important divides between the bio-world and the non-bio-world.

As practical examples of the technology, we can imagine:

- the design of minute drug doses tailored to the individual for optimal treatment of disease and targeted to their site of action, thus reducing toxicity and improving efficacy,
- the establishment of new low-cost, real-time high-resolution (perhaps point-of-care) clinical diagnostic techniques,
- the fabrication of sensors which could test the results of vast numbers of different chemical reactions simultaneously to assist the monitoring of cell or organism function in real time or for remote environmental monitoring.

Non-biomedical applications include a vast range of new materials, components for IT and display applications, environmental sensors, fuel cells, catalysts and solar cells.

Working in this influential technology requires a detailed understanding of the underlying physical, chemical and biological processes across a range of scientific disciplines and at the nanoscale. Indeed, at this scale the full range of sciences begin to come together and the new challenge is to create and share a common scientific, management and regulatory language such that effective interdisciplinary interaction is maximised. The ultimate goal is to produce new materials, devices and systems tailored to meet the needs of a growing range of commercial, scientific, engineering and medical applications — opening new markets and yielding dramatic benefits in product performance.

2. The London Centre for Nanotechnology

The London Centre for Nanotechnology (LCN) is a new UK-based, multidisciplinary research enterprise structured to form the bridge between the physical and biomedical sciences, with a unique strategy and clear focus on exploitation and commercialisation [4]. It brings together two internationally competitive institutions in nanotechnology, namely University College London and Imperial College London, in a unique operating model that accesses the combined skills of eight departments, including medicine, chemistry, physics, electrical and electronic engineering, materials and earth science, and two leading business centres. Of particular note, the LCN combines the capabilities of two leading biomedical universities and has been designed to compete internationally in this strategic area.

There are, of course, a growing number of world-class institutions working in the nanotechnology area spread around the UK. The LCN, which collaborates with many of these institutions, is used here simply as one, highly interdisciplinary and commercial 'best practice'-based model for delivering the science to benefit the UK and further afield.

LCN separates nanoscience from nanotechnology by noting that each nanotechnology requires a clear vehicle for delivery, including not only the research and development activities but also the management and technology transfer processes. Any one technology will typically require substantial development to take it from its basic research stage through to a product. This includes developing and protecting the basic ideas, determining the appropriate market and its needs, augmenting the basic idea with other intellectual property and creating a more credible commercial offering that can be effectively exploited. LCN integrates all of these processes such that a basic technology can be taken through to incubation and industry.

2.1 LCN capabilities

The LCN has clearly differentiated capabilities and a strategic research agenda; these are aligned with industry needs and driven by extensive consultation, and effectively balance the basic science and industry R&D agendas. Research in LCN is organised around three thematic areas — each with a set of high-value deliverables.

- Novel, low cost healthcare

  LCN is uniquely placed, through the vast biomedical expertise it can access locally, to develop new paradigms in healthcare. Under development are low cost diagnostics and novel drug delivery systems, as well as new therapeutic regimes individually tailored to the patient. These aims complement those defined by the National Institutes of Health (NIH) for the application of nanotechnology to medicine [3] where first applications of nanoparticles for image contrast agents and drug delivery are already clinically approved (see section 3).

- New paradigms for information technology and communications

  The computing and communications needs of society continue to grow. Current technology approaches are limited by physical laws and a variety of new methods are being sought by LCN staff to circumvent the limitations, applying nanotechnology-driven paradigms such as quantum-based computing and spintronics to the information technology field (see section 4).

- Earth and environment

  New sources of energy, new approaches to finding, assessing and tracking current supplies, and novel approaches to clean-up are being studied. These cross areas as diverse as fuel-cell research through to catalysts, combining fields that range from geology to biology (see section 5).

Deliverables have been chosen to cover the needs of society and industry (Fig 1). They are selected following a commercial strategy development process that best balances the research competencies of the LCN with market, society and industry needs, and which places the LCN in a complementary rather than competing position with other top-tier nanocentres across the globe. Some of the deliverables in the general area of nanomedicine are:

- real space images of biomolecules,
- label-free rapid protein and DNA diagnostics,
- individually tailored drugs and selective delivery systems,
- trackers for food, pharmaceutical and petrochemical industries,
- biocompatible scaffolds for tissue engineering,
- mobile network-based healthcare.

Deliverables for IT include quantum computing (gates), magnetic and spintronic materials, superconducting materials, new photonic and optoelectronic devices and integrated systems like computer memory. Some of these will include the novel use of hybrid organic (e.g. nanotube) — inorganic devices with improved transport properties. Environmental deliverables include fuel cells, inexpensive and reusable catalysts, a variety of solar cells, novel processing routes for organics, plastic electronics and various low-weight high-durability materials.

In-house capabilities have been built covering areas as diverse as nanotubes and composites, super-conductors, organic and carbon nanostructures, nano-photonics, magnetism, novel nanofabrication in III-V, silicon and organic materials — this extends also to various medical diagnostics and therapy-based nanotechnologies. LCN has an extensive range of core tools for nano-characterisation — the technologies required to see and understand nanostructures in both the biological and non-biological areas, such as

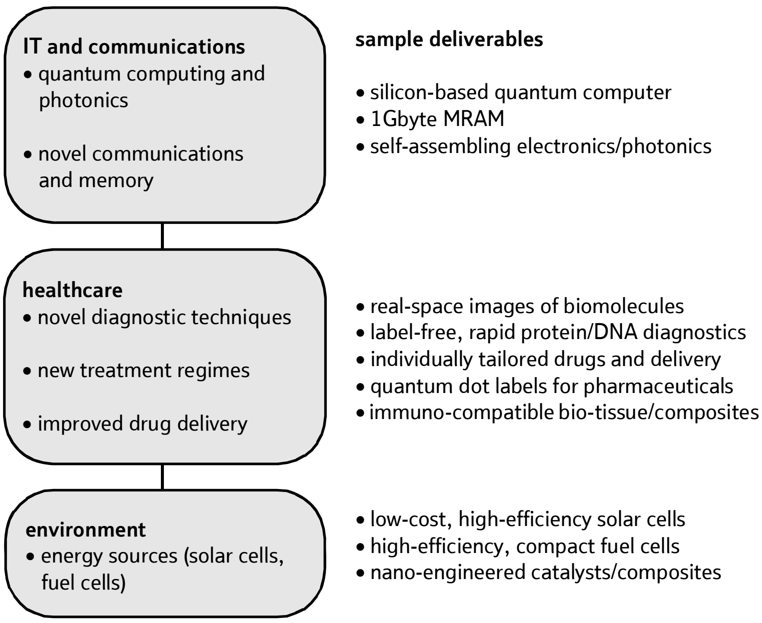

Fig 1 Some sample LCN deliverables.

physically scanned probes and other state-of-the-art microscopy and diffraction-based methods.

Strong connections are being made with UK and international businesses, academia, and other key networks [5—7]. LCN is linked into a broad range of organisations ranging from the London Biotechnology Network [8] and London Technology Network [9], through government-related and inward investment organisations to the broader investment and commercial communities. The Centre also has strong links to other academic institutions and national centres and is constantly and actively pursuing new relationships.

3. Novel, low-cost healthcare

Patient demand for new therapies, diagnostics and mobile information access is placing pressure on healthcare providers, from medical professionals through to the biomedical industries; concurrently the costs of developing new medical products are escalating. The challenge is to improve quality of life at low cost, through the early detection and efficient, effective treatment of disease. Nanotechnology offers many new research avenues that will benefit medical diagnosis and treatments in both the short and longer term [3] (see Fig 2). A taxonomy of the broad areas where nanotechnology will be active have been reviewed recently [10—13] and should form the basis for developing the strategic alignment of 'nano-medicine' with that of traditional medical research. We are developing low cost information-rich diagnostics, drug delivery and drug manufacturing systems based on expertise 'derived from the semiconductor industry'. Likely applications of LCN's nanotechnology include wearable nanoscale biosensors and monitors, label-free DNA and chemical detectors, inhaled and ingested diagnostic and therapeutic tools, *in vivo* monitored implants and smart materials. Some of these research areas and potential deliverable are summarised in Fig 1. The typical examples illustrated herein are based upon highly interdisciplinary working practices at LCN. They range from early stage laboratory studies of novel label-free sensors and new biomaterials for medical devices and tissue engineering to magnetic nanoparticle detectors that are currently under clinical trial. The likely areas to impact patient care early are in improved diagnostic testing and non-invasive imaging [14—16].

Finding the cause of, and therapy for, many diseases lies in a greater understanding of the structure and function of proteins. Nanotechnology brings a powerful tool-kit to medicine, allowing us to understand the processes driving protein formation and operation. Diseases like Alzheimer's, Parkinson's and CJD have been linked to 'misfolded' proteins. Atomic force microscopy can be used to 'grab' and 'pull' proteins and watch proteins unravel and refold in their natural environments. Understanding the fundamental mechanisms of such processes may provide ways to inhibit disease; complementary assay technologies will allow us to recognise the presence of these abnormal proteins in medical samples. Our goal is a set of low-cost, high-throughput screening tools for hospitals, patient point-of-care tests and greater levels of understanding to the drugs industry.

Osteoporosis and arthritis take up substantial hospital resources. Extending the life span of hip implants, or preventing deficiencies in bone function, would make available tens of thousands of hospital

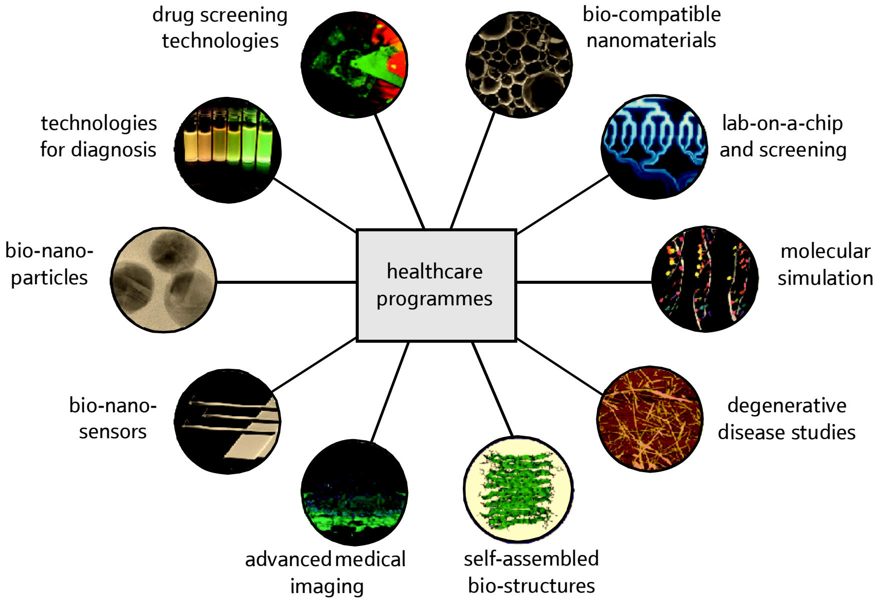

Fig 2 Examples of clinically approved applications.

beds, with positive knock-on effects. We are applying nanoscale cellular biology and other capabilities to provide new routes for drug development for common but major causes of disease. Examples are shown in Fig 3. Our goals also include biocompatible smart materials, artificial bone and long-lasting implants and scaffolds to hasten the healing of fractures.

Nanotechnology will provide new routes to drug manufacture and delivery. Micro-fluidic devices, chips that aid and monitor chemical reactions, can provide low-cost, ultra-pure drug manufacture and portable metered drug delivery. ‘Quantum dots’, nanoparticles with precisely designed structures, can now be attached to molecules or proteins such that, when ingested, they effectively deliver a therapy to a specific location (e.g. a tumour) or fluoresce to show the location of a problem. Similar nanoparticles, with improved magnetic properties, are already ‘in the clinic’ as MRI contrast agents with controlled targeting to specific tissue sites. Indeed, LCN has magnetic particle sensors for cancer entering the advanced prototype phase (see Pankhurst [17]).

4. Information technology and communications

The computing and communications needs of society continue to grow. Current technological approaches are of limited benefit and their costs are rising. The LCN is applying its expertise to a variety of new ways to circumvent the current limitations, applying nanotechnology-driven paradigms such as quantum-based computing, self-assembling electronics and organic and vacuum-based electronics to the IT field.

Since the 1970s the number of devices on a computer chip has grown by a factor of 100 000. The size of the individual devices and the number of electrons required to operate them halves every 1—2 years. Concurrently, the cost and complexity of fabrication plants making the chips doubles every 2—3 years and at present costs are many hundreds of millions of dollars. Compounding this problem, over the last 5 years the number of Internet users has grown to 1.5 bn and the need for computing power continues to grow. To circumvent this, the LCN is looking at nanometre-scale information technology as a way of producing faster, cheaper higher capacity devices with novel operating paradigms (see Fig 4).

In the 20th century, streams of electrons flowing through devices on silicon chips were exploited to give the microelectronics revolution. In the 21st century, it will be the turn of the quantum properties associated with individual electrons that drive a new generation of electronics. As devices shrink to the scale of billionths of a metre, a factor of 1000 below the scale of microelectronics, they start to exhibit unique quantum phenomena that can be harnessed to perform calculations or encode information. This approach will lead to a new generation of computing technology that is completely secure, high-speed, efficient and parallel — with the ability to study completely new problems, e.g. the modelling of biological phenomena.

The LCN is looking to novel nanotechnology-based ‘self-assembling’ approaches to produce a new generation of products. Circuits with atomic scale components (e.g. quantum dots) that form ‘naturally’ during manufacture, through precise control of their growth conditions, are now within reach. In fact, new self-assembly and molecular electronics techniques already produce world-class lasers, LEDs and detectors

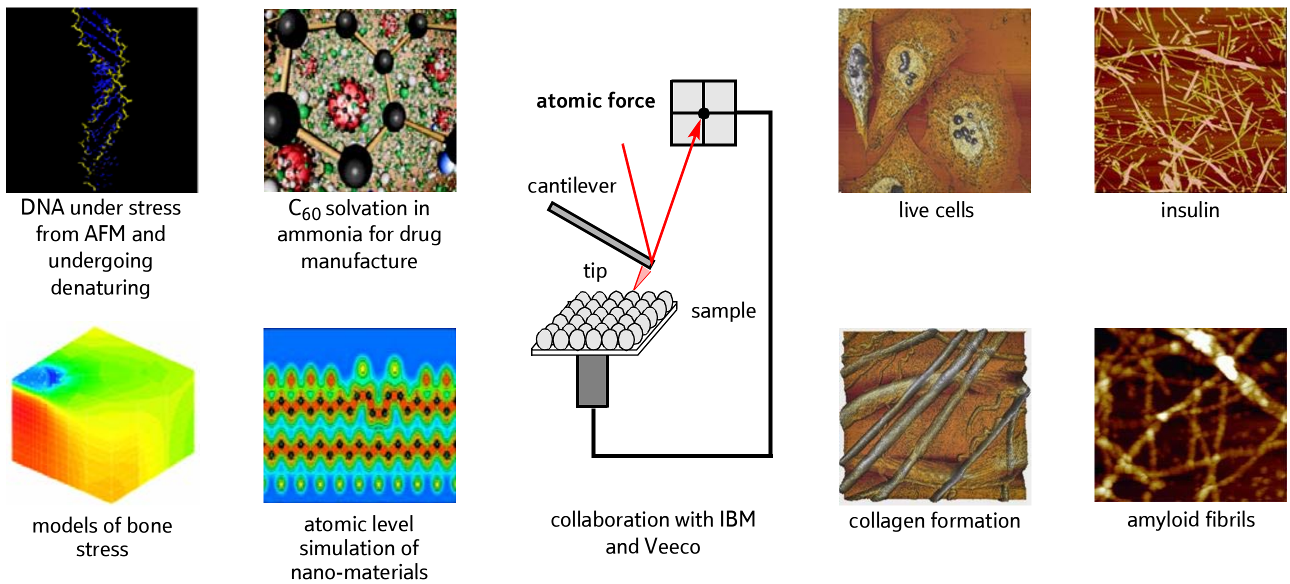

Fig 3 Example nanoscale cellular biology applications.

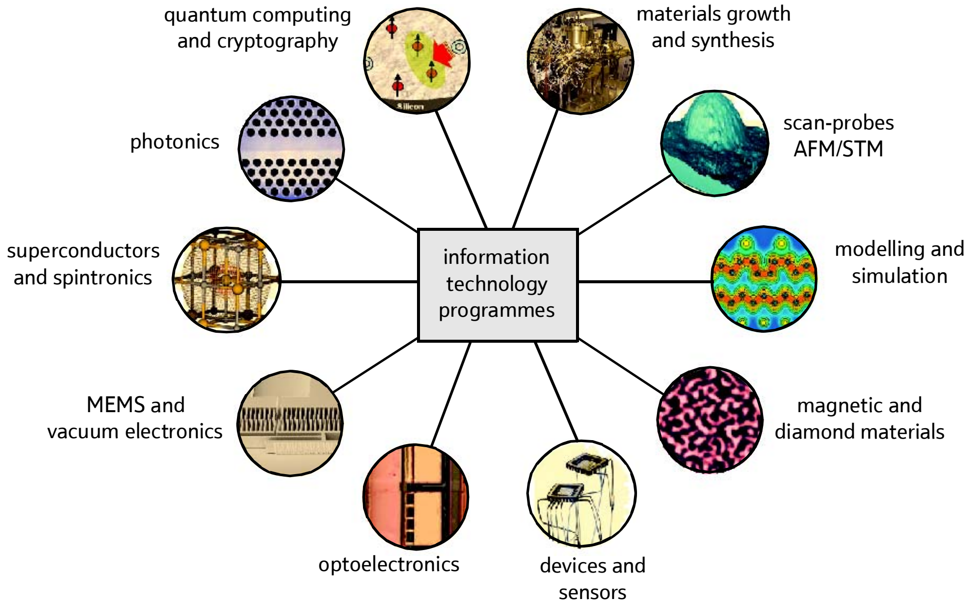

Fig 4 Example information technology and communications nanoscale deliverables.

based on quantum nano-dots. In future, circuits could include electronic or opto-electronic devices, made in semiconductors like silicon or cheaper plastic/organic materials, which could produce, react to or indeed control light, yielding products operating much more quickly and efficiently than any current technology. At the LCN, we are looking both at novel devices for a range of applications and at the new manufacturing approaches required to make them.

The speed of many current electronic devices is limited by the speed electrons can move within them. However, it is known that electrons moving in a vacuum are faster than those moving in a solid, like silicon, and this fact can be used to open up a whole new field based on ultra-fast vacuum micro- and nano-electronics. At the LCN, we are looking at micro-triode devices — vacuum-based electronic components using nanoscale semiconductor tips to produce streams of electrons that fly through a vacuum under the control of electric fields. These components can be used for a range of important applications — particularly where traditional electronics are of limited use, e.g. in harsh environments. These include novel light sources, flat-panel displays, ultra-fast computing, propulsion systems for spacecraft, efficient x-ray tubes, and magnetic and pressure sensing. One important area is THz imaging — a new method of screening for security and medical purposes.

The development of future generations of communications and computing technologies will require a range of powerful tools and cross-disciplinary technical expertise. Techniques like scanning tunnelling microscopy, atomic force microscopy and transmission electron microscopy (TEM), which allow us to study and manipulate atoms with great precision, are at the forefront of creating the new technologies. By providing new insights into how materials are formed and how they behave at the smallest of length scales we can engineer new materials and devices. These tools, coupled to skills in molecular and organic chemistry, physical modelling, systems understanding and new fabrication techniques, will allow us to produce cheaper, faster components with simpler manufacturing processes. The LCN has built a range of world-class capabilities in all of these areas and is using them to deliver the next generation of computers, memories, communication devices and sensors.

5. Earth and environment

Nanotechnology will have an impact on many areas of society, including the way we protect and study the earth and our environment. Nanoscale science will yield new technology and, more importantly, scientific understanding of the way nature works and how we interact with and affect it. Given the high public profile of nanotechnology, the LCN is also studying the impact of nanotechnology itself, and ensures that any technology it develops is properly assessed and managed. To this end, LCN's research is highly transparent to the public and is overseen by an advisory board chosen from a range of public and private institutions.

There is a growing need for low-cost, renewable sources of energy. One approach is to tap the sun's energy using solar cells. The main problem limiting large-scale application of the current generation of solar cells is cost. Current technology relies on semiconductor-based devices which require expensive fabrication. In applications where competing sources of energy are limited, the cost of a solar cell can be traded off against its benefits, for example in powering satellites or for emergency communications in remote areas. But for everyday use, for example to power homes or commercial processes, the costs become prohibitive. At the LCN, we are looking into efficient yet low-cost solar cells for large-scale applications. Solar cells fabricated using nano-structured plastic and organic materials are simpler to manufacture in volume and are flexible; they may even be ink-jet printed over large areas. This work is in collaboration with BP and links to the largest research activity of its kind in the UK, at Imperial College. This work may also lead to more efficient opto-electronic components, such as sensors for environmental monitoring. Another complementary area in alternative fuels research is that of fuel cells. We are investigating numerous ways to reduce the cost and size, while increasing the efficiency and lifetimes of fuel-cell batteries using nano-engineering techniques. Fuel cells will have an impact on a range of applications from the automotive to the IT industry.

Nanotechnology has the potential to positively affect the environment in many ways (see Fig 5). By applying nanotechnology techniques to the catalysts used in chemicals manufacture, we can improve process efficiency, thereby reducing raw materials usage, cost and pollution. In fact, through our deeper understanding of atomic processes, we can nano-engineer catalysts to be reusable, longer lasting and less dependent on expensive materials like platinum. As another example, we can create novel nano-composites, multi-functional materials and eco-materials. These materials include nano-fibres to reinforce their structure, leading to a new range of high-strength, low-weight materials with unique electrical, thermal and friction properties and improved resistance to wear, and made using environmentally sound manufacturing techniques. Through their improved properties, these materials will yield savings in the fuel consumed by vehicles and the energy consumed during the manufacture of products. They will open up a host of novel applications, ranging from new longer-lasting injection moulding components for the plastics industry, through improved electrodes for capacitors in the electronics industry, to lightweight, strong tissue scaffolds for the medical industry.

It is well known that nanotechnology will have a profound impact on the products we use. But few realise that nano-technological approaches can be applied to give us a deeper understanding of the Earth and its functions. By understanding how nano-particles, existing on the smallest scales, interact with their environment, we can create models of the Earth from the bottom-up. This allows us to answer age-old questions like how hot the Earth's core is, what it is made of and how it formed. Most people believe the Earth's core contains iron and sits at 5000—6000 °C, but physical evidence is extremely difficult to come by and to interpret. Yet the issue is hugely important as the core drives the dynamics of the whole Earth and its surface. At the LCN we are bringing together the physical, astronomical and geological sciences to work on new ways of modelling global environmental processes, using nanoscale understanding and quantum mechanics to predict the properties of materials at the extreme pressures and temperatures of the core and beyond.

At the LCN we are attempting to gain a better understanding of the fundamental processes affecting

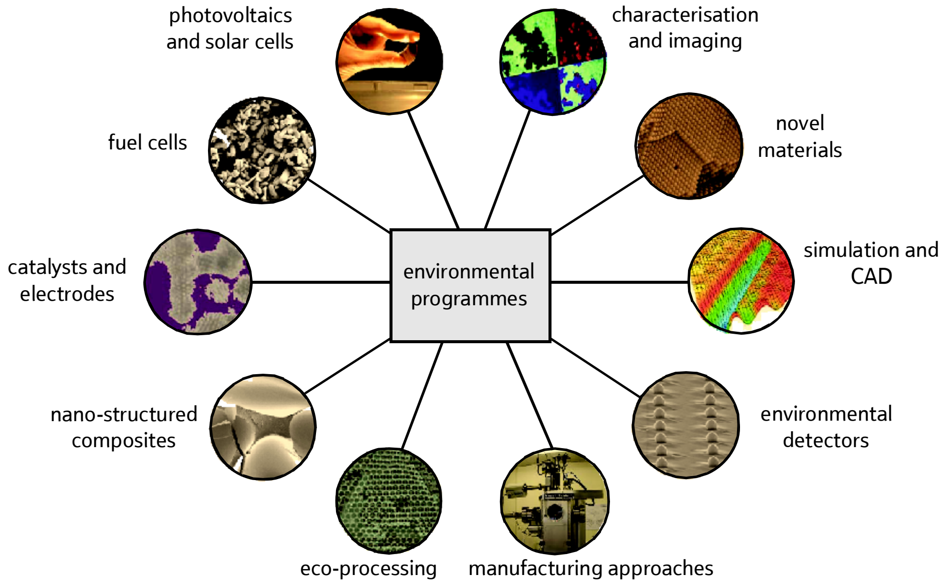

Fig 5 Example environmental programmes.

the environment. We are looking into new ways of producing and storing energy, and for ways to lower the cost of access to this technology. We are also investigating ways to improve the efficiency of various manufacturing processes such that pollution can be reduced, yet with cost savings to industry. Furthermore, we are looking at ways to reduce the weight of parts for the auto and aero-industries, reducing fuel needs.

6. The Bio-Nanotechnology Centre

This is a new development built out of LCN's successful business model. University College London and Imperial College London have jointly established the Bio-Nanotechnology Centre (BNC) with services also being contributed by the National Physical Laboratory (NPL), and the UK metrology centre of excellence, as partners to the project. This was established as part of a peer-reviewed competition with funding from UK Government Department of Trade and Industry [18, 19] and the London Development Agency [20]. The BNC, an internationally unique not-for-profit medical product development and prototyping company, aims to complete the bio-nanotechnology value chain in the UK (see Fig 6), combining the new LCN capabilities at UCL and Imperial College with the vast medical infrastructure in London and with the capabilities at NPL.

7. Conclusions

London and the UK, as is the case across the world, are gaining new and internationally competitive facilities and interdisciplinary research networks to move the perceived prospects of nanotechnology successfully through to the market-place — both for commercial and societal benefit. Nanotechnology is being treated as a core strategic area for London. University College London and Imperial College London are building substantial new infrastructure in the areas associated with medical and bio-nanotechnology, IT and the environment and new staff and capabilities are constantly being brought into London. The LCN is one such university-based organisation that is at the forefront of outward facing research, operating with the clear aim of developing solutions to improve patient care. In particular, we predict a major impact of nanotechnology on healthcare in the 21st century by taking such an approach.

On a final and important note, the LCN has chosen to deliver nanotechnology in a very transparent manner, with all of its deliverables being important to the society it serves. Ethical issues associated with the technology are addressed through its advisory and executive boards and the centre welcomes both debate and education.

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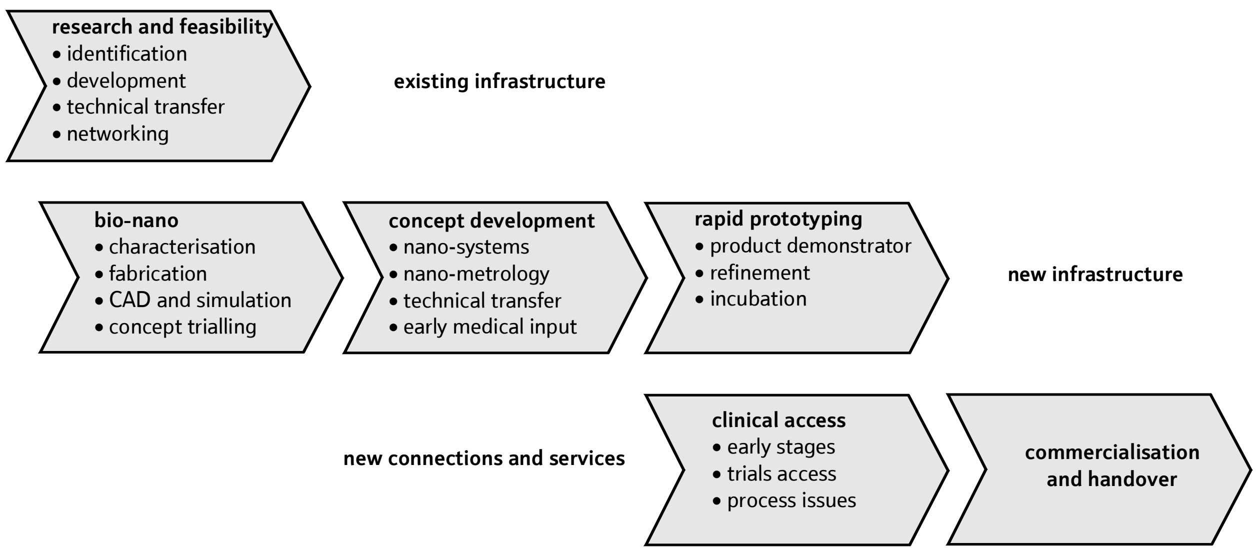

Fig 6 The UK bio-nanotechnology value chain.

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Mike Horton qualified in biochemistry and medicine from London University and pursued a career in haematology at Barts Hospital and Cancer Research UK until moving to the Department of Medicine, University College London, ten years ago. His research interests have evolved towards cellular biophysics and medical nanotechnology — especially the application of atomic force microscopy to biomedical problems with a particular focus on mineralised tissue and collagen-based diseases. Currently, he is lead for life sciences in the London Centre for Nanotechnology and is co-director of the joint Cambridge/Bristol/UCL 'interdisciplinary research collaboration' in nanotechnology, funded by the UK joint research councils. Most recently he has been involved in the establishment of the 'Bio-Nanotechnology Centre', a joint venture between UCL, Imperial and the National Physical Laboratory that is funded as part of the DTI's MNT programme together with the London Development Agency. This new not-for-profit company aims to insert itself into the biomedical nanotechnology value chain for the benefit of UK industry.

Abid Khan is Director of the Monash Institute for Nanosciences at Monash University in Melbourne Australia, which is focused on materials and devices for the biomedical and environmental areas. Prior to this, he was Deputy Director of the London Centre for Nanotechnology, in charge of Business Development and major strategic initiatives, including the creation of London's Bio-Nanotechnology Centre. Previously, he worked in strategy and operations management with Booz Allen & Hamilton, specialising in major organisational and operational change projects and was also a researcher at Oxford University. He holds a PhD from University College London and a Physics degree from Imperial College.

Simon Maddison started his career at the former PO research station at Dollis Hill working on System X, work which he continued at GEC, then followed at Siemens and Mitel. Over the last 20 years he has co-founded five start-up companies, managing the development and commercialisation of cutting-edge communications technology. He is currently with UCL's business group, developing collaborations with industry, and BT in particular. He has a bachelor's degree in Electrical Engineering and a Masters in Computer Science, both from Imperial College, London. He has recently published two books aimed at evangelising technology to school children.