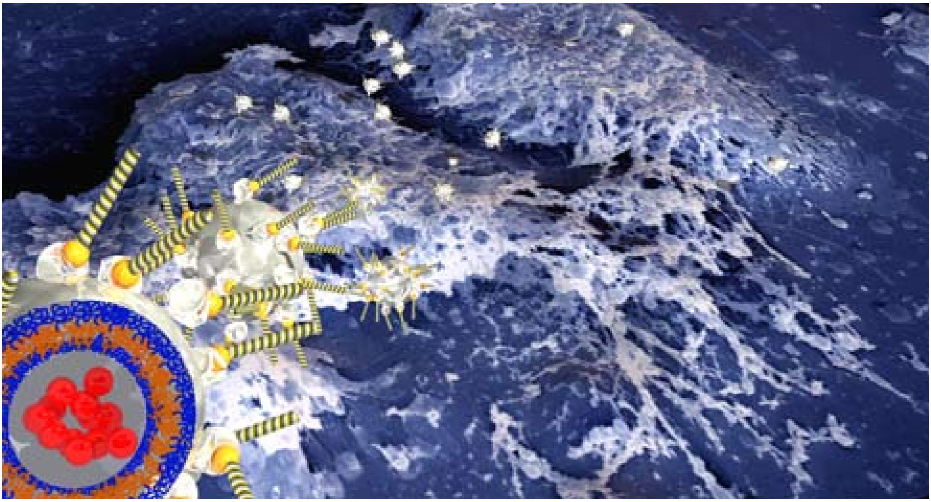
CLINAM

European Foundation for Clinical Nanomedicine

What is Nanomedicine?



Nanomedicine:
The Use of Nano-Scale Science for the Benefit of the Patient

Nanomedicine: The use of nano-scale science for the benefit of the patient

Prof. Dr. med. Patrick Hunziker, CSO of the European Foundation for Clinical Nanomedicine

Introduction

In the development of modern medicine, new scientific findings and technological developments have often served as milestones for a deeper knowledge and more effective treatments: the development of the light microscope, for example, led to the discovery of bacteria as disease pathogens, which in turn provided the platform for the discovery of penicillin as a natural, antimicrobial substance that could be used to cure infections which previously could be expected to run a fatal course. As one of the newest areas of science, nano-scale science and technology are seen by many as the key technology of the 21st century, which of course raises the question as to what role this technology will play in medicine.

This article provides a brief overview of some tools, methods and materials of nanotechnology that offer potential applications in medicine, followed by a series of examples showing applications that are already in development. The importance of these developments will then be discussed in their wider context.

The Nanometer

Nano-scale science deals with very small objects: atoms, molecules, aggregates and surfaces, for which new instruments have to be used so that these objects can be studied, "touched" and structured for specific applications. The historically separate disciplines of physics, chemistry, biology and medicine meet today in realms where things are measured by the nanometre (one thousandth of a thousandth of a millimetre), making nano-scale science a uniquely interdisciplinary field (Figure 1).

Why do we need "Nano" for medicine?

- Life is "Nano".
  The basic unit of all living organisms, the cell, is made up of numerous smaller structures, known as organelles; these consist of biomolecules that interact with one another, bringing together mechanical and biochemical functions at the nano-scale level. The molecular "nano-machines" thus form the foundations of all living organisms. "Nano" is thus not so much a technological invention of the modern age as a fundamental characteristic of all life. The development of nano-scale science has opened our eyes in this respect.
- Nano-objects can be dangerous
  The possibility of visualizing nano-objects has shown that naturally occurring Nano-scale objects can be dangerous: LDL particles (which transport cholesterol), viruses and also nano-particles in exhaust emissions lead to major and common diseases.
- Diseases are often "Nano" – the methods used in medicine today are not ...

Many disease processes begin in specific cell types with a dysfunction at the level of the cell organelles and the cellular biological “Nano-machines”. By contrast, most methods used in medicine today are either macroscopic – scalpel, radiotherapy, cardiac catheter – and thus too crude for the diseased cell, or the medicines used “flood” the body in a very non-specific way and also trigger side effects in organs that are not even involved in the disease process. It would also make sense to treat the disease processes occurring at the nano level in individual cells and organs by using nano-scale tools that can specifically target these cells and organs.

- Limited efficacy of medicine today
  Modern medicine has already achieved a lot, but has still not eradicated the principal medical problems: arteriosclerosis continues to cause myocardial infarction and stroke, leading to suffering and the need for care, as well as early death; cancers are more responsive to treatment than they used to be, but often at the cost of severe side effects; infections such as malaria continue to kill a million children a year in Africa; brain disorders in many cases lead to a loss of independence and the need for care; the incidence of diabetes is rocketing all over the world. New medical approaches for these therapeutic areas would therefore be very welcome.

Nano-scale science
New tools, new methods, new materials

Nano-scale science can be described through the tools, methods and materials used. These include, amongst others:

- Scanning microscopes – visualization and manipulation of individual atoms and molecules.
  It was the development of the Scanning Tunnel Microscope (1) and the Atomic Force Microscope (AFM) that triggered the emergence of nano-scale science. Scanning microscopes “feel their way” over surfaces spot by spot, so that extremely high-resolution images can be created right down to the individual atom. Originally used above all for physical experiments, these methods have acquired a value in biomedical imaging. The use of AFM technology as highly sensitive sensors for processes taking place on surfaces are becoming increasingly important for medical diagnostics. The unique opportunity to “treat” individual atoms and molecules mechanically using atomic force microscopes has hardly been used in medicine as yet.
- Nano-optics
  Nano-optics is concerned with optical phenomena below the wavelength of light, for example the optical visualization of individual molecules. For instance, it allows us to study the interaction of two biomolecules. Of particular medical importance is the possibility of developing sensors based on nano-optics that permit the detection of very small quantities of a biomolecule.
- Nano-materials and nano-surfaces
  The nano-scale structure of a material has an enormous impact on the pro-

perties of objects. The nano-scale sciences have led to the development of novel materials, such as carbon nano-tubes and carbon nano-balls (fullerene) with unique properties. There has also been a substantial growth in our understanding of nano-structured objects such as nano-particles, nano-sleeves, nano-carriers and nano-structured surfaces. Improved surface properties play a key role both in the biocompatibility of implants and vehicles for medicines and also in novel medical laboratory tests.

- Nano-fluidics
  Thanks to the sensitivity of new diagnostic methods based on Nanotechnology, it is possible to manage with very small sample quantities, so that a whole series of different measurements can be performed in a single drop. However, the handling of fluids in such tiny quantities calls for new methods, which fall under the heading “micro- and nano-fluidics”.
- Nano-systems, nano-devices and nano-robots
  To identify specific diseased cells in the body and to home in on them with local treatment that targets only these cells, thereby minimizing side effects while optimizing efficacy calls for nano-scale objects with complex functionality. This development of ever “smarter” systems for combating disease at the nano-level is inspired by biological models in the human body and is highly promising, but it is still very much in its infancy. In certain situations, it is also an advantage that there is no need for transferring genetic material or for the use of stem cells.

Nano-mechanics and nano-optics

- Scanning microscopy
  Scanning microscopes allow very high-resolution images of biological preparations to be produced right down to individual molecules. Since this is possible in a physiological environment, it is even possible to obtain very high-resolution images of live objects (Figure 2), and using microscopic film it is even possible to observe changes over time. This complements the possibilities offered by other microscopes, such as the electron microscope, which is dependent on very thin slices and a vacuum in order to achieve a high resolution.
- Nano-mechanical sensors
  Atomic force microscopy is based on highly sensitive measurements of the deflection made by a microscopically small lever arm as a force sensor for extremely low forces. The binding of molecules to the surface of the lever arm likewise leads to forces acting on the lever arm. This instrument thus becomes a highly sensitive sensor: in the gaseous phase, this kind of nano-sensor is suitable for detecting the complex “odour pattern” of specific diseases in exhaled air, thus allowing a rapid diagnosis (Figure 3).
- Catheter-based scanning microscopes
  Since the components of scanning microscopes may also be built very small, it is possible to construct very compact devices even on the tip of an endo-

scope (2) that is used in medicine. This enables measurements to be made, even inside the body, that are based on the force microscope.

- Nano-optic sensors
  Nano-optic microscopes exploit optical effects in the so-called optical near field, below the wavelength of light, in order to achieve very high resolutions. The transparent tips used for this, with their very small optical aperture, can also be used as highly sensitive sensors for biomolecules when these are furnished with a fluorescence mechanism that can be "switched off"; in experiments, it is even possible to detect the pairing of individual nucleic acid strands with this concept.

Nano-Fluidics

- Laboratory diagnostics
  The miniaturization of diagnostic tests that are based on the measurement of substances in fluids has crucial advantages: The quantity of samples, e.g. blood samples from premature babies or patients in intensive care, can be massively reduced. At the same time, fewer reagents are needed. Tests that are run on a surface and thus depend on the diffusion of the molecules to be measured become faster because the diffusion path is shorter. Miniaturization also allows parallelization and thus simultaneous measurement of multiple parameters in the same test. Figure 4 shows a matrix immunoassay (3) based on micro/nano-fluidics that performs multiple measurements of clinically important parameters in the smallest possible space. The vision of obtaining all parameters that are relevant to a patient from a single drop of blood within minutes appears to be within reach.

Nano-Materials

- Biocompatible implants
  The biocompatibility of implants is becoming an increasingly important issue in medicine: more and more patients, for example, have coronary stents (4), cardiac pacemakers and joint prostheses. Stents are implanted because they improve the prognosis, e.g. in coronary artery disease, by keeping the vessel dilated (5). But they are not perfect: in some patients, the vessel eventually closes again despite the stent, thereby necessitating a new intervention. More recent drug-coated stents only partially solve the problem: while late occlusions now occur less often, there is evidence to suggest that acute stent closure may occur more frequently in certain patients with drug-coated stents. Improving the structural properties of these stents, e.g. by means of Nano-structured surfaces, is one way of avoiding such problems in the future.
- Nano-bio interaction
  The interaction of cells and nano-materials is an important area of current research. Figure 5 shows the binding of polymeric (6), biocompatible and non-toxic nano-carriers (7) to cells, their uptake in the cell and the slow release of an active substance. Data from scientific studies show that optimum

biocompatibility and very low toxicity can be achieved through the selection of suitable materials for the design of such carriers. Long-term studies on the question of unexpected long-term complications, such as organ lesions, tumour development or malformations, are currently under way.

- Targeted therapy
  One of the key weaknesses of drug therapy today is the fact that most medicines entering the body can act on all the cells and organs of the body. They may well lead to the desired therapeutic effects on the diseased cells, but can also induce side effects on cells and organs not involved in the disease process. Not only is this unpleasant or even dangerous, but it also limits the dose of medicine necessary for treating the disease. This is seen especially in cancer therapy, where the high-dose chemotherapy that is often needed to effect a cure leads to nasty side effects in the bone marrow, gut, hair and other organs.
- Designer particles for molecular diagnosis and targeted therapy
  An important area of nano-scale science is therefore the development of nano-structured carriers for medical applications. The wish list of such systems is long (Figure 6): they should selectively home in on the cells and organs of the body that are involved in the disease process, specifically targeting their potent healing effects on these cells and organs, while sparing cells not involved in the disease process. They should be completely non-toxic, biodegradable or capable of natural excretion, not be recognized or eliminated by the body's own immune system before they have reached their target, and not induce any allergic reactions. Ideally, they are generic, i.e. they can be "programmed" to combat a wide variety of diseases by docking onto any target structures one chooses and being capable of carrying any medicines.

Vision: smart nano-systems
Nano-systems with a sensor and effector function

The natural functions of a living creature provide a lot of inspiration for the development of new medical methods: historically, the development of many antibiotics and cancer medicines mimicked the workings of nature. In the era of nano-medicine this fertilization of technological developments through the imitation of physiological processes is equally important.

An interesting example is the immune system: T-Lymphocytes are capable of specifically identifying cells in the body that are infected with a virus and then eliminating these specific cells that are recognized as being diseased. In its simplest form, this kind of "smart" activity requires the presence of a "sensor" that "measures" its environment and an "effector" that can be switched on and is activated when the sensor identifies a particular condition, thereby triggering a biological response. This would open the door to very much more targeted and effective treatments, e.g. of tumours or infectious diseases, than today's pharmaceuticals are able to provide. Can such a system be built in nano-scale dimensions?

Synthetic Nanotechnological organelles
Organelles are building blocks of the living cell that fulfil an independent function in the cell, have a specific biochemical functionality and often possess a biochemical compartment of their own; typical examples of organelles are mitochondria, lysosomes, the cell nucleus, the Golgi apparatus and many more. Many inherited metabolic disorders and also acquired diseases show specific biochemical defects of these organelles: every so-called lysosomal storage disease is characterized by the lack of a single enzyme in these organelles. Synthetic organelles that are furnished with this biochemical functionality could be used for the targeted treatment of these "orphan diseases" by being specifically introduced into the cells where they can substitute for the missing functions. Figure 9 shows a nanotechnologically manufactured prototype of such synthetic organelles.

Many unanswered questions
Nano-medicine is a very young field, which did not come into existence as a field of experimental research in its own right until the beginning of the 21st century. Accordingly, a lot of questions still remain to be fully answered. Research projects currently in progress, for example, are exploring the important question as to how "Nano" interacts with "bio", starting with cell/nano-particle interactions to questions of the uptake, breakdown and elimination of nano-structured objects by the whole body. In what diseases will treatment especially benefit from the new opportunities offered by nanomedicine? What are the most promising molecular "targets" in these diseases? How will these treatments change the long-term course of the disease, the quality of life and the prognosis? What is the tolerability of these treatments in the long term? Also standard toxicological questions, such as the carcinogenicity and teratogenicity of these methods, require sound and often costly and time-consuming studies.

Nano-toxicity
Nano-toxicity is a new term that is currently attracting a lot of attention. Indeed, some naturally occurring nano-structured objects are directly associated with diseases:

- The so-called LDL (low-density lipoprotein) particles that occur naturally in the body are biological nano-particles measuring about 20 nm; they serve as carriers of cholesterol in the body that is both vital and at the same time directly involved in the development of arteriosclerosis – the most common cause of death in the western world.
- Viruses that cause AIDS, bird flu and smallpox are biological nano-particles that are highly pathogenic
- Smoke from diesel engines, heating systems, fires, candles and cigarettes contain huge quantities of carbon nano-particles.

At the same time, finely structured materials have long been manufactured in large quantities by industry, whether as toners for photocopiers, surface coatings for paper, titanium oxide powder for suncreams or fullerene for cell phone batteries. For medicine it is important to understand to what extent such particles can interact with and be absorbed and eliminated by the body, and what this means in the long term. Nano-scale science in particular has opened our eyes to the importance and biological activity of the smallest objects and has also provided us with instruments and methods to study their complexity in detail. Science policy has also acknowledged the importance of these questions, as shown e.g. in forthcoming national and international research programmes on the subject of the "Benefits and risks of nano-particles".

Nanomedicine for early diagnosis and prophylaxis of diseases
Nanomedicine as an approach to diagnosis at the molecular level offers the prospect of detecting and locating diseases such as arteriosclerosis at an early stage, which can already be done in disease models, e.g. with transgenic mice. If this is confirmed in patients, there is a possibility that severe complications such as stroke or myocardial infarction, which lead to a lot of suffering, loss of independence, a chronic need for treatment and high costs, might be avoided by means of prophylactic treatment of people at risk to make the occurrence of these far-reaching events more unlikely. Will it even be possible to eradicate arteriosclerosis as a disease by means of nanomedicine?

Nanomedicine as sustainable medicine
One of the characteristics of nanomedicine is the highly targeted use of very small quantities of substance both for diagnosis and for therapy; in experimental studies, for example, certain therapeutic effects have been achieved using quantities of substance a hundred times lower than with conventional medicines. The miniaturization of diagnostic tests can considerably reduce both the amount of chemical reagents needed and also the materials needed for equipment and samples. The characteristics offer huge potential for sustainable medicine.

In summary
- Nanotechnology is very diverse
- Nanotechnology in the medical laboratory will become very important very quickly.
- In vivo diagnostic nanomedicine will offer more precise diagnosis and early detection.
- The potential for more effective treatments of serious diseases with fewer wide effects is high, and initial successes have already been reported in preclinical studies – clinical studies are under way.
- New and ongoing research programmes and abroad are investigating the benefits and also toxicity issues of nano-structured objects.

Commercial and political dimension
Nanotechnology is seen by many as the key technology of the 21st century, which will not only have a major formative influence in the main foreseeable fields of application, computer technology and medicine, but will also be of fundamental

importance for national industries and economies. As a result, the major industrial nations and political unions, above all the USA, EU, Japan, Russia and China, are investing enormous funds in the development of nanotechnology and nanomedicine.

Responsible medical research

Nanomedicine is aimed at ensuring the wellbeing of the patient and society, and not simply a propagation of new technology regardless of its implications. Responsible research in nanomedicine strives to gain a broad and fundamental understanding of nano-scale scientific tools, methods and materials, as well as their interaction with biological organisms. Basic physical and chemical research in the field of Nanotechnology is of course an indispensable part of this effort. Cell culture experiments, studies in organ sections, methods of systems biology and the use of genomics (9) and proteomics (10) methods can answer a lot of questions and should be used wherever possible to explore the bio/nano interaction. But before the step is taken to perform studies in humans, the responsible use of animal studies is still necessary today in order to arrive at an overall assessment of the interaction between nano-objects and the whole body and to evaluate longer-term favourable or unfavourable effects.

Finally, well-planned studies in humans are necessary with the promising developments of new nanomedicine-based treatment. Clinical research and the early use of new therapy in patients with otherwise untreatable diseases must not be made impossible by excessive regulatory hurdles; on the other hand, well-founded study data will of course be necessary for broad commercial use.

Realistic assessment and the ideological hijack

As with all new technological developments, Nanomedicine, too, prompts us to think about the future and arouses new hopes and old anxieties among experts as well as the wider public.

Technology enthusiasts tend to believe that new technologies are in principle a good thing, that the advantages will outweigh any disadvantages and that the latter can be safely brought under control with further technological developments.

Those who are fundamentally sceptical of technology see in any new development that bears the “technology” label a development which is essentially a threat by virtue of its unpredictability and which brings with it uncontrollable risks, so that the development must be stopped or slowed down.

New technologies are not infrequently hijacked to propagate world views: the vision of transhumanist philosophy (11), for example, declared that the so-called convergent technologies (nanotech - biotech - information technology - cognitive sciences) form the basis for a leap in development to a higher level of existence, but should also be used in the shorter term to “improve” healthy people further.

These differing points of view make it essential that a realistic assessment is made of the technology: enthusiasm for new developments must be linked with a healthy scepticism as regards the possibilities and limits; future medical applica-

tions must undergo thorough pre-clinical testing before they are used in humans, and the longer-term effects on the body must be investigated. Research must take a broad view that also includes the effects on society, ecological sustainability, questions of the developing world and philosophical implications.
This broad view of nanomedicine makes it a fascinating, interdisciplinary research field. But the necessary dialogue between nano-scale science, medicine, the humanities and society is not easy and is a major challenge during a time of ever stronger specialization in society and science (12).

The final test for nanomedicine: the patient's perspective
Ultimately, the value of Nanomedicine will be determined by the perspective of the patient:

- Which diseases that are untreatable today will actually be amenable to nanomedicine-based therapy?
- Which "orphan diseases" will it be able to cure?
- Which major diseases of our times will be better treated?
- Will we be able to afford this medicine?
- Will the developing world also benefit from these treatments?
- Will nanomedicine be ethically responsible and ecologically sustainable?
- How will it affect our society, culture and world view?

Further information can be found here

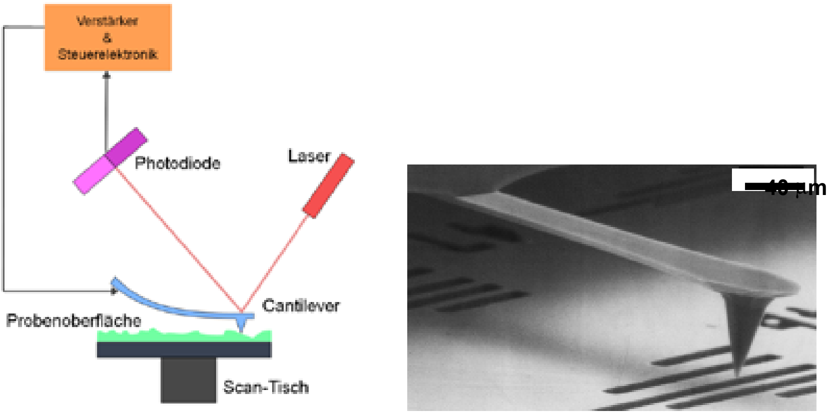
- European Foundation for Clinical Nanomedicine (http://www.clinam.org)
- European Society for Nanomedicine (http://www.esnam.org)
- Nanomedicine Research Group, University Hospital Basel http://www.swiss-Nano.org
- European Technology Platform, Brussels (http://cordis.europa.eu/Nanotechnology/Nanomedicine.htm)
- European Journal for Nanomedicine (http://www.clinam.org/journal)

Footnotes
(1) Heinrich Rohrer (Switzerland) and Gerd Binnig (Germany), both researchers at IBM Research Laboratories in Rüschlikon ZH, won the Nobel Prize for Physics in 1986 for their invention of the scanning tunnel microscope .
(2) Endoscope: an instrument used for examining (and sometimes treating) internal cavities or organs of the body.
(3) Matrix immunoassay: specific test for detecting a substance on the basis of a reaction between this substance and an antibody to it which has been prepared in the laboratory and fixed to the surface of a matrix.
(4) Coronary stents are small tubes that are introduced into the coronary vessels to keep the vessels sufficiently open to ensure that the required blood flow is adequate.
(5) dilatation catheter widening occlusions in a blood vessel
(6) Polymers: large molecular substances comprising chemically linked chains of molecular units (e.g. proteins from amino acid chains or polyethylene from ethylene chains)
(7) Carrier: Particles under 100 nm

(8) Orphan diseases: very rare diseases that are not seen by a general practitioner more than once a year.
(9) Genomics: a branch of science that is concerned with the study of the whole structure of the genome and the way individual genes interact within this structure.
(10) Proteomics: a branch of science that is concerned with the study of all the proteins in a cell or organism and the way they interact.
(11) For an explanation, see http://en.wikipedia.org/wiki/Transhumanism.
(12) The aim of the European Conference for Clinical Nanomedicine, which takes place annually in Basel, is to facilitate intensive interaction between doctors and scientists engaged in Nano-Scale science in a setting that permits both the presentation of new technological developments, clinical experiences and a critical analysis of this field. (http://www.clinam.org/conference)

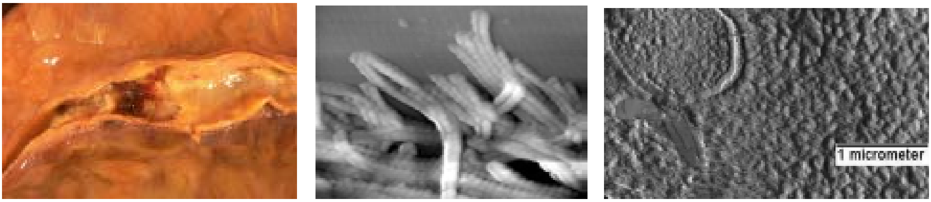
Figures

Figure 1 Atomic force microscopy



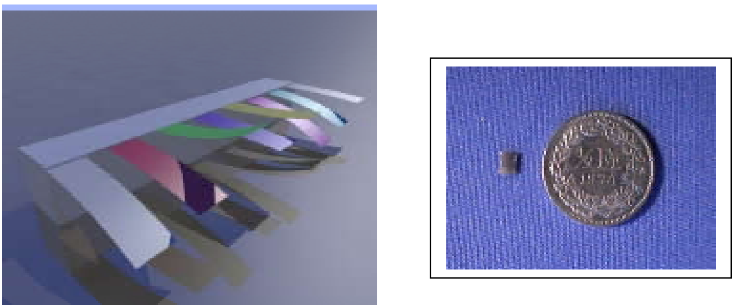
A microscopically small stylus attached to a leaf spring, the so-called cantilever, feels its ways over the surface of a sample line by line. The relief of the surface is transmitted to the leaf spring, which is deflected to varying degrees according to the scan point. This deflection of the stylus is measured by means of optical sensors and serves as a measure of the atomic forces acting between the tip and the surface. Rather as in digital photography, the point-by-point recording of the surface generates an image.
The resolution of the image depends on the radius of curvature of the stylus tip. As a rule, structures can be imaged at orders of magnitude in the range 10 - 20 nm, depending on the roughness of the sample surface, or even 0.1 - 10 nm. Under ideal conditions, even individual atoms can be imaged. The AFM and the scanning tunnelling microscope thus offer the highest resolution of all the microscopic techniques available.

Figure 2 Atomic force microscopy of biological material and live tissue



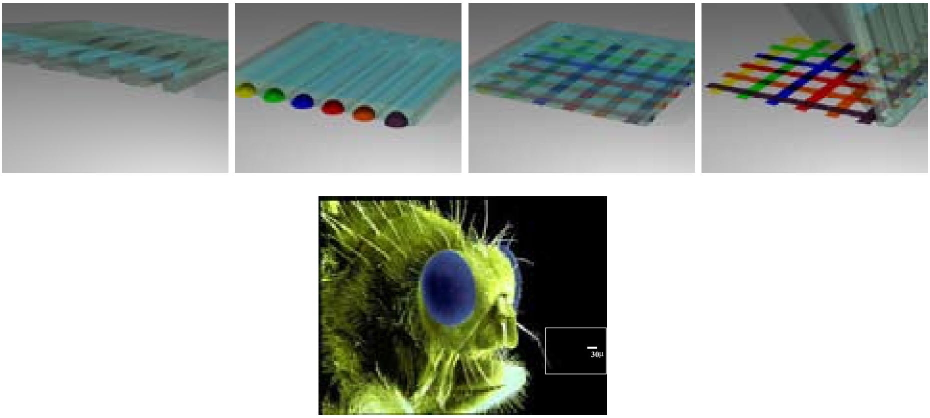
Atomic force microscopy is suitable for high-resolution imaging of biological samples and even live tissue. An artery with sclerotic lesions (above) can be examined in different magnifications: the middle image shows fibrils with a characteristic, repetitive band-like structure where the bands are separated by gaps measuring 67 nm, which corresponds to the supramolecular structure of collagen type I.
The bottom high-resolution image showing the surface of an endothelial cell in an artery goes a step further. The structures shown here measure as little as less than 30 Nanometres. Since the cell is alive, any changes and the effect of medicines on the cell can be directly monitored in real time. (Reichlin, Hunziker, Aebi, Stolz)

Figure 3 Cantilever biosensor (AFM technology) with reactive surface coating



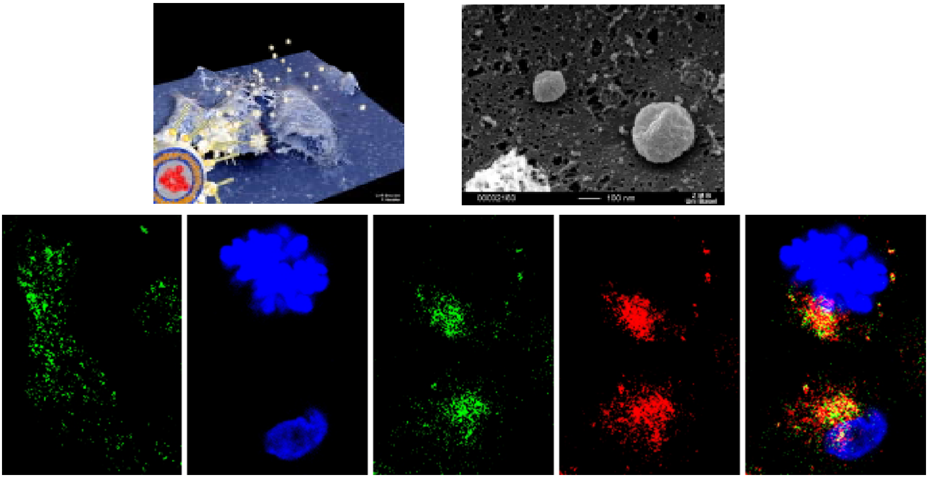
The extremely high sensitivity of the cantilever to mechanical deflections is useful for its function as a sensor. For this purpose, the cantilever on a surface is furnished with a reactive coat. When the molecules to be measured come into contact with this coating, the surface characteristics change slightly, which leads to a small, but very precisely measurable deflection. The large range of possible coatings, e.g. simple polymers of differing chemical composition, and also antibodies and nucleic acid strands, makes this an extremely versatile sensor principle. The miniscule size of the sensor, which is manufactured by means of silicon chip technology, makes its possible to measure multiple parameters in parallel. A sensor chip with 8 sensors is shown here alongside a small 50 centime coin (Schmid, Lang, Gerber, Hunziker, Eur.J.Nanomed 2008)

Figure 4 Nano-fluidics: multianalyte immunoassay in nanolitre samples



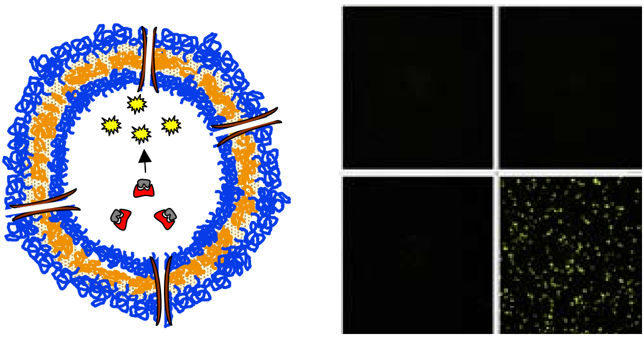
Very small quantities of liquid are used in nano-fluidics. The top pictures show the functional principle of a nano-fluidic sensor for multiple analytes: binding molecules (e.g. antibodies) are applied to a measurement surface through micro-structured channels, as a result of which a very small pattern of lines appears on the surface, which is capable of specifically binding different analytes. After rotation of the channels by 90 degrees, a sample can now be applied: one-hundredth of a drop of blood is enough to fill a sample channel. The binding molecules present on the measurement surface bind the analyte. The last step entails the application of a marker, e.g. a fluorescently labelled second antibody, which shows the position and quantity of the bound analytes. The reading device now shows a pattern that displays a “mosaic” of measurement points, which can be measured automatically. The middle row of images shows the result of such a test (picture insert) in comparison with the size of an insect head. On an area the size of a finger nail there is space for >50,000 measurement points. (Wolf, Delamarche, Hunziker, Michel et al, Biosensors and Bioelectronics, 2003)

Figure 5 Interactions on nano-structures with biological cells



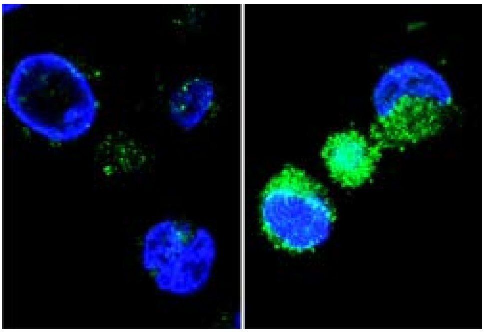
Biocompatible polymers can be used to make ball-like containers whose cavities can be charged with materials of any kind, e.g. medicines, and whose surface can be functionalized in such a way that they bind specifically to cell surfaces of target cells (upper diagram). Below this is an electron microscopic image that shows one such container measuring 100-200 nm (left and centre; right after binding to a cell). The bottom row of images shows the interaction between “Nano” and “bio”: the nano-containers (red) can be transported into the cell, where they find their way to specific intracellular targets: the containers shown in this example are migrating to the so-called Golgi apparatus, which is coloured green in the central image. By contrast, these nano-containers avoid both the mitochondria (left image, green) and the cell nucleus (blue). The bottom series of images shows the degradation of the nano-containers over the course of 2 days with the slow release of a green dye as an example of drug release. (Broz, Benhaim, Hunziker & al.)

Figure 6 Prototype of a “smart” nanocarrier



A nanocarrier that can specifically respond to changes in the surrounding conditions has to possess a sensor function. In the prototype shown here, the shell of the nanocarrier features pores that open and close depending on the surrounding conditions. In addition, the carrier has been charged with an enzyme that switches on when the pH value falls below 6 and then produces an enzymatic product. A fall in the pH from 7.4 to 5 typically occurs when a medicinal nanocontainer binds to its target cell and enters the lysosomes. This sequence of events is shown under fluorescence microscopy: nanocarriers with no channels (2 left images) are unable to detect the surrounding conditions and are therefore not switched on. Nanocarriers fitted with channels and featuring pH-sensitive enzymes (2 right images) are inactive in the blood (top right), but begin their biochemical function when the pH falls to 5 (bottom right), which is shown in the enzymatic production of a yellowish-green fluorescent substrate. (Broz, Hunziker et al, NanoLetters 2006)

Figure 7 Artificial nanomedicine-based organelles



Certain genetic diseases occur as a result of the genetically determined absence of certain enzymes in the subcellular organelles. The miniscule size of the nanocarriers, their high degree of stability when a suitable wall composition is selected, and also the possibility of selectively investing the target cell with a biochemical function that it is lacking enable artificial organelles to be developed: while the cells on the left lack a biochemical function (shown by the low level of production of bright red metabolic product), this function is restored in the cells on the right by means of artificial nanomedicine-based organelles. (Benhaim, Hunziker et al, NanoLetters 2008)

CLINAM

European Foundation for Clinical Nanomedicine

Alemannengasse 12, P.O.Box, 4016 Basel, Switzerland
Tel. +41 61 695 93 95 Fax +41 61 695 93 90
Mail Clinam@clinam.org