Journal of Geoethical Nanotechnology
Vol. 9, Iss. 1 (2014) 76 - 85


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# NANOSCIENCE, NANOENGINEERING AND NANOTECHNOLOGY

LAJOS (LOU) BALOGH, PHD

*Board Member of the American Society for Nanomedicine &*
*Member of the US Technical Advisory Group to ISO Nanotechnology.*
*baloghlp@gmail.com*

Dr. Lou Balogh sheds light on the term ‘nanotechnology’ and its science, engineering and policies for practical and sustainable human purposes.

*Keywords*: Lou Balogh, nanoscience, nanoengineering, nanotechnology, sustainable, nano, biology, chemistry, nanoscale, quantum, National Institute of Health, NIH, Environmental Protection Agency, EPA, Food and Drug Administration, FDA, National Science Foundation, NSF, nanometer, International Organization of Standardization, ISO, Nanotechnology Technical Advisory Group, nanotubes, nanoparticles, nanorod, nanodiamond, nanogold, nanosilver, nanorobot, nanodevice, nanomachine, macro, micro, anthropomorphic, millimeter, micrometer, nanomedicine, nanoscopic, metallofullerenol, metastasizing, nanofiber, tumor, cancer, cells.

Before we can talk about any sustainable nanotechnology[1], we have to find out what “nano” and “technology” really mean. I’m going to discuss nanoscience[2], nanoengineering[3] and nanotechnology. We all know that there are many, many definitions for “nano”, although as a matter of fact, everybody has a different definition or a certain kind of personal understanding of these words. Unfortunately, we use the term “nanotechnology” often without much forethought and project our own understanding behind it. Let me point out that nanotechnology isn’t really different from anything else.

[1] Nanotechnology is the technology to put the nanoscience and nano-engineering to practical use. Technology always requires commercialization and assumes manufacturing, i.e., production of goods.

- The nanoscopic range is transitional between molecular and bulk. Here individual molecular properties are modified by the emerging collective/cooperative behavior between the components of the given system until individual states become indistinguishable from each other.
- Due to the large contact area, surface contribution is prominent.

[2] Nanoscience is the science of nanoscale materials and objects. As such, it is part of all disciplines of natural science.

[3] Nanoengineering is the practice of engineering on the nanoscale. i.e., the process of designing and making predictive models, tools, machines, apparatus, and systems to exploit basic and applied nanoscience. Engineering is always quantitative.

There are so many terms for 'nano' and the number of these definitions seems to be growing every single day. Why do we have so many terms and definitions for 'nano'? What is the reason? We all know that communication may become a serious barrier between people. The example in the graphic at the top of the next page is of a verbal communication, but also thought communication that if you look at it, the person on the left, (I'm 100% certain) is an organic chemist. The redhead is a mathematician and the third guy, with the beard, is a biologist. The fourth one isn't even a scientist; he's probably someone who takes care of the inventory. One little mouse at the bottom of the slide is asking, "Why don't they understand each other?" But, the other little mouse doesn't care. She's just thinking about the cheese.


There are several reasons for the confusion concerning 'nano'-words. First of all, the scientific meaning of nano contradicts to all other recent definitions. The original **meaning of 'nano' is simply $10^{-9}$ times of something**, without telling us what is it. In other words, 'nano' is prefixed to the name of a unit of measurement to denote a factor of $10^{-9}$. Consequently, nanoscale can be assigned to any dimension; for length, which is measured in meters, the nanoscale regime is naturally between 1 and 1000 nanometers. The second major source of confusion is **the way nano related terms are created and used** in every-day life and even in scientific life. Number three reason is **defining "nano" as a "*characteristic property*"** and/**or unique phenomena *within 1-100 nm due to the size of the object.***

These definitions can be divided into three groups. In the **first group** there are the **scientific definitions** that **are created by scientists for scientists**. Scientific definitions themselves are not necessarily identical; there are many versions depending on what specific area the particular research was done. For example, "quantum-dots are nano-meter sized crystals of semiconductors". This is a precise definition, but it could not be efficiently used in public arguments. Without knowing what nanometer, quantum and semiconductor are, it is very hard to understand what is it all about.

The **second group** of definitions is what I call '**decision-enabling'** definitions. These definitions are generated by various agencies, funding, regulatory agencies, and policy makers like the National Institute of Health[4] (NIH), the Environmental Protection Agency[5] (EPA), and the Food and Drug Administration[6] (FDA), etc. The first nanotechnology definition was actually created by the National Science Foundation[7] (NSF), stating that: "Nanotechnology is the understanding and control of matter at dimensions of roughly 1 to 100 nanometers, where unique phenomena enable novel applications." (2004 NNI Strategic Plan). Let me reiterate, these decision enabling definitions (and there are many of them), are **created by agencies for** those **agencies** because they have to draw clear guidelines to make decisions. If NIH comes up with a definition in its "Call for Proposals" and declares (as they have already done), that a nanometer range is below 360 nanometers, that's their own definition for that Call. If your research subject is above that limit, you are not eligible to apply. If your subjects are below that limit, your proposal does qualify. Specific policies, intentions, and interests always influence these definitions. Typically, 'decision-enabling' definitions are created by consensus of committee members. However, as the membership of committees and the interests of committees keep changing, these definitions also change over time. I am a member of the TC-229, the U.S. Technical Advisory Group on Nanotechnology to ISO, the International Organization for Standardization[8]. This committee was initiated several years ago, but there are still recurrent discussions about what nanotechnology is, and what the definition of nanotechnology should be. Once we get to the point that everyone can agreed what the definitions are, then a constant effort is needed from the members to maintain and use those definitions. Then, there is also a need to develop a plain language guide, to make the nano-words more understandable by the public.

And the **third group** of definitions is '**public' definitions**. Journalists create these when they attempt to translate scientific definitions or decision-enabling definitions for the general public, usually attaching the adjective "nano" to examples from the macro-world.

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[4] The National Institute of Health – the medical research agency of the United States and part of the U.S. Department of Health and Human Services. Retrieved from http://www.nih.gov/about/.

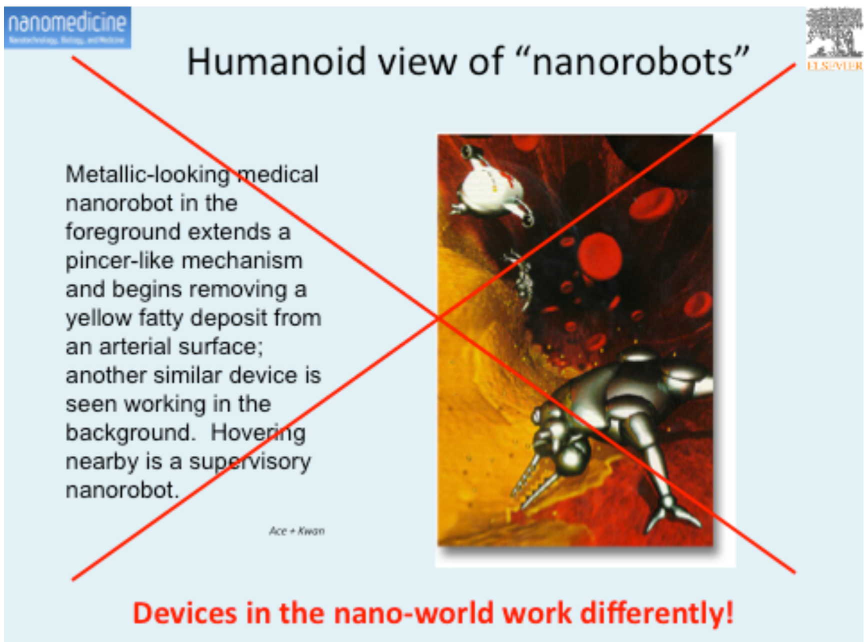
[5] Environmental Protection Agency – established in 1970, one agency within which a variety of federal research, monitoring, standard-setting and enforcement activities to ensure environmental protection. Retrieved from http://www2.epa.gov/aboutepa/epa-history.

[6] Food and Drug Administration - a scientific, regulatory, and public health agency that oversees items accounting for 25 cents of every dollar spent by consumers including: food products (other than meat and poultry), human and animal drugs, therapeutic agents of biological origin, medical devices, radiation-emitting products for consumer, medical, and occupational use, cosmetics, and animal feed. Retrieved from http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm.

[7] National Science Foundation - an independent federal agency created by Congress in 1950 "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense…" Retrieved from http://www.nsf.gov/about/.

[8] ISO Nanotechnology – the International Organization for Standardization is the world's largest developer of voluntary International Standards. Retrieved from http://www.iso.org/iso/home/about.htm.

We must be very careful because our minds work by association of ideas, thoughts, and activity. Macro-word examples using shape and referring to composition (like nanotubes, nanoparticles, nanorods, nanodiamond, nanogold, nanosilver etc.) are correct and okay to use; there's not much confusion there. However, all those nano-words that are associated with some kind of **action or activity** (e.g., nano-robot, nano-device, nano-machine, etc.) may bring up incorrect associations because they suggest that a nano-robot or a nano-device is like its macroscopic or microscopic version, but much smaller, which is not true. It is not true because things work differently on the nanoscale then on the macro or the micro-scale. And we'll go back to that point soon.



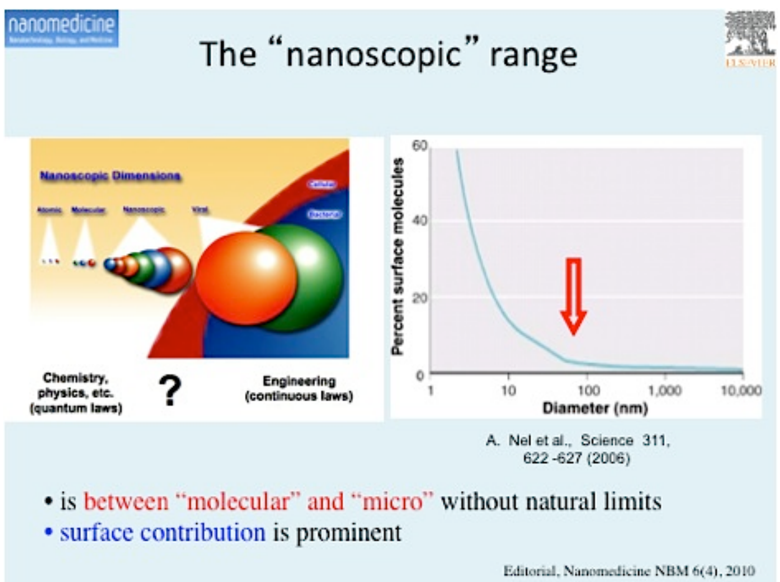

We all have an inappropriate anthropomorphic view of nano-robots. I choose this particular picture because it is a superior example of what to avoid (and I also crossed it to remind us that it is actually not true). Let's read what is written within this graphic: "Metallic-looking medical nanorobot in the foreground extends a pincer-like mechanism and begins removing a yellow fatty deposit from an arterial surface;" … and just to complete the humanoid view of the artist …"another similar device is working in the background. Hovering nearby is a supervisory nanorobot supervising these two guys. Do they really need a supervisor? NO. Devices in the nano-world work very differently than those in the macroscopic range.

In the definition of the International Standardization Organization, there is no mentioning of size - only structure-dependent properties and phenomena are emphasized, to be "distinct from those associated with individual atoms or molecules or with bulk materials". Manipulation and control includes material synthesis. That's just another example; there are many, many agency definitions.

Business is built on technology, engineering and science. Development of any product necessitates crossing these sequential layers of science->engineering->technology to be able to commercialize the product and run a successful business. Adding "nano" to 'science' or 'technology' does not change this hierarchy. The basis is science, followed by engineering. The next layer is the development of a technology. Commercialization is impossible without a technology. A business must earn a solid profit to be sustainable. Of course, these systems are all surrounded by society, and any product, which cannot be sold, will not be put to use e.g., in the clinic. As I've said, adding "nano" does not change this hierarchy. The same drivers work for traditional and 'nano'-products: (a) society needs new knowledge ('pull') and (b) scientific interests often create new knowledge ('push'). For any product, there must be a business opportunity. This also means that just because a product is new, it will not automatically guarantees business success, and the 'new' has to win over the 'old' technology. To further complicate matters, in a society, business interests and technology interests may also differ.

The success of any product is measured in the market. This market could be private enterprises or could be government. This is especially true for medicine and nanomedicine. In fact, 'nanomedicine' does not exist without medicine; nanomedicine is merely a part of medicine.

Development of any nanotechnology-based or enabled product must consist of good science, creative engineering, reliable technology, and rational policies that provide a solid profit for businesses, either private or government, while keeping our world sustainable.




To understand the nanoscopic range on scientific terms, let's carry out a thought-experiment and take a very simple object: a spherical, small object on the nanometer scale. So we have one object with a well-defined shape, composition, architecture, etc.; - everything can be determined. If we have two of these, we can put them together only one way. If we have three, they can be oriented in two ways, now we already have two different kind shape for the same "particle". Let's put together four of them. Now the change is even larger, it's the same material with the same basic components, but we already have three different orientations. After the next step it is five different orientations, and so on, and so on.

The relative change, after adding the first particle, is fifty percent. After the second step, the change is thirty percent. The next step of is twenty-five percent. The relative change between individual is less and less until the number of objects forming an object is large enough that we cannot observe change anymore. In the left (small) side of the nanoscopic range, (by definition), atoms and molecules are not nanoscopic objects. We need at least two atoms or molecules to form a nanoscopic object. In the right side of the graph let's recognize that there is no natural limit, no border, no sudden change, nothing, and it just goes to bulk behavior.

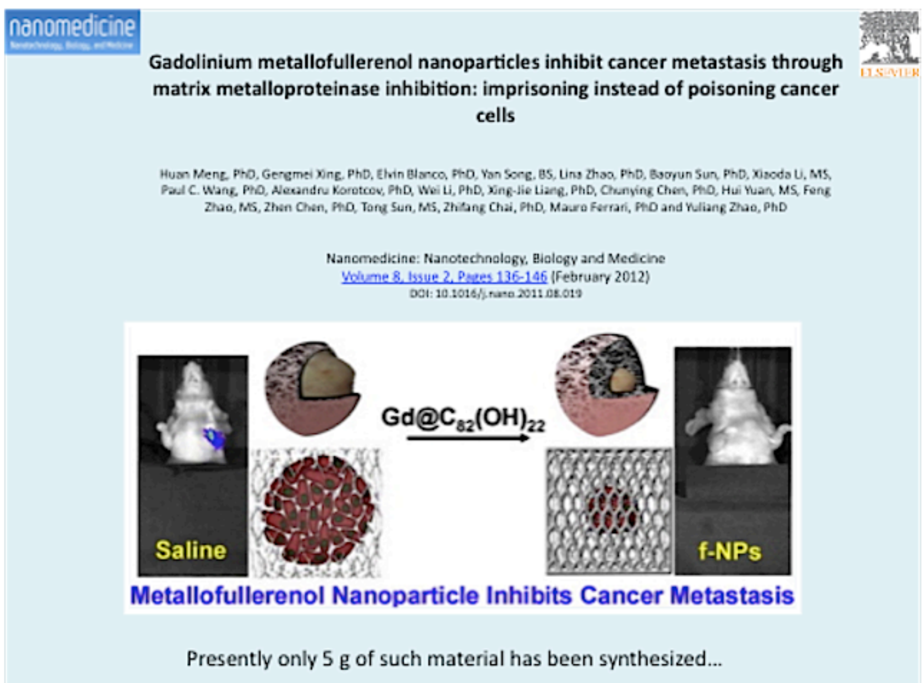
The nanoscopic range is really a transition between molecular and micro (bulk) properties that are modified by the emerging collective / cooperative behavior between all components of the system. Let's remember that even the simplest, spherical nanoparticles can be put together in many, many different shapes.

We can also approach this problem in a different way. On the left side of the graph we have chemistry, physics and those sciences; everything obeys quantum laws. On the right side there is engineering and classic physics, where everything obeys continuous laws. So the question arises, what is in between? Will these laws act simultaneously; or will they transfer from one to the other? The answer is that exactly the in this transitional "nanoscopic" range - between "molecular" and "bulk" - the properties are due to the emergent collective behavior between all component of the system.

Of course, because nanoparticles are very small, the surface contribution is prominent and very important. A rock is a rock, whether it is wet or dry, but if in a system nanoparticles are four nanometers in diameter, the surface of 1 gram material amounts to almost 300 square meters., No, for nanoparticles the medium is not negligible anymore, and whatever is on the surface, becomes part of the system. The red arrow on slide#19 points at 100 nanometer - and this came up in the first NSF definition of nanotechnology -, that value happens to be in the range where the relative change of properties is very small and the surface contribution, is not really prominent anymore. Below that value, the relative change in size-related properties is large, and the surface contribution is much larger (because the smaller size means larger relative surface). That's the origin of the "100 nm" definition, below which we were excited to find new properties.

The nanoscopic range always existed, we were just unaware of it because we didn't have the proper tools to observe, measure, or manipulate things in that range; now we can. That's where the new science, new knowledge is, and we are working on how to use that new knowledge.

Nanoscience is the science of nanoscale man-made materials and objects; and as such, it is **part of all disciplines of natural science,** because in every one of them there is a range that is nanoscale. In Chemistry there is nanoscale, in physics there is nanoscale, it is present in every and all disciplines of natural science. I'll give you two examples:. The first "nanoscopic" concept is not to kill, but to incarcerate cancer cells. Evidence of this scientific leap is the discovery that was made by a Chinese scientist that a certain kind of metallofullerenol nanoparticle[9], (it doesn't matter what is it, exactly), when injected into mice it does not cure the cancer (that little spot on the left side in the graphic below shows the position of the tumor) but these small particles adhere to the surface of the tumor, they surround it, and the nanoparticle completely stops the tumor growth and does not let it to metastasize. The mechanism and that how it happens, doesn't really matter at the moment. What matters is that something new is there now, which we have not observed before. (Very few people die from primary tumors, almost everybody dies from the metastasized tumors.) However, presently only five grams of such material has been synthesized. Clearly it is a great discovery, but it is still in the early scientific stage; we're also beginners at nano-engineering.




My next example is a short circulating peptide nanofiber. These peptide nanofibers are made from blood compatible materials. Their left and right side form strong bonds with each other. Many people are trying to target cancer cells and cancerous tumors by nanoparticles.

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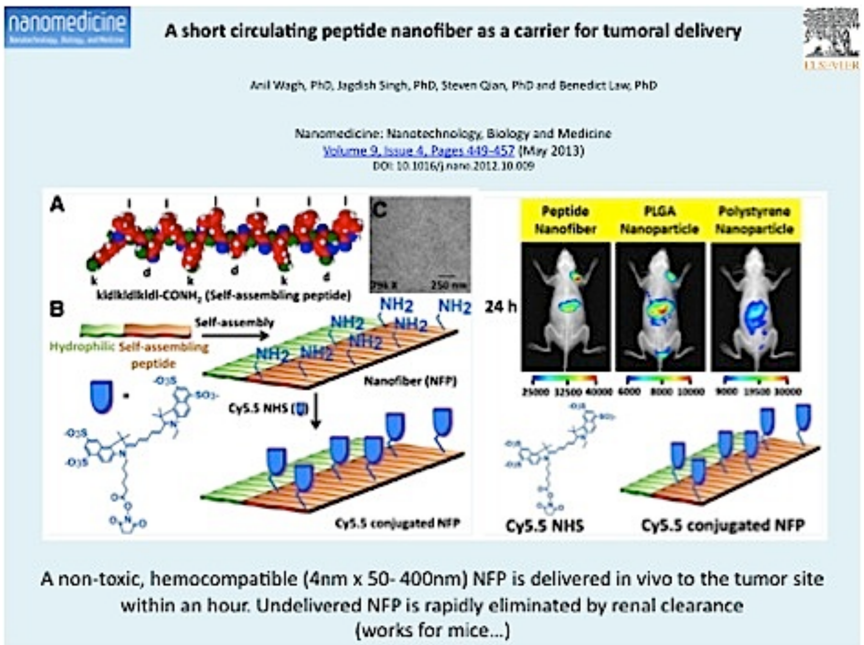
[9] Metallofullerenol nanoparticle – a potent, biocompatible nanomedicine that inhibits and imprisons cancer cells and reverses drug resistance. Meng, H. et al. (2012). Gadolinium metallofullerenol nanoparticles inhibit cancer metastasis through matrix metalloproteinase inhibition: imprisoning instead of poisoning cancer cells. *Nanomedicine, NBM, Vol.* 8:2, pp. 136-146.

Essentially the tumors are not really a problem. The real problem is metastasis, where the individual cells circulate, and initiate very small tumors, which cannot be surgically removed. Now, let's go back to these very small fibers. What the researchers have figured out is that by injecting these very small ('nano-sized') fibers in the blood, they self-assemble on the tumor site and become a large shield surrounding the tumor. That's a very efficient position allowing very efficient imaging. Once the tumor cells are identified, doctors can use all kinds of methods to destroy those cells. This method works perfectly for mice. However, we have no idea at the moment how it would work for people.

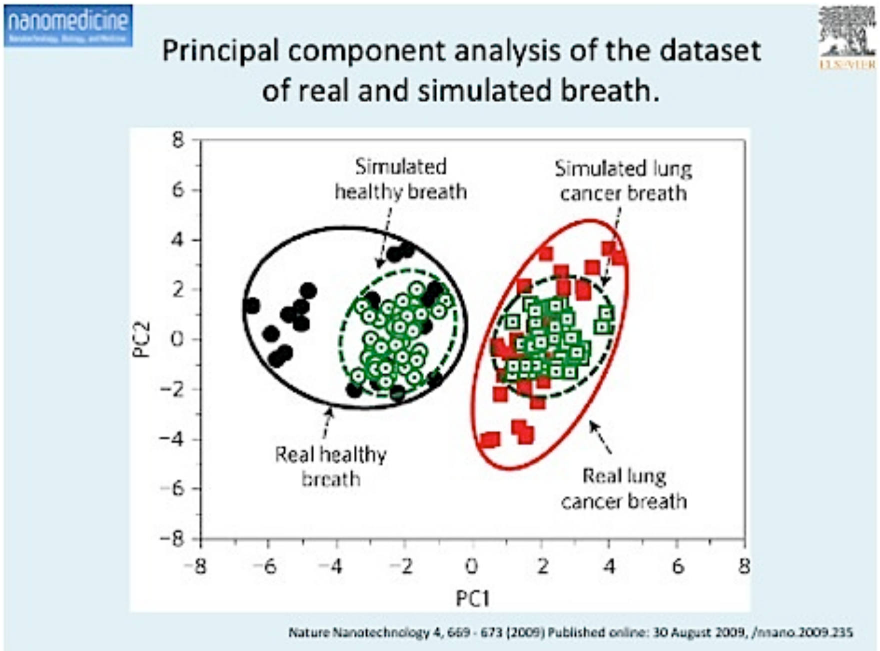



Nanoengineering is the process of designing and making predictive models, tools, machines, apparatus and systems to exploit basic and applied nanoscience for practical human purposes. What is very important that engineering is always quantitative? There is no approximation in engineering. It's not an 'almost' approach, you have to be able to make a device that works. I'll give you three examples.

The first example is nanoengineering detecting lung cancer biomarkers in the air. It's the work of Hossam Haick[10] at Technion in Haifa, Israel[11]. The concept is that when someone has lung cancer, the various biochemical processes in the lung are different from the healthy case, so the air breathing in is the same, but the composition of what you breathe out is a byproduct of

[10] Hossam Haick – Faculty member of the Israeli Institute of Technology (Technion), Department of Chemical Engineering. Retrieved from http://ceweb.technion.ac.il/Hossam_Haick.htm.
[11] http://www.technion.ac.il/en/.

cancerous cells, so the composition is somewhat different because of the cancer cells the lung contain.




The patient breathes into an electronic nose for thirty seconds, the air goes through a whole bunch of sensors, doctors compare the measured signals and they can determine with a high probability whether the air is from a healthy breath or if there some kind of serious issue. This particular graph taken from our journal (above) is of a simulated healthy breath and simulated lung cancer breath responses - they can clearly be differentiated. This project is now in clinical II trial and they are testing the device on thirty to thirty-five lung cancer patients. The identification of lung cancer with this method compared to other methods is ninety-five percent accurate. Wouldn't it be great to have this method commercialized? First, operation of lung cancer is not that easy, Especially in countries, where smoking is dominant (not only cigarette smoking but all other kinds of substances are being smoked), the diagnosis comes often very late and it is very hard to fix this problem after the cancer started.

This is engineering, demonstrating a working instrument. The details are less important than the principle.

There is a need for fast, highly sensitive and quantitative techniques detecting and profiling altered cells. The most precise method to identify a tumor is needle biopsy, and it takes about two weeks to confirm the result by various biological methods. Based on a biopsy, a doctor will definitely be able to tell if there is a breast cancer, what kind of cancer is that exactly, and so on. However, I don't envy anybody who has to spend two weeks waiting for his/her diagnosis.

With this next technique, scientists use a special needle, which is non-magnetic and the biopsy sample in the needle is put into an instrument that is able to determine within fifteen minutes whether it is lung cancer or breast cancer cells are present or not. I think this is a very significant engineering achievement, which is now undergoing technological development and business development as well.

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