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NANOETHICS – A NEW CHAPTER IN ETHICAL STUDIES

NANO-ETIKA – NOVO POGLAVLJE ETIČKIH STUDIJA

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Abstract
Nanotechnology as a natural continuation of microtechnology introduced a new way of building molecular structures through bottom-up methods. The approach provides numerous new opportunities in information technology, medicine and new materials; however, it also brings new risks. In the paper we summarize a brief history of nanoscience and nanotechnology by documenting the main milestones on the roadmap of this branch since the beginning of the 20th century. We discuss new properties of materials and structures appearing in the nanoworld. We highlight the role of social sciences and humanities in nanoscience. Attention is paid to new threats originating in this field, as well as to the code of conduct of responsible nanoscientist. The issues represent subjects of nanoethics – a discipline that opens up a new chapter in the ethical studies. In this context we summarize the basic problems of the contemporary nanoethics, which deal with human enhancement and related religious and theological aspects, nanotoxicology, regulations and specifics of intellectual property rights in nanotechnology. Economic implications, especially the possibility of bridging the nanodivide currently appearing between developed and developing world, are discussed as well. We conclude by arguing that nanoscience and nanotechnology open up new horizons in the field of philosophy. There is a need to overcome the ambivalence of public opinion towards nanoscience and nanotechnology by the means of providing correct and opened information and continuous technology assessment.

Sažetak
Nanotehnologija kao prirodni nastavak mikrotehnologije uvodi novi način izgradnje molekularne strukture kroz metodu „od dna prema gore". Pristup omogućuje brojne nove mogućnosti u informacijskoj tehnologiji, medicini i kod novih materijala; međutim, to također donosi nove rizike. U radu se ukratko daje pregled povijest nanoznanosti i nanotehnologije dokumentirajući glavne prekretnice na razvojnom putu ove grane od početka 20. stoljeća. Raspravlja se o novim svojstvima materijala i struktura koji se pojavljuju u nanosvijetu. Izdvajamo ulogu društvenih i humanističkih znanosti u nanoznanosti. Pozornost se posvećuje novim prijetnjama podrijetlom iz ovog područja, kao i na pravila ponašanja odgovornog nanoznanstvenika. Pitanja predstavljaju predmete nanoetike - discipline koja otvara novo poglavlje u etičkim studijama. U tom kontekstu možemo sažeti osnovne probleme suvremene nano-etike koja se bavi ljudskim poboljšanjima i srodnim vjerskim i teološkim aspektima, nanotoksikologijom, propisima i specifičnostima prava intelektualnog vlasništva u nanotehnologiji. Ekonomske posljedice, pogotovo mogućnost premošćivanja nano-jaza, trenutno se pojavljuje između razvijenog i nerazvijenog svijeta, također se diskutira u radu. U zaključku tvrdimo da nanoznanost i nanotehnologija otvara nove vidike na polju filozofije. Postoji potreba da se prevlada ambivalentnost javnog mnijenja prema nanoznanosti i nanotehnologiji sredstvima koja pravilno i otvoreno prenose informacije i kontinuirano prate tehnologiju.

Introduction

Nanoscience and nanotechnology (N&N) is a rapidly expanding area. They cover design, preparation and applications of materials and structures having at least one dimension within the interval from 1 to 100 nm (1 nm = 10^{-9} m). At the left margin it touches the quantum world. At the right margin the interval adjoins the sub-micrometre region 100 – 1000 nm (1 μm). Typical nano-objects are molecules, atomic clusters, nano-crystallites, nanoparticles (NP), nanowires, nano-layers, etc.

In order to illustrate the fast progress and main principles of N&N, in Box 1 below we provide selected statements by well-known scientists and Nobel Prize (NbP) laureates in the field /**1, 2**/. The last of these statements implicates that politicians, researchers, producers and consumers of nano-products must pay attention to risks and to ethics of N&N.

Box 1 Famous statements about N&N

Atoms cannot be perceived by senses. They exist only in our imagination.

Ernst Mach, 1900

The principles of physics do not speak against the possibility of manipulating things atom-by-atom.

Richard Feynman, 1959

Nanotechnology is the art of building devices at the ultimate level of finesse, atom-by-atom.

Richard Smalley, 2000

Those who control nanotechnology will lead the industry.

M. Nakamura, Hitachi

Biggest breakthroughs in nanotechnology are going to be in the new materials.

T. Kirkpatrick, General Electric

Our ability to reap the long-term benefits of nanotechnology will depend on how well industry and governments manage the safety and performance of the first generation of nanotechnology products.

A. Maynard, University of Michigan

In Box 2 below we enumerate main milestones in N&N as summarized in /**2, 3, 4**/. Many of them have been awarded by NbP. They document that the fundaments of nanoscience have been laid since the early 20th century. N&N currently represent a common denominator for the recent developments in chemistry (nanochemistry), biology (nanobiology) and medicine (nanomedicine), whenever these disciplines touch upon the dimension of a single molecule. The interactions obey the laws of physics which are valid up to the level of elementary particles. Therefore we do not speak about nanophysics.

1. Extrapolation of microtechnology into the nanoworld

N&N are a continuation of five decades of miniaturization and growing level of integration described by the Moore's law /**5**/. Its original formulation was born in 1965 when G. Moore noticed that the number of components per integrated circuit for minimum component cost increased roughly by a factor of 2 annually between 1962 and 1965. He predicted that the rate would remain constant for at least 10 years. His prediction proved to be accurate: the number of transistors on integrated circuits has been doubling approximately every two years since 1965. Nowadays the Moore's law approaches physical barriers and the role of N&N grows.

The breakthrough in N&N was scanning tunnelling microscope (STM) having atomic resolution /**6**/. In this device the information is not obtained by using radiation but by mechanical sharp probe scanning over the surface at a very small distance and imaging its topography**.** Afterwards also other types of scanning probe microscopes were created, especially atomic force microscope (AFM). These devices are also used for manipulation of atoms or molecules. In this way the Feynman vision /**7**/ of manipulating the matter atom-by-atom has been fulfilled at least at the laboratory scale, because the process is too slow for practical applications. Anyway, STM heralded the emergence of N&N /**8**/. Nowadays the structures are not synthesized atom-by-atom but from bigger blocks, e.g. from nanoparticles composed of thousands of atoms. This additive process is called *bottom – up* approach. It is complementary to the *top – down* formation of structures, broadly used in micro- and nanoelectronics.

Box 2	**Summary of main milestones in N&N**
1905	A. Einstein estimated the diameter of sugar molecule at about 1 nm.
1931	M. Knoll and E. Ruska invented electron microscope, NbP.
1959	R. Feynman presented his talk "Plenty of room at the bottom".
1974	N. Taniguchi conceived the word *nanotechnology.*
1981	G. Binnig and H. Rohrer invented scanning tunnelling microscope, NbP.
1985	R. F. Curl, H. W. Kroto and R. E. Samlley discovered fullerenes, NbP.
1986	K. E. Drexler published his book *Engines of creation.*
1988	A. Fert and P. Grünberg discovered GMR, NbP.
1991	S. Iijima discovered carbon nanotubes.
2000	W. Clinton announced NNI of USA.
2004	A. Geim and K. Novoselov isolated graphene, NbP.
2007	M. C. Lemme et al. fabricated graphene FET.
2008	The force to move an atom over surface was measured at Almaden Res. Ctr.
2012	A. Bérut et al. verified the minimum amount of energy kTln2 (Landauer principle, 1961) required to change one bit of information.

2. New phenomena and qualities in the nanoworld

New qualities of materials and structures that appear when we enter the nanoworld are discussed in /**7**/. They originate from classical and quantum phenomena. In the realm of classical physics we must consider at least:
a) Large surface to bulk ratio;
b) Small size of nano-entities.
Ad a) In a 1 nm particle almost all atoms are on the surface /**9**/**.** This manifests itself in the decrease of the melting temperature. Gold nanoparticles with the diameter of 2 nm melt already at 500 ^{o}C because of smaller number of bonds to the neighbouring atoms. *Per analogiam,* in the nano-world many properties are changing dramatically: insoluble substances become soluble, non-inflammable things are burning. Chemically toxic materials like As, Cd, Co show toxicity in bulk. In the nanoworld we also speak about physical toxicity. Large effective surface of structures generates free radicals with threatening consequences, such as inflammations of lungs, fibrosis or tu-

mors /**10**/. In this way a conception that all nanoparticles are toxic was born.
Ad b) Small nanoparticles penetrate through membranes, opaque films become transparent, nanoparticle solutions are coloured depending on their size. Another example of utilizing the small dimensions are nanoclusters in the matrix of material (e.g. ceramics) that increase its strength /**11**/.
The most interesting phenomena are introduced through entering the territory of quantum physics. Some of them could be exploited in the future quantum computing and quantum encryption /**12**/.

3. N&N in the era of productivity

New technologies typically pass through the cycle of hyperbolic expectations. Five phases of this cycle can be characterized as follows /**13**/: launching the technology; over - optimistic expectations; des-illusion; enlightenment and realistic views; expectations matched at the level of productivity. At present N&N enter the phase of productivity and therefore safety and security become the imperative of the day. The progress is tremendous and it manifests itself in many fields /**1**, **14**/: high strength materials; durable composites; new surface coatings; improved medicaments; artificial skin, bones and cardiac tissues; high efficiency plasmonic solar cells; sensors and nanosensors; filters for decontamination of water; plastic items from plant-derived raw materials (instead of petrochemicals).

Nowadays we must ask to which extent could be N&N harmful. The question is related to use or misuse. On one hand, also knife, dynamite or alcohol are harmful if used in an improper way. On the other hand, there is one significant difference - while knife is visible to the naked eye, nanoscale entities are invisible to unmediated senses. Concerns of public belong partly to the category of sci-fi like self-replication nanosystems, uncontrolled nanorobots or transhumans, but on the other side to real danger like biological warfare, toxic nature of nanomaterials, invasion into privacy - molecularly naked patients, latent fingerprints etc. /**15, 16**/. In this connection we speak about big brother technologies. Motivated by these concerns, a new Springer journal *Nanoethics* was launched in 2007. A year later the European Commission (EC) adopted a voluntary Code of Conduct /**17**/. The Code is based on a set of a few of general principles: research should be comprehensible to the public; research activities should be safe, ethical and contributing to sustainable development; research should anticipate potential environmental health and safety impacts. More details are to be found in /**18**/. Short term regulations must be followed by medium and long term measures reflected in the legislation.

4. Ubiquitous nanoparticles

N&N work with many types of nanoparticles (Table 1). Some of them are chemically toxic. Threats like cancerogenity, mutagenity, genotoxicity are related to their composition and size. The essential equation reads: *hazard = risk x exposition* /**10**/. Therefore, the first measure is to avoid exposition. The dangerous channels are inhalation and skin contact. NPs stored in liquids are less dangerous than aerosols. Safety precautions involve activities such as toxicological screening, measuring of particle concentration in the air, water and food, controlling of explosive and flammable mixtures with air or oxygen and pyrophoric matters /**19**/.

Table 1 Basic nanoparticles used in N&N /2/

Metals	Oxides	Compounds	Semiconductors
Ag, Al, Au, Co, Cu, Ni, Pd, Pt, Zn	Al_2O_3, Fe_2O_3, SiO_2, TiO_2, WO_3, ZnO	AgCu, $BaTiO_3$, CuNi, MoS_2	CdS, CdTe, Si, GaAs, InP

On the other hand, nanoparticles can provide remedy to various diseases or health-related problems. Well-known are the antimicrobial properties of silver NPs. However, the overuse of nanosilver products could enable the flourishing of resistant strains /**20**/.

5. The role of social sciences and humanities in N&N

N&N has so far benefited mainly from the results of natural and technical sciences. Nevertheless, social sciences and humanities can increasingly contribute to the development of N&N. The potential fields of intervention include the economic context of N&N, sociology and psychology of consumers, security and protection of privacy, the common denominator of the enumerated activities being ethics /**16**/. Most frequent issues which will be discussed in the following chapters are as follows:

- Basic problems of ethics in N&N,
- Economic context,
- Informed public and ambivalence of attitudes,
- Technology assessment.

6. Basic problems of ethics in N&N

6.1 Human enhancement (HA)

Enhancement of physical and cognitive abilities of man by technical and/or biological means challenges ethical, juridical and religious attitudes. Access to these technologies will be limited due to its high cost. They are non-therapeutic and therefore not covered by health insurance (even minor enhancement drug like Viagra is not covered) /**21**/. Then the standard opinion prevails that HA will impair justice, although, in longer horizon enhanced persons should be capable of developing efficient responses to social and other problems /**21**/. However, at present also the opposite problem is being discussed, i.e. the dis-enhancement of animals. Emblematic is the blind chicken issue: chicken suffer in high density battery cages where they are prone to cannibalism. The considerations develop even toward the methods aimed at disrupting animals´ ability to experience pain. This approach is repulsive and the dignity of creatures is noted /**22**/. In this regard the religious persons worry that HA will contribute to re-defining the human nature and diminishing its religious understanding /**23**/. Nevertheless, it is doubtful that man can emulate the nature, which spent millions of years for perfecting high-performance structures. Moreover, the nature operates at room temperature in aqueous ambiance, while chemists operate at high temperatures, in vacuum or in organic solvents /**24**/.

6.2. Health and safety

Safety in N&N is related mostly to the fields of health, food and environment. Mapping of early literature on the subjects indicates that toxicology is in the centre of interest /**25**/. Nano-entities can penetrate the protective mechanisms of human body, such as the brain-blood barrier, cell membranes, they can trigger inflammation and cause damage to the DNA /**26**/. The cited paper criticizes insufficient funding of nanotoxicology, as well as issues emanating from the conflict of interest: large companies hamper the distribution of information, labelling is often not correct, and data sheets list only restrictions typical for bulk and not for the nano-forms. As *pars pro toto,* the criticism of marketing of TiO_2 nanomaterial in UV protective cosmetics should be mentioned /**27**/. The process suffered from numerous problems, such as the absence of alternatives, low degree of controllability, etc.

6.3. Regulation in N&N

As it was mentioned above, European Commission has issued a Code of Conduct in N&N. However, its implementation is problematic /**28**/. The regulation and decision-making done at three levels (European Commission, European Parliament, and Member States) suffers from the lack of effective coordination. The Code is not propagated and applied in the spirit of confidence building and stakeholders guidance /**29**/. Although Europe has so far not witnessed a large-scale disaster like China has in 2007 /**30**/, this does not mean that people are not intoxicated by N&N products, as it was demonstrated at the conference Nanomedicine in 2012 (University of Zürich).

6.4. Intellectual property rights (IPR) in N&N

Nanotechnology as a form of molecular manufacturing needs new forms of IPR. The boundary between invention and discovery (that can and cannot be patented, respectively), is blurred here /**4**/. Often, N&N involve the sale and distribution of a type or an idea, rather than a token or a device /**31**/. Finally, the fast inflow of new results suffers from the slow patent procedures. In the countries where *grace period* is not implemented /**32**/, the patenting opportunities can be lost because of the conflict of interests between publication and patenting. Attention should be paid also to unethical and corrupt practices in scientific publishing, especially to selling and buying papers, induced by publication boom which appears also in N&N and by promotion requirements /**33**/.

7. Economic context

Focal problem in N&N is the nano-divide developing between the rich and poor worlds. Similarly as in the case of digital divide in the era of information technologies, the bridging of this divide does not seem to be straightforward. This is supported also by the dependence theory in economic development – gains in one region are offset by losses in other regions. While it is assumed that the West will continue to dominate, China and India are likely to narrow the gap. They may challenge the western culture of individualism by emphasizing the compassion /**34**/.

8. Informed public and ambivalence of attitudes

As in the case of many other technologies (nuclear energy is an excellent example), in N&N we have to deal with big expectations and enthusiastic support on one side and concerns about environmental, health and social effects (leading even to the request for a moratorium) on the other side /**35/**. Therefore, openly published attitudes of researchers, journalists, politicians and public are important. Given that developing countries consider N&N to be an accelerator of their progress, the vision of researchers are positive, in anticipation of new projects and grants. For example, the review of 150 papers published in Brazil shows absolute prevalence of attitudes in favour of the N&N /**36**/. In the developed world a broad spectrum of attitudes ranging from enthusiasm to antipathy can be found, which is related also to the experiences gained in the related contexts, e.g. in the case of biotechnology /**37**/.

9. Technology assessment

Technology assessment should be done in the real time with the aim to shed light on both its useful and threatening consequences /**38**/. This is particularly important nowadays, when the holistic NBIC concept (nano-, bio-, info- and cognitive sciences) is being born /**39**/. In this regard, N&N are understood not as a starting point of a new industrial revolution, but as a revolution in the quality of life /**40**/.

Conclusions

N&N have already conquered the markets. Therefore, systemization and standardisation of the discipline is necessary. Enhancement of philosophical and ethical research is a condition *sine qua non* for achieving these goals. New inspiration is provided, for example, by biomimetics that studies the properties of living structures and organisms.

From the point of view of ethics, in the N&N field the common belief that science and technology are neutral and only their applications are liable to moral screening, is being revised. N&N, however, do not create a new category of ethical problems, we observe only new manifestation of the problems that are already known /**41**/.

New qualities in N&N are challenging also from the philosophical point of view. Let us mention the complementarity as a basic physical principle: we observe that with the decreasing size of studied structures, the dimensions and complexity of research facilities increase. The penetration into nano-world facilitates better understanding of macro-world, even of the Cosmos /**42**/.

Symmetry is observed also in terms of the dimensions of the current micro- and macro-world research agendas: in the micro-world the manipulation of matter is done at the level of 10^{-9} m, while in the macro-world the operations (e.g. the top achievement of landing on the Moon) took place at the distance of approximately 10^{9} m from the Earth. The fact that mankind occupies a central position on this scale underlines our responsibility for fostering the ethical and moral development in N&N and other frontier branches of the contemporary research.

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References

/1/ H. Dosch, M. H. van de Voorde (eds.), Genesys White Paper, Max-Planck Inst. für Metallforschung, Stuttgart, 2008, ISBN 978-3-00-027338-4.

/2/ Š. Luby, M. Lubyová, P. Šiffalovič, M. Jergel, E. Majková, A brief history of nanoscience and foresight in nanotechnology, NATO Advanced Study Institute Nanomaterials and Nanostructures, Cork, 2013, Springer, submitted.

/3/ G. Stix, Little big science, Scientific American, 2001, September 26th, p. 26.

/4/ B. Bastani, D. Fernandez, Intellectual property rights in nanotechnology, Thin Solid Films, 420 – 421, 2002, p. 472.

/5/ G. E. Moore, Cramming more components onto integrated circuit, Proc. Electronics, 1965, April 19th, p. 114.

/6/ G. Binnig, H. Rohrer, Ch. Gerber, E. Weibel, Surface studies by scanning tunneling microscope, Phys. Rev. Lett., 49, 1982, p. 57.

/7/ R. P. Feynman, There's plenty of room at the bottom, Caltech Engineering and Science J., 1960, http//www.zyvex.com/nanotech/feynman.html.

/8/ P. Moriarty, Nanostructured materials, Report Prog. Phys. 64, 2001, p. 297.

/9/ C. N. Ramachandra Rao, G. U. Kulkarni, P. J. Thomas, P. P. Edwards, Metal nanoparticles and their assemblies, Chem. Soc. Rev. 29, 2000, p. 27.

/10/ D.B. Warheit, Nanoparticles: health impact? Materials Today 7, 2004, No. 2, p. 32.

/11/ P. Sajgalik, M. Hnatko, Z. Lences, J. Dusza, M. Kasiarova, In situ preparation of Si_3N_4/SiC nanocomposites for cutting tools, Int. J. Appl. Ceram. Technol. 3, 2006, p. 41.

/12/ P. Kaye, R. Laflamme, M. Mosca, An introduction to quantum computing, Oxford University Press, Oxford, 2007.

/13/ M. Hersam, Nanoscience and nanotechnology in the posthype era, ACS Nano, 5, 2011, p. 1.

/14/ Nanotechnology: the invisible giant tackling Europe's future challenges, DG Res. Inov. Ind. Techn. EUR 13325 EN, 2013, ISBN 978-92-79-28892-0.

/15/ C. Toumey, Privacy in the shadow of nanotechnology. Nanoethics 1, 2007, p. 211.

/16/ M. Ebbesen, The role of the humanities and social sciences in nanotechnology research and development, Nanoethics, 2, 2008, p. 1.

/17/ Commission Recommendation on a Code of Conduct for Responsible Nanosciences and Nanotechnology Research, European Comm., Brussels, 2008, Document C (2008) 424, http://ec.europa.eu/research/research-eu.

/18/ R. McGinn, Ethical responsibilities of nanotechnology researchers: a short guide, Nanoethics, 4, 2010, p. 1.

/19/ D. L. Huber, Synthesis, properties, and applications of iron nanoparticles, small 1, 2005, p. 482.

/20/ K. Eggelson, http://www.sciencedaily.com/releases/2012/04/120428000220.htm.

/21/ T. Garcia, R. Sandler, Enhancing justice? Nanoethics, 2, 2008, p. 277.

/22/ P. B. Thompson, The opposite of human enhancement: nanotechnology and the blind chicken problem, Nanoethics, 2, 2008, p. 305.

/23/ C. Toumey, Seven religious reactions to nanotechnology, Nanoethics, 5, 2011, p. 251.

/24/ B. Bensaude-Vincent, Self-assembley, self-organization: nanotechnology and vitalism, Nanoethics, 3, 2009, p. 31.

/25/ K. Kjoelberg, F. Wickson, Social and ethical interactions with nano: mapping the early literature, Nanoethics, 1, 2007, p. 89.

/26/ K. Shrader-Frechette, Nanotoxicology and ethical conditions for informed consent, Nanoethics, 1, 2007, p. 47.

/27/ J. F. Jacobs, I. van de Poel, P. Osseweijer, Sunscreens with titanium dioxide (TiO_2) nanoparticles: a societal experiment, Nanoethics, 4, 2010, p. 103.

/28/ A. M. P. del Castillo, The European and member states' approaches to the regulating nanomaterials: two level governance, Nanoethics, 7, 2013, p. 189.

/29/ B. Dorbeck-Jung, C. Shelley-Egan, Meta-regulation and nanotechnologies: the challenge of responsibilisation within EC's Code of Conduct for responsible N&N research. Nanoethics, 7, 2013, p. 55.

/30/ S. Dalton-Brown, Global ethics and nanotechnology: a comparison of the nanoethics environments in the EU and China. Nanoethics, 6, 2012, p. 137.

/31/ D. Koepsell, Let's get smaller: an introduction to transitional issues in nanotech and intellectual property, Nanoethics, 3, 2009, p. 157.

/32/ J. Strauss, Is the patent system fit to meet the needs of the „triple helix" alliance? In: 20 Jahre Europäische Akademie der Wissenschaften und Künste, ed. M. Eder, Edition Weimar, Salzburg, 2009, p. 371, ISBN 978-3-89739-666-1.

/33/ M. Hvistendahl, China's publication bazaar, Science, 342, 2013, p. 1035.

/34/ S. Hongladarom, Nanotechnology, development and Buddhist values, Nanoethics, 3, 2009, p. 97.

/35/ S. Arnaldi, A. Muratorio, Nanotechnology, uncertainty and regulation, Nanoethics, 7, 2013, p. 173.

/36/ N. Invernizzi, Vision of Brazilian scientists on nanoscience and nanotechnologies, Nanoethics, 2, 2008, p. 133.

/37/ M. Kearnes, B. Wynne, On nanotechnology and ambivalence: the politics of enthusiasm, Nanoethics, 1, 2007, p. 131.

/38/ D. H. Guston, D. Sarewitz, Real-time technology assessment, Technology in Society, 24, 2002, p. 93.

/39/ A. T. Swierstra, M. Boenink, B. Walhout, R. van Est, Converging technologies, shifting boundaries, Nanoethics, 3, 2009, p. 213.

/40/ C. Shelley-Egan, The ambivalence of promising technology, Nanoethics 4, 2010, p. 183.

/41/ F. Bacchini, Is nanotechnology giving rise to new ethical problems? Nanoethics, 7, 2013, p. 107.

/42/ M. L. Schattenburg, From nanometers to gigaparsecs: The role of nanostructures in unraveling the mysteries of the cosmos, J. Vac. Sci. Technol. B, 19, 2001, p. 2319.