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Importance of a Midterm Time Horizon for Addressing Ethical Issues Integral to Nanobiotechnology

George Khushf

Humanities Director, Center for Bioethics, University of South Carolina, Columbia, South Carolina

Address all correspondence to George Khushf, Humanities Director, Center for Bioethics, University of South Carolina, Columbia, SC 29208; Khushfg@gwm.sc.edu.

ABSTRACT: There is a consensus emerging on the importance of upstream ethical engagement in nanobiotechnology. Such a preventive ethic would anticipate downstream concerns that might arise and mitigate them as part of the research and development process. However, there is an unappreciated tension between the time horizon of upstream ethics and that assumed by most bioethical research. Current standards of high-quality research on ethical issues biases the research in favor of near-term, science-based, results-oriented work. A near-term focus would miss many of the important ethical issues integral to nanobiotechnology and undermine the goals integral to upstream ethical engagement. However, if we move to a far-term time horizon, the ethical debates tend to get too speculative and are no longer disciplined by existing research trajectories. This paper addresses the link between the midterm time horizon necessary for upstream ethics and the form, content, and style of ethical reflection. New paradigm cases, standards, and criteria will be needed for high-quality upstream ethics work in the area of nanobiotechnology.

KEY WORDS: human factors engineering, MIT Institute for Soldier Nanotechnologies, nanoethics, upstream ethics, medical error

I. INTRODUCTION

Nanoscale science and technology involve the understanding and manipulation of matter in the 1–100 nm range. The nanoscale is considered especially important for both fundamental scientific research and for engineering/medical applications. In science, this region is seen as the last frontier in our decomposition of bulk level materials and systems into their constituent components. Below this, we move into the realm of atomic and subatomic physics. Above this region, we are in the classical domain. However, within this so-called mesoscale, we have the averaging over quantum effects by which the stable properties of bulk level materials are formed. For living systems, this is likewise seen as the ultimate level of resolution for understanding how the function of higher-level systems arises from the basic molecular components and assemblages that are integral to all life processes. Thus, for example, the National Institutes of Health advance the Nanomedicine Roadmap Initiative as a mapping of this last frontier, providing the foundation for the genuinely molecular medicine of the future.[1] Engineering and medical applications will include not only a refined interface with systems at this scale, but also the capacity to create novel materials, with size-dependent properties. "Nano" thus signifies the ultimate level of understanding and control.[2]

Following the precedent of the Human Genome Project, many funding agencies have called for research addressing the ethical, legal, and social aspects of nanoscale science and technology. As part of an initial, exploratory project in this area, I reviewed research related to bionanotechnology in order to identify areas where reflection on the ethical issues is especially important. A preliminary sketch of some of the ethical challenges integral to nanomedicine has already been published.[3,4] In this paper, I reflect on an interesting problem that arose in the framing of this survey project.

It turns out that in many areas of research currently associated with nanotechnology, the core research directions and culture have already been well established in non-nano-related areas, and the new nano-related tools simply augment or enable the realization of antecedent goals. For example, we might see nanowires used to advance a brain-machine interface.[5] The core framing of the ethical issues will be governed by this antecedent domain and, in many cases, it will be difficult to specify or clarify what novel or additional concerns are introduced by nanotechnology. For example, does the use of nanowires bring any new issues or in some way compound the existing issues already present in the development of brain-machine interfaces?

When trying to refine what is implicit in these questions about novelty, we need to make a choice about the time horizon that is important for the framing of the ethical issues. The problem can be simply stated as follows: If we ignore the more visionary statements and goals and focus on the current research that is being published, the impact of nanotechnology is modest, especially when considering the ethical issues. Much of the work on, e.g., new materials, quantum dots, and sensors provides a quantitative advance over current technologies, but it does not seem to raise qualitatively different ethical issues. Perhaps the most significant near-term development concerns the health and safety of these new particles. It is already clear that existing health and safety standards are not fully adequate, for example, when considering the toxicity of a nanoparticle. But there is now a whole industry focusing on these health and safety issues, including new work on standards.[6]

For the more revolutionary impact of nanoscale science and technology, we thus need to move further out in time. However, here we need to be very careful. If we go too far out, nano becomes a catchword for a radical mastery of the building blocks of matter, and the ethical issues turn into radical utopian or dystopian visions of gray goo, a collapse of the world economy, and transhumans. In such speculation, the ethical debate is no longer disciplined by the specific research initiatives that are underway. The reflections also are framed in ways that do not directly inform the research that is now being conducted.

Put generally, we can identify a trade-off: the nearer the time horizon, the less distinctive or significant the ethical aspects of the research appear, and the more disciplined the ethical deliberation is by the existing science; as you move further out in time, the visionary aspects of the research become more prominent, but they become more discon-

nected from the existing scientific trajectories. The question is, then: What should be the time horizon of early efforts at mapping the ethical issues integral to nanotechnology?

In this paper, I seek to show how the form and content of ethical deliberation is deeply intertwined with the time horizon of the research being considered. This linkage highlights how early choices about the time horizon will condition the kind of analysis provided. After reviewing in greater detail some of the trade-offs in selecting a given time horizon, I argue for the importance of a midterm horizon. Upstream ethical engagement depends on such a time horizon.

II. HOW THE TIME HORIZON CONDITIONS THE FORM AND CONTENT OF ETHICAL DELIBERATION

Today there is much discussion of upstream ethical engagement. Although there is considerable debate about what this should mean, it is generally defined by contrast to a more "reactive ethic" that simply considers the downstream effects of some technological trajectory that is already underway. The phrase thus captures at least two important motifs: First, we should integrate ethical deliberation into the research and development process itself, rather than having it come in post hoc, as a kind of external evaluation or regulatory process. Second, we should preventively manage problems before they ever emerge as problems. This involves a process of foresight or anticipation, which brings into view how humans might eventually utilize the products of research. We can then integrate these anticipated concerns up front into the design process, thereby developing our research in ways that are less likely to be problematic.

Upstream ethical engagement is considered important because technology is increasingly disruptive, involving heightened capacities to significantly alter our natural and social landscapes, and it develops too rapidly for older, post hoc modes of reflection. Upstream ethical engagement is thus seen as better suited for the more radical, rapidly accelerating science and technology of the future. This provides the rationale behind the many calls for ethics and social issues research related to nanotechnology.

Although there now seems to be a consensus in favor of such proactive management of ethical issues, there is an unappreciated disconnect between existing standards and assumptions integral to traditional, post hoc modes of ethical reflection and the assumptions integral to upstream ethical engagement. In order to appreciate this disconnect, we need to first consider an important difference between two kinds of ethical reflection commonly found in academic and research settings. First, we have the more theoretical and speculative reflection on the grand themes of ethics; for example, accounts of justice or of the general nature of human flourishing. This is the kind of work that might be done by traditional philosophers at a university. Often this work is developed in a way that is quite removed from the day-to-day, practical deliberations of people who face more concrete ethical challenges, and many of the leading figures in these academic debates have little experience working in practice settings. In contrast to such "ivory tower" speculation, there is also a more detail-oriented, practical kind of ethics work that is closely coupled with the real-world settings where ethical issues arise. Here I am thinking of work on topics such as equipoise in human subjects research or the appropriate mechanisms for allocating scarce organs.

There is a clear difference in the purpose, style, and criteria integral to these two kinds of ethics work. There is also some tension between practitioners of these competing types of ethics work, a tension that is rooted in the different standards of excellence. Often, the more speculative ethicists view the applied work as an uninteresting, pragmatic compromise, which is too often uninformed by the deeper theoretical questions. They see the applied ethicists as falling short of the best standards of their professional disciplines. On the other hand, the more practically oriented ethicists emphasize the need to be attentive to the rich, often tacit dimensions of a problem; they value the way the real world poses ethical questions, and seek to develop nuanced, balanced answers to these real-world questions. They tend to dismiss the grand questions as too speculative, and normally seek local, practical resolutions to specific ethical problems.

In the context of science, engineering, and medical research, the standards of the applied ethi-

cists tend to dominate. These standards presuppose that you have some existing technology or research stream in which specific problems have already been raised. The style of deliberation emphasizes the kind of detail-oriented, science-based, post hoc reflection that is associated with traditional downstream ethical deliberation. From this perspective, the more open-ended, anticipatory work of upstream ethics appears to be too much like the ivory tower, speculative stuff that is found in academic departments. The existing standards thus pull ethics research in the direction of near-term research, and they work against the anticipatory, proactive management of ethical issues arising from current research efforts. In practice, this amounts to a continual request for, "What's new about nano?" And when some narrowly circumscribed, existing technology is not identified, there is a natural tendency to dismiss the importance of the issues or see the only alternative as the ivory tower speculation.

III. HOW ETHICAL ISSUES DISAPPEAR WHEN WE MOVE FROM A MIDTERM TO A NEAR-TERM FOCUS

In this paper, I explore the conceptual link between the midterm time horizon and the character of an upstream ethic. Although a detailed case study cannot be developed here, I would like to present a case that demonstrates how a near-term focus would miss many of the important ethical issues. The point of this case study is simply to demonstrate how the standards and criteria of excellence integral to a traditional, post hoc applied ethic lead to a kind of blindness.

The initiative we consider is the Massachusetts Institute of Technology (MIT) Institute for Soldier Nanotechnologies (ISN). This was funded in 2002 by the U.S. Army Research Office for $50 million for five years. The contract was just extended in 2007 for another five years. The mission of the ISN is to "develop and exploit nanotechnology to dramatically improve the survivability of soldiers." Here the goal comes from outside the ISN; it is, in fact, a broad Army goal for the "future force warrior." This goal involves the transformation of "today's cotton/nylon fatigues and bulky equipment to a sleek, lightweight battlesuit that provides everything from responsive armor to medical monitoring to communications—and more—in one integrated system."[7]

Although the details of this future battle suit are somewhat fuzzy, the Army clearly has in mind some fairly radical, science fiction–like developments. Such a suit would include ongoing medical monitoring and enhance human performance. It would also enable real-time communication and networking with other soldiers and Army operations, and enable forms of coordinated action that would otherwise be impossible. Monitoring would presumably involve traditional physiological indicators, such as heart rate and temperature, but also include newer, not-yet-specified indicators; for example, some of the research concerns the kinds of molecules that might cross dermal barriers. In some cases, there is a fuzzy line between medical therapy and enhancement. The Army is, for example, interested in hydration status monitoring and "on the move hydration." But any "on-board physiological/medical sensor suite" would also provide a platform for "optimized cognitive and physical fightability."[8,9] They also envisage new forms of enhanced team performance that integrate more traditional cognitive and organizational techniques with the battle suit–enabled modalities of awareness and networking.

The ISN divides its research into several subcategories, and these have changed somewhat with the recent restructuring. Here I will use the earlier subcategories, since these have framed existing research efforts and they can be traced to specific publications arising from the research—something that cannot as easily be done with the newer categories, since we do not yet have their research trajectories. Also, the newly restructured Web site no longer lists publications under specific research initiatives. The pre-restructured ISN listed the following seven research areas:[10]

Team 1: Energy Absorbing Materials
Team 2: Mechanically Active Materials and Devices
Team 3: Sensing and Counteraction
Team 4: Biomaterials and Nanodevices for Soldier Medical Technology
Team 5: Processing and Characterization—the Nanofoundries

Team 6: Modeling and Simulation of Materials and Processes
Team 7: Systems Design, Hardening, and Integration

Under each of these general areas, they also listed subtopics; for example, under "Team 4" there were the following four foci:

Project 4.1: Switchable surfaces
Project 4.2: Noninvasive diagnostics and delivery of injury intervention agents
Project 4.3: Semiactive variable-impedance materials—biomechanical design and control
Project 4.4: Nanostructured biomedical fiber constructs

Finally, they listed specific publications. Here are three that were included under their "Team 4" category:

1. "A simple soft lithographic route to fabrication of poly(ethylene glycol) microstructures for protein and cell patterning," K.Y. Suh, J. Seong, A. Khademhosseini, E. Laibinis, R. Langer, Biomaterials 25, 557, 2004.
2. "Layer-by-layer deposition of hyaluronic acid and poly-L-lysine for patterned cell co-cultures," A. Khademhosseini, K.Y. Suh, J.M. Yang, G. Eng, J. Yeh, S.Levenberg, R. Langer, Biomaterials 25, 3583, 2004.
3. "Construction of nonbiofouling surfaces by polymeric self-assembled monolayers," S. Jon, J. Seong, A. Khadenhosseini, T.N.T. Tran, P.E. Laibinis, R. Langer, Langmuir: ACS J. Surf. Coll. 19, 24, 9989, 2003.

The point I want to make by listing these research areas, subtopics, and publications is that we increasingly lose a sense of what motivates and integrates research efforts as we move from the broader vision of the ISN to the specific research results. Here the whole is clearly more than the sum of the parts. If we were to look at the publications alone, we would get almost no sense of the fairly radical Army project. As our time horizon shifts from the midterm vision toward the near-term activities and results, we also lose any sense of the project's integrity, and the ISN fragments into a disconnected set of efforts on, e.g., layer-by-layer deposition or construction of nonbiofouling surfaces. The criteria of traditional "high-quality ethics research" drives in the direction of near-term, post hoc, science-based research results. Taken to its logical conclusion, such a traditional ethic becomes blind to the visions and values that order and direct many research processes. In the case of the ISN, we would lose the phenomenon we seek to study.

In some ways, this fragmented set of practices is itself instructive. It would be equally problematic to take all of the visionary statements at face value. Scientists are often opportunistic. In many cases, researchers are really interested in these more local projects, and they simply use the ISN alliance as a way of getting Army money to fund what they would like to be doing. There is thus some merit to the bioethicist's impulse to discount the grand, visionary aims and focus on the "real research" being conducted. However, although it may be naive to assume that science teams are functioning in a perfectly coordinated manner to realize ISN goals, it is equally naive to assume that these goals play no role in initiating and directing these research efforts. A midterm focus seeks to explicitly address how these broader visions and social systems concretely motivate, govern, and are informed by the developing research.

If we just focus on the near term and insist that ethics only consider the "real science," the ISN project disappears. We then get the standard question, "What's novel about nano?" and the implication is, "Since there is nothing new here, why worry about it?" When we move to a midterm horizon and attempt to consider the relation between the stated purposes and the specific research efforts, then we have an ambiguous, complex coupling and need to do a lot of work to try understand how these bits and pieces function together. In this case the question, "What's novel about nano?" takes on a different character. It is no longer dismissive. Instead, the question is taken as a research question integral to upstream ethics: What exactly does nanoscale science and research contribute to the realization of the Army future force warrior? How does the Army goal influence the way nanoscale research is conceptualized and conducted? What is the relation between the midterm ISN vision and other goals

and activities, for example, of scientists, the military, etc. Do specific subactivities of this initiative call for special attention? As we start to flesh out answers to these questions, we also bring into view the kinds of factors that might be proactively managed as part of an upstream ethics process.

Where this reflection goes, I must leave open. However, I think this case has given us enough to appreciate two things. First, the traditional criteria and standards of applied ethics work need to be revised if we want to appropriately address the visions and values that inform developing research trajectories. Second, much more work is needed to develop the linkage between upstream ethical engagement and the midterm time horizon. I now close with a few general comments on how these new standards might be developed.

IV. THE MIDTERM TIME HORIZON AND HUMAN FACTORS ENGINEERING

A central challenge for upstream ethical reflection involves specification of the appropriate time horizon. The focus needs to be far enough ahead so downstream effects can be anticipated and proactively managed, but not so far downstream that we lose touch with current research developments. Proactive management implies a realistic coupling between not-yet-existing problems and existing research efforts. I define the horizon of such a coupling as a midterm time horizon.

It should be apparent that such a midterm horizon, with this coupling, involves logics of practical rationality that are significantly different from traditional kinds of risk analysis. Standard precautionary principles or risk management strategies normally assume you have some discrete activity or technological product, which is taken as given. The ethical analysis then considers the environmental or social impact of this discrete development, and manages risk accordingly. Ethical analysis thus assumes a sharp division between the process of research and development, on one hand, and the ethical and regulatory oversight, on the other. In upstream ethical engagement, this division breaks down.

Some precedent for upstream coupling can be found in the field of human factors engineering, and in related areas of operations, systems, and ergonomic research. Some of the important developments in these areas arose in the context of wartime aviation. In early cockpit design, toggle switches were arrayed in a row, and pilots in the midst of combat pressure might quickly flip the wrong switch, leading to disastrous consequences. Engineers came to distinguish between the active error of pilots and the latent error of engineers who would not sufficiently account for "human factors" in their design of the cockpit. Drawing on this insight, human factors engineers would imaginatively enter into the contexts of anticipated use, and then design the cockpit so it better enables pilots to function as they should. In this way, downstream errors could be proactively managed as part of the design process.

Recently, human factors and operations research insights have been used for restructuring health systems so that errors are proactively managed and quality is advanced.[11,12] Central to this initiative is a shift from individuals to systems. Traditionally, a medical professional has been seen as the agent of health care. If there were an error, then this was seen as a failure of the individual. However, research has shown that many errors are better understood in terms of systems; for example, when a patient is given an incorrect dose of some drug, this might arise from an unclear label or from bottles of similar design—a problem analogous to the similar toggle switches in the cockpit of an aircraft. By focusing on the latent errors integral to systems, errors can be proactively managed so they never arise.

This same shift in perspective can inform the way ethical analysis is conducted. However, a deep shift is needed in how we conceptualize and manage the process of research and development. Here, again, there is a useful analogy with the health-care context. Traditionally, we have seen health care as a function of what physicians do; we imagine it as a transaction between an individual doctor and an individual patient. Health systems and administrators are viewed as part of the support structure enabling medicine, but they are not seen as constitutive of the practice. As a result, when systems changes are advanced that limit or condition how clinicians might practice, this is seen as an intrusion into the proper jurisdiction of the physician. The system shift thus entails a deep transformation in how health care is understood and practiced, with associated changes

in the very meaning of quality, standards of care, and even the appropriate authority and responsibility for practicing that care. If error and quality are managed as systems issues, then, by implication, they are not just within the jurisdiction of physicians.

In a similar way, the logic of upstream ethics challenges what has traditionally been viewed as the appropriate jurisdiction of scientists. It also challenges the traditional jurisdiction of ethics and policy work. By means of the coupling of anticipated downstream effects with upstream design processes, the scientist now plays a direct role in the management of ethical issues and the ethics and policy work plays a role in the design. One of the most significant challenges for an upstream ethic will be to develop paradigm cases, methods, and standards for advancing this kind of coupling. As these are developed, the specific character of the midterm time horizon will also become clearer.

At this preliminary stage, the midterm time horizon must thus remain somewhat fuzzy. It is specified by the coupling of anticipated effects and research design, and therefore depends on a more careful specification of that coupling. But to do this, we need to move from general reflection to specific cases, methods, and standards. Human factors, operations, and systems engineering can provide some valuable guidance. But we will also need to deeply rethink these fields. They usually presuppose an engineering application, and thus have not been developed for more academically oriented research in fundamental and applied areas. Any extension of these models to the settings of cutting-edge research where upstream ethics is considered especially important must thus involve a fundamental, critical rethinking of both the research in question and the human factors and systems models.

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