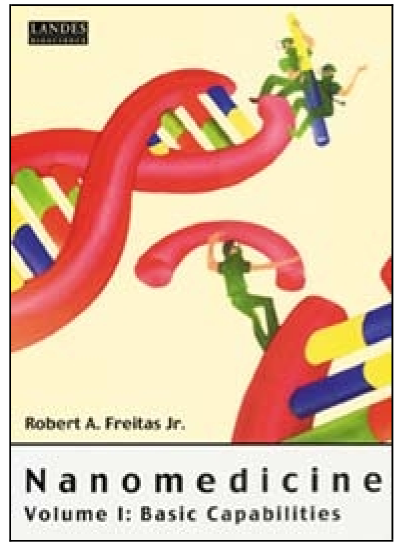
LE Magazine October 2000 **REVIEW**

A Gift From The Future

A review of Nanomedicine, Volume 1: Basic Capabilities, by Robert A. Freitas Jr.

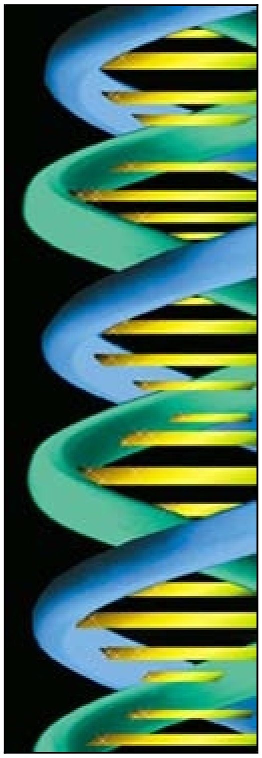


Nanomedicine is an endlessly impressive and uniquely important book. Like Newton's Principia and Drexler's Nanosystems, it stands as a marker between all that has come before, and all that will come in the future. For it is effectively a blueprint for the future—essentially the whole future—of health, longevity and medicine. It is not quite a prediction—predictions are notoriously difficult—but is instead an engineering sketch of what will be possible for medicine based on the laws of physics and chemistry, when humankind can do everything consistent with those laws of physics. Despite its focus on the ultimate future of medicine, Nanomedicine is relevant to nearly everyone alive today and now, in many ways. It may save many lives, and it will certainly elevate many more. It is, in a sense, a gift from the future to those of us living in the present.

The book is at once very easy and very difficult to explain and to understand. It is excellently written and presented, and is about elemental themes of life and the conquest of death, disease, discomfort and ultimately even displeasure, at the hands of technology. But no mere simple statement can convey the staggering depth of the book, the awesome scholarship that has produced it, and the relentlessness with which Freitas has pursued his subject. If you want the full story, you'll have to read the book.

To start at the beginning, Nanomedicine is about just that: nanomedicine. Freitas defines nanomedicine at least twice. On page two, he says "Nanomedicine may be broadly defined as the comprehensive monitoring, control, construction, repair, defense and improvement of all human biological systems, working from the molecular level, using engineered nanodevices and nanostructures." Later, he gives "the broadest possible conception of nanomedicine" as "the science and technology of diagnosing, treating and preventing disease and traumatic injury, of relieving pain, and of preserving and improving human health, using molecular tools and molecular knowledge of the human body." Stated differently, he notes, on page 17, that what is coming is "a molecular technologic medicine in which the molecular basis of life, by then well-known, is manipulated to produce specific desired results," and that "in the coming century, the principal [sic] focus will shift from medical science to medical engineering. Nanomedicine will involve designing and building a vast proliferation of incredibly efficacious molecular devices, and then deploying these devices in patients to establish and maintain a continuous state of human healthiness."

In order to understand what Freitas means by "healthiness," we turn to Freitas' definition of disease. Typically, Freitas doesn't just casually state that disease is such-and-such. Instead, he describes no less than eight previously-proposed definitions of disease, complete with a graphical illustration of opinions as to what constitutes a disease, before proposing his own definition, the "volitional normative model" of disease. Essentially, in the era of nanomedicine, disease is a failure to attain optimal functioning, and optimal functioning is defined by the wishes of the patient. In other words, ideal health is whatever the patient wants it to be. Nanomedicine, Freitas tells us, is charged with the duty of making the patient's wishes, whatever they may be, come true. This begins to hint at the capabilities projected for nanomedicine. Essentially, nanomedicine will mean that, if a given individual wants to, he or she can go beyond being disease-free, and can enjoy the conditions of being free of aging, free of vulnerability to many traumatic events that today would be fatal, and, finally, free of the limitations of the present human body plan. As Freitas says in considering the relevance of a historical perspective on nanomedicine, "another important reason to study the history of medicine is to gain a deeper appreciation of the long, hard struggle to improve human health, a struggle that is expected finally to culminate in victory in the 21st century." That's victory in the final sense, the virtual end of the battle.



The concept of nanomedicine is clearly and squarely based on the concept of molecular nanotechnology, which is a general ability to manipulate matter to atomic precision. This foundation is secure. The intellectual soundness of molecular nanotechnology was established with the monumental work by K. Eric Drexler, Nanosystems: Molecular Machinery, Manufacturing, and Computation (John Wiley and Sons, New York, 1992). As Ralph Merkle states in his excellent Afterword to Freitas' book, “Nanosystems was published in 1992, and no significant flaws have been found. Given the volume of public debate and the number of people who have read the book, the simplest explanation for this absence of reported errors is that its logic is basically correct and its conclusions are basically sound.” If we are made of atoms, and molecular nanotechnology allows us to put our atoms anywhere we want, and attach or detach them from any other atoms as we may please, then it does stand to reason that we'll be able to control our health almost totally. As Eric Drexler states in his masterful Forward to Nanomedicine, “these are not high-risk predictions, but merely the extension of currently-observable progress in biological and medical research. . . . What was visionary a short time ago is now a minimum baseline expectation.”

However, simple assertions have little force unless they are backed up with rigorous analysis. As Carl Sagan once remarked in another context, extraordinary claims require extraordinary evidence. And Robert Freitas is here to give it to us.

Nanomedicine is a book of 509 pages of fine print that could easily have been 2000 pages at a normal font size. The last citation is numbered 3728. There are 210 figures, 58 tables and over 270 equations. Freitas reports in his preface his expenditure of about 19,000 hours of effort, or essentially 10 man-years, in putting together the work, and it shows. The results are such that I believe it will be hard if not impossible for even zealous skeptics, if any still remain, to remain deeply skeptical of Freitas' vision upon close reading of this book, barring the abdication of intellectual honesty and reason. Freitas provides what amounts to an intellectual battering ram capable, I believe, of breaking through the ignorance and resistance of anyone who is actually willing to view nanomedicine on its merits, and capable of understanding what Freitas says.

Nor can Freitas be dismissed as a mere unqualified enthusiast. Freitas has formal credentials for writing such a work. According to the book jacket, he has degrees in physics, psychology and law, has written and published extensively, co-edited a seminal NASA study on the feasibility of self-reproducing factories in space, and wrote the first published technical design study of a medical nanorobot that appeared in a peer-reviewed biomedical journal.

Nanomedicine is organized in a logical series of chapters. The first is entitled “The Prospect of Nanomedicine,” and takes a look at nanomedicine in the context of the broad sweep of history, starting with fossilized pathogens dating back 500 million years, and culminating in a detailed description of modern contributions to the idea of nanomedicine, the differences between nanomedicine and more conventional approaches, and an idea of how a visit to the doctor would be different in the era of nanomedicine.

Chapter two is a vital one, “Pathways to Molecular Manufacturing.” Since we can't build nano devices now, it is imperative to at least provide evidence that we will one day have that capability. Freitas, to his great credit, provides an exceptionally detailed look at how existing capabilities can be channeled into the beginnings of molecular nanotechnology, and how these beginnings can, in turn, develop into full-fledged molecular and machine manufacturing capability. Not only does this provide justification for considering what the results of this process will ultimately be, but it also helps to instruct present-day nanotechnologists on how they can proceed.

Having set this stage, the book then proceeds through a series of chapters on the nuts and bolts issues of creating and safely operating medical nanodevices and networks. Chapter three focuses on “Molecular Transport and Sortation,” chapter four on “Nanosensors and Nanoscale Scanning,” chapter five on adaptable shapes (“Metamorphic Surfaces”) for nanodevices, chapter six on powering medical nanodevices, chapter seven on communication with and between nanomedical devices, chapter eight on the related topic of navigation, and chapter nine on the crucial issues of “Manipulation and Locomotion.” Finally, chapter 10 discusses “Other Basic Capabilities,” including timekeeping, molecular computing, handling of high and low pressures, extermination of viruses and aberrant cells, solubility issues, and a discussion of locomotion through and excavation of ice. Appendices A-C give reference data of various kinds (physical constants and conversion factors in A, a comprehensive list of all of the molecules found in blood and their concentrations in B, and a catalog of most distinct cell types in the human body in C). Following this is an extensive glossary, reference list and index. The glossary is needed since, in addition to the numerous arcane words available before Nanomedicine, Freitas is forced to coin innumerable terms (such as “histonavigation,” “vasculography” and “communicyte”) in order to describe the new devices and capabilities he envisions.

The purpose of chapters 3 to 10 is to establish something akin to a parts list for nanomedical devices and a set of performance standards for such parts. Nanomedical devices have to be made out of components that do specific things, occupy specific volumes, respond at specific rates, and operate with specific tolerances and with specific power requirements. Once these components are characterized, it becomes more feasible to talk about what can be done by combinations of components. In addition, Freitas provides enormous context to such discussions by citing example after example of archaic, contemporary, and projected designs and working examples pertinent to each subtopic being considered.

It isn't possible in a short review to provide a detailed account of or critique of each specific topic area considered in Nanomedicine. Instead, lets take as an example just one topic area of particular interest, the nanomedical computers needed to permit cell repair machines to operate. There isn't much point in talking about what an intracellular computer will be programmed to do if you can't first establish what the intracellular computer's core design limitations will be. Drexler extensively discussed molecular computers in Nanosystems, but didn't consider the problems of running such computers under the biological constraints that exist in a living system, constraints which are a specific nanomedical, as opposed to merely a global nanotechnological, problem. Nanocomputer performance is important to nanomedicine in many different ways in dealing with many different problems, so it's important to think carefully about what can be expected from medical (in vivo) nanocomputers.

I myself had analyzed, in a presentation before the American Academy of Anti-Aging Medicine, the problem of heat production by intracellular nanocomputers, and had to conclude that clock speeds similar to those in today's PCs would be problematic in cells unless more energy-efficient architectures than those described by Drexler were adopted. Nanocomputers as described by Drexler dissipate relatively large amounts of heat compared to the remarkably subtle energy expenditures of typical cells. I was therefore quite interested to see what Freitas would say about these matters.

Surprisingly, it turns out that one could double cell and whole-body energy expenditure with only a 0.4oF increase in body temperature, so efficient are natural body systems for dissipating excess heat. For comparison, a body exercising at maximum capacity increases energy expenditure by a factor of 16 (with a rise of only about 6oF). Given that cells already repair virtually all damage already, it isn't hard to imagine that we could repair all currently-unrepaired biological injury if we devoted equal energy to doing this. It's also not hard to imagine that we could do much to repair traumatic injury if we devoted 15 times our normal energy expenditure to this task during emergencies, even if most of this energy expenditure represented computational "thinking" about repairs rather than the actual conduct of the repairs themselves. (Of course, heat dissipation mechanisms could be limited as a result of certain kinds of trauma, but this still leaves substantial room for augmented healing capacity.) In summary, the simple physiological context provided by Freitas, in his typically near-exhaustive treatment of issues, is reassuring. Incidentally, it is worth pointing out that in order to double your metabolic rate, you would have to eat twice as much in order to avoid losing weight. This is bound to be an attractive "side effect" of nanomedicine. If you didn't want to eat that much, we learn that popping a couple of high-energy pills containing coated powdered diamond could support the extra metabolism for days.

On a more fundamental level, Freitas brings us up to date on a plethora of new, more energy-efficient computer information processing architectures, including even a discussion of the upcoming field of quantum computers, wherein the superposition principle could allow a single carbon atom to retain 100 million bits of information and process it at the rate of around 1026 bits/second! Moreover, a tamer form of logic called helical logic by its developers, Merkle and Drexler, could cut the energy requirements of Drexler's original rod logic system by a factor of around 10,000, and reversible computers could extend this advantage considerably more. The vast scope for creating more energy-efficient nanocomputers in combination with the increased energy expenditure permitted by natural human physiological temperature compensation systems seems ample to allow most nanomedical problems to be tackled with large safety margins.

One notable apparent gap in the argument is Freitas' virtual silence about the required investment of chemical energy needed to carry out the actual biochemical reactions needed to effect repair. Given our long lifespans, it seems likely that elimination of currently-unrepaired damage under baseline conditions would require less than 1% of normal basal metabolic energy expediture, which is well within comfortable working conditions. On the other hand, major trauma might require a vast expansion of chemical reactions on biomolecules, and it will be important for Freitas to specify how the partitioning of the nanomedical energy budget between the requirements of the nanodevices themselves on the one hand and the requirements for producing chemical changes in biomolecules on the other is likely to be constrained. It may be that the energy needs of the nanodevices dwarf or even encompass the additional costs of performing chemistry on the target molecules, but these issues will have to be made more explicit in the future.

Fortunately, additional information will in fact be forthcoming. The current book is only Volume 1 of what will eventually be a three-volume treatise. Although it is hard for this reviewer to endure the present absence of Volumes 2 and 3, Freitas does at least share with us, at the end of chapter one, a glimpse of what these volumes will contain. Volume 2 will be subtitled "Systems and Operations." It will consider such subjects as control, repair and replacement, safety and reliability, deployment configurations, performance, examples of specific nanorobot devices, reading and editing of biological molecules, enabling systems for cell repair, the manufacturing of tissues and organs, and personal defense systems. Volume 3 will be subtitled "Applications." Volume 3 will consider proofs-of-concept, treatment of pathogens and cancer, reversal of trauma and injury from radiation and burns, emergency care, brain repair, control of aging and most causes of death prevalent today, biostasis (suspended animation), human augmentation (meaning the addition of new capabilities and features to the human body), and the social implications of nanomedicine.

The greatest weakness of the book, I believe, is the lack of integration of the reference list. The reference list runs to over 3700 references, but not all references exist—for example, references 2-5, 7, and 22-26 aren't in the list. To exacerbate the situation, the references are listed in no particular order other than the fact that the citation numbers themselves run sequentially, and perhaps a weak correlation between the citation number and the order of citation in the text. It is effectively impossible to infer from the reference number where the reference is cited in the book, and it is impossible to easily find cited authors' names due to the lack of alphabetization of the reference list. This is a clerical issue that can obviously be overcome in a future edition and was undoubtedly the result of a publishing deadline that precluded the herculean task of shuffling so many citations into a coherent pattern. In any case, if one reads any passage of interest in the book, the citations appearing in that passage can be found readily in the list, so the list does serve its primary purpose of backing up what is said in the book.

Another weakness of the book is the figures. They are of admirable content, but of less-than-stellar quality and size in many cases. This was probably a necessary compromise to keep the price of the book in the readily-affordable range. Nevertheless, the figures amply illustrate the points they are intended to illuminate.

From time to time it is apparent that Freitas is a masterful engineer or mathematician, but not a biologist by training. Little quirks such as reference to a "neuron cell" instead of to a "neuron" (Table 6.8) appear infrequently. Such tiny glitches, however, only serve to underscore the magnitude of Freitas' achievement in crossing disciplinary barriers to write a book that is really about biology, a field that is not his area of formal training.

It is possible that Nanomedicine will for many years be like Stephen Hawking's A Brief History of Time, a book that many people considered important enough to buy, but that most people could not read, and that mostly ended up on the coffee table to impress guests. If so, then I urge the reader to decorate his or her coffee table with this book. We should support Freitas' superhuman effort because, in so doing, we will be helping in a very palpable way to create the future we all dream of and that our lives will ultimately depend upon. As Ralph Merkle's Afterword says, "Nanomedicine is more than just a description of what might be, it is a call to action."

Happily, the Foresight Institute has announced that Mr. Freitas is joining Zyvex, the first company devoted to creating a nano-assembler. Zyvex will financially support the completion of Volume 2 and Volume 3, thus freeing up Rob Freitas for this monumental work. This is good news both for the future of Nanomedicine and for the future of nanomedicine. Stay tuned. — Gregory M. Fahy, Ph.D.

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