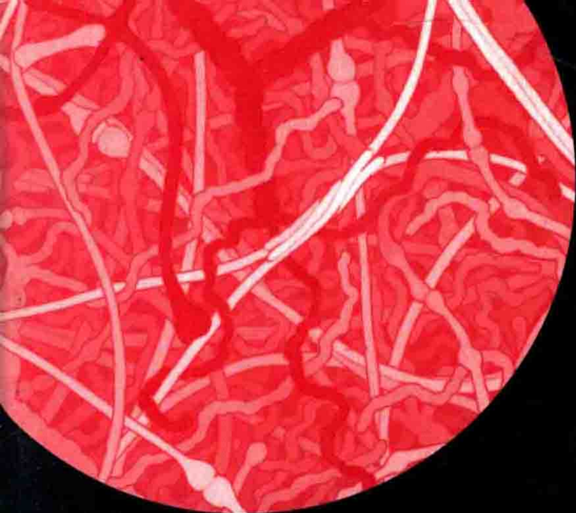
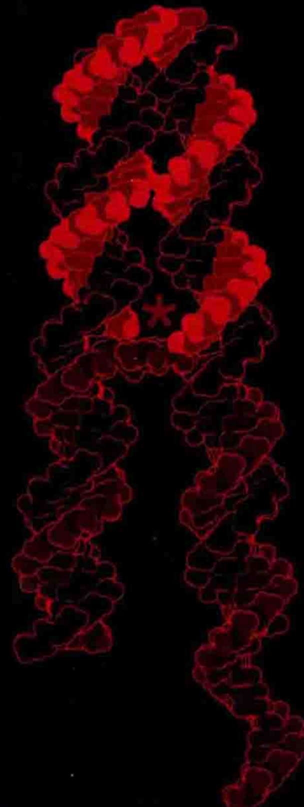


BIONANOTECHNOLOGY



lessons from nature

DAVID S. GOODSELL

BIONANOTECHNOLOGY

Lessons from Nature

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Library of Congress Cataloging-in-Publication Data:

Goodsell, David S.
Biotechnology : lessons from nature / David S. Goodsell.
p. ; cm.
Includes bibliographical references and index.
ISBN 0-471-41719-X (cloth : alk. paper)
1. Biomolecules. 2. Nanotechnology. 3. Biotechnology.
[DNLM: 1. Biotechnology. 2. Nanotechnology. QT 36 G655b 2004] I.
Title.
QP514.2.G658 2004
660.6—dc21 2003006943

Printed in the United States of America

10 9 8 7 6 5 4 3 2

BIONANOTECHNOLOGY

PREFACE

Today is the most exciting time to be working in nanotechnology, and bionanotechnology in particular. Chemistry, biology, and physics have revealed an immense amount of information on molecular structure and function, and now we are poised to make use of it for atomic-level engineering. New discoveries are being made every day, and clever people are pressing these discoveries into service in every imaginable (and unimaginable) way.

In this book, I present many of the lessons that may be learned from biology and how they are being applied to nanotechnology. The book is divided into three basic parts. In the first part, I explore the properties of the nanomachines that are available in cells. In Chapter 2, I present the unfamiliar world of bionanomachines and go on a short tour of the natural nanomachinery that is available for our use. Chapter 3 provides an overview of the techniques that are available in biotechnology for harnessing and modifying these nanomachines.

In the second part, I look to these natural nanomachines for guidance in the building of our own nanomachinery. By surveying what is known about biological molecules, we can isolate the general principles of structure and function that are used to construct functional nanomachines. These include general structural principles, presented in Chapter 4, and functional principles, described in Chapter 5.

The book finishes with two chapters on applications. Chapter 6 surveys some of the exciting applications of bionanotechnology that are currently under study. The final chapter looks to the future, speculating about what we might expect.

Bionanotechnology is a rapidly evolving field, which encompasses a diverse collection of disciplines. This book necessarily omits entire sectors of research and interest and is unavoidably biased by my own interests and my own background as a structural biologist. Biomolecular science still holds many deep mysteries and exciting avenues for study, which should provide even more source material for bionanotechnology in the coming decades. I invite you to explore the growing literature in this field, using this book as an invitation for further reading.

I thank Arthur J. Olson for many useful discussions during the writing of this book.

David S. Goodsell

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THE QUEST FOR NANOTECHNOLOGY

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The principles of physics, as far as I can see, do not speak against the possibility of maneuvering things atom by atom. It is not an attempt to violate any laws; it is something, in principle, that can be done; but in practice, it has not been done because we are too big.

—Richard Feynman*

Nanotechnology is available, today, to anyone with a laboratory and imagination. You can create custom nanomachines with commercially available kits and reagents. You can design and build nanoscale assemblers that synthesize interesting molecules. You can construct tiny machines that seek out cancer cells and kill them. You can build molecule-size sensors for detecting light, acidity, or trace amounts of poisonous metals. Nanotechnology is a reality today, and nanotechnology is accessible with remarkably modest resources.

What is nanotechnology? Nanotechnology is the ability to build and shape matter one atom at a time. The idea of nanotechnology was first presented by physicist Richard Feynman. In a lecture entitled "Room at the Bottom," he unveiled the possibilities available in the molecular world. Because ordinary matter is built of so many atoms, he showed that there is a

*All opening quotes are taken from Richard P. Feynman's 1959 talk at the California Institute of Technology, as published in the February 1960 issue of CalTech's *Engineering and Science.*

Bionanotechnology: Lessons from Nature. By David S. Goodsell
ISBN 0-471-41719-X

remarkable amount of space within which to build. Feynman's vision spawned the discipline of nanotechnology, and we are now amassing the tools to make his dream a reality.

But atoms are almost unbelievably small; a million times smaller than objects in our familiar world. Their properties are utterly foreign, so our natural intuition and knowledge of the meter-scale world is useless at best and misleading at worst. How can we approach the problem of engineering at the atomic scale?

When men and women first restructured matter to fit their needs, an approach opposite from nanotechnology was taken. Instead of building an object from the bottom up, atom-by-atom, early craftsmen invented a top-down approach. They used tools to shape and transform existing matter. Clay, plant fibers, and metals were shaped, pounded, and carved into vessels, clothing, and weapons. With some added sophistication, this approach still accounts for the bulk of all products created by mankind. We still take raw materials from the earth and physically shape them into functional products.

Mankind did not make any concerted effort to shape the atoms in manufactured products until medieval times, when alchemists sowed the seeds of the modern science of chemistry. During their search for the secrets of immortality and the transmutation of lead to gold, they developed methods for the willful combination of atoms. Chemical reaction, purification, and characterization are all tools of the alchemists. Today, chemists build molecules of defined shape and specified properties. Chemical reactions are understood, and tailored, at the atomic level. Most of chemistry, however, is performed at a bulk level. Large quantities of pure materials are mixed and reacted, and the desired product is purified from the mixture of molecules that are formed. Nonetheless, chemistry is nanotechnology—the willful combination of atoms to form a desired molecule. But it is nanotechnology on a bulk scale, controlled by statistical mechanics rather than controlled atom-by-atom at the nanometer scale.

We are now in the midst of the second major revolution of nanotechnology. Now, scientists are attempting modify matter one atom at a time.

Some envision a nanotechnology closely modeled after our own macroscopic technology. This new field has been dubbed *molecular nanotechnology* for its focus on creating molecules individually atom-by-atom. K. Eric Drexler has proposed methods of constructing molecules by forcibly pressing atoms together into the desired molecular shapes, in a process dubbed "mechanosynthesis" for its parallels with macroscopic machinery and engineering. With simple raw materials, he envisions building objects in an assembly-line manner by directly bonding individual atoms. The idea is compelling. The engineer retains direct control over the synthesis, through a physical connection between the atomic realm and our macroscopic world.

Central to the idea of mechanosynthesis is the construction of an *assembler*. This is a nanometer-scale machine that assembles objects atom-by-atom according to defined instructions. Nanotechnology aficionados have speculated that the creation of just a single working assembler would lead immediately to the "Two-Week Revolution." They tell us that as soon as a single assembler is built, all of the dreams of nanotechnology would be realized within days. Researchers could immediately direct this first assembler to build additional new assemblers. These assemblers would immediately allow construction of large-scale factories, filled with level upon level of assemblers for building macroscale objects. Nanotechnology would explode to fill every need and utterly change our way of life. Unfortunately, assemblers based on mechanosynthesis currently remain only an evocative idea.

The subject of this book is another approach to nanotechnology, which is available today to anyone with a moderately equipped laboratory. This is *bionanotechnology*, nanotechnology that looks to nature for its start. Modern cells build thousands of working nanomachines, which may be harnessed and modified to perform our own custom nanotechnological tasks. Modern cells provide us with an elaborate, efficient set of molecular machines that restructure matter atom-by-atom, exactly to our specifications. And with the well-tested techniques of biotechnology, we can extend the function of these machines for our own goals, modifying existing biomolecular nanomachines or designing entirely new ones.

BIOTECHNOLOGY AND THE TWO-WEEK REVOLUTION

The Two-Week Revolution has already occurred, although it has lasted for decades instead of weeks. Biotechnology uses the ready-made assemblers available in living cells to build thousands of custom-designed molecules to atomic specifications, including the construction of new assemblers. This has lead to myriad applications, including commercial production of hormones and drugs, elegant methods for diagnosing and curing infectious and genetic diseases, and engineering of organisms for specialized tasks such as bioremediation and disease resistance.

Biotechnology took several decades to gather momentum. The primary impediment has been the lack of basic knowledge of biomolecular processes and mechanisms. We have been given an incredible toolbox of molecular machinery, and we are only now beginning to learn how to use it. The key enabling technology, recombinant DNA, made the natural protein assembler of the cell available for use. The subsequent years have yielded numerous refinements on the technology, and numerous ideas on how it might be exploited.

Biotechnology has grown, and is still growing, with each new discovery in molecular biology. Further research into viral biology has led to improved vectors for delivering new genetic material. An explosion of enzymes for clipping, editing, ligating, and copying DNA, as well as efficient techniques for the chemical synthesis of DNA, has allowed the creation of complicated new genetic constructs. Engineered bacteria now create large quantities of natural proteins for medicinal use, mutated proteins for research, hybrid chimeric proteins for specialized applications, and entirely new proteins, if a researcher is bold enough to design a protein from scratch.

FROM BIOTECHNOLOGY TO BIONANOTECHNOLOGY

We are now poised to extend biotechnology into bionanotechnology. What is bionanotechnology, and how is it different from biotechnology? The two terms currently share an overlapped field of topics. I will define bionanotechnology here as applications that require human design and construction at the nanoscale level and will label projects as biotechnology when nanoscale understanding and design are not necessary. Biotechnology grew from the use of natural enzymes to manipulate the genetic code, which was then used to modify entire organisms. The atomic details were not really important—existing functionalities were combined to achieve the end goal. Today, we have the ability to work at a much finer level with a more detailed level of understanding and control. We have the tools to create biological machines atom-by-atom according to our own plans. Now, we must flex our imagination and venture into the unknown.

Bionanotechnology has many different faces, but all share a central concept: the ability to design molecular machinery to atomic specifications. Today, individual bionanomachines are being designed and created to perform specific nanoscale tasks, such as the targeting of a cancer cell or the solution of a simple computational task. Many are toy problems, designed to test our understanding and control of these tiny machines. As bionanotechnology matures, we will redesign the biomolecular machinery of the cell to perform large-scale tasks for human health and technology. Macroscopic structures will be built to atomic precision with existing biomolecular assemblers or by using biological models for assembly. Looking to cells, we can find atomically precise molecule-sized motors, girders, random-access memory, sensors, and a host of other useful mechanisms, all ready to be harnessed by bionanotechnology. And the technology for designing and constructing these machines in bulk scale is well worked out and ready for application today.

Nanomedicine will be the biggest winner. Bionanomachines work best in the environment of a living cell and so are tailored for medical applications. Complex molecules that seek out diseased or cancerous cells are already a reality. Sensors for diagnosing diseased states are under development. Replacement therapy, with custom-constructed molecules, is used today to treat diabetes and growth hormone deficiencies, with many other applications on the horizon.

Biomaterials are another major application of bionanotechnology. We already use biomaterials extensively. Look around the room and notice how much wood is used to build your shelter and furnishing and how much cotton, wool, and other natural fibers are used in your clothing and books. Biomaterials address our growing ecological sensitivity—biomaterials are strong but biodegradable. Biomaterials also integrate perfectly with living tissue, so they are ideal for medical applications.

The production of hybrid machines, part biological and part inorganic,