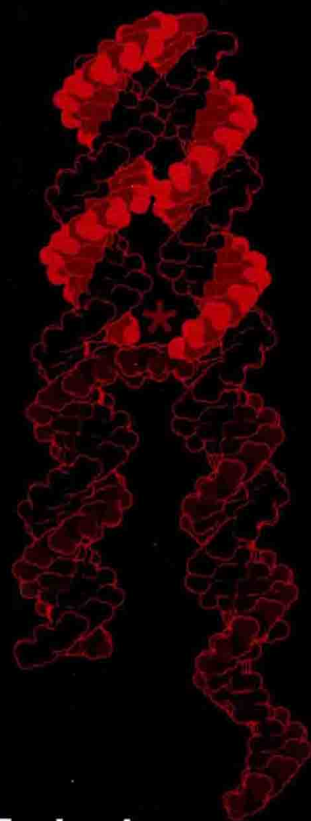


BIONANOTECHNOLOGY

*lessons
from
nature*



DAVID S. GOODSELL

BIONANOTECHNOLOGY

Lessons from Nature

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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. GOODSSELL

CONTENTS

1	The Quest for Nanotechnology	1
	Biotechnology and the Two-Week Revolution	3
	From Biotechnology to Bionanotechnology	4
	What is Bionanotechnology?	6
2	Bionanomachines in Action	9
	The Unfamiliar World of Bionanomachines	10
	Gravity and inertia are negligible at the nanoscale	10
	Nanomachines show atomic granularity	11
	Thermal motion is a significant force at the nanoscale	12
	Bionanomachines require a water environment	13
	Modern Biomaterials	14
	Most natural bionanomachines are composed of protein	15
	Nucleic acids carry information	21
	Lipids are used for infrastructure	24
	Polysaccharides are used in specialized structural roles	27
	The Legacy of Evolution	28
	Evolution has placed significant limitations on the properties of natural biomolecules	31
	Guided Tour of Natural Bionanomachinery	32
3	Biomolecular Design and Biotechnology	43
	Recombinant DNA Technology	45
	DNA may be engineered with commercially available enzymes	46
	Site-directed mutagenesis makes specific changes in the genome	52
	Fusion proteins combine two functions	52

Monoclonal Antibodies	54
Biomolecular Structure Determination	57
X-ray crystallography provides atomic structures	58
NMR spectroscopy may be used to derive atomic structures	61
Electron microscopy reveals molecular morphology	62
Atomic force microscopy probes the surface of biomolecules	64
Molecular Modeling	66
Bionanomachines are visualized with computer graphics	67
Computer modeling is used to predict biomolecular structure and function	68
The protein folding problem	69
Docking simulations predict the modes of biomolecular interaction	72
New functionalities are developed with computer-assisted molecular design	74
4 Structural Principles of Bionanotechnology	75
Natural Bionanomachinery is Designed for a Specific Environment	76
A Hierarchical Strategy Allows Construction of Nanomachines	77
The Raw Materials: Biomolecular Structure and Stability	80
Molecules are composed of atoms linked by covalent bonds	80
Dispersion and repulsion forces act at close range	84
Hydrogen bonds provide stability and specificity	86
Electrostatic interactions are formed between charged atoms	87
The hydrophobic effect stabilizes biomolecules in water	89
Protein Folding	91
Not all protein sequences adopt stable structures	93
Globular proteins have a hierarchical structure	93
Stable globular structure requires a combination of design strategies	95
Chaperones provide the optimal environment for folding	98
Rigidity can make proteins more stable at high temperatures	100
Many proteins make use of disorder	101

Self-Assembly	103
Symmetry allows self-assembly of stable complexes with defined size	105
Quasisymmetry is used to build assemblies too large for perfect symmetry	113
Crowded conditions promote self-assembly	115
Self-Organization	116
Lipids self-organize into bilayers	117
Lipid bilayers are fluid	118
Proteins may be designed to self-organize with lipid bilayers	119
Molecular Recognition	121
Crane principles for molecular recognition	122
Atomicity limits the tolerance of combining sites	127
Flexibility	129
Biomolecules show flexibility at all levels	130
Flexibility poses great challenges for the design of bionanomachines	134
5 Functional Principles of Bionanotechnology	135
Information-Driven Nanoassembly	136
Nucleic acids carry genetic information	136
Ribosomes construct proteins	140
Information is stored in very compact form	142
Energetics	145
Chemical energy is transferred by carrier molecules	146
Light is captured with specialized small molecules	149
Protein pathways transfer single electrons	151
Electrical conduction and charge transfer have been observed in DNA	155
Electrochemical gradients are created across membranes	156
Chemical Transformation	158
Enzymes reduce the entropy of a chemical reaction	162
Enzymes create environments that stabilize transition states	163
Enzymes use chemical tools to perform a reaction	164

Regulation	167
Protein activity may be regulated through allosteric motions	167
Protein action may be regulated by covalent modification	171
Biomaterials	173
Helical assembly of subunits forms filaments and fibrils	174
Microscale infrastructure is built from fibrous components	177
Minerals are combined with biomaterials for special applications	181
Elastic proteins use disordered chains	184
Cells make specific and general adhesives	187
Biomolecular Motors	189
ATP powers linear motors	190
ATP synthase and flagellar motors are rotary motors	194
Brownian ratchets rectify random thermal motions	201
Traffic Across Membranes	203
Potassium channels use a selectivity filter	205
ABC transporters use a flip-flop mechanism	207
Bacteriorhodopsin uses light to pump protons	207
Biomolecular Sensing	211
Smell and taste detect specific molecules	212
Light is sensed by monitoring light-sensitive motions in retinal	213
Mechanosensory receptors sense motion across a membrane	213
Bacteria sense chemical gradients by rectification of random motion	216
Self-Replication	216
Cells are autonomous self-replicators	217
The basic design of cells is shaped by the processes of evolution	220
Machine-Phase Bionanotechnology	221
Muscle sarcomeres	221
Nerves	224
6 Bionanotechnology Today	227
Basic Capabilities	228
Natural proteins may be simplified	228
Proteins are being designed from scratch	230
Proteins may be constructed with nonnatural amino acids	232

Peptide nucleic acids provide a stable alternative to DNA and RNA	235
Nanomedicine Today	237
Computer-aided drug design has produced effective anti-AIDS drugs	238
Immunotoxins are targeted cell killers	240
Drugs may be delivered with liposomes	241
Artificial blood saves lives	243
Gene therapy will correct genetic defects	245
General medicine is changing into personalized medicine	247
Self-Assembly at Many Scales	248
Self-assembling DNA scaffolds have been constructed	248
Cyclic peptides form nanotubes	250
Fusion proteins self-assemble into extended structures	252
Small organic molecules self-assemble into large structures	252
Larger objects may be self-assembled	254
Harnessing Molecular Motors	257
ATP synthase is used as a rotary motor	257
Molecular machines have been built of DNA	259
DNA Computers	261
The first DNA computer solved a traveling salesman problem	262
Satisfiability problems are solved by DNA computing	264
A Turing machine has been built with DNA	265
Molecular Design Using Biological Selection	266
Antibodies may be turned into enzymes	267
Peptides may be screened with bacteriophage display libraries	271
Nucleic acids with novel functions may be selected	273
Functional bionanomachines are surprisingly common	277
Artificial Life	277
Artificial protocells reproduce by budding	278
Self-replicating molecules are an elusive goal	280
ATP is made with an artificial photosynthetic liposome	281
Poliovirus has been created with only a genetic blueprint	283
Hybrid Materials	285
Nanoscale conductive metal wires may be constructed with DNA	285

Patterned aggregates of gold nanoparticles are formed with DNA	286
DNA flexes a sensitive mechanical lever	287
Researchers are harnessing biomineralization	288
Biosensors	290
Antibodies are widely used as biosensors	291
Biosensors detect glucose levels for management of diabetes	292
Engineered nanopores detect specific DNA sequences	294
7 The Future of Bionanotechnology	295
A Timetable for Bionanotechnology	296
Lessons for Molecular Nanotechnology	298
Three Case Studies	300
Case study: Nanotube synthase	301
Case study: A general nanoscale assembler	303
Case study: Nanosurveillance	305
Ethical Considerations	309
Respect for life	309
Potential dangers	310
Final thoughts	311
Literature	313
Sources	320
Index	323

THE QUEST FOR NANOTECHNOLOGY

1

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*.

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 led 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,