The Biologization of Engineering -- and of Engineering Education

- Engineering Education
- Reports, Recommendations, and Predictions
- Biological and BioMedical Engrg----> Man (and Woman)
- Biology--Inspired Engineering---> Creativity
    - 4 Billion Years is a very long time!
    - 30 Million plus Species
    - Energy from the Sky
    - Materials from the Air
- Bio-Based Engineering -- Concepts and Themes
- Examples
- Enjoy

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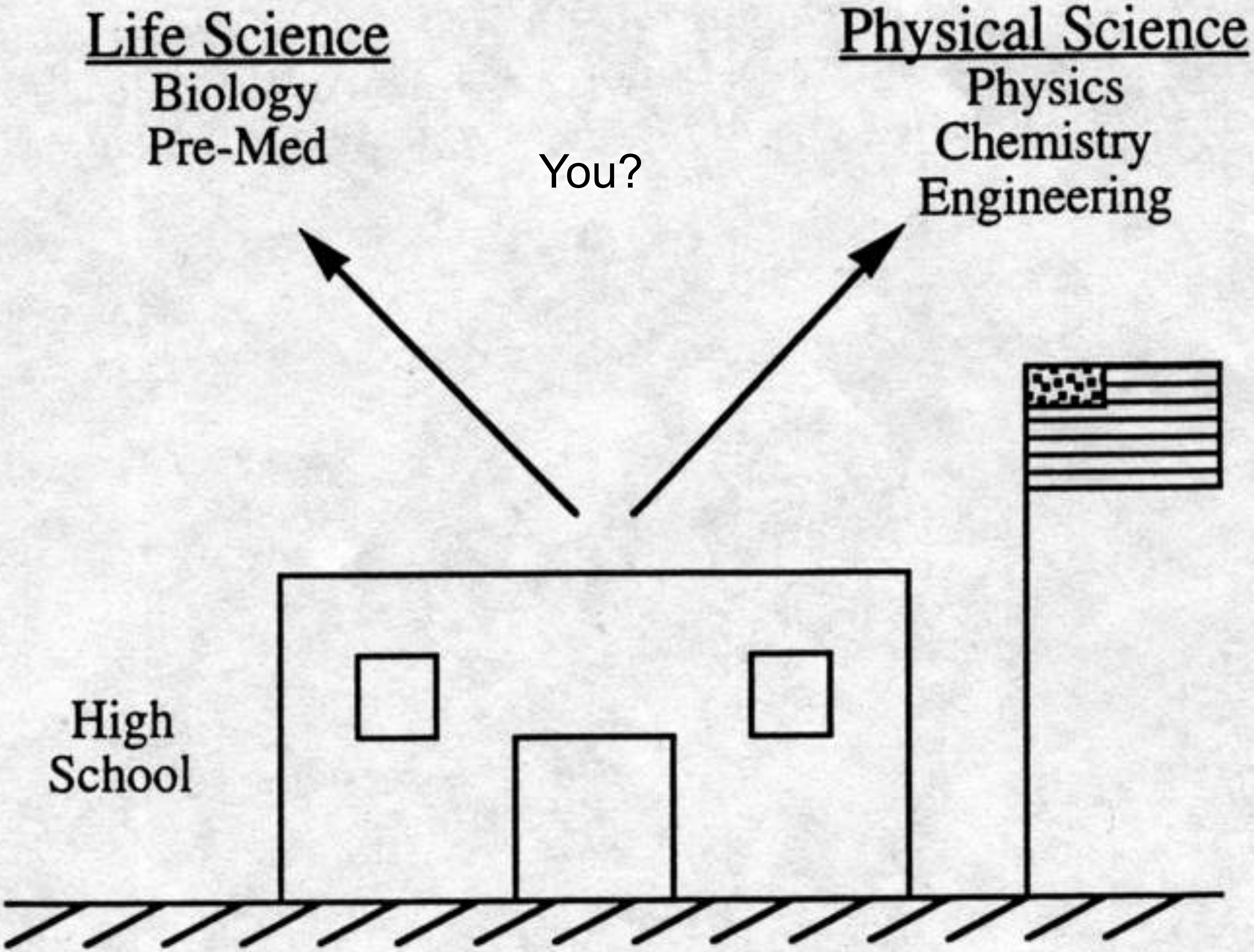
Winona 10/26/00



Life Science
Biology
Pre-Med

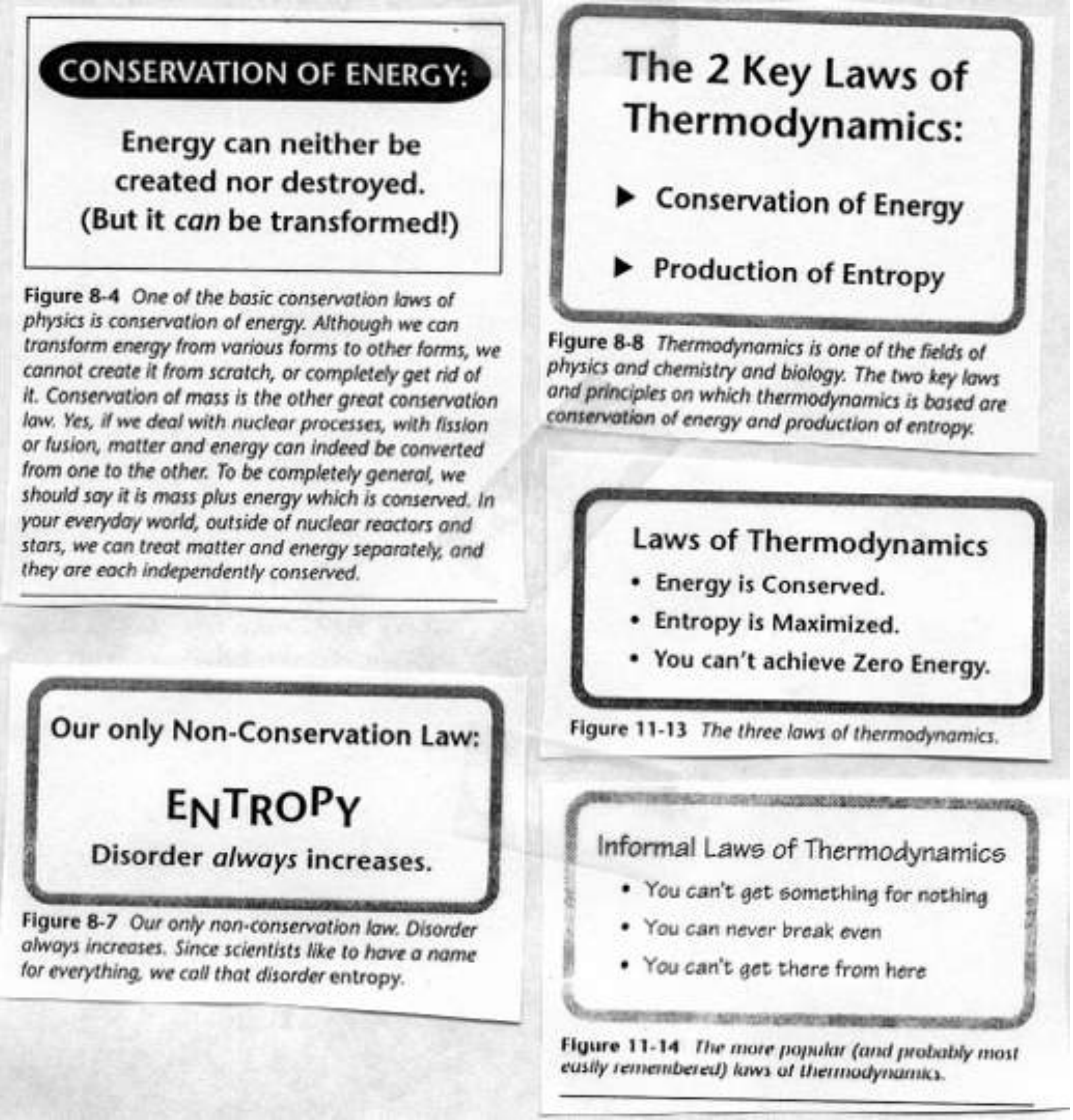
You?

Physical Science
Physics
Chemistry
Engineering

High
School

Engineering Disciplines	Basic Science Fields
Electrical Engineering	Physics (electricity and magnetism)
Mechanical Engineering	Physics (mechanics)
Civil Engineering	Physics (mechanics)
Chemical Engineering	Chemistry
Computer Engineering	Physics
Materials Engineering	Chemistry/Physics
Biomedical Engineering	Biology/Physiology
ALL	Mathematics

Rules:
Physics



CONSERVATION OF ENERGY:

Energy can neither be created nor destroyed. (But it *can* be transformed!)

Figure 8-4 *One of the basic conservation laws of physics is conservation of energy. Although we can transform energy from various forms to other forms, we cannot create it from scratch, or completely get rid of it. Conservation of mass is the other great conservation law. Yes, if we deal with nuclear processes, with fission or fusion, matter and energy can indeed be converted from one to the other. To be completely general, we should say it is mass plus energy which is conserved. In your everyday world, outside of nuclear reactors and stars, we can treat matter and energy separately, and they are each independently conserved.*

Our only Non-Conservation Law:

ENTROPY

Disorder *always* increases.

Figure 8-7 *Our only non-conservation law. Disorder always increases. Since scientists like to have a name for everything, we call that disorder entropy.*

The 2 Key Laws of Thermodynamics:

- ▶ **Conservation of Energy**
- ▶ **Production of Entropy**

Figure 8-8 *Thermodynamics is one of the fields of physics and chemistry and biology. The two key laws and principles on which thermodynamics is based are conservation of energy and production of entropy.*

Laws of Thermodynamics

- **Energy is Conserved.**
- **Entropy is Maximized.**
- **You can't achieve Zero Energy.**

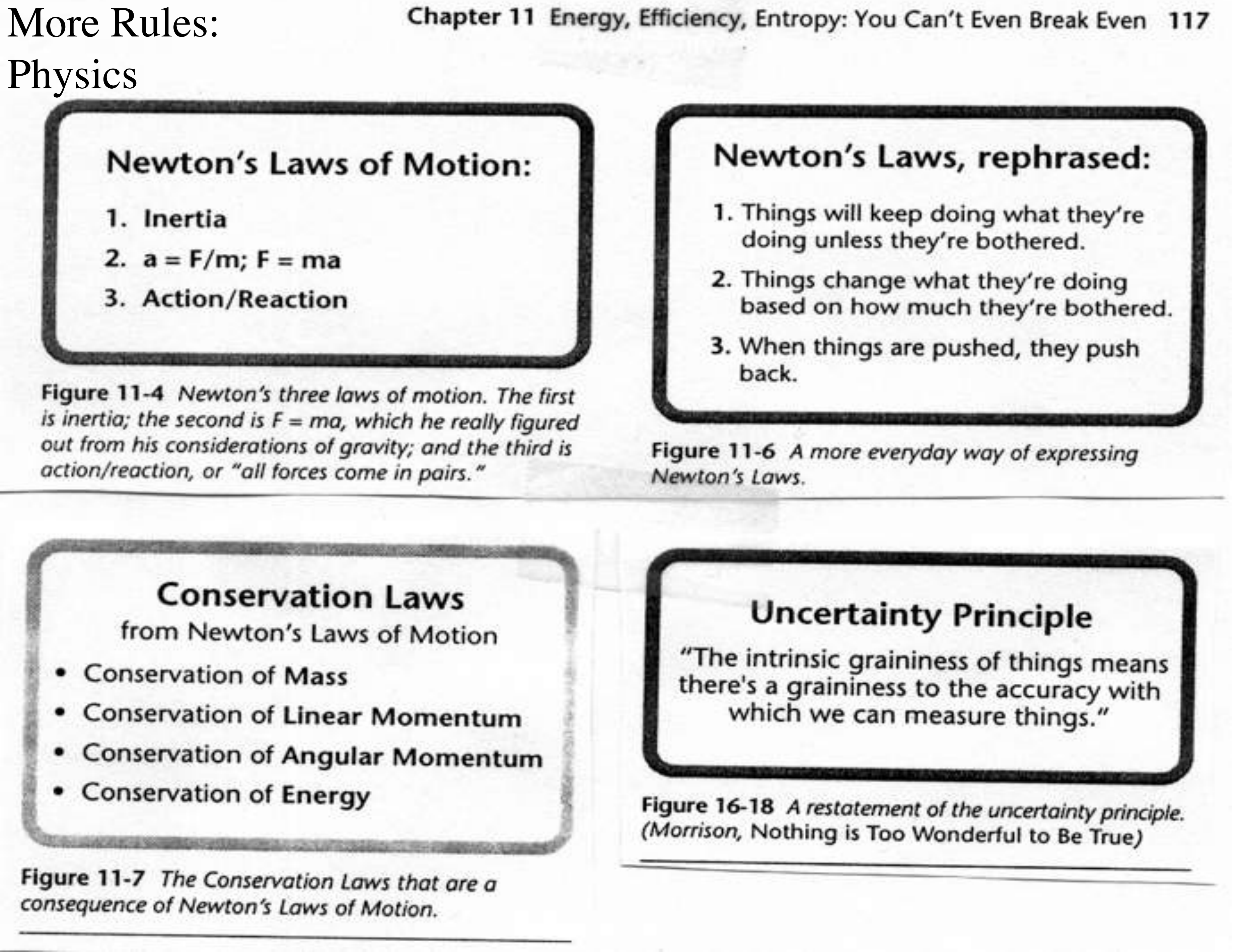
Figure 11-13 *The three laws of thermodynamics.*

Informal Laws of Thermodynamics

- You can't get something for nothing
- You can never break even
- You can't get there from here

Figure 11-14 *The more popular (and probably most easily remembered) laws of thermodynamics.*

More Rules: Physics



Newton's Laws of Motion:

1. Inertia
2. a = F/m; F = ma
3. Action/Reaction

Figure 11-4 *Newton's three laws of motion. The first is inertia; the second is F = ma, which he really figured out from his considerations of gravity; and the third is action/reaction, or "all forces come in pairs."*

Newton's Laws, rephrased:

1. Things will keep doing what they're doing unless they're bothered.
2. Things change what they're doing based on how much they're bothered.
3. When things are pushed, they push back.

Figure 11-6 *A more everyday way of expressing Newton's Laws.*

Conservation Laws

from Newton's Laws of Motion

- Conservation of **Mass**
- Conservation of **Linear Momentum**
- Conservation of **Angular Momentum**
- Conservation of **Energy**

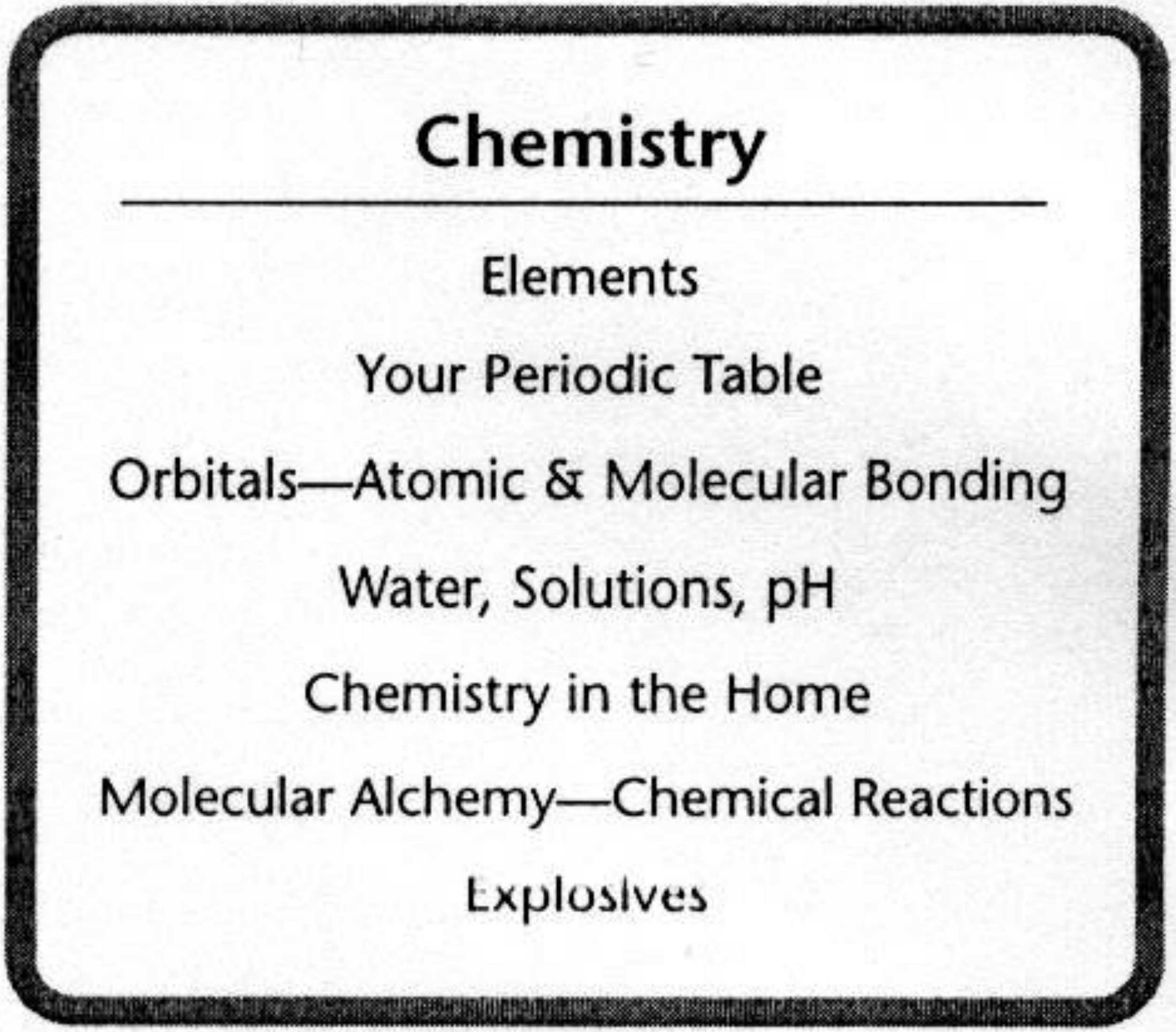
Figure 11-7 *The Conservation Laws that are a consequence of Newton's Laws of Motion.*

Uncertainty Principle

"The intrinsic graininess of things means there's a graininess to the accuracy with which we can measure things."

Figure 16-18 *A restatement of the uncertainty principle. (Morrison,* Nothing is Too Wonderful to Be True*)*

Stuff: Chemistry



Chemistry

Elements

Your Periodic Table

Orbitals—Atomic & Molecular Bonding

Water, Solutions, pH

Chemistry in the Home

Molecular Alchemy—Chemical Reactions

Explosives

Figure 24-23 *Key topics of chemistry.*

Ages of Engineering and Engineering Education

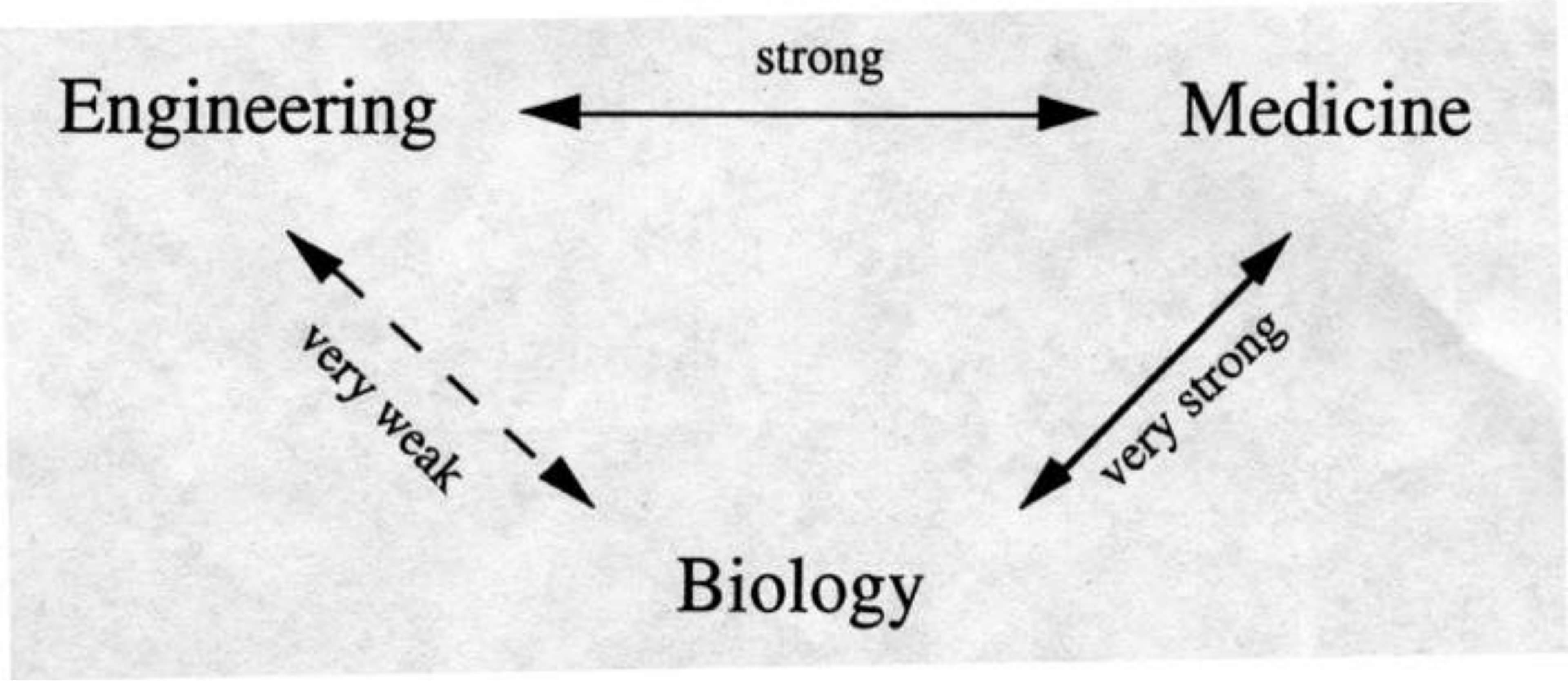
(based in part on speeches by N.R. Augustine, former Chair and CEO, Lockheed--Martin)

- Structural Age -- Statics-- fighting gravity
- Mechanical Age -- Dynamics -- fighting friction
- Energy Age -- Industrial Revolution and fossil fuels
- Information Age -- Electronics and Computers
- Socioengineering (according to Augustine in 1993):
  - Communication skills
  - Environmental skills
  - Political skills
  - Economics skills
  - International skills
- But, says Andrade: Biology Age

A Time Perspective --

YOU: 20 to 50 plus years (now)
Your Life: +20-60 years (hopefully!)
Chemistry: 150 years (since Mendeleev)
Physics: 300 years (since Newton)
Civilization: 10,000--50,000 years
Life (Biology): 3.5±0.5 Billion years

3.5-4.0 billion years is a long, long time!!



3.5-4.0 billion years is a long, long time!!

Rules and Principles:Biology

Chapter 26 What is Life? Diversity and Extinction **283**

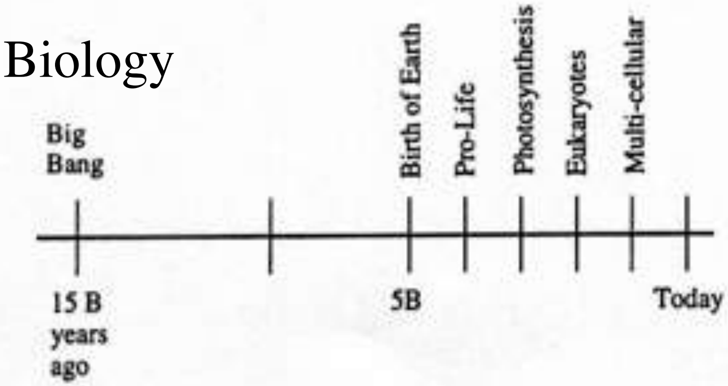
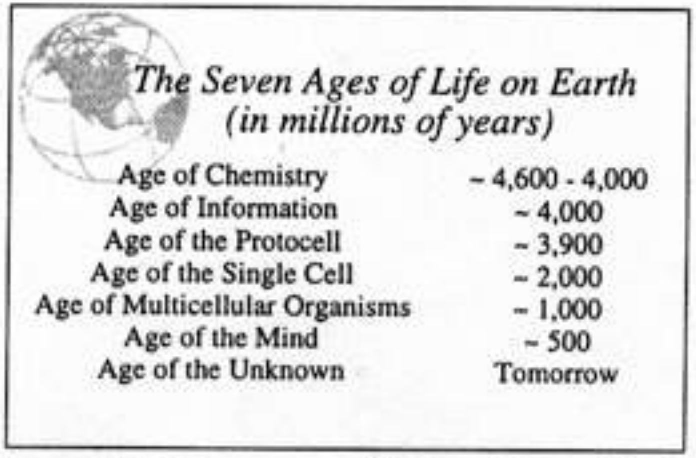


Figure 26-13 *A very rough clock! In billions of years.*

Chapter 27 What is Life? The Very Early Days **293**



The Seven Ages of Life on Earth (in millions of years)

Age of Chemistry	~ 4,600 - 4,000
Age of Information	~ 4,000
Age of the Protocell	~ 3,900
Age of the Single Cell	~ 2,000
Age of Multicellular Organisms	~ 1,000
Age of the Mind	~ 500
Age of the Unknown	Tomorrow

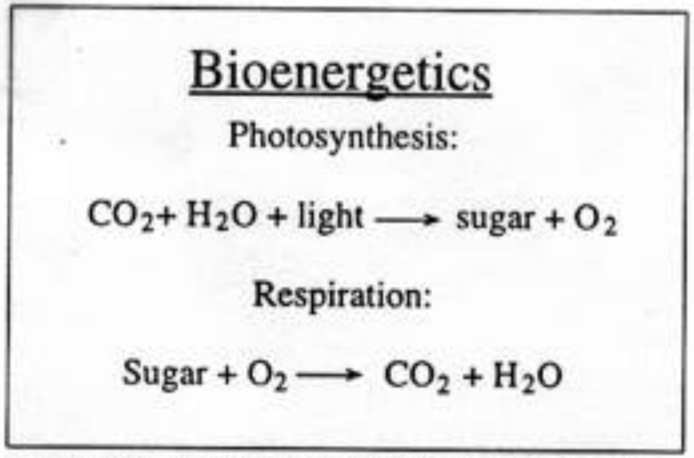
Figure 27-3 *The seven ages of life, from de Duve's book.*

30+ Million species!

Five Kingdoms

Monera	Prokaryotes: Bacteria
Protoctista ..	Eukaryotes: Mainly single cell protists
Fungi	Multi-celled Eukaryotes: Mainly molds & mushrooms
Animalia	Multi-celled Eukaryotes: The Animals
Plantae	Multi-celled Eukaryotes: Green Plants

Figure 26-5 *A summary of the Five Kingdoms.*



Bioenergetics

Photosynthesis:

$$CO_2 + H_2O + \text{light} \longrightarrow \text{sugar} + O_2$$

Respiration:

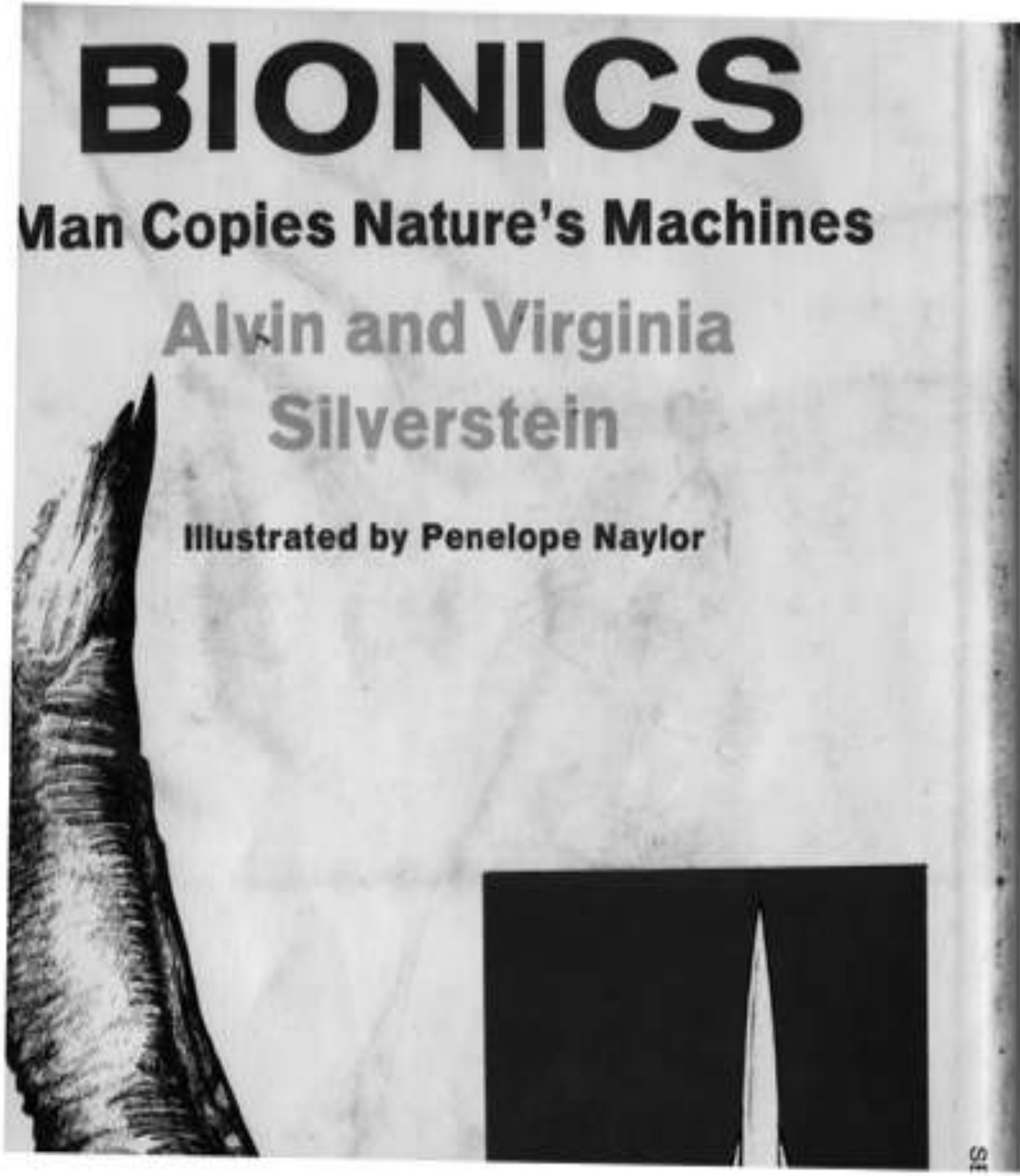
$$\text{Sugar} + O_2 \longrightarrow CO_2 + H_2O$$

Figure 29-1 *Bioenergetics is that part of biology and biochemistry which deals with transformations of energy. There are two major fields of bioenergetics: photosynthesis, which produces oxygen and "fuels," and respiration, which produces CO_2 and water.*

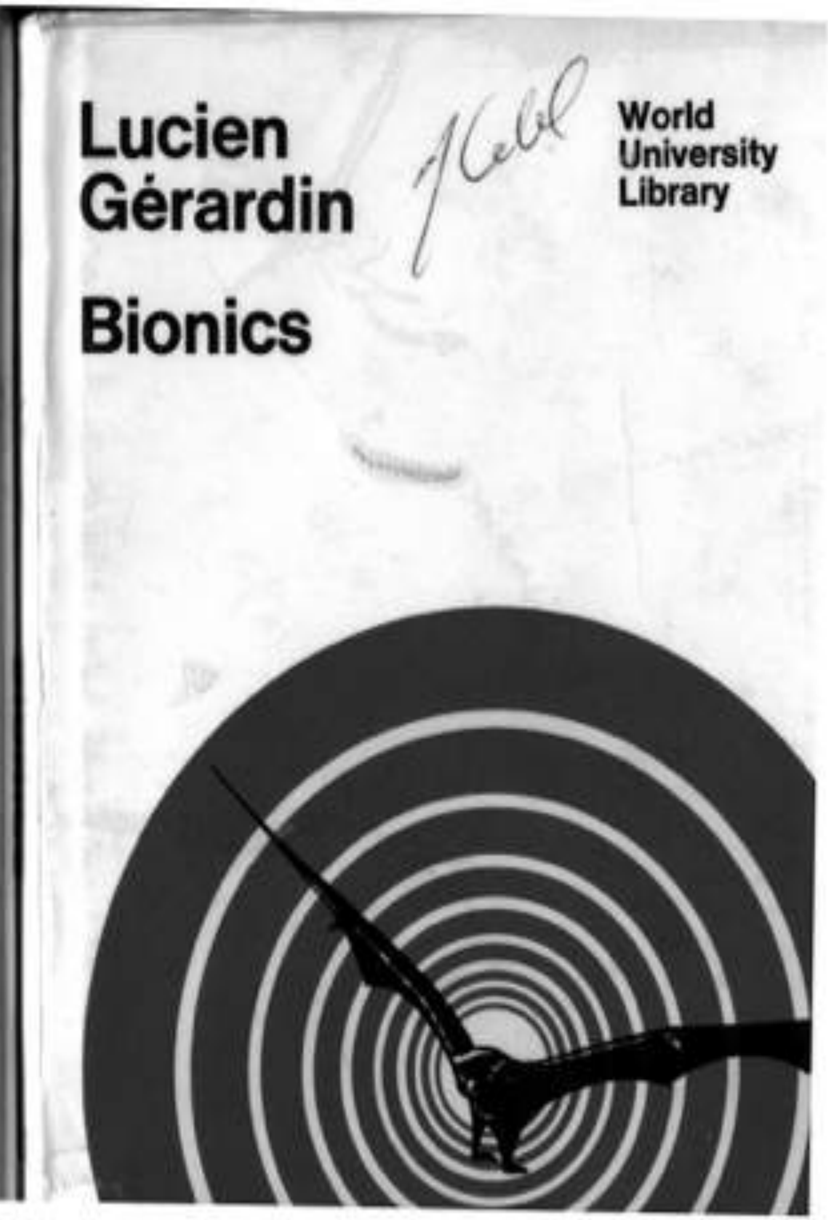
Bio-Based Engineering:

Looking to Biology for Inspiration and Ideas --

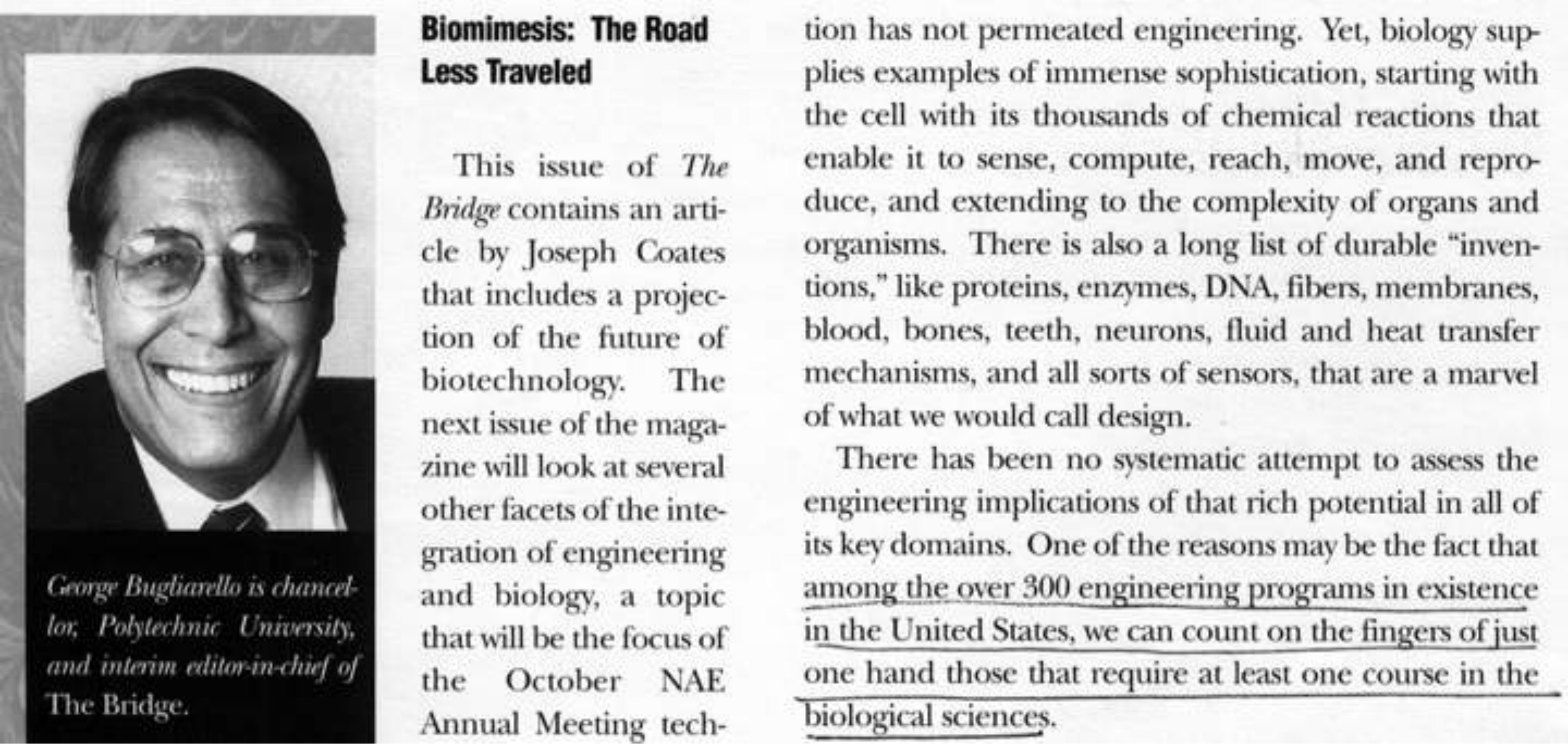
4 billion years is a long, long time!!



McCall
Publ.,1970



McGraw-Hill,
1968



George Bugliarello is chancellor, Polytechnic University, and interim editor-in-chief of The Bridge.

Biomimesis: The Road Less Traveled

This issue of *The Bridge* contains an article by Joseph Coates that includes a projection of the future of biotechnology. The next issue of the magazine will look at several other facets of the integration of engineering and biology, a topic that will be the focus of the October NAE Annual Meeting tech-

tion has not permeated engineering. Yet, biology supplies examples of immense sophistication, starting with the cell with its thousands of chemical reactions that enable it to sense, compute, reach, move, and reproduce, and extending to the complexity of organs and organisms. There is also a long list of durable "inventions," like proteins, enzymes, DNA, fibers, membranes, blood, bones, teeth, neurons, fluid and heat transfer mechanisms, and all sorts of sensors, that are a marvel of what we would call design.

There has been no systematic attempt to assess the engineering implications of that rich potential in all of its key domains. One of the reasons may be the fact that among the over 300 engineering programs in existence in the United States, we can count on the fingers of just one hand those that require at least one course in the biological sciences.

The Bridge, 27-3 (1997) 2

The Emergence of Bioengineering

Robert M. Nerem

The melding of engineering and the biological sciences will require bold and creative changes in the engineering profession.

The Bridge, 27-4 (1997) 4

Areas of Bioengineering Application

Agricultural Engineering
Animal Systems Engineering
Aquacultural Engineering
Biomedical Engineering
Bioprocess Engineering
Ecological Systems Engineering
Environmental Engineering
Food Engineering
Genetic Engineering
Horticultural Engineering
Human Engineering
Microbial Systems Engineering
Rehabilitation Engineering

“…we need to make biology a part of the science foundation required of any person with a university education...
This includes ... engineering students...
There clearly is a need for a true integration of biology and engineering.”

Robert M. Nerem, The Bridge, 27 (4), 1997, pp. 4-8

Biological Concepts and Topics:

- Energy transduction and storage
  - Mechano-chemical mechanisms
  - Electrical/chemical gradients
  - Photoreception
  - Light production: Bioluminescence
  - Heat production: Thermogenesis
- Bio-optics
  - Wave length shifting
  - Filtering
  - Polarization
  - Simple and compound lenses

Biological Concepts and Topics:

- Structure and Materials
  - Novel geometries
  - Functional compounds
  - Nano and micro building blocks
- Chemical processes
  - Catalytic enzymes
  - Unique reaction environments
  - Mining the air
- Environmental adaptation
  - Survival
  - Extreme environments
  - Rapid, combinatorial experiments

Biological Concepts and Topics:

- Sensory mechanisms
  - Electromagnetic field detection
  - Thermal field detection
  - Stress and strain field detection
  - Chemical potentials and gradients
- Information processing
- Communications strategies and modalities

My Course on Bio-Based Engineering

Photon transduction	photosynthesis
Photon production	bioluminescence
Heat generation	thermogenesis
Drought resistance	anhydrobiosis
Frost resistance	antifreeze
Extreme environments	extremophilia
Hydrogen production	metabolism
Electric field generation	electric organs

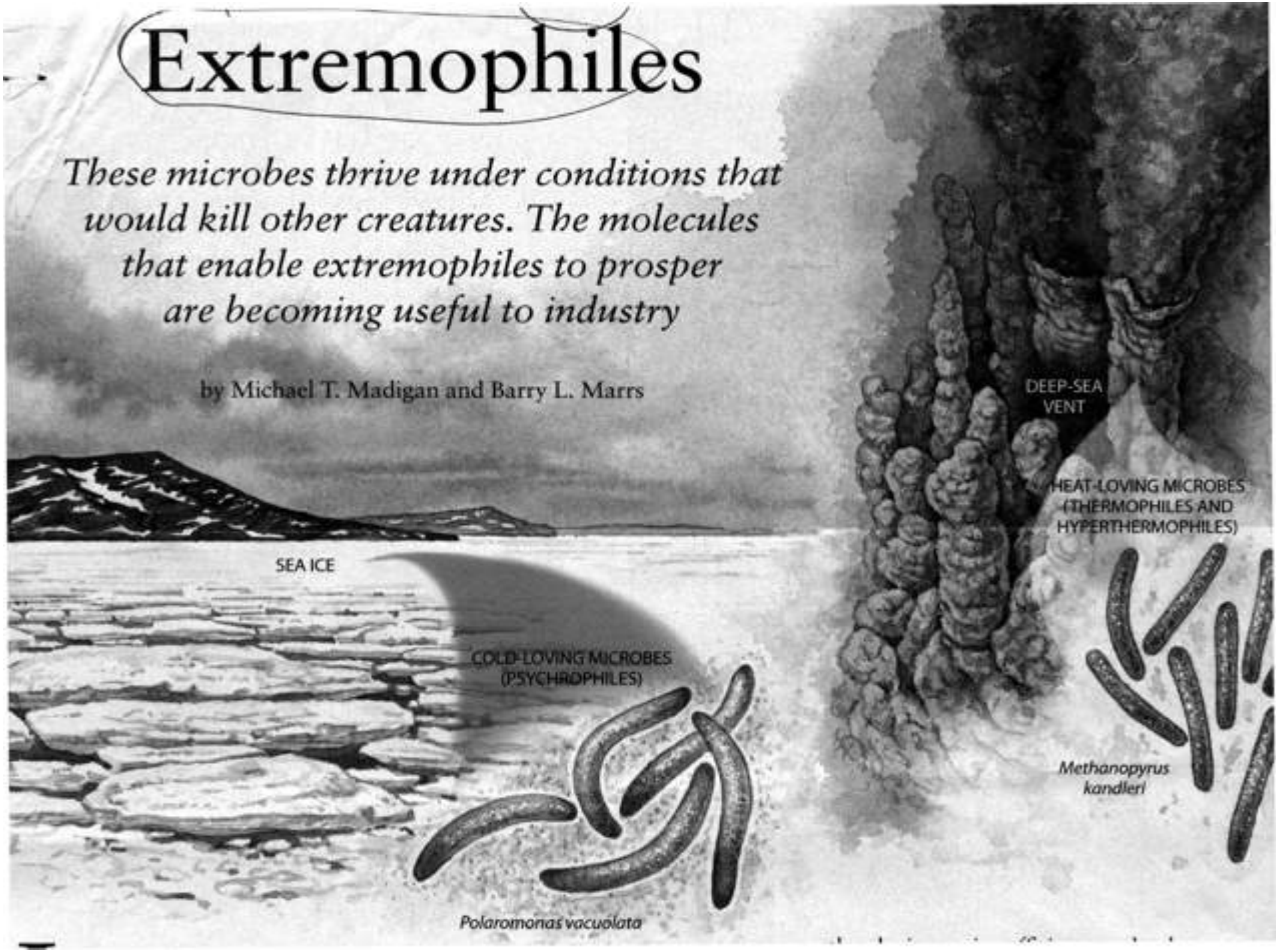
And now for some examples

- Put on your creativity and invention caps--

Biological Concepts and Topics:

From Microorganisms

Photosynthesis
Bioluminescence
Thermogenesis
Psychrophilia (cold loving)
Barophilia (pressure loving 250 atm!)
Halophilia (salt loving 4-5M!)
Nitrogen reducing
High and low pH (pH 1 to 10 !!)
Magnetotaxis
Drought tolerance

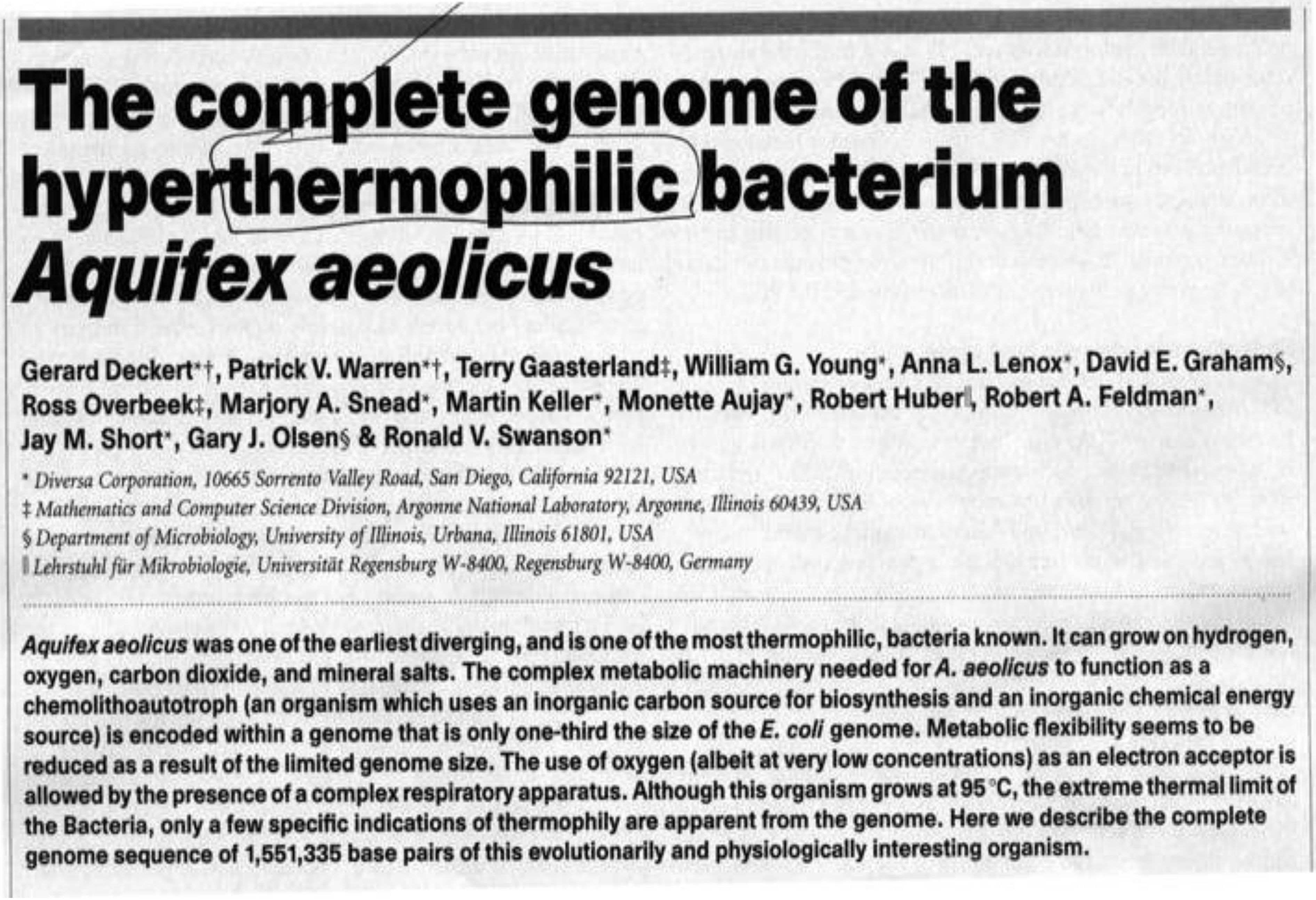


Extremophiles

These microbes thrive under conditions that would kill other creatures. The molecules that enable extremophiles to prosper are becoming useful to industry

by Michael T. Madigan and Barry L. Marrs

Scient. Amer. April, 1997, pp. 82-87



The complete genome of the hyperthermophilic bacterium *Aquifex aeolicus*

Gerard Deckert[*,†], Patrick V. Warren[*,†], Terry Gaasterland[‡], William G. Young[*], Anna L. Lenox[*], David E. Graham[§], Ross Overbeek[‡], Marjory A. Snead[*], Martin Keller[*], Monette Aujay[*], Robert Huber[‖], Robert A. Feldman[*], Jay M. Short[*], Gary J. Olsen[§] & Ronald V. Swanson[*]

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[‡] *Mathematics and Computer Science Division, Argonne National Laboratory, Argonne, Illinois 60439, USA*
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[‖] *Lehrstuhl für Mikrobiologie, Universität Regensburg W-8400, Regensburg W-8400, Germany*

Aquifex aeolicus was one of the earliest diverging, and is one of the most thermophilic, bacteria known. It can grow on hydrogen, oxygen, carbon dioxide, and mineral salts. The complex metabolic machinery needed for *A. aeolicus* to function as a chemolithoautotroph (an organism which uses an inorganic carbon source for biosynthesis and an inorganic chemical energy source) is encoded within a genome that is only one-third the size of the *E. coli* genome. Metabolic flexibility seems to be reduced as a result of the limited genome size. The use of oxygen (albeit at very low concentrations) as an electron acceptor is allowed by the presence of a complex respiratory apparatus. Although this organism grows at 95 °C, the extreme thermal limit of the Bacteria, only a few specific indications of thermophily are apparent from the genome. Here we describe the complete genome sequence of 1,551,335 base pairs of this evolutionarily and physiologically interesting organism.

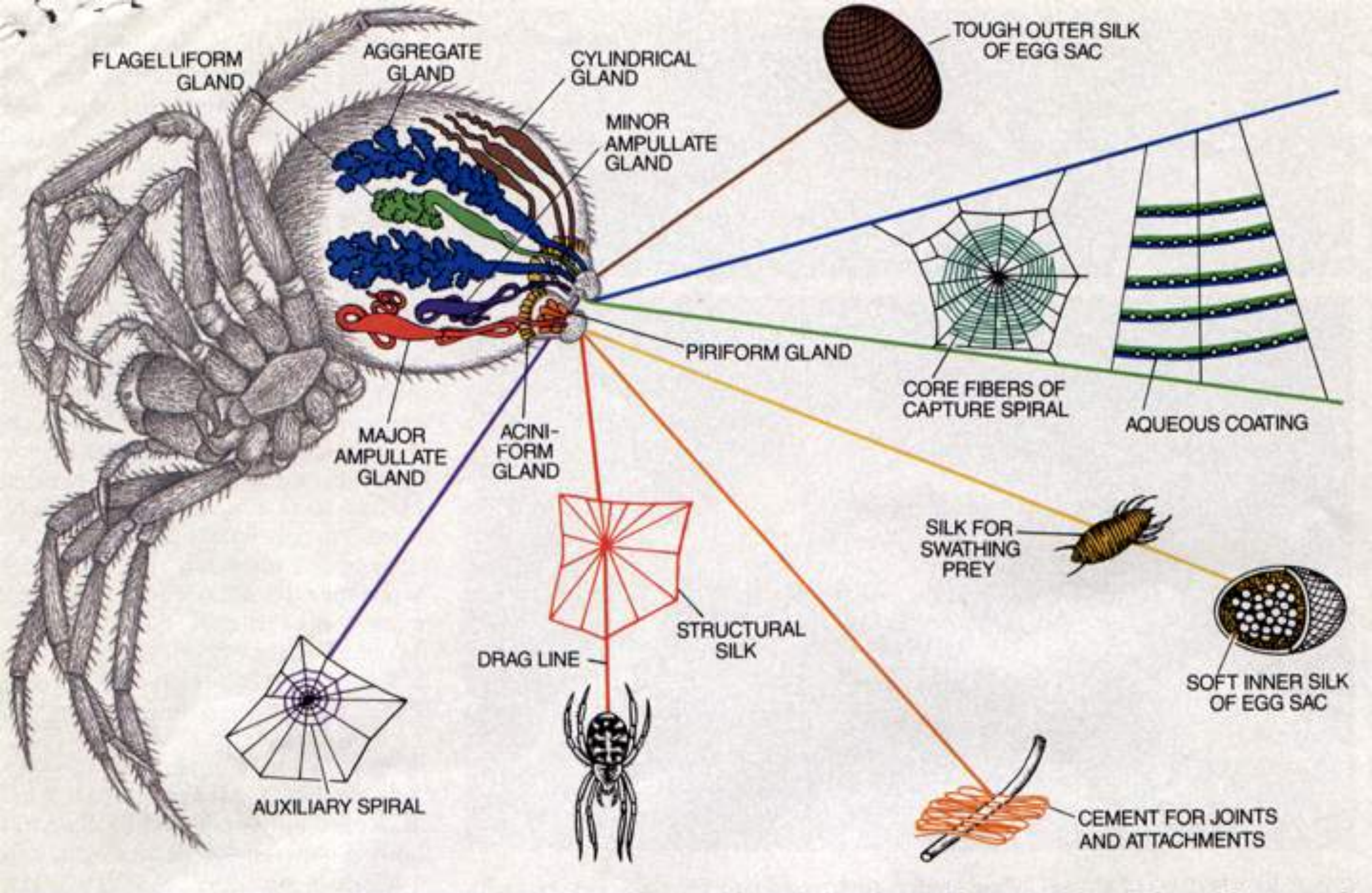
Just 1 of 30 -- soon ~100

Nature, 393 (1998) 353

Biological Concepts and Topics:

From Animals:

- Bioluminescence (fireflies)
- Electric fields (fish)
    - production
    - detection
- Magnetotaxis...
- Thermal fields
    - organs for Thermogenesis (and hibernation)
    - Heat detection (snakes)
- Drought resistance -- Anhydrobiosis
- Salt tolerance and salt glands (sea birds)
- Water conservation and production
- Materials -- Webs, Shells, Skeletons, etc.



DIFFERENT SILKS for different functions can be produced by the same spider. *A. diadematus* can switch between silks with varied amino acid compositions. The spider uses abdominal glands and spigots to produce seven kinds of silk.

F. Vollrath, Spider Webs and Silks, Scient. Amer. Mar. 1992, 70-76

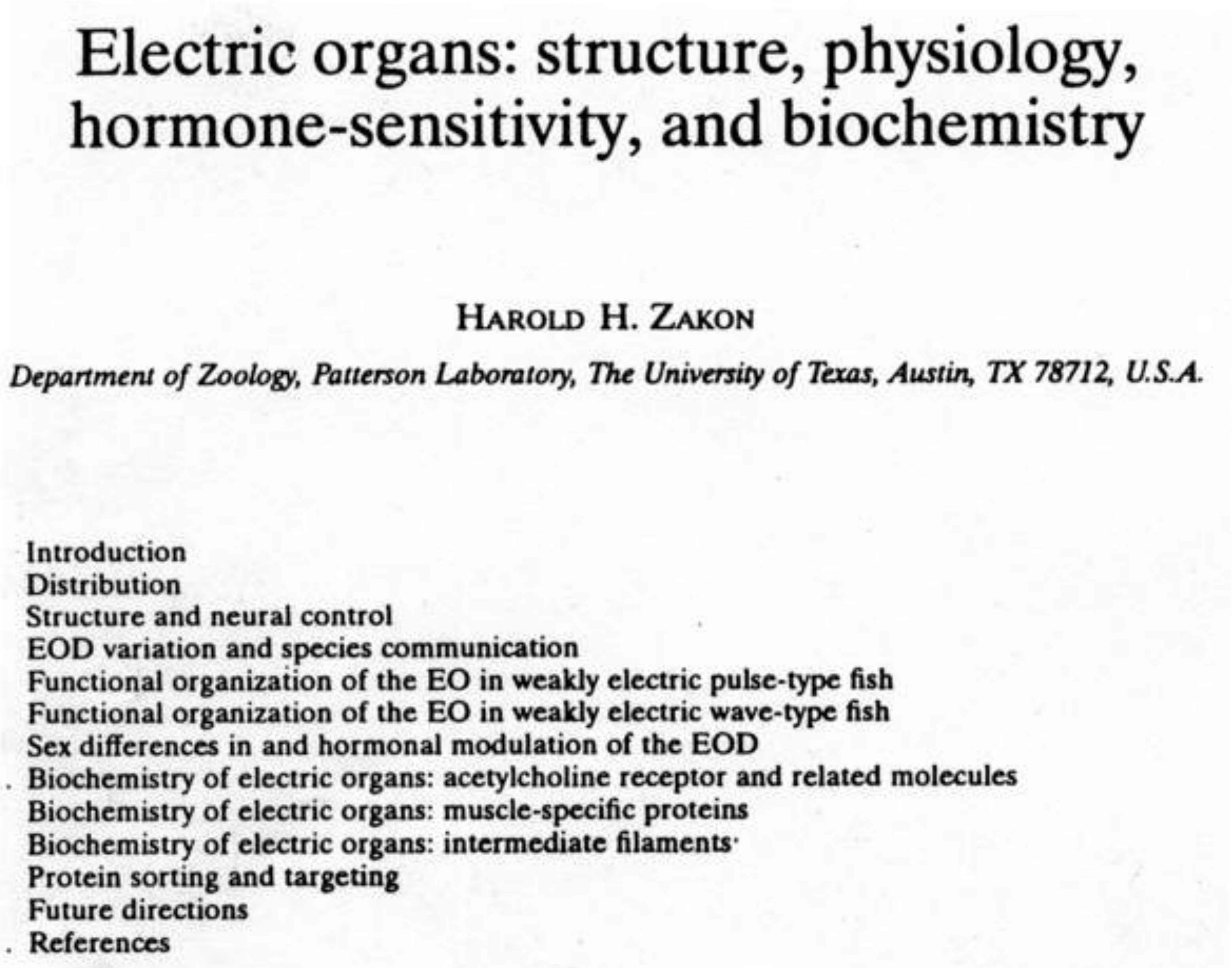
AMER. ZOOL., 31:726–742 (1991)

Evolutionary Novelties: How Fish Have Built a Heater Out of Muscle[1]

BARBARA A. BLOCK

Department of Organismal Biology and Anatomy, The University of Chicago, Chicago, Illinois 60637

SYNOPSIS. The evolution of any complex morphology or physiological adaptation involves the historical transformation of numerous interacting components from an ancestral to a derived state. How such transformations occur are central to our understanding of how novel morphologies arise. The rapid explosion of technology in the field of molecular biology provides new tools that can be incorporated into studies examining the origin of novel phenotypes. Molecular biological techniques can now be used to probe how changes in gene expression result in pathways leading to novel or altered morphologies. The integration of molecular approaches into problems in organismal biology provides a promising new direction for the analysis of form and function. Interdisciplinary studies, combining the resolving power of molecular biology with the complex problems of organismal biology, will shed new light on whole animal function and evolution.

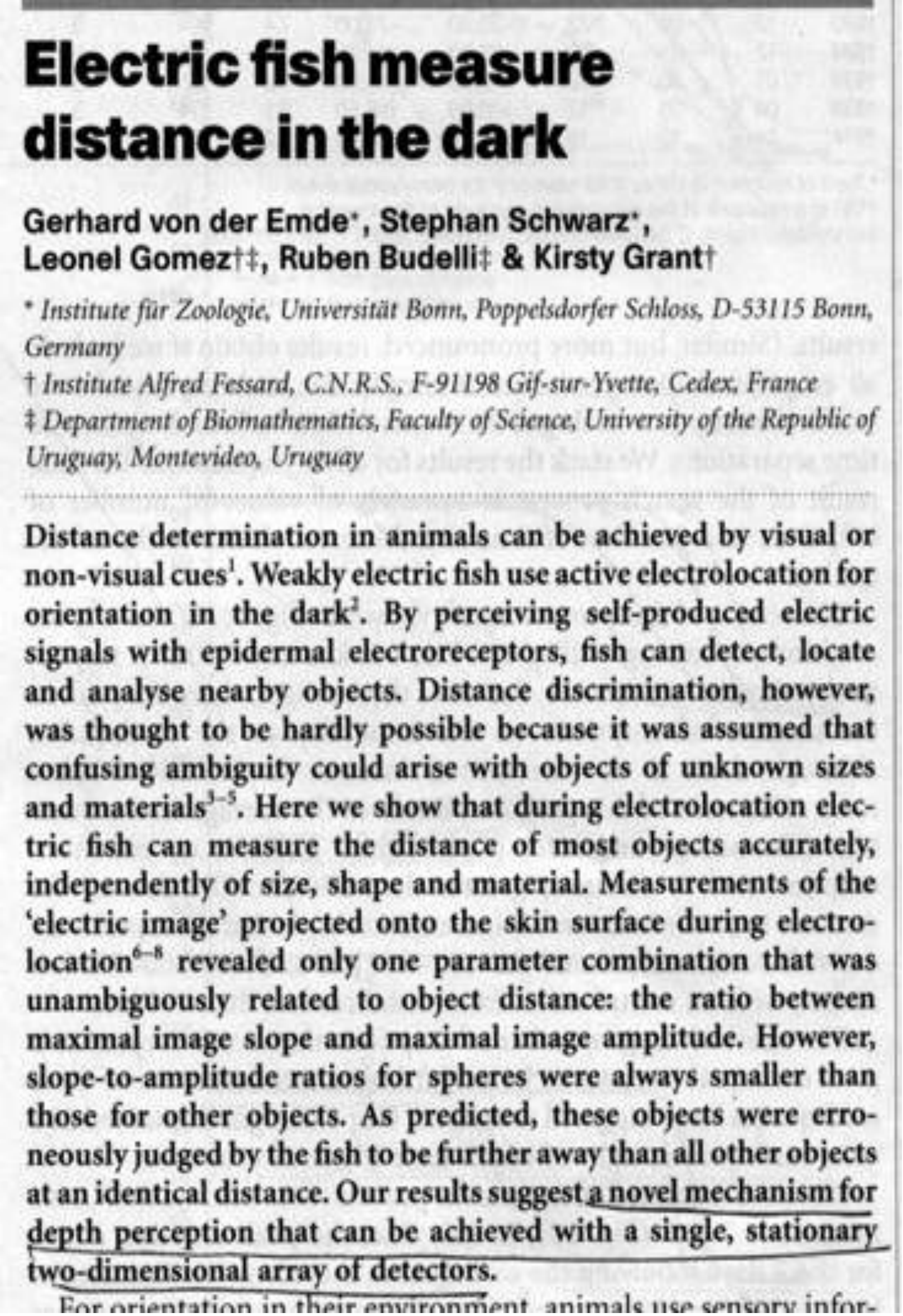


Electric organs: structure, physiology, hormone-sensitivity, and biochemistry

HAROLD H. ZAKON

Department of Zoology, Patterson Laboratory, The University of Texas, Austin, TX 78712, U.S.A.

Chapter in Hochachka and Mommsen, eds., Biochem. Molec. Biol. of Fishes, V. 4, 1995, Elsevier



Electric fish measure distance in the dark

Gerhard von der Emde[*], Stephan Schwarz[*], Leonel Gomez[†‡], Ruben Budelli[‡] & Kirsty Grant[†]

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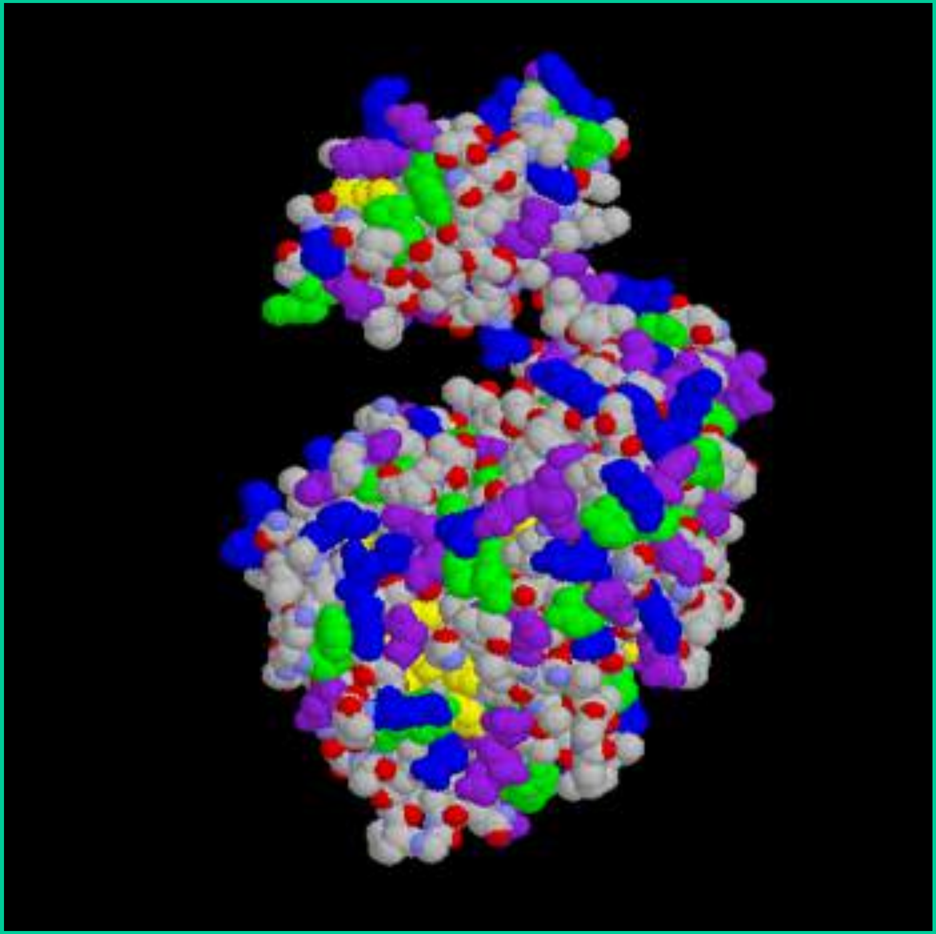
[‡] *Department of Biomathematics, Faculty of Science, University of the Republic of Uruguay, Montevideo, Uruguay*

Distance determination in animals can be achieved by visual or non-visual cues[1]. Weakly electric fish use active electrolocation for orientation in the dark[2]. By perceiving self-produced electric signals with epidermal electroreceptors, fish can detect, locate and analyse nearby objects. Distance discrimination, however, was thought to be hardly possible because it was assumed that confusing ambiguity could arise with objects of unknown sizes and materials[3–5]. Here we show that during electrolocation electric fish can measure the distance of most objects accurately, independently of size, shape and material. Measurements of the 'electric image' projected onto the skin surface during electrolocation[6–8] revealed only one parameter combination that was unambiguously related to object distance: the ratio between maximal image slope and maximal image amplitude. However, slope-to-amplitude ratios for spheres were always smaller than those for other objects. As predicted, these objects were erroneously judged by the fish to be further away than all other objects at an identical distance. Our results suggest a novel mechanism for depth perception that can be achieved with a single, stationary two-dimensional array of detectors.

For orientation in their environment, animals use sensory infor-

Nature 395 (1998) 890-894

Firefly Luciferase



Aromatic Groups - Green

(Histidine, Tyrosine, & Tryptophan)

Basic Groups - Blue

(Lysine & Arginine)

Sulfur-Containing Groups - Yellow

(Cysteine & Methionine)

Acidic Groups - Purple

(Glutamic Acid & Aspartic Acid)

BCCP Domain, (His)6 tail;
R. Stewart

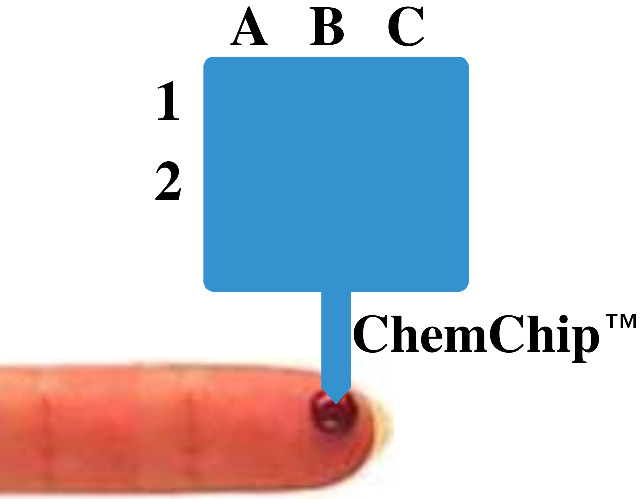
ATP SENSOR PLATFORM

CORE BIOCHEMISTRY - THE FIREFLY LUCIFERASE REACTION

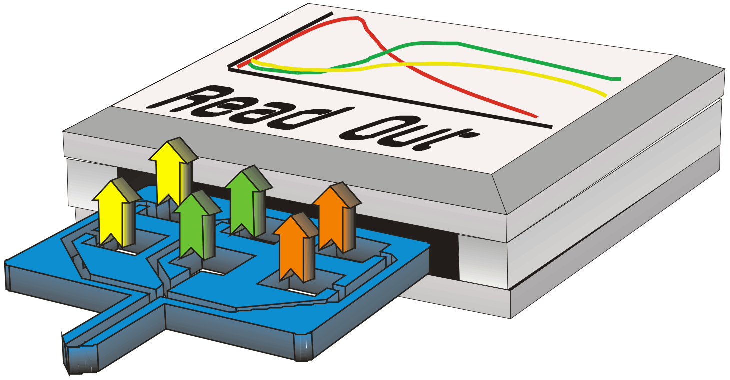
$$\mathrm{ATP} + \mathrm{O_2} + \mathrm{Luciferin} \xrightarrow[\mathrm{Mg^{++}}]{\text{Firefly Luciferase}} \mathrm{AMP} + \mathrm{CO_2} + \mathrm{PPi} + \mathrm{Oxyluciferin} + \mathrm{Light}$$

Quantify Light at 563 nm

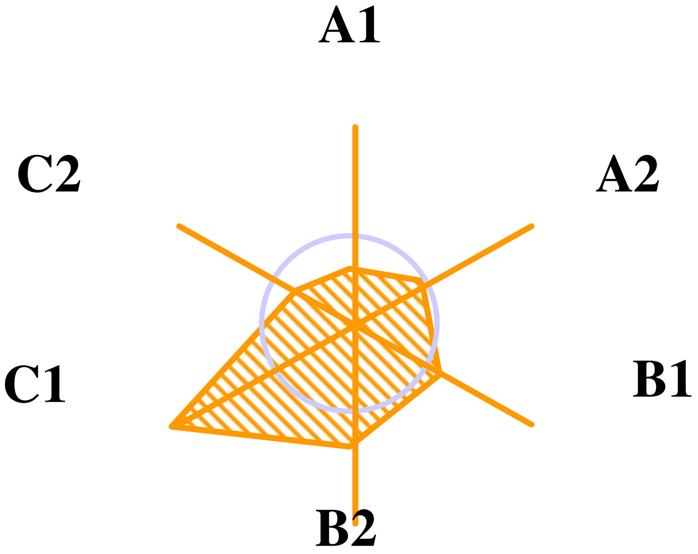
Multi-Metabolite Biosensor -- ChipWare™



Sample Acquisition



Handheld Luminometer



Galactosemia

Biological Concepts and Topics:

From Plants:

Mining the Air--Photosynthesis

Drought tolerance

    resurrection plant

Thermal tolerance

    skunk cabbage
    via thermogenesis

Salt tolerance

    via reverse osmosis

Journal of Experimental Botany, Vol. 51, GMP Special Issue, pp. 319–328, February 2000

Journal of Experimental Botany

6

Modelling photosynthesis and its control

Mark G. Poolman[1], **David A. Fell and Simon Thomas**

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Received 19 April 1999; Accepted 31 August 1999

Abstract

The dynamic and steady-state behaviour of a computer simulation of the Calvin cycle reactions of the chloroplast, including starch synthesis and degradation, and triose phosphate export have been investigated. A major difference compared with previous models is that none of the reversible reactions are assumed to be at equilibrium. The model can exhibit alternate steady states of low or high carbon assimilation flux, with hysteresis in the transitions between the steady states induced by environmental factors such as phosphate and light intensity. The enzymes which have the greatest influence on the flux have been investigated by calculation of their flux control coefficients. Different patterns of control are exhibited over the assimilation flux, the flux to starch and the flux to cytosolic triose phosphate. The assimilation flux is mostly sensitive to sedoheptulose *bis*phosphatase and Rubisco, with the exact distribution depending on their relative activities. Other enzymes, particularly the triose phosphate translocator, become more influential when other fluxes are considered. These results are shown to be broadly consistent with observations on transgenic plants.

Key words: Computer modelling, photosynthesis, genetic manipulation techniques.

carbon assimilation, and the techniques to modify them, are well known, there have been no reports to date of useful increases in carbon assimilation brought about by GM techniques. Progress appears hampered not by technological constraints, but by the absence of a coherent body of theory that allows the *a priori* prediction of the effect of changes in enzyme activities on the behaviour of a given biochemical system, or that, more usefully, can identify the enzyme(s) which must be modified in order to bring about a particular change in behaviour.

A useful first step in developing such an all-embracing body of knowledge is the field of Metabolic Control Analysis (MCA) first proposed in the early 1970s (Kacser and Burns, 1973; Heinrich and Rapoport, 1974; for current reviews and introductory material see Fell 1992, 1997; Kacser *et al*., 1995). For the purposes of this paper, the use of MCA lies in the fact that it provides a precise, quantitative definition of the amount of influence that a given enzyme has over the properties of the system of which it is a part: the control coefficient.

An important consequence of MCA is that the value of any particular control coefficient for a given enzyme is a function not of the kinetic characteristics of that enzyme alone, but of those of all reactions in the system (see previous citations). From this it follows that the influence that a particular enzyme has, cannot be inferred solely from the properties of that enzyme; all enzymes in the system must be considered.

Plants That Warm Themselves

Some plants produce extraordinary heat when they bloom. A few even regulate their temperature within narrow limits, much as if they were warm-blooded animals

by Roger S. Seymour

In the spring of 1972 George A. Bartholomew, a leader in the study of animal physiology, invited a group of his students and co-workers from the University of California at Los Angeles to a dinner party. Among his guests was Daniel K. Odell, now of Sea World in Florida. En route to the affair, Dan noticed some striking flowers. They consisted of a rather phallic projection that was about nine inches long and partly enveloped by a leaflike structure. Intrigued, he picked one to show the other partygoers. When he handed the cutting to Kenneth A. Nagy and me, we were astonished to find it was warm. What is more, the flower grew hotter as the evening progressed, appearing to become warmer than the human body. As zoologists, we were dumbfounded. How could a mere plant heat itself more than the pinnacle of organic evolution—the warm-blooded animal?

From that moment on, I have hunted for and analyzed hot plants whenever I could steal time from my research into animals. I continue to be amazed by what my colleagues and I—and several other researchers—have found. Among our discoveries is that some plants produce as much heat for their weight as birds and insects in flight, the greatest heat producers of all. And a few plants actually thermoregulate, almost as if they were birds or mammals: they not only generate warmth, they alter their heat production to keep their temperature surprisingly constant in fluctuating air temperatures.

We were not, it turns out, the first to realize that some plants give off heat. When we delved into the botanical literature, we learned that almost 200 years earlier, in 1778, the French naturalist Jean-Baptiste de Lamarck reported that the European arum lily, probably *Arum italicum*, became warm when it flowered. This plant is a member of the huge family Araceae, which includes *Philodendron*, the kind of plant Dan had plucked. It also includes jack-in-the-pulpit, skunk cabbage and many other familiar plants. In these so-called aroids, or arum lilies, the flowering part is termed a spadix and is not a true flower; it is an "inflorescence," or clustering of small flowers (florets). The aroid spadix, which consists of hundreds of florets assembled on a common stalk, is partly enveloped by a large bract, or specialized leaf, known as a spathe. Dan's "flower"—from *P. selloum*—was therefore not technically a flower; it was an inflorescence.

Scientists had subsequently discovered that other species of this bizarre family heat up, and they had noted weak heat production by a few plants outside the aroids—by the flowers of the Amazon water lily and of the custard apple, by the inflorescences of a few palms, and by the male cones of certain cycads (fernlike plants that resemble palms). Some investigators, among them Bastiaan J. D. Meeuse of the University of Washington, had even uncovered clues to how the cells of various plants generate warmth [see "The Voodoo Lily," by Bastiaan J. D. Meeuse; Scientific American, July 1966].

For instance, they found that to make heat, aroids activate two biochemical pathways in mitochondria, which are often called the power plants of cells. These pathways are distinguished by their sensitivity to cyanide. The one that can be poisoned by the chemical is common to plants and animals; the one that is insensitive to cyanide occurs in heat-pro-

ONLY THREE PLANTS have yet been shown to regulate their temperature. Such control is exhibited by the flowering parts of *Philodendron selloum*, *Symplocarpus foetidus* (skunk cabbage) and *Nelumbo nucifera* (sacred lotus).

Philodendron selloum
Flower temperature: 38 to 46 degrees C
In air temperatures of: 4 to 39 degrees C
Period of regulation: 18 to 24 hours

New and novel materials and structures:

BIOTECHNOLOGY

Silk from Milk

PEOPLE HAVE KNOWN about the superior strength of silk at least since the days of Genghis Khan, whose warriors wove the material into their armor to stop arrows. Khan's silk, made by silkworms, would be no match for modern bullets. But today's armies are looking to spider silk, the strongest material known, for the next generation of armor.

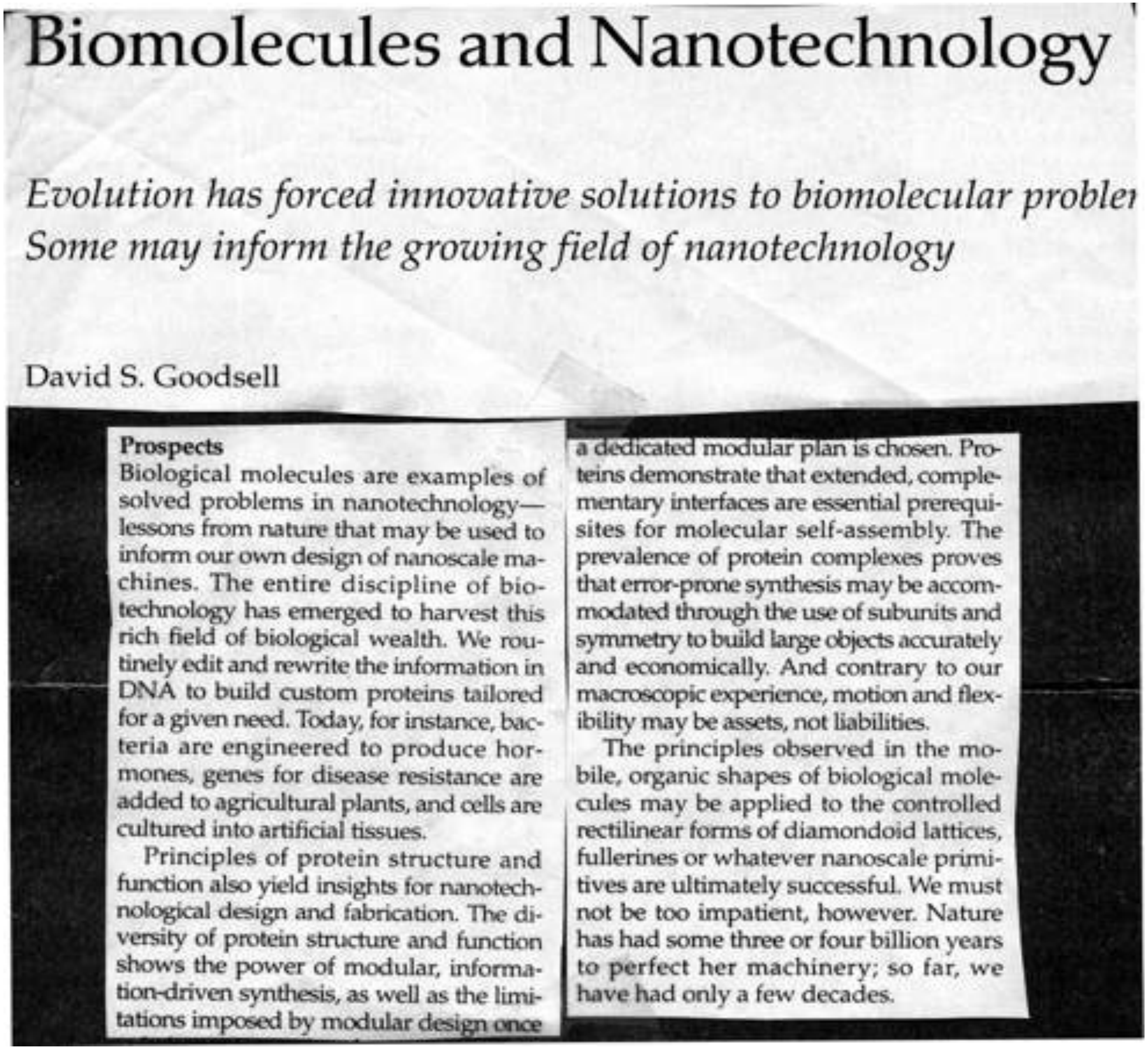
Unlike worms, spiders can't be raised in large numbers because they're territorial. But scientists at Montreal-based Nexia Biotechnologies realized that the spider's silk gland is anatomically similar to a goat's mammary gland. "We popped the spider gene into cells taken from a goat's mammary, and lo and behold, they secreted beautiful spider silk," says Nexia CEO Jeffrey Turner.

When the gene is inserted into the mammary glands of live goats, the animals produce silk protein in their milk. The protein must be extracted from the milk and spun into a fiber, just as a spider spins a web.

Nexia already has a herd of more than 20 "BioSteel goats," each of which may produce as much silk as 10,000 spiders. The U.S. and Canadian armies are interested in using spider silk to make lighter, stronger bulletproof vests and other gear. "A silk

Pop.Sci., Oct., 2000

P. 25



Biomolecules and Nanotechnology

Evolution has forced innovative solutions to biomolecular proble
Some may inform the growing field of nanotechnology

David S. Goodsell

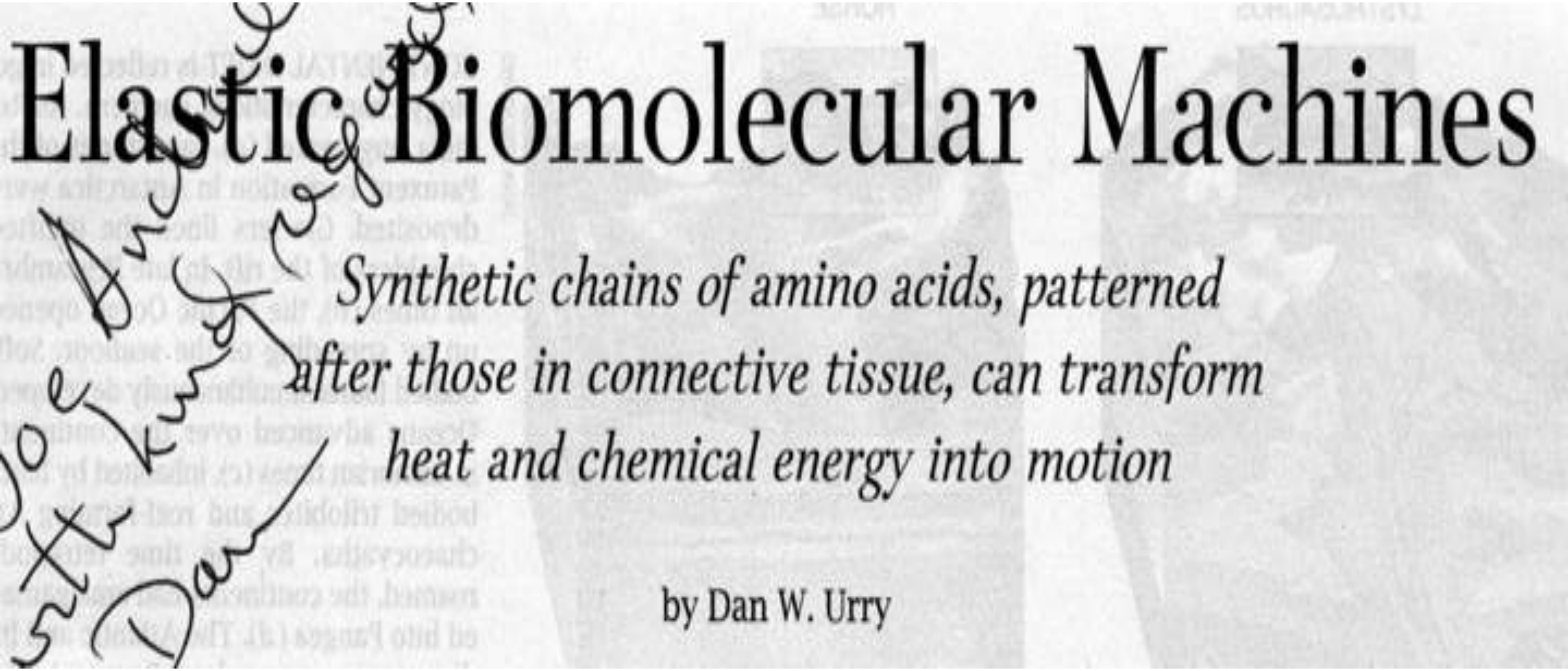
Prospects

Biological molecules are examples of solved problems in nanotechnology—lessons from nature that may be used to inform our own design of nanoscale machines. The entire discipline of biotechnology has emerged to harvest this rich field of biological wealth. We routinely edit and rewrite the information in DNA to build custom proteins tailored for a given need. Today, for instance, bacteria are engineered to produce hormones, genes for disease resistance are added to agricultural plants, and cells are cultured into artificial tissues.

Principles of protein structure and function also yield insights for nanotechnological design and fabrication. The diversity of protein structure and function shows the power of modular, information-driven synthesis, as well as the limitations imposed by modular design once a dedicated modular plan is chosen. Proteins demonstrate that extended, complementary interfaces are essential prerequisites for molecular self-assembly. The prevalence of protein complexes proves that error-prone synthesis may be accommodated through the use of subunits and symmetry to build large objects accurately and economically. And contrary to our macroscopic experience, motion and flexibility may be assets, not liabilities.

The principles observed in the mobile, organic shapes of biological molecules may be applied to the controlled rectilinear forms of diamondoid lattices, fullerines or whatever nanoscale primitives are ultimately successful. We must not be too impatient, however. Nature has had some three or four billion years to perfect her machinery; so far, we have had only a few decades.

Amer. Scientist, 88 (2000) 230.



Elastic Biomolecular Machines

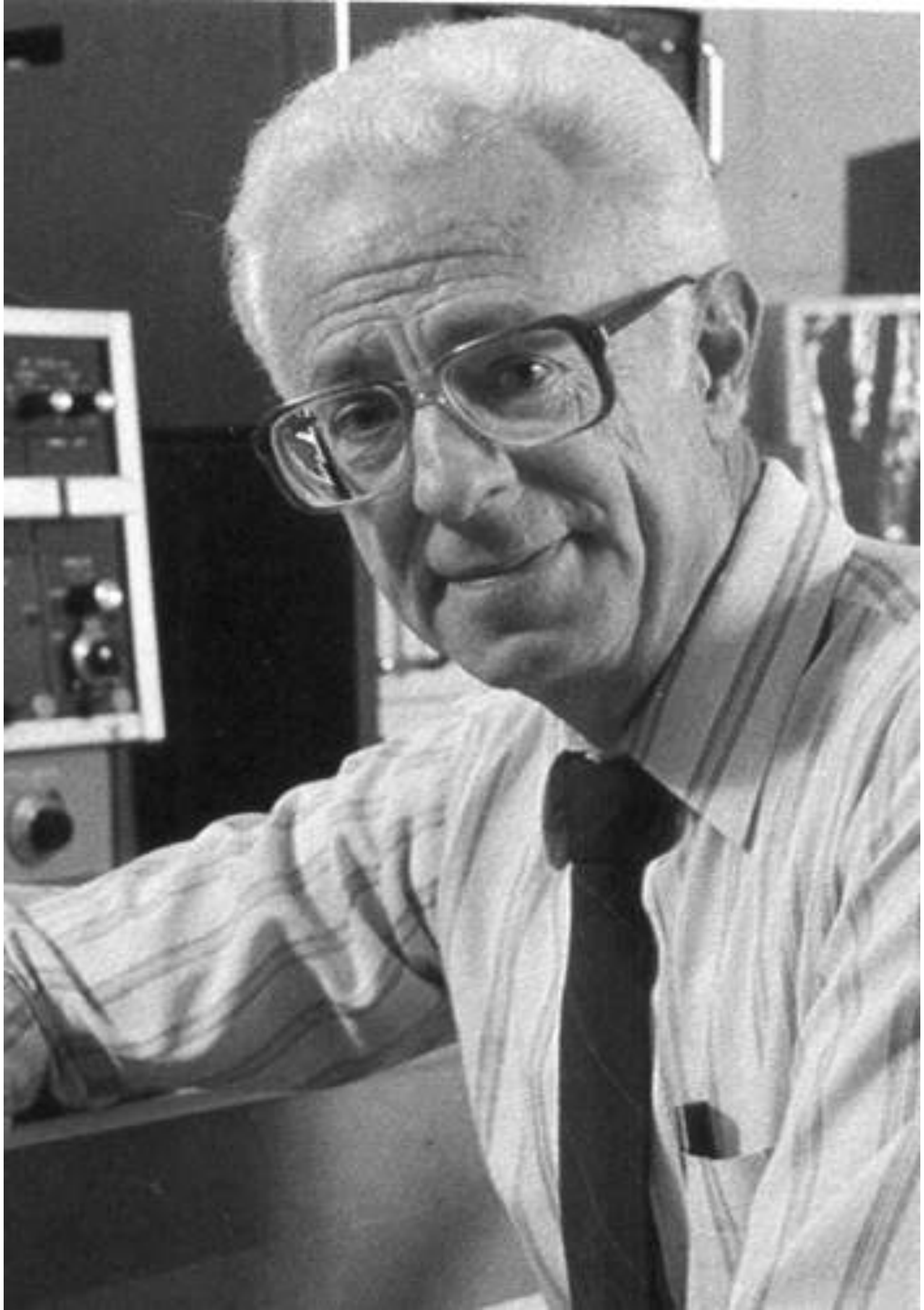
Synthetic chains of amino acids, patterned after those in connective tissue, can transform heat and chemical energy into motion

by Dan W. Urry

Joe Andrade with kind regards Dan

Scient. Amer. 272 (Jan. 1995) pp.44-49

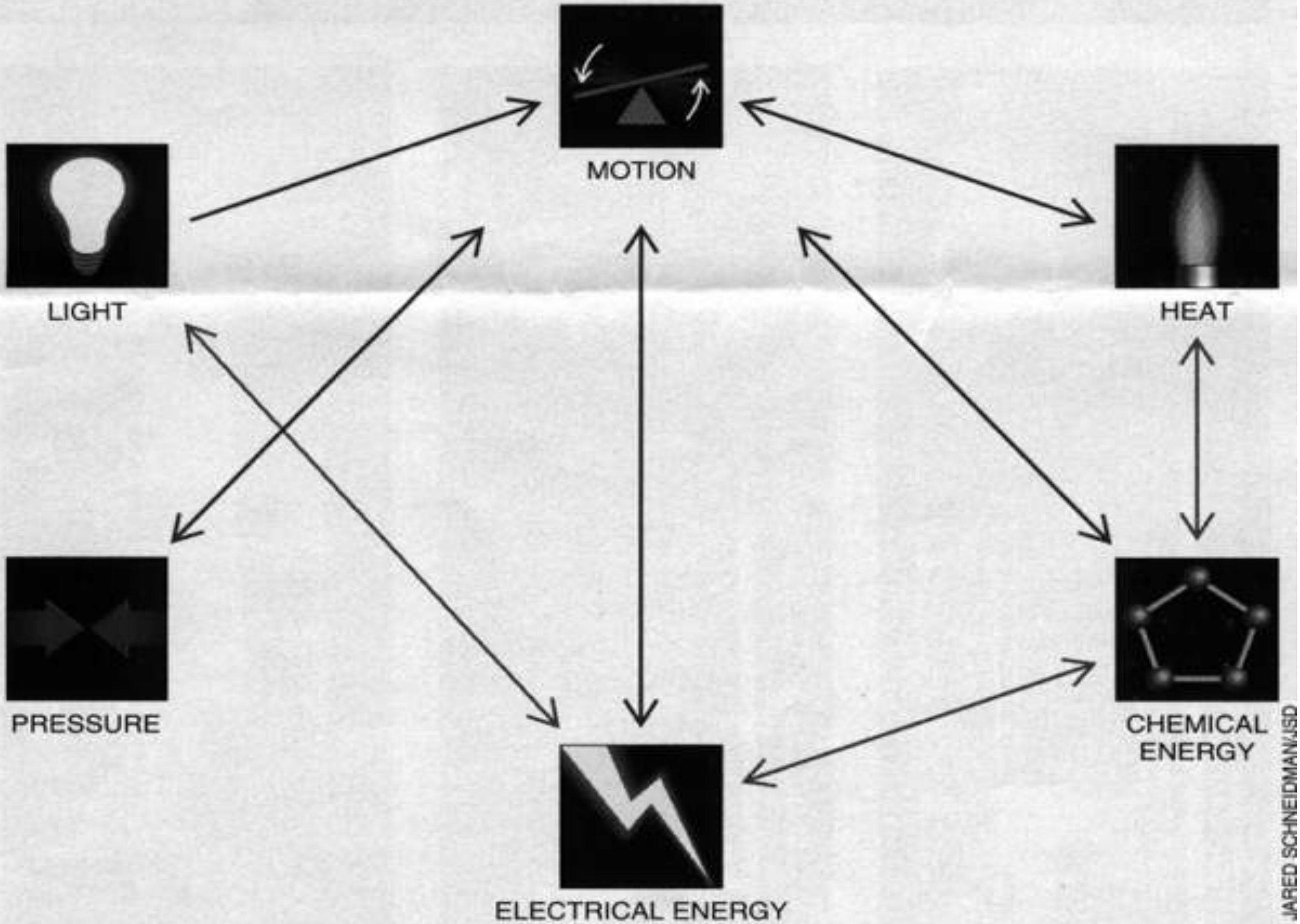
From Elastin to "Polymers"



Dr. Dan Urry

Res. Devel.

Oct., 1988, p. 56



JARED SCHNEIDMAN/JSD

ENERGY can be converted between many different forms by biomolecular machines. Some conversions (such as heat to motion) proceed directly (*red arrows*), whereas others require an intermediate step (*gray arrows*).

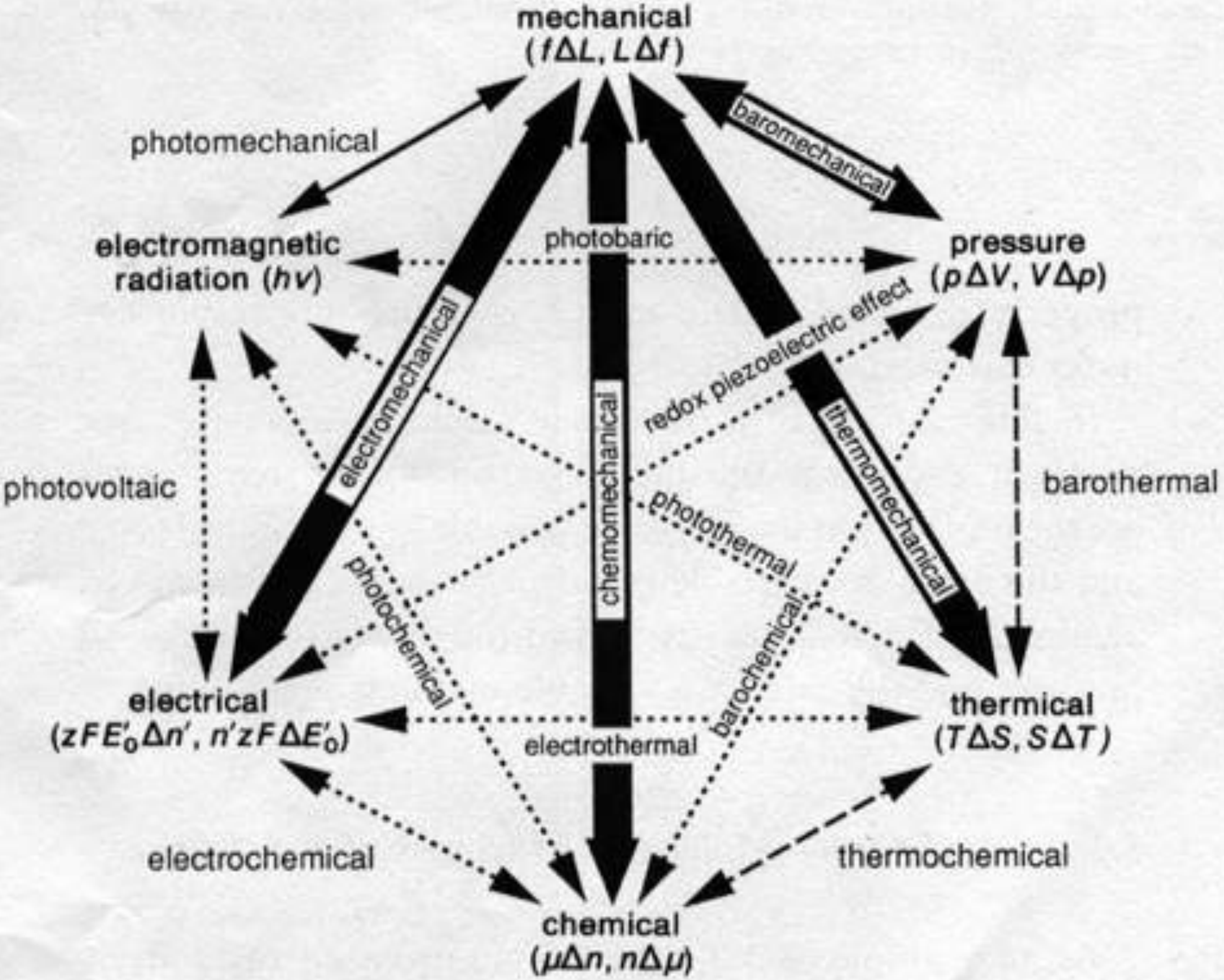


Fig. 12. Demonstrated and putative energy conversions with molecular machines of the T_t type. The bold arrows indicate the energy conversions that have been observed with the elastic protein-based matrices. Photomechanical energy conversion is inferred from photoreduction of nicotinamide [90] and, for example, from photoisomerism of a cinnamic acid chromophore attached to a side chain. To our knowledge these arrows include all energy conversions that can occur in the living organism, and all appear possible by T_t-type molecular machines.

Angew.Chemie
32 (1993) 819

R. Cingolani, “Biological Software for Materials Engineering”

“The cross-fertilization of biology, chemistry, materials science is opening up tremendous opportunities for innovation in previously unrelated disciplines such as electronics and information processing. The extraordinary recognition capability of biomolecules has suggested their use as a means for direct recognition and binding of inorganic materials--in other words acting as a sort of natural software for programming the formation of matter.”

“The main idea is to exploit the highly specific binding properties characteristic of naturally formed organisms to drive the formation of hybrid inorganic structures containing semiconductors or metals.”

Nature Biotechnology 18 (2000) 828-9.

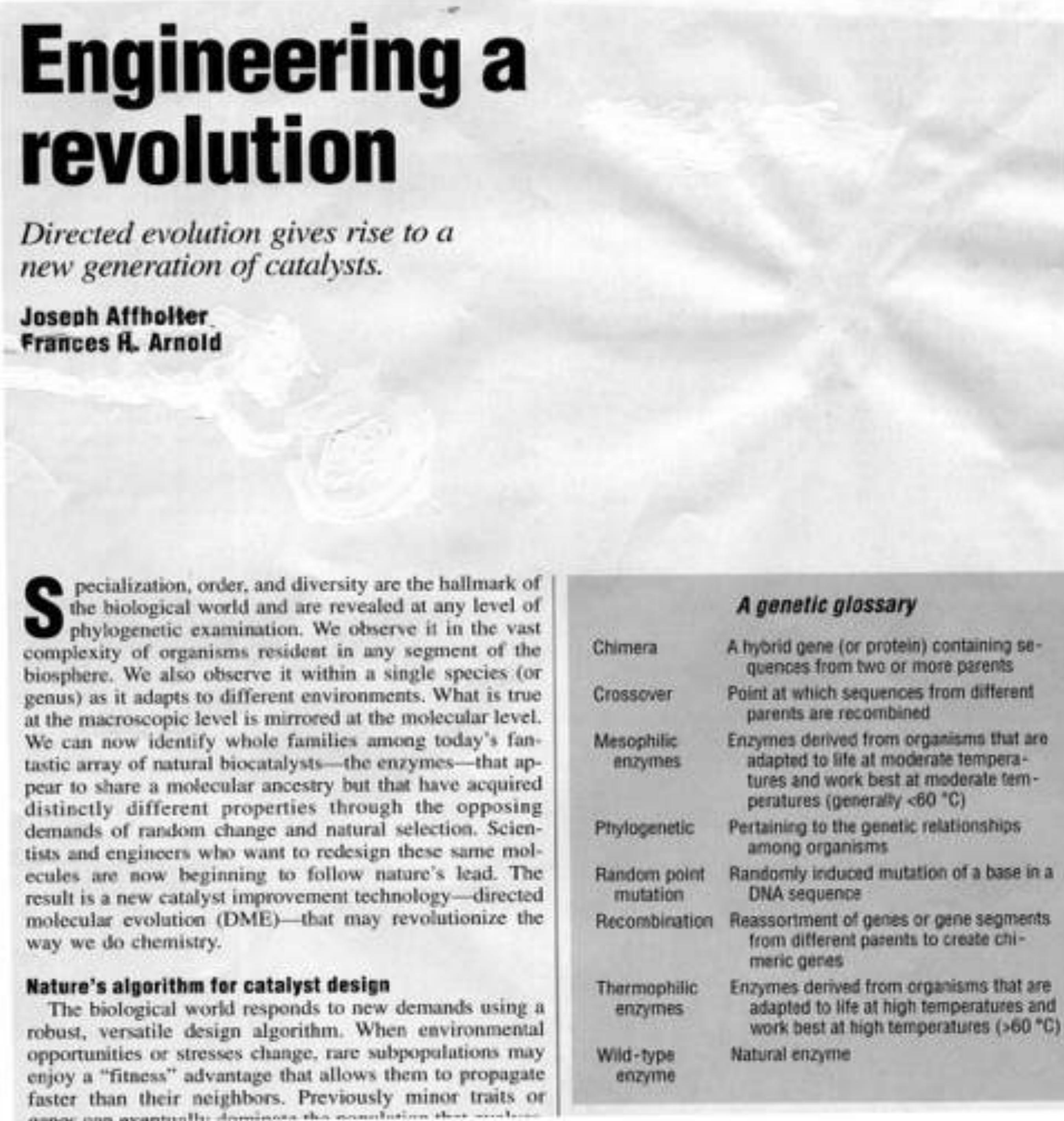
R. Cingolani, “Biological Software for Materials Engineering” (cont’ed)

“…specific peptide sequences can distinguish different crystallographic planes of the most important semiconductors to control the positioning and the assembly of materials at the nanoscale.

The experiments “…exemplify the increasing overlap between biology, chemistry, and physics.”

“Biological molecules offer considerable advantages over inorganic matter in terms of recognition and self-assembly for materials engineering. We are clearly only just beginning to glimpse the potential of biology as software for programming the formation of complex systems.”

Nature Biotechnology 18 (2000) 828-9.



Engineering a revolution

Directed evolution gives rise to a new generation of catalysts.

Joseph Affholter
Frances H. Arnold

Specialization, order, and diversity are the hallmark of the biological world and are revealed at any level of phylogenetic examination. We observe it in the vast complexity of organisms resident in any segment of the biosphere. We also observe it within a single species (or genus) as it adapts to different environments. What is true at the macroscopic level is mirrored at the molecular level. We can now identify whole families among today's fantastic array of natural biocatalysts—the enzymes—that appear to share a molecular ancestry but that have acquired distinctly different properties through the opposing demands of random change and natural selection. Scientists and engineers who want to redesign these same molecules are now beginning to follow nature's lead. The result is a new catalyst improvement technology—directed molecular evolution (DME)—that may revolutionize the way we do chemistry.

Nature's algorithm for catalyst design

The biological world responds to new demands using a robust, versatile design algorithm. When environmental opportunities or stresses change, rare subpopulations may enjoy a "fitness" advantage that allows them to propagate faster than their neighbors. Previously minor traits or

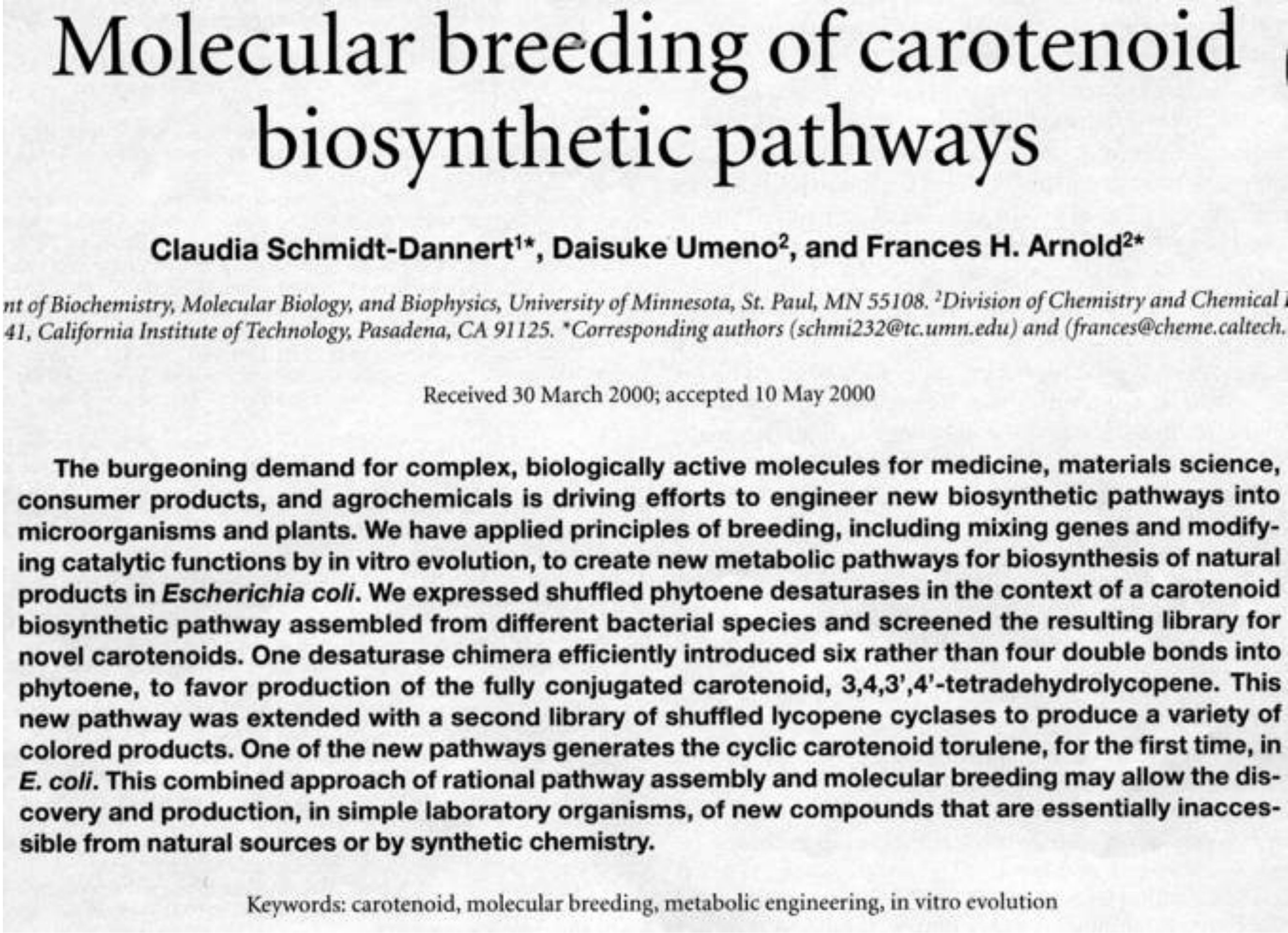
A genetic glossary

Chimera	A hybrid gene (or protein) containing sequences from two or more parents
Crossover	Point at which sequences from different parents are recombined
Mesophilic enzymes	Enzymes derived from organisms that are adapted to life at moderate temperatures and work best at moderate temperatures (generally <60 °C)
Phylogenetic	Pertaining to the genetic relationships among organisms
Random point mutation	Randomly induced mutation of a base in a DNA sequence
Recombination	Reassortment of genes or gene segments from different parents to create chimeric genes
Thermophilic enzymes	Enzymes derived from organisms that are adapted to life at high temperatures and work best at high temperatures (>60 °C)
Wild-type enzyme	Natural enzyme

ChemTech

Sept 99.

P. 34



Molecular breeding of carotenoid biosynthetic pathways

Claudia Schmidt-Dannert[1]*, Daisuke Umeno[2], and Frances H. Arnold[2]*

nt of Biochemistry, Molecular Biology, and Biophysics, University of Minnesota, St. Paul, MN 55108. [2]Division of Chemistry and Chemical
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Received 30 March 2000; accepted 10 May 2000

The burgeoning demand for complex, biologically active molecules for medicine, materials science, consumer products, and agrochemicals is driving efforts to engineer new biosynthetic pathways into microorganisms and plants. We have applied principles of breeding, including mixing genes and modifying catalytic functions by in vitro evolution, to create new metabolic pathways for biosynthesis of natural products in *Escherichia coli*. We expressed shuffled phytoene desaturases in the context of a carotenoid biosynthetic pathway assembled from different bacterial species and screened the resulting library for novel carotenoids. One desaturase chimera efficiently introduced six rather than four double bonds into phytoene, to favor production of the fully conjugated carotenoid, 3,4,3',4'-tetradehydrolycopene. This new pathway was extended with a second library of shuffled lycopene cyclases to produce a variety of colored products. One of the new pathways generates the cyclic carotenoid torulene, for the first time, in *E. coli*. This combined approach of rational pathway assembly and molecular breeding may allow the discovery and production, in simple laboratory organisms, of new compounds that are essentially inaccessible from natural sources or by synthetic chemistry.

Keywords: carotenoid, molecular breeding, metabolic engineering, in vitro evolution

Nature Biotech 18 (2000) 750

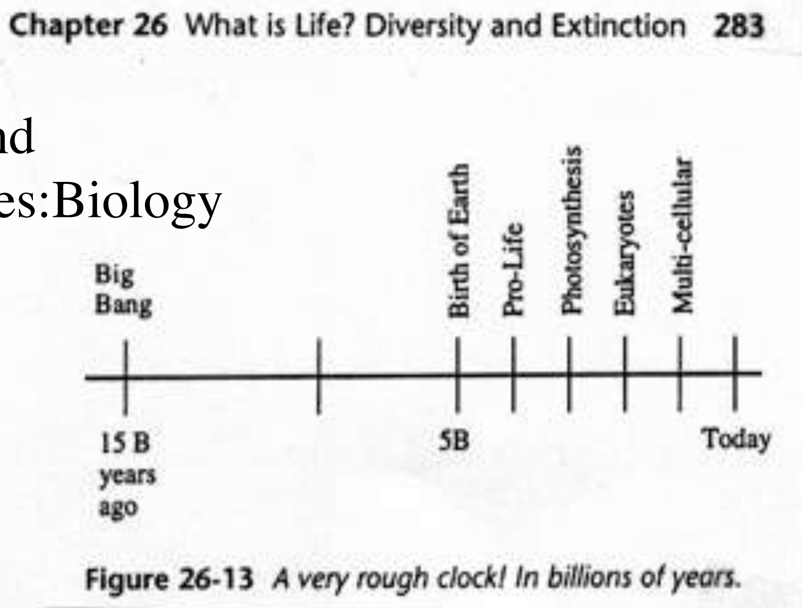
P. Cohen, “Life—the Sequel,” New Scientist, 30 Sept. 2000, p. 33

“Poor, pitiful evolution. Sure, over the aeons it has managed to compiled a noteworthy list of accomplishments--beetles, butterflies, birds of paradise and Beethoven, to name a few.” But when one “...contemplates the primitive building blocks it has to work with --proteins constructed from just 20 amino acids and DNA stitched together from an alphabet of four measly chemical letters... one can't help but lament what might have been.”

"There are millions of compounds it could play with and what does it settle on? Chemicals that are rather uninteresting, “ says
David Liu, biochemist, Harvard University. “Imagine what it could do with some real tools.”

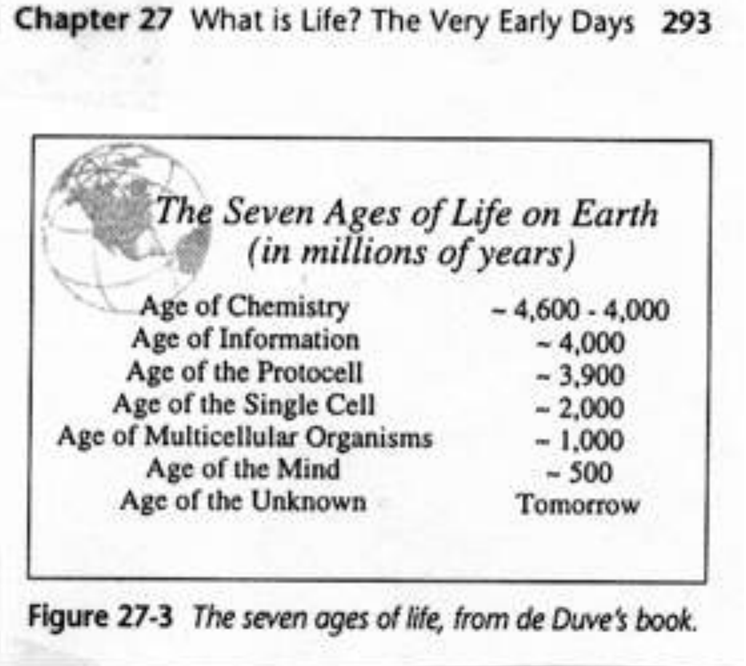
“...re-engineering of the machinery that transforms genetic code into protein..” by creating completely new DNA letters
and to “...use DNA as a templated assembly platform for entirely new chemicals--in essence, to write a new genetic code for plastic, paint or penicillin.”

Rules and Principles:Biology



Chapter 26 What is Life? Diversity and Extinction **283**

Figure 26-13 *A very rough clock! In billions of years.*

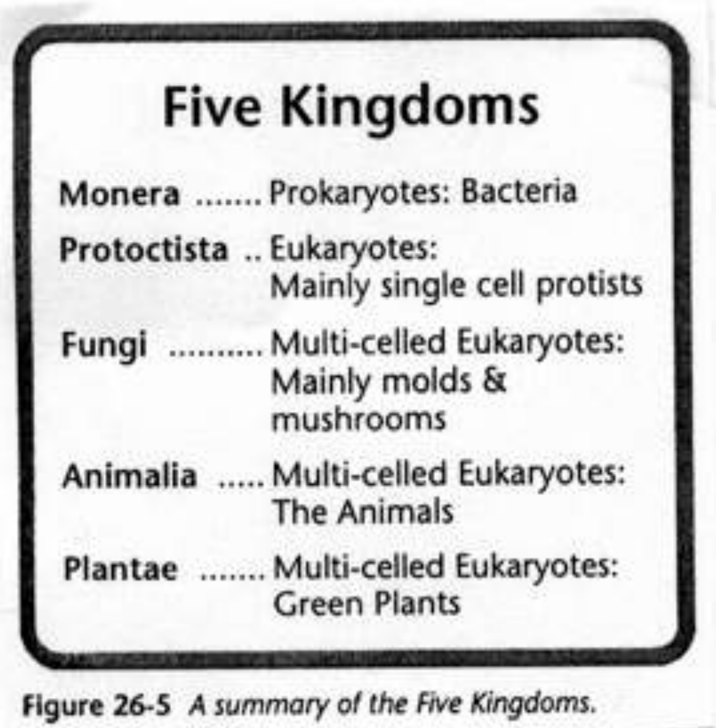


Chapter 27 What is Life? The Very Early Days **293**

The Seven Ages of Life on Earth
(in millions of years)

Age of Chemistry	~ 4,600 - 4,000
Age of Information	~ 4,000
Age of the Protocell	~ 3,900
Age of the Single Cell	~ 2,000
Age of Multicellular Organisms	~ 1,000
Age of the Mind	~ 500
Age of the Unknown	Tomorrow

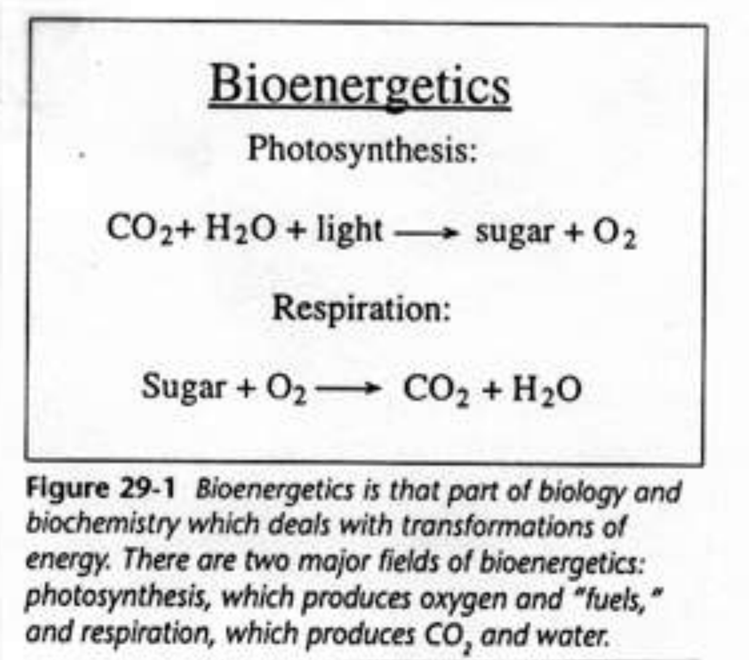
Figure 27-3 *The seven ages of life, from de Duve's book.*



Five Kingdoms

Monera	Prokaryotes: Bacteria
Protoctista ..	Eukaryotes: Mainly single cell protists
Fungi	Multi-celled Eukaryotes: Mainly molds & mushrooms
Animalia	Multi-celled Eukaryotes: The Animals
Plantae	Multi-celled Eukaryotes: Green Plants

Figure 26-5 *A summary of the Five Kingdoms.*



Bioenergetics

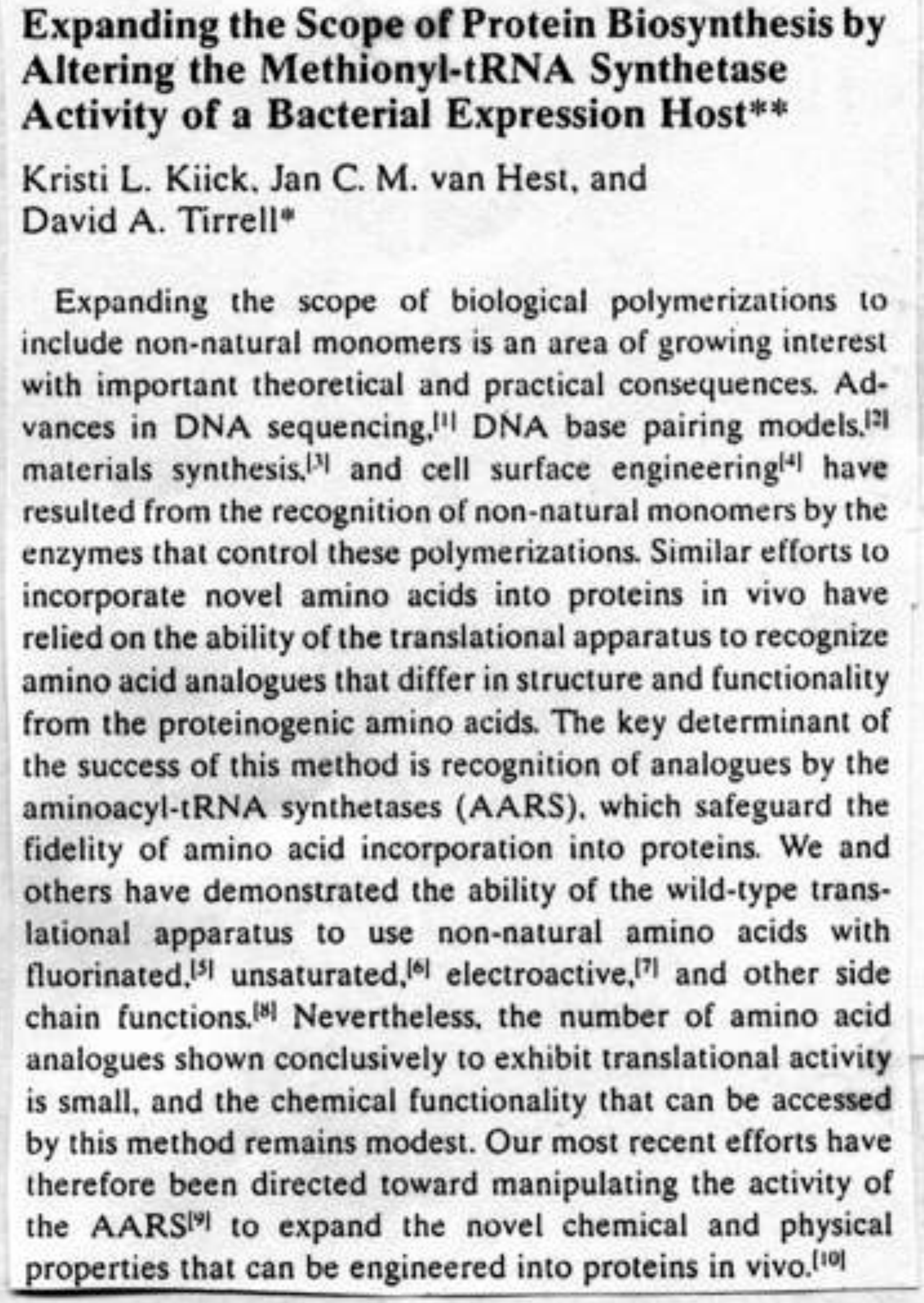
Photosynthesis:

$$CO_2 + H_2O + \text{light} \longrightarrow \text{sugar} + O_2$$

Respiration:

$$\text{Sugar} + O_2 \longrightarrow CO_2 + H_2O$$

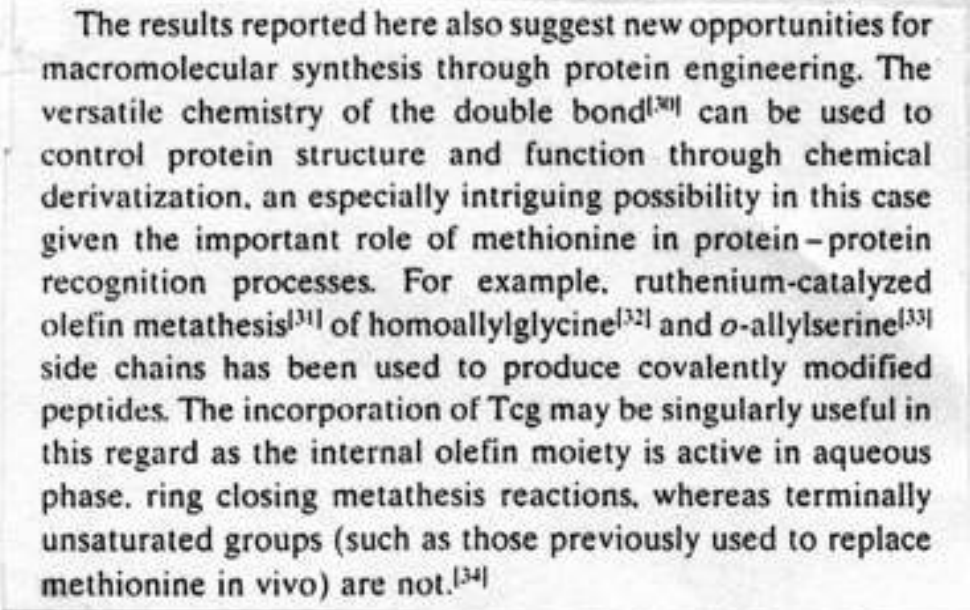
Figure 29-1 *Bioenergetics is that part of biology and biochemistry which deals with transformations of energy. There are two major fields of bioenergetics: photosynthesis, which produces oxygen and "fuels," and respiration, which produces CO_2 and water.*



Expanding the Scope of Protein Biosynthesis by Altering the Methionyl-tRNA Synthetase Activity of a Bacterial Expression Host**

Kristi L. Kiick, Jan C. M. van Hest, and
David A. Tirrell*

Expanding the scope of biological polymerizations to include non-natural monomers is an area of growing interest with important theoretical and practical consequences. Advances in DNA sequencing,[1] DNA base pairing models,[2] materials synthesis,[3] and cell surface engineering[4] have resulted from the recognition of non-natural monomers by the enzymes that control these polymerizations. Similar efforts to incorporate novel amino acids into proteins in vivo have relied on the ability of the translational apparatus to recognize amino acid analogues that differ in structure and functionality from the proteinogenic amino acids. The key determinant of the success of this method is recognition of analogues by the aminoacyl-tRNA synthetases (AARS), which safeguard the fidelity of amino acid incorporation into proteins. We and others have demonstrated the ability of the wild-type translational apparatus to use non-natural amino acids with fluorinated,[5] unsaturated,[6] electroactive,[7] and other side chain functions.[8] Nevertheless, the number of amino acid analogues shown conclusively to exhibit translational activity is small, and the chemical functionality that can be accessed by this method remains modest. Our most recent efforts have therefore been directed toward manipulating the activity of the AARS[9] to expand the novel chemical and physical properties that can be engineered into proteins in vivo.[10]



The results reported here also suggest new opportunities for macromolecular synthesis through protein engineering. The versatile chemistry of the double bond[30] can be used to control protein structure and function through chemical derivatization, an especially intriguing possibility in this case given the important role of methionine in protein–protein recognition processes. For example, ruthenium-catalyzed olefin metathesis[31] of homoallylglycine[32] and *o*-allylserine[33] side chains has been used to produce covalently modified peptides. The incorporation of Tcg may be singularly useful in this regard as the internal olefin moiety is active in aqueous phase, ring closing metathesis reactions, whereas terminally unsaturated groups (such as those previously used to replace methionine in vivo) are not.[34]

Angew. Chemie Int Ed., 39 (2000) 2148.

Polymer Paradigms

- Mendeleev-- Periodic Table -- Elements -- mid1800s
- Organic Chem -- early Polymers -- early 1900s
- Polymer Chem -- Nylons -- Dacron -- mid 1900s
  - Addition and Condensation -- Statistics -- Paul Flory
- Stereoregular, Coordination Polymers -- later 1900s
  - Block Copolymers -- “Intelligent” Polymers
- Biopolymers from Biology -- Organisms -- next 10 years
  - Silk, Cellulose, Elastin, Hybrids CHNOPS
- Biopolymers from “Plants” -- photosynthesis -- CHNOPS
  - Materials from air and water!! -- next 20 years
- Materials from and beyond Biology -- beyond CHNOPS
  - New elements, new energetics, new templates -- next 30 years?

Bottom Line? Energy, Matter, 02/CO2

“It is not enough that you should understand about applied science in order that your work may increase man's blessings. Concern for man himself and his fate must always form the chief interest of all technical endeavors, concern for the great unsolved problems of the organization of labor and the distribution of goods -- in order that the creations of our mind shall be a blessing and not a curse to mankind.

Never forget this in the midst of your diagrams and equations.”

Albert Einstein, 1931

Food, Water, Shelter, Health, Environment, Population, Transportation --for ALL 6 Billion *homo sapiens*, 30+ Million other species, and Planet Earth.

Your future…your world…your turn!!

- …
- …
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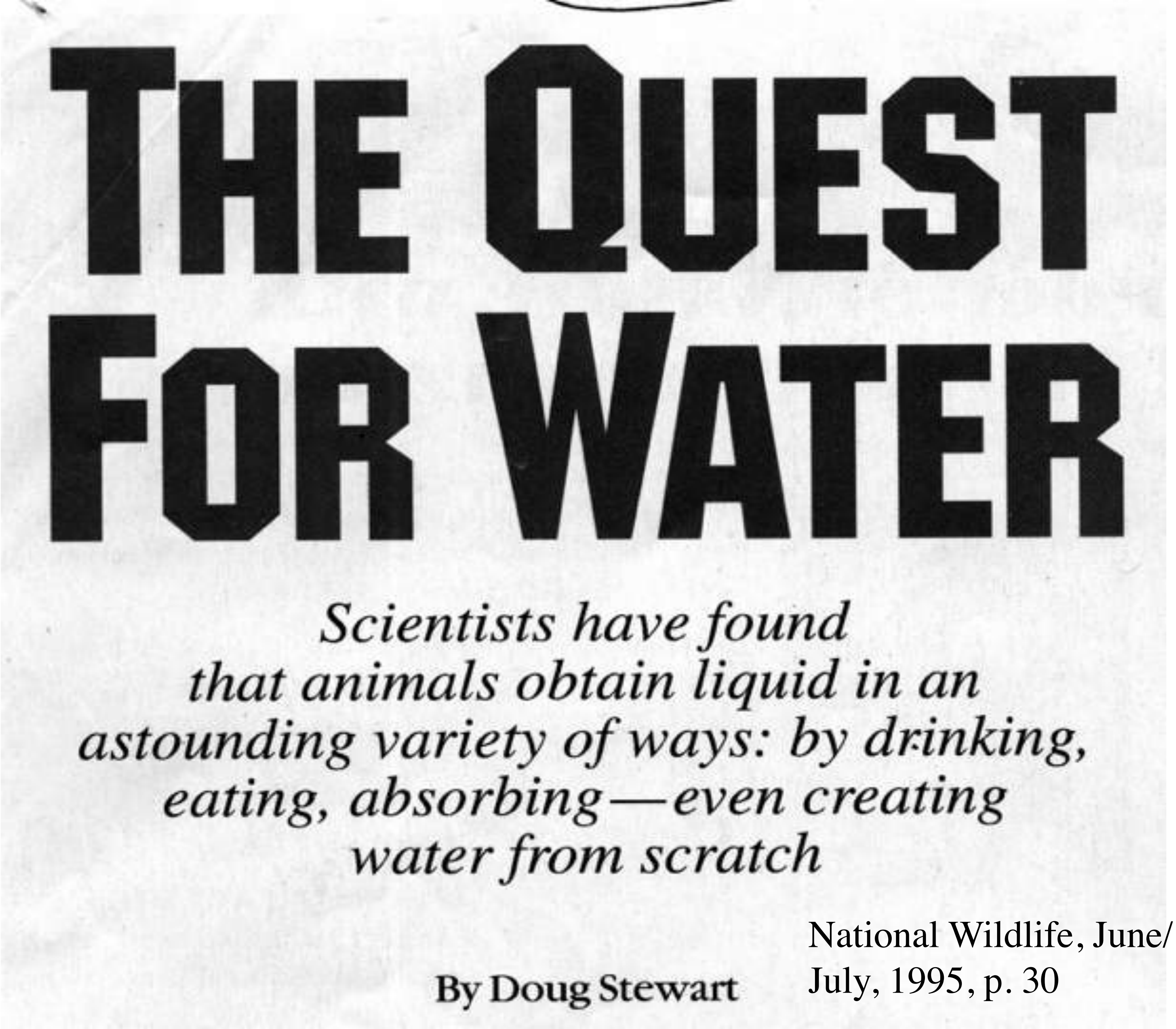
- …

Thanks

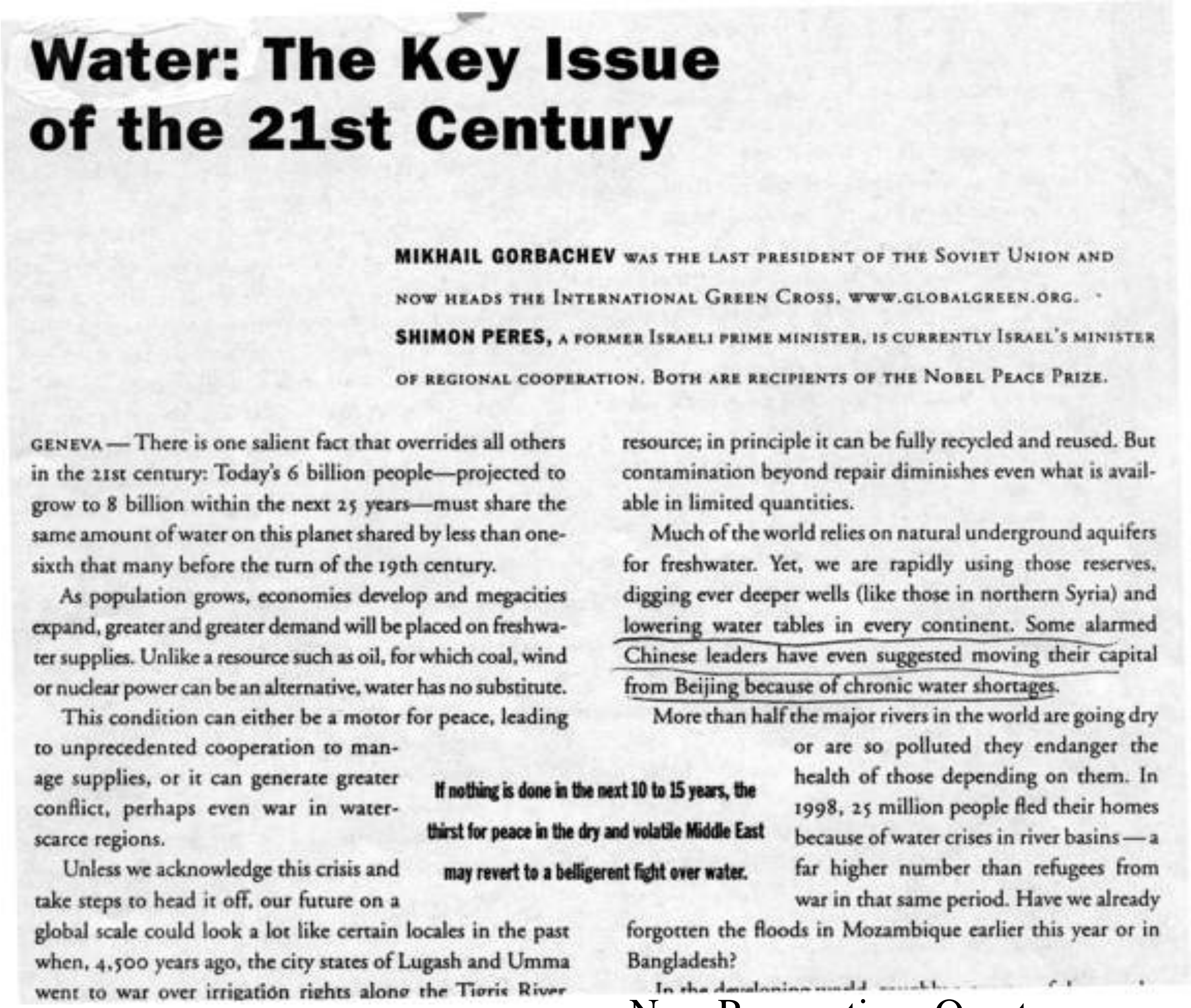


THE QUEST FOR WATER

Scientists have found that animals obtain liquid in an astounding variety of ways: by drinking, eating, absorbing—even creating water from scratch

By Doug Stewart

National Wildlife, June/
July, 1995, p. 30



Water: The Key Issue of the 21st Century

MIKHAIL GORBACHEV WAS THE LAST PRESIDENT OF THE SOVIET UNION AND NOW HEADS THE INTERNATIONAL GREEN CROSS, WWW.GLOBALGREEN.ORG. **SHIMON PERES,** A FORMER ISRAELI PRIME MINISTER, IS CURRENTLY ISRAEL'S MINISTER OF REGIONAL COOPERATION. BOTH ARE RECIPIENTS OF THE NOBEL PEACE PRIZE.

GENEVA — There is one salient fact that overrides all others in the 21st century: Today's 6 billion people—projected to grow to 8 billion within the next 25 years—must share the same amount of water on this planet shared by less than one-sixth that many before the turn of the 19th century.

As population grows, economies develop and megacities expand, greater and greater demand will be placed on freshwater supplies. Unlike a resource such as oil, for which coal, wind or nuclear power can be an alternative, water has no substitute.

This condition can either be a motor for peace, leading to unprecedented cooperation to manage supplies, or it can generate greater conflict, perhaps even war in water-scarce regions.

Unless we acknowledge this crisis and take steps to head it off, our future on a global scale could look a lot like certain locales in the past when, 4,500 years ago, the city states of Lugash and Umma went to war over irrigation rights along the Tigris River

If nothing is done in the next 10 to 15 years, the thirst for peace in the dry and volatile Middle East may revert to a belligerent fight over water.

resource; in principle it can be fully recycled and reused. But contamination beyond repair diminishes even what is available in limited quantities.

Much of the world relies on natural underground aquifers for freshwater. Yet, we are rapidly using those reserves, digging ever deeper wells (like those in northern Syria) and lowering water tables in every continent. Some alarmed Chinese leaders have even suggested moving their capital from Beijing because of chronic water shortages.

More than half the major rivers in the world are going dry or are so polluted they endanger the health of those depending on them. In 1998, 25 million people fled their homes because of water crises in river basins — a far higher number than refugees from war in that same period. Have we already forgotten the floods in Mozambique earlier this year or in Bangladesh?

New Perspectives Quart.
Summer, 2000, p. 56