THE CONFLUENCE OF CHEMICAL AND BIOLOGICAL SCIENCES
IMPLICATIONS, OPPORTUNITIES AND CHALLENGES

International Conferences on Biosciences: State of the Art Advancements

Kumarakom, Kerala

September 11, 2014

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OUTLINE

- A brief history of natural science and the origins of biology
- Chemistry and Biology : The two cultures
- Integrated Chemistry and Biology : Motivation
  - *Bio-inspired Materials*
  - *Bio-catalysis and synthetic biology for sustainable chemistry*
  - *Bio inspired molecular devices for sustainable energy*
  - *Drugs and Pharmaceuticals*
- Integrating Chemistry and Biology : Challenges to education

ORIGINS OF BIOLOGY

- Biology has its early origins in medicine, human anatomy and physiology (Harvey, Vesalius)
- Naturalists (Linnaeus, Gregor Mendel) artists and sculptors (Leonardo da Vinci) and explorers (Darwin, Alexander von Humboldt) through careful observations of the nature around us created some of the profound theories in genetics and natural selection
- The use of the term biology, as we understand today, first appeared in 1799, attributed to Thomas Beddoes
- As a discipline of natural history and science, many believed that living matter are fundamentally different from non-living matter because they contain some non physical element or governed by different principles than are inanimate things (Vitalism)

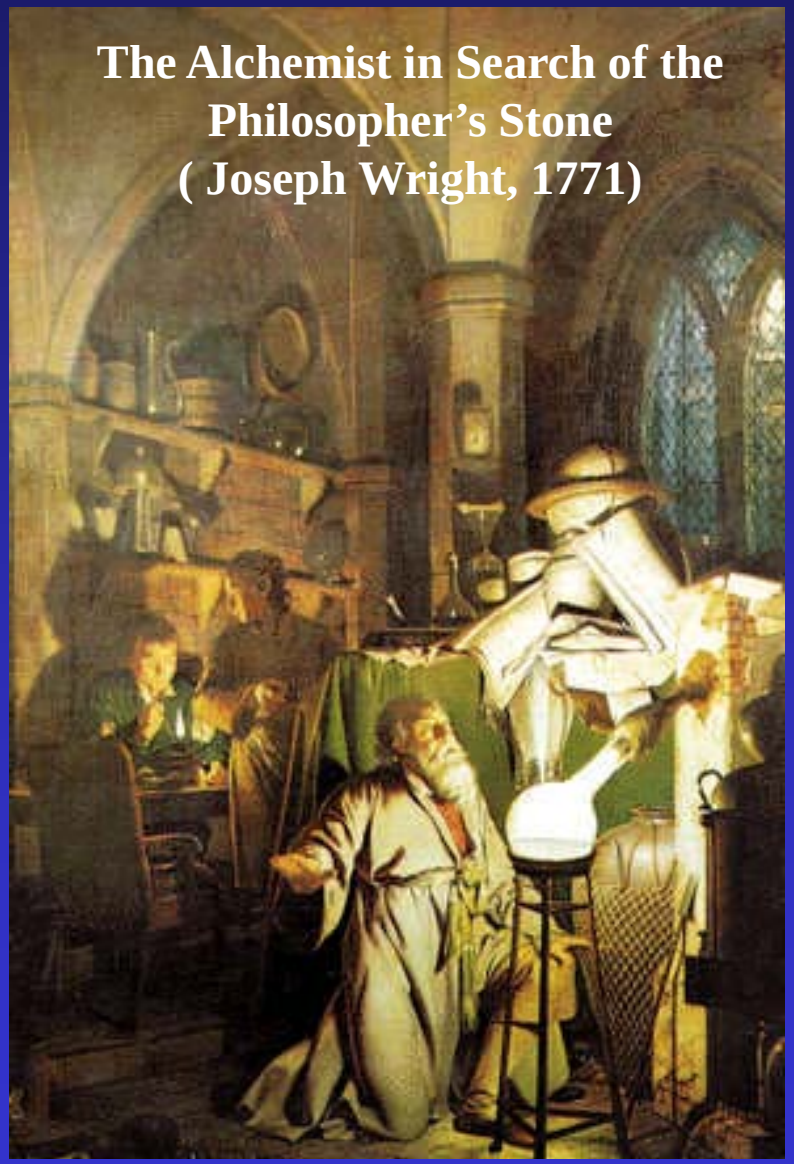
Vesalius
1578-1657

William Harvey
1514-1564

Leonardo da Vinci
1452-1519

Thomas Beddoes
1760-1808

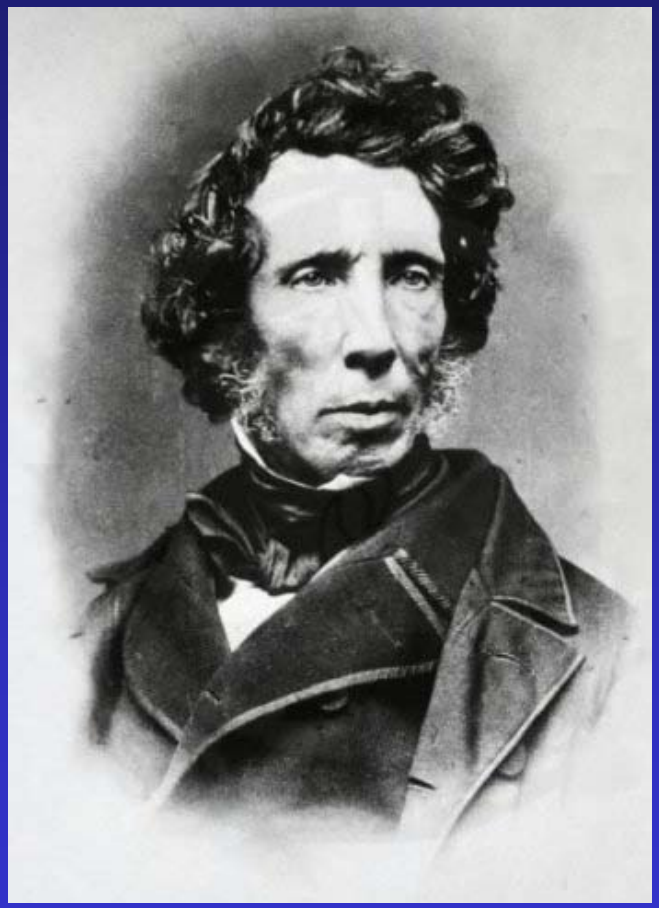
HENNIG BRANDT OF HAMBURG (1630 -1710)



The Alchemist in Search of the Philosopher's Stone (Joseph Wright, 1771)

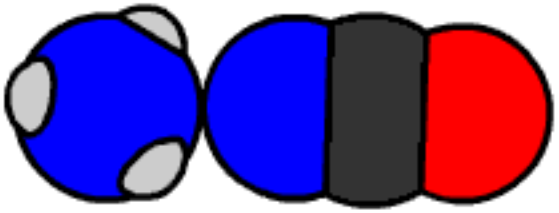
- in 1699 Brandt heated human urine to high temperatures leading to the formation of elemental phosphorus which comes off as a gas. Phosphorus condenses to a liquid below about 280° C and then solidifies (to the white phosphorus allotrope) at about 44° C
- White phosphorous glows with a white light; hence he called it phosphorous the "bearer of light"
- He used about 5,500 litres of urine to produce just 120 grams of phosphorus. (1 litre of adult human urine contains about 1.4 g phosphorus)
- When Brandt observed the white light in the flask, he thought he has discovered the "vital force" which was believed to be the basis of all life ! Little did he realize that he has discovered the element phosphorous. Phosphorous was established as an element by Lavoisier only in in 1777 !

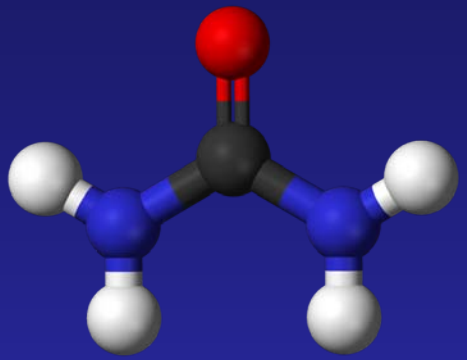
CHEMICAL SYNTHESIS OF UREA : THE END OF VITALISM



Friedrich Wohler (1800 – 1882)

$[NH_4^+][NCO^-]$

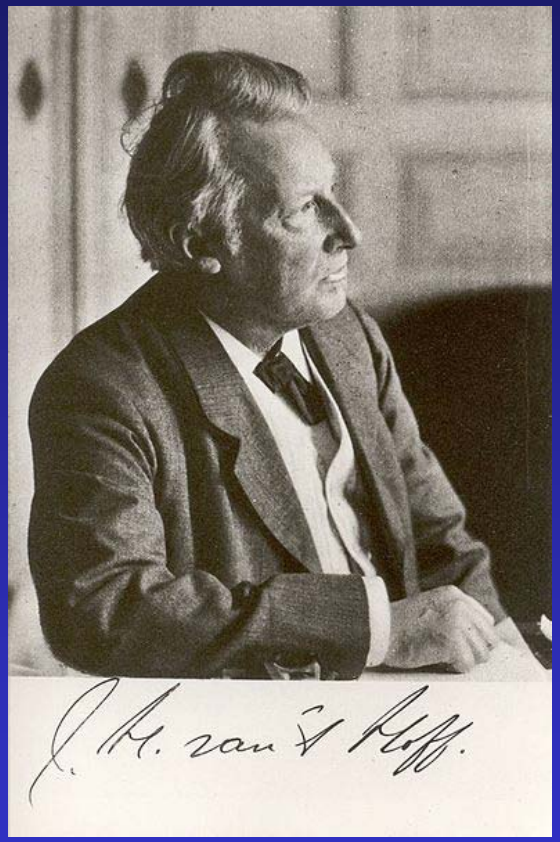




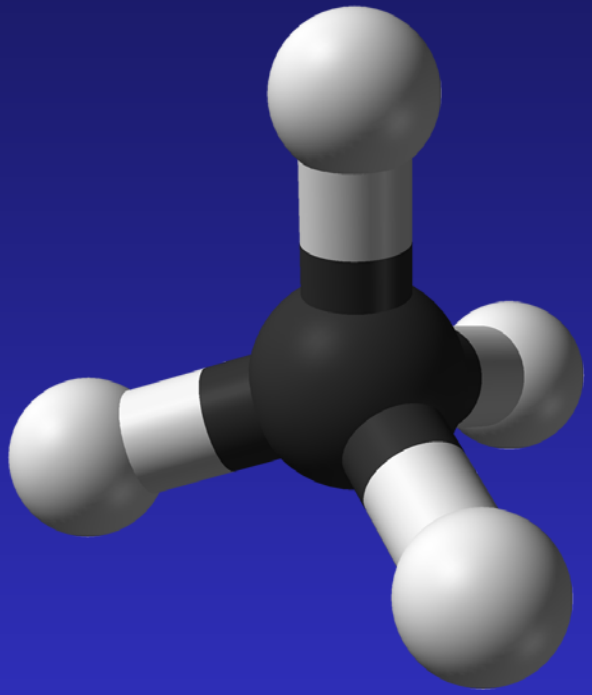
" I must tell you that I can make urea without the use of a kidney of either man or dog" ***: Wohler in a letter to his teacher Berzelius***

Annalen der Physik und Chemie, 88(2), 253-256 (1828)

CHEMICAL REVOLUTION : UNDERSTANDING CHEMICAL STRUCTURES



Jacobus van't Hoff (1852-1911)



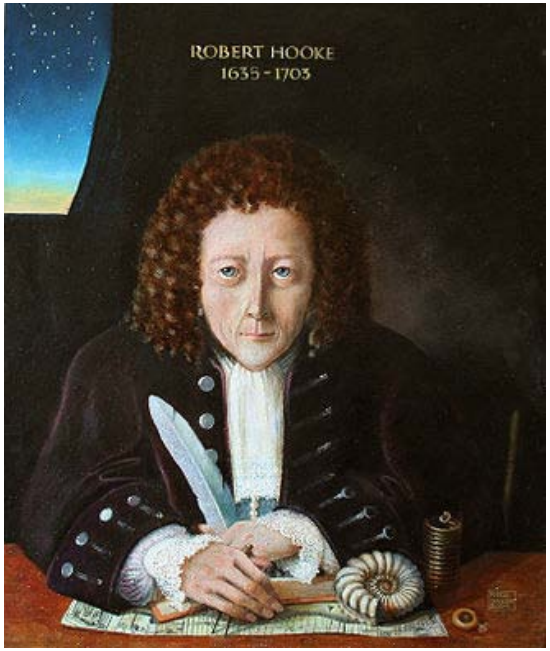
The tetrahedral nature of carbon
(La Chimie dans l'espace, 1874)

First Nobel Prize in 1901

THE EMERGENCE OF REDUCTIONISM AND THE BEGINNING OF THE CHEMISTRY - BIOLOGY DIVIDE

- Nineteenth century marked the end of vitalism and beginning of the reductionism as a philosophical thought in science
- Vitalism was the dominant philosophical thought up to that time
- The reductionists believed that all complex systems can be understood as a sum of its parts
- Evolution of quantum mechanics and their applications to chemistry gave rise to the belief that one can understand chemical and physical states of matter *ab initio,* based on atomic and electronic theory
- The chemists and physicists of the period focused attention on problems that can be solved by the reductionist approach
- Biology proved too complex for this approach; hence was abandoned by most chemists and physicists

THE TOOL THAT LAUNCHED BIOLOGY AS A SCIENCE



Robert Hooke
1635-1703

MICROGRAPHIA:

OR SOME

Physiological Descriptions

OF

MINUTE BODIES

MADE BY

MAGNIFYING GLASSES

WITH

OBSERVATIONS and INQUIRIES thereupon.

By *R. HOOKE*, Fellow of the ROYAL SOCIETY.

Nanpeſſis oculis quantum contendere Lincus,
Non tamen idcirco contemnas Lippus inungi. Horat. Ep. lib. 1.

LONDON, Printed by *Jo. Martyn*, and *Ja. Allestry*, Printers to the ROYAL SOCIETY, and are to be sold at their Shop at the *Bell* in S. *Paul's* Church-yard. M DC LX V.

LEEUWENHOEK : FATHER OF MICROBIOLOGY

Antonie van Leeuwenhoek
1632-1673

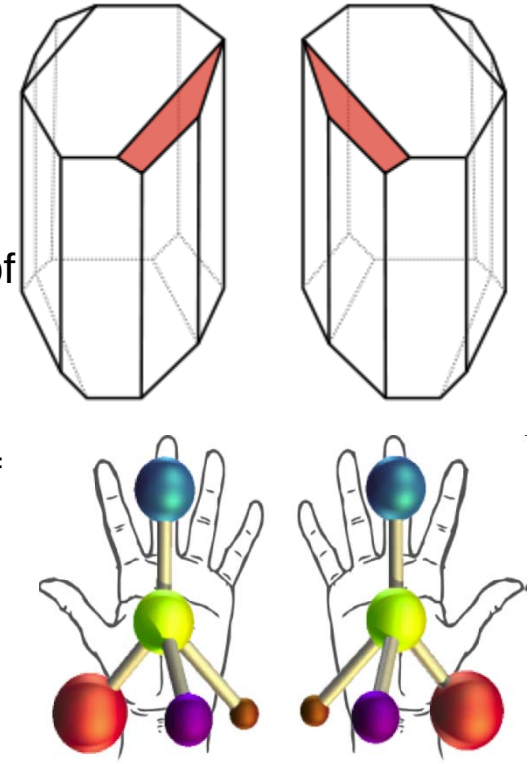
- Builder of Microscope superior to Hook's microscope
- 300 to 500 X magnification
- His microscopic observations were reported in over 190 letters to the Royal Society, London and published in the Philosophical Transactions of the Royal Society
- He observed protozoa, blood cells and a single cell organism, bacteria

Antony van Leeuwenhoek considered that what is true in natural philosophy can be most fruitfully investigated by the experimental method, supported by the evidence of the senses; for which reason, by diligence and tireless labour he made with his own hand certain most excellent lenses, with the aid of which he discovered many secrets of nature, now famous throughout the whole philosophical World.

Epitaph, New Church at Delft, Netherlands

LOUIS PASTEUR AND THE REVIVAL OF VITALISM

- Known for his epochal work on the study of microorganisms and laid the foundations of stereochemistry, microbiology and immunology
- Trained as a chemist, his early fame came from isolation of D and L form of crystals of tartaric acid
- He suggested that only “living organisms” can produce molecules of exclusively one symmetry; whereas, chemical synthesis can produce only “racemic” mixtures
- This led to his firm belief that only “living organisms” could be responsible for biological processes, a view that was rejected by chemists who had embraced “reductionism” as the basis of understanding matter..



Louis Pasteur
1822-95

Every one in this argument were wrong!

CONFLICT BETWEEN CHEMISTRY AND BIOLOGY

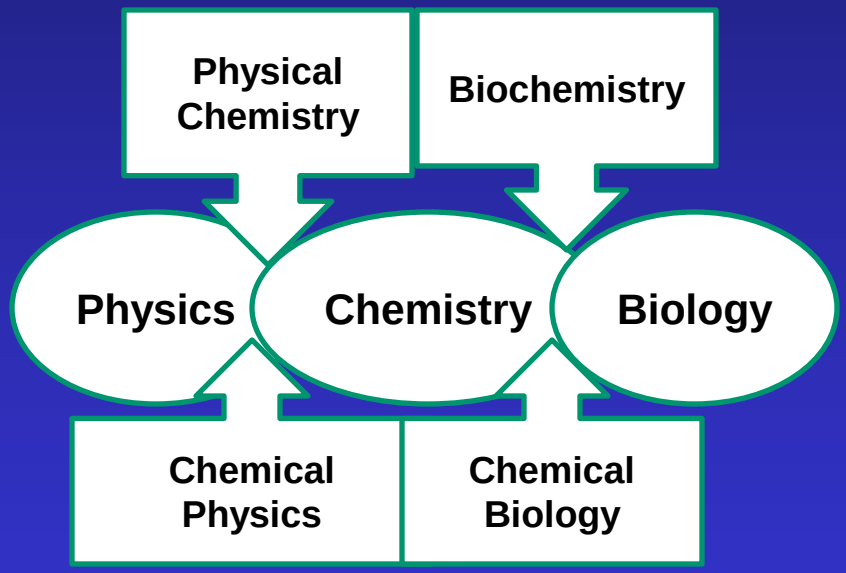
- Process for converting grape juice to wine was known since antiquity; yet the nature of the process was obscure till the 19th century
- Antony Von Leeuwenhoek, in 1676, saw yeast cells in fermentation sediments
- Yet the leading chemists of the 19th century (Berzelius, Lavosier, Liebig or Wohler) did not recognize the central role of yeast in fermentation. They believed that "catalytic" breakdown of sugar led to alcohol. The chemists were enamored by the concept of "reductionism" and threw out "vitalism" as an antiquated idea
- Even Pasteur, though trained as a chemist, missed the discovery of enzymes, the key to fermentation

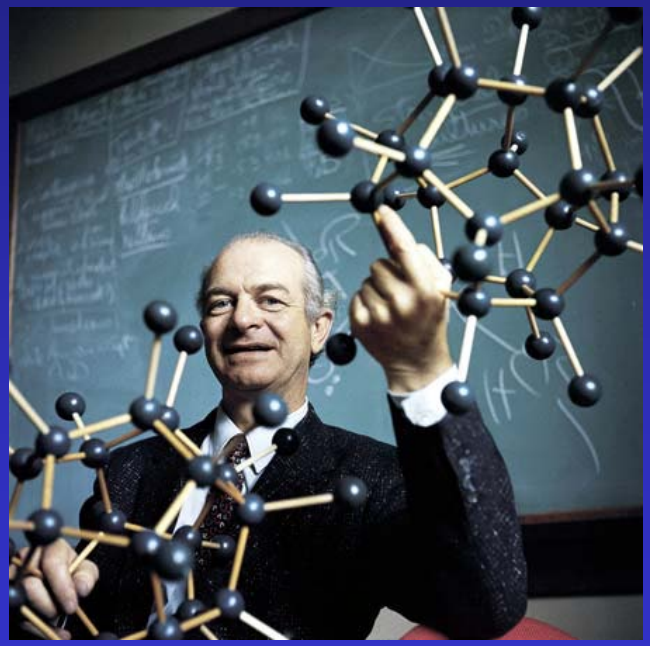
It will take another thirty years before Eduard Buchner in Munich would discover that enzymes from cell free extract of yeasts were responsible for fermentation

Eduard Buchner
1860-1917
Nobel 1907

LINUS PAULING AND THE NATURE OF THE CHEMICAL BOND

Established chemistry as an overarching science that bridges physics on one side and biology on the other





1901- 1994
Nobel Laureate, 1954

STRUCTURAL ORGANIC CHEMISTRY

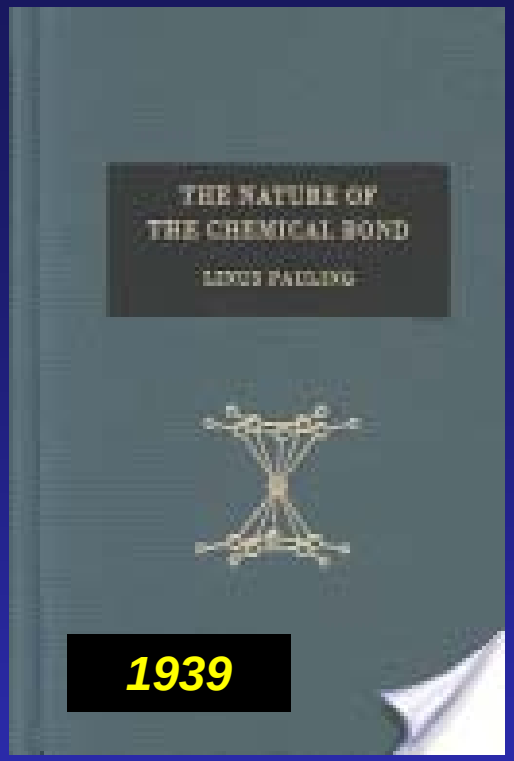
Reproduced from" Linus Pauling in His Own Words",1995

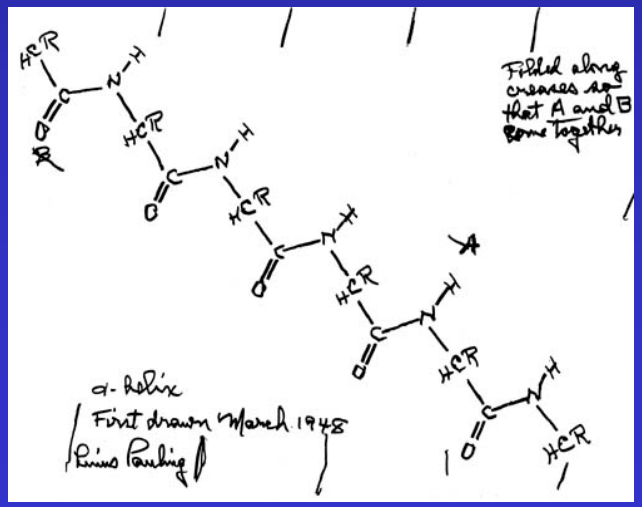
" By 1932 I felt reasonably well satisfied with my understanding of inorganic compounds , including such complicated ones like silicate minerals. The possibility of getting a better understanding also of organic compounds then presented itself. Very little information on bond lengths and bond angles were available for organic compounds. In 1930, when I visited Germany, I learned about a new method of determining the structure of molecules that had been invented by Dr Herman Mark. This was the method of electron diffraction "

ANOTHER TOOL EMERGES : X RAY AND ELECTRON DIFFRACTION

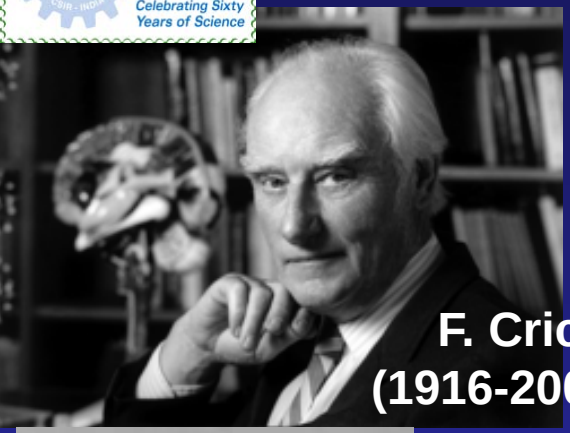
- *" My student Brockway began in 1930 to construct the first electron diffraction apparatus for studying organic molecules that had been built anywhere except in Herman Mark`s laboratory in Vienna*

Within a few years we had amassed a large amount of information, leading to new ideas in structural chemistry, such as the theory of resonance, orbital hybridization and valence bonds. These results were in accordance with the results of quantum mechanical calculations and it became clear by 1935 that a far more extensive, precise and detailed understanding of organic compounds have been developed than that had been available to chemists in earlier decades"



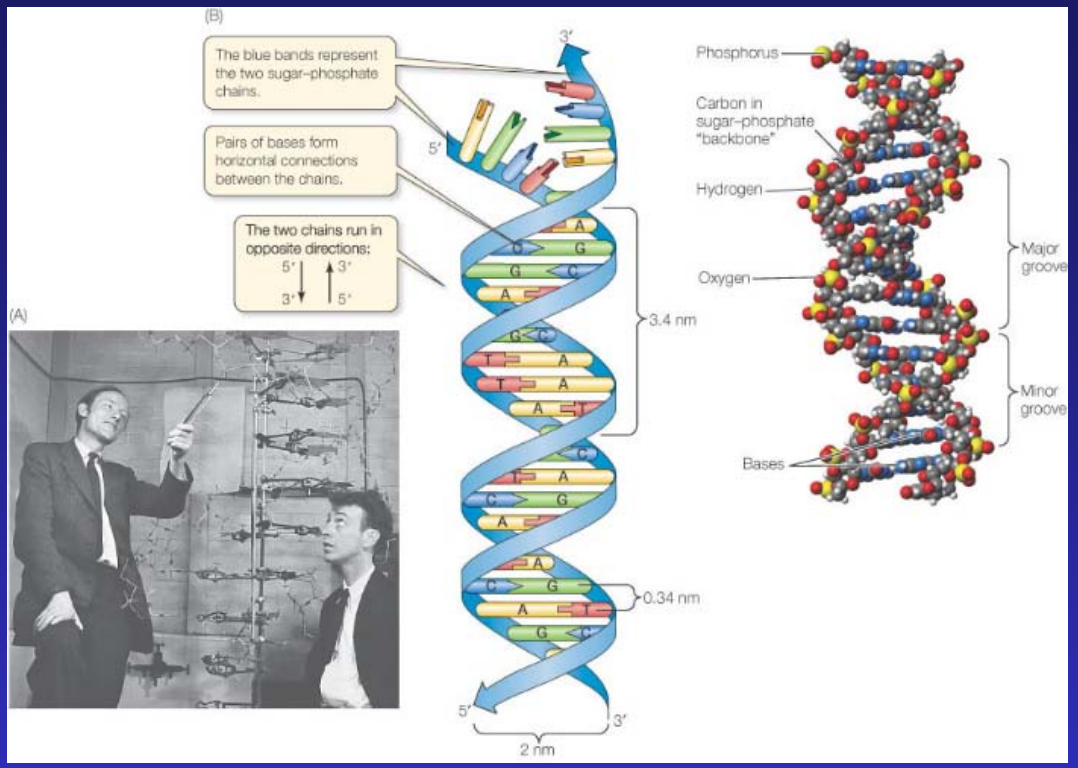


THE DOUBLE HELIX : AN ICON OF 20 th CENTURY SCIENCE



F. Crick
(1916-2004)

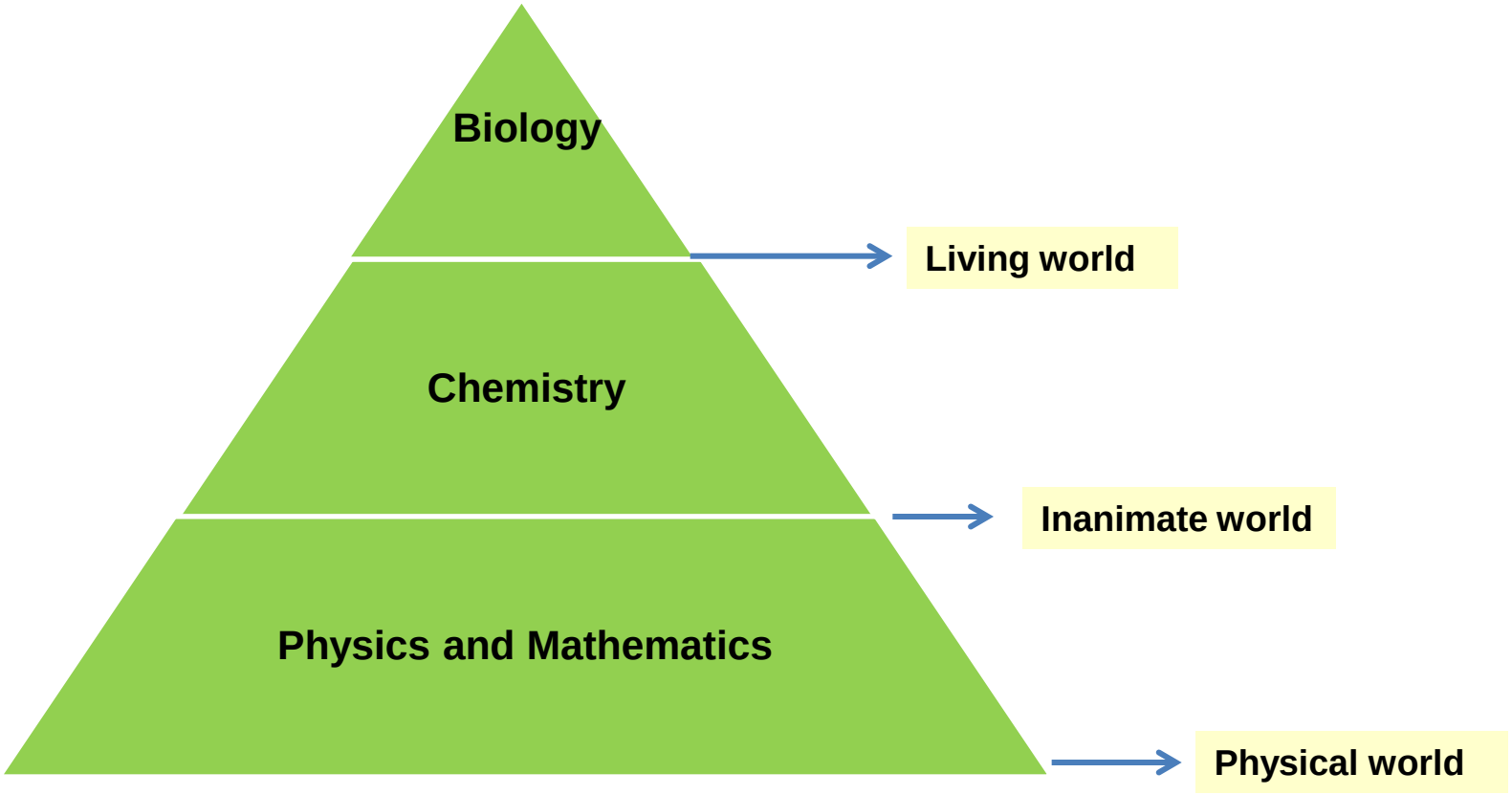
J. D. Watson
(1928-)



"This structure has novel features which are of considerable biological interest"……It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material"

Watson and Crick in Nature, April 25, 1953
(Discovered on 28 February 1953)

HEIRARCHY OF SCIENCE



P. Oppenheim and H. Putnam, Unit of science as a working hypothesis, H. Feigl, M. Scriven, G. Maxwell (eds.), Concepts, Theories and the Mind – Body Problem, Vol.2, University of Minnesota Press, 1958

PHYSICS, CHEMISTRY AND BIOLOGY: STYLE AND APPROACH

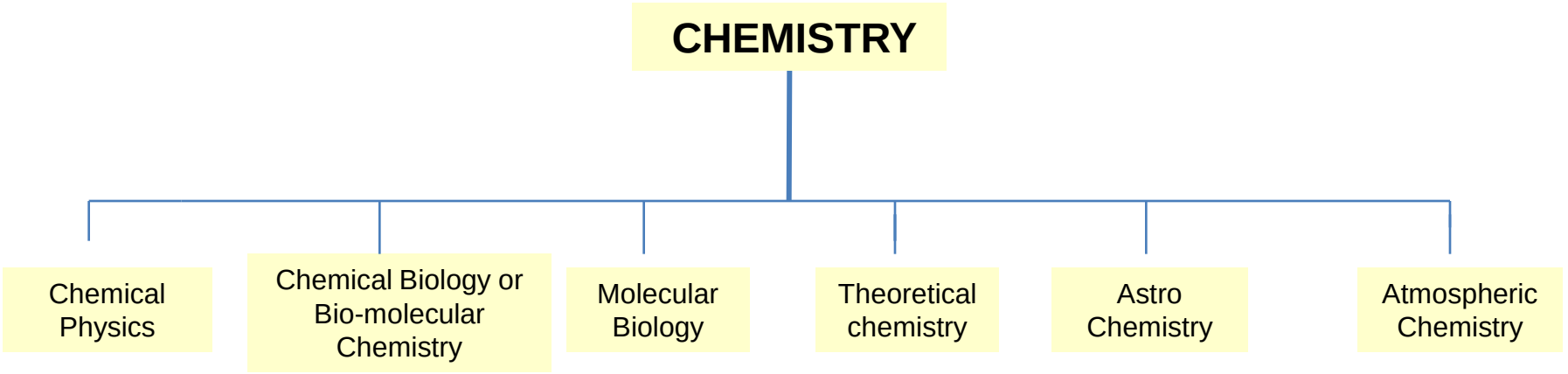
Physics	Search for “simple” systems to test “theory” based hypothesis on the structure of matter
Chemistry	Understand molecular and structural diversity in the organization of matter, mostly “non-living”
Biology	Understand molecular and structural diversity in the organization of matter, mostly living

Chemistry and Biology are two distinctive cultures and the rift between them is serious, generally unappreciated and counter productive.

Arthur Kornberg, 1987

CENTRALITY OR BRANCHING OF CHEMISTRY

S.Ritter, C&EN, November 29, 2004, p.31; Wilson C.K. Poon, Studies in History and Philosophy of Biological and Biomedical Sciences, 42, 115 (2011)



- Science began centuries ago as a unitary discipline and included mathematics, astronomy, anatomy and alchemy; During the 1700's, in the Age of Reason, scientific disciplines as we broadly understand today took shape
- Now science is evolving again, back into a multidisciplinary endeavor with key focal points as the interface between chemistry and physics, chemistry and biology and biology and physics.
- From a study of elements to molecules the study of molecular interactions and functions , leading to the creation of many sub disciplines, seemingly away from the core discipline of chemistry and into increasingly multidisciplinary space

COMPLEXITY IN BIOLOGICAL SYSTEMS

- The beginning of the concept of *Emergent Properties : when whole becomes larger than the sum of the parts*
- Biology is characterized by emergent properties, systems more important than molecule or assembly of molecules; shape or form is more important than chemical composition or structure
- Emergent properties are characteristic of complex systems – Ant colonies, flight of birds, behaviour of crowds, droplets of water and ice, behaviour of cells, neural networks, cognitive science, musical notes, traffic on a road, climate and atmospheric science etc . These systems are characterized by high level of collective or cooperative behaviour.
- Does reductionist approach limit our ability to understand emergent properties?
- Is there need for a new stream of thought to connect the simple molecular understanding of matter provided by chemistry with the complex emergent behavior of biological system ?

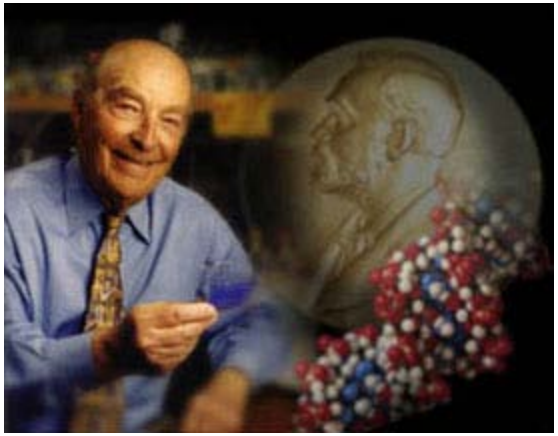
LANGUAGE OF CHEMISTRY

Language of Chemistry

Physical World

Biological World

The Two Cultures: Chemistry and Biology,
A. Kornberg, Biochemistry, 26, 68888 (1987)



Arthur Kornberg 1918-2007 Nobel, 1959

LANGUAGE OF CHEMISTRY

Letters	Atoms
Words	Molecules
Grammar	Rules of bonding and reactions
Sentences	Assembly of molecules
Paragraphs	Sets of molecular assemblies
Chapter	Expression of information by assemblies
Book	Transmission of information
Story	?

COMPLEX MATTER via SUPRAMOLECULAR SELF ASSEMBLY

Supramolecular Chemistry

Molecular Recognition and Self Organization

Physical World

Biological World

Jean-Marie Lehn, Science, 295, 29 March 2002

J-M Lehn
1939
Nobel, 1987

BIOINSPIRED MATERIALS

NATURE'S APPROACH TO SUSTAINABLE MATERIALS

Nature designs material with great care and attention to details

- Economy in the use of raw materials
- Minimum use of energy
- Easy to recycle under ambient conditions

Nature achieves this sophistication through highly organized fabrication methods and hierarchies of structures

WHICH COMPANY IN THE WORLD PRODUCES ……

- Biodegradable fibers stronger than steel
- Biodegradable photo-detectors more sensitive than the most advanced photonics technology
- Biodegradable super-hydrophobic surfaces
- Toughest ceramic biodegradable nano-composites
- Biodegradable data storage media that carry one bit of information for every three molecules

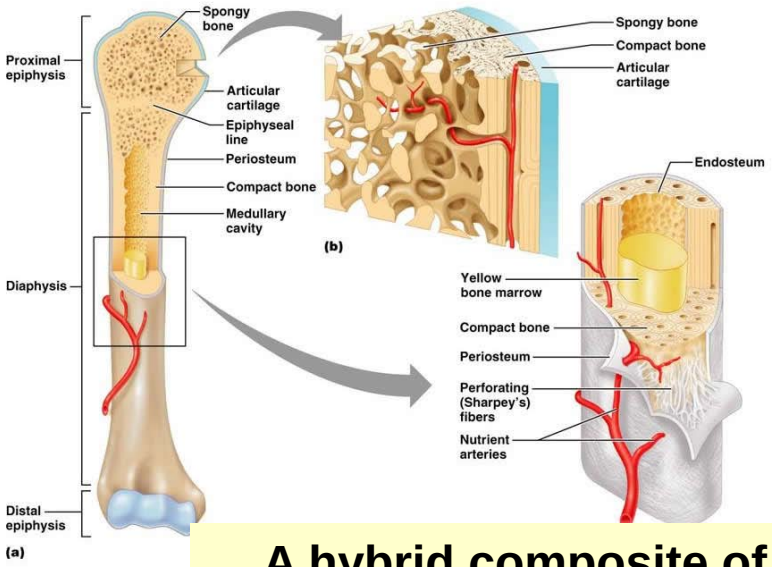
Superhydrophobic surface

Abalone shell

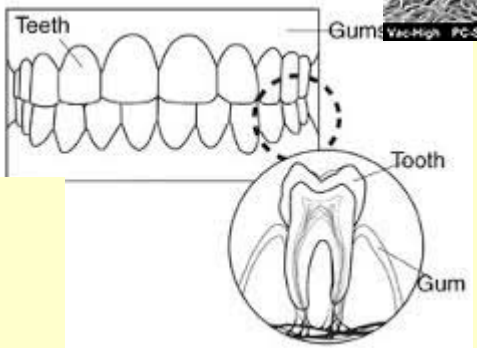
Surface Photonic Gratings

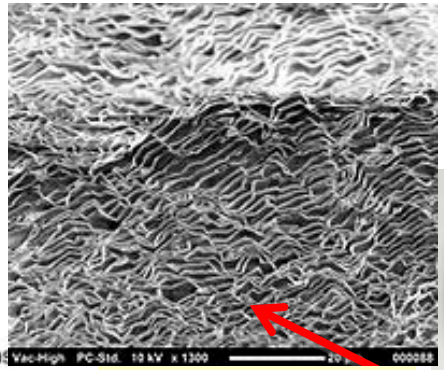
This company is called Life Inc.,

Its materials are the most advanced on this planet



A hybrid composite of Hydroxyapatite and Collagen Type II





Aragonite layers in the nacre of a blue mussel

MATERIAL SYNTHESIS : NATURE'S PRINCIPLES

- Optimal use of energy and raw materials
- Minimal energy consumption – most synthesis occurs at <45^{o}C
- Molecular control leading to flawless materials: Self healing and self-correcting principles
- Use of compatible chemistries
  - Ceramics : $CaCO_3$, SiO_2
  - Non-ceramics : Proteins, polysaccharides
  - Water : Plasticizer
  - Partitioning and separations : Lipid (Bilayer membranes)
  - Hydrophobic interaction : Orientation
  - Liquid crystallinity : Processing of materials

Will the twenty first century be the age of bio-inspired organic materials

ADVANTAGES OF MATERIALS MADE BY NATURE

- Efficient synthesis, if you are prepared to wait long enough
  - Fastest rate of bone growth : 1 μm/day
  - Growth of egg shells : 5 g/day
- Recycling
  - Animals/Plant continuously recycle/ repair their constituent materials
  - Choice : make materials that are strong/ tough with finite probability of catastrophic failure (man)

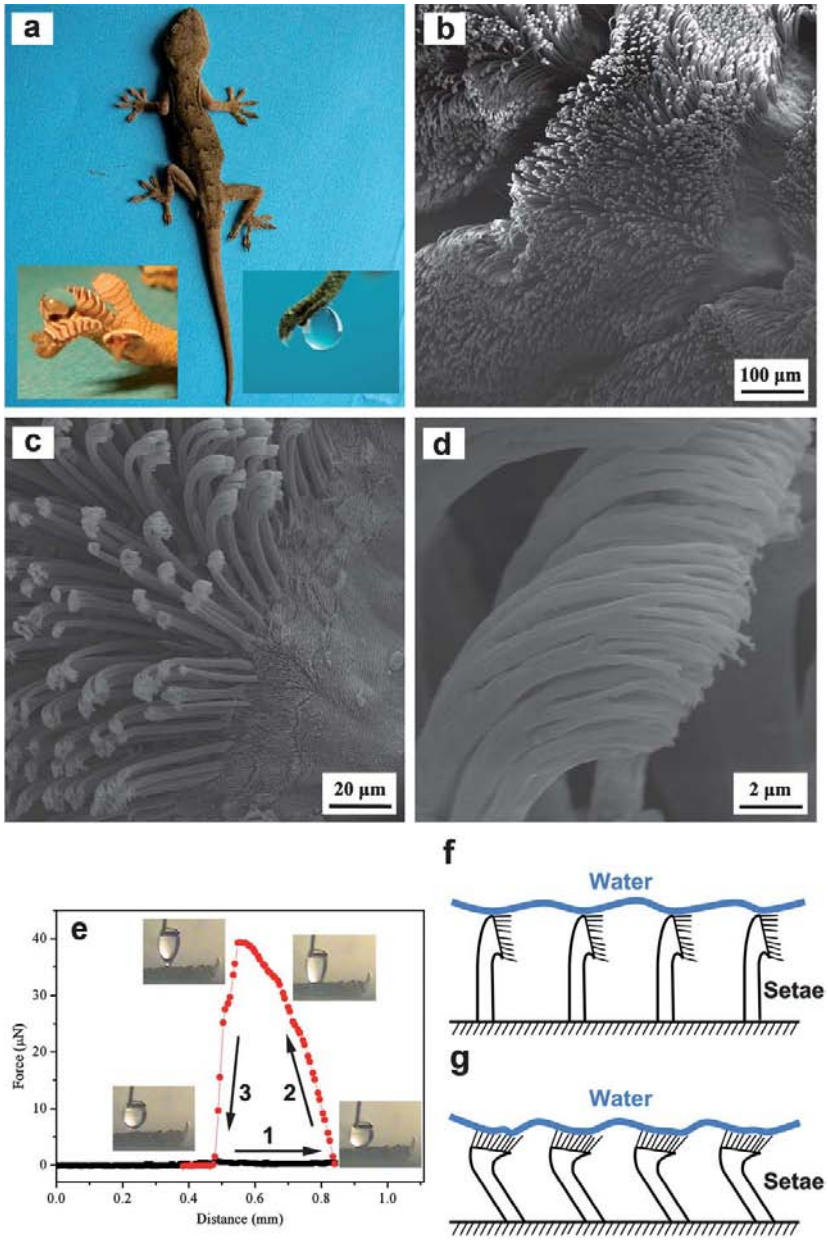
    or

    make materials that are relatively weaker, but have self healing or repair capabilities (nature)

Self-healing structures and tough materials are emerging from an understanding of nature's processes

SUPER HYDROPHOBIC GECKO FEET WITH HIGH ADHESIVE FORCE TOWARDS WATER

An illustration of functional integration of multiscale structures in biological materials



K. Liu et al.,Nanoscale, 4, 768 (2012)

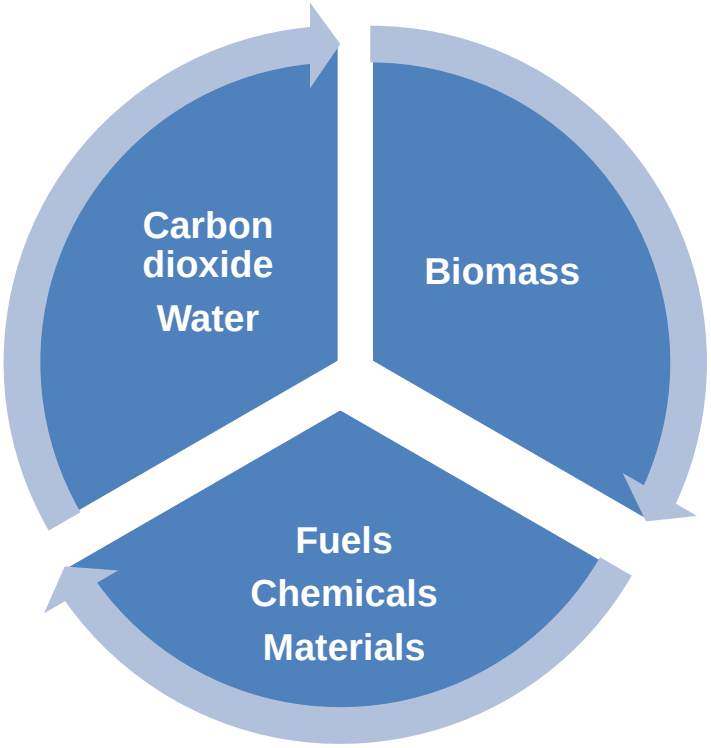
BIO-INSPIRED MATERIALS CHEMISTRY

- Bio-smart Surfaces
- Bio-mineralization
- Bio-glass and Bio-ceramics
- DNA nanomaterials via conjugation
- Bio-nanomaterials
- Bio-composites

E.Dujardin and S. Mann, Adv. Mater.,14, 1 (2002)

BIO CATALYSIS AND SYNTHETIC BIOLOGY FOR SUSTAINABLE CHEMISTRY

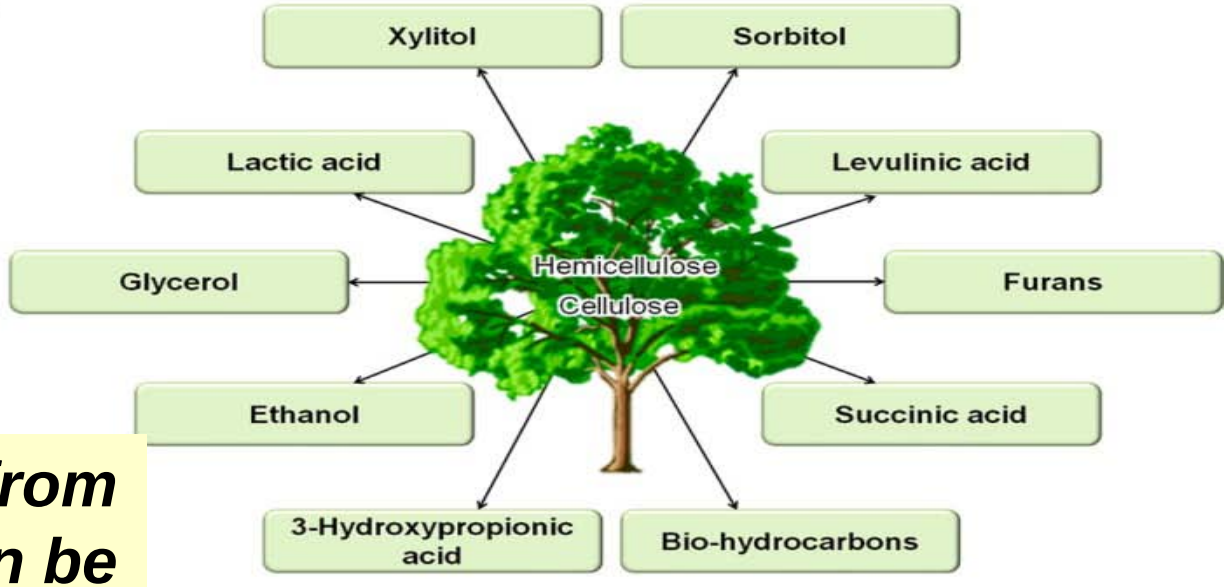
FROM HYDROCARBONS TO CARBOHYDRATES : FROM NON RENEWABLES TO RENEWABLES



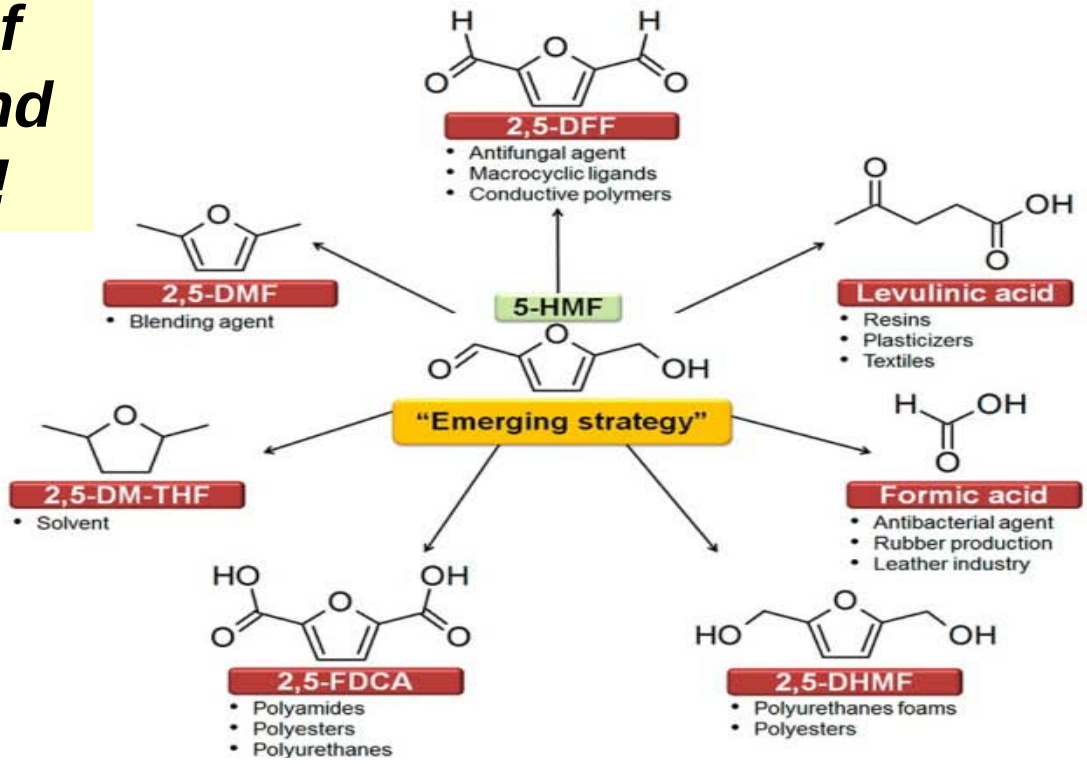
Can a part of the chemicals / materials/ fuel needs of humankind progressively shift to renewable carbohydrate resources (biomass) ?

Is such a virtuous cycle just a dream ?

(a)



Biomass from a plant can be a source of chemical and materials !



BIO-REFINERY : A PLATFORM FOR SUSTAINABLE CHEMISTRY

The refinery based on fossil resources

Source	Transformation	Products	Downstream process
Oilfields	Refining & Cracking	Chemical Transformation	Formulation
Crude Oil	Naphtha	Monomers & polymers	End Product

The bio-refinery based on renewable resources

Source	Transformation	Products	Downstream process	
Agricultural Fields and Forests	Starch & Sugar production	Biotech Trans-formation	Chemical Trans-formation	Formulation
Biomass	Sugars	Monomers & polymers		End Product

Leading role of biology
Shared role between biology and chemistry
Leading role of chemistry

BIOLOGY TOOLS THAT ARE SHAPING THE FUTURE OF CHEMISTRY

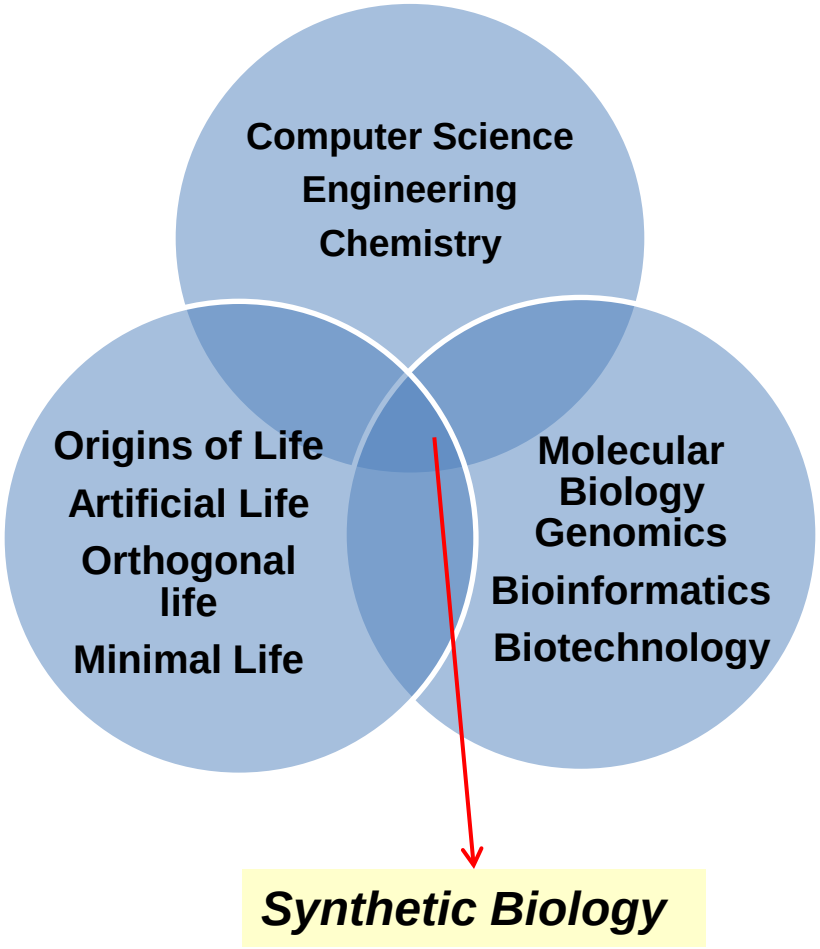
- Plant molecular biology
- Genetic engineering
- Protein engineering
- Genomics and metabolomics
- Industrial microbiology
- Catalytic thermo-philic enzymes
- Bioreactor engineering and fermentation
- Directed evolution to create adaptive organisms
- Metabolic pathway engineering
- ***Synthetic biology***

SYNTHETIC BIOLOGY: APPLYING ENGINEERING TO BIOLOGY

Synthetic biology is the engineering of biology; the synthesis of complex, biologically based (or inspired) systems which do not exist in nature. The engineering perspective may be applied to all levels of the hierarchy of biological structures- from individual molecules to whole cells, tissues and organisms

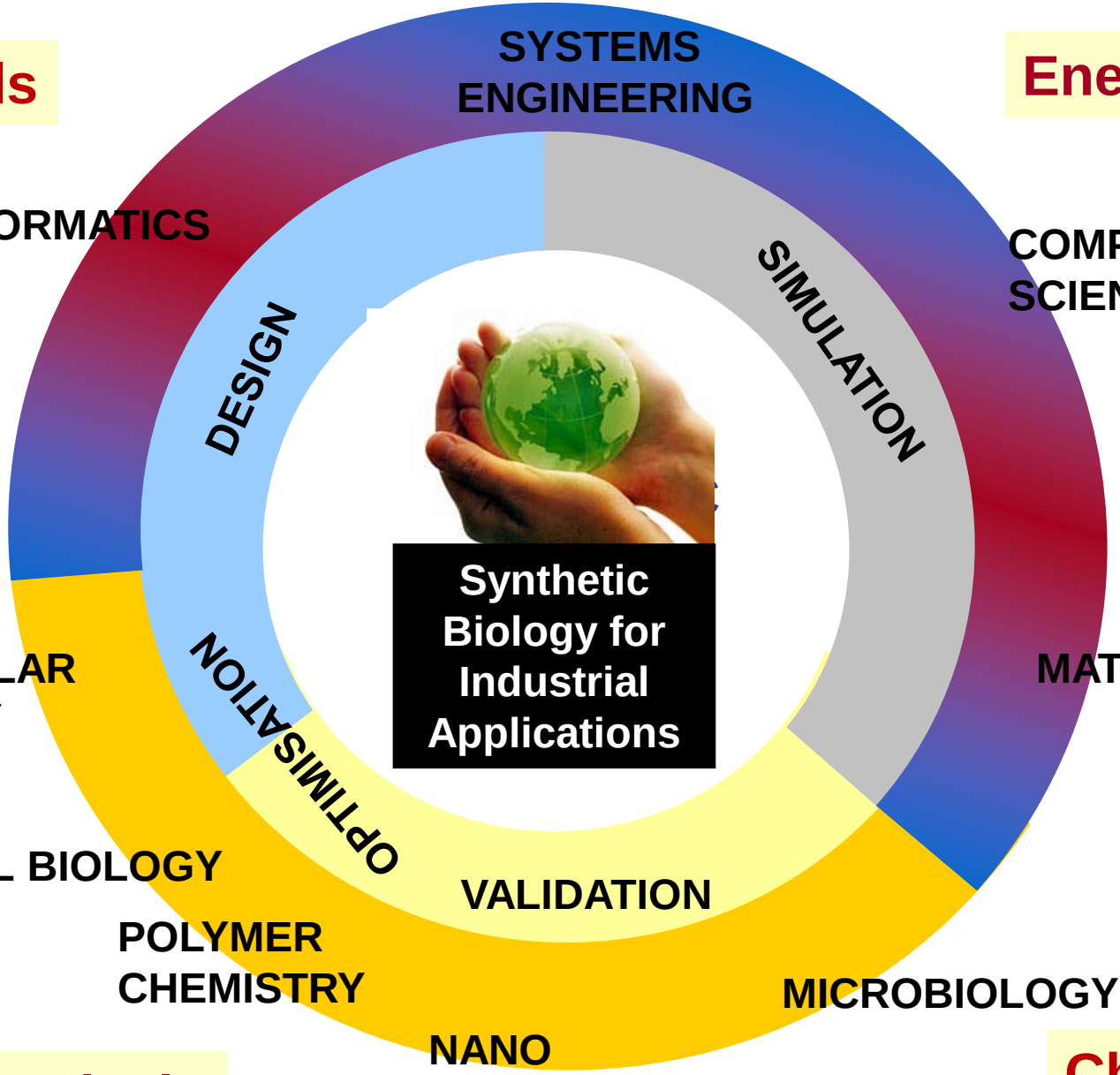
European Union , 2005

Objective
Engineering new biological pathways
Creating, de novo, new organisms



D. Endy, Nature, 438, 449 (2005)
D. Endy and I.Deese, Adventures in Synthetic Biology, Issue 1, 2005

SYNTHETIC BIOLOGY: AN INTEGRATIVE SCIENCE



Materials

Energy

BIOINFORMATICS

COMPUTER SCIENCE

MOLECULAR BIOLOGY

MATHEMATICS

CHEMICAL BIOLOGY

POLYMER CHEMISTRY

MICROBIOLOGY

NANO TECHNOLOGY

Pharmaceuticals

Chemicals

THE THIRD WAVE IN BIOTECHNOLOGY

- First Wave : Food Security
- Second Wave : Health Security
- Third Wave : Energy and Resource Security

From reading of a genetic code to writing it, from random selection to designed selection, from creating the gene to creating the chromosome

SYNTHETIC BIOLOGY

Provides the tools and processes to manipulate life

Steps

- Understand the genes responsible for function called “parts” (metabolic pathway engineering, DNA sequencing and Genomics)
- Take the “parts” (DNA sequences, promoters or sequences that facilitate gene expression) and assemble them into a “device”
- Insert the “device” into a cell of an organism and allow them to perform the desired function
- Use “Directed Evolution” to perfect the functions of the synthetic organism

SYNTHETIC BIOLOGY

- "Parts" available from Gene Foundries
  - Registry of Standard Biological parts @ MIT
    www.parts.mit.edu
  - BioFAB at UC, Berkeley and Stanford
- How reproducible are the parts and with what reliabilty we can go from parts to functions : open question
- As of today, synthetic biology requires massive efforts. Keasling's creation of a synthetic microbe that will produce an antimalarial compound, Artemisinin, was a result of 150 person years effort !
- The synthesis of a bacteria in the laboratory has also been accomplished (Craig Venter)

Roberta Kwok, www. nature. com/news/2010/100120/pdf/4632888a

We must either succeed in producing living matter artificially, or we must find the reasons why this is impossible.

Jacques Loeb, The Mechanistic Conception of Life, 1912

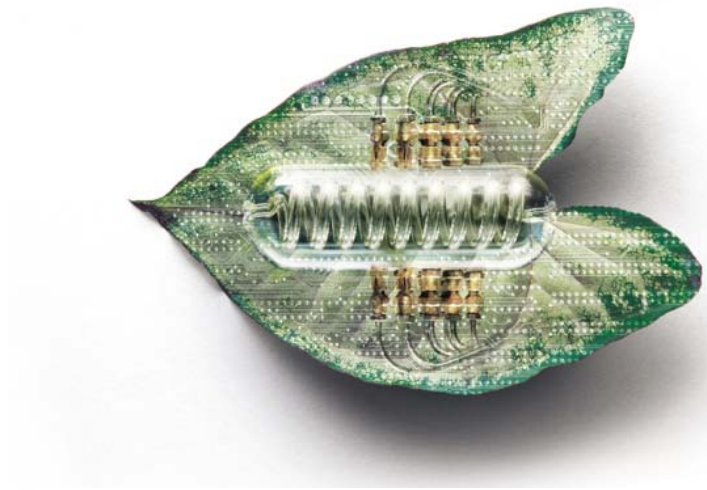
SYNTHETIC BIOLOGY : SOME QUESTIONS

- Will synthetic biology provide humans the ability to “hack” life, or even play God ? No or Yes?
- If yes, when ?
- Is there an ethical dimension to this kind of research?

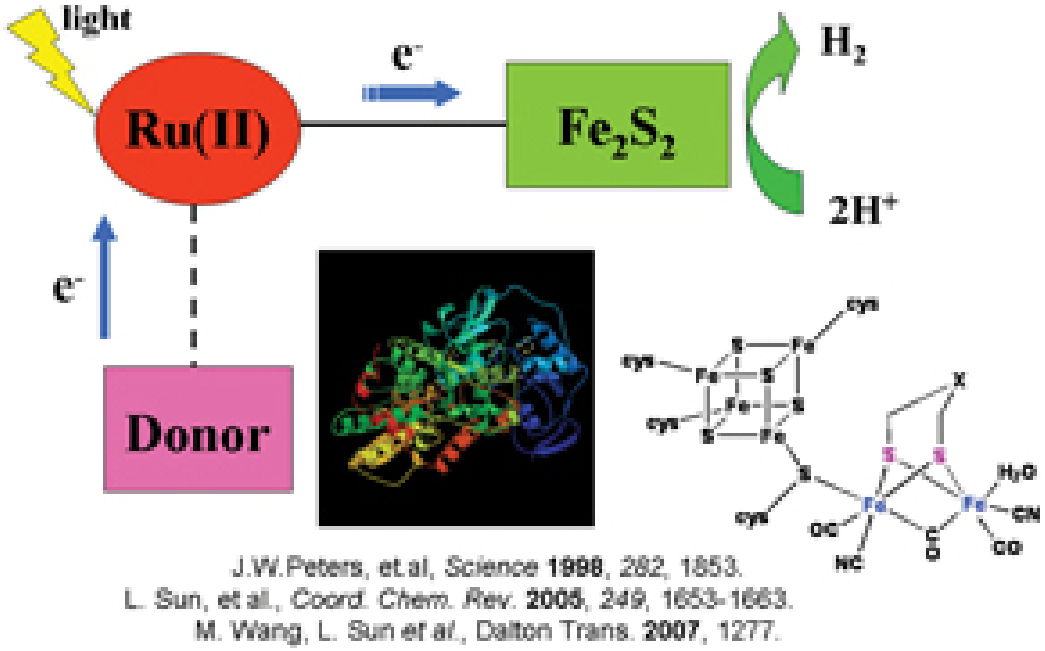
One hundred years ago, when Wright Brothers first flew their plane made of wood and paper, no one believed that men can fly. Where will synthetic biology take us in the next hundred years ?

BIO IINSPIRED MOLECULAR DEVICES FOR SUSTAINABLE ENERGY

AN ARTIFICIAL LEAF



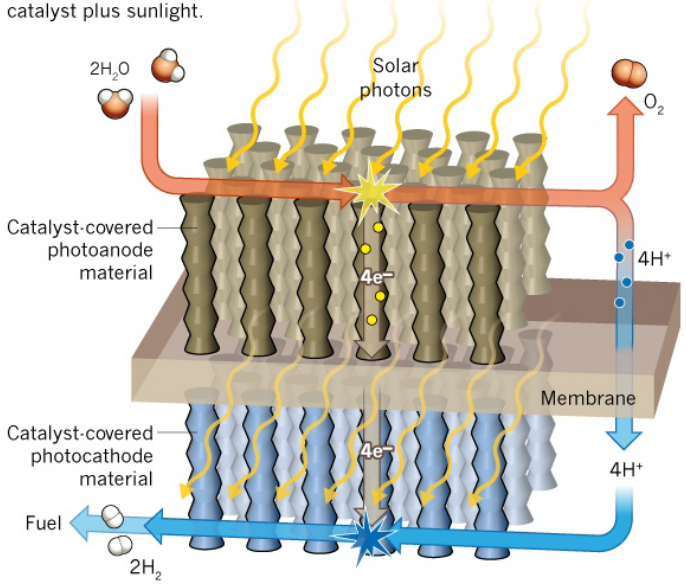
To mimic the function of FeFe-hydrogenase active site



J.W.Peters, et al, *Science* **1998**, 282, 1853.
L. Sun, et al., *Coord. Chem. Rev.* **2005**, 249, 1653-1663.
M. Wang, L. Sun *et al.*, Dalton Trans. **2007**, 1277.

SPLITTING WATER

Artificial photosynthesis uses photons from sunlight to split water molecules into oxygen and hydrogen, which can be used to make fuel. Every two molecules of water yield one oxygen molecule (O_2), as well as four pairs of protons (H^+) and electrons (e^-). The protons and electrons migrate across a membrane, where a photocathode recombines them into hydrogen using a catalyst plus sunlight.



T. Norin, U. Pandit, Chemistry Int.,p.4 (2008)
J. Marshall, Nature, p.22, 5 June 2014

INTEGRATING CHEMISTRY AND BIOLOGY : CHALLENGES TO EDUCATION

INTEGRATIVE LEARNING

" **Making connections within disciplines, between fields, between curriculum, co-curriculum, or between academic knowledge and practice"**

Awbrey, S.M, Dana, D., Miller, V.W., Robinson, P., Ryan, M.M. and Scott, D.K. (Eds.), (2006). Integrative Learning and Action: A Call to Wholeness (Studies in Education and Spirituality),New York: Peter Lang Publications

INTEGRATIVE SCIENCE IS NOT NEW

- **Science, when it began as an organized body of knowledge was essentially integrated or holistic.**
- **Science was part of a larger domain of knowledge called Natural Sciences, that included the study of chemistry, biology, physics, mathematics, logic and philosophy**
- **Most departments of sciences in the nineteenth century and early twentieth century were called Department of Natural Sciences**
- **As science expanded during the second half of twentieth century, fragmentation of disciplines became more prevalent**
- **Integrative Science recognizes the absence of borders between sciences. Science finds its strengths in the unity of its diverse disciplines**

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CHANGING FACE OF BIOLOGY AND CHEMISTRY

- **Chemistry and biology are becoming more and more an interdisciplinary pursuit**
- **However, students usually learn chemistry and biology in isolation**
- **Is there a case for teaching science in an integrative fashion ?**
- **Can principles of chemistry be illustrated using familiar biological phenomena or ecosystem behavior and vice versa ?**
- **Structure, function and dynamics constitute the central theme of chemistry. All chemistry must be taught in the context of this theme**

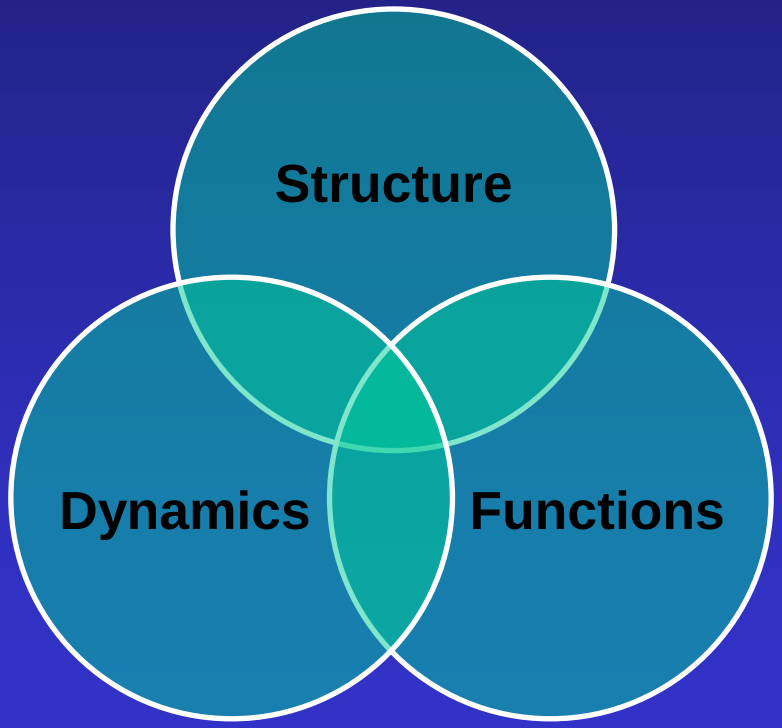
Why don't we teach chemistry and biology the way it is practiced today ?

INTEGRATION OF CHEMISTRY AND BIOLOGY

Molecules can be organic, inorganic or biologically derived, small or big, single or assemblies and involving a range of inter and intra -molecular forces

CHEMISTRY

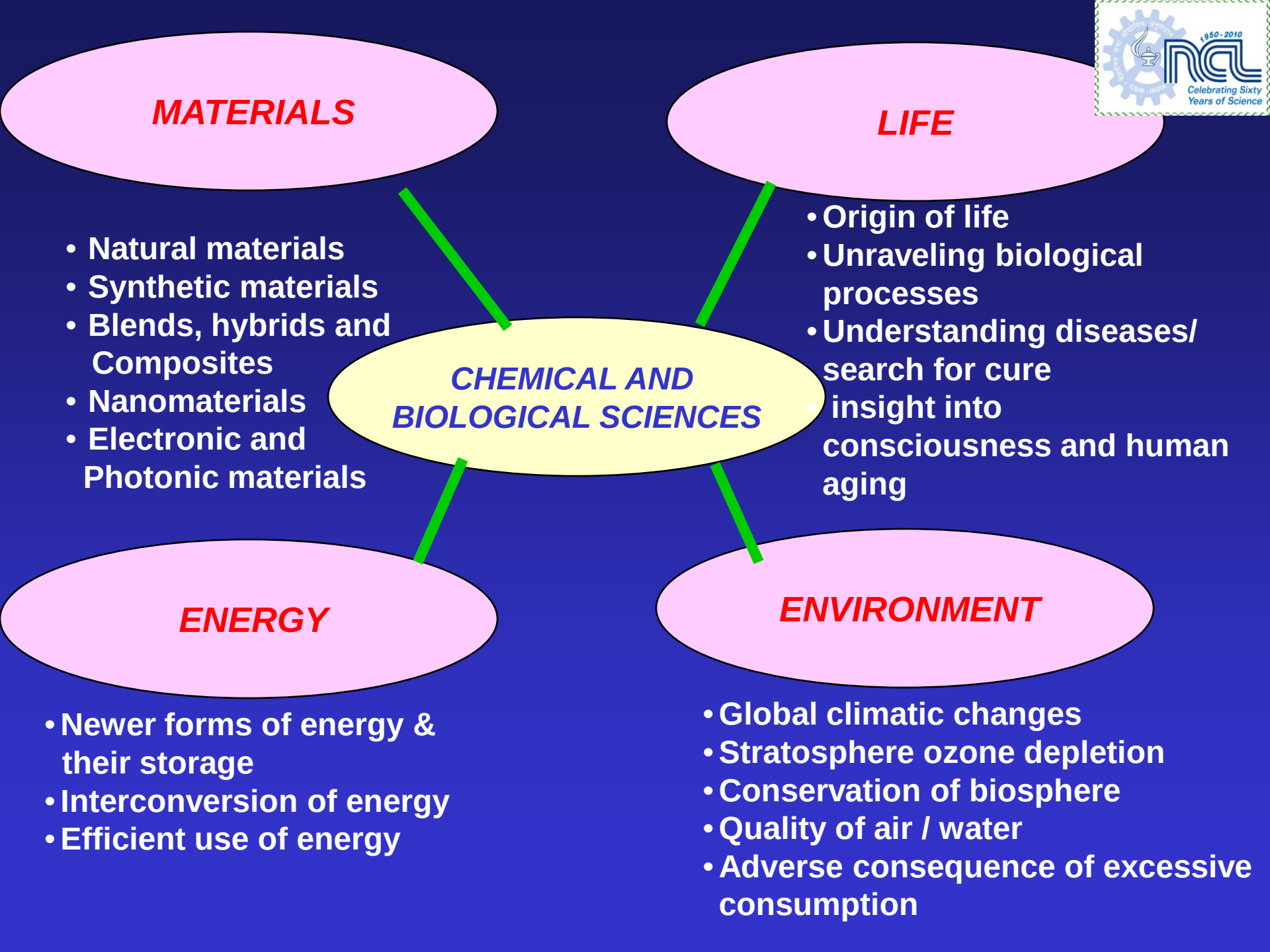
Progression from atoms to molecules to larger molecular assemblies



BIOLOGY

Progression from whole organisms to molecular structure

J. Chemical Education, 88, 1257 (2011)


MATERIALS
• Natural materials
• Synthetic materials
• Blends, hybrids and Composites
• Nanomaterials
• Electronic and Photonic materials
LIFE
• Origin of life
• Unraveling biological processes
• Understanding diseases/ search for cure
• insight into consciousness and human aging
CHEMICAL AND BIOLOGICAL SCIENCES
ENERGY
• Newer forms of energy & their storage
• Interconversion of energy
• Efficient use of energy
ENVIRONMENT
• Global climatic changes
• Stratosphere ozone depletion
• Conservation of biosphere
• Quality of air / water
• Adverse consequence of excessive consumption
1950-2010
Celebrating Sixty Years of Science

FOUR QUESTIONS A TEACHER MUST ASK

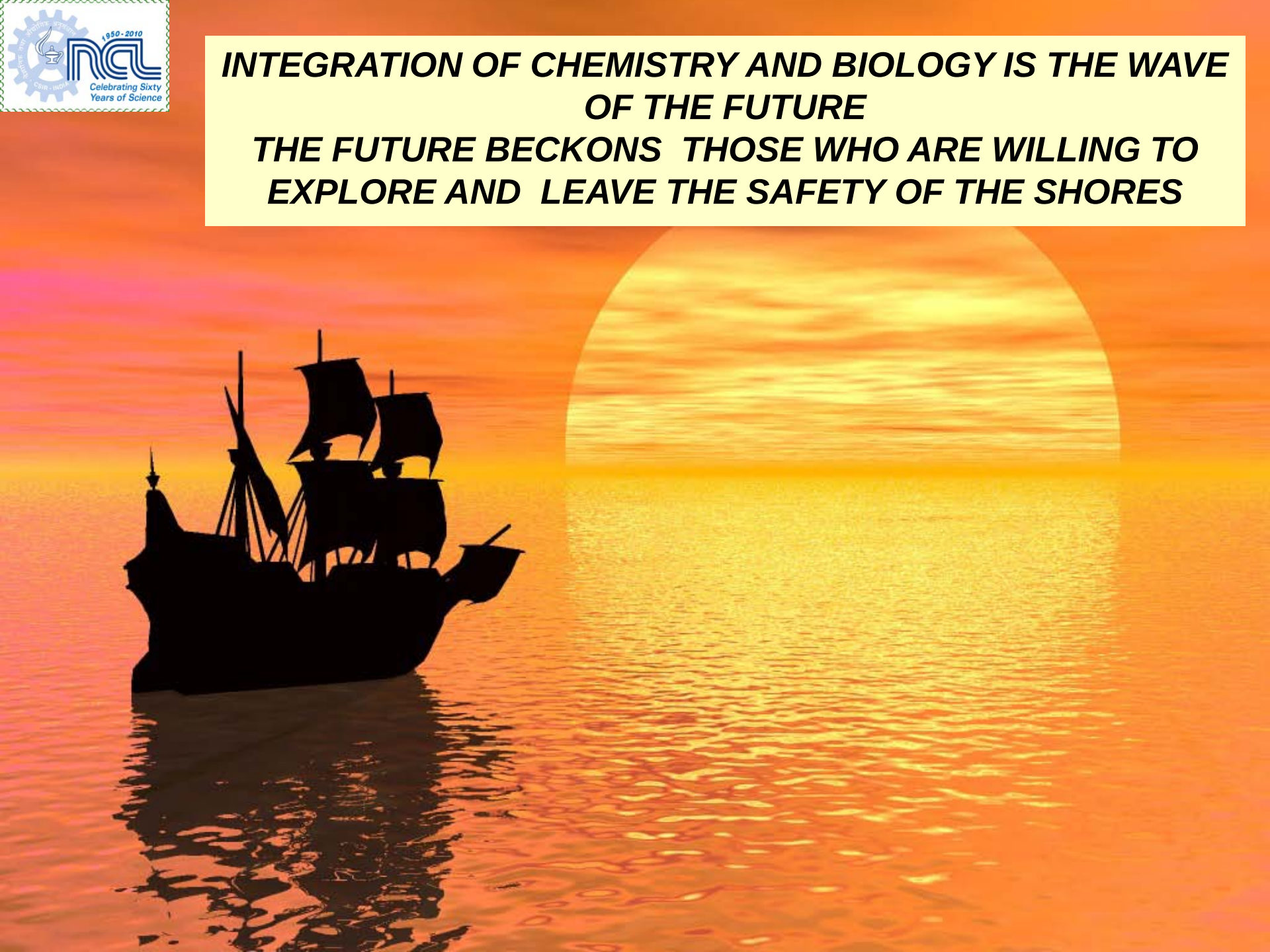
- *What should we be teaching ?*
- *How should we be teaching ?*
- *Why should we be teaching ?*
- *How do we know that we have managed to teach ?*

“ Biological concepts and models are becoming more quantitative and biological research has become critically dependent on concepts and methods drawn from other disciplines. The connections between the biological sciences and physical sciences are becoming deeper and more extensive. However, the way in which we educate future biologists is not geared to the biology of the future. Connections between biology and other scientific disciplines need to be reinforced so that interdisciplinary work and thinking become second nature”

NRC Committee on Undergraduate Education, National Academy Press, Washington DC, USA, 2002; www.nap.edu/books/0309085357/html/

INTEGRATION OF CHEMISTRY AND BIOLOGY IS THE WAVE OF THE FUTURE

THE FUTURE BECKONS THOSE WHO ARE WILLING TO EXPLORE AND LEAVE THE SAFETY OF THE SHORES



1950 - 2010

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THANK YOU