Understanding Complexity in Biological Systems:

From Simple Description to Synthetic Design

Dr. George Poste
Chief Scientist, Complex Adaptive Systems Initiative
and Del E. Webb Chair in Health Innovation
Arizona State University
george.poste@asu.edu
www.casi.asu.edu

Presentation: "Transcending Our Origins"
Origins 5th Anniversary Celebration and Workshop
Arizona State University
5 April 2014

Biological Diversity and Variation: "Endless Forms Most Beautiful"

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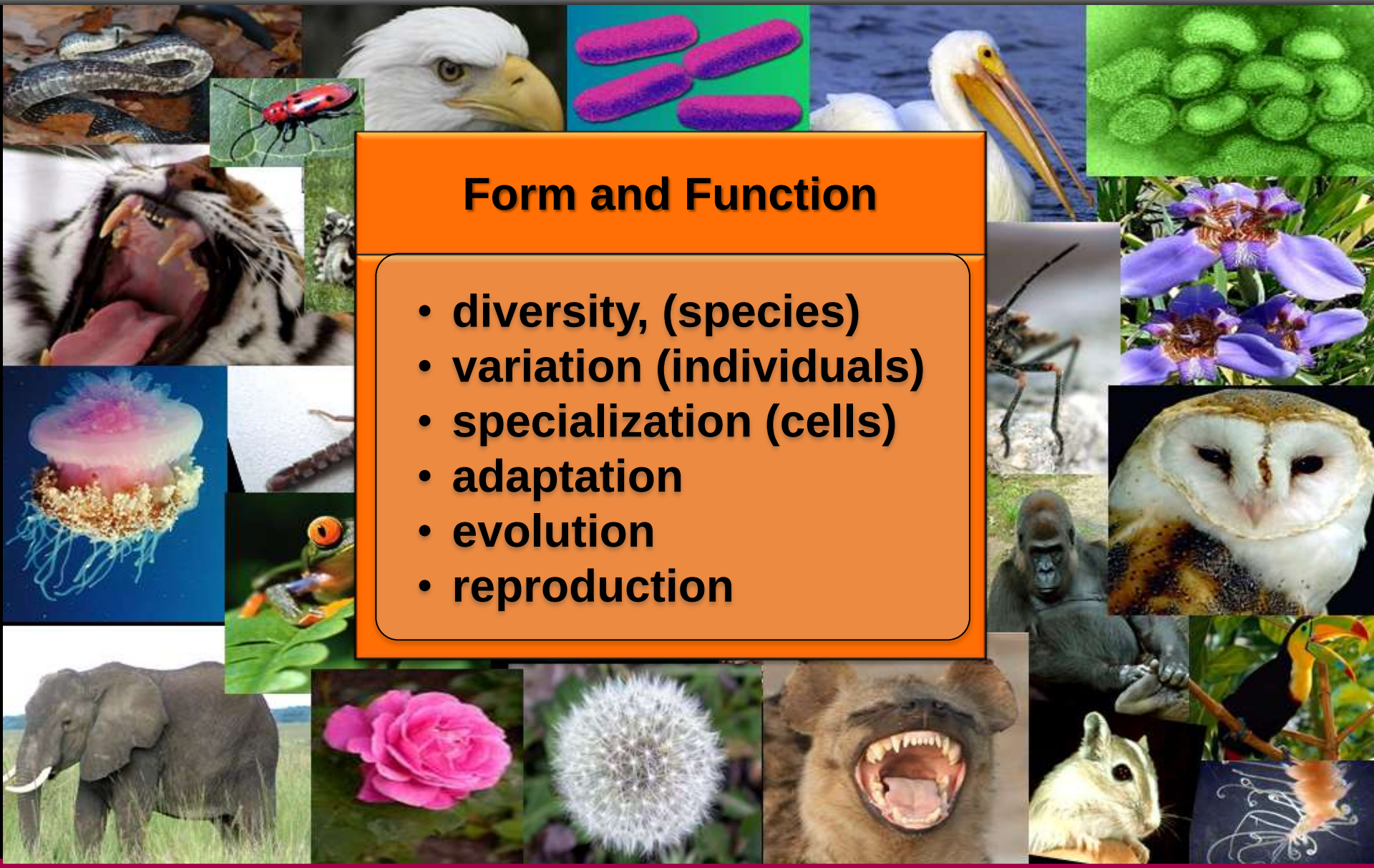
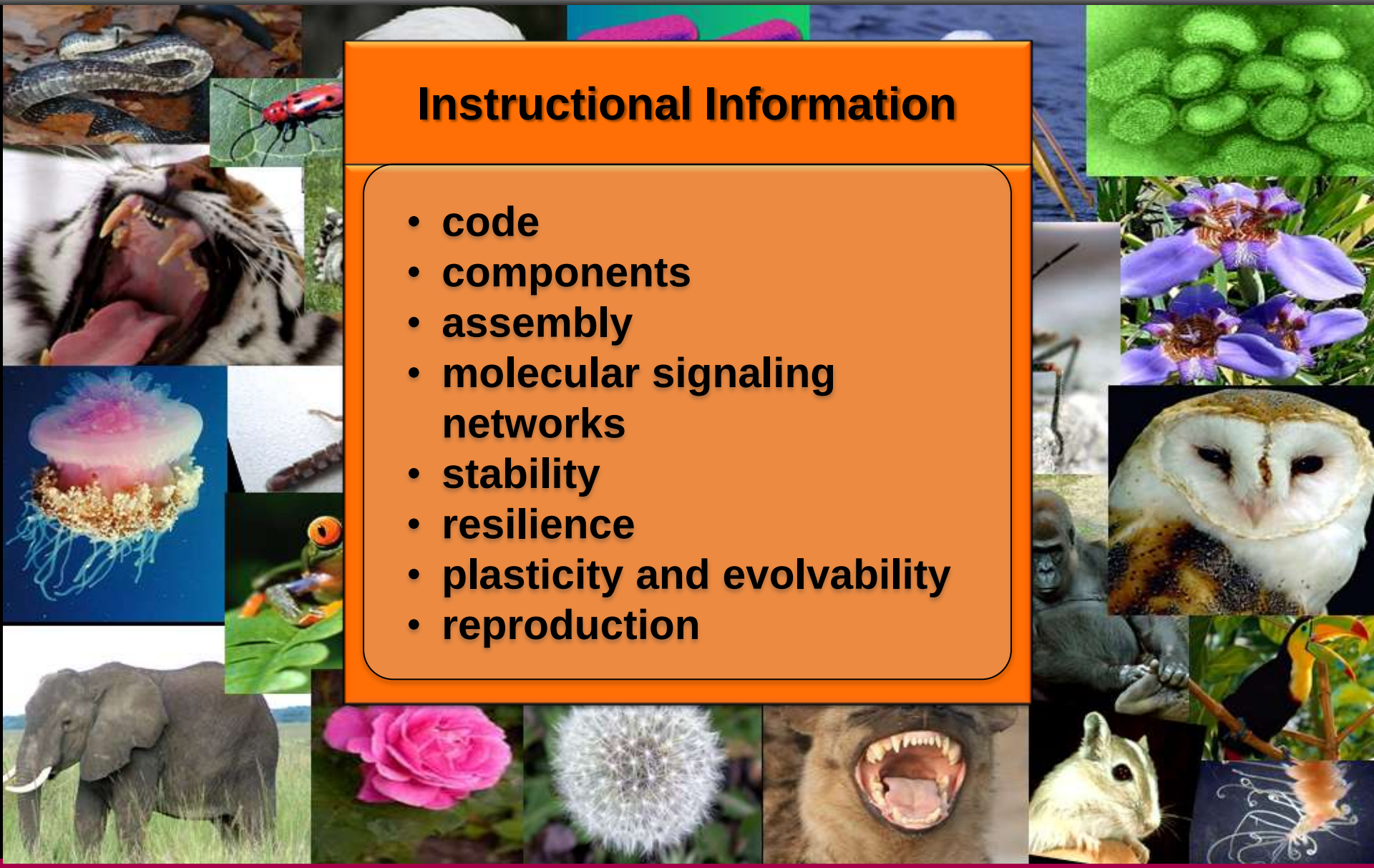


Form and Function

- diversity, (species)
- variation (individuals)
- specialization (cells)
- adaptation
- evolution
- reproduction

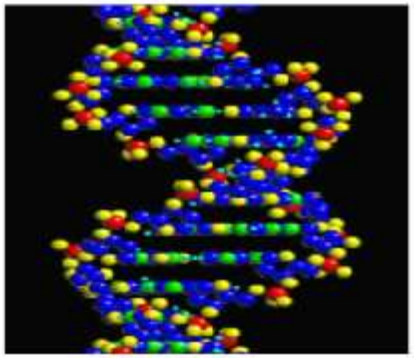
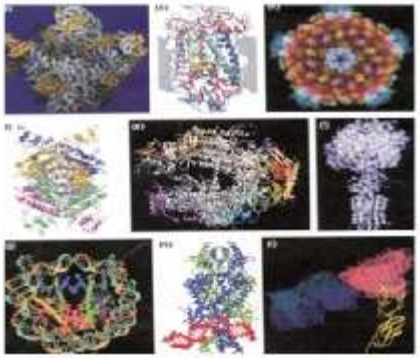
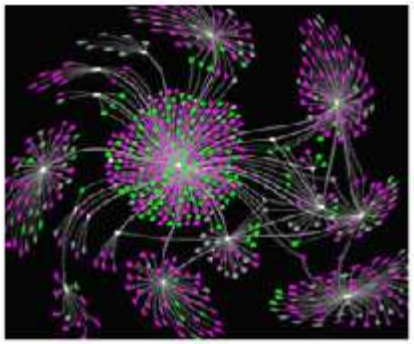
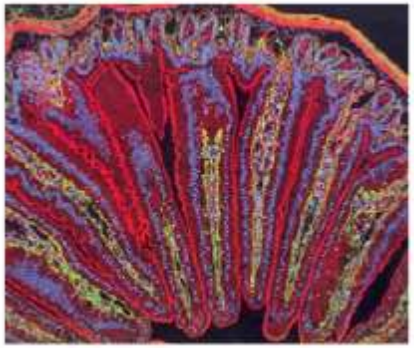
Biological Diversity and Variation: "Endless Forms Most Beautiful"



Instructional Information

- code
- components
- assembly
- molecular signaling networks
- stability
- resilience
- plasticity and evolvability
- reproduction

Understanding Biological Organization: The Construction of Increasing Hierarchical Complexity and Mapping the Underlying Instructional Information

common genetic (digital) code in all life forms	tool box of protein motifs for combinatorial assembly ("molecular lego")	assembly of structurally and functionally diverse proteins	protein interactions and nanoscale intracellular structures
			
			
molecular signaling networks	cells and tissues	organs	organism

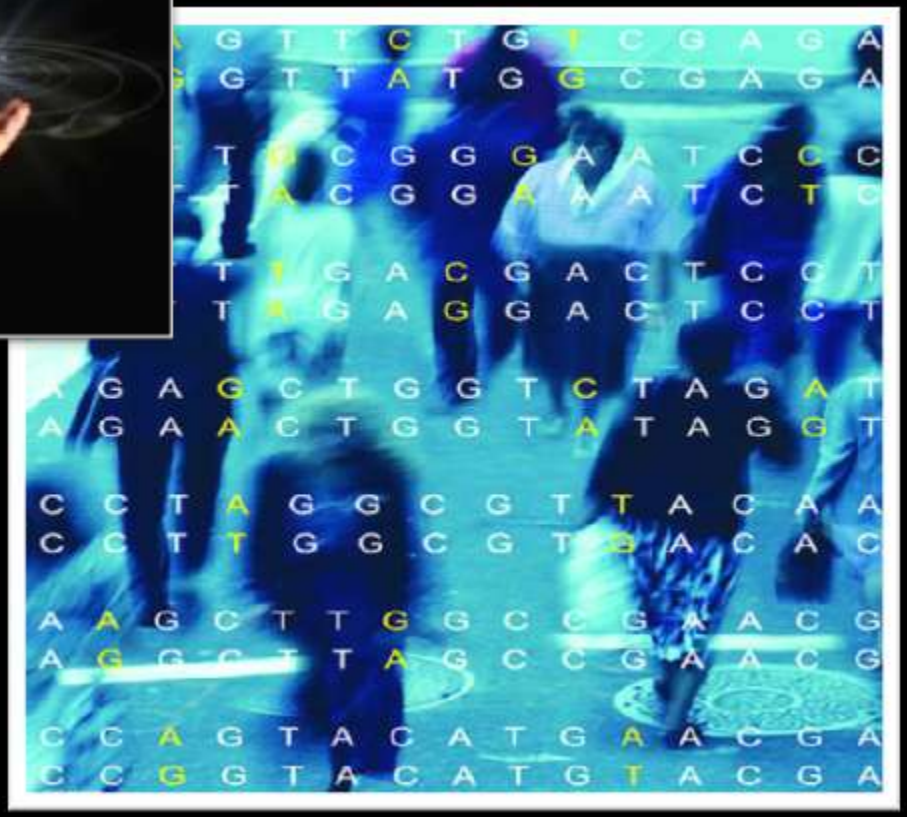
Systems and Synthetic Biology: "Exploring Biospace"

Understanding the Coding Systems for Highly-Specific Programs of Regulated Information Flow and Processing in Dynamic Biological Systems

Digital Biology: "It from Bits"

Digital Biology and Synthetic Biology
“It from Bits”

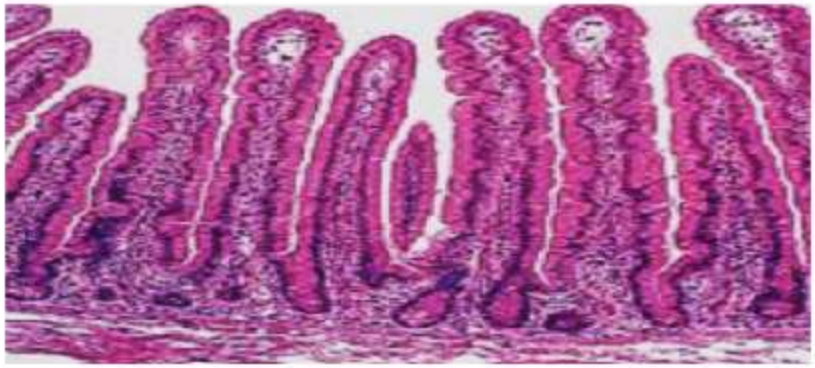
- ‘It’

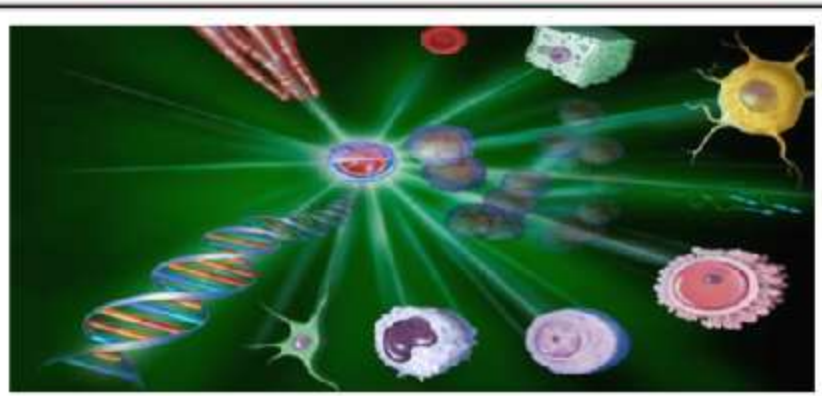


- ‘Bits’

Digital Biology and Molecular Medicine
Mapping Instructional Coding Landscapes and Information Networks

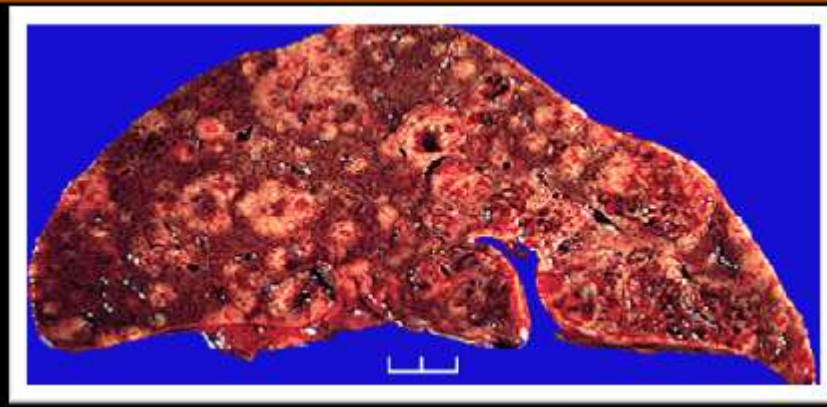
stable information signaling networks (health)





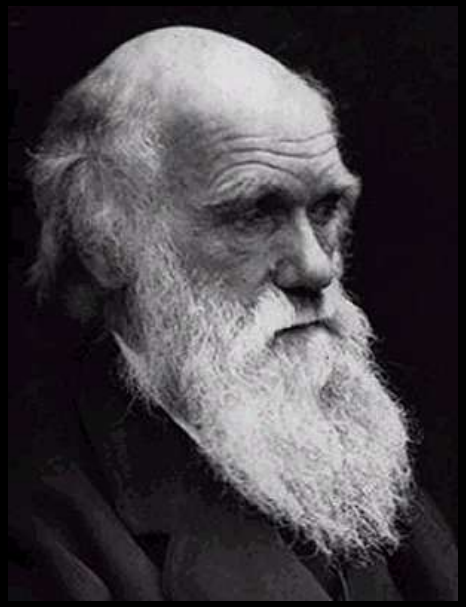
reprogramming information networks (stem cells and regenerative medicine)

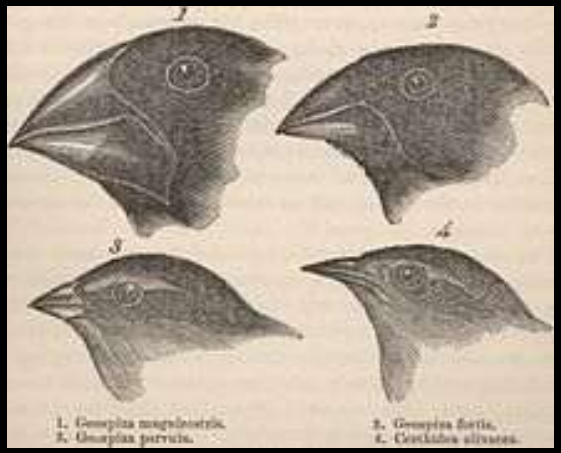
disrupted (dysregulated) information signaling networks (disease)



engineering novel gene constructs (code) to program biological information networks

Darwinian Evolution





….the inheritance of
“profitable variation”

Synthetic Biology:
Accelerated and Directed Evolution

"Creating artificial life with DNA synthesis.
That's sort of the equivalent
of machine-language programming.
If you want to change the world in some big way,
use biological molecules."

Bill Gates
Wired 2010

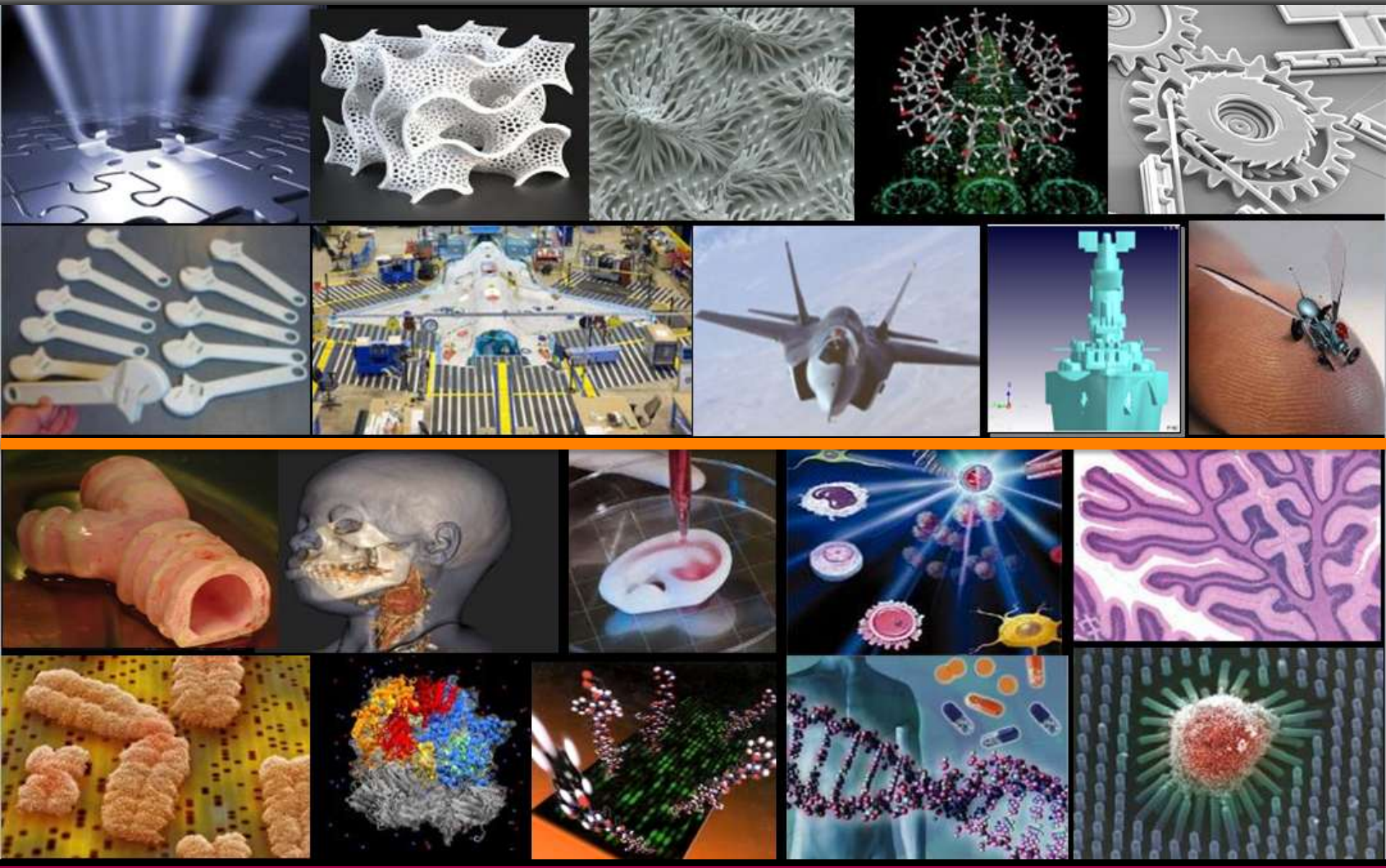
Life as Evolving Software

- DNA as a universal programming language
- origin of life is the origin of software (G. Chaitin)
- all that counts is the information – the rest will take care of itself via programmed self-assembly (S. Brenner)
- immense, combinatorial space (DNA and gene regulatory networks as software)
- generation of biological diversity (inventiveness, plasticity, adaptation, evolvability)
- phylogeny is software archeology

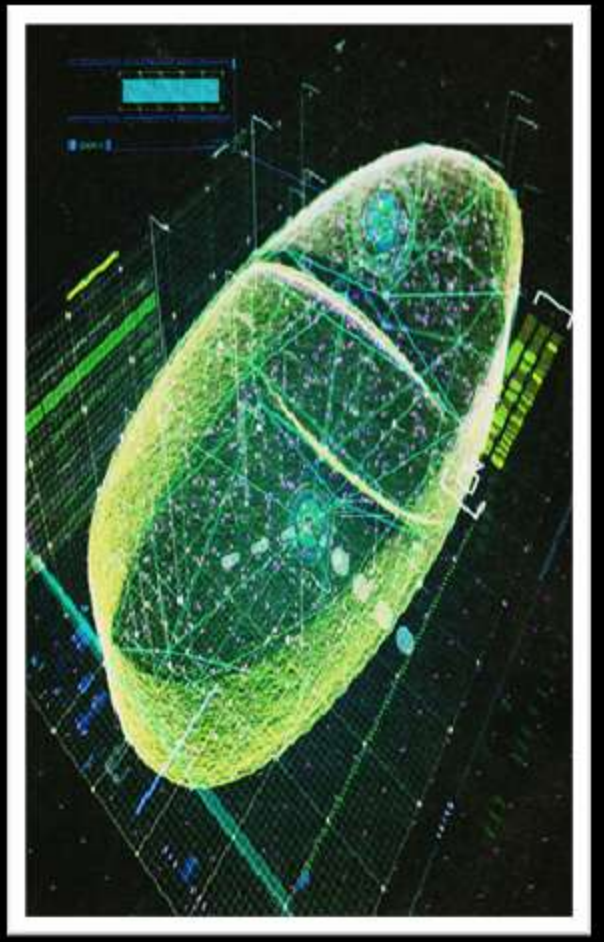
Synthetic Biology

- to program and assemble biological functions and organisms based on knowledge of the ‘rule sets’ underlying hierarchical biological organization
  - reprogramming existing biological signaling pathways and networks
- exploring “biospace”
  - design, simulation and construction of novel functions/organisms
  - novel biotic (living): abiotic (inert materials) combinations

Advanced Manufacturing
Digital Programming of 3-D Fabrication and New Assembly Technologies



Emerging Technologies for Precision Modification of Genomes and Their Coding Instructions (Biological Software)



Cost-Effective Synthetic Production of DNA

Genome Editing

Construction of ‘Cellular Chassis’ For Designed Genes

“Mapping Possibility Space”

"Mapping Possibility Space"
The Power of Combinatorial Molecular Interactions and Self-Assembly of Complex Molecular Networks

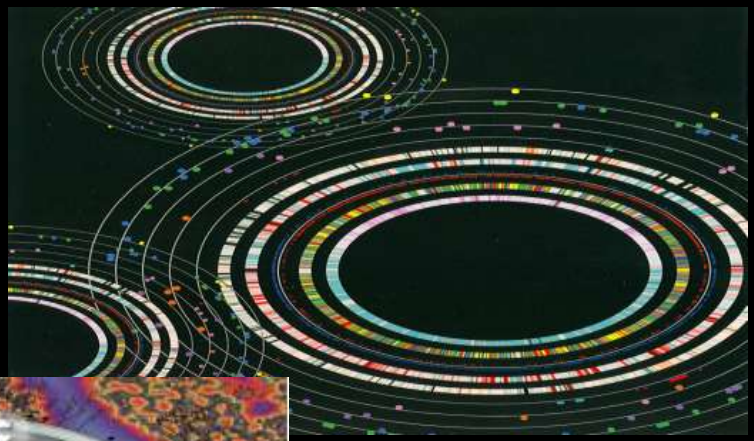
- number of theoretical possibilities for synthetic assembly far exceeds the narrow space sampled in evolutionary time (existing and extinct species)
  - DNA and RNA nucleotide sequence permutations
  - amino acid sequence permutations
  - gene regulatory networks (gene-gene interactions, RNA-mediated gene regulation)
  - protein-protein interaction networks

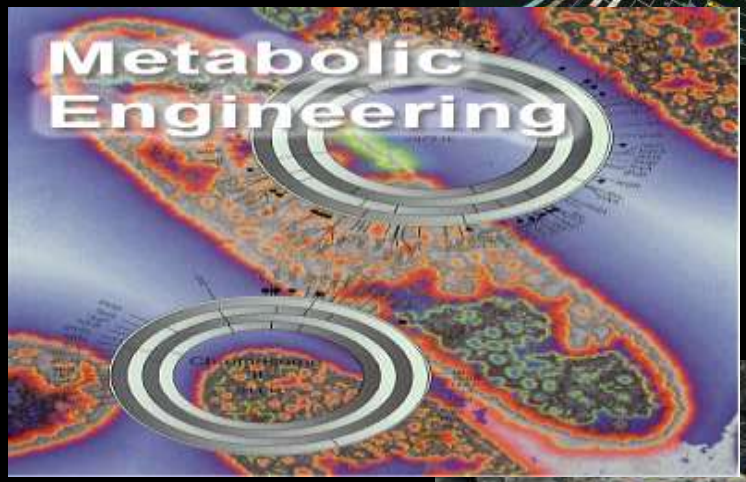
Exploring Biospace
The Power of Combinatorial Interactions and Molecular Assembly

- 22,000 genes
- two genes cooperate to create a function =(22,000 x 21,999)/2 = 241,989,000 potential combinations
- 100 genes generate a complex function $=10^{65794}$ potential combinations
- number of theoretical possibilities for synthetic assembly (biospace) far exceed narrow molecular space sampled in evolutionary time to date

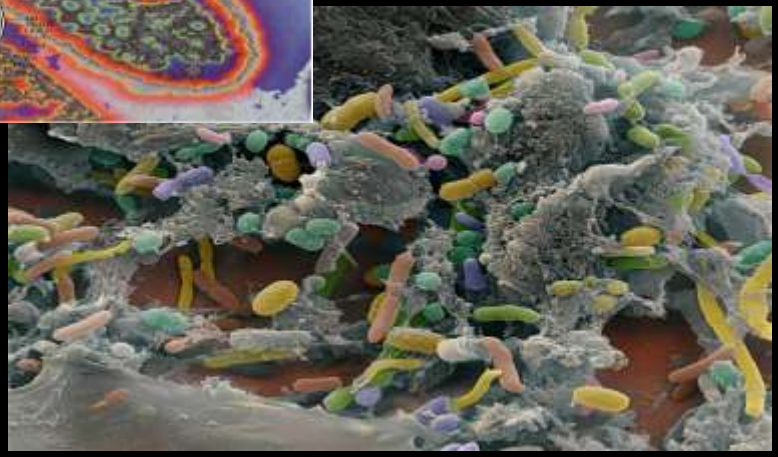
Synthetic Biology:
Engineering Novel Organisms with Novel Functions

Programmable Microbial Genomes





A New Industrial Ecology and Novel Biosyntheses



reversal of abnormal microbiome (dysbiosis) in human

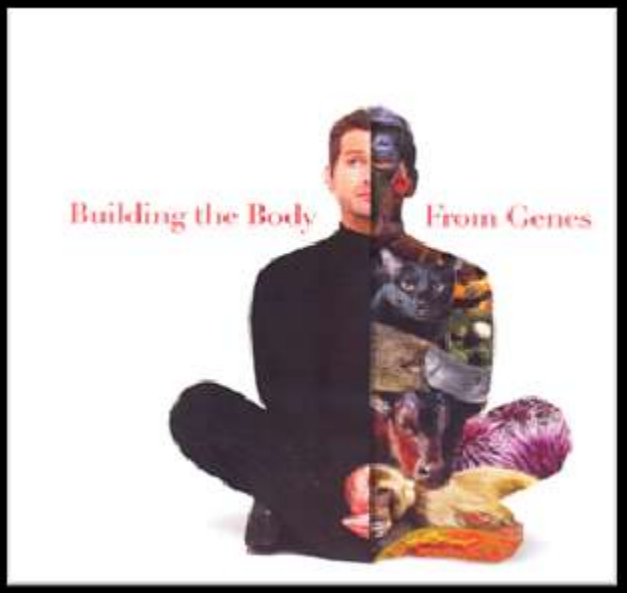
Synthetic Biology and Engineering Enhanced Traits in Food, Feed and Fiber Products

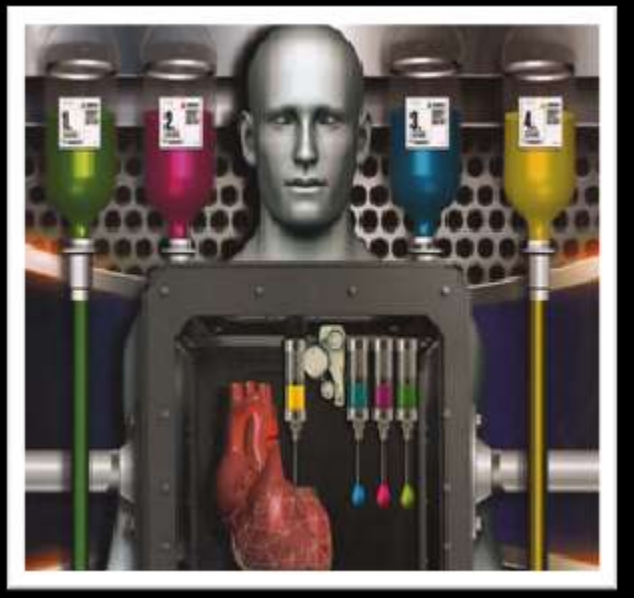




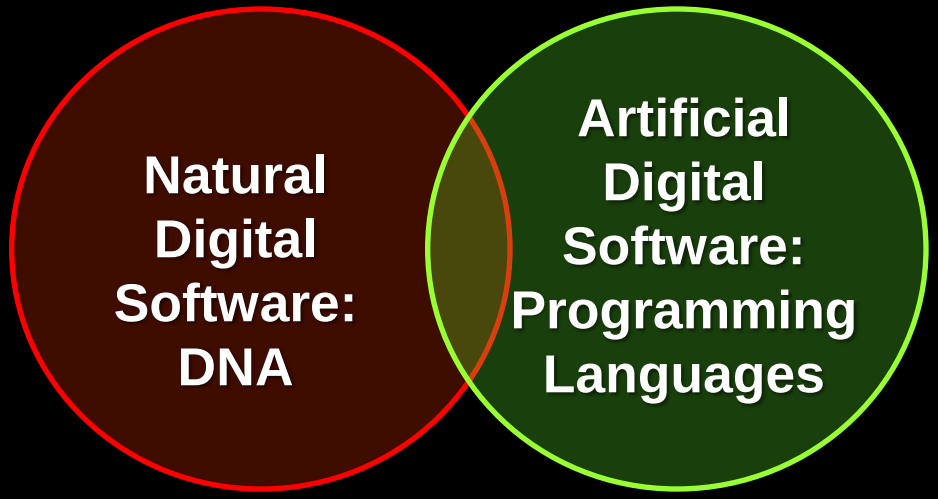



Regenerative Medicine:
The Union of Synthetic Biology and Tissue Engineering





Convergence



$3 – 4 \times 10^9$ years old	60 - 70 years old

Digital Biology and Synthetic Biology

- the reduction of biological complexity to modularity to rebuild complexity
- using silicon to make DNA that makes something with no evolutionary counterpart
- silicon encodes digital DNA for e.transfer to any location

“The Matternet”

- internet for objects
- digital coding of fabrication specifications to distributed, point-of-need (PON) synthesis units
  - digital “omics” and synthetic biology
  - broader concept of digital 3D printing/manufacturing of diverse materials

The Digital-Biological Converter

“We can now send biology at the speed of light”

J. Craig Venter

**“Oh, God help us!
We’re in the hands of
engineers.”**

**Dr. Ian Malcolm
‘Chaotician’: Jurassic Park**

Digital Biology

Biodiversity and Natural Evolution

Synthetic Biology, Directed (accelerated) Evolution and Novel Biodiversity

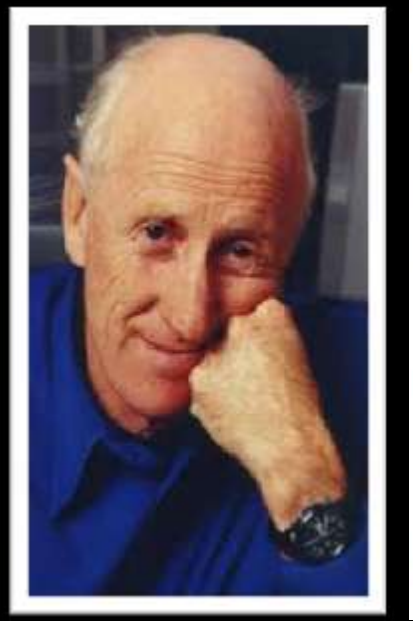
Synthetic Biology and New Metrics for Biodiversity

- diversity = net rate of addition of novel genomes versus net rate of genome extinctions
- rethinking biodiversity
  - the sum total of novel genome sequences (natural or synthetic) or simply the number of distinct species?

Advances in Genome Biology and Flights of Imagination

Theoretical Scenarios versus Current Technological Capabilities

De-extinction: the Revive and Restore Project



Science (2013) 340, 32

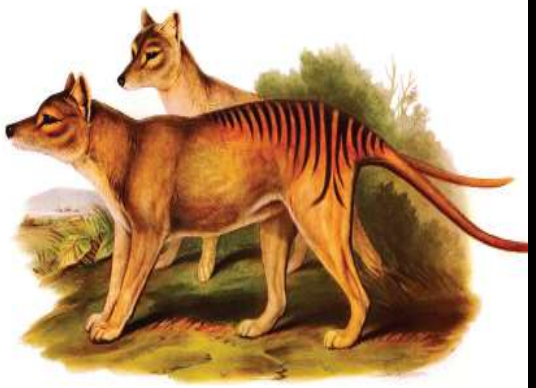
What If Extinction Is Not Forever?

Although new technologies may make it possible to bring extinct species back to life, there are ethical, legal, and social ramifications to be addressed

Jacob S. Sherkow[1] and Henry T. Greely[2]

A 1930s film shows a dog running and jumping inside a fenced enclosure (*1*)—except that the dog has a strange-shaped head, odd stripes, and a rigid tail that can only move side-to-side. The "dog" is actually one of the last thylacines, a marsupial predator also called the Tasmanian tiger. The film was taken shortly before humans extinguished the species forever. Or did we? Recently, new technologies have made it plausible to try to revive many recently extinct species. Scientists around the world are discussing, and working toward, "de-extinction" (*2*).

Currently, three approaches to de-extinction seem most likely to succeed: back-breeding, cloning, and genetic engineering. If the extinct species left closely related descendants, it might be possible to use selective breeding to produce progeny with the phenotypes of the extinct species, as the auroch project in Europe has been doing



Tasmanian tiger. By the 1930s, settlers, encouraged by government bounties, had hunted the thylacine to extinction in the wild. Well-preserved specimens could pave a way to bringing it back.

Not Immediately Available!

Site: geekologie.com

Source: Wired 10-10

The Expansion of Conceptual Horizons in Biology

Living Systems

- mapping molecular information networks and the origin of biological complexity and biodiversity

Life in Simulation

- computational biology and exploration of new architectures for biological signaling (information) networks

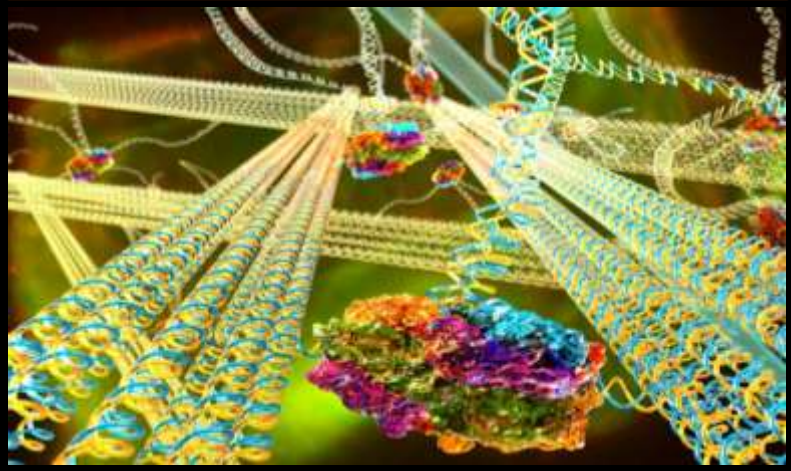
Synthetic Systems

- production of novel structures and functions with no known evolutionary precedent or precursor

Technology Convergence and Synthetic Biology: Biology and Medicine Meet Engineering and Computing

Automation/Miniaturization and Robotic Production Suites and Advanced Machine Learning Tools

Modeling and Simulation of Biological Networks

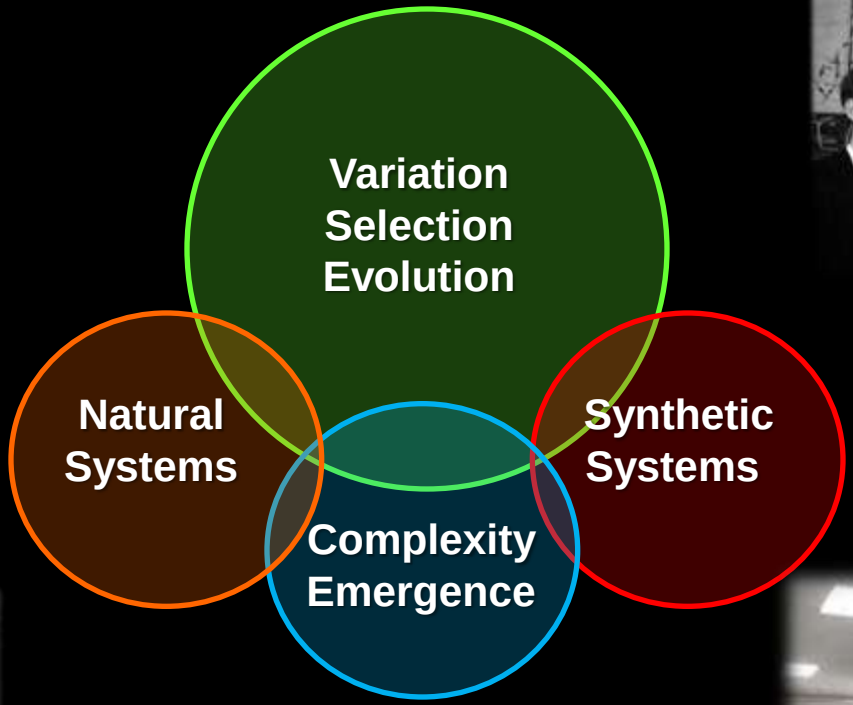


Exabyte and Zettabyte Computing Scale

Advanced Computing, New Analytical Tools and Machine Intelligence

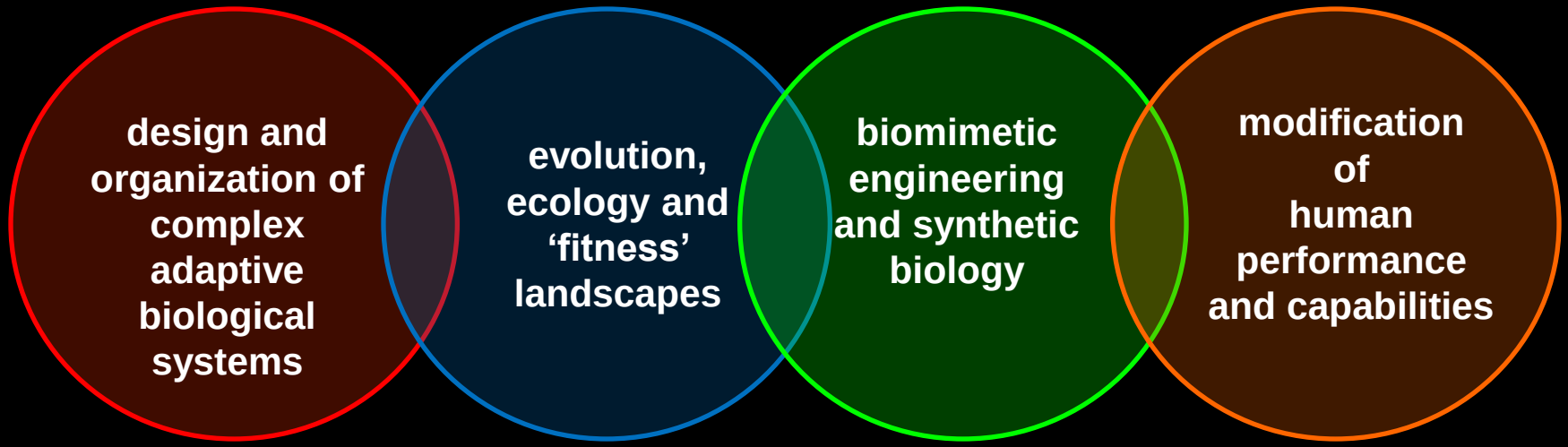
The Evolution of Biological Complexity: A Contemporary Synthesis

Evolutionary Theory

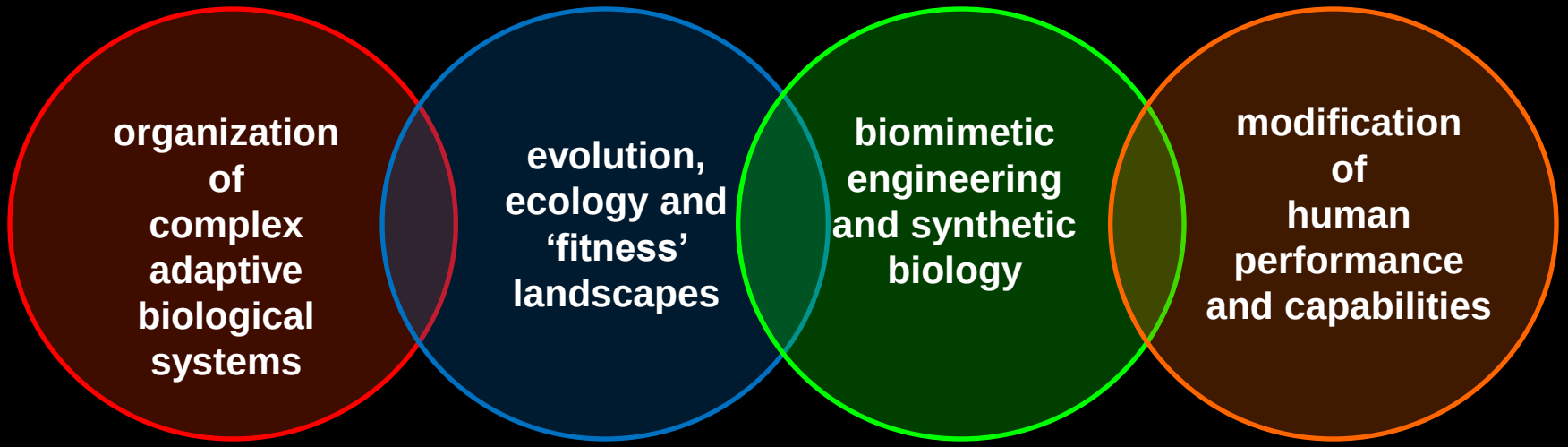


Information Theory

Mapping the Coding Information for Organizational Complexity, Diversity and Variation in Biological Systems



Mapping the Coding Information for Organizational Complexity, Diversity and Variation in Biological Systems



- form and function
- instructional codes and information content

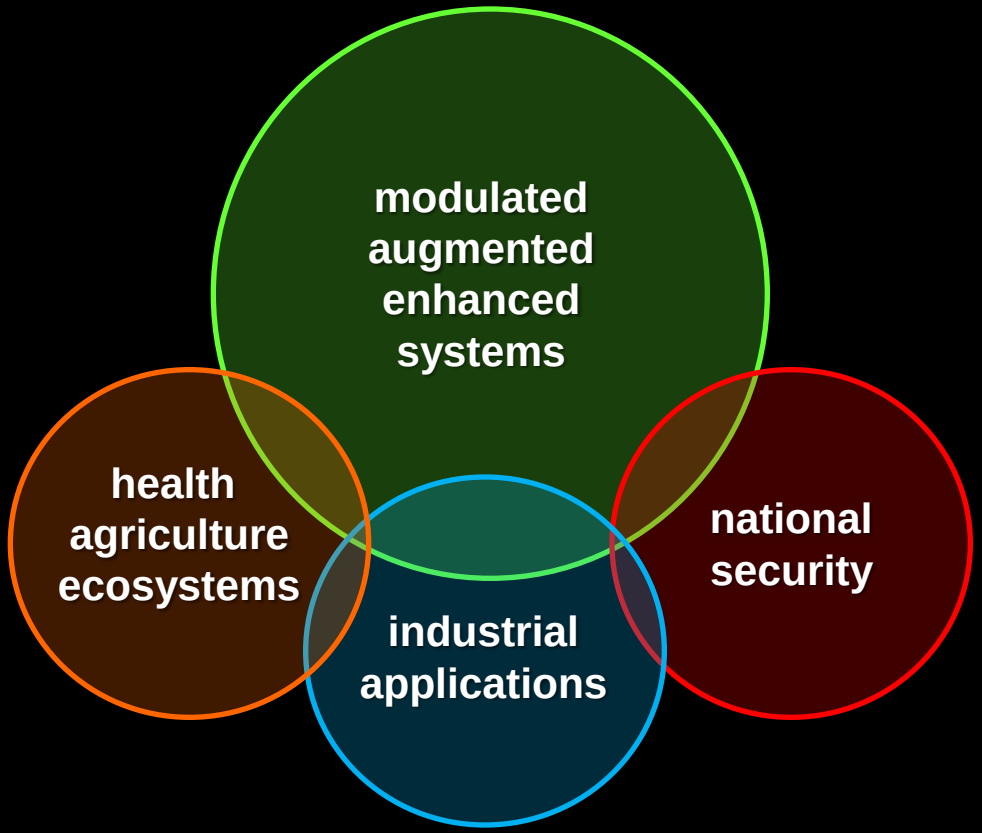
- mapping existing biospace

- exploring novel biospace (possibility space)
- oversight and regulation

- modulation or augmentation (non-heritable)
- enhancement (heritable)

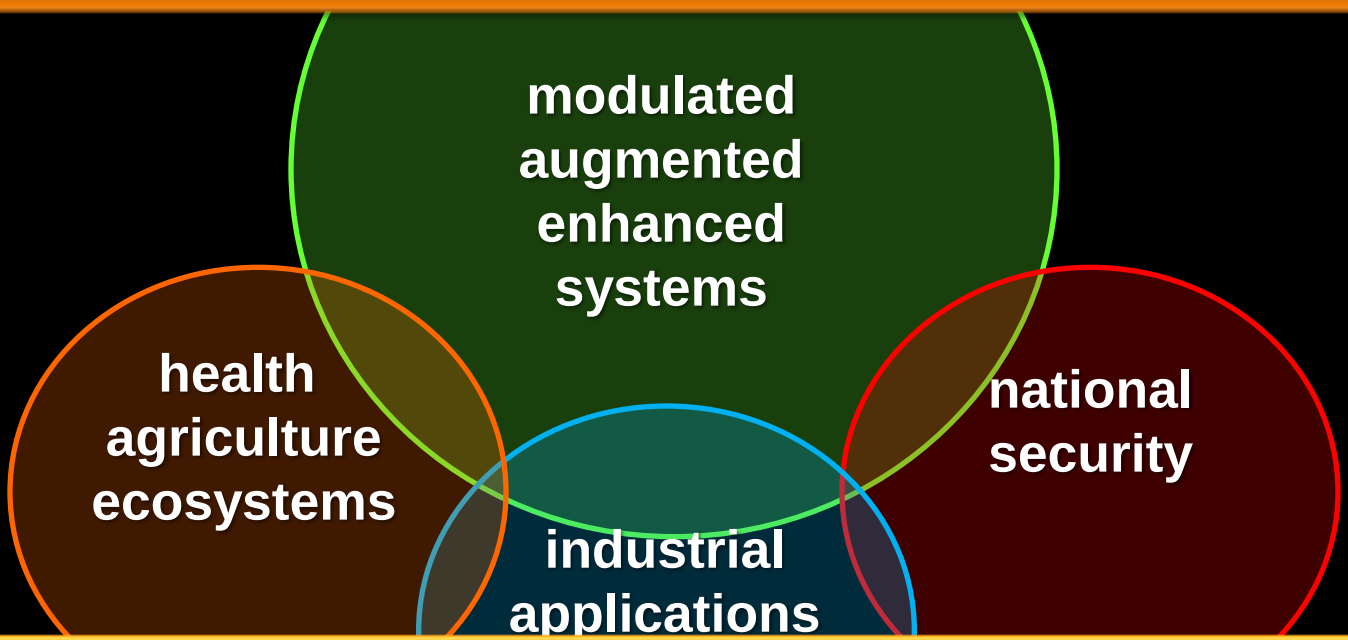
Synthetic Biology and Expanded, Novel Biodiversity

Complex Ethical, Legal and Social Implications and New 'Dual-Use' Dilemmas



Synthetic Biology and Expanded, Novel Biodiversity: Complex Ethical, Legal and Social Implications and New 'Dual-Use' Dilemmas

Impact on Human Identity and Societal Structure



Oversight: Regulation and Legislation