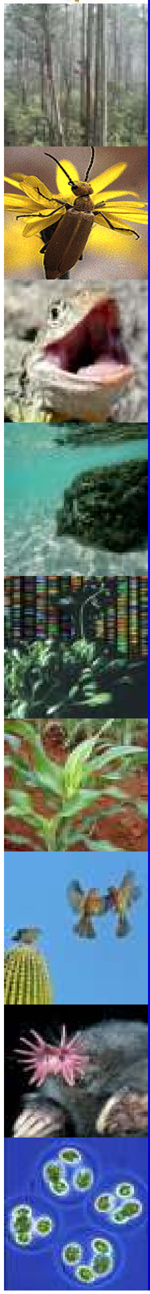
Biological Sciences in the 21st Century

Science and Engineering without Borders

James P. Collins
School of Life Sciences
Arizona State University

NSF EPSCoR 21st National Conference
Washington, DC



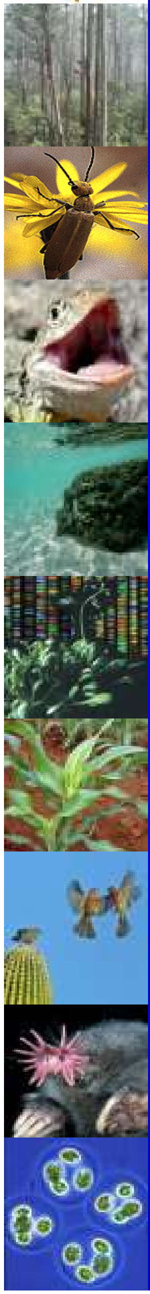
Outline

- **Life in Transition:**
  Questions without borders

- **Life Sciences in Transition:**
  When disciplines merge

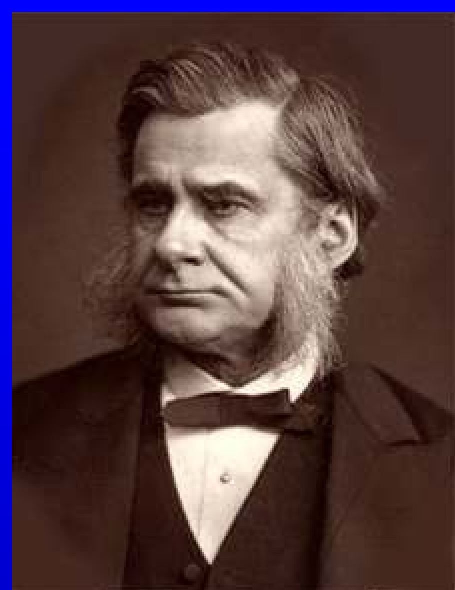
- **Managing the Sciences in Transition:**
  Innovating in the midst of excellence

The Arc of Biology: *19th & 20th Centuries*

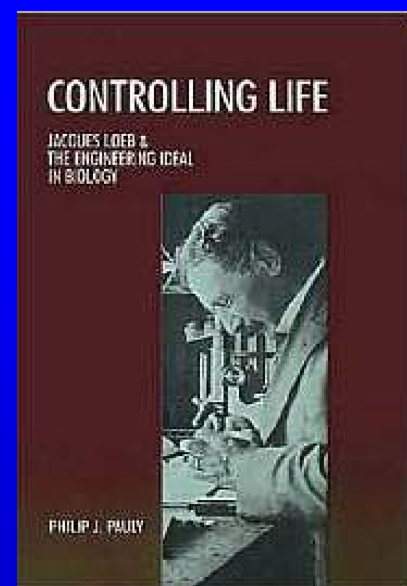


- In the early 20th century biology emerged from natural history and physiology around the question: What is life?
- Biologist Jacques Loeb (1859-1924) helped to shape modern biological research through his emphasis on reductionism, experiments, and the engineering ideal.

Charles Darwin



T.H. Huxley



Jacques Loeb

The Arc of Biology: *Understanding and Controlling Life*

Addition of purple gene copies

- **RNA Interference (RNAi) - An ancient evolutionary mechanism for silencing gene expression**
- **An innate and adaptive response that protects a cell from foreign genes by targeting invading gene messenger RNAs**

Rich Jorgensen, University of Arizona

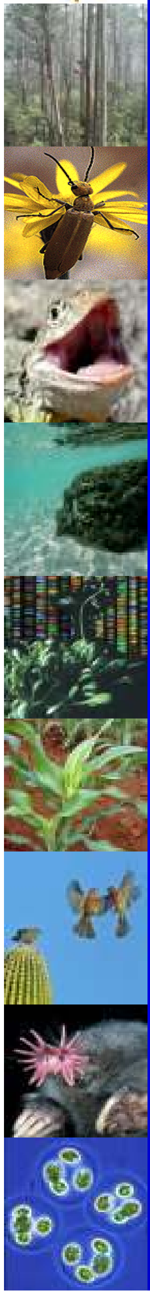
The Arc of Biology: *To Improve the Quality of Human Life*

Practical application of RNAi in agricultural and medical biotechnology

Resistance to papaya virus

Therapeutic RNAi macular degeneration

2006 Nobel Prize in Physiology and Medicine to Fire and Mello



The Arc of Biology: *What is Life?*

Theoretical Constructs in Biology

- All living things are made from cells, the chemical factories of life: *CELL BIOLOGY*
- All life is based on the same genetic code organized as DNA or RNA: *GENETICS*
- All forms of life evolved by natural selection or genetic drift: *EVOLUTION*
- All life is connected to form ecosystems: *ECOLOGY*

Life in Transition

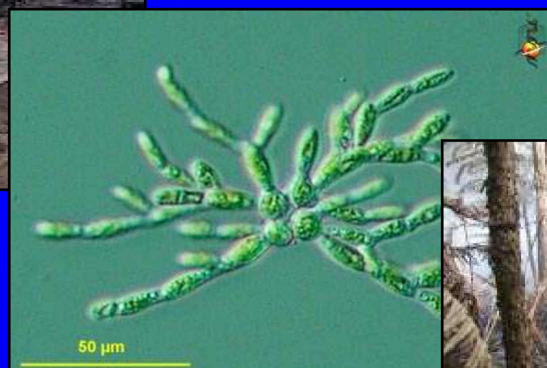
Life put Earth under New Management

Origins
Energy
Adaptation

Pu'u 'Ō'ō Crater, Hawaii

Anoxic World

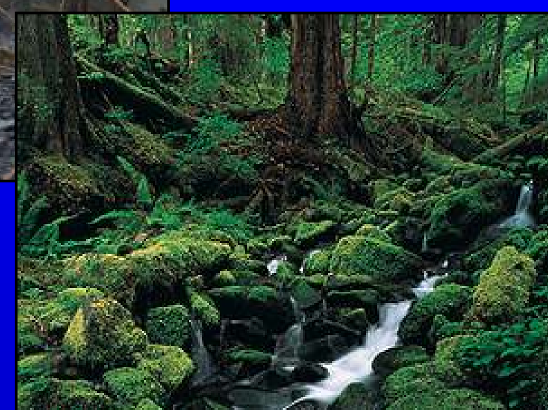
Cyanobacteria



Photosynthesis

Whisk fern on lava

Life on Land



O_2 Rich World

Origins

When, Where, and How did Life on Earth begin?

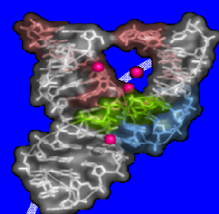
Open system chemistry

Basic elements

$H_2 + CO_2$ => $[\ HCO\ ]_n$

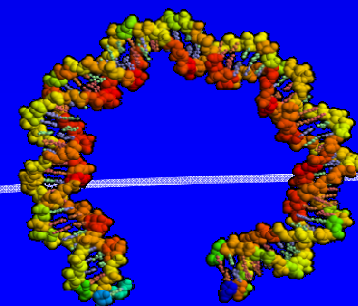
Self-sustaining biochemistry

Self-replication



RNA world

DNA world



How did the biological complexity of life emerge from pre-biotic chemistry and geochemistry?

- **Self-contained – The Cell**
- **Self-sustaining - Energy**
- **Self-replicating – RNA, DNA**
- **Evolving - Biodiversity**

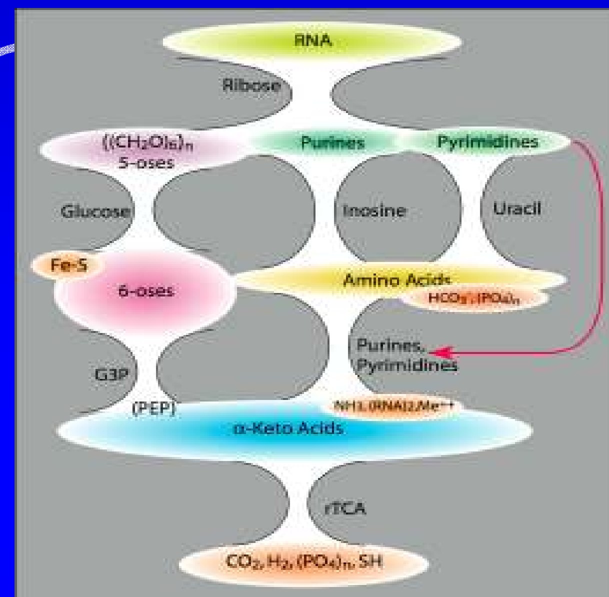
Systems & Synthetic Biology

What are the Indispensable Requirements for Life?

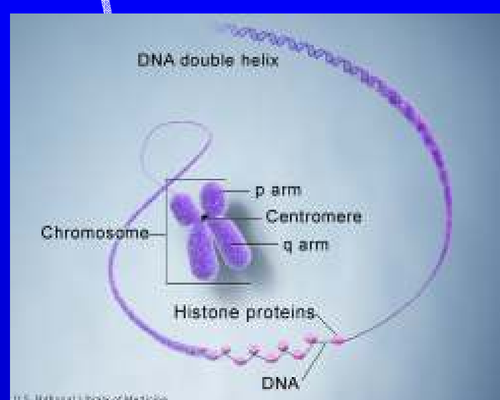
Membrane Encapsulation

Are There Alternative Routes to Life?

New Chemical Theories



Eric Smith, SFI



Genome Stability

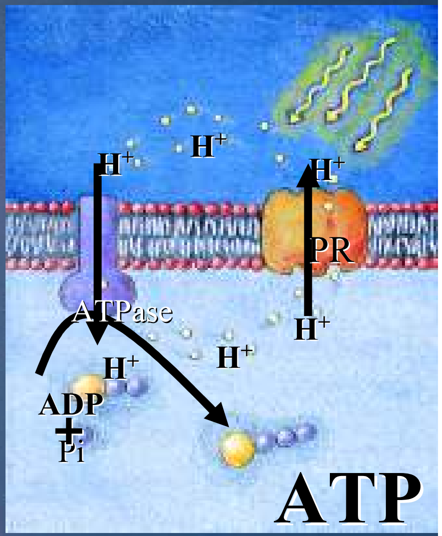
What are:

- **The physical rules for cell membrane assembly?**
- **The minimum gene set required to sustain life?**
- **The fundamental requirements for genome stability?**
- **Chemical constraints?**

Energy

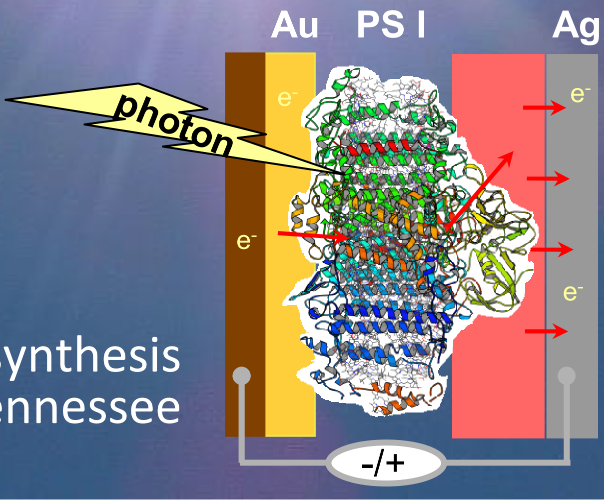
How can natural energy transduction systems inspire biology-based technologies capable of delivering clean, sustainable, and renewable energy?

Light-Driven Energy Transduction
Rhodobacter sphaeroides

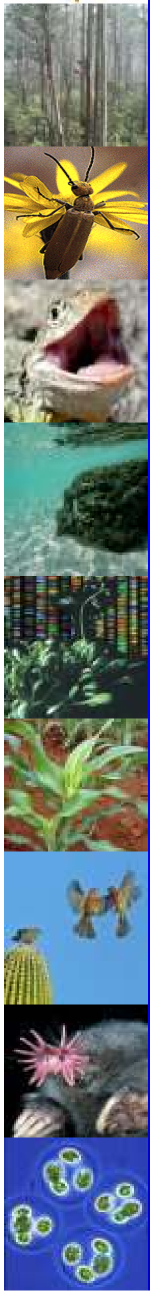


Proteorhodopsins
Edward Delong, MIT

Chloroplasts



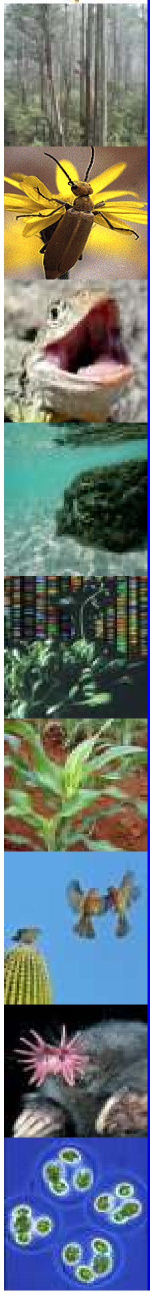
Applied Photosynthesis
Barry Bruce, U. Tennessee



New Energy Systems

- From the application of systems and synthetic biology to:
  - Microbial fuel cells
  - Microbial / algal production of hydrocarbons
- From potential chemical sources of energy in the living world:
  - Arsenate, Iron, Manganese, Nitrate, Selenate, Sulfate, Uranyl oxide

Anna-Louise Reysenbach, Portand State U
Everett Schock, Washington U - St. Louis

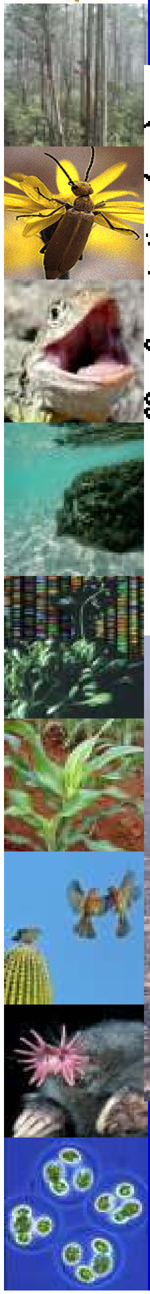


Adaptation

Life in a Time of Planetary Change

Earth's climate and life support systems are changing in novel and unexpected ways.

Life in a Time of Planetary Change



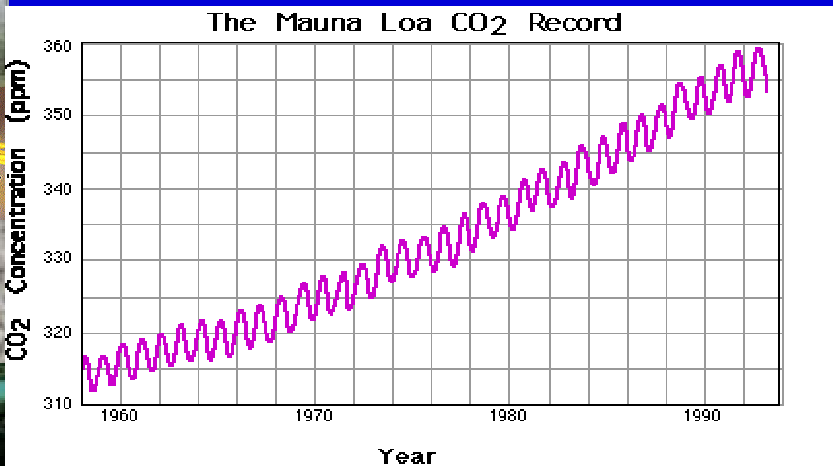


Figure 7.01 The record of CO_2 measured at Mauna Loa, Hawaii shows seasonal cycles — related to the activity of plants in the Northern Hemisphere — on top of an increasing trend to higher values. The record also shows a subtle increase in the seasonal amplitude over time.

We are only now beginning to explore the <u>biological drivers</u> of climate change.

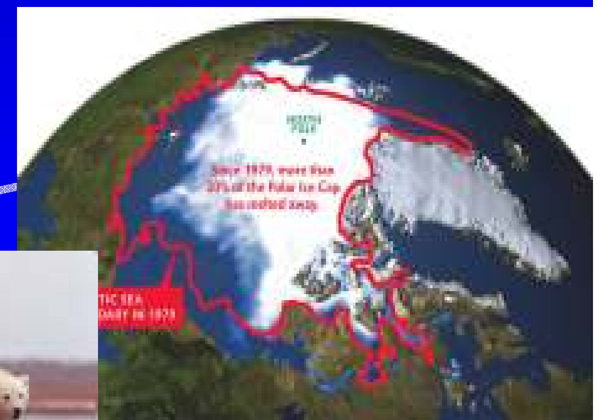
Adaptation

Life in a Time of Planetary Change

Extinction

Transformations

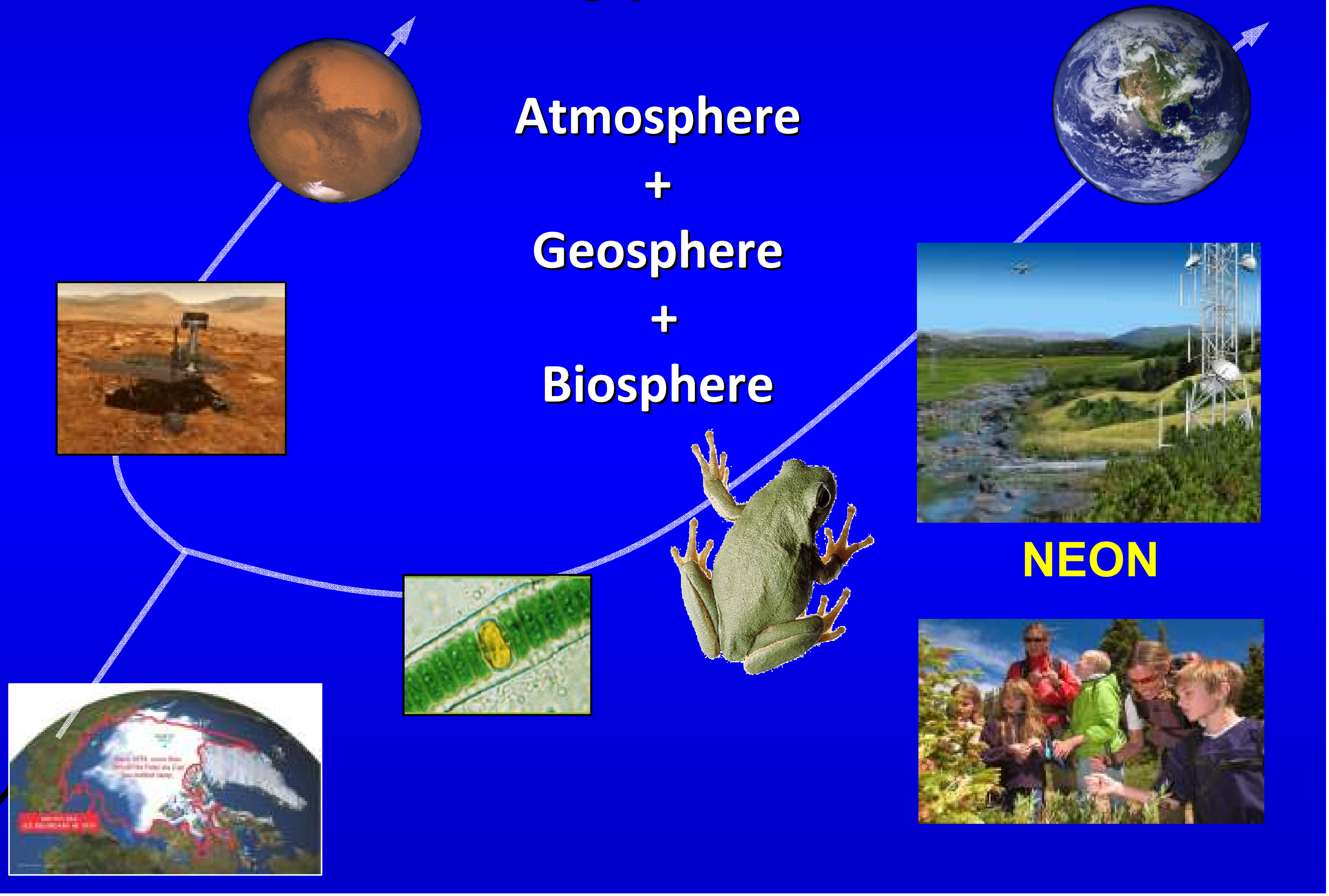
Adaptation and survival



- **Adaptation as a concept - what can we learn?**
- **How do life forms adapt to planetary change?**
- **How does the living world change the planet?**

Making New Connections

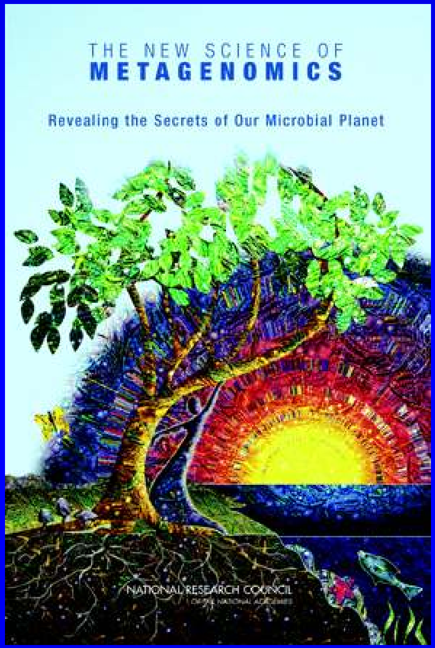
in an Increasingly Connected World



Making Connections

Connecting Genomes to Ecosystems

Community DNA

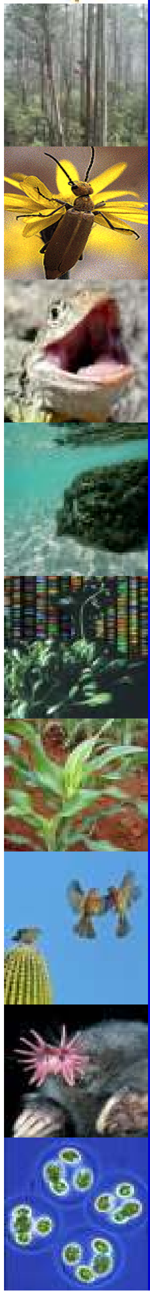


Ecophysiology

Ecosystem Metabolism

EVOLVING GENOMES → **EVOLVING POPULATIONS** → **CHANGING ECOSYSTEMS**

***Adaptation Science:* How will living systems respond to rapidly changing environments?**



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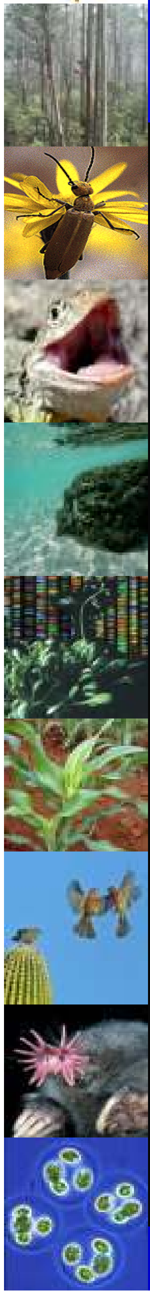
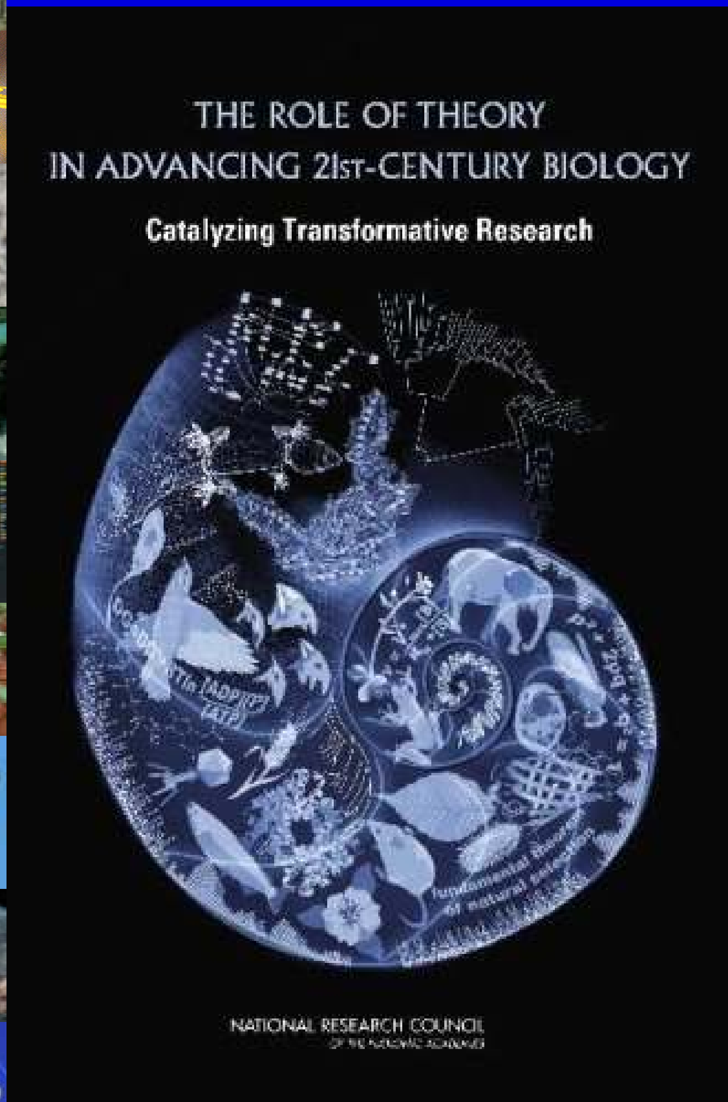
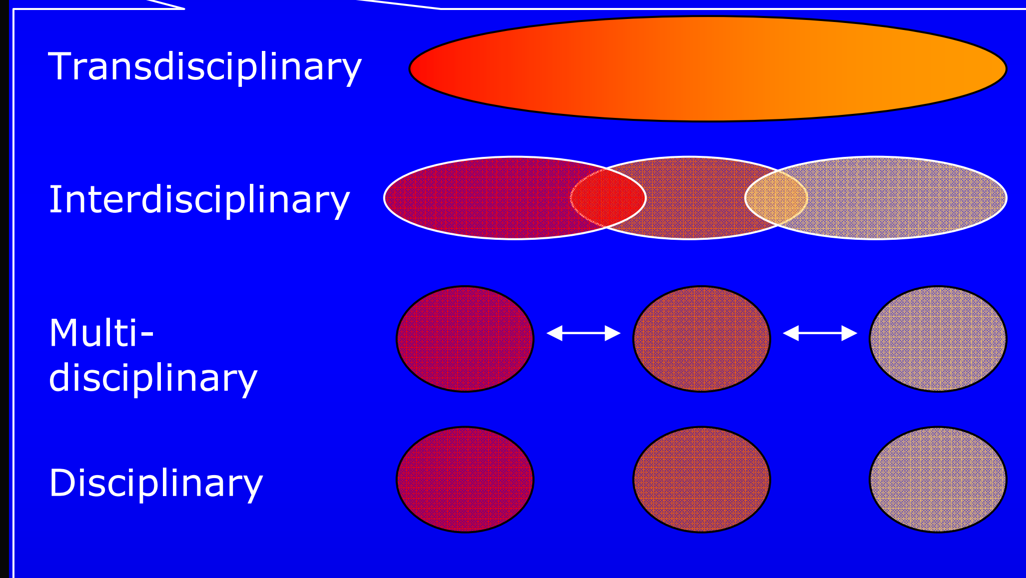
Life Sciences in Transition

Challenges for 21st Century Biology







Is this the science that we are teaching right now?

Shifting Science Priorities

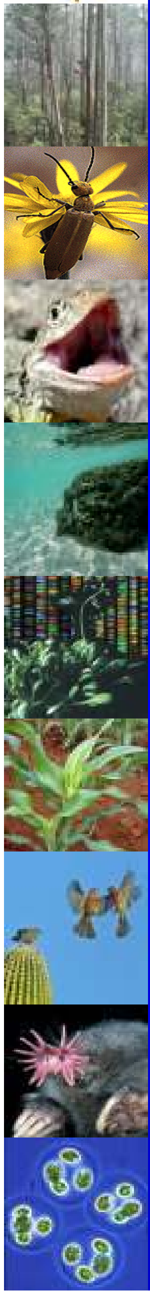
Energy & Environment

Barack H. Obama

John P. Holden

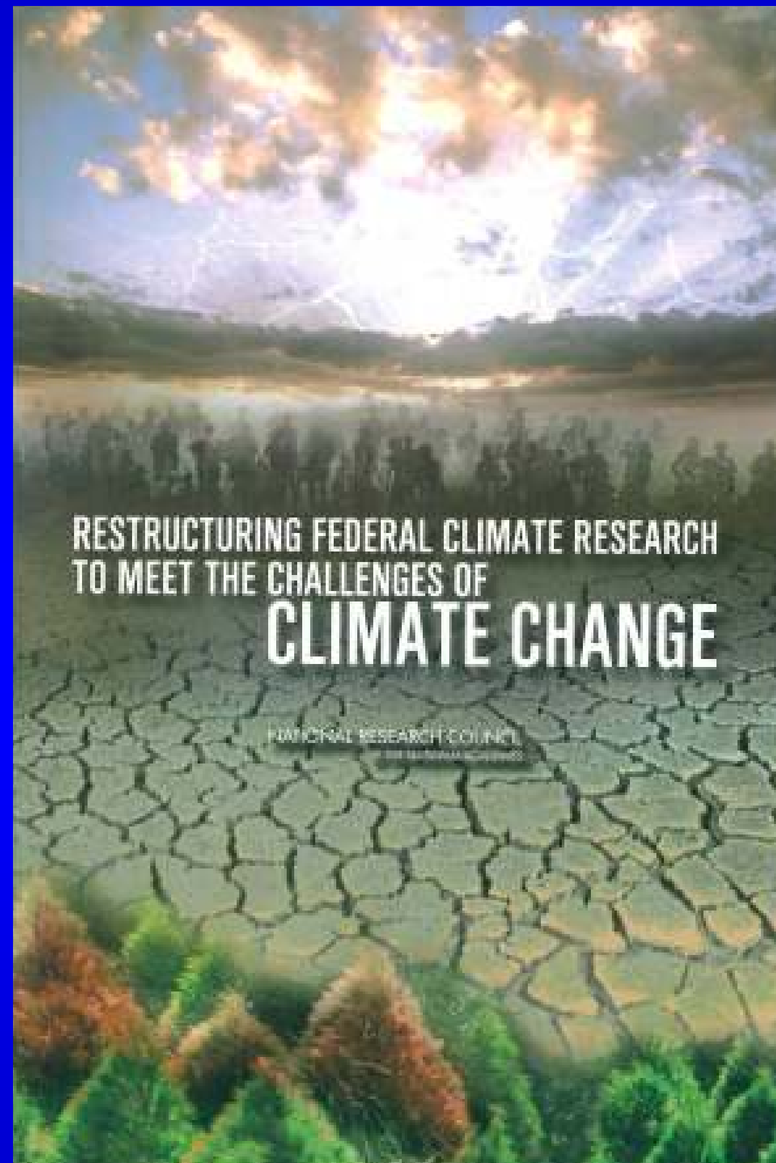
"Of all the challenges we face as a nation and as a planet, none is as pressing as the three-pronged challenge of climate change, sustainable development and the need to foster new and cleaner sources of energy."

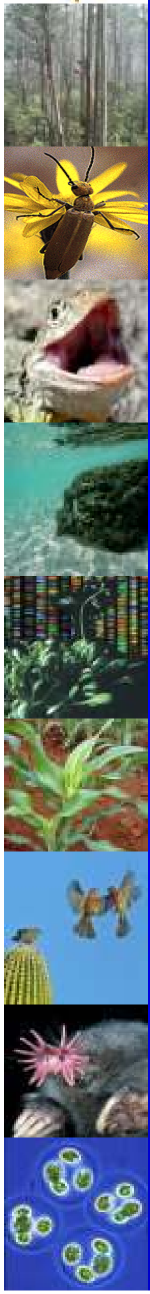
Office of Science Technology and Policy

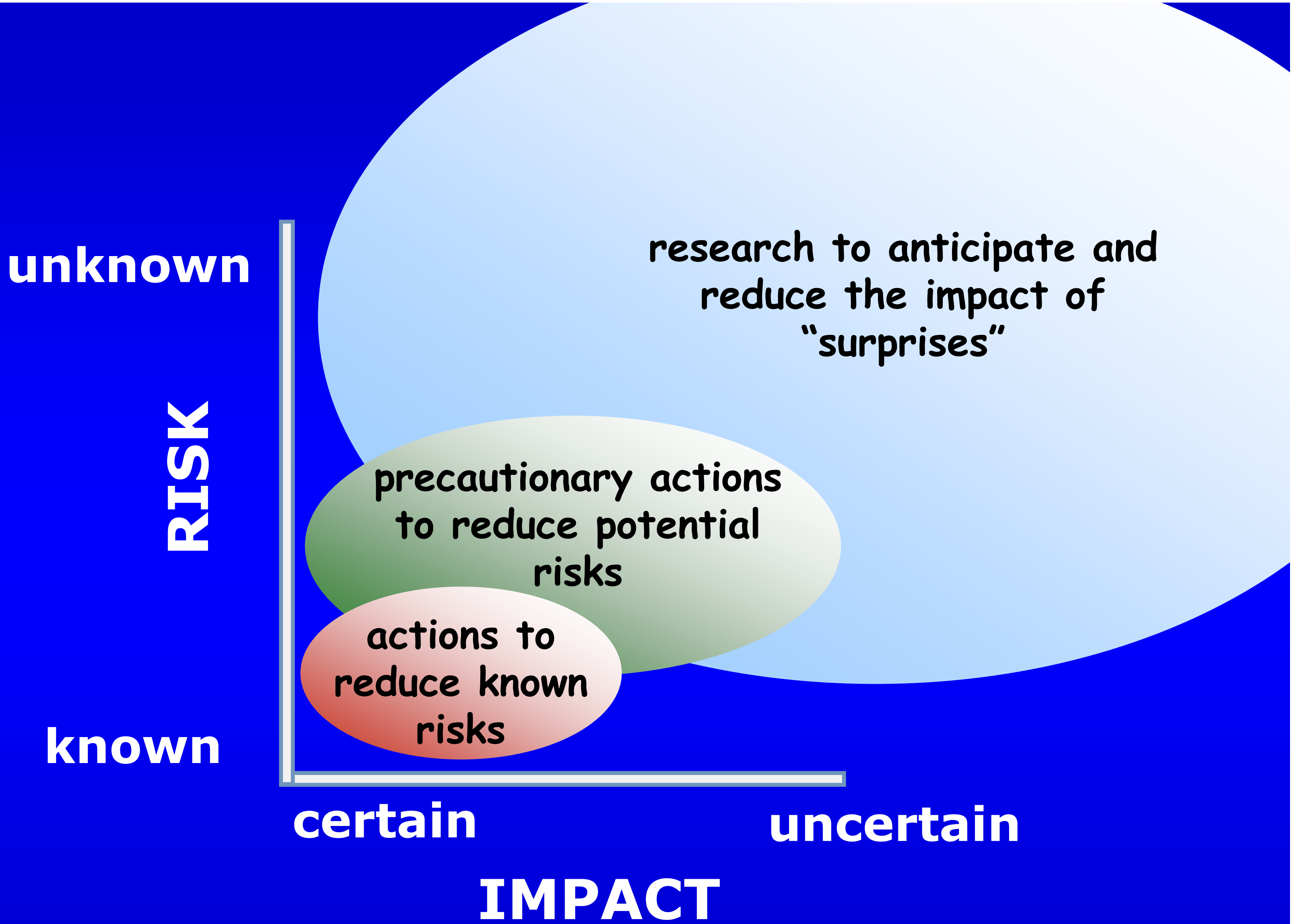


National Research Council of the National Academies of Sciences

Released 2009

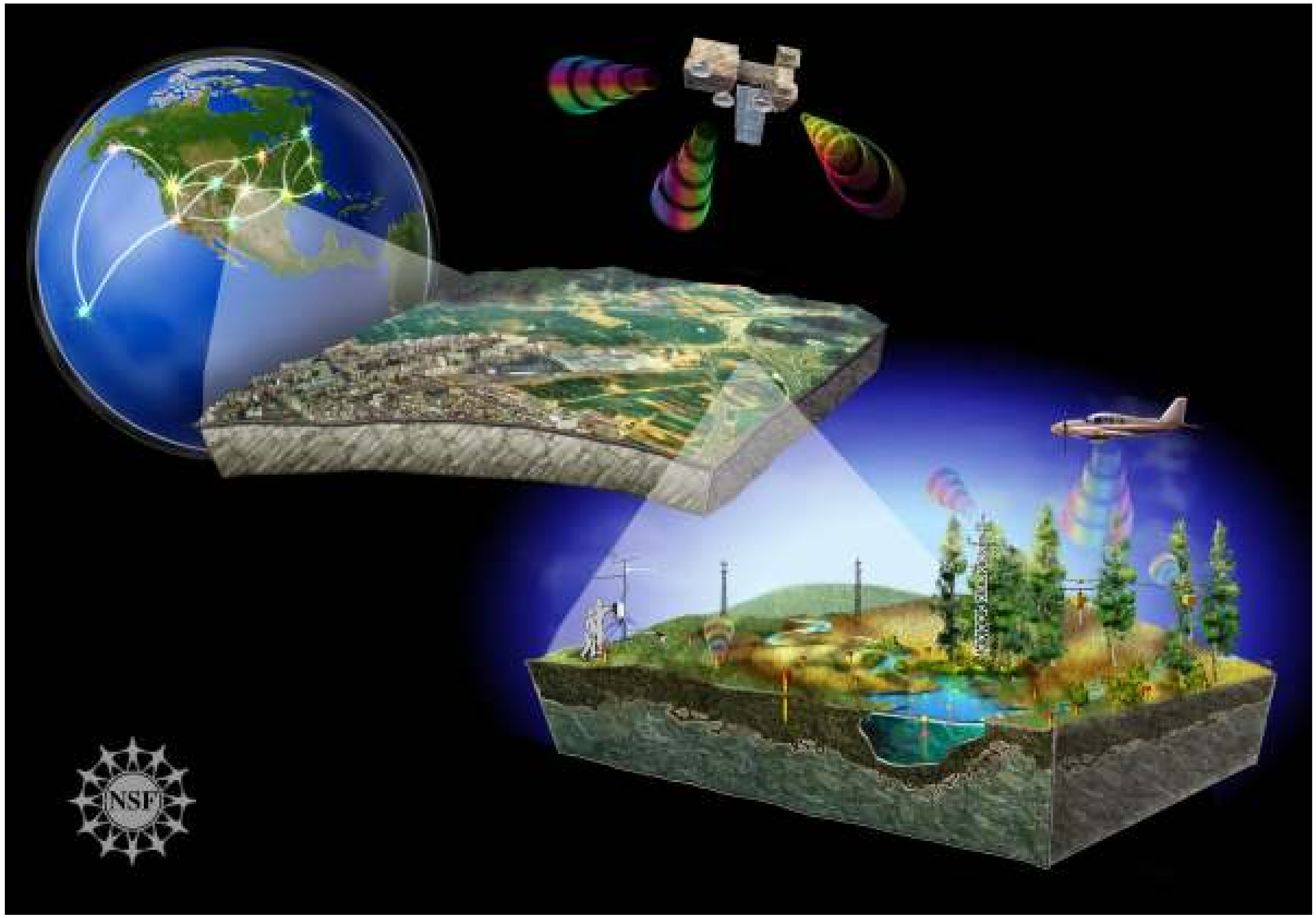






Based on: *Late Lessons from Early Warnings*, European Environment Agency (2001)

New Tools and Approaches



National Ecological Observatory Network (NEON)

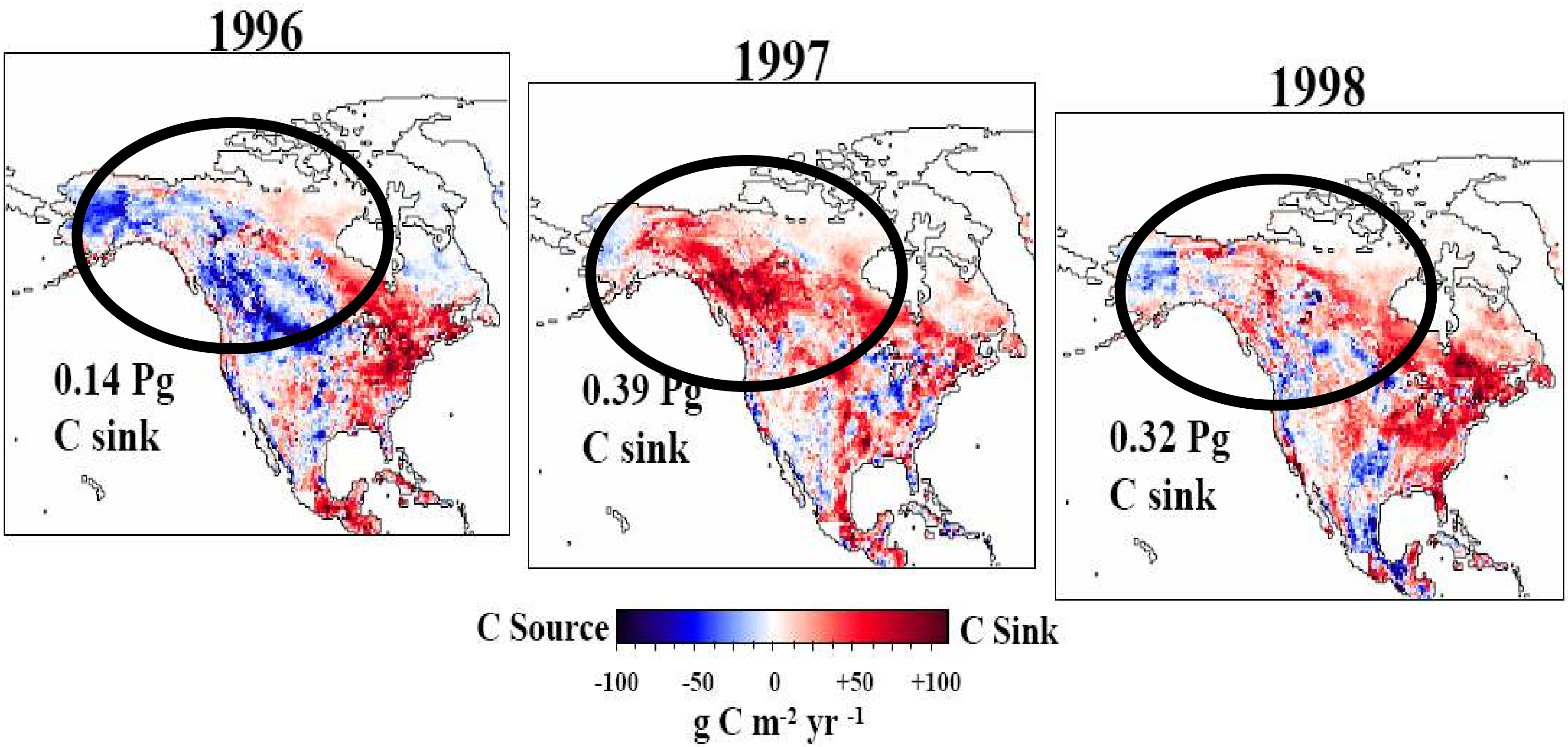
Science for a Sustainable Planet

NEON enabled science provides the fundamental scientific understanding needed for a sustainable planet

Spatial Dimensions: Biological Feedbacks at Continental Scales

Prediction of the North American Carbon Sink

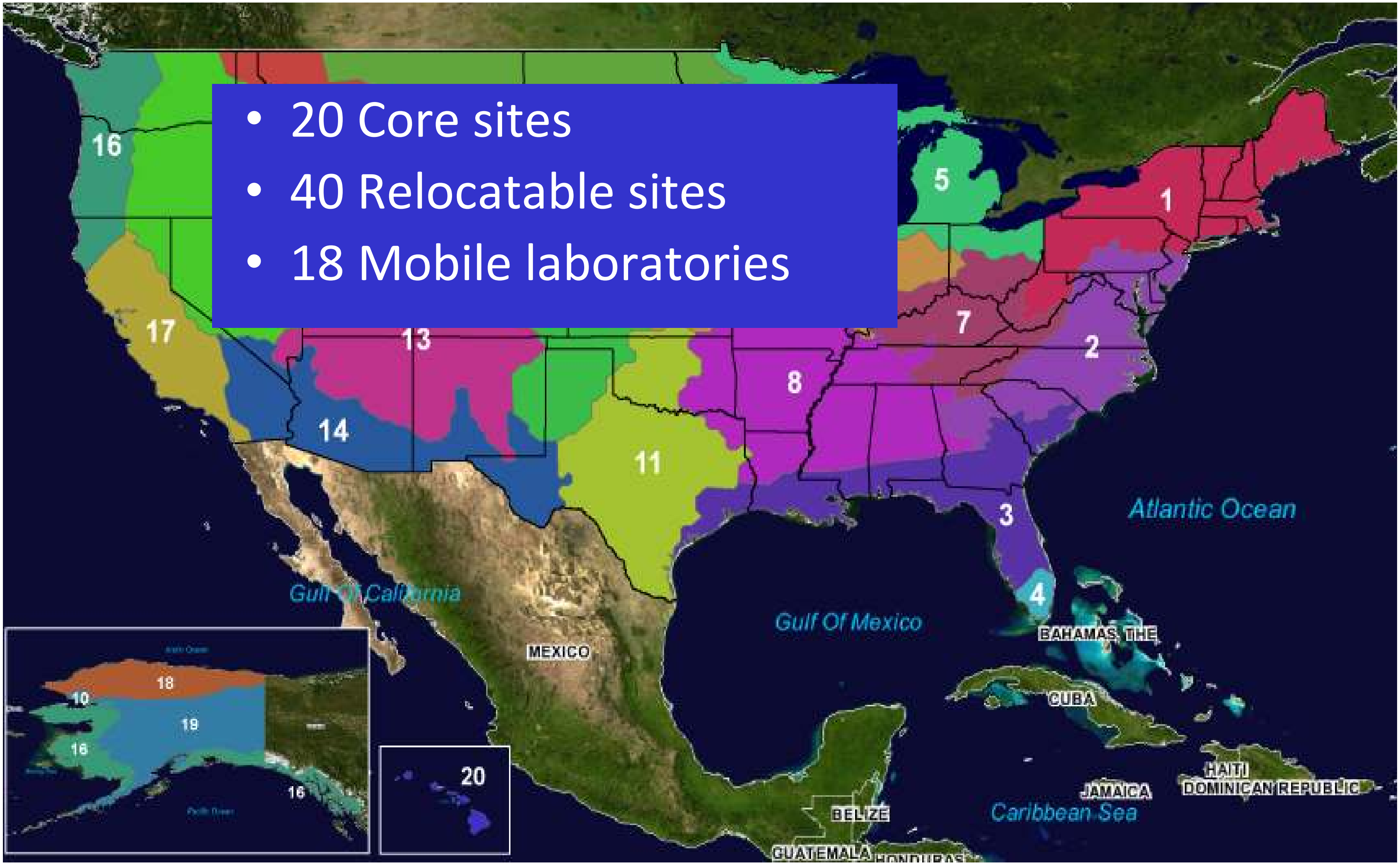
Potter et al. 2003 "The North America Carbon Sink from 1982-1998 Estimated using MODIS Algorithm Products"

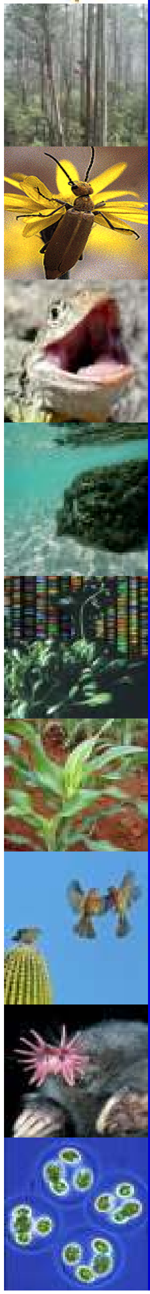


NEON Domains

domains
- 1 North East
- 2 Mid Atlantic
- 3 Southeast
- 4 Atlantic Neo Tropical
- 5 Great Lakes
- 6 Praire Peninsula
- 7 Appalachia
- 8 Ozarks
- 9 Northern Plains
- 10 Central Plains
- 11 Southern Plains
- 12 Northern Rockies
- 13 Southern Rockies
- 14 Desert Southwest
- 15 Great Basin
- 16 Pacific Northwest
- 17 Pacific Southwest
- 18 Trundra
- 19 Taiga
- 20 Pacific Tropical

- 20 Core sites
- 40 Relocatable sites
- 18 Mobile laboratories





NSF EPSCoR Cohorts

1980
Arkansas
Maine
Montana
South Carolina
West Virginia

1985
Alabama
Kentucky
Nevada
North Dakota
Oklahoma
Puerto Rico
Vermont
Wyoming

1987
Idaho
Louisiana
Mississippi
South Dakota

1992
Kansas
Nebraska

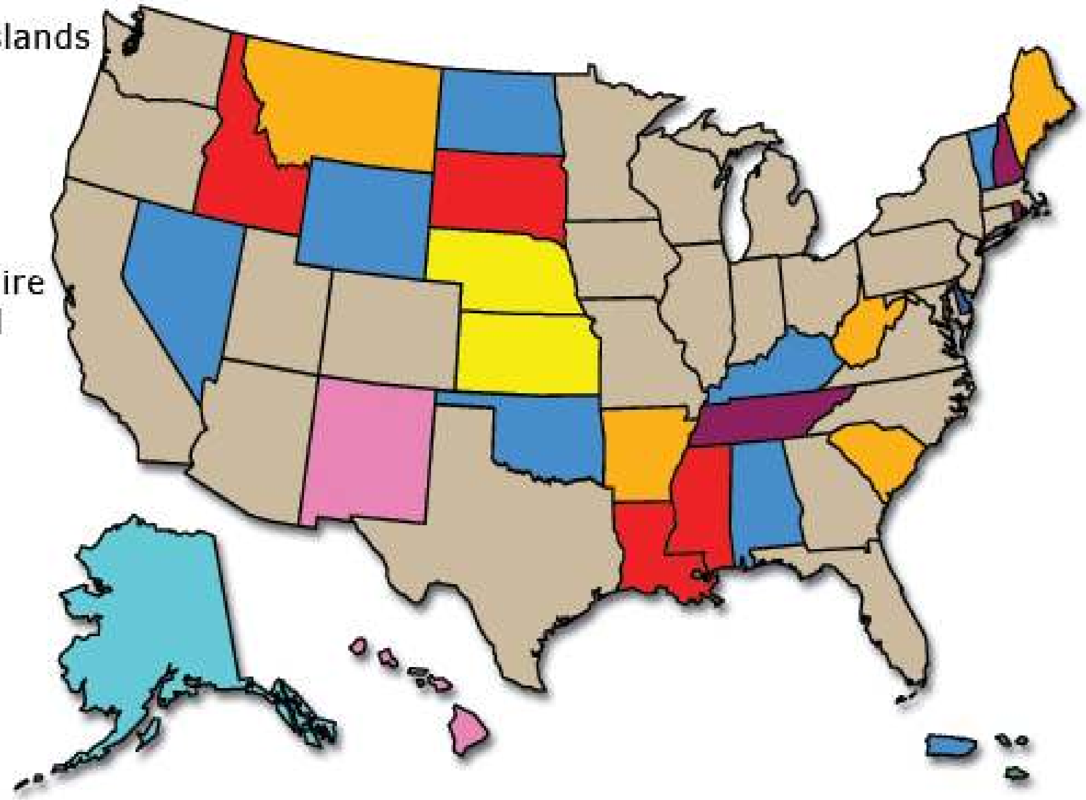
2000
Alaska

2001
Hawaii
New Mexico

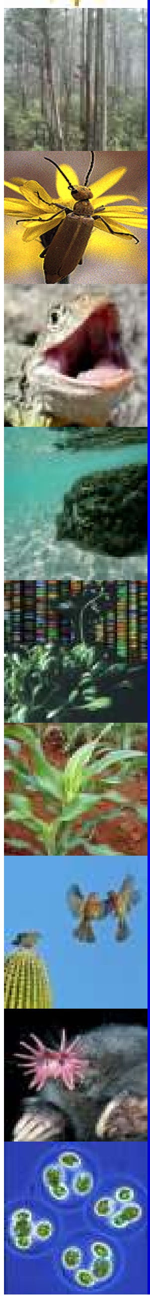
2002
U.S Virgin Islands

2003
Delaware

2004
New Hampshire
Rhode Island
Tennessee



Integrated Research Approach

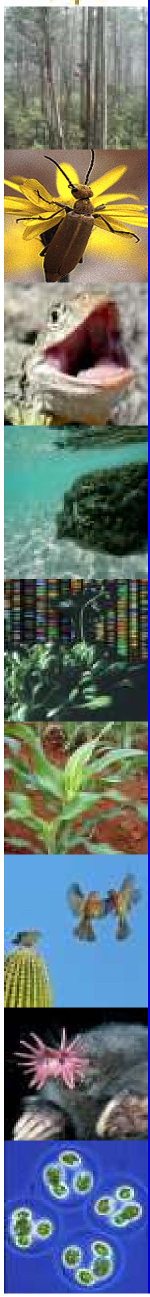


MODELING
of basic natural & human processes & their interactions

EXPERIMENTS
at large scales

ENVIRONMENTAL OBSERVATION
including changes from human activities, adaptation, and mitigation

NEON Data & Data Products



Data Generated	TB/Yr
Sensors (~18,000)	
Raw	75
Processed	12
Sentinel	1
Remote Sensing	124
Total	212

nature

www.nature.com/nature Vol 460 | Issue no. 7255 | 30 July 2009

Information overload

A report released last week by the US National Academies makes recommendations for tackling the issues surrounding the era of petabyte science.

Geneticists spent more than a decade getting their first complete reading of the 3 billion base pairs of the human genome, which they finally published in 2003. But today's rapid sequencing machines can run through that much DNA in a week, and are busily churning out multiple sequences from an ever-expanding list of species. Meanwhile, astronomers working with the Sloan Digital Sky Survey telescope in New Mexico have mapped some 25% of the sky since 2000, obtaining data on more than 200 million objects. The Large Synoptic Survey Telescope, scheduled for completion atop Chile's Cerro Pachón in 2015, will gather that much data in one night.

Statistics tell a similar story in many scientific fields. This is great news for research; data glut is always better than data famine. But it

their fields, and institutions should ensure that training is in place to make this possible.

The access principle asserts the value of openness: only if results are shared can other researchers check the data's accuracy, verify analyses and build on previous work. So unless there are very good reasons for researchers to withhold data — reasons that should be publicly posted and available for comment by other researchers — they should make provisions to supply public access in a timely manner, possibly as early as their grant proposals.

Finally, the stewardship principle addresses the need for long-term pres-

"Each researcher is ultimately responsible for ensuring the

EDUCATION

Computing Has Changed Biology—Biology Education Must Catch Up

Biologists need better computational education so that researchers can benefit from the bioinformatics revolution.

Pavel Pevzner[1]* and Ron Shamir[2]

Advances in computing have forever changed the practice of biological research. Computational biology, or bioinformatics, is as essential for biology in this century as molecular biology was in the last. In fact, it is difficult to imagine modern molecular biology without computational biology. For example, a difficult algorithmic puzzle had to be solved in order to successfully assemble the human genome sequence from millions of short pieces.

However, the computational components of undergraduate biology education have hardly changed in the past 50 years. New courses for biologists should be more relevant to their discipline, complementing the standard mathematical courses that were and mathematicians from various branches of bioinformatics agreed that the time has come to shift the paradigm in biology education by adding new computational courses to standard curricula. This realization is not new: *BIO2010*, a National Research Council report (*1*), recommended substantial changes in the mathematics curricula for research-oriented biology undergraduates. Bialek and Botstein (*2*) and Pevzner (*3*) acknowledged the problem and outlined some creative approaches to its solution. However, the question of how best to deliver computational ideas to biologists remains.

Because bioinformatics is a computational science, courses should strive to present the ideas that drive an algorithm's design and computational ideas and ensures that they are able to apply them?

Consider the problem of analyzing gene expression data by principal component analysis (PCA), a powerful computational technique used by thousands of biologists. PCA is not typically covered in mathematics courses taken by biologists, so many may use PCA without understanding how it works or even what it does. A biologist who "blindly" uses PCA or other bioinformatics tools may misapply the method, miss important observations, misinterpret the results, and derive erroneous biological conclusions [see (*4*) for examples of misinterpretations of BLAST results].

Thus, we believe that undergraduate cur-

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EDUCATION

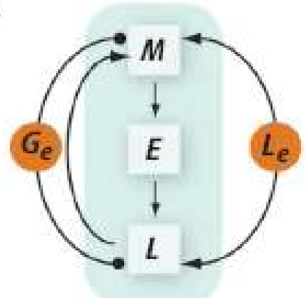
Mathematical Biology Education: Beyond Calculus

Training in developing algebraic models is often overlooked but can be valuable to biologists and mathematicians.

Raina Robeva[1*] and Reinhard Laubenbacher[2]

In 2003, the National Research Council's *BIO2010* report recommended aggressive curriculum restructuring to educate the "quantitative biologists" of the future (*1*). The number of undergraduate and graduate programs in mathematical and computational biology has since increased, and some institutions have added courses in mathematical biology related to biomedical research (*2*, *3*). The National Science Foundation (NSF) and the National Institutes of Health are funding development workshops and discussion forums for faculty (*4*, *5*), research-related experiences (*6*, *7*), and specialized research conferences in mathematical biology for students (*8*, *9*).

This new generation of biologists will



$$\dot{M} = Dk_M P_D(G_e)P_R(A) - \gamma_M M \qquad f_M = \neg G_e \wedge (L \vee L_e)$$

$$\dot{E} = k_E M - \gamma_E E \qquad f_E = M$$

$$\dot{L} = k_L \beta_L(L_e)\beta_G(G_e)Q - 2\phi_M \mathcal{M}(L)B - \gamma_L L \qquad f_L = \neg G_e \wedge E \wedge L_e$$

DE and Boolean models of the *lac operon* mechanism. Each component of the shaded part of the wiring diagram is a variable in the model, and the compartments outside of the shaded region are parameters. Directed links represent influences between the variables: A positive influence is indicated by an arrow; a negative influence is depicted by a circle.

systems biology. At the molecular level, this involves understanding a complex network of interacting molecular species that incorporates gene regulation, protein-protein interactions, and metabolism. Two types of models have been used successfully to organize

regulatory networks (*10*). They have proven useful in cases where network dynamics are determined by the logic of interactions rather than finely tuned kinetics, which often are not known. Published algebraic models include the metabolic network in *Escheri-*

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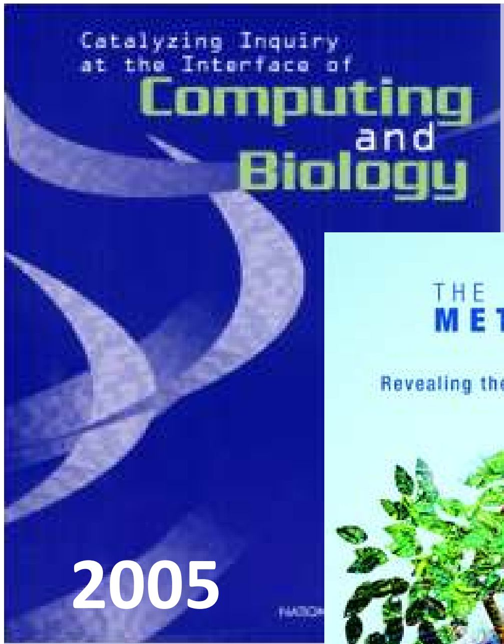
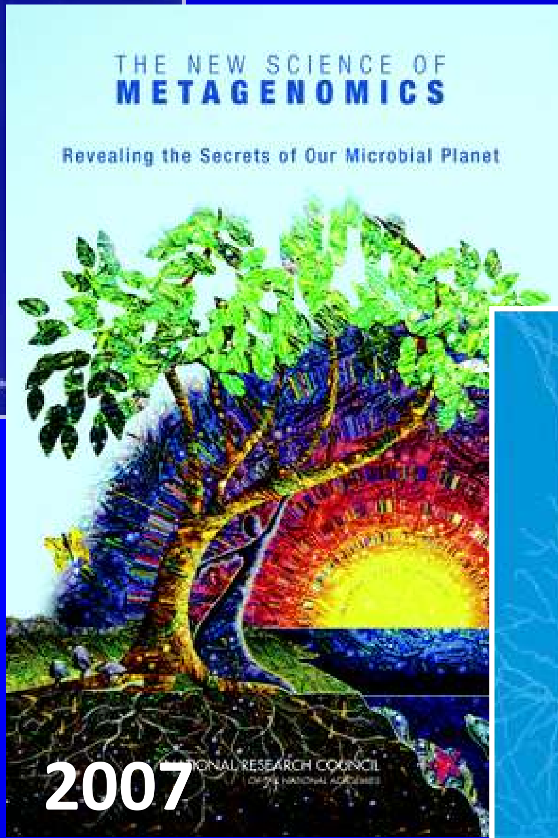
Thinking beyond disciplines



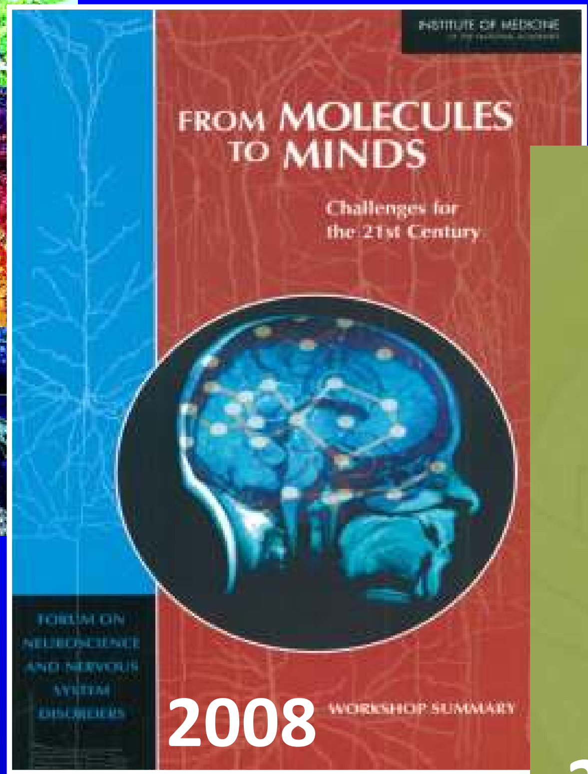
2005

Computational Thinking



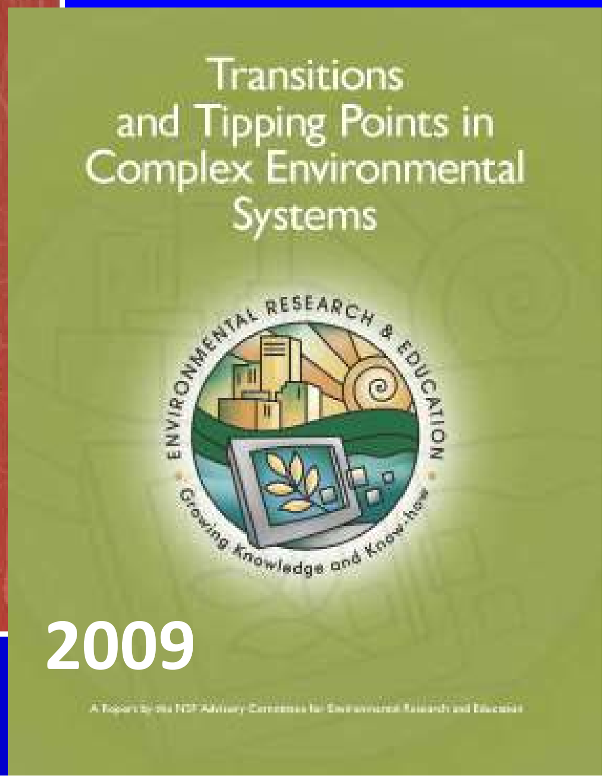
2007

Synthetic Thinking



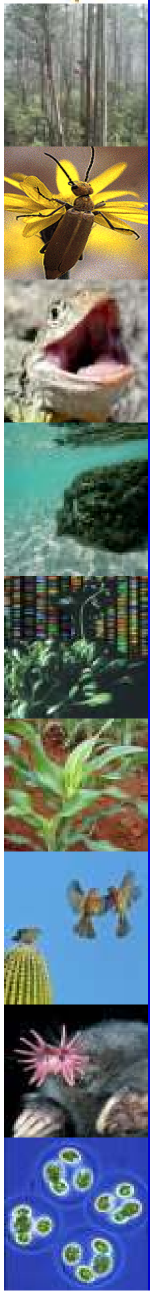
2008

Multiscale Thinking



2009

Systems Thinking

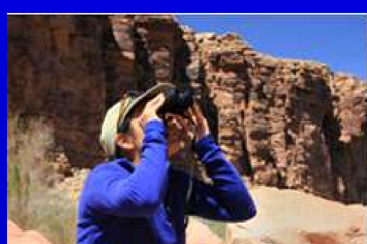


Life Sciences in Transition

Challenge: Catalyzing Community Change in Biology Education

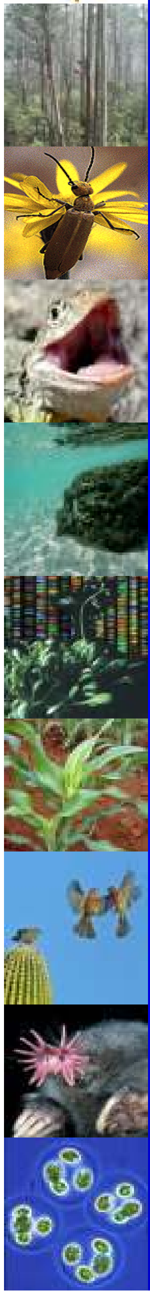
Prepare a new generation of scientists to communicate science as a precise, predictive, and reliable way of knowing the world.

Transforming Undergraduate Education in Biology: Mobilizing the Community for Change Conference (July 2009)



Vision & Change in Undergraduate Biology Education

A VIEW FOR THE 21st CENTURY



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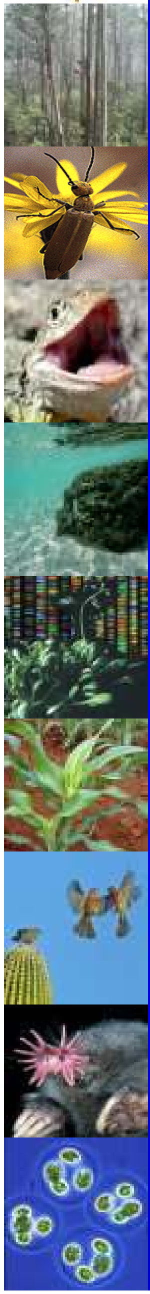
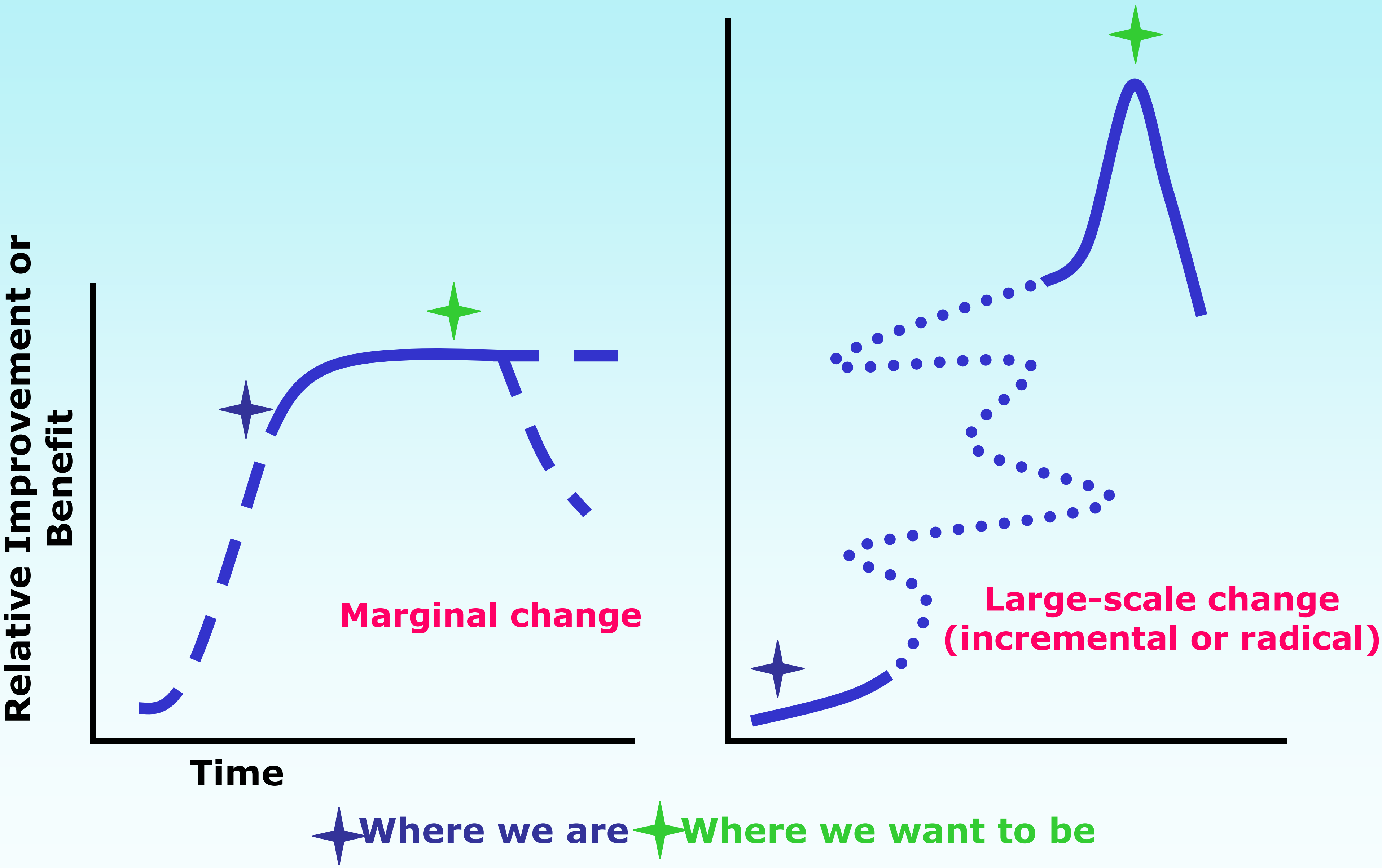


Innovating in the Midst of Excellence

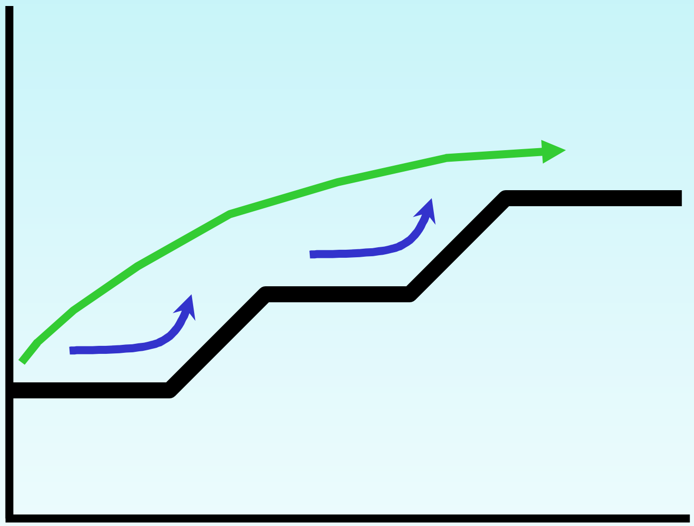
"The goal is an organization that is constantly making its future rather than defending its past."

Hamel & Valiksngas, 2003

“Improvement Landscapes”



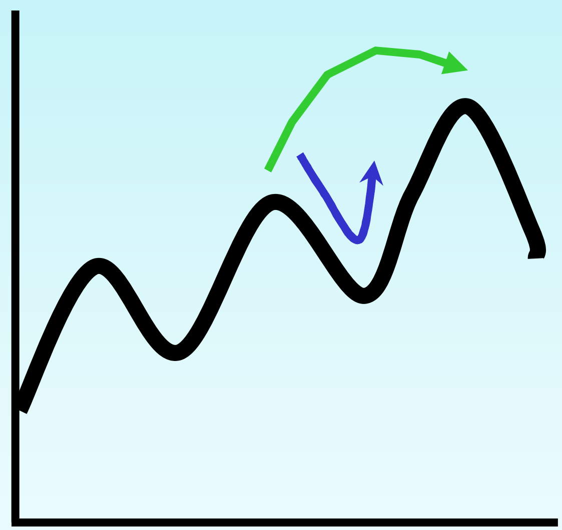
Stair Step Model



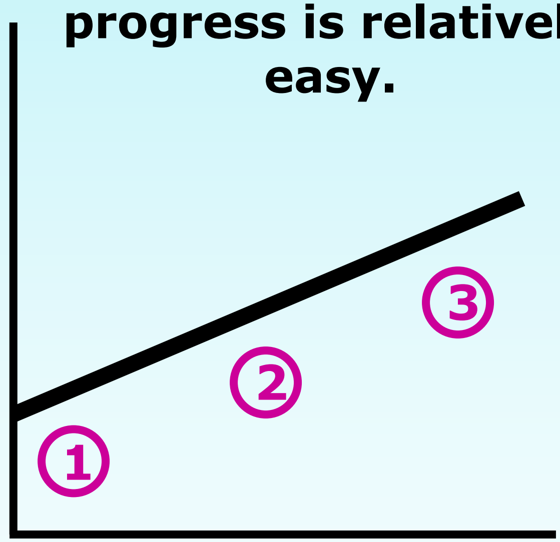
- **Incremental** change may be easy to achieve once there is a shared vision of benefits.
- **Revolutionary** change can support rapid gains.
- A prediction: given the structure of universities and funding agencies, the pressures would be towards incremental change.
- What are the costs of each model?
- How can performance of each model be assessed?

Peak Model

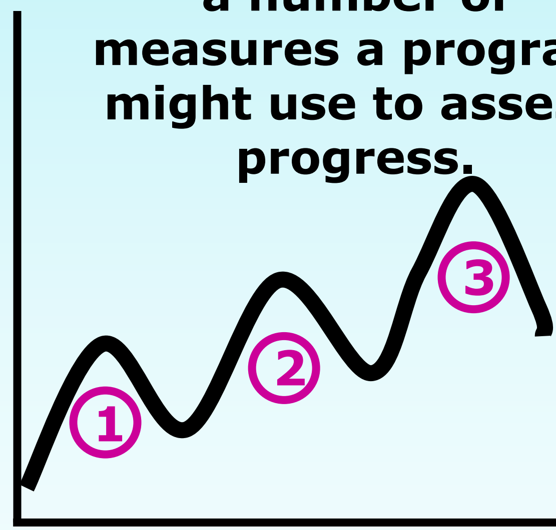
- **Incremental change**
  - Possible in institutions, but requires patience, leadership, and resources to offset possible erosion in quality.
  - Institutional pressure to avoid troughs is often high, and could prevent progress.
- **Revolutionary change**
  - May be difficult to achieve in institutions because of colleagues "left on a prior peak."
  - What are the costs of sustaining both peaks? In business this type of change is characterized as the "Innovator's Dilemma."



A model of institutional change in which bottom-up, self-organized efforts can prevail. Progress is possible without significant costs, and achieving recognition of the merits of progress is relatively easy.

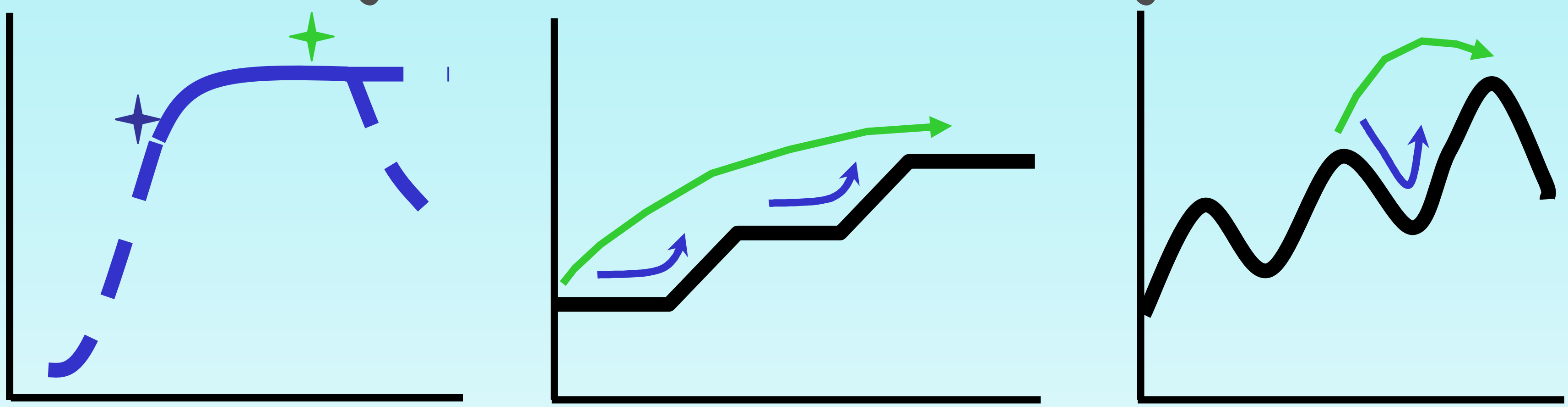


A model of institutional change in which significant investments of leadership and resources need to be made to negotiate the "troughs." The ordinate can be any of a number of measures a program might use to assess progress.



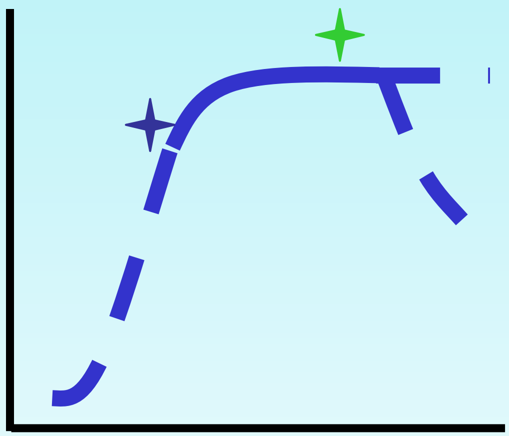
Developmental Stage

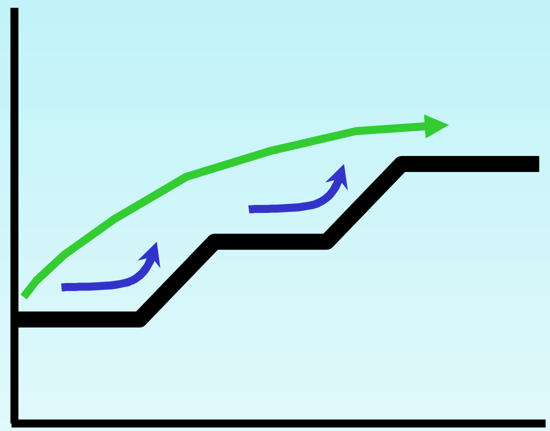
Challenges

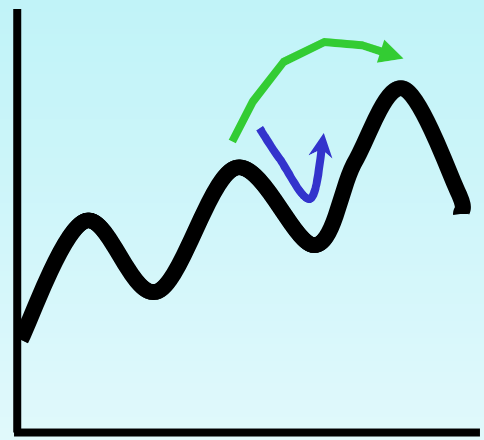


- Which model applies? Does it matter? Does the appropriate model differ for research, education, and outreach activities? For universities versus funding agencies?
- What does this mean for the steps we take in creating the science units of the 21st Century? What are the biggest potential gains and the largest potential pitfalls?

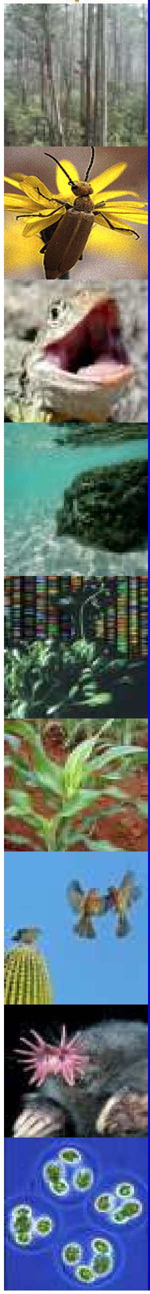
Some questions for consideration…







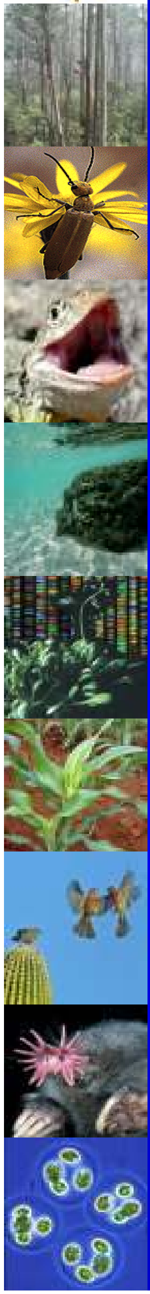
- If only marginal change is needed, why is progress in causing change often so slow?
- Will incremental change be fast enough to meet institutional responsibilities?
- How do we foster radical change? How do we ensure we land on a peak? How do we know we're on a peak?



The Innovator's Dilemma

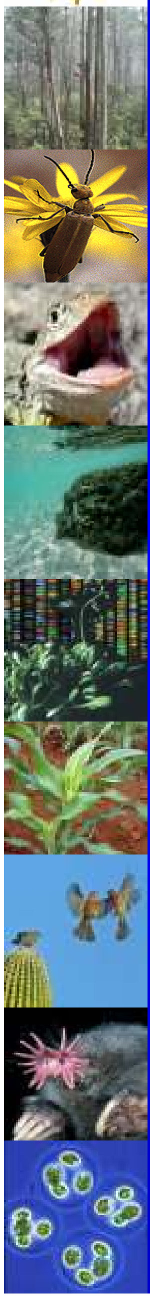
"Incumbents very seldom invent the future."

Eric Schmidt, CEO, Google
New York Times, April 15, 2009



"In all affairs it's a healthy thing now and then to hang a question mark on the things you have long taken for granted."

Bertrand Russell



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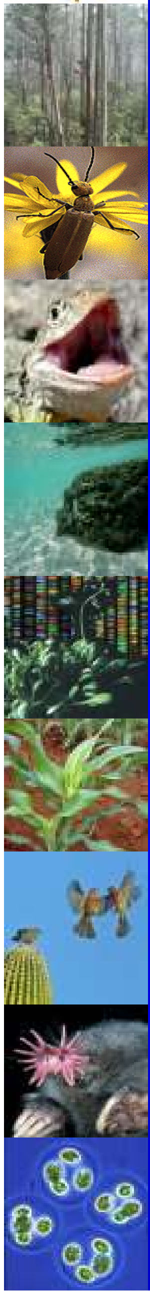
What really matters?

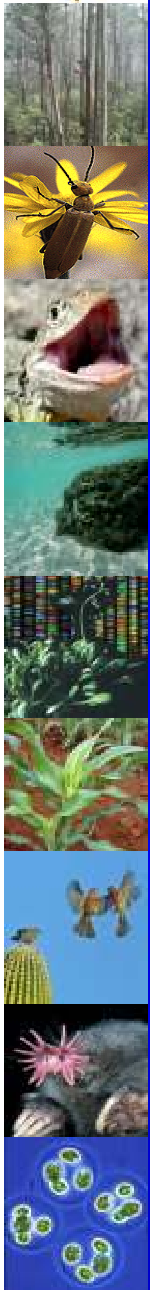
Whose view counts?

How do values vary?

Experiments in Innovation: The process of discovery



- Exploring novel processes for identifying frontier research:
  - Crowd sourcing
  - Clean slate
  - Creativity training for faculty members
  - Synthesis centers
  - Prediction markets
  - Sandpits



Outline

- **Life in Transition:**
  Questions without borders

- **Life Sciences in Transition:**
  When disciplines merge

- **Managing the Sciences in Transition:**
  Innovating in the midst of excellence


Sustainability, Innovation, and EPSCoR