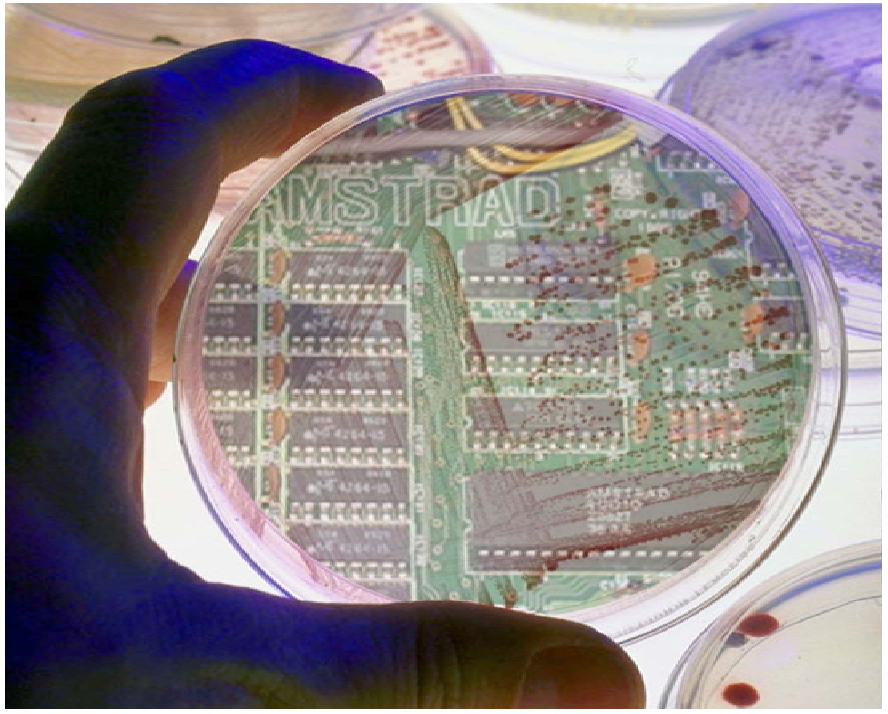
SynBio for the Environment



Víctor de Lorenzo

http://www.cnb.csic.es/~meml

Centro Nacional de Biotecnología (CNB)

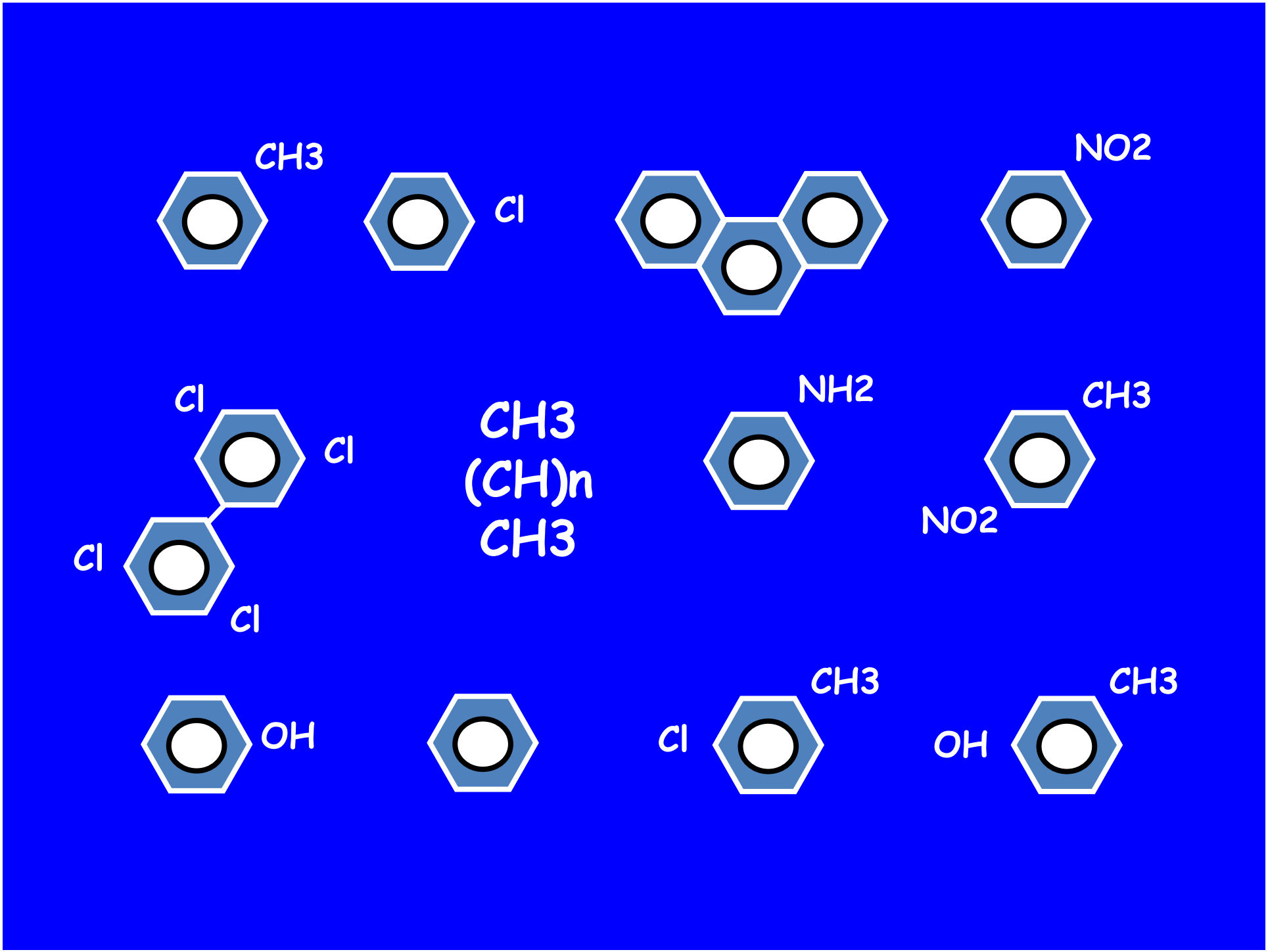
Consejo Superior de Investigaciones Científicas (CSIC)

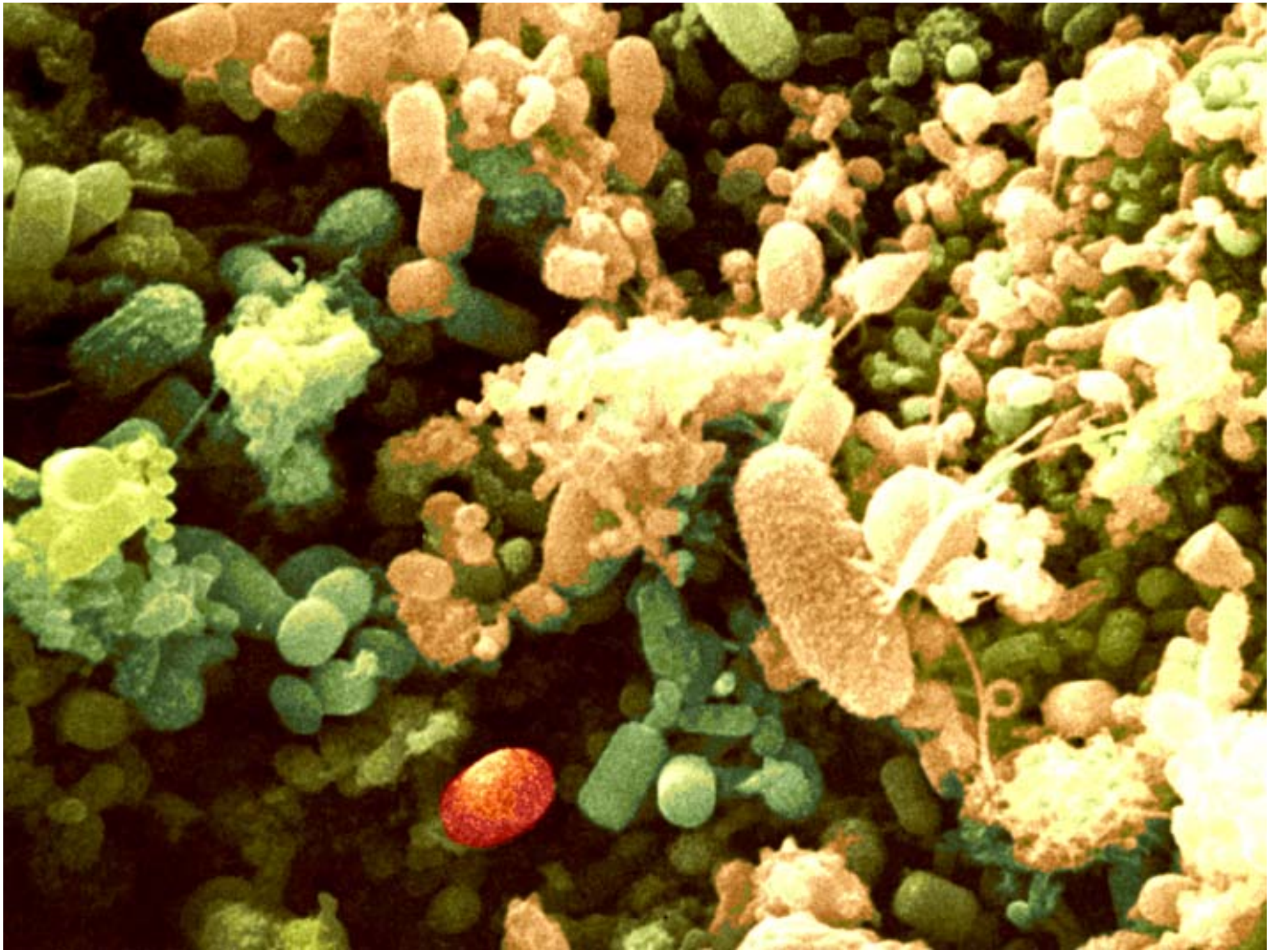
Madrid (Spain)

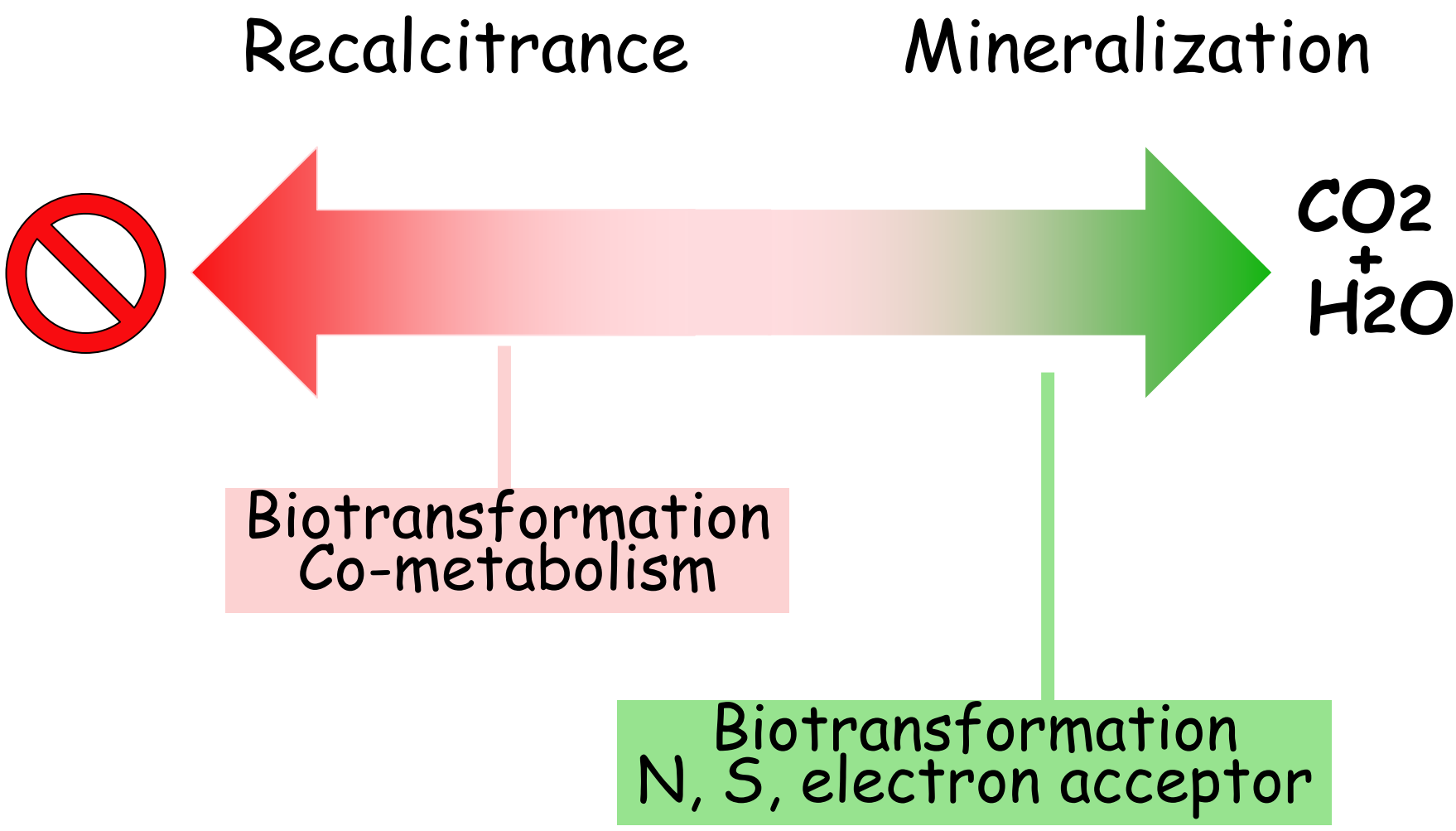

Our scenario ...

Accessing the catabolic landscape

Repsol - YPF Oil Refinery. Puertollano (Spain)


CH3
Cl
NO2
Cl
Cl
Cl
CH3
(CH)n
CH3
NH2
CH3
NO2
OH
CH3
Cl
CH3
OH




Recalcitrance
Mineralization
CO2
+
H2O
Biotransformation
Co-metabolism
Biotransformation
N, S, electron acceptor

Engineered Biological agents for environmental application

- *In situ* biodegradation
- Bio-transformation
- Detection
- Immobilization

Physics, Computation and Engineering

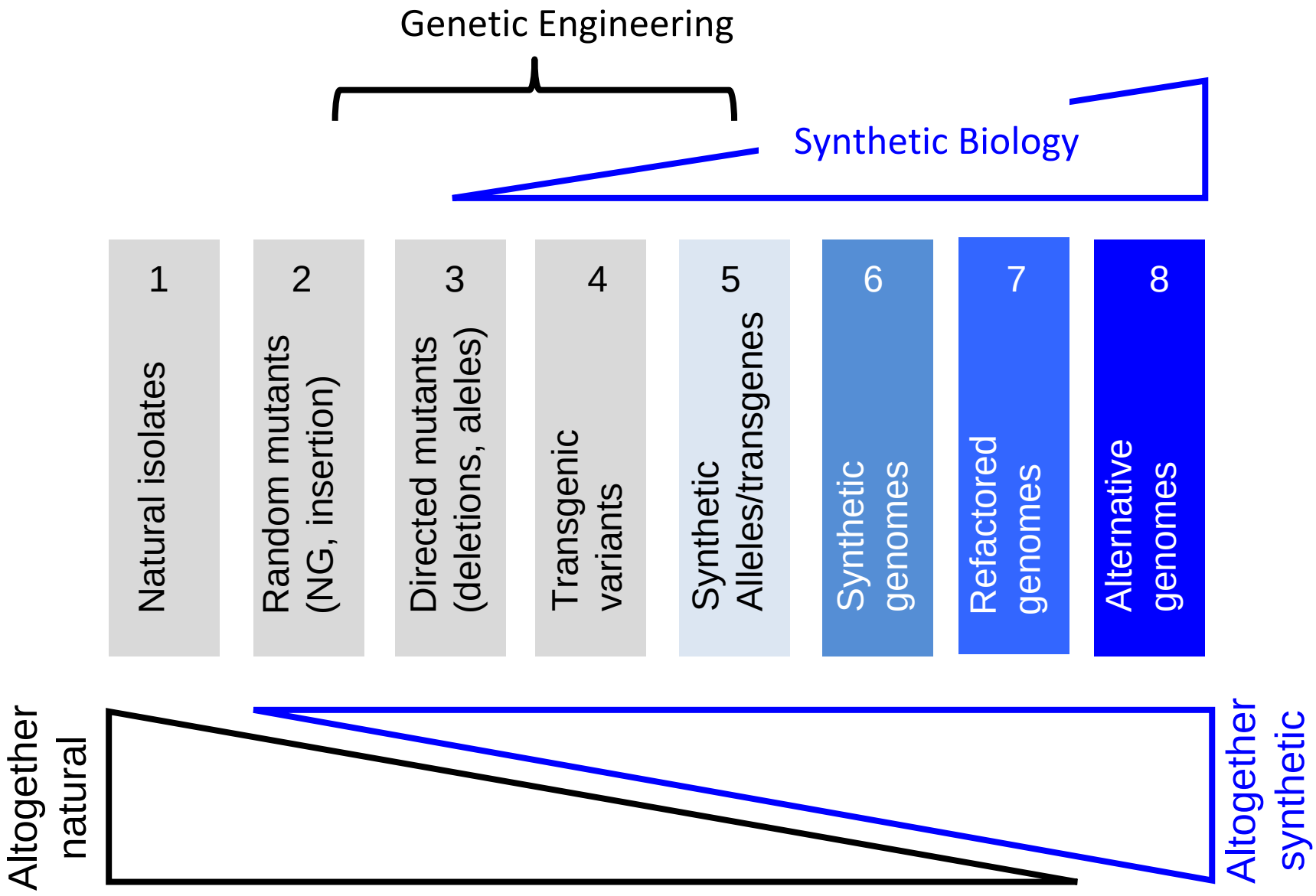
From servants to Masters of the (biotech) House?

Service	Molecular Biology (hypothesis-driven experimentation)
Partnership	Systems Biology (data-driven information mining; model-driven experimentation)
Leadership?	Synthetic Biology (forward design of biological properties)

Proposition #1

The criterion for identifying new scenarios associated to the application of Synthetic Biosystems is not the way the agent is engineered, but the divide between familiar and non-familiar Biology.

The roadmap from Genetic Engineering to Synthetic/Non-natural MO

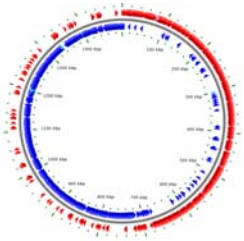


E. coli Nissle 1917


MUTAFLOR®
Wirkstoff: E. coli Stamm Nissle 1917
Zusammensetzung:
1 magensaftresistente Hartkapsel
enthält: Escherichia coli Stamm
Nissle 1917 entsprechend 2,5 – 25 x 10⁹
vermehrungsfähigen Zellen (KBE)

Synthetic DNA fragments

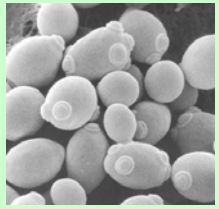
Synthetic Genomes



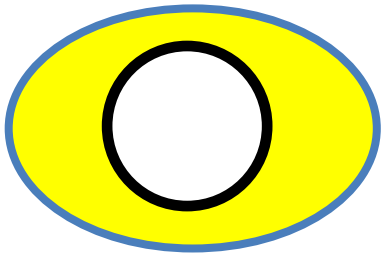
Plasmid & Transposon vectors

Viral vectors

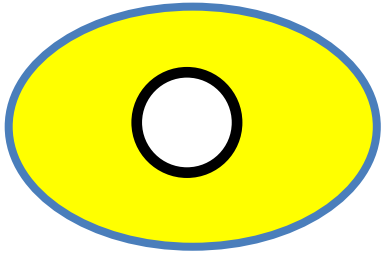
Yeast vectors



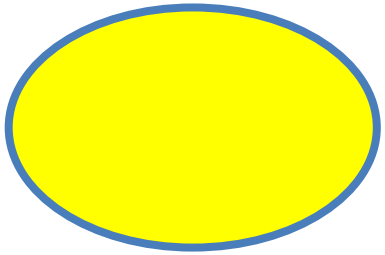
Natural bacterium



Streamlined genome

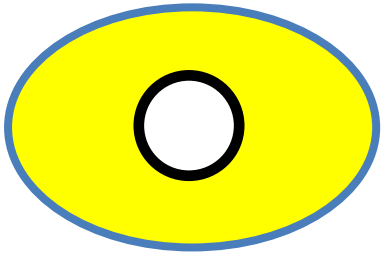


Genome-less cells



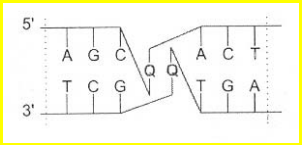
- Orthogonal ribosomes
- Alternative/expanded genetic codes
- Proteins with non-natural amino acids

Streamlined genome



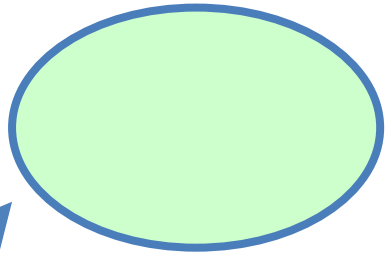
Familiar Biology

Xeno-Nucleic acids (XNAs)

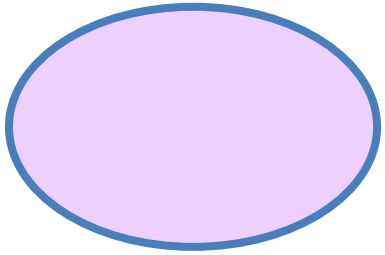


Alternative information-bearing molecules / genomes

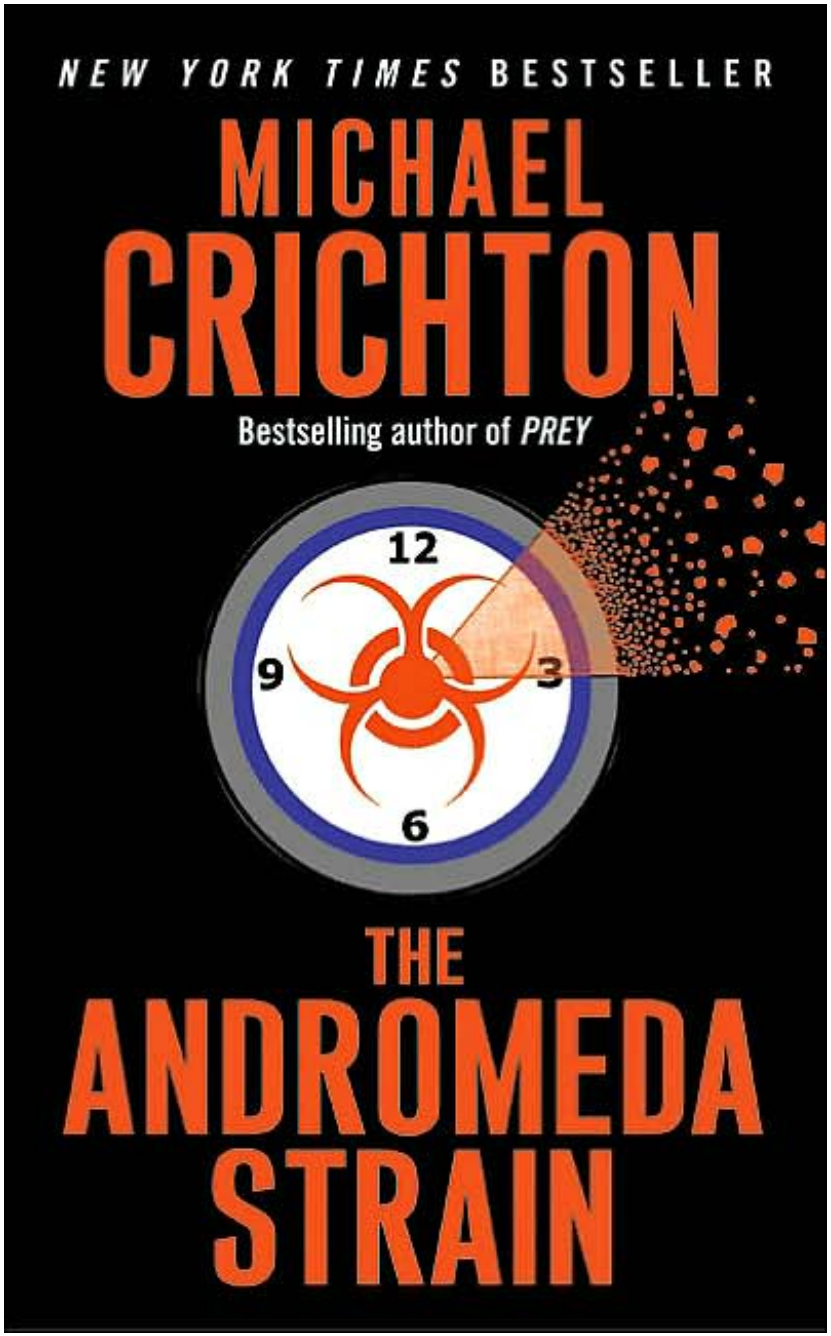
Vesicles/artificial cells



Orthogonal cells



Non-familiar Biology


NEW YORK TIMES BESTSELLER
MICHAEL
CRICHTON
Bestselling author of PREY
12
3
6
9
THE
ANDROMEDA
STRAIN

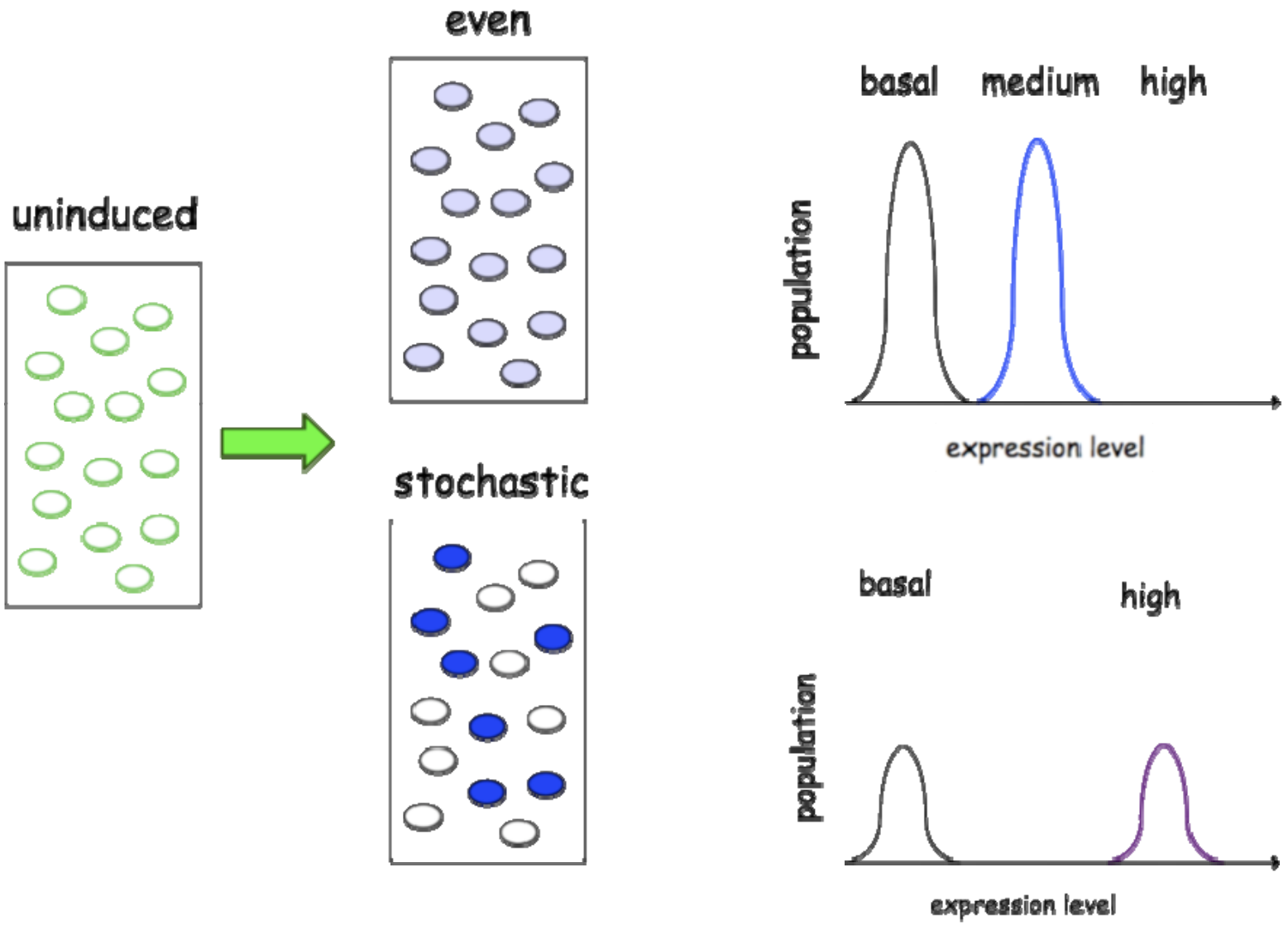
The 10 questions on environmental risks borne by Engineered/synthetic/non-natural microorganisms (SEMs)

1. Can SEMs colonize and eventually takeover natural microbial communities?
2. Is there a chance that SEMs enter new niches that natural bacteria cannot?
3. Might SEMs go into a stage of uncontrolled growth?
4. What are the chances of horizontal transfer of the synthetic genes to novel recipients?
5. Is there a tradeoff between safety and biotechnological efficacy of SEMs?
6. Could traits engineered in SEMs evolve towards virulence or other deleterious behavior?
7. Are there scenarios of SEMs capable of damaging life or property?
8. What is the environmental fate of synthetic genes?
9. Are there chances of malicious misuse of SEMs
10. Should SEMs be endowed with traits to increase their safety and predictability?

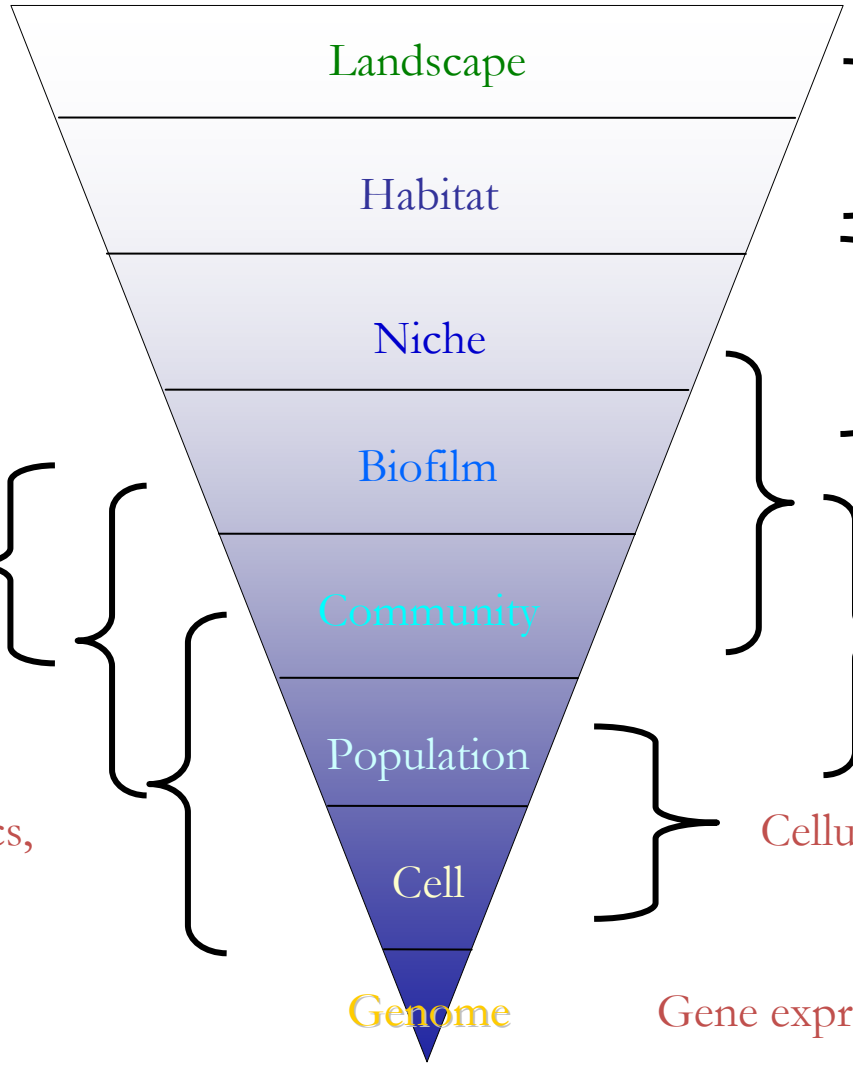
Proposition #2

The biggest challenge of SB re. Environmental applications is the projection of stochastic behaviour of individuals into population performance.

Projection of stochastic-single cell events into population behaviour



The Complexity Pyramid



Experimental Approaches

Process Analysis

Activities, Microprobes

Community Profiling, Tracer Technology

Metabolic networks

Transcriptomics, Proteomics, Metabolomics, Phenotype

Genetics, Genomics

Biological questions

Global Processes, Interactions

Local Interactions

Community Dynamics, Activities, Invasions

Metabolic Networks And Interactions

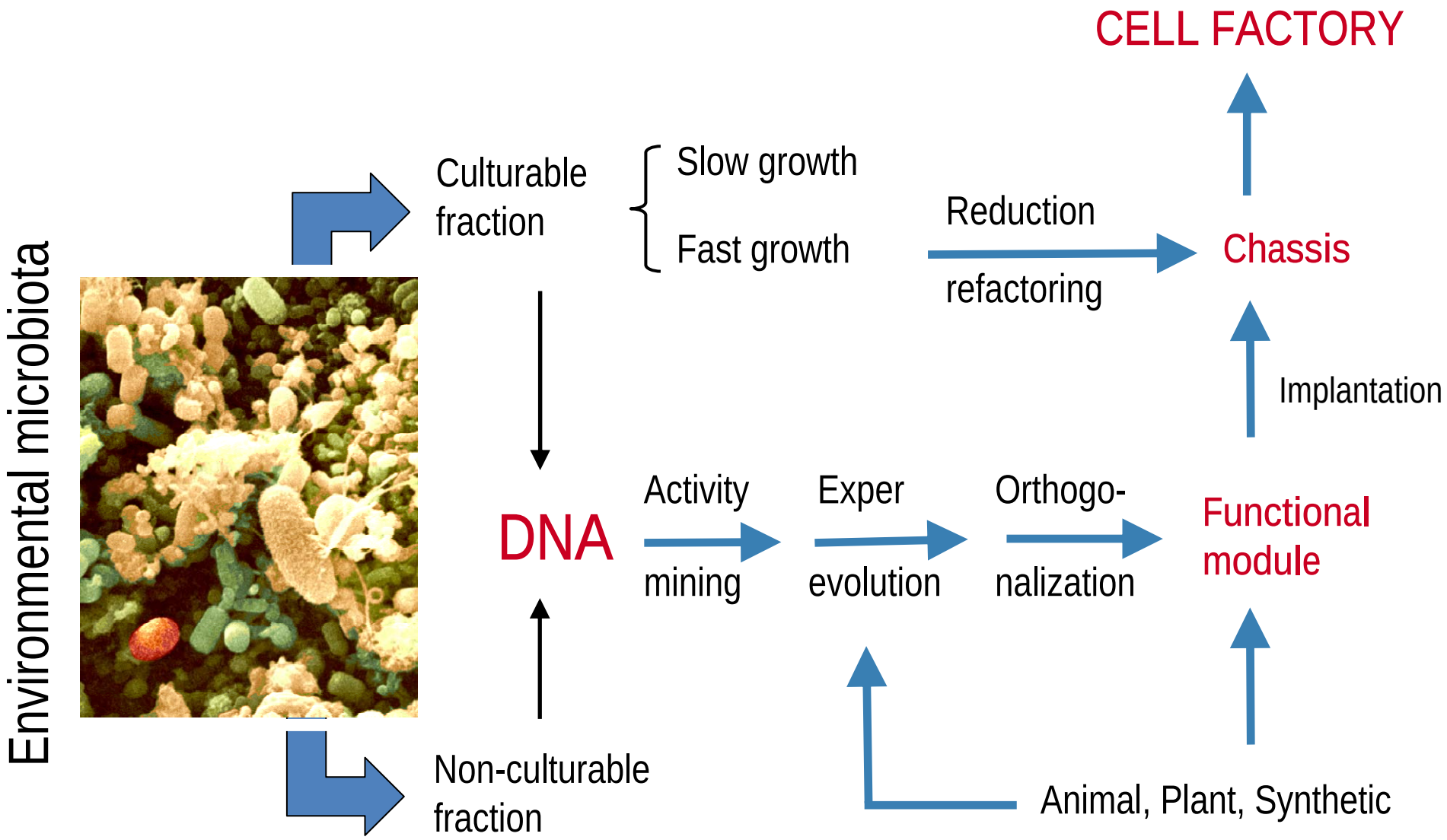
Cellular Activities

Gene expression, Regulation

Proposition #3

For the next 10 year (at least), frontline Environmental Biotech research will rely the combination of Metagenomics with Synthetic Biology.

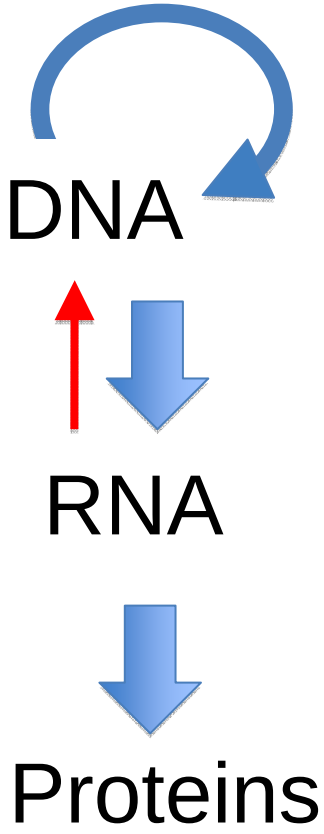
Combining Synthetic Biology with Metagenomics



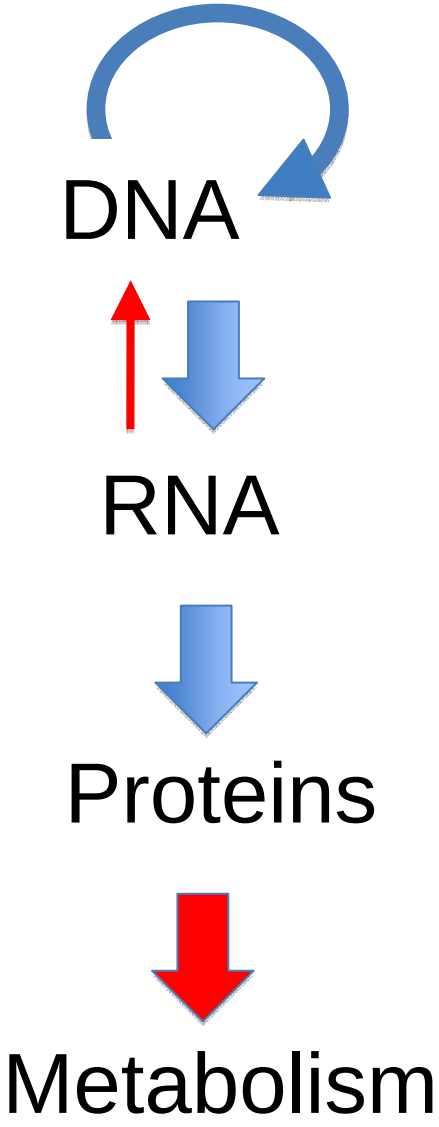
Proposition #4

Synthetic Biology will bring about a transition from a Geno-centric Environmental Biotech to a Chemo-centric discipline

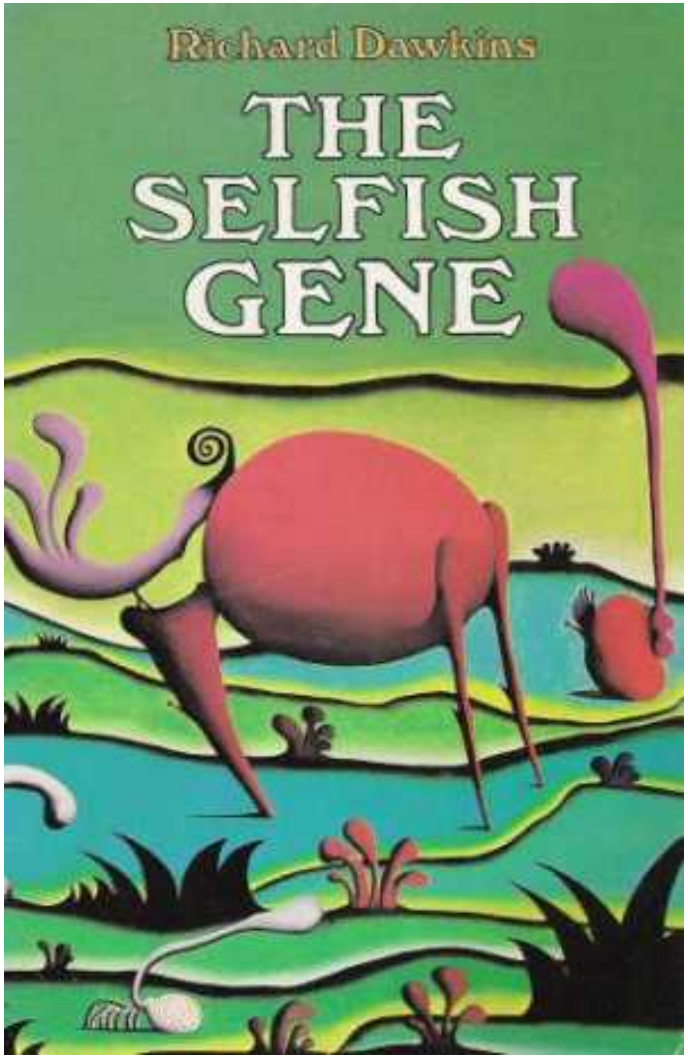
The geno-centric syndrome



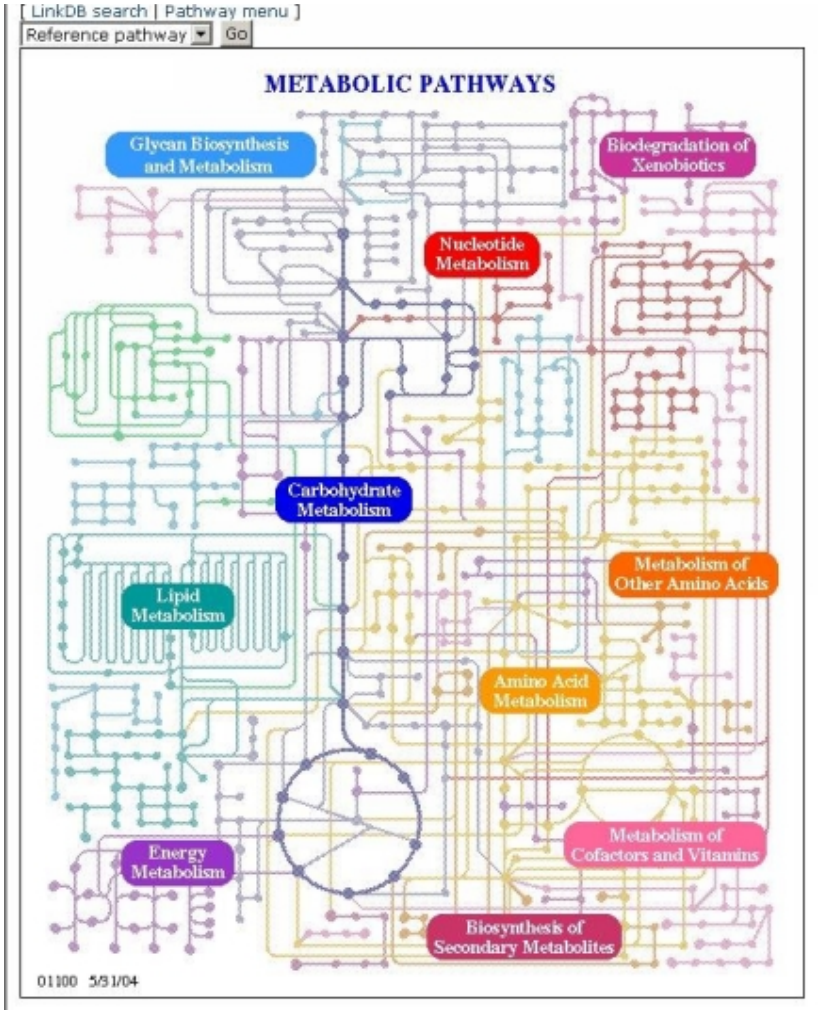
The geno-centric syndrome



The ongoing shift in understanding live systems



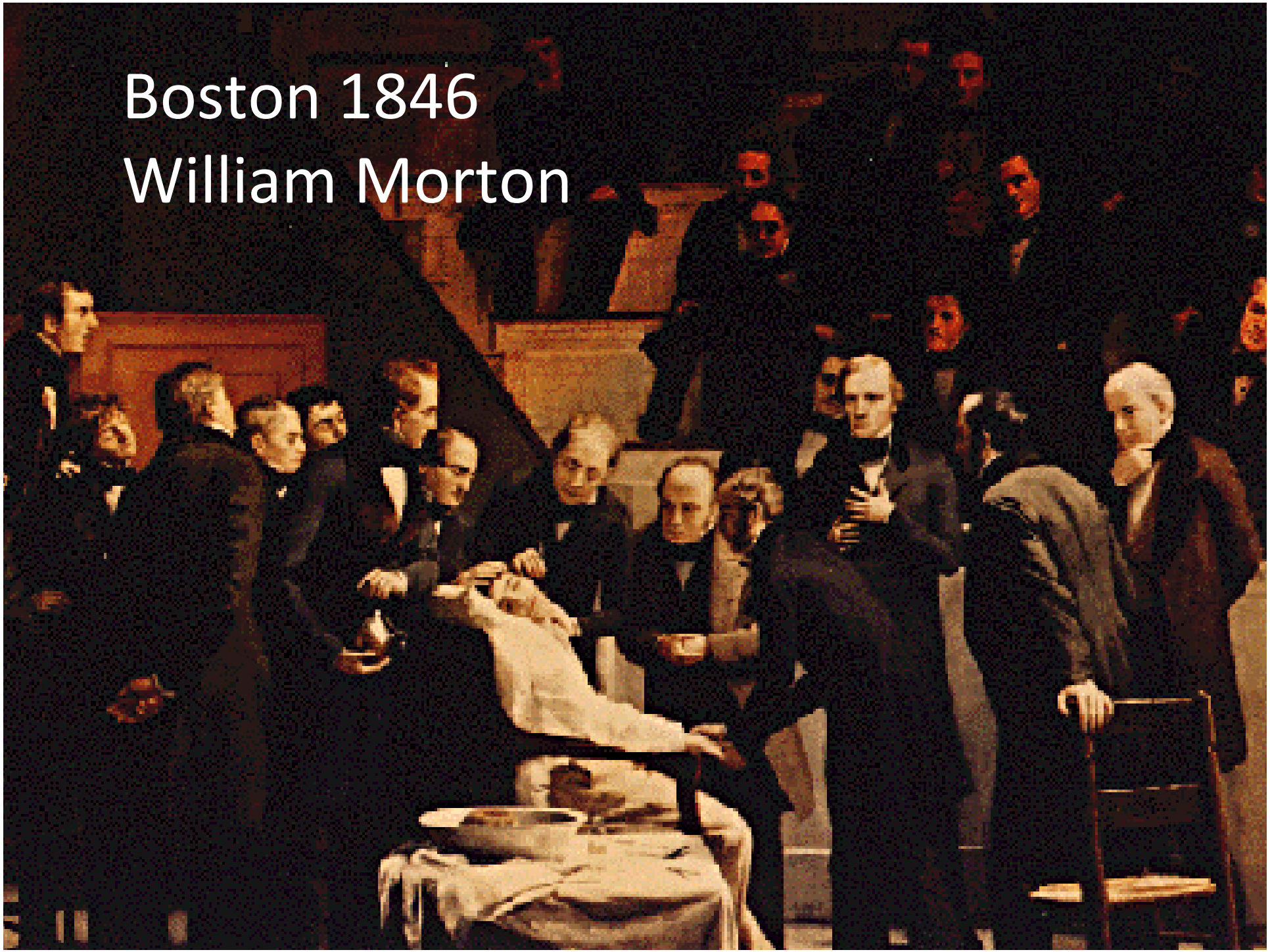
The selfish metabolism



Proposition #5

Adress public debates with a historical perspective:

- Learn from past controversies
- Study mistakes and try better
- Do not alarm the public
- Find societal allies


Boston 1846
William Morton

Questions raised by every new groundbreaking Technology related to Life Siences

- What is the Science behind?
- Is it safe? ¿Risks?
- Who owns intellectual property?
- Who benefits?
- Should it be regulated / controlled? By whom?
- Natural *vs*. Non-natural: Are we playing God?

and by all means…

Do not play the arsonist fireman!

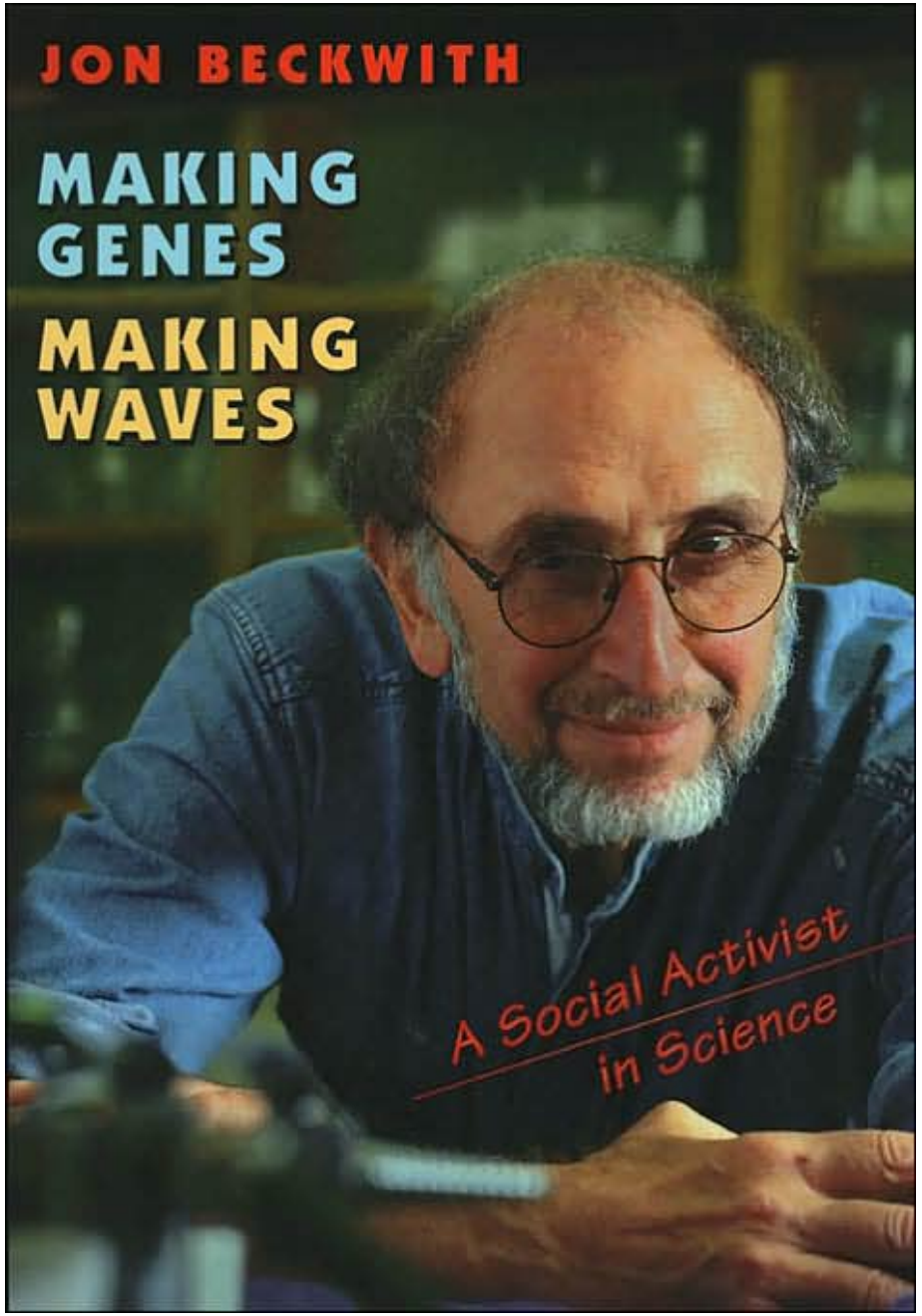
Nature **224**, 768-774 (22 November 1969)
Received 18 September 1969

Isolation of Pure *lac* Operon DNA*

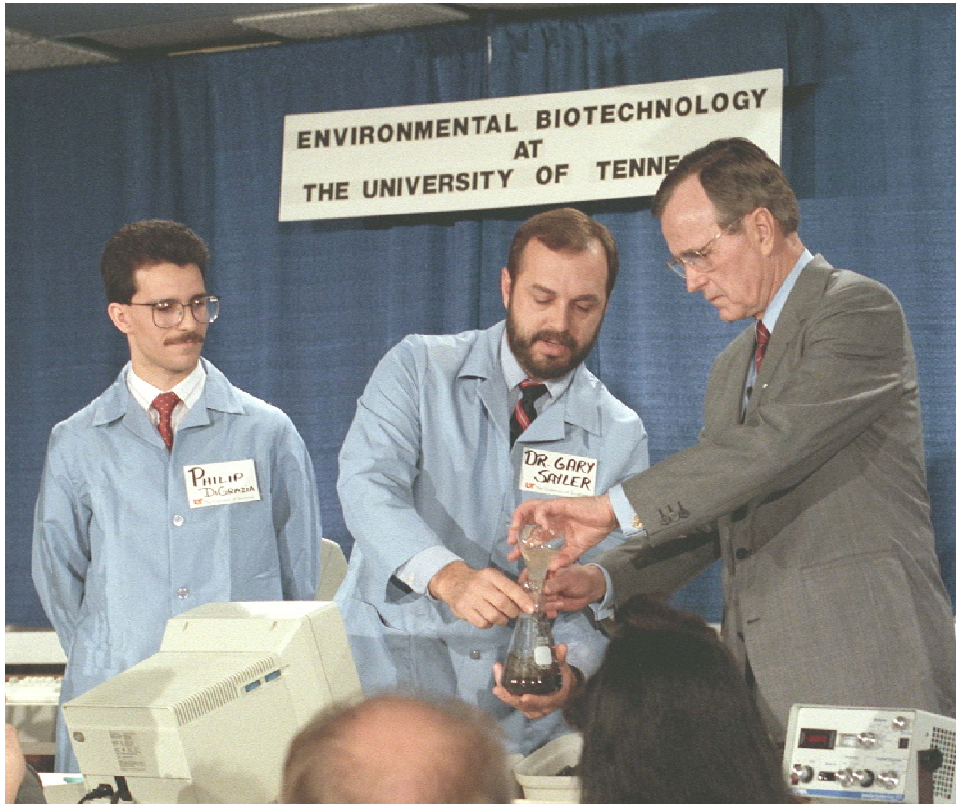
JIM SHAPIRO, LORNE MACHATTIE†, LARRY ERON, GARRET IHLER‡, KARIN IPPEN§ & JON BECKWITH

1. Department of Bacteriology and Immunology, and Department of Biological Chemistry, Harvard Medical School, Boston, Massachusetts 02115
2. Present addresses: †Department of Cell Biology, University of Toronto, Ontario.
3. ‡Department of Biochemistry, University of Pittsburgh, Pittsburgh, Pennsylvania.
4. §MRC Microbial Genetics Research Unit, Department of Molecular Biology, University of Edinburgh, West Mains Road, Edinburgh.

Two specialized transducing phages, which carry the *lac* operon of *Escherichia coli* inserted into their DNA in opposite orientations, are used as a source of complementary sequences from which to prepare pure *lac* operon duplex. The availability of a single pure promoter will facilitate many new experiments on genetic transcription.



Paris, 1800



Knoxville, 1990

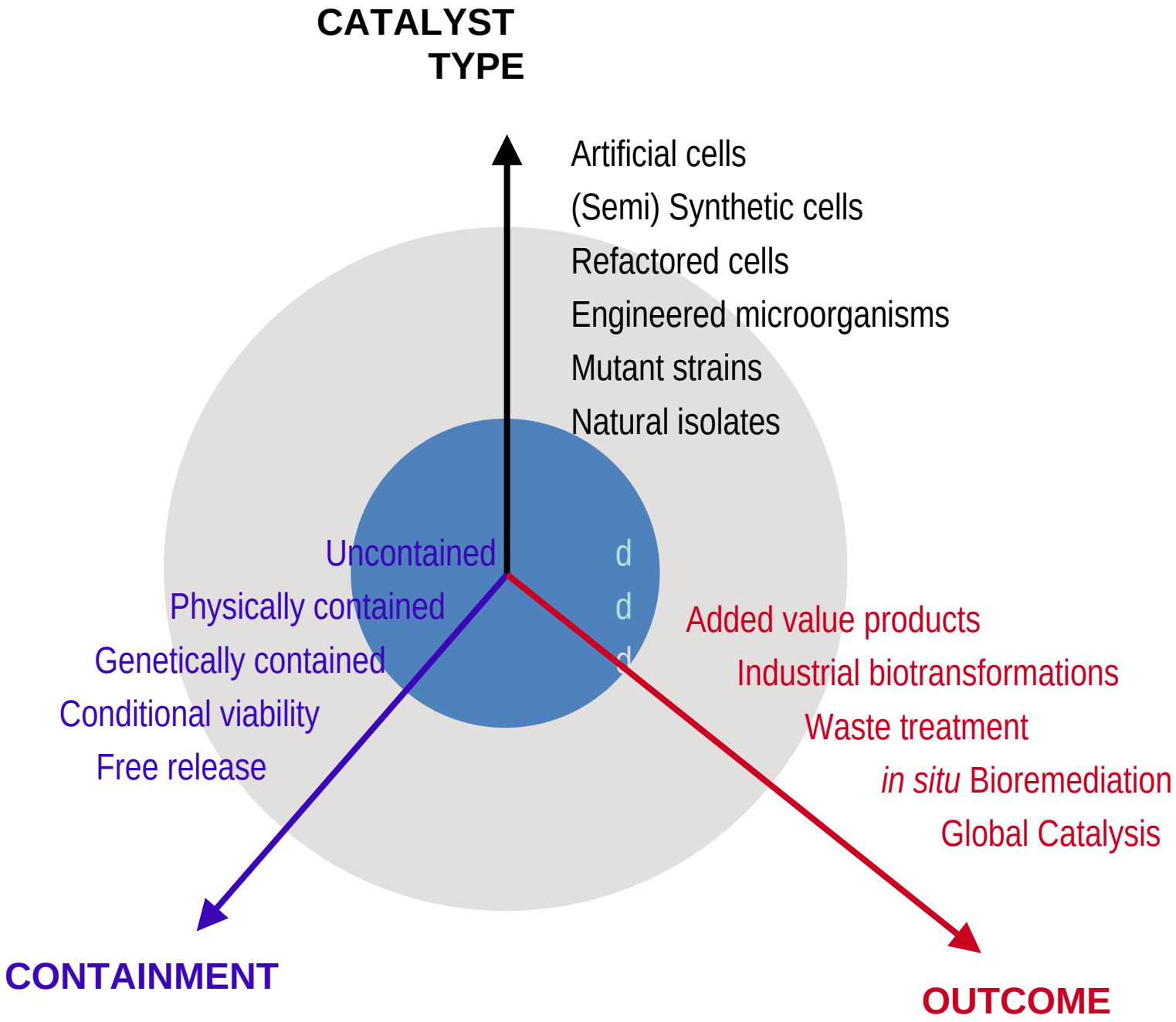
Centro Nacional de Biotecnología (CNB)

Consejo Superior de Investigaciones Científicas (CSIC)

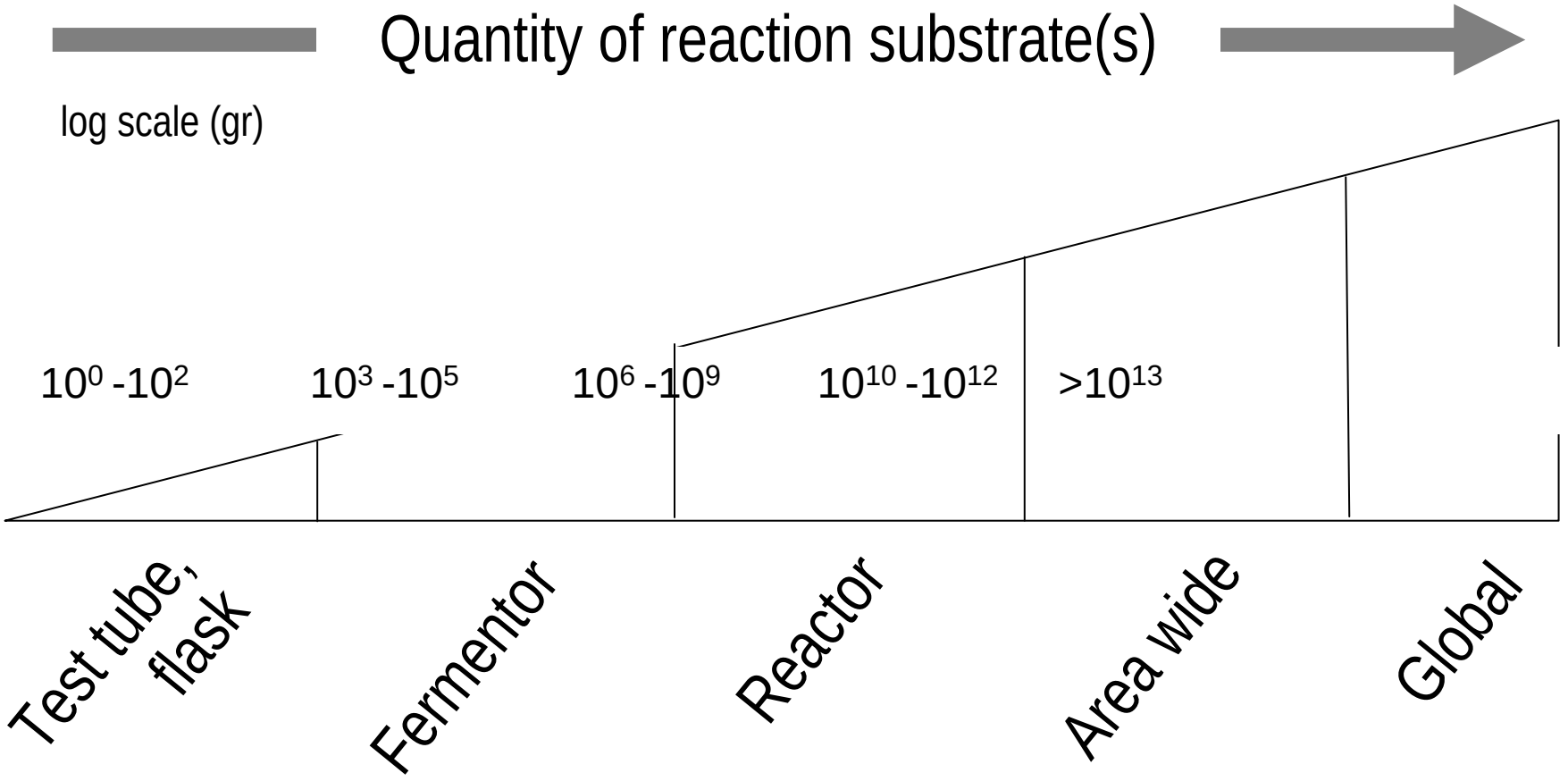
Madrid-Cantoblanco (Spain)

Proposition #5

Think BIG! For the first time we can entertain scenarios for engineering global biocatalysis interventions

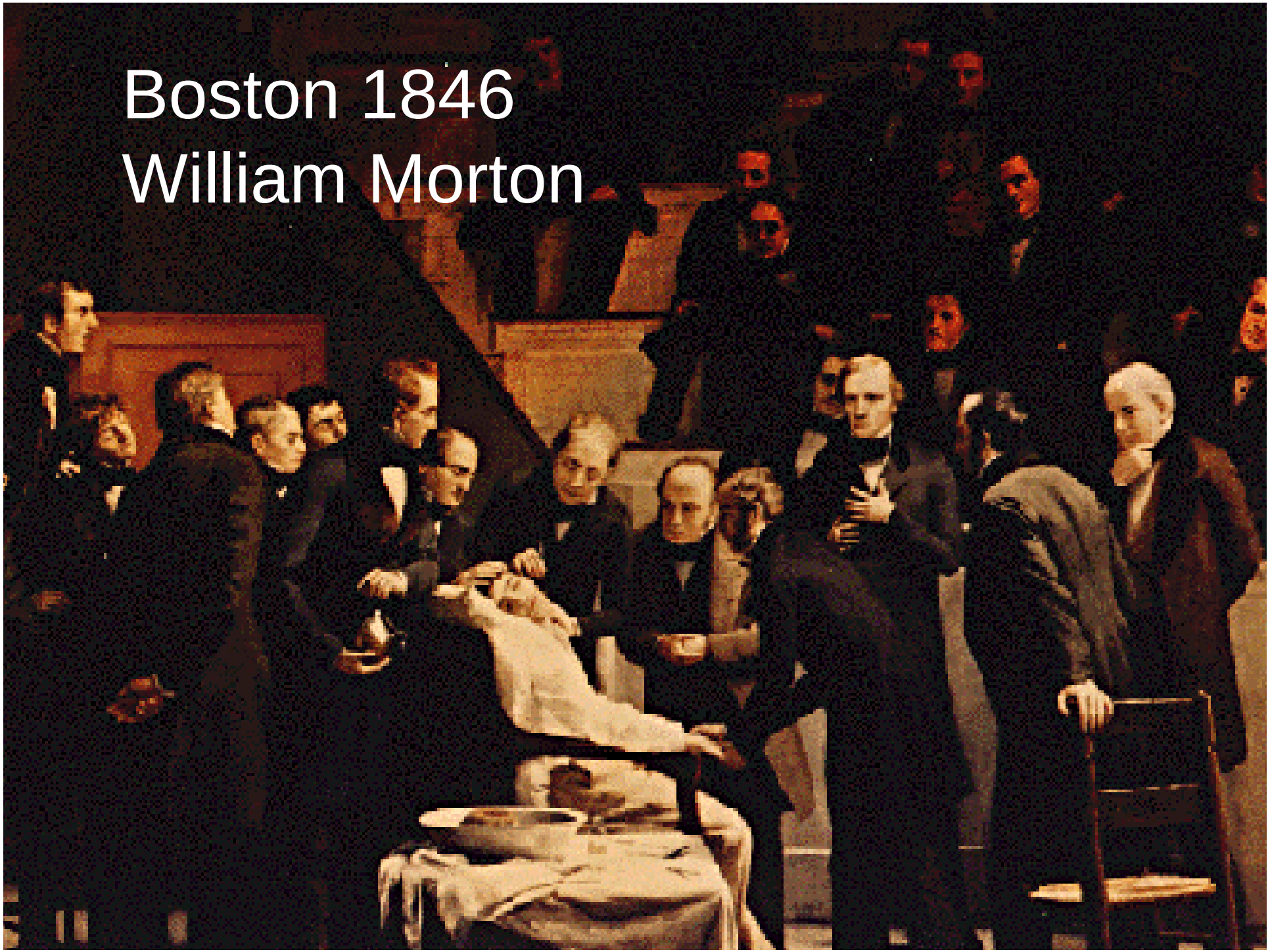

CATALYST TYPE
Artificial cells
(Semi) Synthetic cells
Refactored cells
Engineered microorganisms
Mutant strains
Natural isolates
Uncontained
Physically contained
Genetically contained
Conditional viability
Free release
CONTAINMENT
Added value products
Industrial biotransformations
Waste treatment
in situ Bioremediation
Global Catalysis
OUTCOME

SIZE MATTERS



Proposition #6

Look at societal/ethical debates with a historical perspective – do not re-invent the wheel by over-emphasizing issues that were tackled time ago


Boston 1846
William Morton

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- Who owns intellectual property?
- Who benefits?
- Should it be regulated / controlled? By whom?
- Natural *vs*. Non-natural: Are we playing God?

Proposition #7

Pursue societal allies and identify end-users beyond lobbing/impressing/entertaining the powerful

Paris, 1800

Knoxville, 1990