

Function-centred (meta-) genomics applied to biochemical knowledge



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Institute of Catalysis: general view

R&D activities of the ICP in the frame of the Spanish National Research Council (CSIC)

Who we are

Largest public research institution in Spain

What we do

- Scientific and technological research (multidisciplinary)
- Training of researchers and specialized personnel
- Dissemination of knowledge to the society
- Transfer of technology to the market

Where we are

SPAIN

Research centres

Own and joint research centres geographical distribution



Institute of Catalysis
Madrid, SPAIN

Institute of Catalysis: general view

- To develop new advanced (bio)catalysts for
- To develop innovative (bio) catalytic processes
- To increase the competitiveness of our (bio)chemical industry

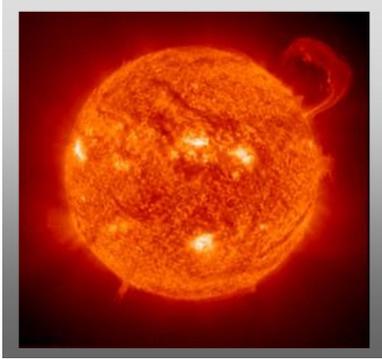
within the concept of

SUSTAINABLE (BIO)CHEMISTRY

ICP is a mixed chemical and biological institute devoted to catalysis



Institute of Catalysis: general view



Energy

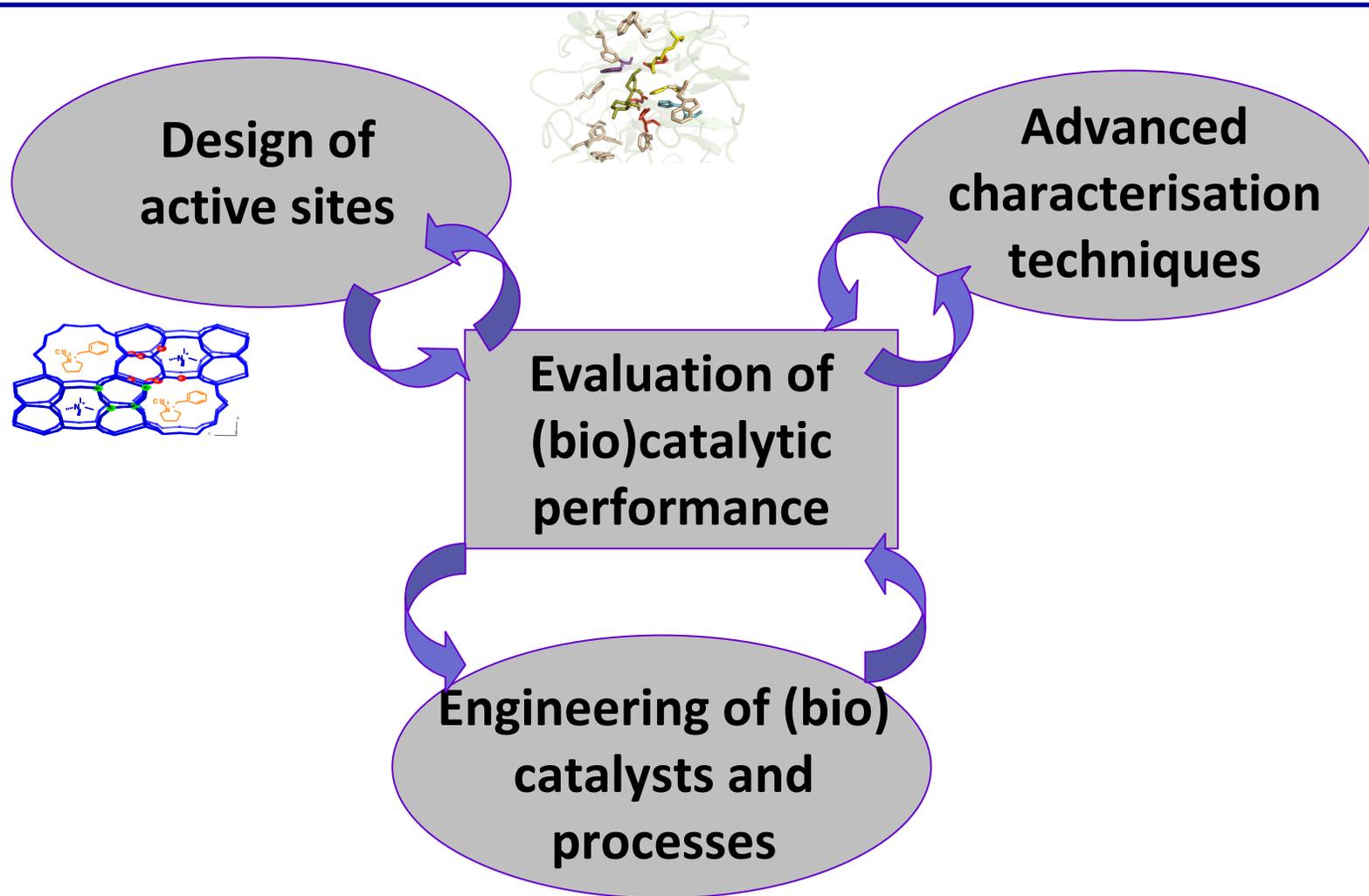


**Environment
protection**



**Selective
synthesis of
chemicals**

Institute of Catalysis: general view

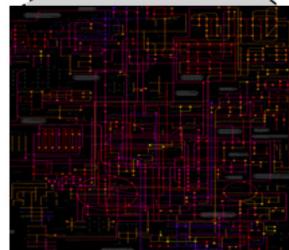


Biochemical networking: a “Google” map-like view

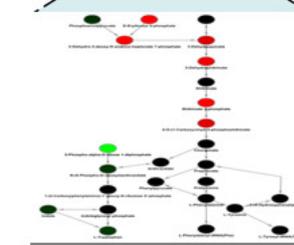
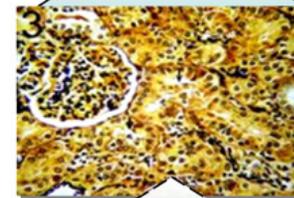
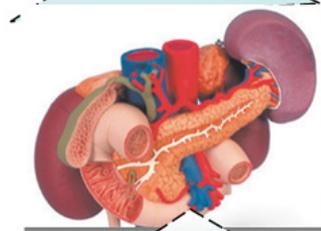
Land



Environment

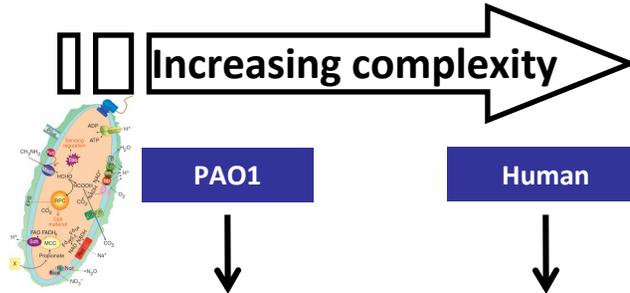


Organism

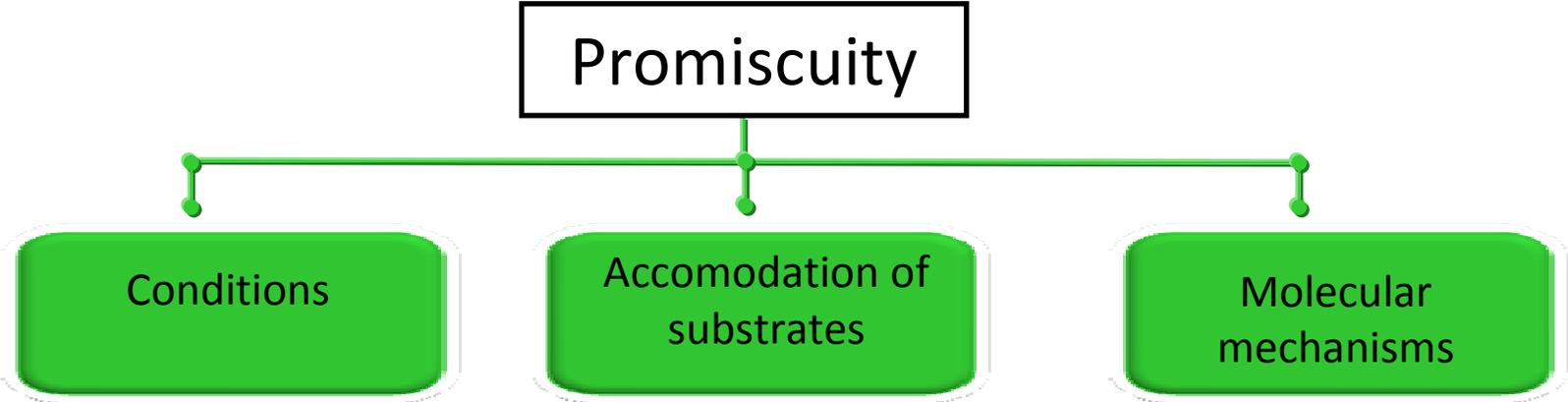


Biochemical networking: too complex?

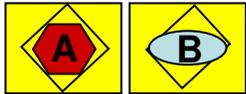
Size	KT2440	PAO1	Human	ENV. SAMPLE and HUMAN MICROBIOME
Species	1	1	1	> 20,000
Genome	6.18 Mbp	6.3 Mbp	3.4 Bbp	1-100 Gbp
mRNA & Proteome	5437	5570	25000	$\sim 10^{12}$
Metabolome	1482 reactions representing 1216 molecules and 838 enzymes	1576 reactions representing 1339 molecules and 876 enzymes	2250 reactions representing 1445 molecules and 2289 enzymes	$\sim 10^{12}$ reactions representing 10^5 molecules and 10^9 enzymes



Promiscuity: implications in biochemical networking



Differential expression



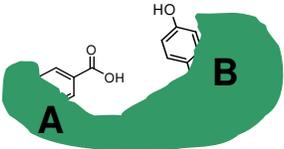
Partial recognition



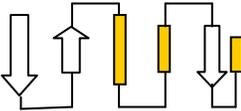
Flexibility and plasticity



Environmental



Multiple interactions



Fold



Concentration

Such evolution process may provide a significant competitive advantage in organisms thriving in environments containing complex “food” webs₈

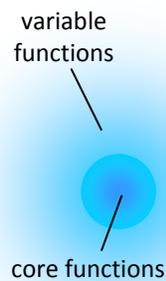
“-Omics” applied to promiscuity investigations

•(Meta-) DNA sequencing

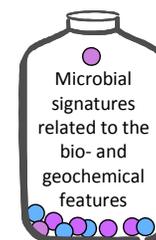


Genetic determinants

- Significant differences exist in single cells and communities under different environmental conditions



•HT 2D and shotgun (meta-) proteomics



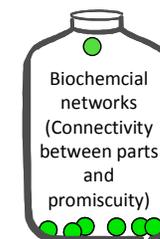
Proteomic determinants

- Significant differences
- Factors:
Co-lateral genetic effect, lifestyle, environmental stimuli

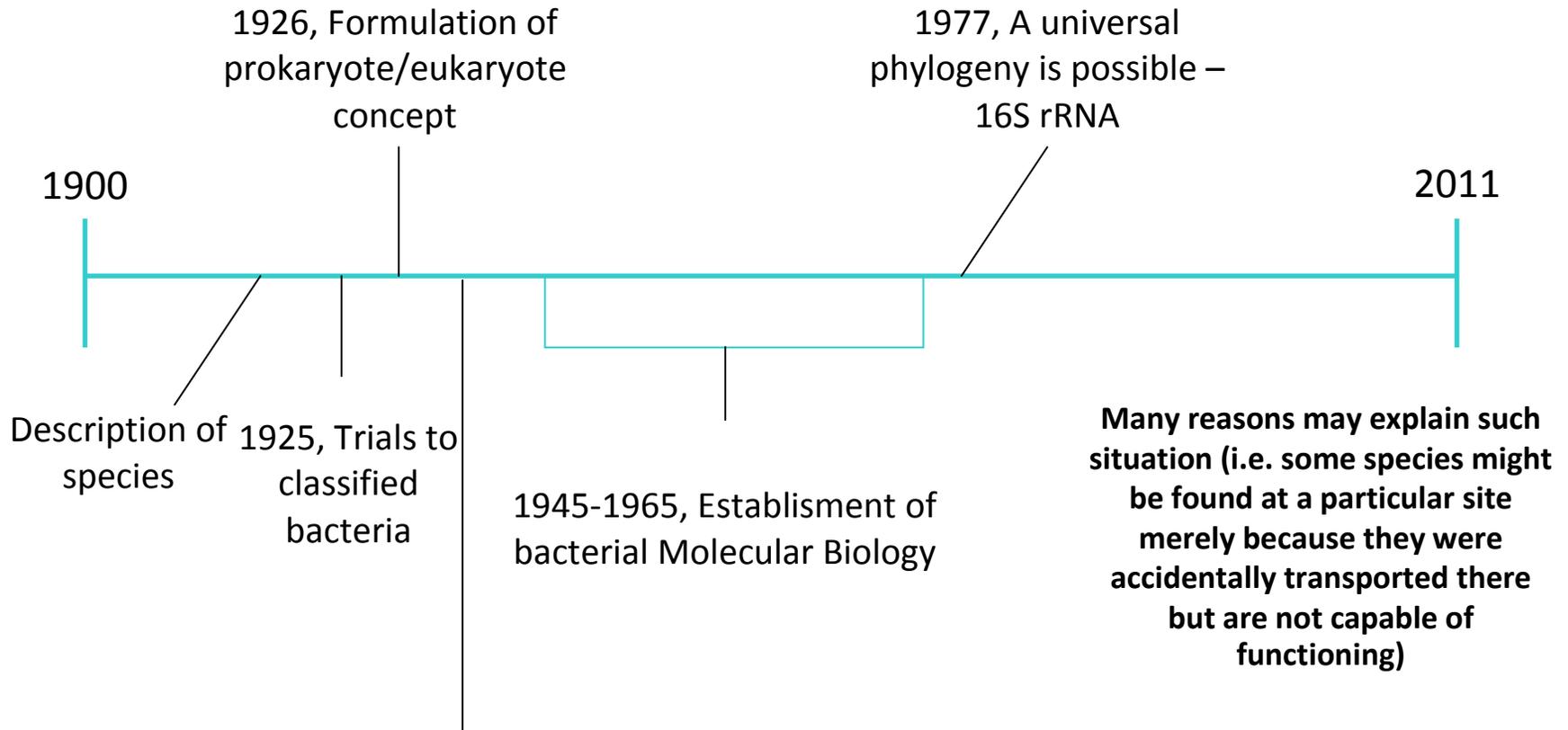
•HT metabolomic (HPLC, NMR, etc) •(Meta-)genomics

Biochemical network determinants

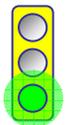
- Functional consequences?
- Functional equivalence?
- Promiscuous phenotypes remains unclear



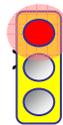
The history of “-Omics”



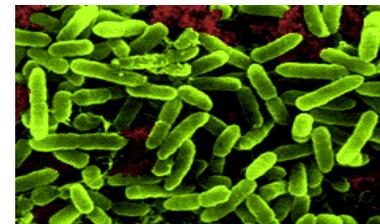
1935, Observation about micro-organisms



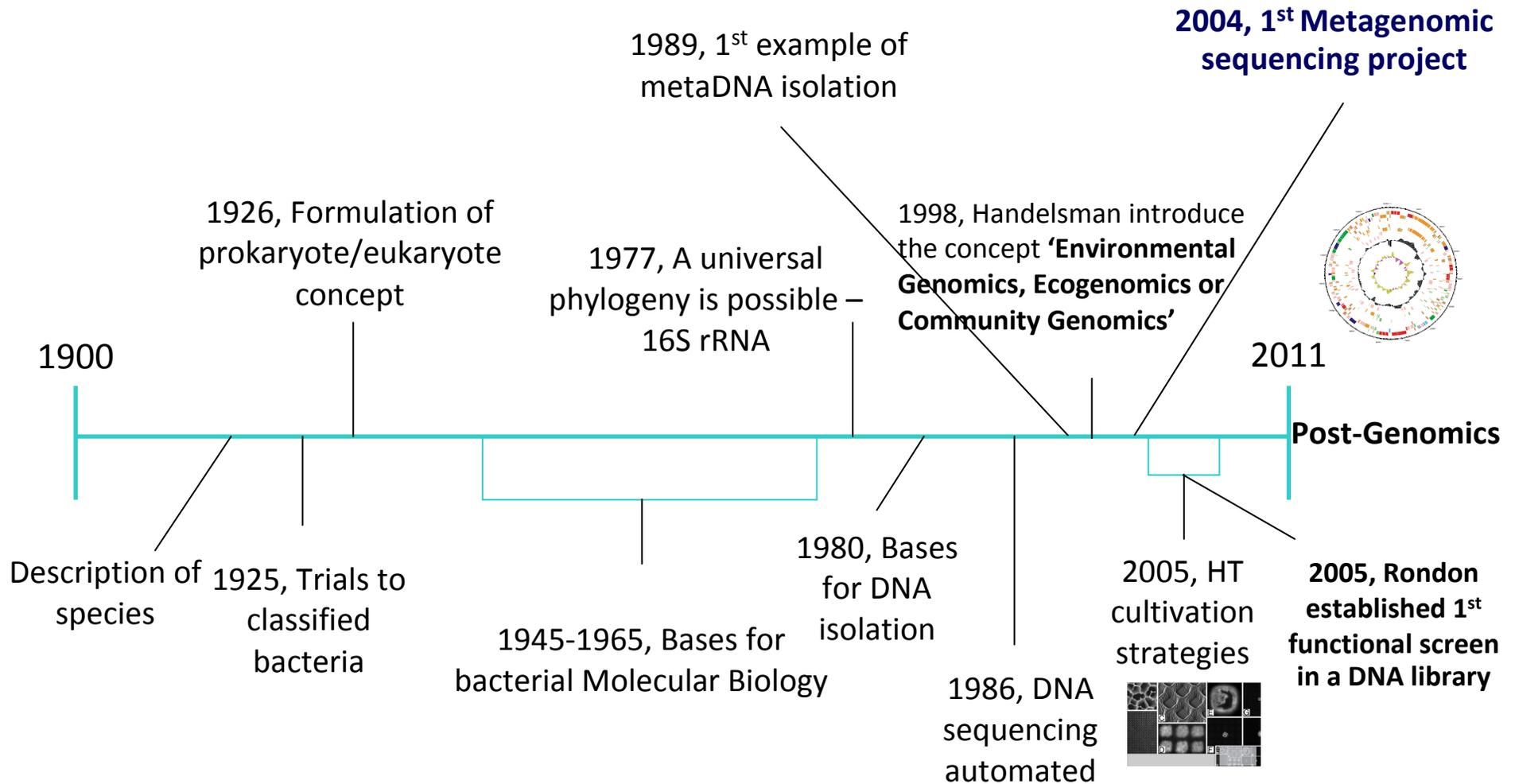
Abundance
Industrial supply



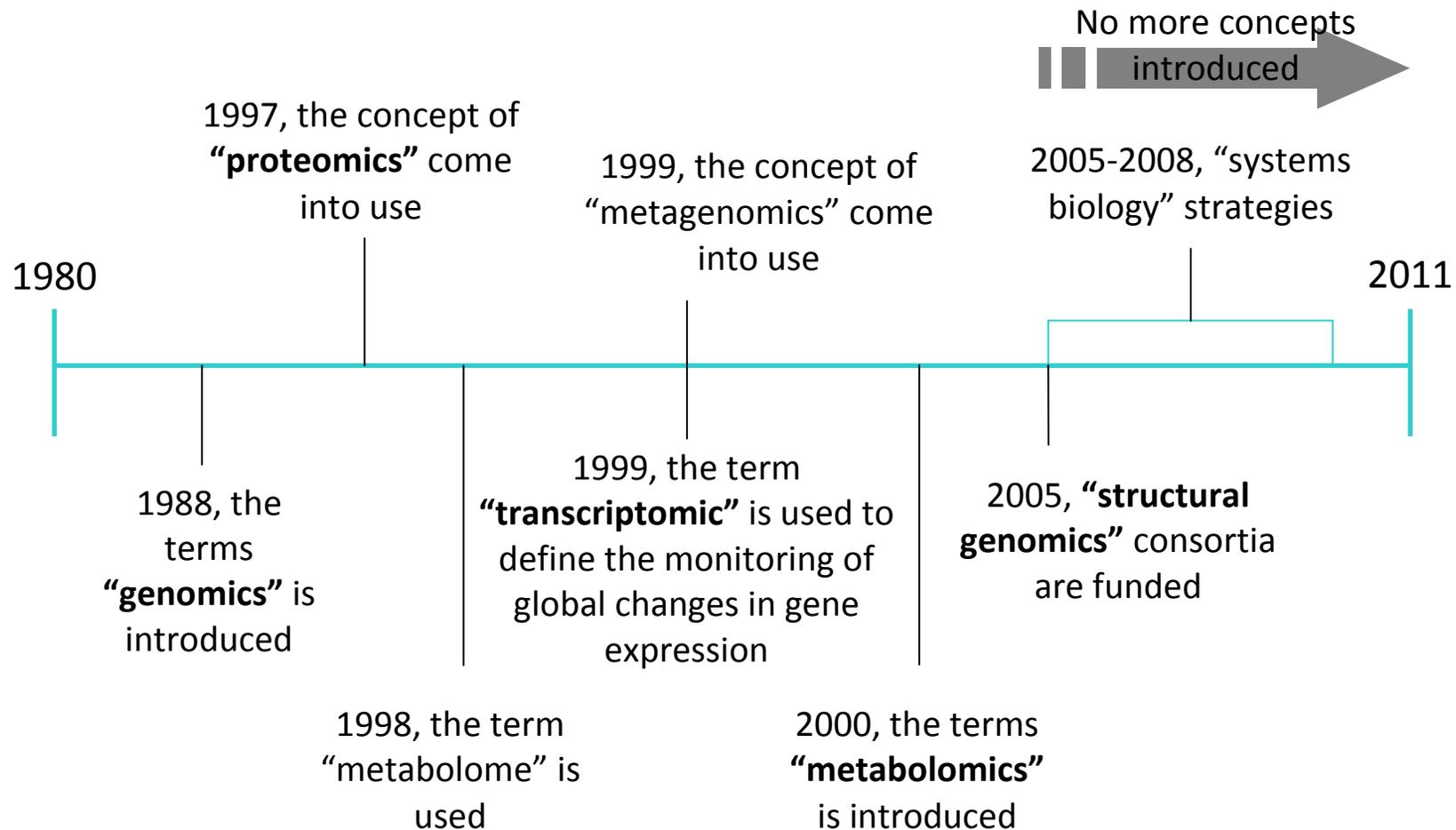
9% non-cultivable



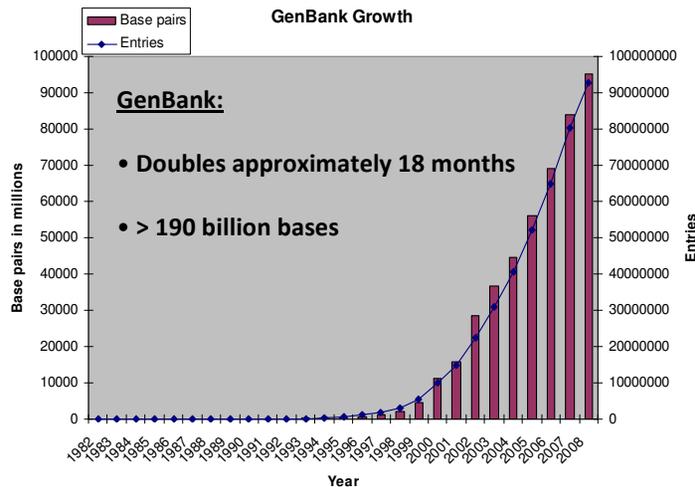
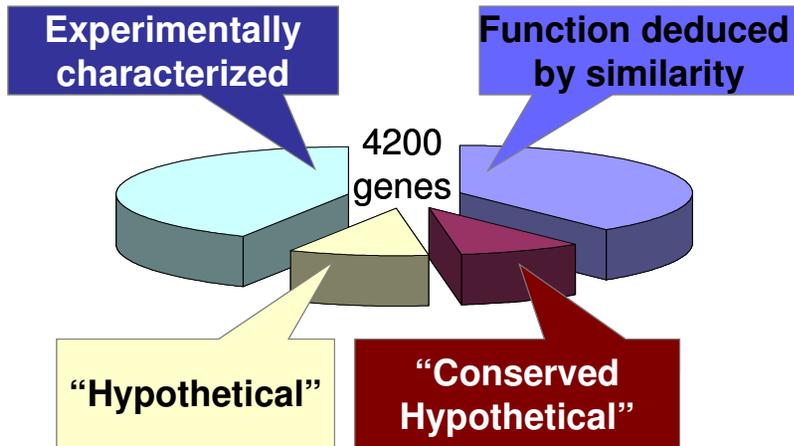
The history of “-Omics”



The history of “-Omics”



“-Omic” applied to promiscuity investigations



Problems of “-omic” investigations

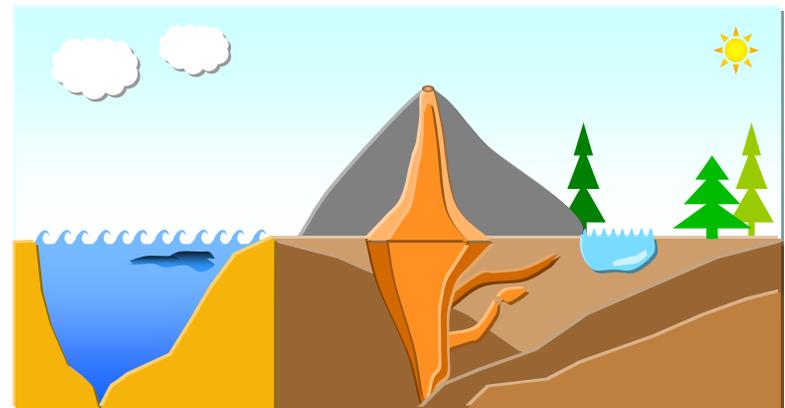
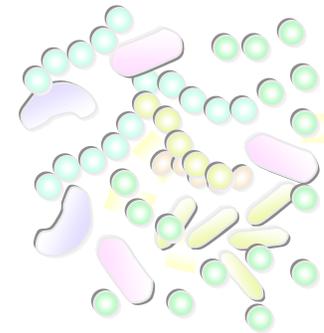
- The existing sequence resources have a valuable potential for bioinformatics-based screens
- There is a **serious problem** in relation to the **quality and degree of completeness of the annotation** of (meta-) genomes
- Majority of proteins will be never manually annotated
- Thus, **wrong annotations** in enzyme super-families containing multiple families that catalyse different reactions are a large problem that has been recognized
- Inferred **biochemical information** are **incomplete**
- **Mutations** at residues may provide variants from which **new specificities** can evolve

“-Omics” applied to promiscuity investigations

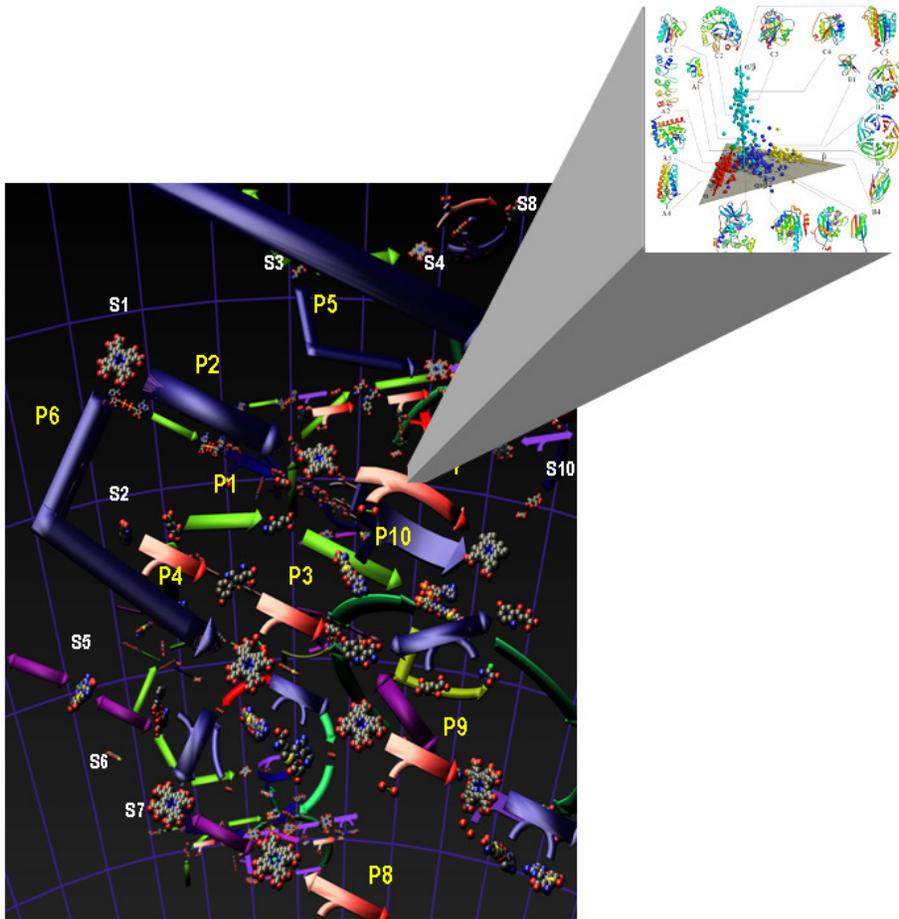
Outstanding Research Questions at microbial level:

- The relative abundance of a certain group of microorganisms is not necessarily linked to their importance in the community functioning
- Common organisms may not necessarily play a critical role in a community despite their numbers
 - Organisms that only muster 0.1% fraction can be of pivotal importance
- What is the “*functional*” complement in different organisms and how does it evolve?

“Some organisms are present in high numbers whereas others can be found at concentrations below 10 cells per gram of soil”



“-Omics” applied to promiscuity investigations



Outstanding Research Questions at enzymatic level:

- How is metabolism performed?
 - Principles of new metabolism
- How has evolution produced an incredible variety of metabolic activities from a limited number of ancestral activities?
- How do they evolve?
- Can “*environmental pressure*” forces “*alternative*” evolution pathways?
- Promiscuity and evolution

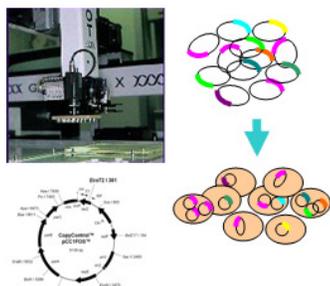
The function-driven analysis of (meta-) genomes guarantees identification of enzymes acting on defined substrates

To identify
niches of interest



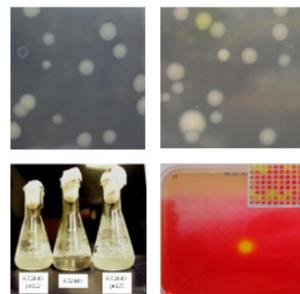
Distinct environmental
conditions

To isolate and
construct DNA libraries



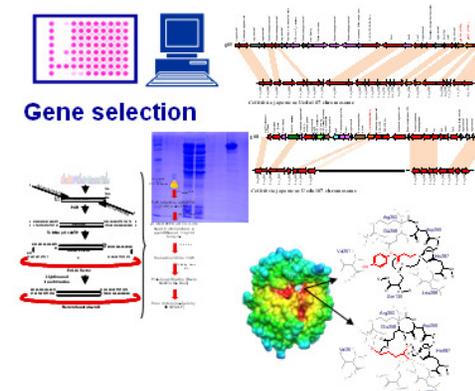
Distinct DNA nature,
vectors, libraries

To perform
HTP screens



Distinct solid
and liquid screens

To create collection of
(variant) enzymes



- Metagenomic is essential to create wide collections of ***a-la-carte* enzymes** for both basic research and industrial applications
- In terms of basic research metagenomic can be applied to find **promiscuos enzymes** able to perform chemically different reactions