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Future -omics developments

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National and Kapodistrian
University of Athens

Brussels October 2016, ERA-NET MBT

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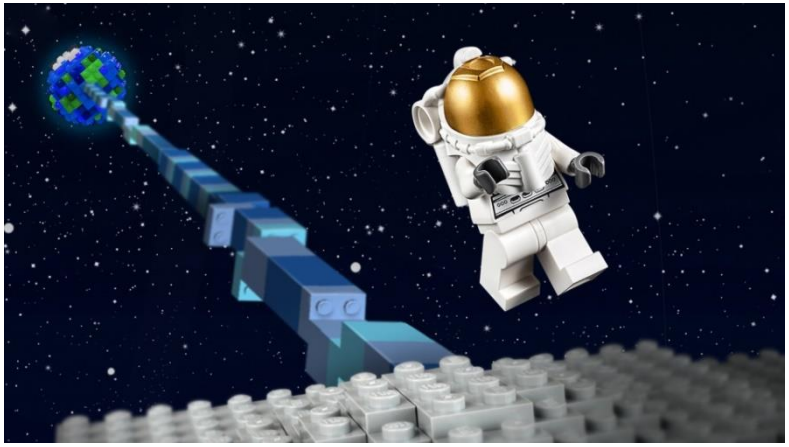
Where do we stand?



Points to work

- An **aging population** mainly in Europe/USA - **HEALTH**
- Consumption continuously increasing/**waste production** - **ENVIRONMENTAL DEGRADATION**
- **Exhaustive use of natural sources** - **RESOURCES**
- Huge differences in **food access/poverty rates –LIMITED ACCESS**

Where do we want to be?

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ERA-NET MBT

ROADMAP

- Exploration of the marine environment
- Support biomass production and processing
- Contribute to product innovation and differentiation
- Enabling technologies and infrastructure
- Providing policy support and stimulation

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MARINE ORGANISMS

✓Described land species ~ 1.5 million (85%)

✓Described marine species ~ 250,000

✓There are more phyla and classes in the oceans (of 33 animal phyla, 21 exclusively marine, only 1 terrestrial)

Biodiversity

TYPE OF ECOSYSTEM	TYPE OF ORGANISM	TYPE OF ZONATION	TYPE OF TROPHIC RELATIONSHIP
* *Deep sea*	* *Plankton*	* *Neritic*	* *Autotrophs*
* *Cold coral reefs*	* *Nekton*	* *Epipelagic*	* *Heterotrophs*
* *Seamounts*	* *Benthos*	* *Photic*	
* *Pelagic ecosystems*		* *Mesopelagic*	
* *Coastal waters*		* *Bathypelagic*	
* *Intertidal ecosystems*		* *Aphotic*	
* *Estuaries*		* *Abyssopelagic*	
		* *Hadal*	

The exploration of marine ecosystems has only began in the mid 1970

Mar. Drugs 2014, 12, 1066-1101; doi:10.3390/md12021066

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OMICS TECHNOLOGIES

GENOMICS

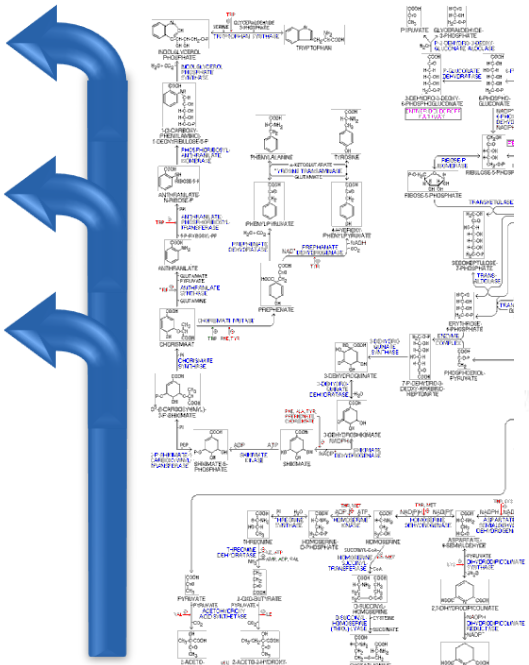
TRANSCRIPTOMICS

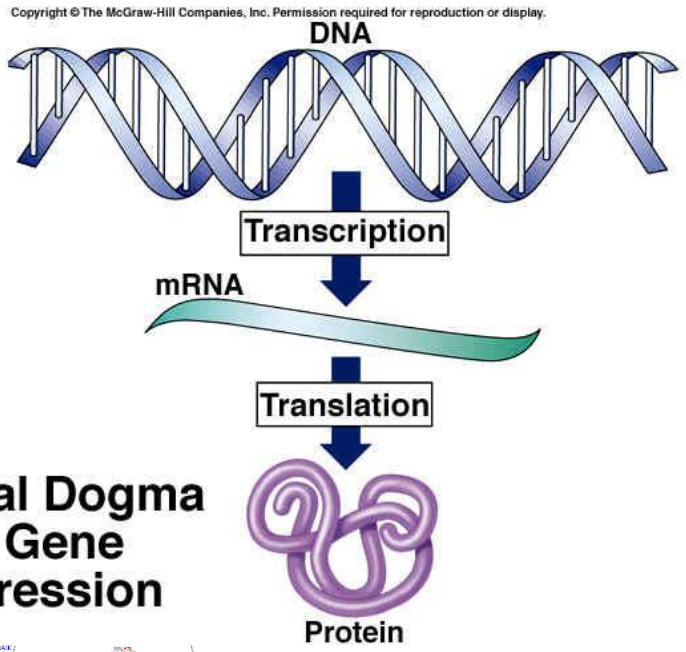
PROTEOMICS

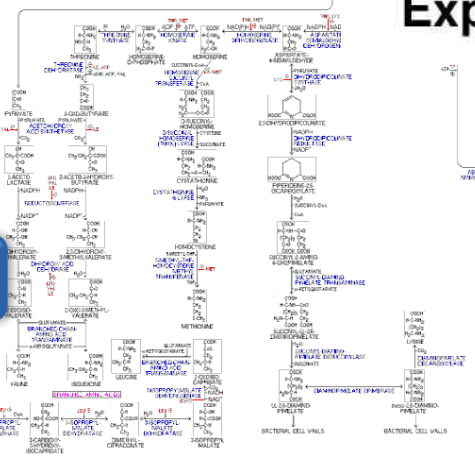
METABOLOMICS

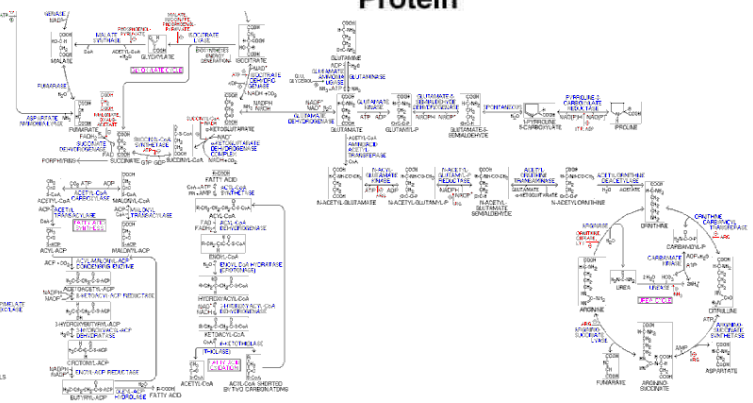
PHENOTYPE

ENVIRONMENT









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MARINE –OMICS APPLICATIONS

➢ GENOMICS

The life aquatic: advances in marine vertebrate genomics

Joanna L. Kelley, Anthony P. Brown, Nina Overgaard Therkildsen & Andrew D. Foote

Affiliations | Corresponding author

Nature Reviews Genetics **17**, 523–534 (2016) | doi:10.1038/nrg.2016.66

METAGENOMICS

Marine genomics goes viral

Linda Koch

Nature Reviews Genetics (2016) | doi:10.1038/nrg.2016.130

Published online 03 October 2016

- **HAB**s are present in nearly all aquatic environments as naturally occurring phenomena

ARTICLE

Received 5 Sep 2013 | Accepted 14 Mar 2014 | Published 16 Apr 2014

DOI: 10.1038/ncomms4652

Forensic genomics as a novel tool for identifying the causes of mass mortality events

Pierre De Wit[1,2], Laura Rogers-Bennett[3], Raphael M. Kudela[4] & Stephen R. Palumbi[1]

- More than 1/3 **of Reef building corals** threatened with extinction

Genomic basis for coral resilience to climate change

Daniel J. Barshis[1,2], Jason T. Ladner, Thomas A. Oliver, François O. Seneca, Nikki Traylor-Knowles, and Stephen R. Palumbi

Department of Biology, Hopkins Marine Station, Stanford University, Pacific Grove, CA 93950

PNAS | January 22, 2013 | vol. 110 | no. 4 | 1387–1392

MARINE –OMICS APPLICATIONS

- **PROTEOMICS**
  - Existing methodological limitations
  - Non-model organisms
  - Lack of the proteomes of species commonly used in aquaculture

Proteomics for the authentication of fish species
Journal of Proteomics, Volume 147, 2016, 119–124

MARINE –OMICS in DRUG DISCOVERY

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Mar. Drugs **2014**, *12*(6), 3416-3448; doi:10.3390/md12063416

Open Access

Article

Metabolomic Tools for Secondary Metabolite Discovery from Marine Microbial Symbionts

Lynsey Macintyre [1,*], Tong Zhang [1], Christina Viegelmann [1], Ignacio Juarez Martinez [1], Cheng Cheng [1,2], Catherine Dowdells [1], Usama Ramadan Abdelmohsen [2], Christine Gernert [2], Ute Hentschel [2] and RuAngelie Edrada-Ebel [1,*]

Mar. Drugs **2014**, *12*(6), 3681-3705; doi:10.3390/md12063681

Open Access

Article

Accurate Dereplication of Bioactive Secondary Metabolites from Marine-Derived Fungi by UHPLC-DAD-QTOFMS and a MS/HRMS Library

Sara Kildgaard, Maria Mansson, Ina Dosen, Andreas Klitgaard, Jens C. Frisvad, Thomas O. Larsen and Kristian F. Nielsen *

Microbial Strain Prioritization Using Metabolomics Tools for the Discovery of Natural Products

Yanpeng Hou†, Doug R. Braun†, Cole R. Michel†, Jonathan L. Klassen‡, Navid Adnani†, Thomas P. Wyche†, and Tim S. Bugni*†

† Pharmaceutical Sciences Division, School of Pharmacy, University of Wisconsin, Madison, Wisconsin 53705, United States

‡ Department of Bacteriology, University of Wisconsin, Madison, Wisconsin 53705, United States

Anal. Chem., **2012**, *84* (10), pp 4277–4283

DOI: 10.1021/ac202623g

Challenging issue for metabolomics analysis of marine organisms is the **high number of compounds** with unknown structures

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INTEGRATIVE OMICS

DNA- protein, protein-protein and protein-ligand interactions

GENOMICS

TRANSCRIPTOMICS

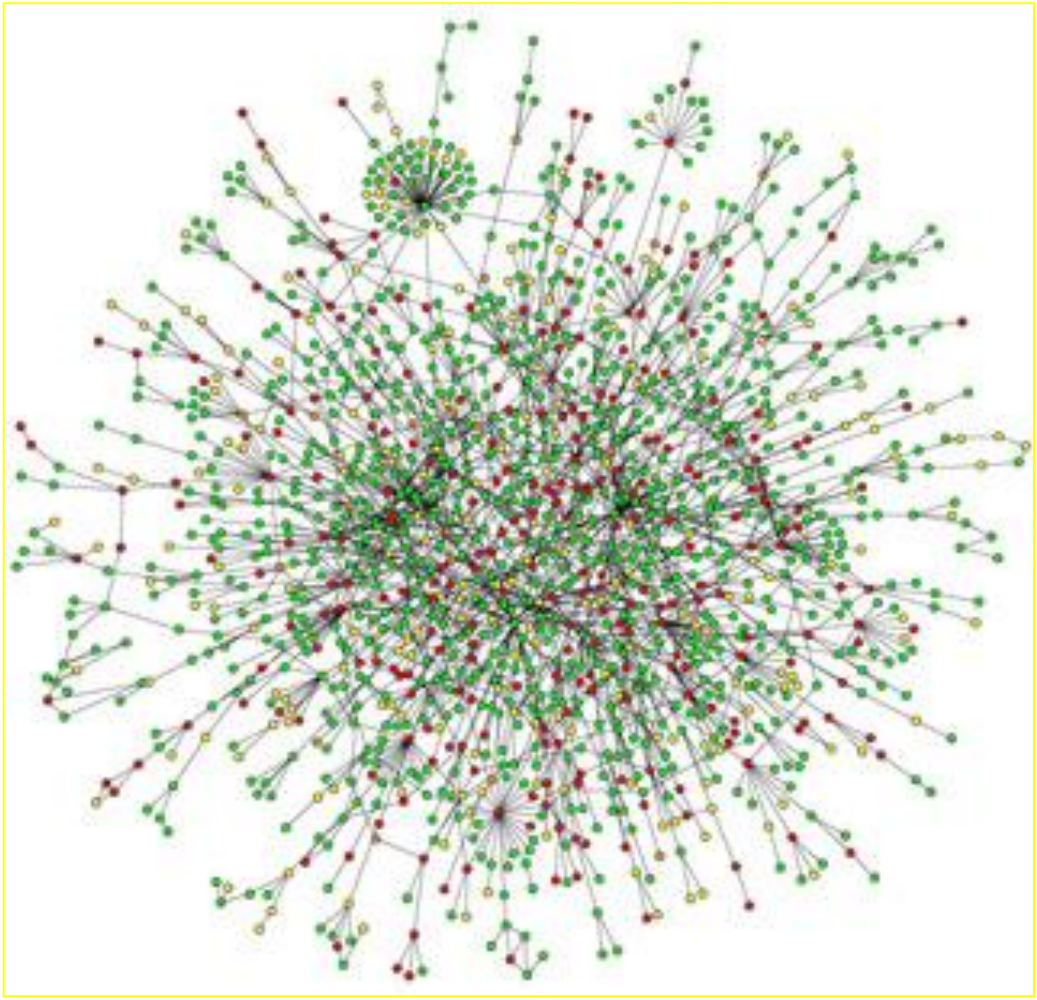
PROTEOMICS

METABOLOMICS

PHENOTYPE

INTERACTOMICS

ENVIRONMENT



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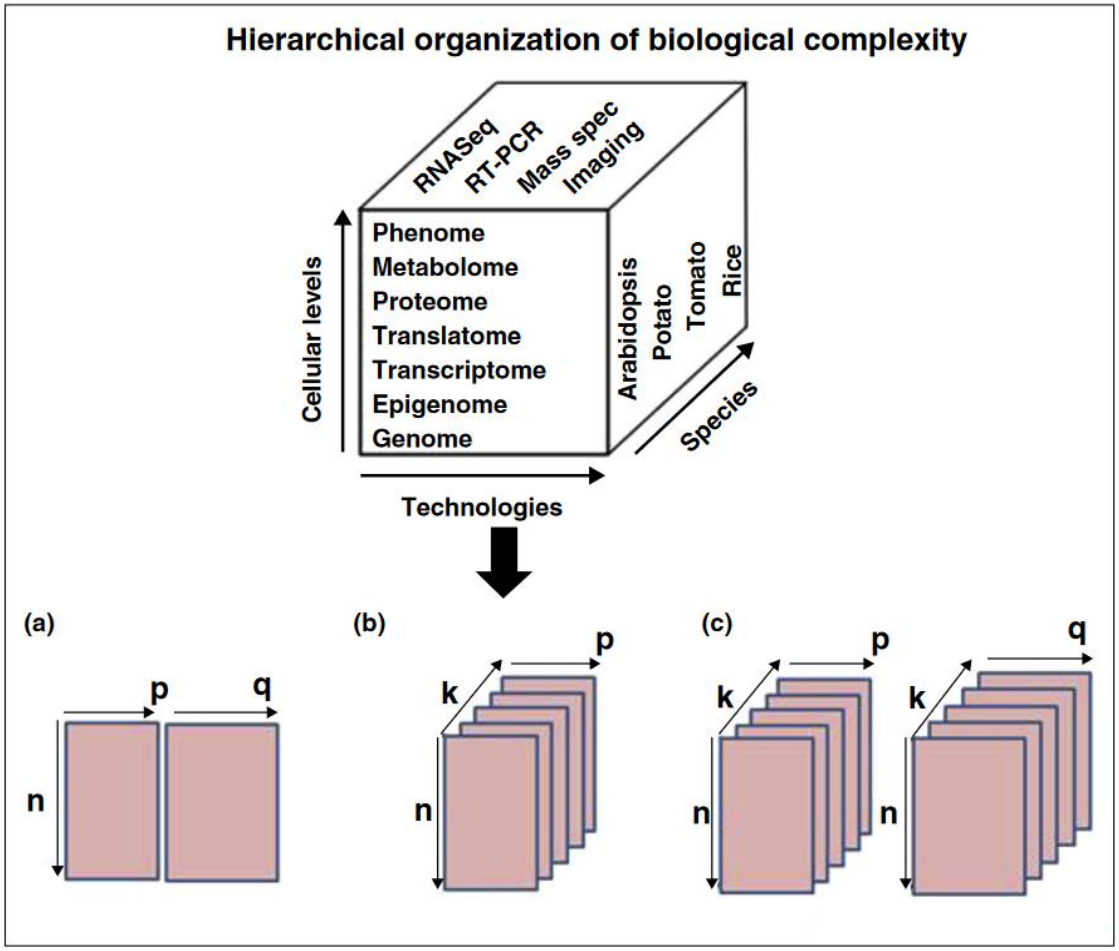
INTEGRATIVE OMICS

1+1>2

Systems biology is based on the understanding that the whole is greater than the sum of the parts

<u>Statistical Correlation of Heterogeneous Data</u>

- **Detection of hidden features**
- **Explore new dimension of data space**



Current Opinion in Plant Biology 2016, 30:57–61

PROPER DESIGN OF EXPERIMENTS

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CASE STUDY

A success story of the correlation of heterogeneous data

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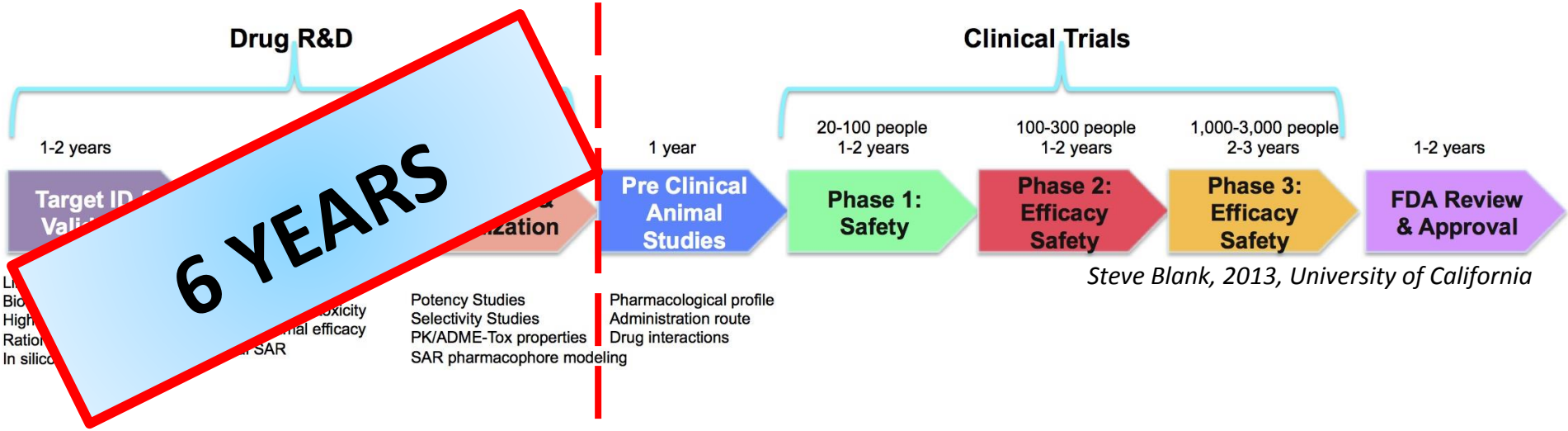
DISCOVERY OF NOVEL NATURAL PRODUCTS

Drug discovery pipeline:



Steve Blank, 2013, University of California

t=0

- **Pure Compounds**
- **Compound Libraries**
- **High Throughput Computer Automated Screening**

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DISCOVERY OF NOVEL NATURAL PRODUCTS

Biological evaluation

Biological evaluation

Raw material

Extraction

Fractions

Isolation

Identification

Pure compounds

Active NP

Challenges

- Complex Extracts
- Low concentration / Big concentration variance
- Diverse Structures

Advance Analytical Techniques

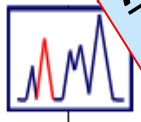
- Isolation - Chromatographic
- Identification - Spectroscopic

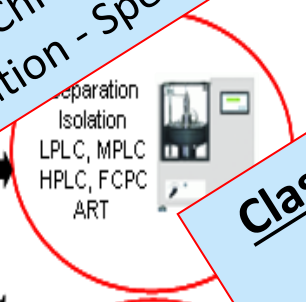
Classical pipeline pitfalls

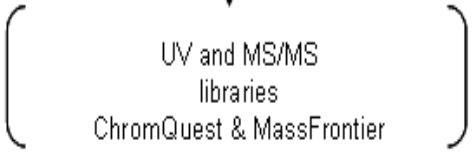
Expensive

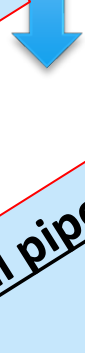
Laborious

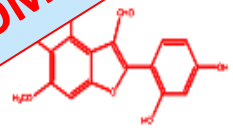
KNOWN COMPOUNDS











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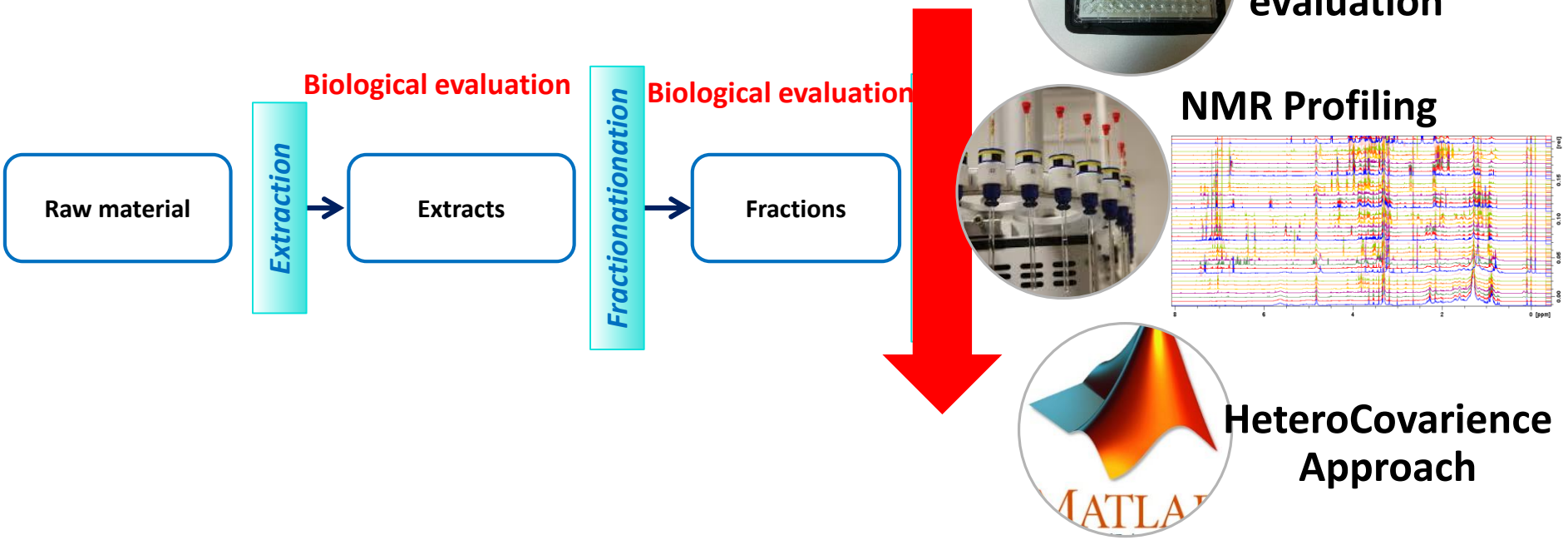
DISCOVERY ACCELARATION

Dereplication methods have been emerged aiming to rationalize the entire discovery process

How –omics tools can accelerate our efforts from research bench to new products of natural origin?

Skip the classical pipeline



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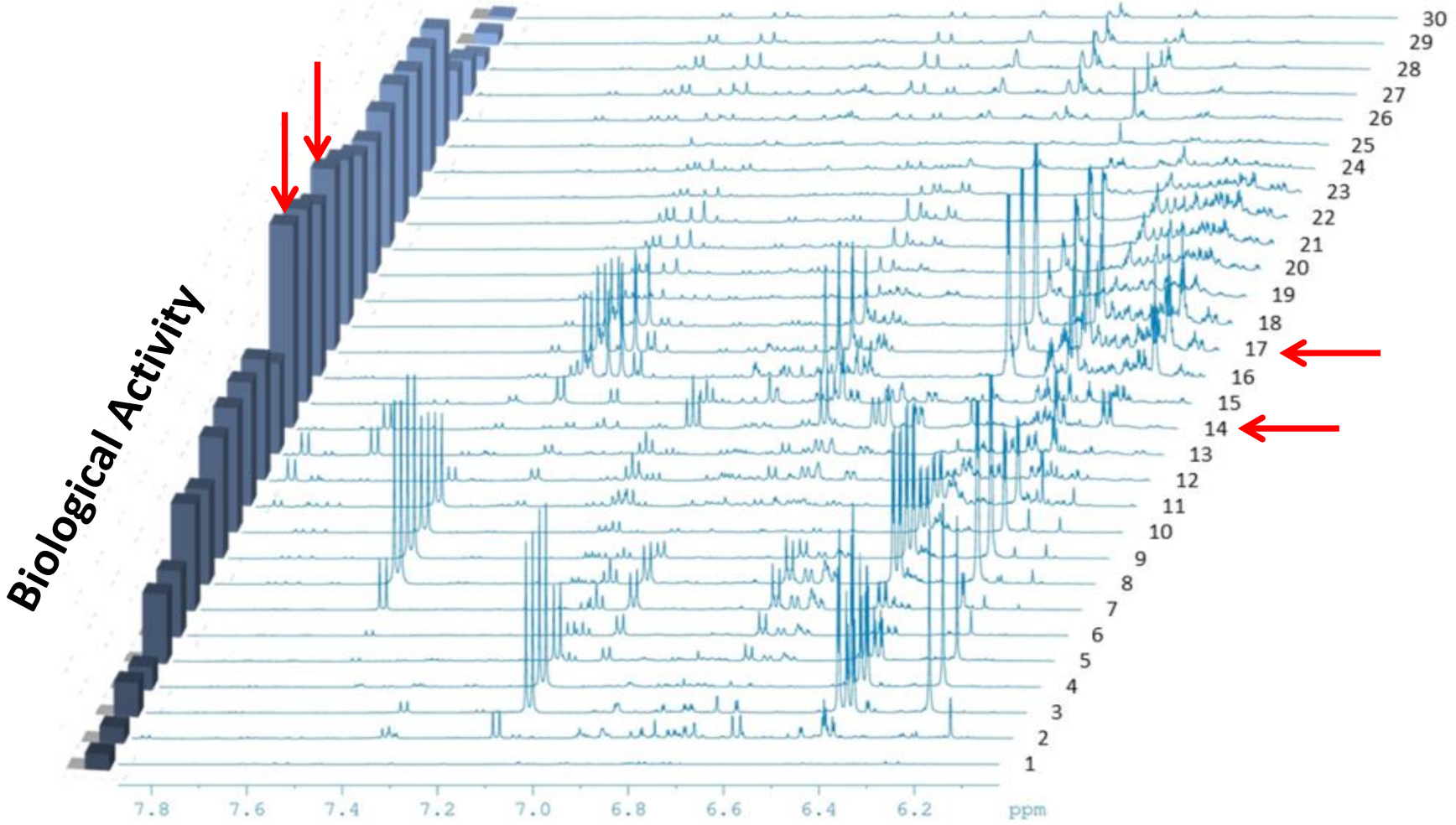
HeteroCovariance Approach

Spectroscopic Features (NMR)



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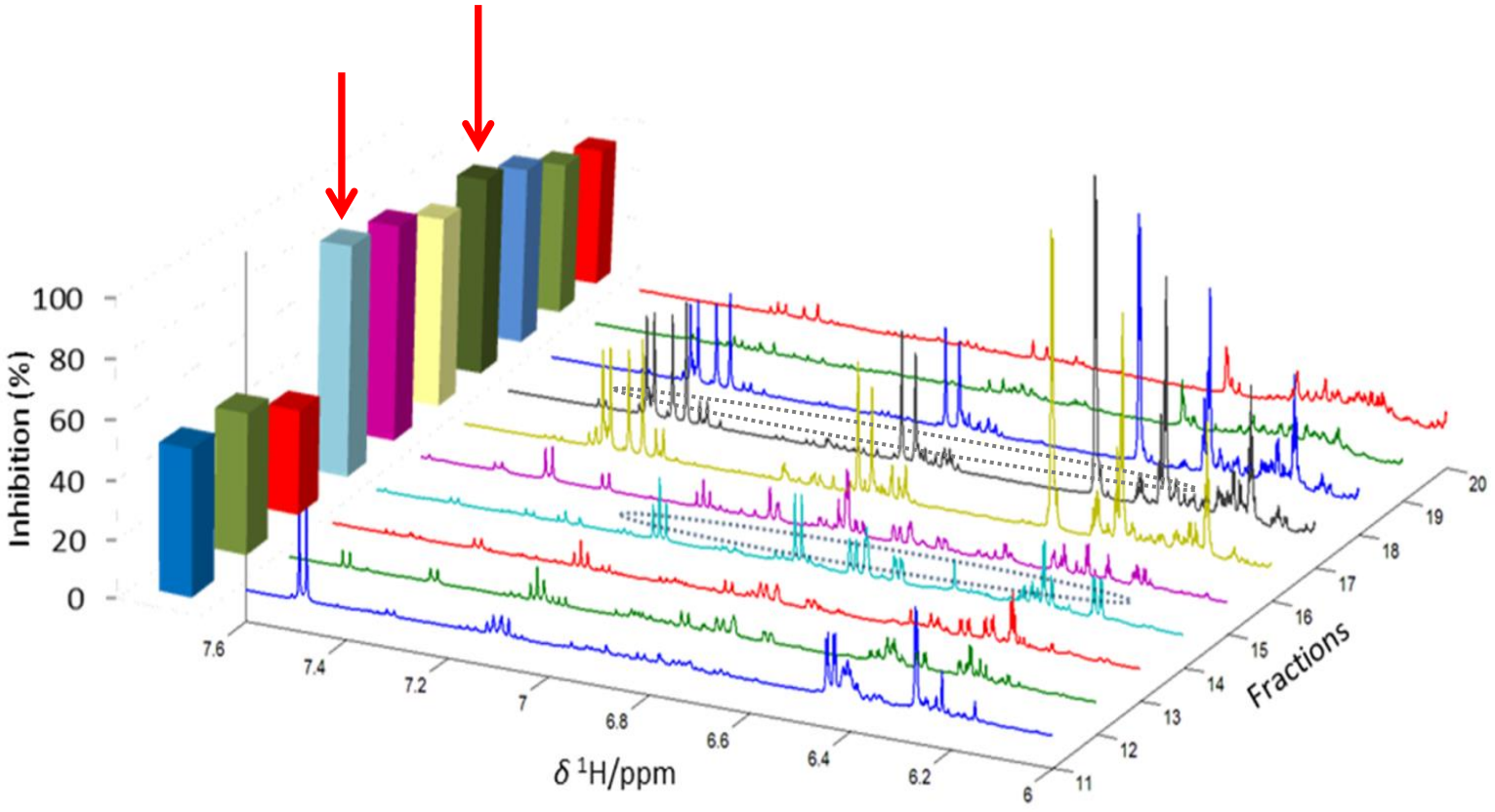
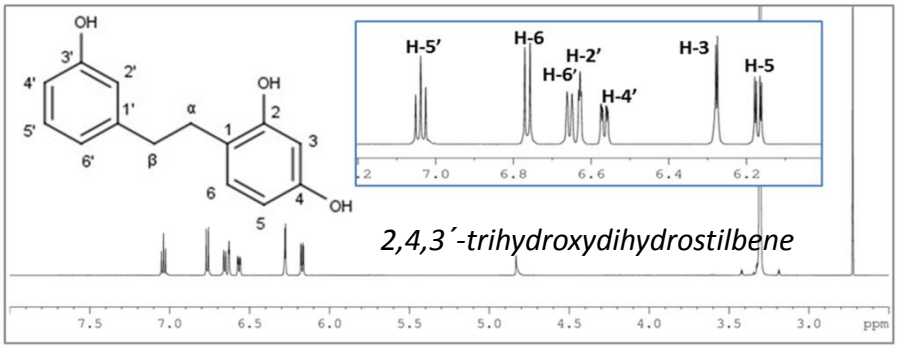
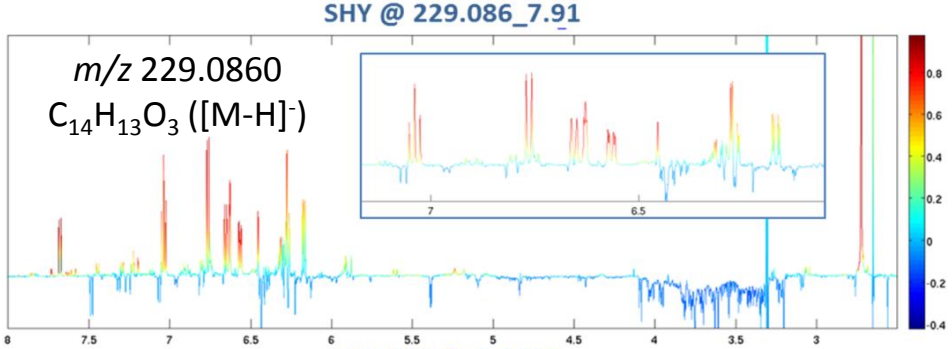
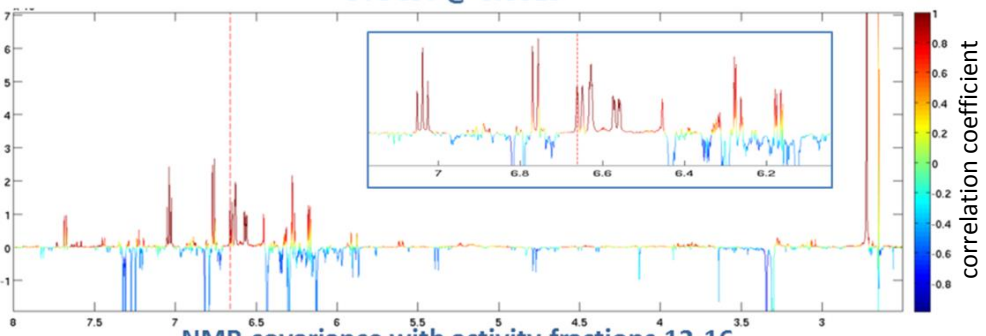
HeteroCovariance Approach (HetCA)

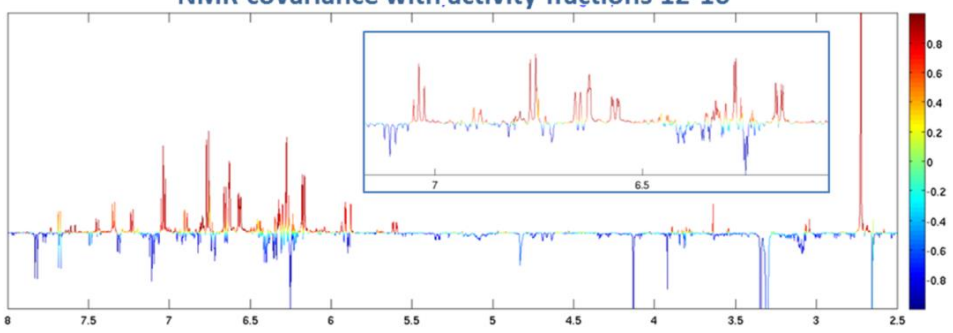


HetCA TOOLBOX

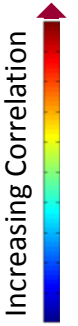








- **Statistical HeterospectroscopY**
  (SHY, NMR – MS)
- **Statistical Total Correlation Spectroscopy**
  (STOCSY, NMR-NMR)
- **Hetero Covariance Approach**
  (HetCA, Spectr. Features – Activity)



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HetCA TOOLBOX

HetCA unmasks minor compounds with major activity from complex mixtures!

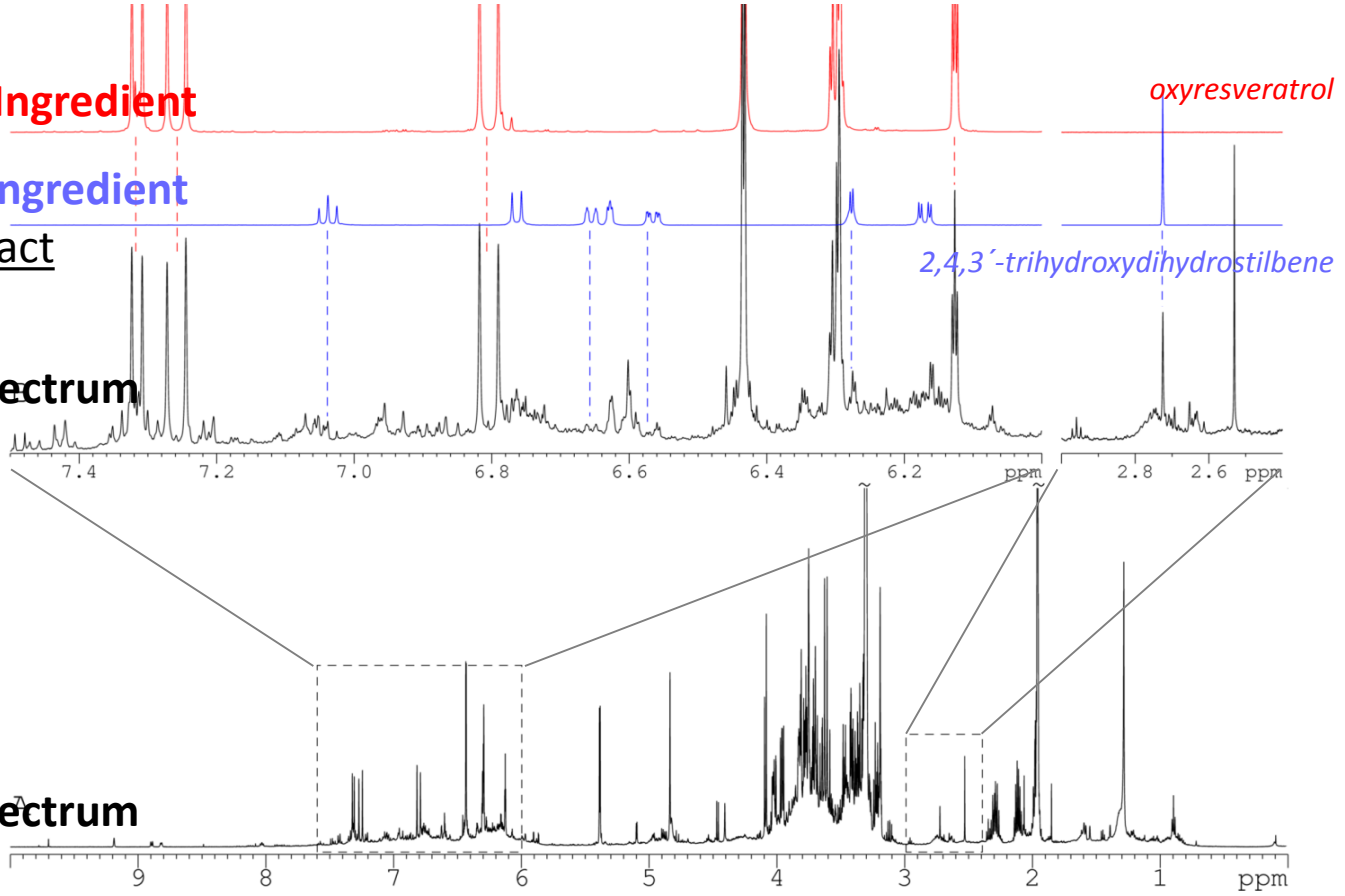
High Concentration Active Ingredient

Low Concentration Active Ingredient

<1% of the total extract

total extract 1D ^{1}H NMR spectrum

total extract 1D ^{1}H NMR spectrum



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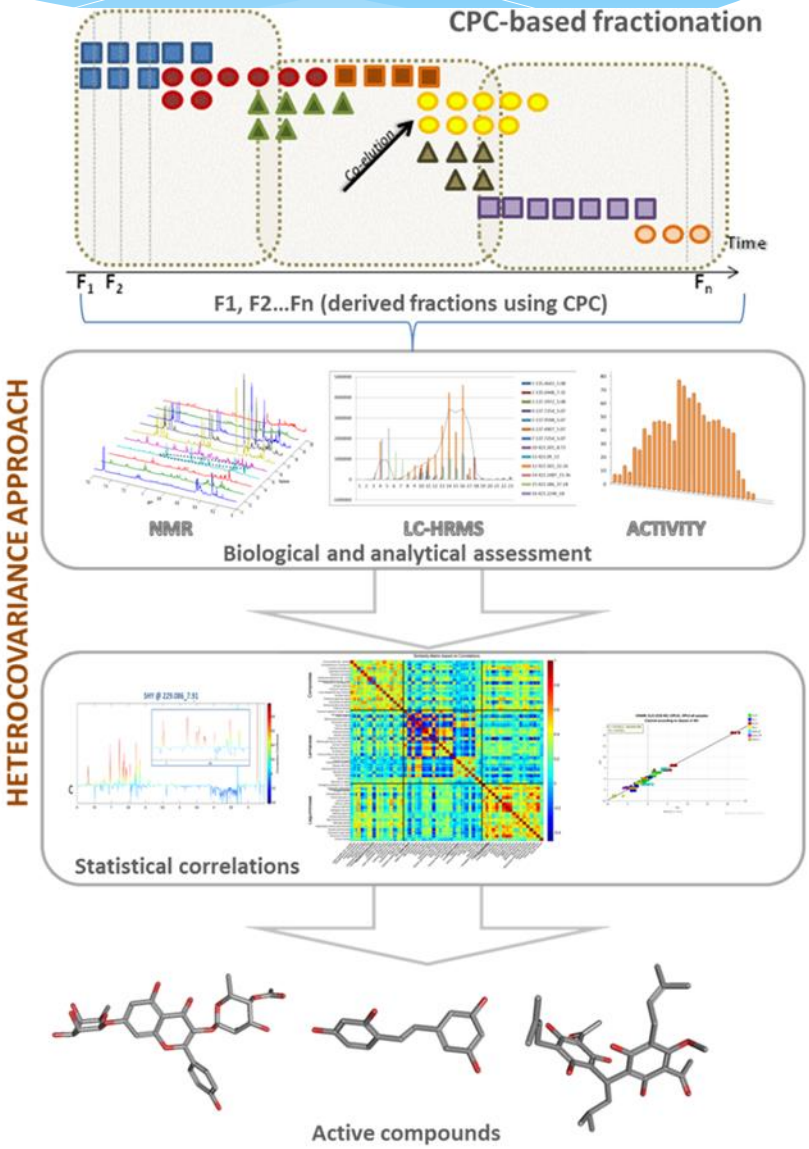
HetCA TOOLBOX

- **Create an Artificial Variance**
- **Statistical correlation of heterogeneous data**
- The **same spectral data** can be utilized for screening against any **possible pharmacological target** or any other **dose dependent property** on the basis of the HeteroCovariance Approach
- This highly innovative activity-based-metabolite-profiling approach can dramatically **accelerate the discovery of active natural products** challenging global biodiversity and chemodiversity



Aligiannis et al., ChemistrySelect 2016; 1(10): 2531–2535

Tascmar

Tools **A**nd **S**trategies to access original bioactive compounds from **C**ultivation of **MAR**ine invertebrates and associated symbionts

Coordinator; CNRS

Budget: 6.7 Million euros

13 partners (100 researchers), among which 6 industrials

Project duration: 4 years starting the 1st April 2015

Participating countries: France, Greece, Israel, Germany, Italy, Spain, Sweden, Thailand

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AVAILABLE TOOLS

✓ We have the tools

- Advance analytical techniques (NMR, uHPLC-HRMS, bioautographic HPTLC, etc)

- **Compound Libraries**
  - **Lack of NMR spectra**
  - **MS annotations**
  - **Non user-friendly**

MarinLit
A database of the marine natural products literature

ANTIBASE 2014
The Natural Compound Identifier

Search My Searches My Account Help Tour
Dictionary of Marine Natural Products

- Bioinformatics - "Big Data Era"

GitHub

MZmine 2

mix Omics

Exploration and Integration of Omics datasets

R

MATLAB
The Language of Technical Computing

Xcms

METLIN

SIMCA
BY UMETRICS

Bioconductor
OPEN SOURCE SOFTWARE FOR BIOINFORMATICS

MetaboAnalyst 3.0

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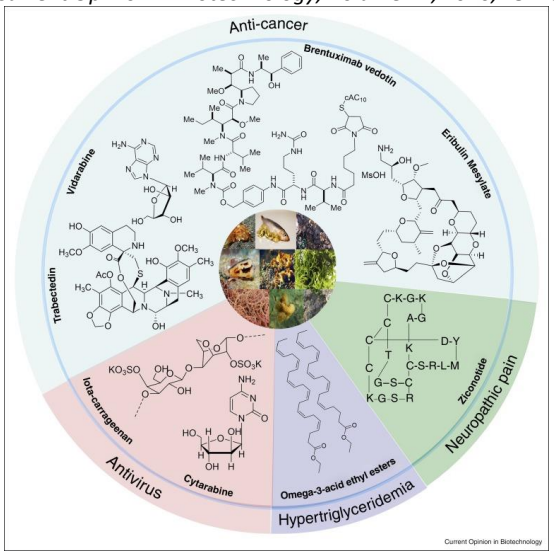
FUTURE PROPOSAL

Current Opinion in Biotechnology, Volume 42, 2016, 13–23

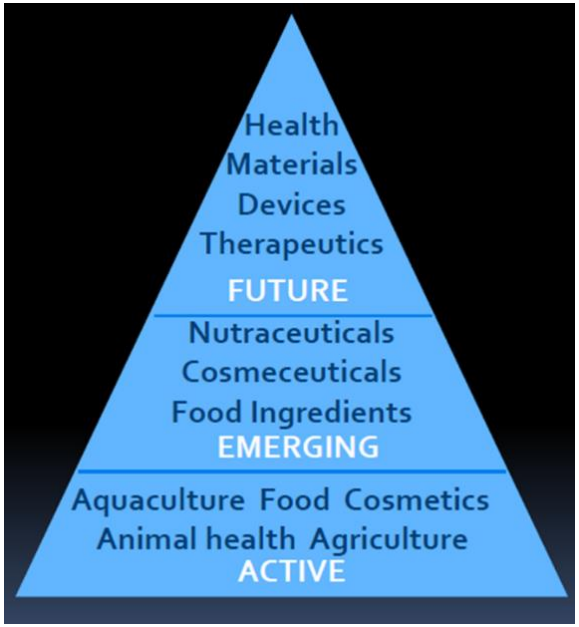


- **Only 8 Drugs of marine origin have been approved by FDA and EMA in *ca.* 40 years**

✓ **Smart connection of Heterogeneous Data**

✓ **Interdisciplinary Collaborations**

✓ **Fast Productive Solutions**



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Thank you for your attention