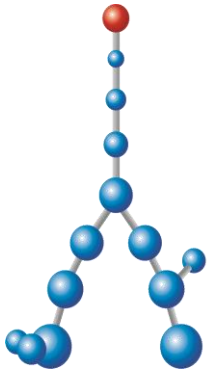


DSTF

Dipartimento di Scienza e Tecnologia del Farmaco

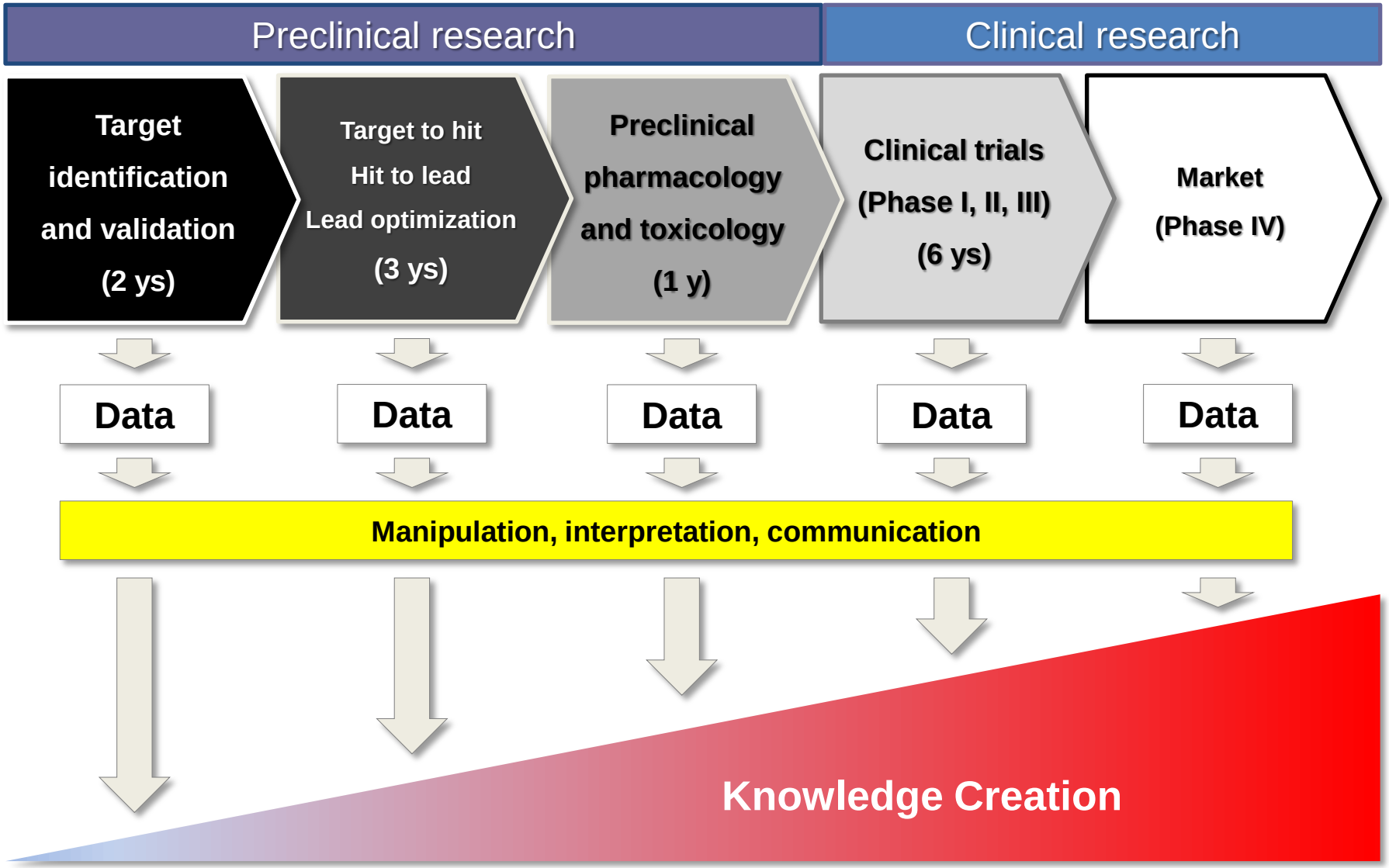
UNIVERSITÀ DEGLI STUDI DI TORINO

Il Calcolo Scientifico nella Ricerca sul Farmaco

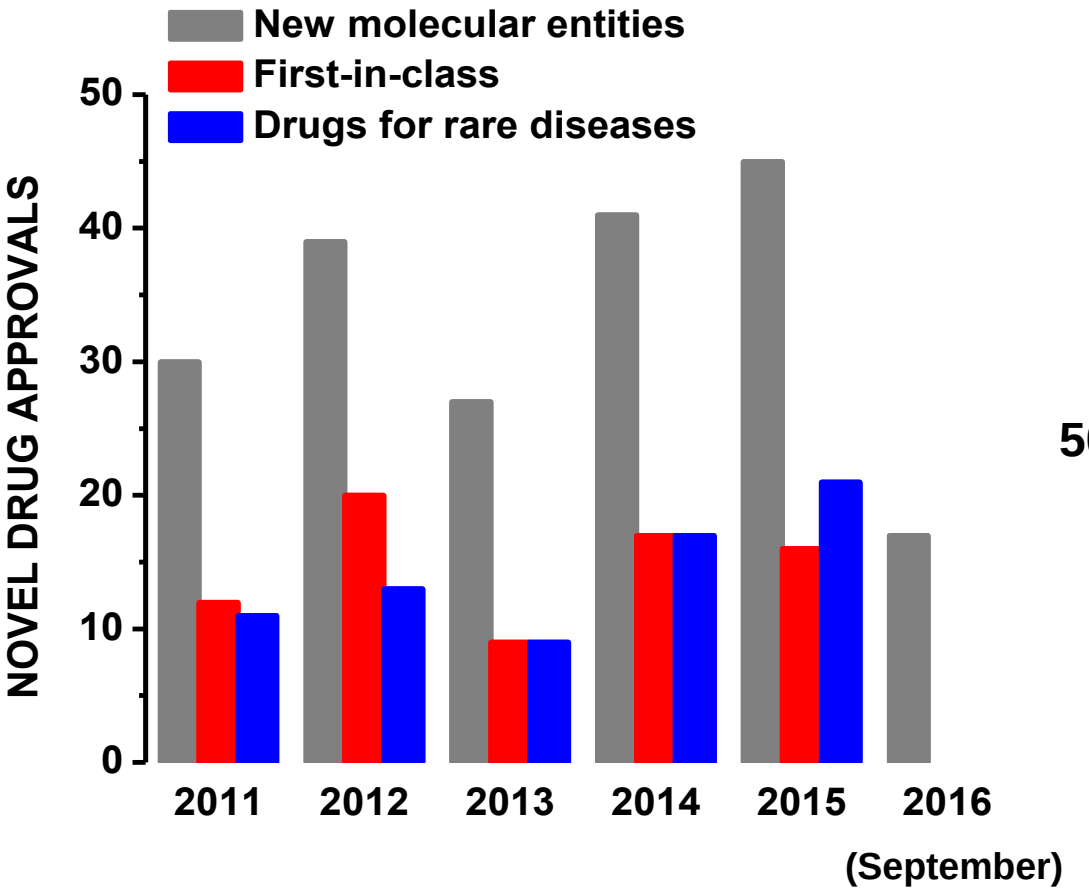
Gianluca Miglio

7 ottobre 2016

Drug Discovery & Development



Number of new molecular entities (FDA)



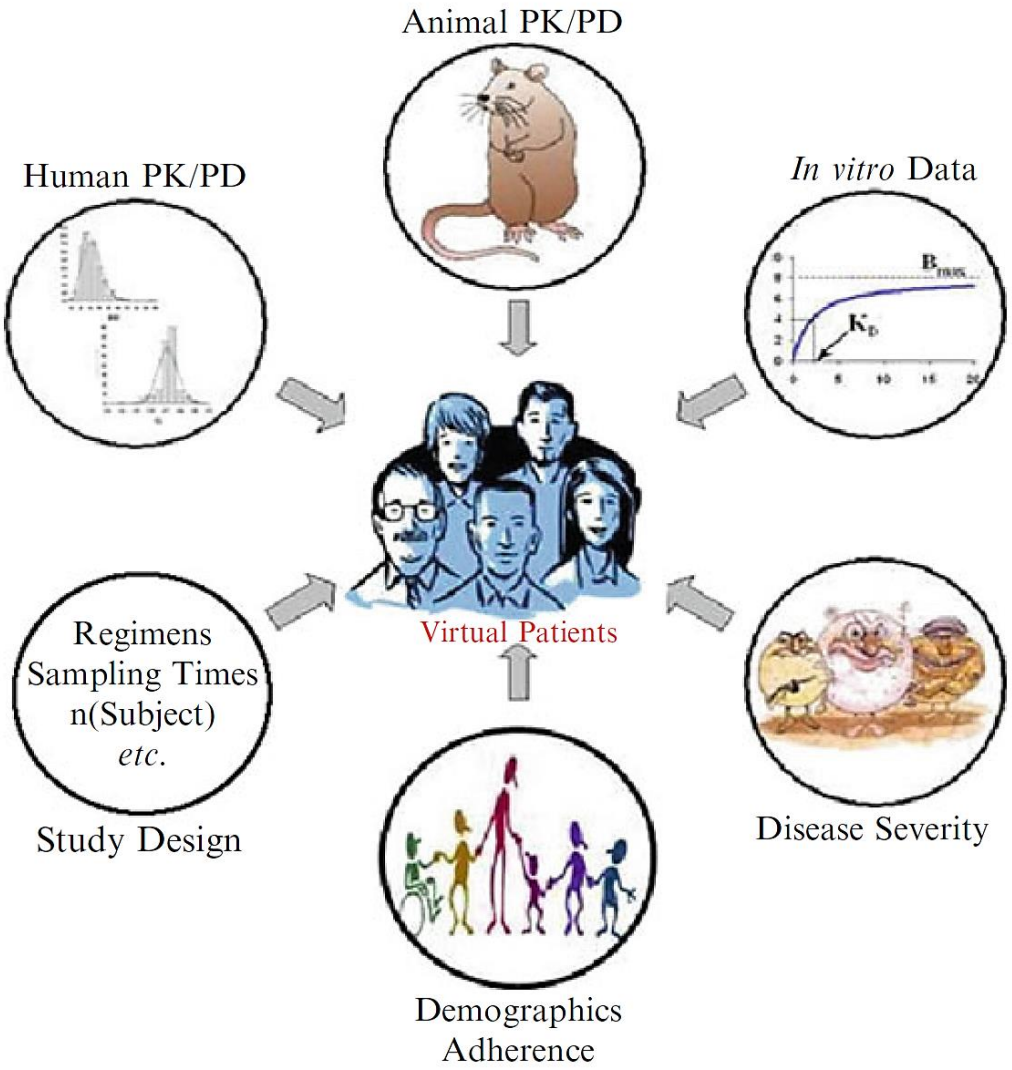
50 MLD $ / y

www.fda.gov

"…Not enough applied scientific work has been done to create *new tools to get fundamentally better answers about how the safety and effectiveness of new products* can be demonstrated in faster time frames, with more certainty, and at lower costs. . . . A new product development toolkit—containing powerful new scientific and technical methods such as animal or ***computer-based predictive models***, biomarkers for safety and effectiveness, and new clinical evaluation techniques—is urgently needed *to improve predictability and efficiency along the critical path from laboratory concept to commercial product*. We need superior product development science to address these challenges..."

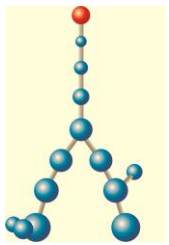
– FDA (2004)
Challenge and Opportunity on the Critical Path to New Products

Clinical Trial Simulations



Kimko and Peck, 2011

Department of Drug Science and Technology



Medicine

Biology and System Biology

Informatics and Bioinformatics

Analytical Chemistry

Biochemistry and Molecular Biology

Physics

Medicinal Chemistry

Organic Chemistry

Pharmaceutical Biology and Food Chemistry

Pharmaceutical Technologies and Cosmetics

Physiology

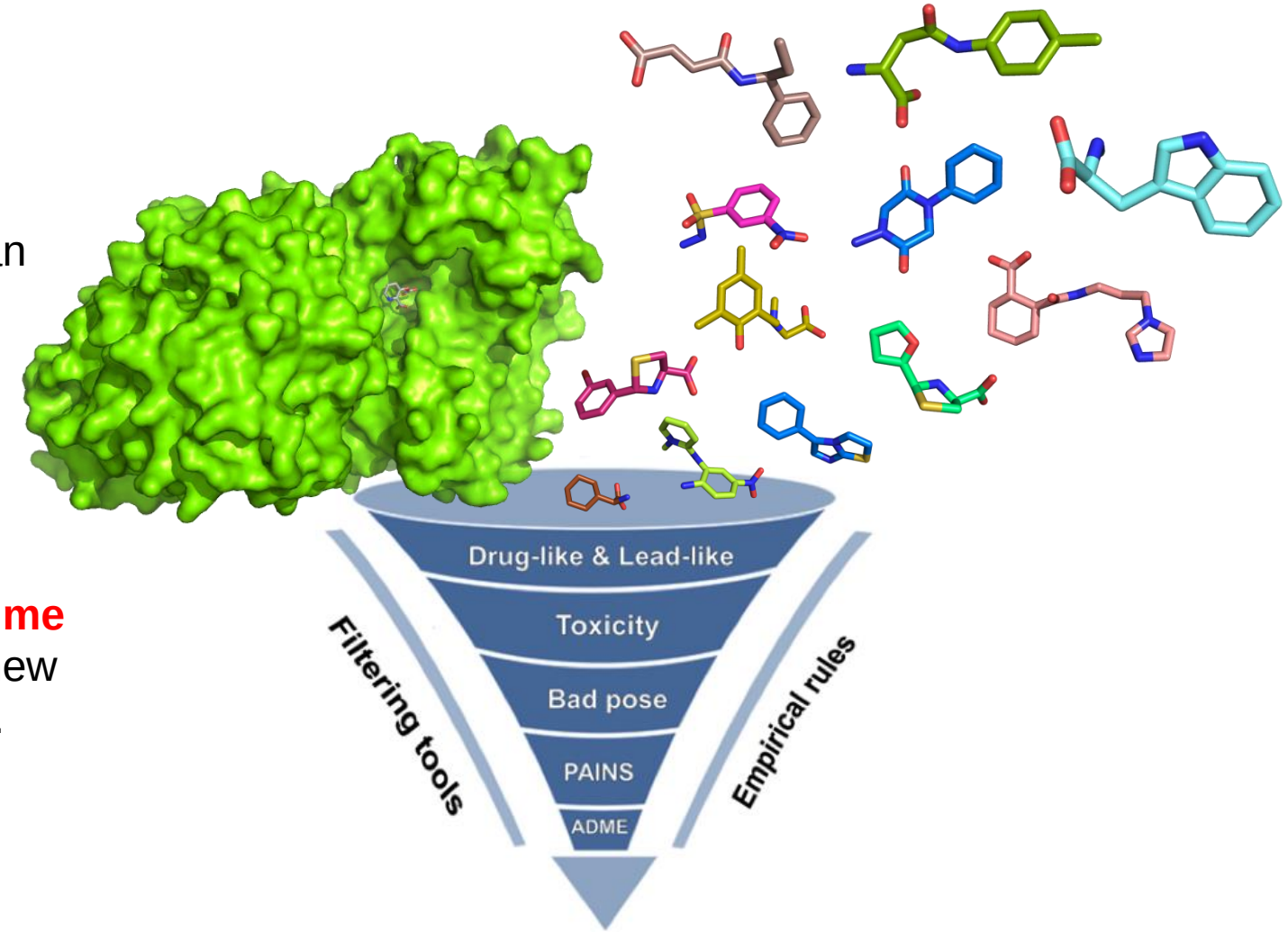
Pharmacology and Toxicology

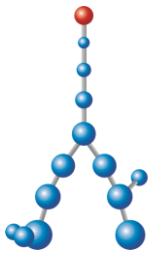
Mathematics and Statistics

Economics

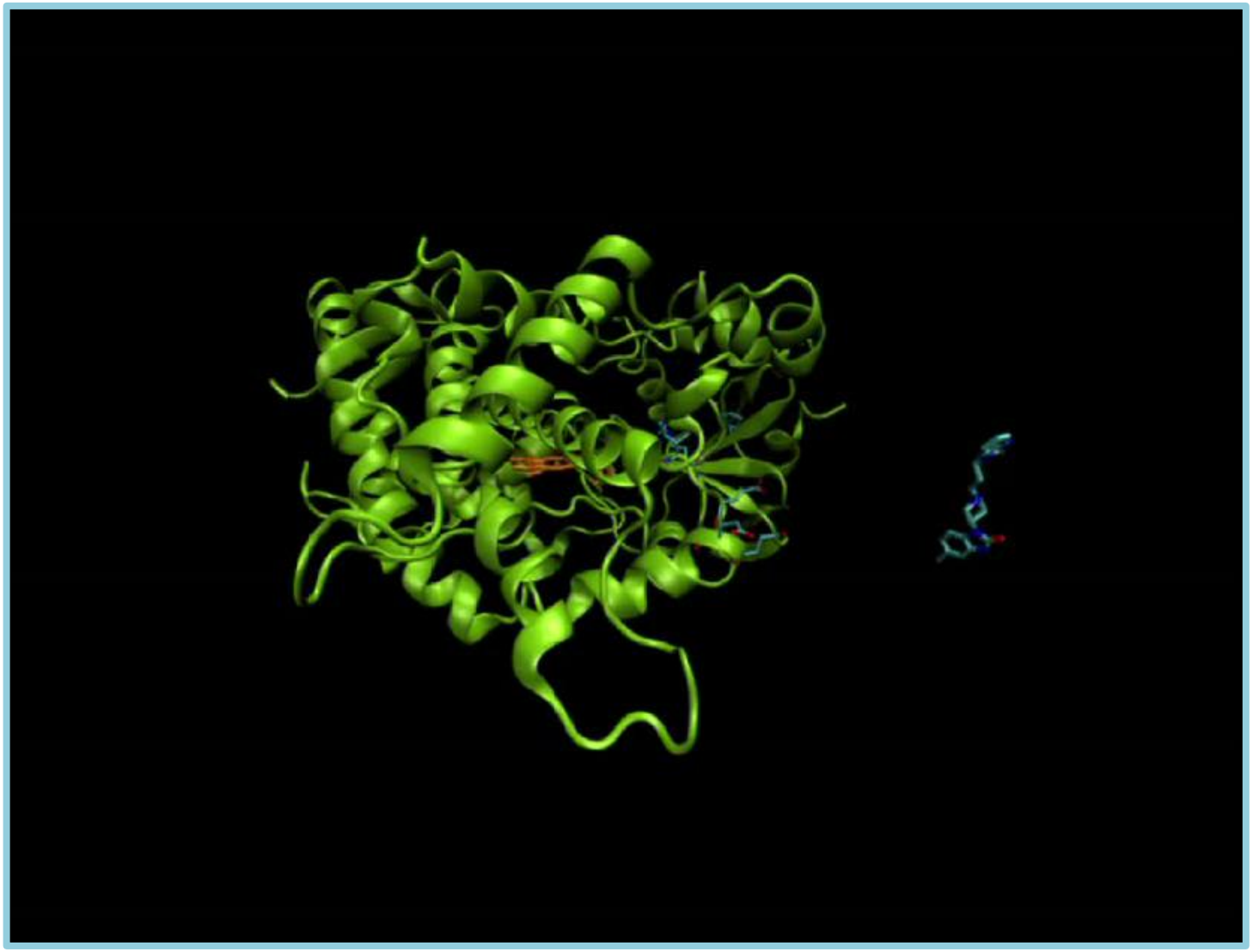
- ***Identifying new ligands*** **for relevant pharmacological targets**

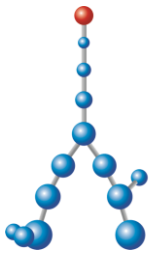
Computational simulations coupled with experiments can dramatically **improve the success of screening campaigns, reducing the cost and the time** for identifying new potential drugs.



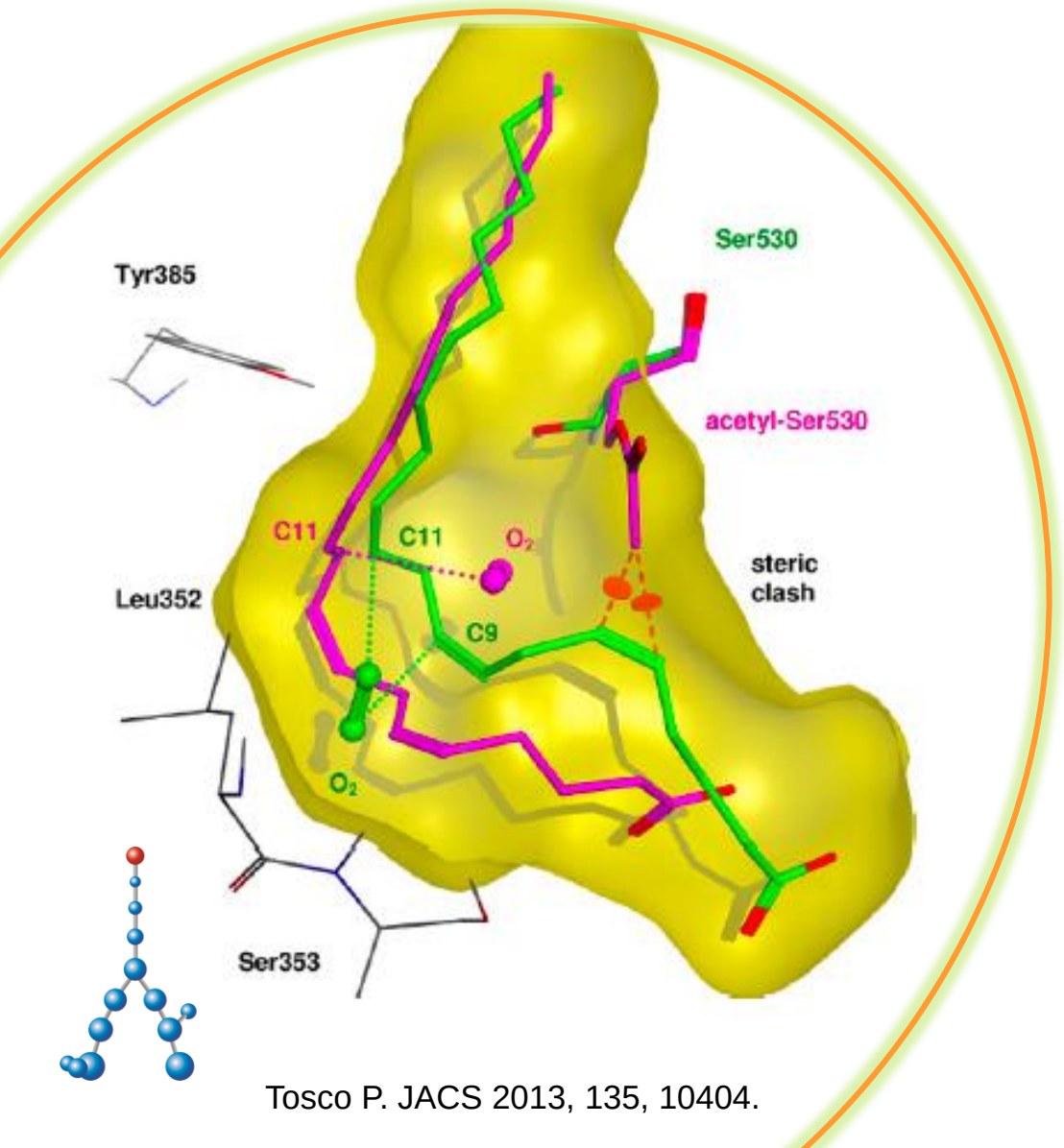


- ***Molecular Dynamics simulations*** **for better tuning drug-target interactions and predict the duration of drug effects**





- ***Mechanistic study*** **of enzymatic reactions catalysed**



Tosco P. JACS 2013, 135, 10404.

Quantum Mechanics

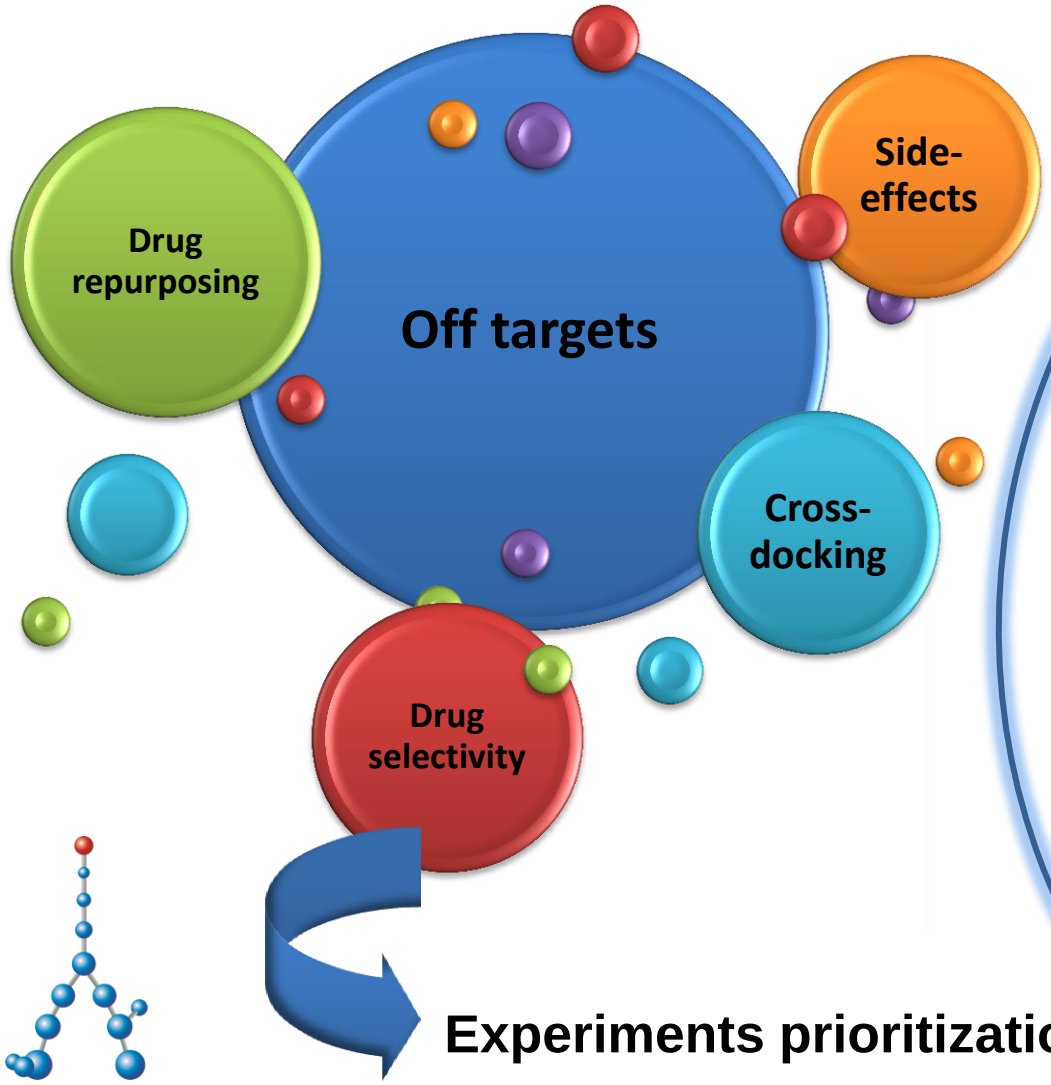
Hybrid QM/MM approaches

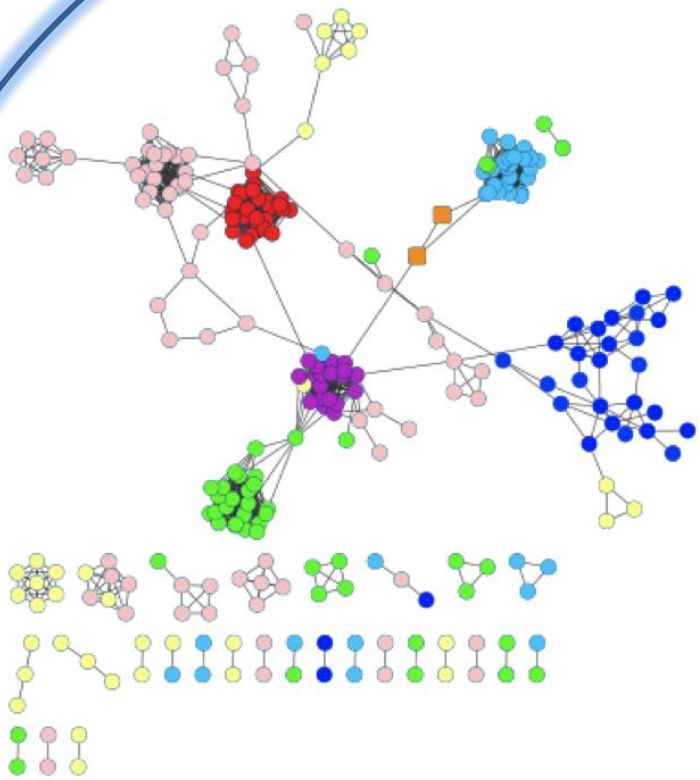
Mechanistic insights on enzymatic reactions/ mechanism of inhibition of potential drugs

Design and development of **more specific and effective drugs**

- ***Identifying similarities among drug targets***

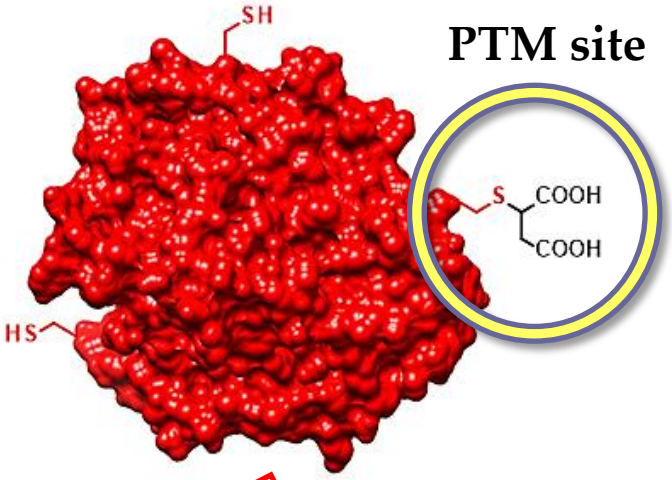
(Structural comparison of large repositories of protein structures)

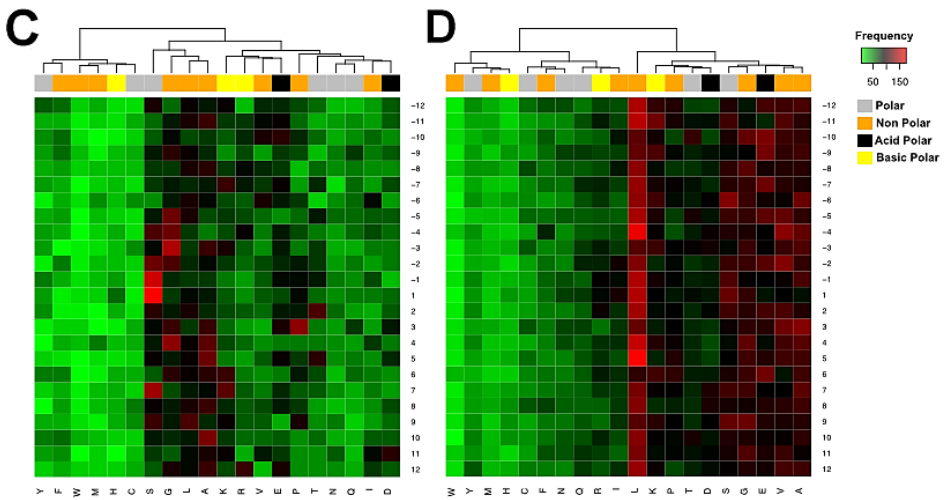


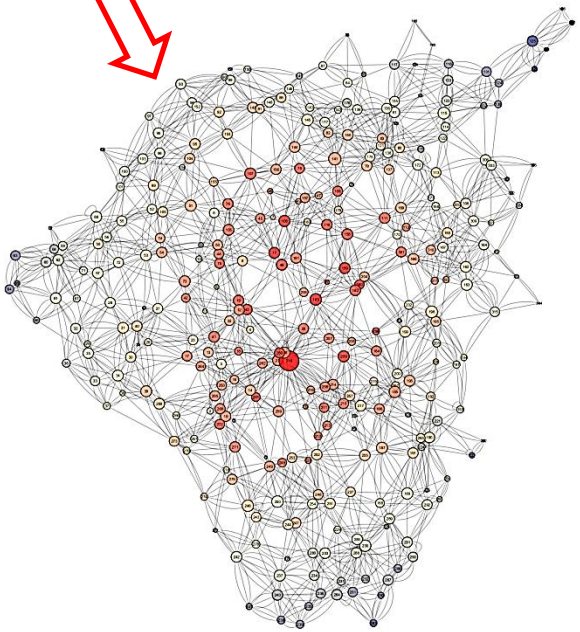


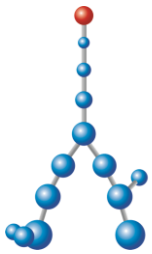
Nuclear Receptor binding sites are grouped accordingly with their similarity suggesting repurposing opportunities

- ***Exploring PTM sites*** **for identifying new targets**









Computational analysis of protein sequence & structure

to identify sites involved in regulatory mechanisms

Miglio et al., BBA Proteins and Proteomics 2016.

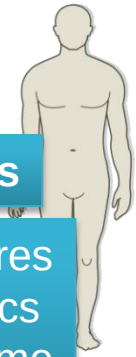
- ***OMICS @ DSTF***

Foodomics & Sensomics

Food authentication
Food quality assessment
Food signatures
Sensomics

Plant Volatilomics

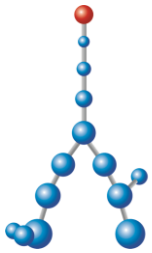
Botanical origin
Plant-insects interactions
Volatile fraction profiling
Sensomics

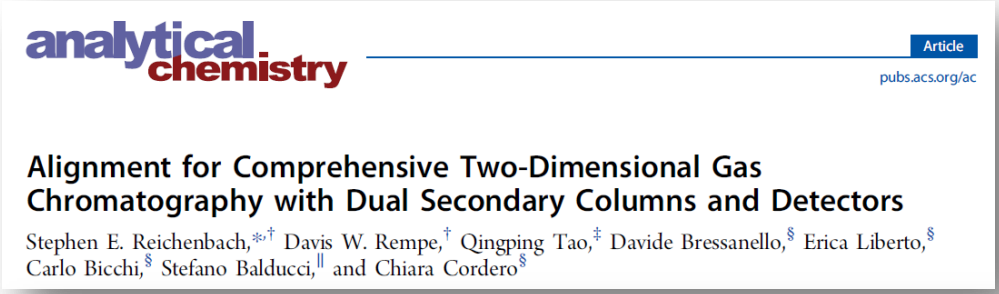


Metabolomics biofluids

Urinary metabolic signatures
Blood serum metabolomics
Urine and faecal volatimome
Dietary intake markers

Data mining requires intensive and extensive processing by dedicated software
Pattern recognition approaches based on the principles of biometric fingerprinting.





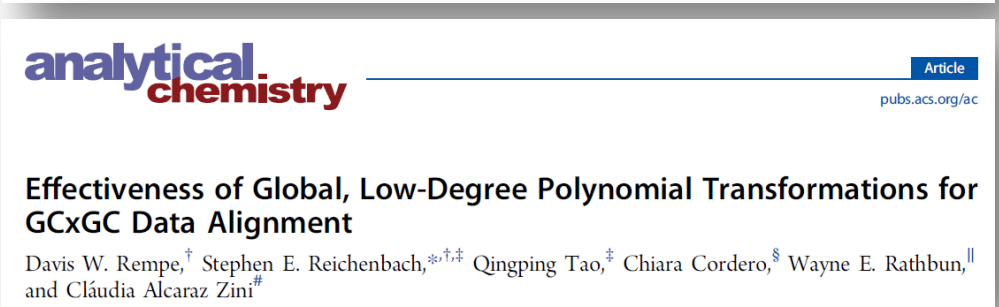
analytical chemistry

Article

pubs.acs.org/ac

Alignment for Comprehensive Two-Dimensional Gas Chromatography with Dual Secondary Columns and Detectors

Stephen E. Reichenbach,[*,†] Davis W. Rempe,[†] Qingping Tao,[‡] Davide Bressanello,[§] Erica Liberto,[§] Carlo Bicchi,[§] Stefano Balducci,[∥] and Chiara Cordero[§]



analytical chemistry

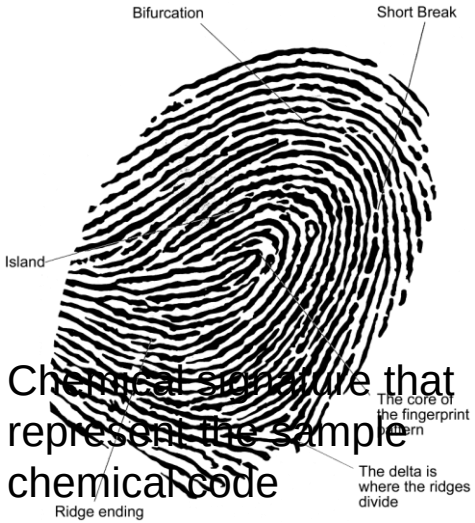
Article

pubs.acs.org/ac

Effectiveness of Global, Low-Degree Polynomial Transformations for GCxGC Data Alignment

Davis W. Rempe,[†] Stephen E. Reichenbach,[*,†,‡] Qingping Tao,[‡] Chiara Cordero,[§] Wayne E. Rathbun,[∥] and Cláudia Alcaraz Zini[#]

- ***OMICS @ DSTF***



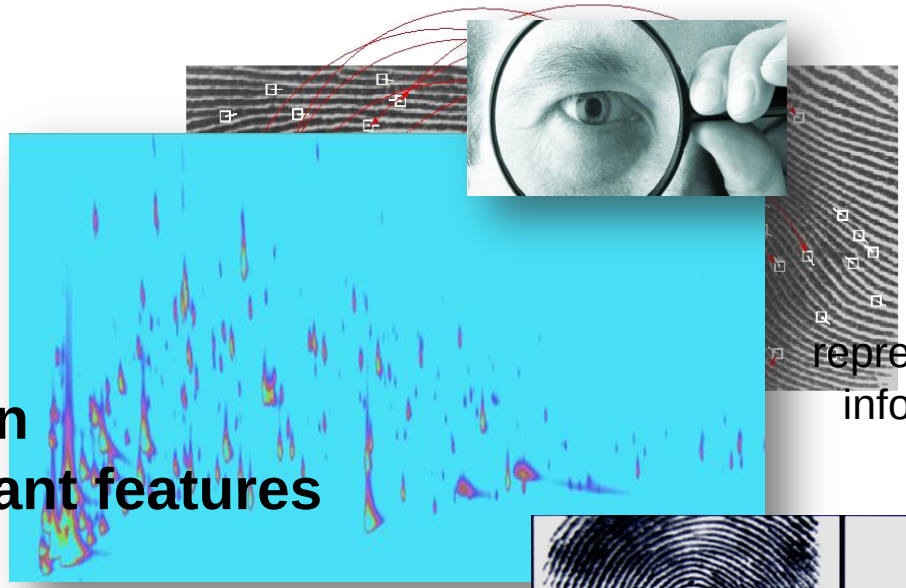
Chemical signature that represent the sample chemical code

Image Acquisition

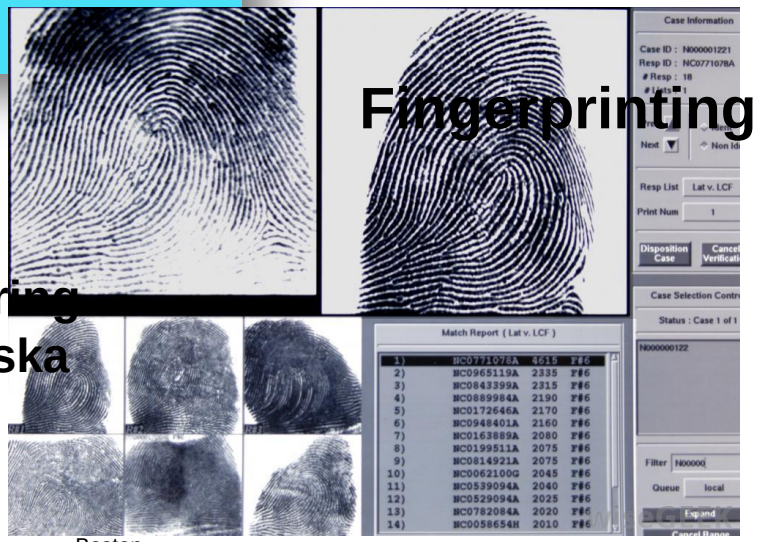
Profiling of relevant features

(Detailed) Profiling

Comparison within stored templates

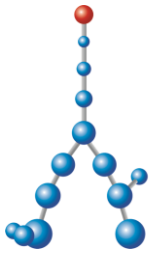


Each 2D pattern is unique and representative of sample informative dimensions



Fingerprinting

Identification



Prof. S.E. Reichenbach
Computer Science and Engineering
Department University of Nebraska
Boston

Conclusions

- **Drug discovery is a data-intensive research**

- ***‘Computer-based predictive models’*** **can quickly transform data into results, improve predictability and efficiency along the critical path from laboratory concept to commercial product**

- **Robust methodologies (e.g., algorithms, software) and technologies are needed to address current and future challenges in the field of drug discovery**

Lo speziale
Pietro Longhi (1752)
(Venezia, Galleria dell’Accademia)