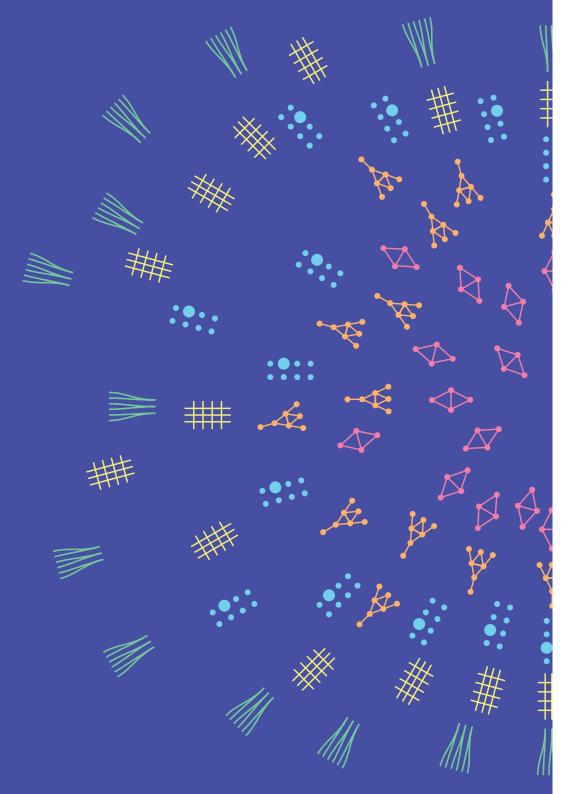






#### COSBI 2005-2025

Celebrating 20 years of Computational Excellence in Systems Biology







2005-2025:

## Two Decades of Research, Innovation, and Scientific Advancement

Celebrating 20 years of pioneering work at the intersection of computational science and biology, transforming data into actionable knowledge for personalized health.

#### THE JOURNEY OF COSBI

# From inception to global recognition



#### FOUNDATION OF COSBI IN 2005: A VISIONARY PARTNERSHIP

The Microsoft Research - University of Trento Centre for Computational and Systems Biology (COSBI) opened its doors in December 2005, marking the beginning of an extraordinary scientific journey, led by Corrado Priami. The founding agreement for this groundbreaking joint venture between Microsoft Research and the University of Trento was signed in Prague on February 2, 2005.

A clear mission: to conduct research and development in conceptual approaches, programming languages, and supporting software tools for modeling biological systems



#### FIVE YEARS OF PROGRESS: "MERGING KNOWLEDGE" IN 2010

COSBI celebrated its fifth anniversary with the international conference "Merging Knowledge", held in Trento from November 30 to December 3, 2010. This landmark event brought together distinguished scientists from around the world to discuss the relevance of computer science to systems biology and explore the emerging field of nutrigenomics, which combines personalized medicine with personalized diet.



#### 10 YEARS OF ACHIEVEMENT: "CONVERGING SCIENCE" IN 2015

COSBI marked its 10th anniversary with an event underscoring its transition from a pioneering research initiative to a global computational biology leader. The workshop focusing on systems nutrition and pharmacology, was attended by institutional leaders and industry partners from Nestlé, Sanofi, and the FDA. By this decade mark, COSBI had assembled a multinational team and secured industrial contracts funding 85% of operations through pioneering data analysis methods and modeling algorithms established in its first five years.

## NEW LEADERSHIP AND CONTINUED GROWTH: COSBI IN 2020

In 2017, a significant leadership transition: Enrico Domenici, a biologist with extensive experience in the pharmaceutical sector, was appointed as President, succeeding founding director Corrado Priami. COSBI continued to expand its research portfolio and strengthen its position as a leader in computational biology. In 2019, COSBI became a Foundation, keeping focus on its mission of developing computational platforms for personalized medicine and nutrition, and translating information into actionable knowledge.



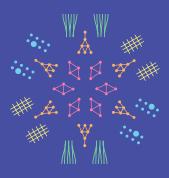
#### COSBI TODAY

## Transforming biological data into actionable knowledge

## A SYSTEMS BIOLOGY APPROACH TO COMPLEX CHALLENGES

An integrative approach, focusing on extracting knowledge from multiple sources and framing it within a systems-level context to address complex biological questions, bridging the gap between massive amounts of biomedical data and actionable scientific insights.

## Systems Pharmacology



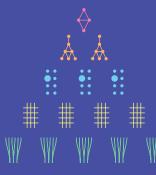
#### BUILDING COMPUTATIONAL FRAMEWORKS TO SUPPORT DRUG DISCOVERY AND PERSONALIZED MEDICINE

Combining molecular, cellular, preclinical, and clinical data from different sources to build a systems view of biological processes in healthy and disease condition, setting the basis for mechanistic models and mathematical descriptions of both complex and rare disorders:

- identify new targets and biomarkers
- simulate disease progression
- identify patient subgroups
- predict drug efficacy

guiding the advance of small molecules and biological agents through the various phases of their development.

## Systems Metabolism & Nutrition



#### EXPLORING THE ROLE OF NUTRITION ON HUMAN METABOLISM IN HEALTH AND DISEASE

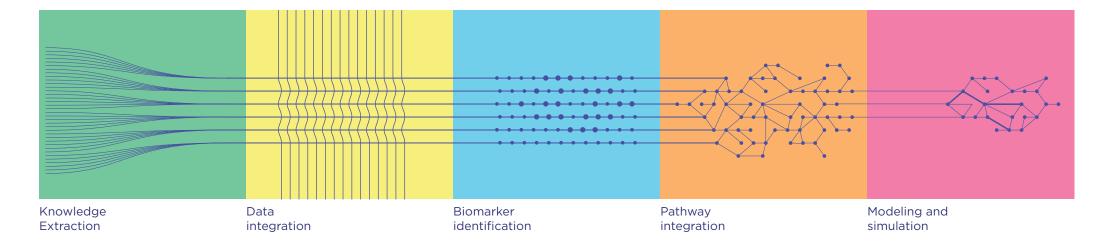
Integrating genomic, metabolomic, and microbiome (high dimensional) to construct computational models that data that elucidate metabolic pathways and their regulation at cellular, tissue, and organism levels, while also assessing the impact of dietary factors on metabolic health and disease:

- identify novel targets for metabolic disorders
- simulate metabolic responses to nutritional interventions

guiding the advance of personalized dietary strategies for metabolic health.

## Core Technologies

Our research pillars in Systems Pharmacology and Systems Nutrition & Metabolism are powered by a core suite of computational technologies in continuous development, designed to extract insights from complex biological data and accelerate discovery.



#### **KNOWLEDGE EXTRACTION & SYNTHESIS**

- Automated literature mining and NLP pipelines mapping disease mechanisms, drug actions, and nutrient-metabolism interactions.
- Interactive knowledge networks linking molecular targets, pathways, and biomarkers.

#### PREDICTIVE BIOMARKER/ TARGET DISCOVERY

- Multi-omics integration (genomic, transcriptomic, metabolomic) for patient stratification and disease driver identification.
- Hybrid AI-mechanistic models prioritizing drug repurposing candidates and biomarkers.

#### ADVANCED SIMULATION PLATFORMS

- Hybrid stochastic-deterministic models capturing the complexity of common and rare disorders.
- Quantitative Systems Pharmacology (QSP) models predicting disease progression or treatment efficacy in various conditions.
- Virtual patient platforms for in-silico testing of therapies and dietary interventions.

#### **OUR GLOBAL NETWORK**

## Partnerships and Collaborations

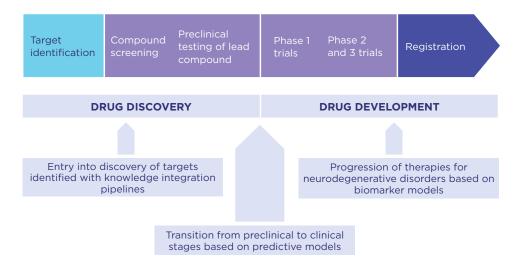
#### BUILDING BRIDGES BETWEEN ACADEMIA AND INDUSTRY

Over its two decades of existence, COSBI has established an impressive network of collaborations with leading academic institutions, research organizations, and industry partners around the world. These partnerships have been instrumental in advancing our research goals and translating scientific discoveries into practical applications.

## INDUSTRIAL PARTNERSHIPS: DRIVING INNOVATION AND DATA-DRIVEN DECISION MAKING

COSBI has established strong partnerships with leading companies in the pharmaceutical and biotechnology sectors. Our expertise has offered key contributions to drug discovery and development, such as supporting target selection, biomarker identification, transition between preclinical and clinical stages, and guiding clinical decision-making with advanced computational models.





#### SPOTLIGHT ON

## Internal Research Projects

#### FROM SCIENTIFIC LITERATURE TO ACTIONABLE KNOWLEDGE

COSBI tools can automatically discover, extract, and link relevant information from scientific literature leveraging semantic search, AI-based Natural Language Processing and LLM-powered analysis for advanced drug repurposing and mechanistic modeling.

#### SINGLE CELL NETWORK-BASED DRUG REPURPOSING

By analyzing biological data at the singlecell level, COSBI researchers can identify subtle patterns and relationships that might be missed by traditional approaches, opening new avenues for therapeutic intervention.

#### RANK-BASED MULTI-OMICS BIOMARKERS

Innovative multi-omics approaches being developed at COSBI will help researchers and clinicians better understand disease by jointly analyzing genes, proteins, and metabolism, ultimately enabling earlier diagnosis and more personalized treatments.

#### MECHANISTIC MODELS FOR THE ADVANCEMENT OF PARKINSON'S THERAPIES

By mathematically describing the molecular mechanisms that lead to a-synuclein aggregation—a key driver of Parkinson's disease pathogenesis— COSBI research aims to improve our understanding of the disease and support the development of new therapeutic strategies.

#### MULTI SCALE QSP MODELS FOR THE DEVELOPMENT AND OPTIMIZATION OF MRNA VACCINES

With mechanistic models describing the immune responses following mRNA vaccine administration, COSBI intends to support the design and optimization of dosing regimens for current and future mRNA vaccines.

#### THE INTEGRATION OF MACHINE LEARNING AND MECHANISTIC MODELING

By integrating machine learning and traditional modeling methods, COSBI is developing advanced hybrid models that address key simulation challenges and enable more robust and interpretable systems biology applications.

# The Next Decade of Innovation

As we look ahead to the next decade of our journey, we remain committed to developing cutting-edge computational tools and approaches that transform biological data into actionable knowledge. Our future research directions include:

- Further advancement of QSP models for rare diseases and complex disorders.
- Integration of artificial intelligence and machine learning with mechanistic modeling approaches,
- Development of patient-specific computational models for truly personalized medicine.
- Expansion of our computational platforms to address emerging global health challenges.



## Selected recent publications

1: Dasti L et al. A Multiscale Quantitative Systems Pharmacology Model for the Development and Optimization of mRNA Vaccines. CPT Pharmacometrics Syst Pharmacol. 2025

2: Visintainer R et al. stormTB: a web-based simulator of a murine minimal-PBPK model for anti-tuberculosis treatments. Front Pharmacol. 2025.

3: Boggi C et al. Longitudinal transcriptomic analysis of the hyperoxia-exposed preterm rabbit as a model of BPD. Front Pediatr. 2025

4: Giampiccolo S et al. Robust parameter estimation and identifiability analysis with hybrid neural ordinary differential equations in computational biology. NPJ Syst Biol Appl. 2024

5: Tomasoni D et al. Strengths and limitations of non-disclosive data analysis: a comparison of breast cancer survival classifiers using VisualSHIELD. Front Genet. 2024

6: Reali F et al. A minimal PBPK model to accelerate preclinical development of drugs against tuberculosis. Front Pharmacol. 2024

7: Berquez Me t al. Lysosomal cystine export regulates mTORC1 signaling to guide kidney epithelial cell fate specialization. Nat Commun. 2023.

8: Parolo S et al. Single-cell-led drug repurposing for Alzheimer's disease. Sci Rep. 20239: Real F. et al. Use of quantitative systems pharmacology pipelines to bridge in vitro and in vivo results in drug discovery. Front Syst Biol. 2023

10: Paris A et al. A pediatric quantitative systems pharmacology model of neurofilament trafficking in spinal muscular atrophy treated with the antisense oligonucleotide nusinersen. CPT Pharmacometrics Syst Pharmacol. 2023

11: Righetti E et al. Mechanistic models of a-synuclein homeostasis for Parkinson's disease: A blueprint for therapeutic intervention. Front. Appl. Math. Stat. 2022 12: Selvaggio G et al. Computational Analysis of Cytokine Release Following Bispecific T-Cell Engager Therapy: Applications of a Logic-Based Model. Front Oncol. 2022.

13: Coletti R et al A Model-Based Framework to Identify Optimal Administration Protocols for Immunotherapies in Castration-Resistance Prostate Cancer. Cancers (Basel). 2021

14: Selvaggio G et al. A quantitative systems pharmacology approach to support mRNA vaccine development and optimization. CPT Pharmacometrics Syst Pharmacol. 2021

15: Leonardelli L et al. Literature Mining and Mechanistic Graphical Modelling to Improve mRNA Vaccine Platforms. Front Immunol. 2021

16: Tomasoni D et al. QSPcc reduces bottlenecks in computational model simulations. Commun Biol. 2021

17: Fiorentino G et al. MOUSSE: Multi-Omics Using Subject-Specific SignaturEs. Cancers (Basel). 2021

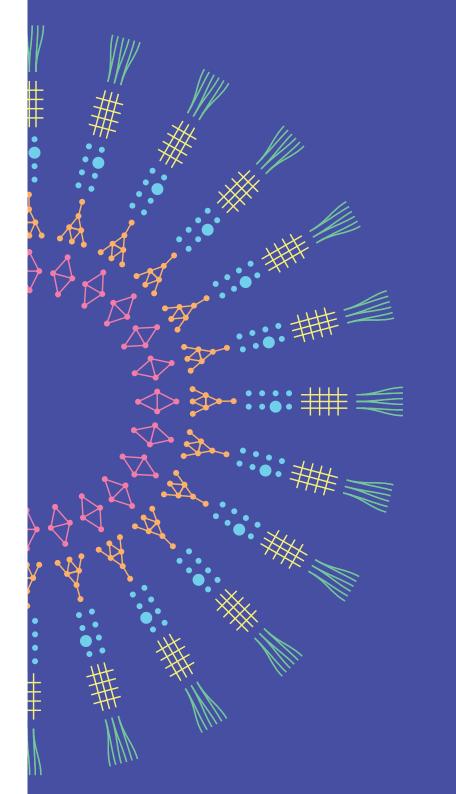
18: Simoni G et al. A robust computational pipeline for model-based and data-driven phenotype clustering. Bioinformatics. 2021

19: Abrams R et al. A Quantitative Systems Pharmacology Model of Gaucher Disease Type 1 Provides Mechanistic Insight Into the Response to Substrate Reduction Therapy With Eliglustat. CPT Pharmacometrics Syst Pharmacol. 2020

20: Coletti R et al. QSP model of prostate cancer immunotherapy to identify effective combination therapies. Sci Rep. 2020

21: Ciciani M et al. rScudo: an R package for classification of molecular profiles using rankbased signatures. Bioinformatics. 2020

22: Misselbeck K et al. A network-based approach to identify deregulated pathways and drug effects in metabolic syndrome. Nat Commun. 2019





Fondazione The Microsoft Research University of Trento Centre for Computational and Systems Biology

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