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# Integration and analysis of heterogeneous biological data modelled with multilayer graphs for a better understanding of feed efficiency

Camille Juigné

## ► To cite this version:

Camille Juigné. Integration and analysis of heterogeneous biological data modelled with multilayer graphs for a better understanding of feed efficiency. Séminaire DIGIT-BIO INRAE, Dec 2022, Ecully, France. hal-03880428

**HAL Id: hal-03880428**

**<https://inria.hal.science/hal-03880428>**

Submitted on 1 Dec 2022

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# Integration and analysis of heterogeneous biological data modelled with multilayer graphs for a better understanding of feed efficiency

## Metaprogram DIGIT-BIO

- ✓ Axe 1 : Multiscale deciphering of living functions
- Axe 2 : Prediction of phenotypes
- Axe 3 : Transfer and generalisation

PhD (01/12/2020 – 30/11/2023)

### Supervisors

Florence GONDRET, INRAE, UMR PEGASE  
Emmanuelle BECKER, Univ Rennes 1, UMR IRISA

## Context – What is feed efficiency in swine?

The relative ability of the animal to convert feed into weight gain

- Reducing feed costs and wastage
- While maintaining physiological functions and health

⇒ Profitability and sustainable of the animal production

## Key but complex phenotype summarizing multiple biological routes

⇒ Determining the biological basis for inter-individual by analyzing the dependency structure of the data : key regulators and important networks

## Objectives

### 1. Starting hypothesis

Key drivers of the phenotypic divergence can be better defined by considering the different levels of biological organization between biological entities

### 2. Research questions

- How can we link high-throughput data (transcriptomics and metabolomics) collected in different tissues to animal phenotype?
- What is the plus-value of adding open-source knowledge on biological entities?

### 3. Objectives

- Identify important sub-networks at different –omics levels
- Determine the interdependence between entities through reactions in which they participate
- Evaluate the most efficient scenarios through path lengths of reactions between entities

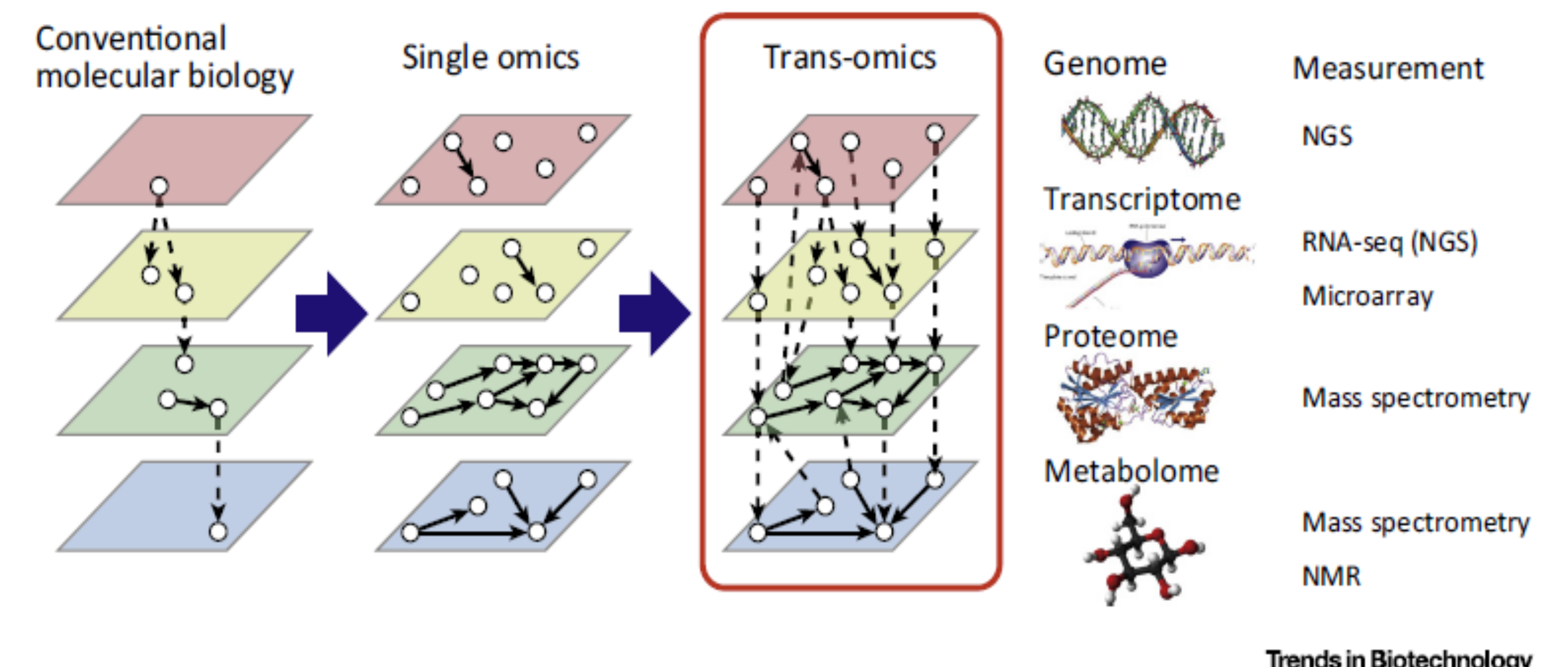


Fig. 1. Linking the different levels of biological organization allows for a holistic view of biological entities (source: K. Yuri et al.)

## Methods

### 1. Statistical approach

#### 1. WGCNA on microarray data from blood

- Analyze pair-wise correlations to find modules of genes = co-expression modules
- Link these modules to feed efficiency measures, such as Feed Conversion Ratio (FCR)

#### 2. PCA on <sup>1</sup>H-NRM data and target metabolites from blood and muscle

- Identify new coordinates (=profiles) summarizing metabolomic data
- Link these profiles to co-expression networks of genes

## Results (1)

- 33 modules identified in microarray data (from 13 to 2,490 unique genes)
- 6 of which are significantly correlated to FCR
- Functional annotation bioinformatics with enrichment scores made biological sense to these modules
- 5 modules of genes ↔ metabolic profiles in blood

### 2. Multilayer network approach

#### 1. Data integration : Interactions connecting transcriptome and metabolome

- Biological Pathway Exchange format (BioPAX) used to represent pathways at cellular and molecular levels
- Reference ontologies (UniProt, ChEBI) and Semantic Web technologies (SPARQL) to retrieve molecules from the modules in graphs of interactions

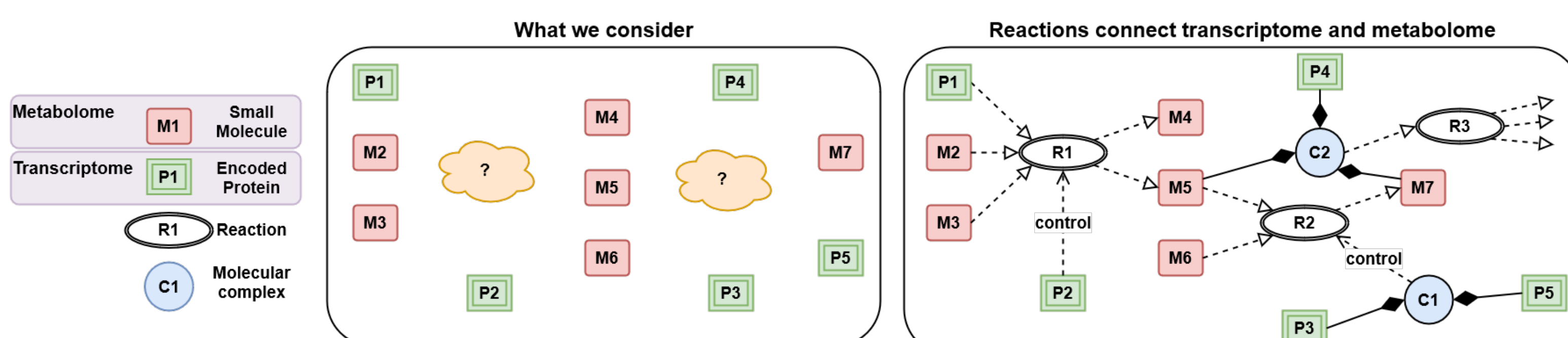


Fig. 2. Interactions connect transcriptome and metabolome through the proteomic level

#### 2. To be continued : graph analysis

Path-finding algorithms to describe the interactions between entities within a module and connecting gene networks to metabolic profiles

## Results (2)

- SPARQL queries allowed identifying and fixing non-compliance with BioPAX specifications for complexes of molecules, to avoid indirection between reactions during path finding

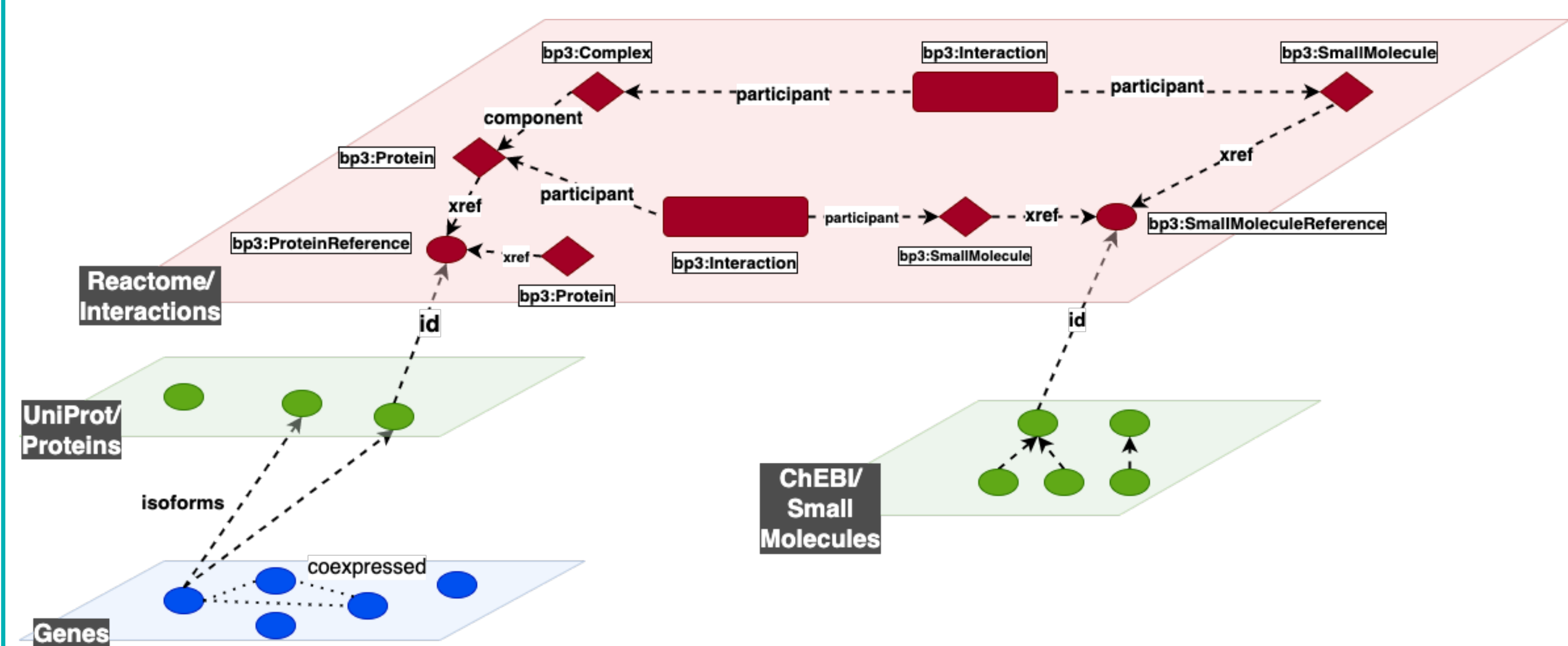


Fig. 3. Integration schema. Each layer represents a type of data from a different data source linked to the others layers by different properties