

# Cross-species metabolic pathways comparison

## Focus on mouse, human and chicken lipid metabolism

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### Context

Lipid assimilation in animals is a major agronomic challenge. Furthermore, the human associated lipid diseases (e.g. obesity) is an important public health concern in industrialized countries. Lipid metabolism relies on some genetic factors which are mostly conserved among species. Thus, it is necessary to qualify and to quantify the differences and the similarities to compare the lipid metabolism between species.

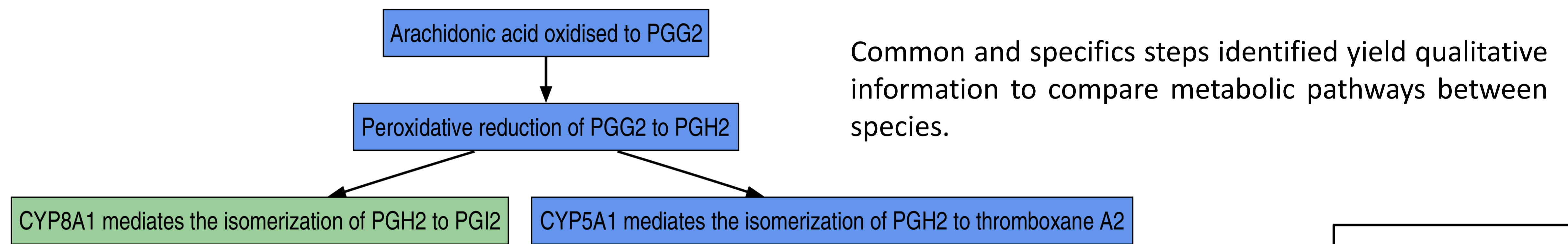
### Objectives and strategy

#### A new knowledge-based method to compare metabolic pathways between species.

- Compare data from pathways databases like Reactome, KEGG and BioCyc. The low level of consistency, comprehensiveness and compatibility between these databases [1] forces us to use them all.
- Use the knowledge from Gene Ontology and its inference rules [2]. Measure the semantic similarities between the genes products by extending Wang's method [3].

#### 1 - Identify automatically common and species specific steps

Extract of prostanoid metabolism: global comparison between mouse and chicken



Common and specific steps identified yield qualitative information to compare metabolic pathways between species.

#### 2 - Quantify semantically the similarities and the differences

Common steps may not be functionally identical...

Let's zoom on the first step of prostanoid metabolism:

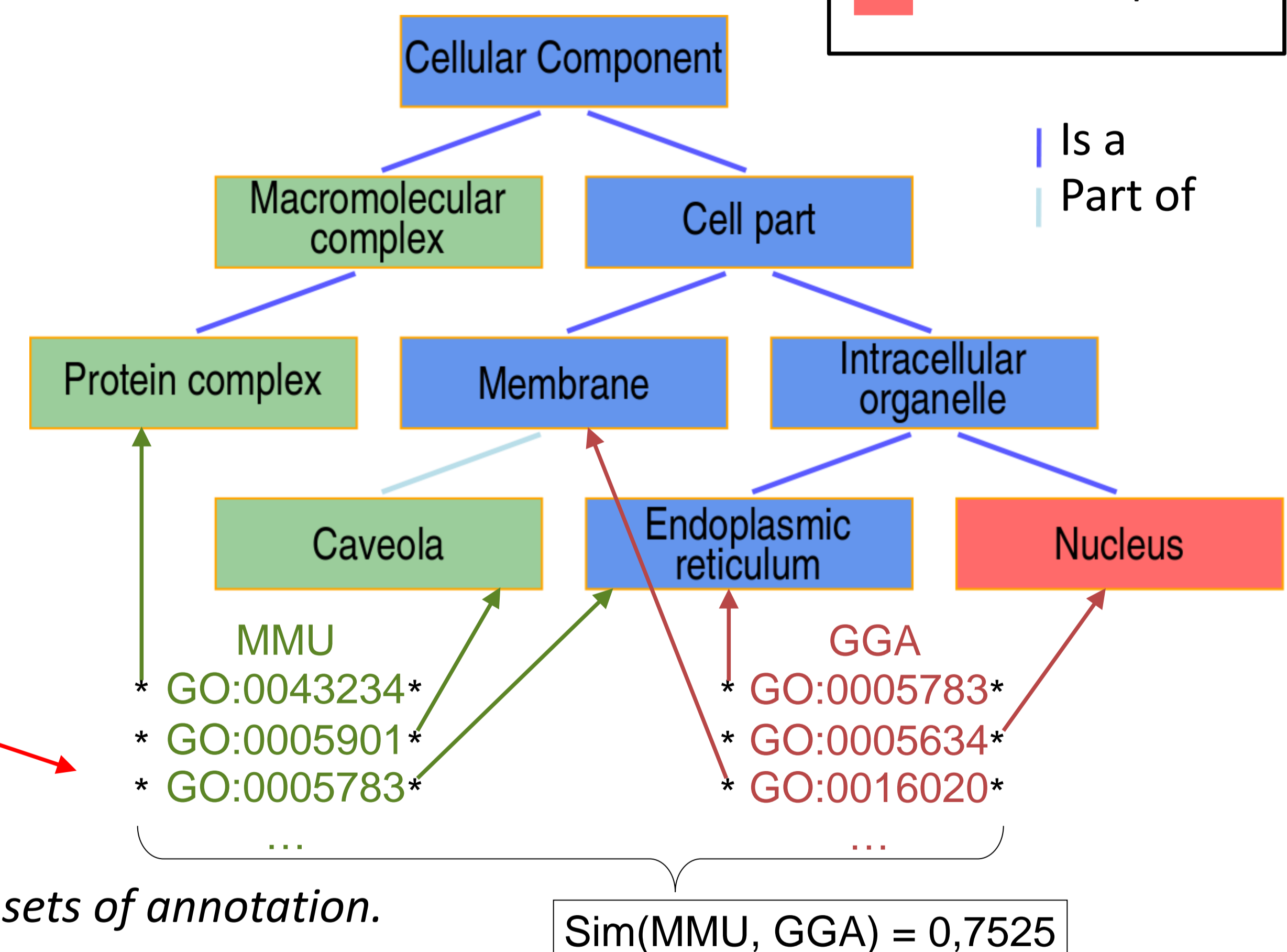
Arachidonic acid oxidised to PGG2							
Reactants				Products			
#	Name	ChEBI	Localization	#	Name	ChEBI	Localization
2	Arachidonate	15843	ER Lumen	1	Prostaglandin G2	27647	ER Lumen
1	O2	15379	ER Lumen				

Enzyme: Prostaglandin G/H synthase (EC = 1.14.99.1)

Gene Ontology annotation of the enzyme

The genes products of a common step between 2 species are described by different Gene Ontology terms.

The *semantics* of GO has to be taken into account to compare the sets of annotation.



#### 3 - Validate the method using simulated and bibliographic data

- Final result of the comparison between 2 species for a metabolic pathway provides estimations of similarity and specificity.
- The first validation step uses a simulated pathway with fictive gene products annotations to compare obtained and expected results. This step allows us to adjust the weight of the different parameters of our method.
- In order to find well documented pathway that are necessary to evaluate the method, we develop and use a search tool called GO2PUB (<http://go2pub.genouest.org>) that enable retrieving bibliography on PubMed using the Gene Ontology terms.
- Final validation will be provided by comparing the results of our automatic method and human expectations. This step will be performed for several well known pathways.

[1] D. Soh, D. Dong, Y. Guo and L. Wong, Consistency, comprehensiveness, and compatibility of pathway databases. BMC Bioinformatics, 11:449, 2010.

[2] S.Y. Rhee, V. Wood, K. Dolinski and S.F. Draghici, Use and misuse of the gene ontology annotations. Nat Rev Genet., 9(7):509-15, 2008.

[3] J.Z. Wang, Z. Du, R. Payattakool, P.S. Yu and C.-F. Chen, A new method to measure the semantic similarity of GO terms. Bioinformatics, 23:1274-1281, 2007.