Supplement

Outline

- **KEGG to BEL:** Transformation process from KGML to BEL
- **Reactome to BEL**: Transformation process from RDF to BEL
- **WikiPathways to BEL**: Transformation process from RDF to BEL
- **BEL Harmonization:** Summary of the harmonization process
- **PathMe Viewer:** A web application for exploring pathway knowledge
- **Implementation Details**
- **Integration in the ComPath Ecosystem:** Integration of inter-database pathway mappings
- **Case Scenario**
- **Availability and Future Directions**

KEGG to BEL

The KEGG PATHWAY Database (Kanehisa *et al.,* 2016) provides a custom, XML based exchange format for each pathway map contained in the database, known as KEGG Markup Language, or KGML. KEGG pathway maps are drawn and updated manually and KGML facilitates the representation of these pathways as graph objects, with entries corresponding to entity nodes and relations and reactions as edges between them.

These KGML files were accessed through the KEGG REST API and subsequently parsed by Pythons' element tree module. The resultant element tree was then traversed for KEGG entry elements to populate corresponding entity type dictionaries. Of the entity types represented in KEGG pathway maps, a subset of types relevant to our purposes were extracted. The selected subset included those entity types which could be readily transformed into BEL nodes. The mapping of KEGG entities to their equivalent BEL nodes is summarized in *Table S1*.

KEGG Node	**Equivalent in BEL**	**Explanation**
Gene/Enzyme	proteinAbundance(x)	Gene, enzyme or protein
Group	complexAbundance(x)	Complex of gene products
Compound	abundance(x)	Chemical compound
Map	bioprocess(x)	Pathway node
Reaction	reaction(reactants(x)), products(y))	Reaction node

Table S1. Mappings between nodes in KGML to BEL v2.0.

The representation of genes in KGML can be by way of single entities or groups of entities which are either similar, of the same family or those which are grouped together because of the ambiguity concerning the role of the genes. Similarly, KEGG compounds may also be represented as single or grouped entities, presumably contingent on their degree of similarity. KEGG genes, compounds and groups representing a complex of gene products were processed into BEL equivalents by optionally constructing BEL composites consisting of similar elements as defined by single identifiers in KGML files or flattened lists of similar entities.

Entities present in KEGG but with no clear BEL equivalence include KEGG hierarchies (i.e. BRITE) and unclassified types termed other. Additionally, KEGG orthologs also remain to be translated into BEL equivalents as we focus here exclusively on human pathways. However, in future we do intend to incorporate orthologs into our framework, hence KEGG orthologs are currently retrieved by our parser.

Similarly, we traversed the element tree for interaction types and extracted those which could be readily mapped to BEL edges. This amounted to the KEGG to BEL equivalencies outlined in *Table S2*. Those KEGG interactions which were not transformed into BEL edges because of ambiguity in translation or due to the absence of a BEL equivalent included state change, dissociation, missing interaction and hidden compound.

A significant portion of KEGG pathway nodes and edges have been directly captured with BEL. Those aforementioned types which we do not directly map to BEL are minimally represented in KEGG pathways, thus, though this is a source of information loss, this loss is mostly negligible. *Figure 1* summarizes the overall statistics for KEGG pathways under two conditions; in the first, unflattened condition, KGML nodes which are represented as grouped entities are translated into BEL composite abundances. In the second, flattened condition, KGML nodes represented as groups are not combined in their translation into BEL and are represented solely as individual entities. Thus, the number of BEL nodes in the unflattened condition is greater than that of the flattened condition by way of the inclusion of composites. In addition to the discrepancy between BEL nodes in the flattened versus unflattened condition, the number of BEL nodes is notably less than the number of entities in the XML file *(Figure*

1). Though a minority of those entities that were not translated from XML into BEL include orthologs, the majority of ostensible information loss is in genes and compounds. While entries in KGML files can be repeated, with the possibility of multiple, identical entries with unique IDs, all nodes are unique in BEL graph representations. Thus, this discrepancy in the number of entities can be largely attributed to the removal of duplicates.

KEGG Edge	Equivalent in BEL	Explanation
Activation	x increases activity(y)	Subject increases the activity of object
Inhibition	x decreases activity(y)	Subject decreases the activity of object
Expression	x increases rnaAbundance(y)	Subject increases expression object
Repression	x decreases rnaAbundance(y)	Subject decreases expression object
Phosphorylation	activity(x) increases proteinAbundance(y, proteinModification(Ph))	Subject increases phosphorylation of object
Dephosphorylation	activity(x) decreases proteinAbundance(y, proteinModification(Ph))	Subject decreases phosphorylation of object
Glycosylation	activity(x) increases proteinAbundance(y, proteinModification(Glyco))	Subject increases glycosylation object
Ubiquitination	activity(x) increases proteinAbundance(y, proteinModification(Ub))	Subject increases ubiquitination object
Methylation	activity(x) increases proteinAbundance(y, proteinModification(Me))	Subject increases methylation object
Indirect effect	x association y	Subject affects object but details are not given
Compound	x association y	Association event
Binding/association	x association y	Association event
Irreversible reaction	catalyticActivity(x) increases reaction(reactants(y), products(z))	Uni-directional reaction
Reversible reaction	catalyticActivity(x) increases reaction(reactants(y), products(z)), catalyticActivity(x) increases reaction(reactants(z), products(y))	Bi-directional reaction

Table S2. Mappings between edges in KGML to BEL v2.0.

A noticeable difference in the number of edges can be seen in BEL relative to those present in KGML *(Figure 2)*. This difference can be attributed to the generation of additional edges including those edges which delineate membership of entities in complexes and those formed between reaction elements. A significantly more pronounced difference between BEL edges and KGML interactions in the flattened condition can also be seen in *Figure 2*. This is due to the generation of edges between all composite components and the neighbours of the composites while in the unflattened mode, edges are formed exclusively between composites and their neighbours.

A detailed look into the KGML to BEL statistics can be seen in the KEGG to BEL Jupyter notebook [https://github.com/ComPath/pathme_resources/blob/master/kegg_to_bel_statistics.ipynb].

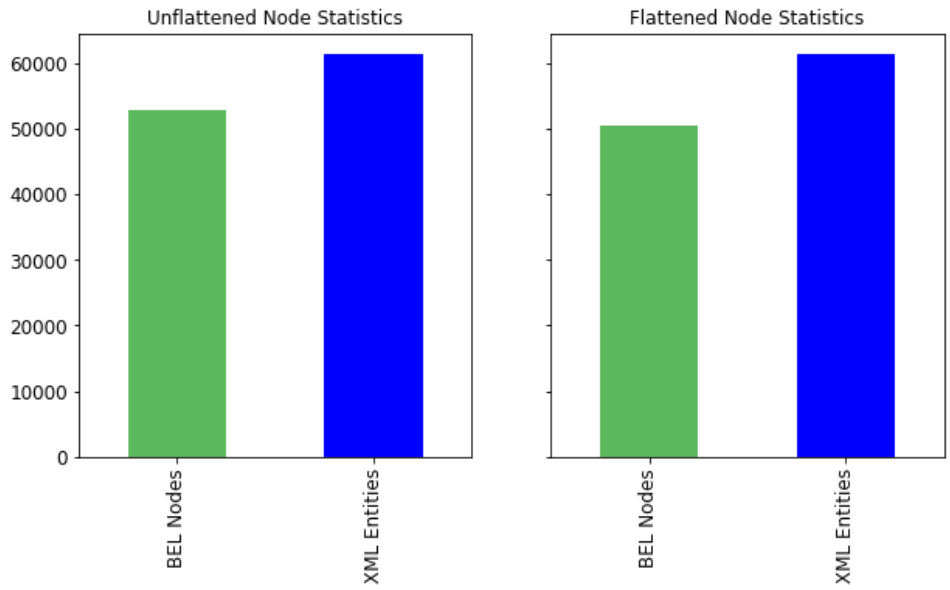

Figure S1. BEL and XML (KGML) node statistics in unflattened versus flattened conditions for all KEGG pathways. The difference in the number of BEL nodes in the unflattened versus flattened condition, where the value of the former is slightly larger, can be attributed to the inclusion of composites in the unflattened condition. The discrepancy in the number of nodes in BEL versus KGML can be largely attributed to the removal of duplicate nodes present in KGML files.

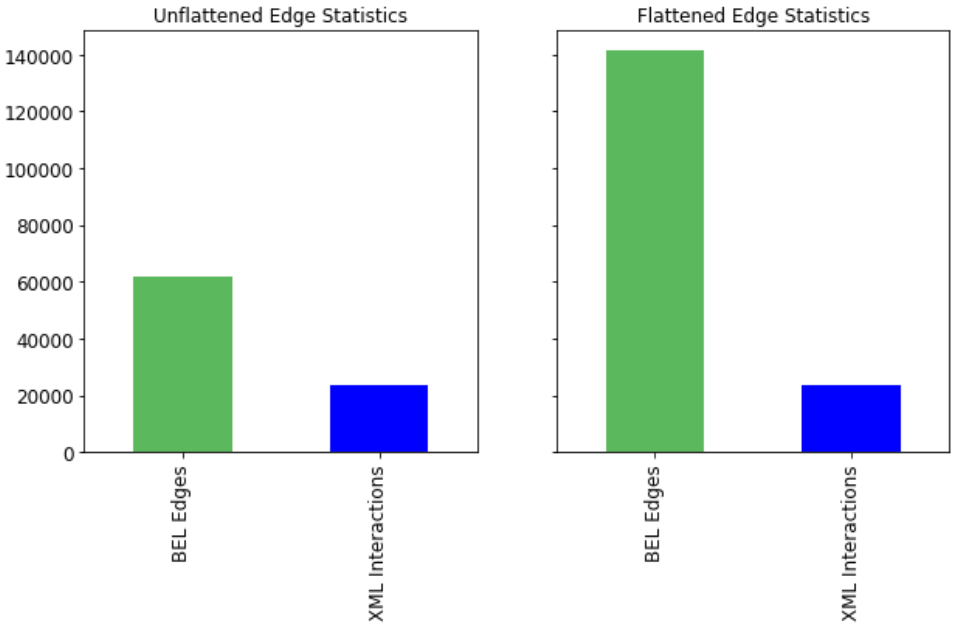

Figure S2. BEL and XML (KGML) edge statistics in unflattened versus flattened conditions for all KEGG pathways. The difference between the number of BEL edges in the unflattened condition is due to the generation of additional edges (ex. Designating membership in complexes, edges between reaction nodes and their reactants and reaction nodes and their products). The more pronounced difference between BEL edges and KGML interactions is partly due to this aforementioned generation of additional edges and largely due to the generation of edges between all composite *components* to each of the composites' neighbours. In contrast, in the un-flattened condition, edges are restricted to those between composites and their neighbours.

Reactome to BEL

Pathways from the Reactome (Fabregat *et al.*, 2017) database can be downloaded in the PSI-MITAB, SBML, SBGN and BioPAX level 2 and 3 formats. Additionally, the database can be downloaded in Neo4j as an interconnected Reactome Graph.

We downloaded Reactome pathways in the BioPAX format through the European Bioinformatics Institutes' (EBI) File Transfer Protocol (FTP) which provides access to RDF datasets in bulk. Because BioPAX is defined using the standard OWL (RDF/XML) syntax, this format can also be used with RDF/OWL tools such as reasoners or triplestores. The RDF file for pathways in humans was then parsed using various SPARQL queries to extract those entity and interaction types which could be directly mapped to nodes and edges in BEL. The mappings are summarized in *Table S3*. The final transformation to BEL is done using the *PyBEL* package (Hoyt *et al*., 2018), where similarly to KEGG, each node/edge is translated to the PyBEL data structure in order to serialize Reactome to BEL. It is important to remark that RDF files were available for pathways from other species for which the parser can also be applied.

Reactome Node	**Equivalent BEL Node**	**Explanation**
Protein	proteinAbundance(x)	Node is gene or protein
SmallMolecule	abundance(x)	Node can be any small molecule
Pathway	biologicalProcess(x)	Node is a pathway
DNA	geneAbundance(x)	Node is the abundance of the gene
RNA	rnaAbundance(x)	Node is the abundance of RNA
Complex	complexAbundance(x)	Node is a complex
Reactome Node	**Equivalent BEL Node**	**Explanation**
Activation	x increases activity(y)	Subject increases the activity of object
Inhibition	x decreases activity(y)	Subject decreases the activity of object

Table S3. Mappings between nodes and edges in the BioPAX format to BEL v2.0.

The statistics of the conversion of Reactome entities and interactions into BEL nodes and edges are presented in the Reactome to BEL Jupyter notebook [https://nbviewer.jupyter.org/github/ComPath/pathme_resources/blob/master/notebooks/reactome/reactome_to_bel_statistics.ipynb]. The results are summarized in *Figure S3*.

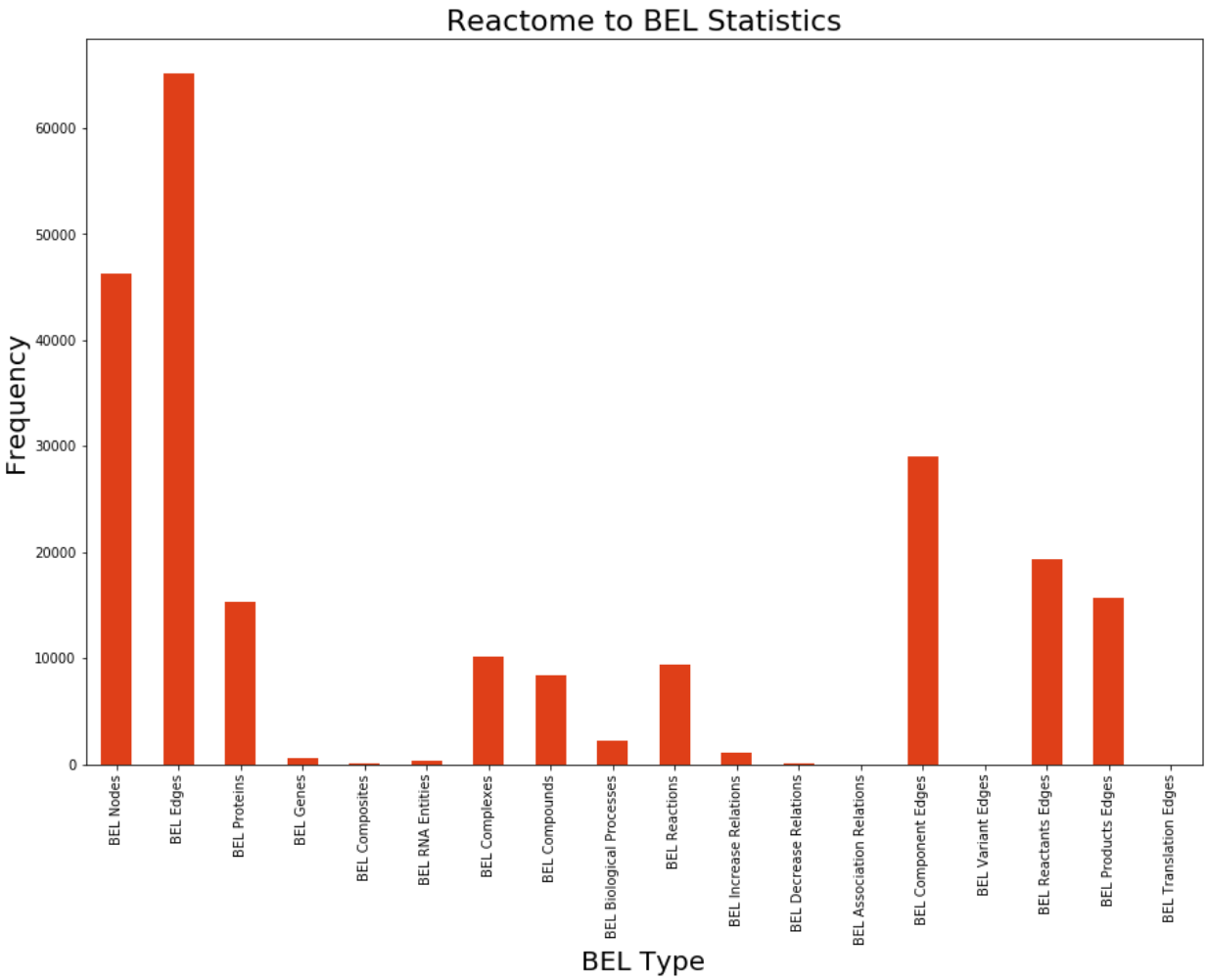

Figure S3. Statistics of the conversion of Reactome entities and interactions into BEL nodes and edges, respectively. All human pathways from the Reactome RDF file were considered.

WikiPathways to BEL

WikiPathways (Slenter *et al*., 2018) provides a *Semantic Web Portal* where its content can be downloaded as RDF (Waagmeester *et al*., 2016). The RDF files contain pathway information that we parsed using multiple SPARQL queries in order to extract the meta-information corresponding to each node/edge in the RDF graph. At this point, we would like to remark that by default the package only parses the original WikiPathways pathways and not other imported pathways from other resources such as Reactome. Additionally, this package parses only human pathways, though pathways from other species can also be applied.

After we extracted and classified the data from RDF, we translated it to BEL. For that, we had to reach a consensus between the types of nodes and edges WikiPathways and their equivalence in BEL. *Table S4* below shows the equivalences. The final transformation to BEL is done using the *PyBEL* package (Hoyt *et al*., 2018), where similarly to Reactome, each node/edge is translated to the PyBEL data structure in order to serialize WikiPathways to BEL.

WikiPathways RDF Node	Equivalent in BEL	Explanation
Protein/GeneProduct	proteinAbundance(x)	Node is a protein or gene product
DataNode	abundance(x)	Node can be abundance of any entity
Metabolite		
Pathway	biologicalProcess(x)	Node is a pathway
Rna	rnaAbundance(x)	Node is abundance of RNA
Complex	complexAbundance(x,y)	Node is a complex
Conversion	reaction(reactants(x), products(y))	Node is a reaction
WikiPathways RDF Edge	**Equivalent in BEL**	**Explanation**
Stimulation	x increases activity(y)	Subject increases the activity of object
Catalysis	x increases reaction(y)	Activity of subject increase transformation of reactants to products
Inhibition	x decreases activity(y)	Subject decreases the activity of object
DirectedInteraction	x association y	Subject has association with object
TranscriptionTranslation	x translatedTo y	RNA members translated to protein members
ComplexBinding	complexAbundance(x,y)	This information is duplicated with the Complex node, since a Complex can also be considered as an interaction

Table S4. Equivalencies between WikiPathways RDF and BEL v2.0.

The statistics for the translation of WikiPathways entities and interactions into BEL nodes and edges can be found in the WikiPathways to BEL Jupyter notebook [https://nbviewer.jupyter.org/github/ComPath/pathme_resources/blob/master/notebooks/wikipathways/wikipathways_to_bel_statistics.ipynb]. The results for the conversion of WikiPathways to BEL are summarized in *Figure S4*.

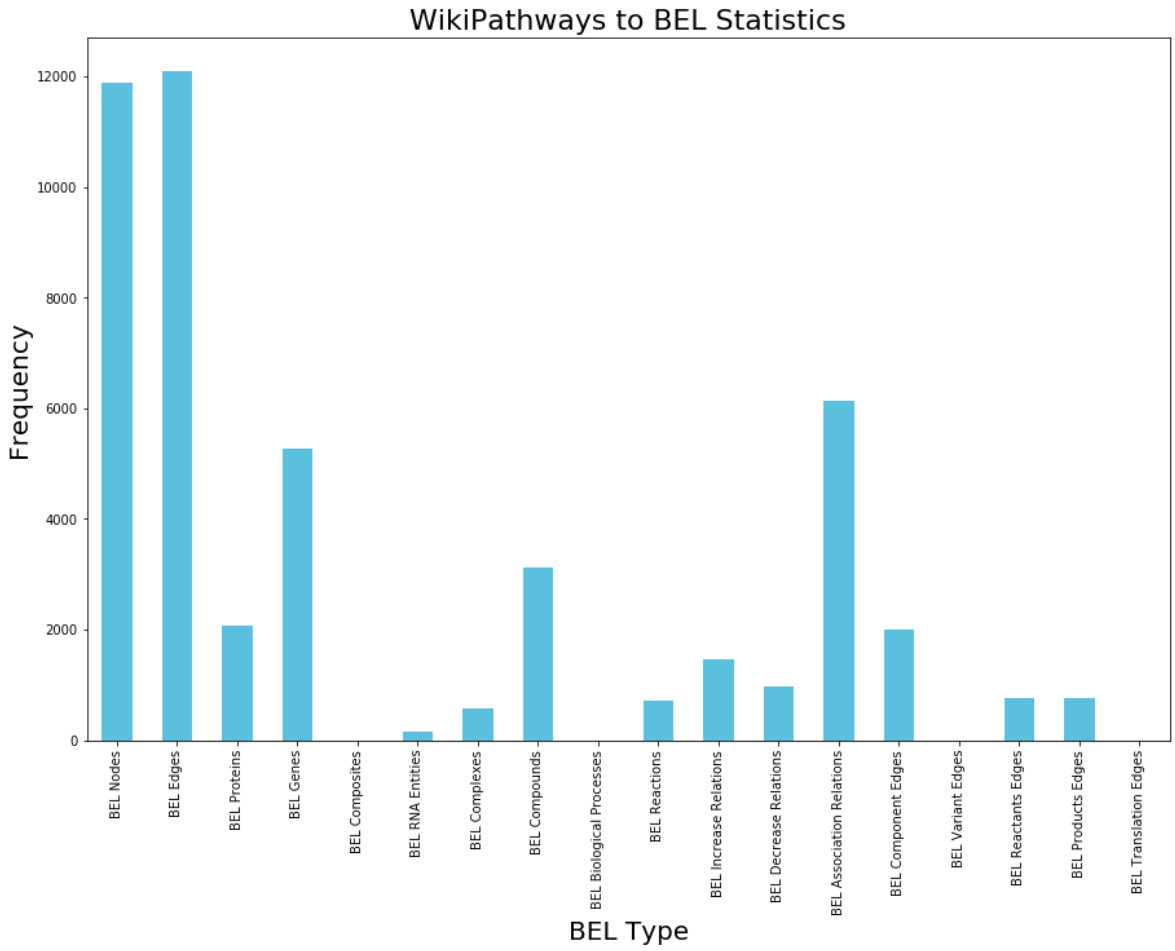

Figure S4. Statistics of the conversion of WikiPathways entities and interactions into BEL nodes and edges, respectively.

BEL Harmonization

As we have shown in the previous sections, BEL v2.0 is capable of capturing almost all of the information from the three different databases and thus, harmonizing the pathway knowledge in a fully interoperable, specified and structured schema. However, as Sales and colleagues discussed in their work, one can represent nodes containing multiple entities or group nodes (e.g., protein complexes, protein families, etc.), by one of two approaches *(Figure S5)*. The first approach represents a set of member entities as participants in a group, corresponding to a single node which can then be connected to its neighbours by its original edges. Conversely, the latter approach creates individual nodes for each of the member entities of a defined group. These member entities can then be connected with the original neighbours of the group node. While both approaches lead to a completely different network topology, they are both valid since they are suited for different applications.

The first formalism, which represents group nodes as individual nodes, is particularly well suited in cases where the node groups represent a protein complex. Whilst generating edges between member parts of a complex and its neighbours would alter the biological meaning of a relationship between a complex and its interacting entity, this first approach preserves the biological context, and thus, facilitates interpretation and visualization. On the other

hand, the latter approach which segregates group node member entities into individual nodes, results in the generation of a comparatively large number of edges and is readily suitable for manipulating the network structure to facilitate working with graph algorithms (e.g., signaling and propagation) and for the representation of protein families, groups of similar proteins or where there is ambiguity concerning the role of the proteins involved in interactions.

Both of these approaches are accounted for in PathMe; by tuning the module with different settings, group nodes can be in the non-flattened *(Figure S5.b)* or flattened *(Figure S5.a)* condition, thus enabling a customized yet transparent pathway reconstruction in BEL.

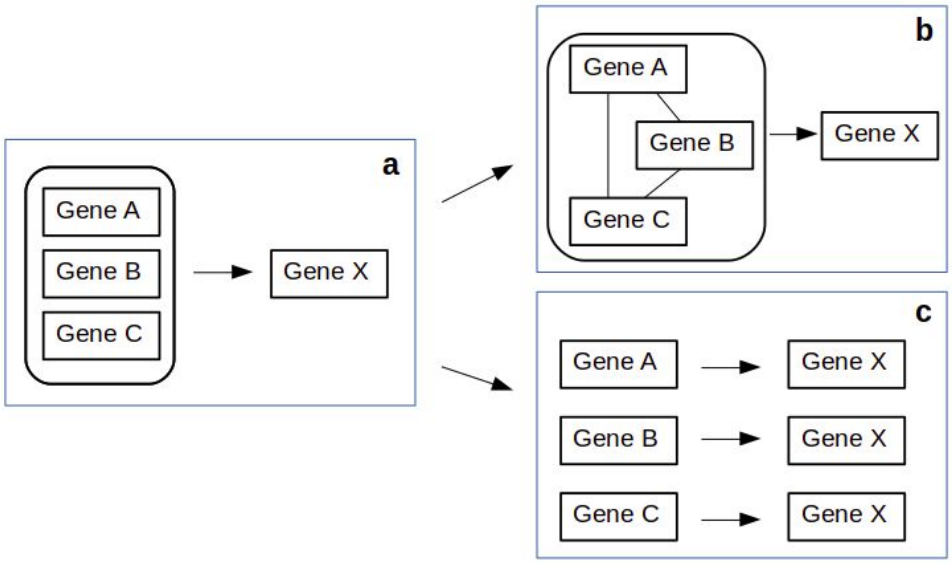

Figure S5. Group nodes representation approaches. Node groups, (**a**), can have edges between each member of the group and a single edge from the group to its neighbours (**b**), or edges between each member of the group to the groups' neighbours (**c).**

PathMe Viewer

The BEL transformation process lays the groundwork for fully interoperability across pathways from different databases. However, we must not forget about the ultimate goal of this work which is exploring coverage, agreements, or discrepancies between pathway databases. While the BEL community already offers a variety of software solutions (i.e., PyBEL (Hoyt *et al*., 2018)) and web applications (i.e., BEL-Commons (Hoyt *et al*., 2018), or BEL.bio (https://bel.bio/)) to explore BEL networks, the particular use case of this work called for customized solutions (e.g., delineating boundaries or highlighting agreements when multiple pathways are being visualized). Therefore, we reused and extended part of the BEL-Commons visualizations to implement PathMe Viewer; thus, benefiting from the variety of functionalities already implemented (e.g., format export, graph transformations and enrichment functions, etc.). This web application, as we present below, provides an intuitive front-end layer designed for visualizing and exploring pathway knowledge represented in BEL.

Since the main target audience for this manuscript are pathway curators and users, we decided to implement the viewer in the form of a user-friendly web application compatible with any device. First, the PathMe main page presents a comprehensive menu where users can quickly explore pathway(s) of interest by using the search functionality on the top of the page *(Figure S6)*. This query leads to the network visualization page where the

corresponding network of the selected pathway(s) is presented using the D3 force-directed layout. The visualization also highlights pathway boundary and contradictory edges between pathways (if any) *(Figure S7)*. Finally, we would like to note that this is an open project and can be deployed internally by any other researcher using Docker/PyPI.

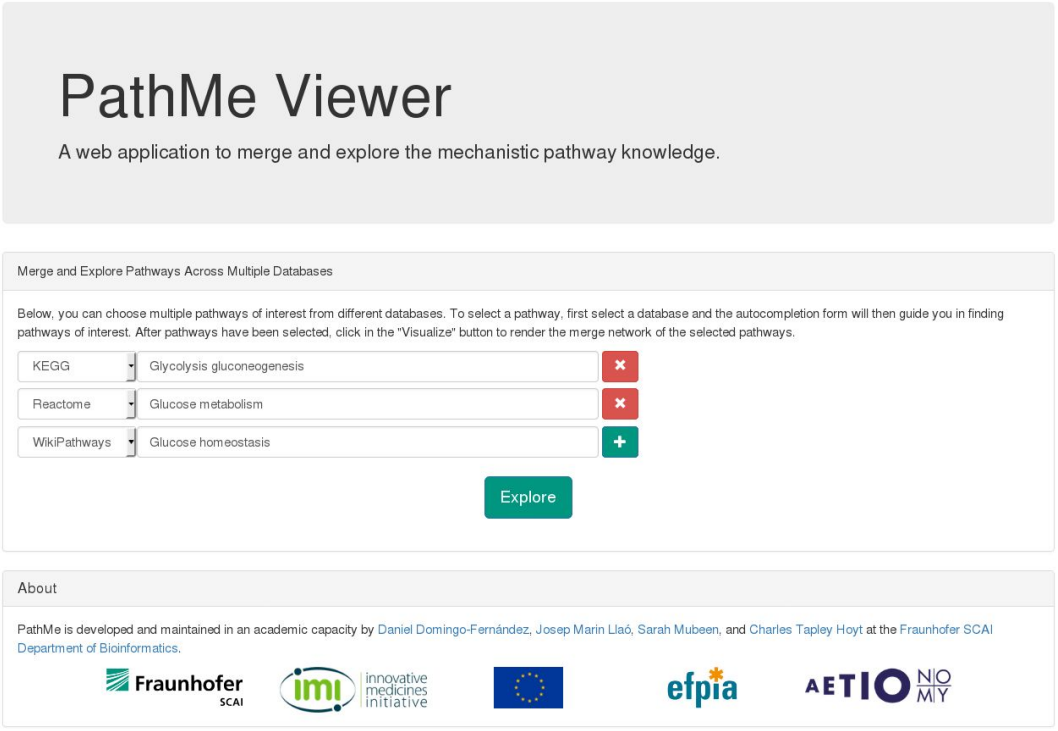

Figure S6. PathMe Viewer main page.

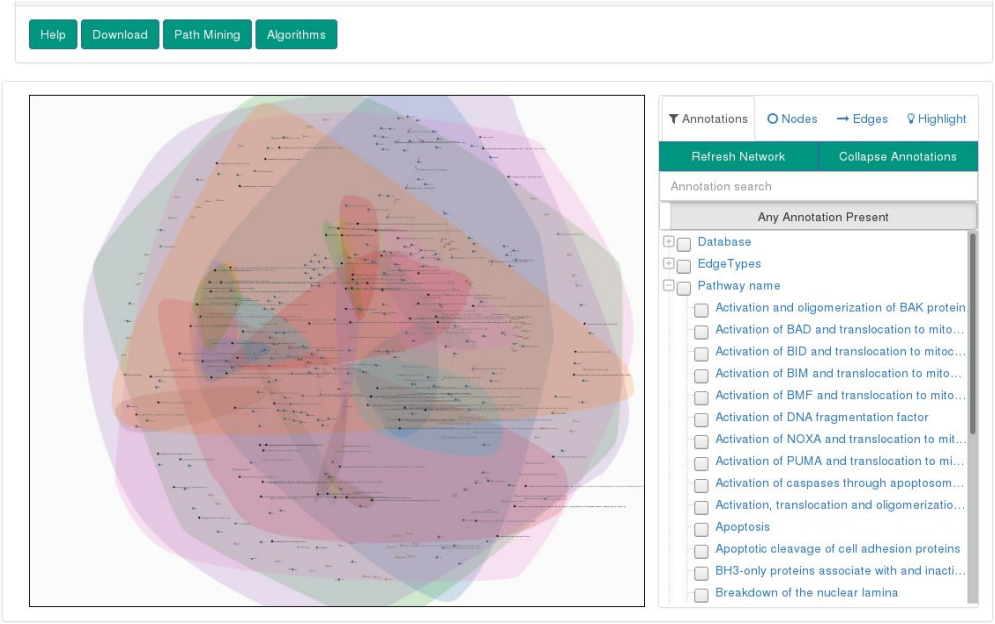

Figure S7. PathMe Viewer network visualization.

Implementations Details

Library	Purpose	Reference
RDFLib	Parsing and handling of RDF resources in WikiPathways and Reactome	https://pypi.org/project/rdflib/
Python XML Module	Parsing and handling of KGML files in KEGG	https://docs.python.org/3/library/xml.html
PyBEL	Handling and creating BEL graphs	https://pypi.org/project/pybel/
PyBEL-Tools	Enrichment of BEL graphs	https://pypi.org/project/pybel-tools/
Pandas	Data handling, statistics generation	https://pypi.org/project/pandas/
Bio2BEL KEGG	Query updated KEGG pathways	https://pypi.org/project/bio2bel-kegg/
Bio2BEL Reactome	Query updated Reactome pathways	https://pypi.org/project/bio2bel-reactome/
Bio2BEL WikiPathways	Query updated WikiPathways pathways	https://pypi.org/project/bio2bel-wikipathways/

Table 1. Python packages used for the harmonization of pathway database content into BEL.

Technology	Functionality
MySQL	Relational database management system
Flask toolbox	An integrated web server and template manager that wraps many of the low level functions in an easy-to-manage programming interface
Docker	Reproducible deployment in any OS

Table 2: A summary of back-end technologies used by the PathMe Viewer.

Javascript Library	Functionality
jQuery	Provides manipulation of DOM, CSS, and general-purpose javascript
D3.js	Network visualization
InspireTree	Builds tree for annotation browser
Bootstrap Toggle	User interface for Toggle buttons
SVG.js	Export SVG images

Table 3: A summary of front-end technologies used by the PathMe Viewer.

Integration in the ComPath Ecosystem

Even after databases have been harmonized into a common schema, one cannot directly explore agreements and pathway demarcations due to the lack of cross-references and mappings. As we point out in the main manuscript, there are several reasons that make automatically linking pathways from disparate database difficult, thus necessitating an exhaustive manual evaluation of the possible mappings for each database and for each pathway. Since the mappings for the three databases showcased in this paper were already generated (Domingo-Fernández *et al*., 2018), we demonstrate the utility of PathMe in the application presented in the main manuscript where we explore the cross-talks of equivalent pathways in the three databases. We would like to remark that this approach is only possible when pathways have been mapped and made fully interoperable. Therefore, the development of PathMe should be tightly related to the curation aspect of the ComPath project to generate more mappings in the future.

In order to facilitate the cross-talk between both web applications, we implemented the PathMe Viewer in a modularized manner so it can be deployed jointly with ComPath while maintaining its independence. While ComPath benefits by linking each pathway information page to the corresponding network using the PathMe Viewer, the latter can use the pathway mappings from ComPath.

Case Scenario

As an application for PathMe, we used the 21 equivalent pathways across the three databases stored in ComPath to demonstrate how PathMe can consolidate the pathway knowledge around them.

Similarity Index

To evaluate the degree of overlap between the three representations of each equivalent pathway, we used a variation of the Szymkiewicz–Simpson/Overlap coefficient *(Equation 1),* calculated for common molecular nodes shared between the networks. To calculate a pathway similarity index, we summed the three coefficients obtained for each individual pairwise comparison. In other words, each pathway similarity index corresponds to the sum of the individual overlaps between i) the KEGG and Reactome representation, ii) the KEGG and WikiPathways representations, and iii) the Reactome and WikiPathways representations. Therefore, the pathway similarity index (S) lies between $0 \leq S \leq 3$ (with 0 corresponding to no overlap between any of the three sets, and 3 corresponding to three equal sets).

$$S_{(X,Y)} = \frac{|X \cap Y|}{min(|X|,|Y|)}$$

Equation 1. The Szymkiewicz-Simpson coefficient calculates the similarity between two sets (X and Y) where $0 \leq S \leq 1$. The similarity is the size of the intersection of the two sets divided by the size of the smaller set. In this case the sets correspond to the number of individual molecular entities excluding group nodes in the BEL graph.

The group nodes (i.e., composites, complexes, and reactions) (see section BEL Harmonization and *Figure S5)* were intentionally excluded when calculating the similarity index. There were two main reasons for doing so:

1. There are an unlimited number of possibilities when generating group nodes because of the combinatorial complexity of grouping members (i.e., a group node has n^n possible combinations). This directly conflicts with the formalism of a set, which is by definition limited. Therefore, by exclusively using individual nodes in the pathway similarity calculations, the number of possible nodes are restricted to a finite number (i.e., the number of known/characterized molecular entities).

2. It is unlikely to find a match between two group nodes since all members in the group must be identical. This can distort the results when comparing a pathway to one having numerous group nodes versus one that possesses relatively few groups or none altogether. In such a case, the former would have a lower similarity score than the latter even if the group nodes are composed of components that are nearly identical.

Results

The results of the similarity analysis between the 21 equivalent pathways are summarized in *Table 4*. A detailed analysis with the scripts to replicate the results and comments on the identified overlaps is available at the following link[https://nbviewer.jupyter.org/github/ComPath/pathme_resources/blob/master/notebooks/similarity_analysis/pathway_similarity.ipynb].

KEGG	Reactome	WikiPathways	Pathway Similarity Index	Merged Network
Cell cycle	Cell Cycle	Cell Cycle	2.10	Link to the merged Cell cycle pathway
Toll-like receptor signaling pathway	Toll-Like Receptors Cascades	Toll-like Receptor Signaling Pathway	1.85	Link to the merged Toll-like receptor signaling pathway
mTOR signaling pathway	mTOR signalling	Target Of Rapamycin (TOR) Signaling	1.75	Link to the merged mTOR signaling pathway
Hedgehog signaling pathway	Signaling by Hedgehog	Hedgehog Signaling Pathway	1.67	Link to the merged Hedgehog signaling pathway
Apoptosis	Apoptosis	Apoptosis	1.31	Link to the merged Apoptosis pathway
IL-17 signaling pathway	Interleukin-17 signaling	IL17 signaling pathway	1.27	Link to the merged IL-17 signaling pathway
PI3K-Akt signaling pathway	PI3K/AKT activation	PI3K-Akt Signaling Pathway	1.25	Link to the merged PI3K/AKT signaling pathway
Wnt signaling pathway	Signaling by WNT	Wnt Signaling Pathway	1.21	Link to the merged Wnt signaling pathway
MAPK signaling pathway	MAPK family signaling cascades	MAPK Signaling Pathway	1.19	Link to the merged MAPK signaling pathway
B cell receptor signaling pathway	B Cell Receptor Signaling Pathway	Signaling by the B Cell Receptor (BCR)	1.11	Link to the merged B cell receptor signaling pathway
Pentose phosphate pathway	Pentose phosphate pathway (hexose monophosphate shunt)	Pentose Phosphate Pathway	1.00	Link to the merged Pentose phosphate pathway
Citrate cycle (TCA cycle)	Citric acid cycle (TCA cycle)	TCA Cycle	1.00	Link to the merged TCA cycle pathway
Synthesis and degradation of ketone bodies	Ketone body metabolism	Synthesis and Degradation of Ketone Bodies	1.00	Link to the merged Ketone body metabolism pathway
Notch signaling pathway	Signaling by NOTCH	Notch Signaling Pathway	0.87	Link to the merged Notch signaling pathway
DNA replication	DNA Replication	DNA Replication	0.83	Link to the merged DNA replication pathway
Prolactin signaling pathway	Prolactin receptor signaling	Prolactin receptor signaling	0.83	Link to the merged Prolactin signaling pathway
TGF-beta signaling pathway	Signaling by TGF-beta family members	TGF-beta Signaling Pathway	0.78	Link to the merged TGF-beta signaling pathway
Thyroid hormone synthesis	Thyroxine biosynthesis	Thyroxine (Thyroid Hormone) Production	0.60	Link to the merged thyroxine synthesis pathway

Sphingolipid metabolism	Sphingolipid metabolism	Sphingolipid Metabolism	0.49	Link to the merged Sphingolipid metabolism pathway
Mismatch repair	Mismatch Repair	Mismatch repair	0.23	Link to the merged mismatch repair pathway
Non-homologous end-joining	Nonhomologous End-Joining (NHEJ)	Non-homologous end joining	0	Link to the merged Non-homologous end joining pathway

Table 4: Consolidated pathway representations, their similarity indexes, and links to visualize the merged networks in the PathMe Viewer. The URLs for the merged networks can also be found at [https://nbviewer.jupyter.org/github/ComPath/pathme_resources/blob/master/notebooks/similarity_analysis/visualized_merged_pathways.ipynb].

Availability and Future Directions

PathMe and PathMe Viewer are both respectively available at https://github.com/ComPath/PathMe and https://github.com/ComPath/PathMe-Viewer with documentation available at https://pathme.readthedocs.io (PathMe) and https://pathme-viewer.readthedocs.io/en/latest/ (PathMe Viewer). Tutorials and the experiments presented in the case scenario are available https://github.com/ComPath/PathMe-Resources. Future work will be focusing on evaluating the equivalent pathways and their cross-talk aiming to complement the knowledge from different databases.

References

1. Domingo-Fernández, D., *et al*. (2018). ComPath: An ecosystem for exploring, analyzing, and curating pathway databases. *BioRxiv* 353235.
2. Fabregat, A., *et al.* (2017). The reactome pathway knowledgebase. *Nucleic Acids Res*., 46(D1), D649-D655.
3. Hoyt, C. T., *et al.* (2018). PyBEL: a computational framework for Biological Expression Language. *Bioinformatics (Oxford, England)*, *34*(4), 703–704.
4. Kanehisa, M., *et al.* (2016). KEGG: new perspectives on genomes, pathways, diseases and drugs. *Nucleic Acids Res*., 45(D1), D353-D361.
5. Sales, G., *et al.* (2012). graphite-a Bioconductor package to convert pathway topology to gene network. *BMC bioinformatics*, *13*(1), 20.
6. Slenter, D. N., *et al.* (2018). WikiPathways: a multifaceted pathway database bridging metabolomics to other omics research. *Nucleic Acids Research*, *46*(D1), D661–D667.
7. Waagmeester, A., *et al.* (2016). Using the semantic web for rapid integration of WikiPathways with other biological online data resources. *PLoS Comput Biol* 12 (6), e1004989+. doi:10.1371/journal.pcbi.1004989