Knowledge Reconciliation of \( n \)-ary Relations* 

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Abstract. In the expanding Semantic Web, an increasing number of sources of data and knowledge are accessible by human and software agents. Sources may differ in granularity or completeness, and thus be complementary. Consequently, unlocking the full potential of the available knowledge requires combining them. To this aim, we define the task of knowledge reconciliation, which consists in identifying, within and across sources, equivalent, more specific, or similar units. This task can be challenging since knowledge units are heterogeneously represented in sources (e.g., in terms of vocabularies). In this paper, we propose a rule-based methodology for the reconciliation of \( n \)-ary relations. To alleviate the heterogeneity in representation, we rely on domain knowledge expressed by ontologies. We tested our method on the biomedical domain of pharmacogenomics by reconciling 50,435 \( n \)-ary relations from four different real-world sources, which highlighted noteworthy agreements and discrepancies within and across sources.

Keywords: Reconciliation · Multidimensional Relation · Order · Ontology

1 Introduction

The Semantic Web [5] offers numerous actors the ability to publish, edit, access, and interpret data and knowledge. Actors are inherently working concurrently, which may lead to different data or knowledge sources describing similar units. These sources may differ in quality, completeness, granularity, and vocabularies. Unlocking the full potential of the knowledge they conjointly express requires identifying, within and across sources, equivalent, more specific or similar knowledge units. This task that we call knowledge reconciliation may highlight agreements, differences, and deficiencies within and across sources, providing a consolidated view of a domain, potentially useful in many applications, such as knowledge fusion and fact-checking.

Here, we focus on the reconciliation of units in knowledge bases expressed using Semantic Web standards. In this case, Uniform Resource Identifiers (URIs)
represent entities of a world, e.g., places, drugs, etc. Statements, expressed with the Resource Description Format (RDF) language, link URIs together or to literals (e.g., string, integers) using predicates. These latter (e.g., has-side-effect, has-name) give access to the link semantics. The use of ontologies, i.e., formal representations of a domain [10], enables the association of domain knowledge with entities. Ontologies consist of definitions of classes and predicates, partially ordered by the subsumption relation, denoted by $\sqsubseteq$. This relation states that a class (respectively a predicate) is more specific than another.

We illustrate the task of knowledge reconciliation in the biomedical domain of pharmacogenomics (PGx), which studies the influence of genetic factors on drug response phenotypes. PGx knowledge originate from distinct sources: reference databases such as PharmGKB, biomedical literature, or the mining of Electronic Health Records of hospitals. Knowledge represented in these sources may differ in levels of validation, completeness, and granularity. Consequently, reconciling PGx relations from these sources would provide a consolidated view on the knowledge of this domain, certainly beneficial in precision medicine, which aims at tailoring drug treatments to patients to reduce adverse effects and maximize drug efficacy [6,7]. PGx knowledge consists of $n$-ary relations relating sets of drugs, sets of genomic variations, and sets of phenotypes. Such an $n$-ary relation states that a patient being treated with the specified sets of drugs, while having the specified genomic variations will be more likely to experience the given phenotypes, e.g., adverse effects. For example, Figure 1 depicts the relation stating that patients treated with warfarin may experience cardiovascular diseases because of variations in the CYP2C9 gene.

![Fig. 1. Representation of a PGx relation between gene CYP2C9, drug warfarin and phenotype cardiovascular_diseases. The relation is reified through the individual pgr_1, connecting its components through the causes predicate.](image)

Motivated by this real-world application, we propose a general and mathematically well-founded methodology for reconciling $n$-ary relation instantiations, for an arbitrary $n$. For simplicity, relation instantiations will be called relations throughout the paper. Given two relations $r_1$ and $r_2$, we aim at deciding on their relatedness degree among the five degrees we propose (e.g., equivalent, more specific). In the Semantic Web standards, only binary predicates exist, requiring to reify $n$-ary relations to represent them properly: relations are individualized and linked to their components by predicates (see Figure 1) [14]. We consider here that an $n$-ary relation is fully defined by its components that consist of sets of individuals. In this context, reconciling two relations comes down to comparing
each of their components, which we achieve by defining five general rules. To
tackle the potential heterogeneity in the representation of relations (e.g., gran-
ularity, vocabularies), we propose to enrich this structure-based comparison by
considering domain knowledge (e.g., classes of ontologies and links between indi-
viduals). Finally, some of our rules are designed to ensure some desired properties
such as transitivity and symmetry.

Knowledge reconciliation is close to several other research works. Indeed, it
is tightly related to database reconciliation, i.e., managing co-existing and inde-
pendently modified replicas of the same database [1]. It is also associated with
ontology matching [8], which aims at finding alignments between units of two
ontologies (e.g., equivalences, or subsumptions between classes, predicates, or in-
stances). In this field, existing works use different features to suggest align-
ments. For example, some methods rely on the syntax of units label (e.g., string
matching). However, labels may not always be available. Structure-based tech-
niques can alleviate such limitations. They rely either on the internal structure
of a unit (i.e., predicates used to link a unit to literals) or the relational structure
of a unit (i.e., its links with other units). Two examples of frequently considered
relational structures are the hierarchy of classes and partOf links in an ontology.
For example, Atencia et al. [3] define linkkeys, a structure-based method to align
individuals. A linkkey consists of a pair of classes and a set of pairs of properties
from two ontologies. Instances of these classes that share common values for
all properties in the linkkey are regarded as identical. Alternatively, Suchanek
et al. [16] propose a holistic method called PARIS to align individuals, classes,
and predicates. In this framework, alignments for each type of unit fertilize the
others. Particularly, they define rules that rely on the internal and relational
structures of units and the functionality of predicates. Similarly, Galarraga et
al. [9] mine specific rules to align ontologies under the Partial Completeness
Assumption, which also relies on the functionality of predicates. Other works
explore knowledge reconciliation in the domain of Natural Language Processing,
to extract knowledge from multiple natural language sources and merge them
into a unique representation [11]. Such a reconciliation can be performed by ma-
chine learning techniques that learn vector representations of units respecting
their similarities [2].

The rest of this paper is organized as follows. In Section 2, we formalize the
problem of knowledge reconciliation for n-ary relations. In Section 3, we propose
two preorders to compare sets of individuals by considering domain knowledge:
links between individuals and classes instantiated. These preorders are used in
Section 4 to define reconciliation rules deciding on the relatedness between two
n-ary relations. Rules are experimented on PGx knowledge in Section 5. Finally,
we discuss our method and conclude in Sections 6 and 7.

Main contributions of this paper:

– We propose a general framework for the reconciliation of n-ary relations
whose components are sets of individuals.

– We propose five reconciliation rules, each ensuring some desired properties,
e.g., transitivity and symmetry. These rules use preorders arising from do-
main knowledge (classes instantiated and links between individuals).
2 Problem Setting

We aim at reconciling $n$-ary relations within a knowledge base $\mathcal{K}$, i.e., given two relations $r_1$ and $r_2$, we determine their relatedness degree (e.g., equivalent, more specific or similar). $\mathcal{K}$ is represented in the formalism of Description Logics (DL) [4] and thus consists of a TBox and an ABox. Accordingly, our knowledge reconciliation methodology uses the DL reasoning mechanisms of satisfiability, instance retrieval, and classification.

More precisely, we consider a set $\mathcal{R}$ of $n$-ary relations ($n$ fixed) whose components are sets of individuals in $\mathcal{K}$. As DL only accounts for binary relations, we assume each relation $r \in \mathcal{R}$ is reified as an individual within $\mathcal{K}$. Such a relation $r$ can be formally represented as $r = (\pi_1(r), \ldots, \pi_n(r))$. $\pi_i : \mathcal{R} \rightarrow 2^\Delta$ associates a relation $r$ with its component $i$ denoted by $\pi_i(r)$, which is a set of individuals included in the domain of interpretation $\Delta$. Relations in $\mathcal{K}$ come from potentially noisy sources and some components may be missing. As $\mathcal{K}$ verifies the Open World Assumption, we can only consider such components to be unknown since they are not explicitly specified as empty. In this case, such unspecified components are set to $\Delta$ to denote that all individuals may apply. For example, we could use a ternary relation to model $\text{pgr}_1$ from Figure 1, giving $\text{pgr}_1 = (\{\text{warfarin}\}, \{\text{CYP2C9}\}, \{\text{cardiovascular diseases}\})$. In this modeling, components respectively represent the sets of drugs, genomic factors, and phenotypes involved in the relation. In Section 5, we propose a finer definition of components by considering predicates (such as causes or influences) in addition to the class of associated individuals (drugs, genetic factors, etc.).

In view of our formalism, reconciling two $n$-ary relations $r_1$ and $r_2$ comes down to deciding on their relatedness degree by comparing their components $\pi_i(r_1)$ and $\pi_i(r_2)$ for each $i \in \{1, \ldots, n\}$. To illustrate, if $\pi_i(r_1) = \pi_i(r_2)$ for all $i$, then $r_1$ and $r_2$ are representing the same knowledge unit. Such a result highlights an agreement between the sources of $r_1$ and $r_2$. In the next section, we consider other tests between components.

3 Ontology-Based Preorders

As illustrated in Section 2, the reconciliation of two $n$-ary relations $r_1$ and $r_2$ relies on the comparison of each of their components $\pi_i(r_1)$ and $\pi_i(r_2)$. Comparing such sets of individuals can be achieved by testing their inclusion or equality. Thus, if $\pi_i(r_1) \subseteq \pi_i(r_2)$, then $\pi_i(r_1)$ can be considered as more specific than $\pi_i(r_2)$. It is noteworthy that testing inclusion or equality implicitly considers owl:sameAs links that indicate identical individuals. For example, the comparison of $\{e_1\}$ with $\{e_2\}$ while knowing that owl:sameAs(e_1, e_2) results in an equality. However, additional domain knowledge can be considered. For instance, some individuals can be part of others. Individuals may also instantiate different ontological classes, which are themselves comparable through subsumption. Such domain knowledge help tackle the heterogeneous representation of relations. To consider this domain knowledge in the process of reconciliation, we propose two preorders, i.e., reflexive and transitive binary orderings.
3.1 Preorder $\leq^p$ Based on Links Between Individuals

Individuals in $\pi_i(r_j)$ may be involved in $K$ in several links with other individuals. Some predicates $p$ used in such links are transitive and reflexive. Thus, for each of these predicates $p$, we define a preorder $\leq^p$ parameterized by $p$ as follows:

$$\pi_i(r_1) \leq^p \pi_i(r_2) \iff \forall e_1 \in \pi_i(r_1), \exists e_2 \in \pi_i(r_2), K \models p(e_1, e_2) \quad (1)$$

Note that, from the reflexivity of $p$, $\pi_i(r_1) \subseteq \pi_i(r_2)$ implies $\pi_i(r_1) \leq^p \pi_i(r_2)$.

The equivalence relation $\sim^p$ associated with $\leq^p$ is defined as usual by:

$$\pi_i(r_1) \sim^p \pi_i(r_2) \iff \pi_i(r_1) \leq^p \pi_i(r_2) \text{ and } \pi_i(r_2) \leq^p \pi_i(r_1) \quad (2)$$

Example 1. By its transitivity and reflexivity, $\text{partOf}$ is a suitable candidate for such a preorder. Consider three individuals $e_1, e_2, e_3$ such that $K \models \text{partOf}(e_3, e_1)$. Then it follows that:

$$\{e_1\} \leq^\text{partOf} \{e_1, e_2\}, \{e_3, e_2\} \leq^\text{partOf} \{e_1, e_2\}, \text{ and } \{e_3\} \leq^\text{partOf} \{e_1, e_2\}$$

Furthermore, we also have that $\{e_3, e_1\} \sim^\text{partOf} \{e_1\}$, since $e_3$ is a part of $e_1$. Thus, adding $e_3$ in a set that already contains $e_1$ is redundant. Such a case may arise due to noise in $K$ induced by source heterogeneity.

3.2 Preorder $\leq^O$ Based on Instantiation and Subsumption

The second preorder we propose takes into account classes of an ontology $O$ instantiated by individuals in $\pi_i(r_j)$ and ordered by subsumption. We denote the set of all classes of $O$ by $\text{classes}(O)$. As it is standard in DL, $\top$ denotes the top level class in $O$. Given an individual $e$, we denote the set of classes of $O$, except $\top$, instantiated by $e$ with:

$$\text{ci}(O, e) = \{ C \in \text{classes}(O) \setminus \{ \top \} \mid K \models C(e) \}$$

Note that $\text{ci}(O, e)$ may be empty. We explicitly exclude $\top$ from $\text{ci}(O, e)$ since $K$ may be noisy: individuals may lack instantiations of specific classes but instantiate $\top$ by default. This motivation to exclude $\top$ is illustrated by Example 2.

Example 2. Consider two PGx relations involving the same drug and genetic factor. Regarding the phenotype, one is linked with an individual representing $\text{headache}$ that does not instantiate the class $\text{Headache}$ in $O$ (e.g., MeSH) but instantiates $\top$ by default. The other relation is linked with an individual $\text{pain}$ that instantiates $\text{Pain}$, with $\text{Headache} \subseteq \text{Pain}$. Intuitively, the first relation is more specific than the second. However, by considering instantiated classes and knowing that $\text{Pain} \subseteq \top$, we would conclude that the first relation is more general than the second. We avoid this unwanted behavior by excluding $\top$ from $\text{ci}(O, e)$, leading to the relations being incomparable.

The proof that $\leq^p$ is a preorder is available in Appendix A.
Given $\mathcal{T} = \{C_1, C_2, \ldots, C_n\} \subseteq \text{classes}(\mathcal{O})$, we denote by $\text{msc}(\mathcal{T})$ the set of the most specific classes of $\mathcal{T}$, i.e., $\text{msc}(\mathcal{T}) = \{C \in \mathcal{T} \mid \not\exists D \in \mathcal{T}, \ D \sqsubset C\}$\footnote{\[ D \sqsubset C \] means that $D \sqsubset C$ and $D \neq C.$}. Similarly, we denote by $\text{msc}(\mathcal{O}, e)$ the set of the most specific classes of $\mathcal{O}$, except $\mathcal{T}$, instantiated by an individual $e$, i.e., $\text{msc}(\mathcal{O}, e) = \text{msc}(ci(\mathcal{O}, e))$.

Given an ontology $\mathcal{O}$, we can now define the preorder\footnote{The proof that $\preceq^O$ is a preorder is available in Appendix \ref{proof}.} $\preceq^O$ based on set inclusion and subsumption as follows:

$$\pi_i(r_1) \preceq^O \pi_i(r_2) \iff \forall e_1 \in \pi_i(r_1), \left[ e_1 \in \pi_i(r_2) \right] \bigvee \left[ \text{msc}(\mathcal{O}, e_1) \neq \emptyset \land \Box \right]$$

$$\forall C_1 \in \text{msc}(\mathcal{O}, e_1), \exists e_2 \in \pi_i(r_2), \exists C_2 \in \text{msc}(\mathcal{O}, e_2), \ C_1 \sqsubseteq C_2$$  \hspace{1cm} (3)\footnote{\[ \Box \]}

Clearly, if $\pi_i(r_1)$ is more specific than $\pi_i(r_2)$ and $e_1 \in \pi_i(r_1)$, then \footnote{\[ \Box \]} $e_1 \in \pi_i(r_2)$, or \footnote{\[ \Box \]} all the most specific classes instantiated by $e_1$ are subsumed by at least one of the most specific classes instantiated by individuals in $\pi_i(r_2)$. Thus individuals in $\pi_i(r_2)$ can be seen as “more general” than those in $\pi_i(r_1)$.

As before, $\preceq^O$ induces the equivalence relation $\sim^O$ defined by:

$$\pi_i(r_1) \sim^O \pi_i(r_2) \iff \pi_i(r_1) \preceq^O \pi_i(r_2) \text{ and } \pi_i(r_2) \preceq^O \pi_i(r_1)$$ \hspace{1cm} (4)

The preorder $\preceq^O$ can be seen as parameterized by the ontology $\mathcal{O}$, allowing to consider different parts of the TBox of $\mathcal{K}$ for each component $\pi_i(r_j)$, if needed.

**Example 3.** Figure\footnote{\[ \Box \]} depicts six examples for the application of $\preceq^O$:

(a) $\{e_1\}$ is more specific than $\{e_2, e_3\}$ even if $e_3$ instantiates a more specific class than $e_1$, because of the more general individual $e_2$.

(b) $\{e_1\}$ is more specific than $\{e_2, e_3\}$ since classes in $\text{msc}(\mathcal{O}, e_1)$ are either the same than those in $\text{msc}(\mathcal{O}, e_2)$ or more specific than those in $\text{msc}(\mathcal{O}, e_3)$.

(c) $\{e_1\}$ is more specific than $\{e_2, e_3\}$ since the class in $\text{msc}(\mathcal{O}, e_1)$ is more specific than the one in $\text{msc}(\mathcal{O}, e_2)$. There is no need to compare it with the class in $\text{msc}(\mathcal{O}, e_3)$.

(d) This example, similar to (c), illustrates the occurrence of the same behavior regardless of classes being instantiated by a single or by several individuals.

(e) $\{e_1\}$ and $\{e_2\}$ cannot be compared. Unlike the two latter examples, here, $e_1$ instantiates a class that is more specific than the class instantiated by $e_2$, but also a class that is not comparable.

(f) $\{e_1\}$ and $\{e_2\}$ are equivalent by instantiating the same most specific class.

## 4 Using Preorders to Define Reconciliation Rules

Let $r_1, r_2 \in R$ be two $n$-ary relations to be reconciled. Assuming each component $i \in \{1, \ldots, n\}$ is endowed with a preorder $\preceq_i \in \{\subseteq, \preceq^p, \preceq^O\}$ enabling the
Fig. 2. Examples of use cases of the preorder ≼\(\mathcal{O}\). Circles represent ontology classes. Solid arrows depict class subsumptions and dashed arrows depict class instantiations by individuals \(e_1\), \(e_2\), and \(e_3\). The light gray color identifies classes in msci(\(\mathcal{O}\), \(e_1\)). The dark gray color identifies classes in msci(\(\mathcal{O}\), \(e_2\)) and msci(\(\mathcal{O}\), \(e_3\)).
comparison of \( \pi_i(r_1) \) and \( \pi_i(r_2) \), we can define rules for aggregating such comparisons for all \( i \in \{1, \ldots, n\} \) and compare \( r_1 \) and \( r_2 \) globally. Thus, such rules conclude on the relatedness degree of \( r_1 \) and \( r_2 \), performing their reconciliation.

Here, we propose the following five relatedness degrees: =, \( \sim \), \( \preceq \), \( \preceq \), and \( \prec \) (from the strongest to the weakest). Accordingly, we propose five reconciliation rules of the form \( B \Rightarrow H \), where \( B \) expresses the conditions of the rule, testing equalities, equivalences, or inequalities between components of \( r_1 \) and \( r_2 \). Classically, these conditions can be combined using conjunctions or disjunctions, respectively denoted by \( \land \) and \( \lor \). If \( B \) holds, \( H \) expresses the relatedness between \( r_1 \) and \( r_2 \) to add to \( K \). Rules are applied from Rule 1 to Rule 5. Once conditions in \( B \) hold for a rule, \( H \) is added to \( K \) and the following rules are discarded, meaning that at most one relatedness degree is added to \( K \) for each pair of relations. When no rule can be applied, \( r_1 \) and \( r_2 \) are considered as incomparable and nothing is added to \( K \). The first four rules are the following:

**Rule 1.** \( \forall i \in \{1, \ldots, n\}, \pi_i(r_1) = \pi_i(r_2) \Rightarrow r_1 = r_2 \)

**Rule 2.** \( \forall i \in \{1, \ldots, n\}, \pi_i(r_1) \sim_i \pi_i(r_2) \Rightarrow r_1 \sim r_2 \)

**Rule 3.** \( \forall i \in \{1, \ldots, n\}, \pi_i(r_1) \preceq_i \pi_i(r_2) \Rightarrow r_1 \preceq r_2 \)

**Rule 4.** \( \forall i \in \{1, \ldots, n\}, [ (\pi_i(r_1) = \pi_i(r_2)) \lor (\pi_i(r_2) \neq \Delta \land \pi_i(r_1) \preceq_i \pi_i(r_2)) \lor (\pi_i(r_1) \neq \Delta \land \pi_i(r_2) \sim_i \pi_i(r_1)) ] \Rightarrow r_1 \preceq r_2 \)

The relatedness degrees resulting of these rules are respectively encoded in \( K \) by owl:sameAs, skos:closeMatch, skos:broadMatch, and skos:relatedMatch links. Rule 1 states that \( r_1 \) and \( r_2 \) are identical (=) whenever \( r_1 \) and \( r_2 \) coincide on each component. Rule 2 states that \( r_1 \) and \( r_2 \) are equivalent (\( \sim \)) whenever each component \( i \in \{1, \ldots, n\} \) of \( r_1 \) is equivalent to the same component of \( r_2 \). Rule 3 states that \( r_1 \) is more specific than \( r_2 \) (\( \preceq \)) whenever each component \( i \in \{1, \ldots, n\} \) of \( r_1 \) is more specific than the same component of \( r_2 \) w.r.t. \( \preceq_i \). Rule 4 states that \( r_1 \) and \( r_2 \) have comparable components (\( \preceq \)) whenever they have the same specified components (i.e., different from \( \Delta \)), and these components are comparable w.r.t. \( \preceq_i \). Rules 1 to 4 ensure the transitivity property. Additionally, Rules 1, 2, and 4 ensure the symmetry property.

In Rules 1 to 4, comparison is made component-wise. However, other relatedness cases may require aggregating over components. For example, we may want to compare all individuals involved in two relations, regardless of the components they are involved in. Additionally, we may want to state that two relations are weakly related if each of their components have a specified proportion of comparable individuals. To this aim, we propose Rule 5. Let \( I = \{I_1, \ldots, I_m\} \) be a partition of \( \{1, \ldots, n\} \), defined by the user at the beginning of the reconciliation process. Let \( \pi_{I_k}(r_j) = \bigcup_{\pi_i(r_j) \neq \Delta} i \in I_k \pi_i(r_j) \), i.e., the aggregated component \( I_k \) of \( r_j \) is the union of all specified \( \pi_i(r_j) \) (i.e., different from \( \Delta \)) for \( i \in I_k \). We assume each aggregated component \( I_k \in I \) is endowed with a preorder \( \preceq_k \in \{\subseteq, \subseteq^p, \subseteq^o\} \). We denote by \( \text{SSD}(\pi_{I_k}(r_1), \pi_{I_k}(r_2)) \) the semantic set difference between \( \pi_{I_k}(r_1) \) and \( \pi_{I_k}(r_2) \), i.e., \( \text{SSD}(\pi_{I_k}(r_1), \pi_{I_k}(r_2)) = \{e_1 \mid e_1 \in \pi_{I_k}(r_1) \text{ and } \{e_1\} \neq_k \pi_{I_k}(r_2)\} \).
SSD(πIk(r1), πIk(r2)) is the set of elements in πIk(r1) preventing it from being more specific than πIk(r2) w.r.t. ≲Ik. We define the operator ◦Ik as follows:

$$\pi_{Ik}(r_1) \bowtie Ik \pi_{Ik}(r_2) = \begin{cases} 1 & \text{if } \pi_{Ik}(r_1) \equiv_{Ik} \pi_{Ik}(r_2) \text{ or } \pi_{Ik}(r_2) \not\equiv_{Ik} \pi_{Ik}(r_1) \\ 1 - \frac{|\text{SSD}(\pi_{Ik}(r_1), \pi_{Ik}(r_2)) \cup \text{SSD}(\pi_{Ik}(r_2), \pi_{Ik}(r_1))|}{|\pi_{Ik}(r_1) \cup \pi_{Ik}(r_2)|} & \text{otherwise} \end{cases}$$

This operator returns a number measuring the similarity between πIk(r1) and πIk(r2). This number is equal to 1 if the two aggregated components are comparable. Otherwise, it is equal to 1 minus the proportion of incomparable elements.

We denote by $I_\Delta(r_1, r_2) = \{I_k \mid I_k \in I \text{ and } \pi_{Ik}(r_1) \not\equiv \Delta \text{ and } \pi_{Ik}(r_2) \not\equiv \Delta\}$ the set of aggregated components that are specified for both $r_1$ and $r_2$ (i.e., different from $\Delta$). Then, Rule 5 is defined as follows:

**Rule 5.** Let $I = \{I_1, \ldots, I_m\}$ be a partition of $\{1, \ldots, n\}$, and let $\gamma_{\not\equiv \Delta}$, $\gamma_S$, and $\gamma_C$ be three parameters, all fixed at the beginning of the reconciliation process.

$$\left(\bigcup_{I_j \in I_{\not\equiv \Delta}(r_1, r_2)} \left[\forall I_k \in I_{\not\equiv \Delta}(r_1, r_2), \pi_{Ik}(r_1) \bowtie Ik \pi_{Ik}(r_2) \geq \gamma_S \right] \lor \left[\sum_{I_k \in I_{\not\equiv \Delta}(r_1, r_2)} \left(\pi_{Ik}(r_1) \bowtie Ik \pi_{Ik}(r_2) = 1\right) \geq \gamma_C\right]\right) \Rightarrow r_1 \bowtie r_2$$

Rule 5 is applicable if at least $\gamma_{\not\equiv \Delta}$ aggregated components are specified for both $r_1$ and $r_2$. Then, $r_1$ and $r_2$ are weakly related ($\bowtie$) whenever all these specified components have a similarity of at least $\gamma_S$ or when at least $\gamma_C$ of them are comparable. Rule 5 ensures the symmetry property. The relatedness degree $\bowtie$ is encoded by skos:related links.

In the end, reconciling $n$-ary relations from $\mathcal{K}$ comes down to applying these five reconciliation rules on every ordered pair $(r_1, r_2)$ of $n$-ary relations from $\mathcal{R}$.

## 5 Application to Pharmacogenomic Knowledge

Our methodology was motivated by the real-world problem of reconciling pharmacogenomic (PGx) knowledge. Consequently, we experimented this methodology with PGxLOD, a PGx knowledge base represented in the ALCHI Description Logic [4]. In PGxLOD, 50,435 PGx relations are available, coming from four different sources: (i) structured data of PharmGKB, (ii) textual portions of PharmGKB called clinical annotations, (iii) biomedical literature, and (iv) results found in EHR studies. PGx relations are represented using classes and predicates of the PGxO ontology [5]. As PGx relations are $n$-ary, they are reified as instances of the PharmacogenomicRelationship class. All the individuals involved in PGx relations instantiate the Drug, GeneticFactor, or Phenotype classes. They are linked with reified PGx relations by predicates qualifying their association to relations. Predicates are organized in a hierarchy defined by subsumption

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[4] https://pgxlod.loria.fr

[5] https://pgxo.loria.fr
relations, such as \texttt{causes} \sqsubseteq \texttt{influences} \sqsubseteq \texttt{isAssociatedWith}. It is noteworthy that, in PGxLOD, \texttt{partOf} links indicate that instances of \texttt{GeneticFactor} compose others such instances. For example, a genomic variation may be part of a gene. Similarly, instances of \texttt{Phenotype} may have dependencies, expressed with \texttt{dependsOn} links. These dependencies enable representing complex phenotypes that refer to other phenotypes or drugs. For example \texttt{warfarin-caused hemorrhage} is a phenotype linked with \texttt{dependsOn} to \texttt{hemorrhage} and \texttt{warfarin}. The TBox of PGxLOD contains, alongside PGxO, three other ontologies: individuals representing drugs may instantiate classes from ATC or ChEBI, and individuals representing phenotypes may instantiate classes from MeSH. Table 1 provides global statistics about PGxLOD.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|}
\hline
Class & \# instances & Predicate & \# links \\
\hline
Drug & 47,584 & \texttt{partOf} & 16,697 \\
GeneticFactor & 464,302 & \texttt{dependsOn} & 23,976 \\
Phenotype & 61,330 & & \\
PharmacogenomicRelationship & 50,435 & & \\
\quad From PharmGKB (structured data) & 3,650 & & \\
\quad From PharmGKB (clinical annotations) & 10,240 & & \\
\quad From biomedical literature & 36,535 & & \\
\quad From EHRs & 10 & & \\
\hline
\end{tabular}
\caption{Statistics about PGxLOD. \# denotes “number of”. Instances linked by \texttt{owl:sameAs} are counted separately. \texttt{partOf} links are counted without transitivity inference. All PGx relations were programmatically extracted from their sources, except the ten relations from EHRs that were manually added as a proof of concept.}
\end{table}

To apply the reconciliation rules on PGx relations, we specified their components. Each component of a relation is the set of individuals with a specific type (Drug, GeneticFactor, or Phenotype) that are linked with a specific predicate to the relation. For example, given \texttt{pgr} a PGx relation, \( \pi_{\text{Phenotype.cause}(pgr)} \) contains all the phenotypes caused by \texttt{pgr}. Hence, as there are 3 types of individuals and 38 predicates, PGx relations have \( 3 \times 38 = 114 \) components. Once components of relations are specified, their associated preorders can be defined. Based on the available data and knowledge in PGxLOD, it makes sense to use the \( \preceq_{\text{Drug}} \) preorder for components involving instances of \texttt{GeneticFactor}. Similarly, we use \( \preceq_{\text{Drug}} \) and \( \preceq_{\text{Phenotype}} \) as preorders for components respectively involving instances of \texttt{Drug} and \texttt{Phenotype}, where \( \preceq_{\text{Drug}} \) is the concatenation of ATC and ChEBI, and \( \preceq_{\text{Phenotype}} \) is the MeSH ontology.

Finally, to apply Rule 5, a natural three-way partition of components appears based on the three types of involved individuals. Therefore, discarding predicates, we gather all drugs, genetic factors, and phenotypes involved in a relation in three aggregated components. To benefit from dependencies of complex phenotypes,
we choose to add them to the correct aggregated components based on their type. For example, in warfarin-caused hemorrhage, hemorrhage is added to the aggregated component representing phenotypes and warfarin is added to the one representing drugs. We arbitrarily set $\gamma_\neq = 3$, $\gamma_S = 0.8$, and $\gamma_C = 2$. These values mean that two PGx relations $pgr_1$ and $pgr_2$ will be reconciled by Rule 5 if their three aggregated components are specified (i.e., different from $\Delta$). Additionally, each of the three aggregated components of $pgr_1$ must have 80% of comparable individuals with the same aggregated component of $pgr_2$, or at least two aggregated components of $pgr_1$ must be comparable with the same aggregated components of $pgr_2$.

To illustrate the interest of this formalization as well as reasoning mechanisms from DL, let $pgr_1$ and $pgr_2$ be two PGx relations. $pgr_1$ causes a phenotype $ph_1$ and is associated with a phenotype $ph_2$, and $pgr_2$ is associated with both phenotypes. Thus, by applying reasoning mechanisms along the hierarchy of predicates, it follows that:

$$\pi_{\text{Phenotype, causes}}(pgr_1) = \{ph_1\}; \pi_{\text{Phenotype, isAssociatedWith}}(pgr_1) = \{ph_1, ph_2\}$$

$$\pi_{\text{Phenotype, causes}}(pgr_2) = \Delta; \pi_{\text{Phenotype, isAssociatedWith}}(pgr_2) = \{ph_1, ph_2\}$$

By definition of $\bowtie_{\text{Phenotype}}$, $\pi_{\text{Phenotype, causes}}(pgr_1) \bowtie_{\text{Phenotype}} \pi_{\text{Phenotype, causes}}(pgr_2)$ as well as $\pi_{\text{Phenotype, isAssociatedWith}}(pgr_1) \bowtie_{\text{Phenotype}} \pi_{\text{Phenotype, isAssociatedWith}}(pgr_2)$. Therefore, by applying Rule 5 $pgr_1$ is more specific than $pgr_2$. This makes sense as the predicate connecting $ph_1$ with $pgr_1$ is more specific with than the one used with $pgr_2$.

We implemented our knowledge reconciliation methodology in C++ with multithreading. Our code is available on GitHub. Our program interacts with the knowledge base thanks to SPARQL queries. Previously, we indicated that an unspecified component of an $n$-ary relation is set to $\Delta$. Accordingly, when a SPARQL query returns $\emptyset$ for a component of a relation, it is interpreted as if it is returning $\Delta$. On PGxLOD, the reconciliation rules led to perform $(50,435) = 1,271,819,395$ comparisons in approximately 54 hours using 4 cores and 15 GB of RAM. Results are provided in Table 2 and discussed in Section 6.

### Discussion

In Table 2, we observe that most links are intra-source as only Rules 2, 3, and 5 generated links across sources. This predominance of intra-source links may come from the use of different vocabularies to represent individuals in sources. In such a case, our reconciliation process requires mappings between such vocabularies to compare individuals. Thus, missing mappings prevent reconciliation rules to be applied. This result underlines the importance of enriching the knowledge base with ontology-to-ontology mappings, for example, those defined in the NCBO BioPortal. We also notice that Rule 5 generates more links than the other rules.
Table 2. Number of links resulting from each rule. Links are generated between relations of distinct sources or within the same source. PGKB stands for “PharmGKB”, sd for “structured data”, and ca for “clinical annotations”. As Rules 1, 2, 4, and 5 ensure symmetry, links from $r_1$ to $r_2$ as well as from $r_2$ to $r_1$ are counted. Similarly, as Rules 1 to 3 ensure transitivity, transitivity-induced links are counted. Regarding skos:broadMatch links, rows represent origins and columns represent destinations.

|                        | PGKB (sd) | PGKB (ca) | Literature | EHRs |
|------------------------|-----------|-----------|------------|------|
| owl:sameAs             |           |           |            |      |
| Rule 1                 | PGKB (sd)| 166       | 0          | 0    |
|                        | PGKB (ca)| 0         | 10,134     | 0    |
|                        | Literature| 0         | 0          | 122,646|
|                        | EHRs     | 0         | 0          | 0    |
| skos:closeMatch        |           |           |            |      |
| Rule 2                 | PGKB (sd)| 0         | 5          | 0    |
|                        | PGKB (ca)| 5         | 1,366      | 0    |
|                        | Literature| 0         | 0          | 16,692|
|                        | EHRs     | 0         | 0          | 0    |
| skos:broadMatch        |           |           |            |      |
| Rule 3                 | PGKB (sd)| 87        | 3          | 15   |
|                        | PGKB (ca)| 9,325     | 665        | 42   |
|                        | Literature| 0         | 0          | 75,138|
|                        | EHRs     | 0         | 0          | 0    |
| skos:relatedMatch      |           |           |            |      |
| Rule 4                 | PGKB (sd)| 20        | 0          | 0    |
|                        | PGKB (ca)| 0         | 110        | 0    |
|                        | Literature| 0         | 0          | 18,050|
|                        | EHRs     | 0         | 0          | 0    |
| skos:related           |           |           |            |      |
| Rule 5                 | PGKB (sd)| 100,596   | 287,670    | 414  |
|                        | PGKB (ca)| 287,670   | 706,270    | 1,103|
|                        | Literature| 414       | 1,103      | 1,082,074|
|                        | EHRs     | 2         | 19         | 15   |

These numbers emphasize the importance of considering weaker relatedness degrees to establish connections between sources and overcome their heterogeneity. Here, by only considering a specified proportion of comparable individuals, this rule allows alleviating missing class instantiations or mappings.

By looking more closely at the results, we notice that all owl:sameAs links are intra-source and thus indicate duplicates. This is expected in the case of the literature since several articles could mention the same relation. The 5 skos:closeMatch links between relations from structured data and clinical annotations of PharmGKB highlight expected agreements between these two related sources. However, linked relations are expressed with different individuals instantiating the same ontology classes, preventing their reconciliation with owl:sameAs.

Some relations from the literature appear more general than PharmGKB structured data and clinical annotations (respectively 15 and 42 skos:broad-
Match links). These links are a foreseen consequence of the completion process of PharmGKB. Indeed, curators achieve this completion after a literature review, inevitably leading to relations more specific or equivalent to the ones in reviewed articles. Interestingly, our methodology could ease such a review by pointing at articles describing similar relations. Clinical annotations of PharmGKB are in several cases more specific than structured data, as 9,325 skos:broadMatch links were produced between these two sources. This is also expected as structured data are a broad-level summary of more complex phenotypes detailed in clinical annotations.

The results of Rule 4 underline that sources may contain relations with comparable components. These results may benefit source owners by encouraging them to add a relation formed by the most specific components of reconciled relations. Finally, we notice that only Rule 5 generates links between the relations from EHRs and other sources. As relations from EHRs are manually represented, there are only a few of them, minimizing the chance of overlap with other sources. Additionally, phenotypes involved in relations from EHRs are very specific, making their comparison with phenotypes from biomedical literature or PharmGKB difficult.

Regarding our method, using rules is somehow off the trends that invest machine learning approaches for reconciliation [13,15]. However, writing simple and well-founded rules constitutes a valid first step before applying machine learning approaches. Indeed, rules are readable and may be analyzed and confirmed by domain experts. This eases the explanation of reconciliation results. Our rules are simple enough to be generally true, and thus, to be useful in other domains. By relying on instantiated classes and partOf links, we illustrate how domain knowledge and reasoning mechanisms can serve a structure-based reconciliation. In future works, conditions under which preorders $\preceq^p$ and $\preceq^O$ could be merged into one unique preorder deserve to be studied.

Other reconciliation rules may appear, either given by experts or automatically learned by machine learning approaches. In this context, such well-founded and explicit rules enable generating a “silver” standard for reconciliation, which may be useful to either train or evaluate supervised approaches. Then, in this view, results obtained from rules constitute a baseline to generalize from or compare to when experimenting with alternative reconciliation methods.

7 Conclusion

In this paper, we considered the reconciliation of $n$-ary relations fully defined by their components. For each pair of relations, we aimed at deciding on their relatedness degree among the five degrees we proposed. We defined a general and mathematically well-founded methodology that relies on reconciliation rules and preorders leveraging domain knowledge and associated reasoning capabilities. We applied our methodology to the real-world use case of reconciling pharmacogenomic relations, i.e., relations that represent the impact of genomic factors on drug response phenotypes, and obtained insightful results. In the future, our
results could be compared with reconciliation results obtained from machine learning approaches. Additionally, the integration of this purely symbolic approach with machine learning approaches deserves to be studied.

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A Proof that $\preceq^p$ is a preorder

Proof. From the fact that $p$ is reflexive, it immediately follows that $\preceq^p$ is reflexive. Indeed, for every $E \subseteq \Delta$, $E \preceq^p E$ since for every $e \in E$, $p(e, e)$.

To prove that $\preceq^p$ is a preorder, it remains to show that $\preceq^p$ is transitive. Consider $E_1, E_2, E_3 \subseteq \Delta$ such that:

$$ E_1 \preceq^p E_2 \text{ and } E_2 \preceq^p E_3. $$

In other words, $\forall e_1 \in E_1$, $\exists e_2 \in E_2$, $K \models p(e_1, e_2)$ and $\forall e_2 \in E_2$, $\exists e_3 \in E_3$, $K \models p(e_2, e_3)$. By the transitivity of $p$, we then have that

$$ \forall e_1 \in E_1$, $\exists e_3 \in E_3$, $K \models p(e_1, e_3), $$
i.e., $E_1 \preceq^p E_3$. This shows that $\preceq^p$ is transitive, and the proof is complete. $\square$

B Proof that $\preceq^O$ is a preorder

Recall that, for every $E_1, E_2 \subseteq \Delta$,

$$ E_1 \preceq^O E_2 \iff \forall e_1 \in E_1, \left[ e_1 \in E_2 \right] \lor \left[ \text{msci}(O, e_1) \neq \emptyset \land \right.$$

$$ \forall C_1 \in \text{msci}(O, e_1), \exists e_2 \in E_2, \exists C_2 \in \text{msci}(O, e_2), C_1 \sqsubseteq C_2 \left]. \quad (5) \right.$$

Proof. The reflexivity of $\preceq^O$ follows immediately from (5a). To see that it is also transitive, consider distinct $E_1, E_2, E_3 \subseteq \Delta$ such that $E_1 \preceq^O E_2$ and $E_2 \preceq^O E_3$. We need to prove that $E_1 \preceq^O E_3$, that is,

$$ \forall e_1 \in E_1, \left[ e_1 \in E_3 \right] \lor \left[ \text{msci}(O, e_1) \neq \emptyset \land \right.$$

$$ \forall C_1 \in \text{msci}(O, e_1), \exists e_3 \in E_3, \exists C_3 \in \text{msci}(O, e_3), C_1 \sqsubseteq C_3 \left]. \quad (5) \right.$$

So let $e_1 \in E_1$. If $e_1 \in E_2$, then it follows from $E_2 \preceq^O E_3$ that

$$ \left[ e_1 \in E_3 \right] \lor \left[ \text{msci}(O, e_1) \neq \emptyset \land \right.$$

$$ \forall C_1 \in \text{msci}(O, e_1), \exists e_3 \in E_3, \exists C_3 \in \text{msci}(O, e_3), C_1 \sqsubseteq C_3 \left], \quad (6) \right.$$

and we are done. Otherwise, $\text{msci}(O, e_1) \neq \emptyset \land \forall C_1 \in \text{msci}(O, e_1), \exists e_2 \in E_2, \exists C_2 \in \text{msci}(O, e_2), C_1 \sqsubseteq C_2$.

As $E_2 \preceq^O E_3$, we have two possible cases for each $e_2 \in E_2$:
– $e_2 \in E_3$ and for each $C_1 \in \text{msci}(O, e_1)$ we also have:

$$\exists e_3 \in E_3, \exists C_3 \in \text{msci}(O, e_3), \ C_1 \sqsubseteq C_3,$$

or

$$\exists e_3 \in E_3, \exists C_3 \in \text{msci}(O, e_3), \ C_2 \sqsubseteq C_3.$$ 

Since the subsumption relation is transitive, $C_1 \sqsubseteq C_3$, and

$$\exists e_3 \in E_3, \exists C_3 \in \text{msci}(O, e_3), \ C_1 \sqsubseteq C_3$$

From these two cases, it follows that for each $e_1 \in E_1$ such that

$$\text{msci}(O, e_1) \neq \emptyset \land \forall C_1 \in \text{msci}(O, e_1), \ \exists e_2 \in E_2, \ \exists C_2 \in \text{msci}(O, e_2), \ C_1 \sqsubseteq C_2,$$

we have that

$$\exists e_3 \in E_3, \exists C_3 \in \text{msci}(O, e_3), \ C_1 \sqsubseteq C_3.$$

From Equations (6) and (7), it then follows that:

$$\forall e_1 \in E_1, \ \left[ e_1 \in E_3 \right] \lor \left[ \text{msci}(O, e_1) \neq \emptyset \land \forall C_1 \in \text{msci}(O, e_1), \ \exists e_3 \in E_3, \ \exists C_3 \in \text{msci}(O, e_3), \ C_1 \sqsubseteq C_3 \right],$$

thus showing that $E_1 \preceq^O E_3$. As the latter holds for every $E_1, E_2, E_3 \subseteq \Delta$, $\preceq^O$ is transitive. \qed