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Abstract

Researchers in neuroscience have a growing number of datasets available to study the brain, which is made possible by recent technological advances. Given the extent to which the brain has been studied, there is also available ontological knowledge encoding the current state of the art regarding its different areas, activation patterns, keywords associated with studies, etc. Furthermore, there is inherent uncertainty associated with brain scans arising from the mapping between voxels—3D pixels—and actual points in different individual brains. Unfortunately, there is

currently no unifying framework for accessing such collections of rich heterogeneous data under uncertainty, making it necessary for researchers to rely on ad hoc tools. In particular, one major weakness of current tools that attempt to address this task is that only very limited propositional query languages have been developed. In this paper we present NeuroLang, a probabilistic language based on first-order logic with existential rules, probabilistic uncertainty, ontologies integration under the open world assumption, and built-in mechanisms to guarantee tractable query answering over very large datasets. NeuroLang's primary objective is to provide a unified framework to seamlessly integrate heterogeneous data, such as ontologies, and map fine-grained cognitive domains to brain regions through a set of formal criteria, promoting shareable and highly reproducible research. After presenting the language and its general query answering architecture, we discuss real-world use cases showing how NeuroLang can be applied to practical scenarios.

Keywords: Datalog, Open-world Assumption, Probabilistic Programming, Query Answering, Meta-Analysis, Neuroimaging

1 Introduction

Recent technological advances in neuroscience have sparked enormous growth in the amount of datasets—containing text, images, and knowledge graphs—available for analysis of the human brain. To take advantage of the full breadth of this heterogeneous, and often noisy data, a unifying framework is needed. This framework should allow researchers to represent their theories, definitions, and perform inferences on them in a structured, formal way. The main hypothesis of this paper is that a probabilistic language based on first-order logic carefully extended with negation and aggregation is a useful tool for such tasks.

Meta-analysis tools are examples of central neuroscience use cases requiring the combination of the aforementioned datasets. This application constitutes a fertile ground to show how current knowledge representation advancements can combine heterogeneous datasets, pushing forward neuroimaging research. Meta-analysis is a set of techniques used to combine a finite number of published articles, which often disagree, to infer consensus-based findings (Poldrack and Yarkoni, 2016). Hence, its main application is aggregating noisy knowledge across articles in the field. While recent advances in automated meta-analysis techniques are mostly centered on better representing spatial correlations (Samartsidis et al, 2017), to the best of our knowledge, none have formally addressed expressivity limitations of query languages and the feasibility of a more expressive resolution.

Current standard tools for neuroimaging meta-analysis are Neurosynth (Yarkoni et al, 2011) and BrainMap (Laird et al, 2011), which harness automatically extracted as well as manually-curated information present across

neuroscientific articles. Briefly, these tools interpret each article as an independent sample of *neuroscientific knowledge*, and then develop query systems centered on study subset selection and posterior probabilistic inference on such subsets. For instance, selecting all studies mentioning "fear" and inferring the most common areas of the brain reported as active—i.e., deferentially oxygenated—in such studies. In these tools, queries select a subset of a total of around 15k full-text articles reporting involvement of several brain locations each, and a brain tessellation of 300k cubes, or voxels, then infer commonalities across these articles through maximum likelihood estimations combined with spatial information smoothing. Such queries can express questions like "*Where do articles reporting the term 'emotion' show activations?*", or "*Which terms associated with cognitive processes are most likely associated with articles reporting activations in the amygdala?*". Finally, after the inferential tasks, the obtained probabilities are manipulated and aggregated to frame results into the frequentist language neuroscientists commonly use to communicate the significance of their results (Yarkoni et al, 2011; Samartsidis et al, 2017). These meta-analyses are performed in under 30 seconds on a regular laptop computer—however, these tools are limited in terms of the expressivity of their associated query languages.

Neurosynth combines text mining, meta-analysis, and machine learning techniques to generate probabilistic mappings relating text-mined terms with activations in the human brain. While NeuroSynth has proven to be of great value to the neuroscience community, the language used to infer these relationships is based on propositional logic, which can limit the expressiveness of its query system. This limitation excludes, for instance, the use of existential quantifiers and negation, forbidding queries such as "*What are the terms most probably mentioned in articles reporting activations in the parietal lobe and no other brain region*", which we dub *segregation queries*. Another example is BrainMap, which has a hand-curated dataset of great precision and an ontology for structuring all this knowledge and annotating the articles. Nonetheless, Brainmap's query system is also based on propositional logic and only allows to select terms mentioned in articles knowing them in advance, which again cannot express segregation queries or harness the full information of neuroscience ontologies—such as CogAt (Poldrack et al, 2011)—that use open knowledge.

Breaching the expressivity limitations of current approaches and handling heterogeneous data requires tackling several issues: handling noisiness in neuroimaging data and conclusions reported across studies calls for a unifying formalism with probabilistic modeling capabilities; being able to leverage ontological information modeled under the open world assumption; finally, performance cannot be ignored since the amount of information needed to model the human brain is considerable. In short, we need to design a logic-based language capable of: (i) performing negation and aggregation; (ii) performing probabilistic inference; (iii) dealing with open knowledge; (iv) post-processing inferred probabilities; and (v) dealing with neuroimaging databases having, at least, a similar performance to current meta-analytic tools.

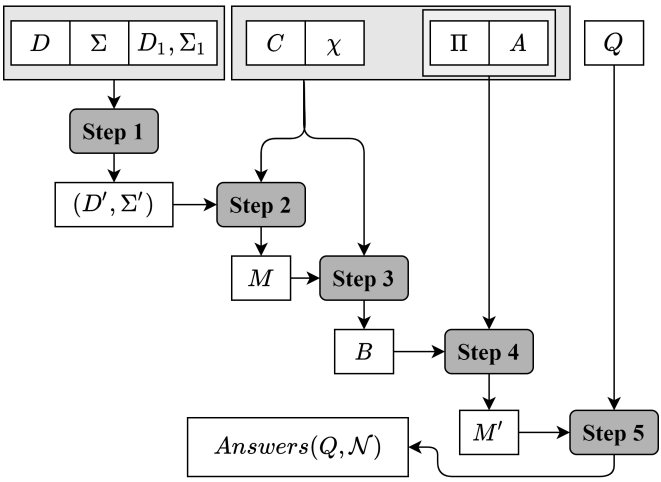


Fig. 1: Overview of the NeuroLangQA algorithm. Step numbers refer to those described in Algorithm 1

Our main proposal in this paper is the development of a subset of Datalog+/–, extended with probabilistic semantics, aggregation, and negation, focused on meta-analytic applications. Such an approach allows us to have a language based on first-order logic with negation and existential ($\text{FO}^{\neg\exists}$), enabling more complex queries such as segregation queries or manipulation of information under the open-world. In all, we produce a language able to express the full breadth of the pipeline needed for meta-analytic applications: from data preprocessing to probabilistic modeling and inference, and finally the post-processing of probabilistic results into images and reports that are easily interpretable in terms of current reporting used in neuroscience publications. Our main contribution is the introduction and evaluation of NeuroLang, a probabilistic language based on Datalog+/– developed to express and solve rich logic-based queries meeting the functional requirements of neuroimaging meta-analyses.

The rest of this paper is organized as follows: Section 2 introduces the probabilistic semantics, which is based on a classical possible world approach adopted in many approaches to reasoning under uncertainy; Section 3 then formally introduces the NeuroLang language and the NeuroLangQA query answering algorithm; Section 4 presents a set of real-world use cases showing how our formalism can be applied in neuroscientific research; finally, Section 5 discusses conclusions.

2 Basic Probabilistic Ontological Model

In this section, we recall the basics on relational databases, conjunctive queries, Datalog, and ontology-mediated query answering (including tuple-generating

dependencies and negative constraints), all based on a probabilistic extension with a corresponding query answering semantics.

We assume an infinite universe of *(data) constants* Δ, an infinite set of *(labeled) nulls* Δ_N (used as "fresh" Skolem terms) that are placeholders for unknown values, and an infinite set of variables $\mathcal{V}$. Different constants represent different values (*i.e., unique name assumption*), while different nulls may represent the same value. Sequences of $k \geq 0$ variables, namely $X_1, \ldots, X_k$, are denoted by $\mathbf{X}$.

Furthermore, we assume a *relational schema* $\mathcal{R}$, which is a finite set of *predicate symbols*, we also allow built-in predicates (with finite extensions) and equality. As expected, a *term* t is a constant, null, or variable. An *atomic formula* (or *atom*) $\mathbf{a}$ has the form $p(t_1, \ldots, t_n)$, where p is an n-ary predicate, and $t_1, \ldots, t_n$ are terms. We denote with $\mathcal{F}$ the set of all ground atoms built from $\mathcal{R}$ and Δ. A negated atom is of the form $\neg a$ where a is an atom. We assume that $\mathcal{R} = \mathcal{R}_D \cup \mathcal{R}_P$, with $\mathcal{R}_D \cap \mathcal{R}_P = \emptyset$, containing predicates that refer to deterministic and probabilistic events, respectively.

A *database instance* D for a relational schema $\mathcal{R}_D$ is a (possibly infinite) set of atoms with predicates from $\mathcal{R}_D$ and arguments from Δ. On the other hand, let a *probabilistic atom* be of the form $\mathbf{a} : p$, where p is a real number in the interval $[0, 1]$ and $\mathbf{a}$ is an atom with a predicate from $\mathcal{R}_P$. We do not allow negation in probabilistic atoms.

A *probabilistic constraint* c has the form

$$\mathbf{a}_1 : p_1 \quad \ldots \quad \mathbf{a}_k : p_k,$$

where $k > 0$, each $\mathbf{a}_i : p_i$ is a probabilistic atom, and $\sum p_i \leq 1$. If the p_i's in a probabilistic constraint do not sum to 1, then there exists also the possibility that none of them happen. The probability of this complementary event is $1 - \sum p_i$. Given a probabilistic constraint $c = \mathbf{a}_1 : p_1 \quad \ldots \quad \mathbf{a}_k : p_k$, we will make use of the notation $atoms(c) = \{\mathbf{a}_1, \ldots, \mathbf{a}_k\}$. We will also denote the probability of any atom $\mathbf{a}$ with $p(\mathbf{a})$. We have that $p(\mathbf{a}_i) = p_i$ whenever $\mathbf{a}_i : p_i$ belongs to a probabilistic constraint c.

Given a set of probabilistic constraints C, note that each ground atom can only appear in one constraint in C. From a practical point of view, this assumption restricts the number of possible worlds by limiting the potential combinations. Vennekens et al (2009, Eq. 5) propose more complex semantics where this assumption is relaxed. This approach is similar to *probabilistic databases* (Suciu et al, 2011) where each tuple comes from a general probability distribution over tuples and inexistence is one of the options. This allows to incorporate beliefs about the likelihood of tuples and cell values.

Example 1. *Consider the following database instance D and a set of probabilistic constraints C (recall that t_i atoms cannot appear in C).*

$$D = \{t_1(a), t_1(c), t_2(a), t_2(b)\}$$

$$C = \left\{ \begin{array}{l} c_1 = s(a,b) \ : 0.3 \\ c_2 = s(b,c) \ : 0.7 \\ c_3 = r(b) \quad : 0.4 \mid r(c) \ : 0.1 \end{array} \right\} \tag{1}$$

Tuple Generating Dependencies

Given a relational schema $\mathcal{R}$, a *tuple-generating dependency (TGD)* σ is a first-order formula of the form:

$$\forall \mathbf{X} \forall \mathbf{Y} \, \Phi(\mathbf{X}, \mathbf{Y}) \rightarrow \exists \mathbf{Z} \, \Psi(\mathbf{X}, \mathbf{Z}),$$

where $\Phi(\mathbf{X}, \mathbf{Y})$ and $\Psi(\mathbf{X}, \mathbf{Z})$ are conjunctions of atoms over $\mathcal{R}$ (without nulls), called the *body* and the *head* of σ, denoted $body(\sigma)$ and $head(\sigma)$, respectively. Such σ is satisfied in a database D for $\mathcal{R}$ if and only if, whenever there exists a homomorphism h that maps the atoms of $\Phi(\mathbf{X}, \mathbf{Y})$ to atoms of D, there exists an extension h' of h that maps the atoms of $\Psi(\mathbf{X}, \mathbf{Z})$ to atoms of D. All sets of TGDs are finite here and we assume without loss of generality that every TGD has a single atom in its head. Furthermore, we say that a TGD σ is *full* whenever there are no existential variables in the head. Let's extend our example further:

Example 2. *Based on Example 1 we can add the following set of rules:*

$$\begin{aligned} \Sigma = \{ & \forall X \ t_1(X) \rightarrow \exists Z \ o(X, Z), \\ & \forall X \forall Y \ t_2(X) \wedge o(X, Y) \rightarrow t(X), \\ & \forall X \forall Y \ s(X, Y) \wedge r(Y) \rightarrow w(X, Y) \} \end{aligned}$$

$$A = \{\forall X \forall W \ v(X, W) \rightarrow u(X, \max(W))\}$$

TGDs can be extended to allow negation—in this work we only allow stratified negation (Abiteboul et al, 1995) for full TGDs. Furthermore, as shown by the rule in set A in the previous example, we extend the language so aggregation functions can be used in the head of full TGDs (Abiteboul et al, 1995). As we see in the following section, we restrict the syntax of this type of rules so that neither negation nor recursion is allowed.

Definition 1. *A* probabilistic ontology $\mathcal{O} = (D, C, \Sigma)$ *consists of a database instance D, a set C of probabilistic constraints, and a set Σ of arbitrary TGDs.*

Note that a database instance can be thought of as a set of probabilistic constraints with only probabilistic atoms, each one annotated with probability 1. Furthermore, the structure (D, Σ) corresponds to a knowledge base with existential rules as defined in Calì et al (2012), whenever rules in Σ do not involve atoms that appear in probabilistic constraints.

Semantics

We take the notion of possible world (or interpretation) of a probabilistic ontology as a subset of $\mathcal{F}$ and we denote with Ω the set of all possible worlds. Each possible world $\omega \in \Omega$ satisfies the following property:

$$\forall F \in \mathcal{F} : \omega \models F \text{ iff } F \in \omega; \qquad \text{otherwise } \omega \models \neg F$$

This means that ω is a complete interpretation of every element of $\mathcal{F}$. The usual semantics of a classical Datalog program P is the least Herbrand model that contains exactly all ground facts in P plus every ground atom inferred from it, i.e. the intersection of all worlds that satisfy P.

However, in the probabilistic case, we need to consider a generalization of this semantics so that every ground fact has associated with a probability value. According to this idea, we are going to take the models of a set of non-probabilistic ontologies, induced by total choices, so that they all share the same TGDs but the corresponding database instances differ. As mentioned before, in our approach, we have two ways of associating probability with facts. In the first one, a fact corresponds to a Boolean random variable that is true with probability p and false with probability $1 - p$. In the second, we interpret facts as multi-valued random variables instead of binary ones. We use probabilistic constraints to represent both and assume that the facts within the same constraint are mutually exclusive events, whereas facts in different constraints are mutually independent events. According to this idea, we give the following definition:

Definition 2. *Given a probabilistic ontology $\mathcal{O} = (D, C, \Sigma)$, for each $1 \leq j \leq |C| : c^j = \mathbf{a}_1^j : p_1^j \mid \ldots \mid \mathbf{a}_k^j : p_k^j$, with $c^j \in C$, we have:*

$$choices(c^j) = \{\mathbf{a}_i^j \mid 1 \leq i \leq k\} \cup \{\bot_{c^j}\}.$$

For each $b = \mathbf{a}_i^j \in c^j$, we have $p(b) = p_i^j$ and $p(\bot_{c^j}) = 1 - \sum_{1 \leq i \leq k} p_i^j$. The set of total choices for $\mathcal{O}$ is defined as total_choices(C) =

$$\{[b_1, \ldots, b_l] \mid l = |C|, 1 \leq j \leq |C| : b_j \in choices(c^j)\}$$

The probability of a particular total choice $\lambda \in total\_choices(C)$ is defined as $p(\lambda) = \prod_{1 \leq j \leq l}^{[b_1,\ldots,b_l] \in \lambda} p(b_j)$. We use notation $atoms(\lambda) = \{\mathbf{b}_j \neq \bot_{c^j} \mid 1 \leq j \leq l : [b_1, ..., b_l] \in \lambda\}$ and $atoms(C) = \bigcup_{\lambda \in total\_choices(C)} atoms(\lambda)$.

Definition 3. *Let ω and λ be a possible world and a total choice, respectively. Then, we will say that ω satisfies λ, denoted $\omega \models \lambda$, if and only if $atoms(\lambda) \subseteq \omega$. Also, $\|\lambda\|$ will denote the set of possible worlds of a total choice, i.e. $\|\lambda\| = \{\omega \in \Omega \mid \omega \models \lambda\}$.*

Example 3. *The set of all total choices for probabilistic ontology* (D, C, Σ) *from Examples 1 and 2 is the following:*

$$\begin{array}{llll}
\lambda_1 & = [s(a,b),\ s(b,c),\ r(b)] & p(\lambda_1) & = 0.084 \\
\lambda_2 & = [s(a,b),\ \bot_{c_2},\ r(b)] & p(\lambda_2) & = 0.036 \\
\lambda_3 & = [\bot_{c_1},\ s(b,c),\ r(b)] & p(\lambda_3) & = 0.196 \\
\lambda_4 & = [\bot_{c_1},\ \bot_{c_2},\ r(b)] & p(\lambda_4) & = 0.084 \\
\lambda_5 & = [s(a,b),\ s(b,c),\ r(c)] & p(\lambda_5) & = 0.021 \\
\lambda_6 & = [s(a,b),\ \bot_{c_2},\ r(c)] & p(\lambda_6) & = 0.009 \\
\lambda_7 & = [\bot_{c_1},\ s(b,c),\ r(c)] & p(\lambda_7) & = 0.049 \\
\lambda_8 & = [\bot_{c_1},\ \bot_{c_2},\ r(c)] & p(\lambda_8) & = 0.021 \\
\lambda_9 & = [s(a,b),\ s(b,c),\ \bot_{c_3}] & p(\lambda_9) & = 0.105 \\
\lambda_{10} & = [s(a,b),\ \bot_{c_2},\ \bot_{c_3}] & p(\lambda_{10}) & = 0.045 \\
\lambda_{11} & = [\bot_{c_1},\ s(b,c),\ \bot_{c_3}] & p(\lambda_{11}) & = 0.245 \\
\lambda_{12} & = [\bot_{c_1},\ \bot_{c_2},\ \bot_{c_3}] & p(\lambda_{12}) & = 0.105
\end{array}$$

It is easy to see that *total_choices*(C) defines a partition on Ω by using the following equivalence relation on $\Omega \times \Omega$: $\omega \equiv \omega'$ if and only if $\forall \lambda \in$ *total_choices*$(C) : \omega \models \lambda \Leftrightarrow \omega' \models \lambda$.

We define the semantics of a probabilistic ontology based on the semantics of a classical ontology with existential rules (TGDs). Intuitively, each total choice induces a classical (i.e., non-probabilistic) ontology.

Definition 4. *Let* $\mathcal{O} = (D, C, \Sigma)$*, be a probabilistic ontology, and let* λ *be a total choice of* C*. Then, the (non-probabilistic) ontology induced by* $\lambda = [b_1, \ldots b_l]$ *is defined as* $O_\lambda = (D_\lambda, \Sigma)$*, with* $D_\lambda = D \cup \{b_1, \ldots b_l\}$*.*

Example 4. *Based on the total choices from Example 3 and probabilistic ontology* $\mathcal{O} = (D, C, \Sigma,)$*, each* λ_i *with* $1 \leq i \leq 12$*, induces a non-probabilistic ontology* $\mathcal{O}_{\lambda_)} = (D_{\lambda_i}, \Sigma)$ *where* $D_{\lambda_i} = \mathcal{D} \cup \{b_1, \ldots, b_l\}$ *with* $b_k \in \lambda_i$ *and* $b_k \neq \bot_{c_j}$ *for every* $c_j \in C$*.*

We recall the notion of models and satisfaction for classical ontologies in Calì et al (2012).

Definition 5. *Given an ontology* (D, Σ)*, the set of* models*, denoted mods*(D, Σ)*, is the set of all (possibly infinite) databases* B *such that (i)* $D \subset B$*, and (ii) every* $\sigma \in \Sigma$ *is satisfied in* B*.*

Note that each B in the above definition can be considered as a possible world under the closed world assumption, i.e. every tuple that does not appear in B is false. It is important to recall that for full TGDs (pure Datalog rules), an ontology (D, Σ) has a unique least model (Abiteboul et al, 1995).

Definition 6. *Let* $\mathcal{O}$ *be a probabilistic ontology, and* Φ *be a conjunction of ground atoms built from predicates in* $\mathcal{R}$*. The probability that* Φ *holds in* $\mathcal{O}$*,*

denoted $Pr^{\mathcal{O}}(\Phi)$*, is the sum of the probabilities of all total choices* λ *such that* $(D_\lambda, \Sigma) \models \Phi$*; that is,* $Pr^{\mathcal{O}}(\Phi) = \sum_{(D_\lambda,\Sigma)\models\Phi}^{\lambda \in total\_choice(C)} p(\lambda)$.

At this point, it is interesting to remark the connection between our approach and the one considered by Riguzzi (2008, 2006). The Logic Programs with Annotated Disjunctions (LPADs) mentioned in their paper make an implicit treatment of mutually exclusive facts, whereas our approach does it explicitly. In fact, LPADs are more expressive than our language since they use non-Horn clauses. In addition, they use well-founded semantics in order to deal with negation as failure. Both aspects have a computational cost that we wish to avoid.

Semantics for Query Answering

A *conjunctive query (CQ)* over $\mathcal{R}$ has the form $Q(\mathbf{X}) = \exists\Phi(\mathbf{X}, \mathbf{Y})$, where $\Phi(\mathbf{X}, \mathbf{Y})$ is a conjunction of atoms (possibly equalities, but not inequalities) with the variables $\mathbf{X}$ and $\mathbf{Y}$, and possibly constants, but without nulls. Probabilistic answers to CQs are defined via *homomorphisms*, which are mappings $\mu\colon \Delta \cup \Delta_N \cup \mathcal{V} \to \Delta \cup \Delta_N \cup \mathcal{V}$ such that (i) $c \in \Delta$ implies $\mu(c) = c$, (ii) $c \in \Delta_N$ implies $\mu(c) \in \Delta \cup \Delta_N$, and (iii) μ is naturally extended to atoms, sets of atoms, and conjunctions of atoms.

Definition 7. *The set of all* probabilistic answers *to a CQ* $Q(\mathbf{X}) = \exists\mathbf{Y}\, \Phi(\mathbf{X}, \mathbf{Y})$ *over a probabilistic ontology* $\mathcal{O} = (D, C, \Sigma)$*, denoted with* $ans(Q, D, C, \Sigma)$*, or* $ans(Q, \mathcal{O})$*, is a set of pairs* (t, p_t) *with* t *a tuple over* Δ *such that there exists a homomorphism* $\mu\colon \mathbf{X} \cup \mathbf{Y} \to \Delta \cup \Delta_N$ *with* $\mu(X) = t$ *and* $(D_\lambda, \Sigma) \models \mu(\Phi(\mathbf{X}, \mathbf{Y}))$ *for all* $\lambda \in total\_choice(C)$*. The probability of each tuple* t *is then* $p_t = \sum_{(D_\lambda,\Sigma)\models\mu(\Phi(\mathbf{X},\mathbf{Y}))}^{\lambda\in total\_choice(C)} p(\lambda)$.

Observations

If a probabilistic ontology $\mathcal{O} = (D, C, \Sigma)$ is such that C is empty, then the semantics for (B)CQs as defined above coincides with that for classical ontologies (Calì et al, 2012).

Note that query answering under general TGDs for non-probabilistic ontologies is undecidable (Beeri and Vardi, 1981), even when the schema and TGDs are fixed (Calì et al, 2008). The two problems of CQ and BCQ evaluation under TGDs are LOGSPACE-equivalent (Fagin et al, 2005a; Deutsch et al, 2008). As mentioned above, in the non-probabilistic case, for arbitrary full TGDs there exists exactly one minimal model (Abiteboul et al, 1995) over which Q is evaluated. Furthermore, it has been shown that for full TGDs CQ evaluation can be done in polynomial time in data complexity (*i.e., assuming* σ *and* Q *fixed*) (Dantsin et al, 2001).

3 NeuroLang Programs

In addition to our model, we assume the existence of a separate schema $\mathcal{T}$, the target schema, that defines the language by means of which users of NeuroLang can query about the probability of certain events. Predicates in $\mathcal{T}$ have a distinguished term in the n-th position (for n-ary predicates) reserved exclusively for real numbers in the interval $[0, 1]$; i.e., for any predicate $p \in \mathcal{T}$, atoms of the form $p(a_1, \ldots, a_n)$ are such that $a_1, \ldots, a_{n-1}$ are variables or constants from Δ, while a_n is a variable or a constant from $[0, 1]$. Below we show an example of how this language is used.

A NeuroLang program $\mathcal{N}$ is comprised of the following components:

- D, Σ: where D is a set of ground atoms from $\mathcal{R}_D$, and Σ is a set of full TGDs that only use atoms from $\mathcal{R}_D$ and can have recursion and stratified negation.
- (D_1, Σ_1): a classical ontology, where D_1 is a set of ground atoms from $\mathcal{R}_D$, Σ_1 is a set of TGDs that belong to the Sticky fragment (Cali et al, 2012), and the bodies and heads are atoms built from predicates in $\mathcal{R}_D$.
- C: a set of probabilistic constraints only involving atoms from $\mathcal{R}_P$.
- χ: a set of full TGDs, whose bodies and heads may contain atoms from $\mathcal{R}_D \cup \mathcal{R}_P$. Neither negation nor recursion is allowed in this set of rules.
- Π: a set of *probability encoding rules* (PERs) with the following form:

$$\sigma^* : \forall \mathbf{X} \forall \mathbf{Y} (\Phi(\mathbf{X}, \mathbf{Y})) \rightarrow \psi(\mathbf{X}, \rho_X)$$

  where Φ is a conjunction of atoms from $\mathcal{R}_D \cup \mathcal{R}_P$, ψ is an atom in $\mathcal{T}$ and ρ_X is the distinguished term that in this case must be a variable (ranging over the reals in $[0, 1]$).
- A: a set of rules of the form

$$\forall \mathbf{X} \forall \mathbf{Y} (\Phi(\mathbf{X}, \mathbf{Y}, \mathbf{Z}) \rightarrow \psi(\mathbf{X}, agg(\mathbf{Z})) \tag{2}$$

  where Φ is a conjunction of atoms in $\mathcal{R}_D \cup \mathcal{T}$ and agg is an aggregation function (e.g., sum, count, avg, etc.). Neither negation nor recursion is allowed in these rules.

Informally, the above sets together provide the following functionalities:

(i) Σ, Σ_1, $\mathcal{C}$, and χ are used by the probabilistic inference mechanism, which applies ontological rules and ultimately associates probabilities to atoms (following the semantics described in Section 2);
(ii) Π incorporates probabilities as values inside atoms; and
(iii) rules in A manipulate these probabilities via aggregation functions to present them as requested by the user.

Algorithm 1: NeuroLangQA

Input : NeuroLang program $\mathcal{N} = (D, \Sigma, (C, \chi), (D_1, \Sigma_1), \Pi, A)$ and query $Q(\mathbf{X}) = \exists \mathbf{Y} \Phi(\mathbf{X}, \mathbf{Y})$

Output: $ans(Q(\mathbf{X}), \mathcal{N})$

Step 1: Obtain database instance D' and set of full TGDs Σ' such that $D^{'} = D \cup D_1$ and $\Sigma^{'}$ is the rewriting of Σ with respect to Σ_1.

Step 2:

2a: Let Aux be the set of TGDs in $\Sigma^{'}$ whose bodies do not depend on $C \cup \chi \cup \Pi$.

2b: Let M the set of ground atoms a such that $(D', Aux \cup A) \models a$

Step 3:

$B := \emptyset$

foreach *PER* $\pi \in \Pi$ **do**

```
// Rule bodies are taken as queries
```

Let $Q_\pi(\mathbf{X}) = body(\pi)$

```
// Obtain probability values
// associated with each query answer
```

$probAnsPairs := ans(Q_\pi(\mathbf{X}), (M, C, \chi))$

foreach $(t, p) \in probAnsPairs$ **do**

```
// Add query answers and PER
// heads to set B
```

Let h' be the instantiation of $head(\pi)$ with values from (t, p)

$B := B \cup \{h', Q_\pi(t)\}$

end

end

Step 4: Let M' the set of ground atoms a such that $(B, (\Sigma' - Aux) \cup A) \models a$

Step 5: Return $ans(Q(\mathbf{X}), \mathcal{N})$ computed from atoms in set M'.

Note that PERs are full TGDs that will be used to translate from a source schema to a target one, in the same spirit as source-to-target TGDs for data exchange (Fagin et al, 2005b). Effectively, they reify the probability of an atom, given by the semantics, as a term in a new atom that can be further manipulated by other rules. For instance, a set of probabilistic constraints $C = \{s(a, b) : 0.3\}$ will be reified by the PER $\forall X \forall Y s(X, Y) \rightarrow t(X, Y, \rho_X)$ as $\{t(a, b, 0.3)\}$. On the other hand, for rules in A we incorporate functional symbols agg to the distinguished term in ψ to indicate that its value takes the result of applying the function agg to all ρ_X that satisfy the body of the rule. Note that users here can define arbitrary rules that manipulate probabilities by means of aggregation functions. It's defined as a post-processing step that builds a view as defined by the user issuing the query. Therefore, it's the user's responsibility that the handling of the probabilities obtained in the previous steps complies with the laws of probability. For more information, we refer the reader to appendix A. We extend notation *body* and *head* used for TGDs to

all types of rules defined in this section. The following is a simple example of query answering using PERs.

Example 5. *Consider the following NeuroLang program $\mathcal{N}$. We add a set of PERs and rules with aggregations.*

$$
\begin{aligned}
D_1 &= \{t_1(a), t_1(c)\},\\
\Sigma_1 &= \{\forall X t_1(X) \rightarrow \exists Z\ o(X, Z)\},\\
D &= \{t_2(a), t_2(b)\},\\
\Sigma &= \{\forall X \forall Y\ t_2(X) \wedge o(X, Y) \rightarrow t(X)\},\\
C &= \left\{ \begin{array}{l} s(a,b)\ : 0.3 \\ s(b,c)\ : 0.7 \\ r(b) \quad : 0.4 \mid r(c)\ : 0.1 \end{array} \right\},\\
\chi &= \{\forall X \forall Y\ s(X, Y) \wedge r(Y) \rightarrow w(X, Y)\}\},\\
\Pi &= \{\forall X \forall Y\ w(X, Y) \rightarrow v(X, \rho_X)\},\\
A &= \{\forall X \forall W\ v(X, W) \rightarrow u(\max(W))\},\\
Q_1(X, P) &= v(X, P), t(X),\\
Q_2(X, P) &= v(X, P), u(P).
\end{aligned}
$$

Now, the partition of possible worlds used to compute queries Q_1 and Q_2 is the following (excluding atoms from D and (D_1, Σ_1) for clarity, and including probabilities):

$$
\left\{ \begin{array}{lllll}
\{s(a,b) & s(b,c) & w(a,b) & r(b) & t(a)\} : 0.084 \\
\{s(a,b) & & w(a,b) & r(b) & t(a)\} : 0.036 \\
\{ & s(b,c) & & r(b) & t(a)\} : 0.196 \\
\{ & & & r(b) & t(a)\} : 0.084 \\
\{s(a,b) & s(b,c) & w(b,c) & r(c) & t(a)\} : 0.021 \\
\{s(a,b) & & & r(c) & t(a)\} : 0.009 \\
\{ & s(b,c) & w(b,c) & r(c) & t(a)\} : 0.049 \\
\{ & & & r(c) & t(a)\} : 0.021 \\
\{s(a,b) & s(b,c) & & & t(a)\} : 0.105 \\
\{s(a,b) & & & & t(a)\} : 0.045 \\
\{ & s(b,c) & & & t(a)\} : 0.245 \\
\{ & & & & t(a)\} : 0.105
\end{array} \right\}
$$

Answering Q_1, Q_2 leads to the target schema solution $\{v(a, 0.141),\ v(b, 0.154),\ u(0.154)\}$. Hence, the resulting answer set is $\{Q_1(a, 0.141), Q_2(b, 0.154)\}$.

Query Answering in NeuroLang

A *NeuroLang query* Q is any conjunction of atoms in $\mathcal{R}_D \cup \mathcal{T}$, such that atoms in $\mathcal{T}$ have as distinguished term a variable; these variables will be instantiated with the probability of certain events as computed by the inference mechanism. Algorithm 1 describes the pseudocode for answering queries in the NeuroLang framework—fig. 1 provides a high-level view of the main steps involved in this process, where inputs are as defined above.

There are two steps in which NeuroLangQA makes external calls. First, in Step 1 the rewriting of Σ w.r.t. Σ_1 is done by means of the XRewrite algorithm developed in Gottlob et al (2014) for rewriting queries with respect to the Sticky fragment of existential rules (also known as Datalog+/–). Note that here the algorithm is used to rewrite every appearance of heads of rules in Σ_1 in the bodies of rules in Σ, yielding a potentially larger set of full TGDs (rules without existentials in the head).

Then, Step 3 derives the probabilities associated with atoms. This is done by dynamically choosing the best algorithm for the job: if π is liftable according to Dalvi and Suciu (2012), then lifted query answering is applied; otherwise, the query is compiled to an SDD representation and model counting is applied (Vlasselaer et al, 2014). Both cases are implemented in relational algebra with provenance (Senellart, 2017). Note also that up to Step 3 we can guarantee the correctness of the semantics of NeuroLangQA, i.e., the probabilities associated with atoms in set B correspond to the probability with which they are entailed in the probabilistic ontology. However, since after this step users can manipulate the probabilities of atoms through aggregation functions provided in A, it cannot be guaranteed that this relationship holds in the next steps, so users have the responsibility of making a sound use of such values. This manipulation is intentionally incorporated to increase the expressive power of the languages; similar additions occur in other languages, like Prolog. This feature is useful in our application case allowing, for instance, to aggregate probabilistic values into voxel overlays (cf. section 4.2), or select the 95th percentile top probabilities of a result set (cf. section 4.3).

The final step of the algorithm returns the answers to query Q as the set of all tuples t built from Δ such that there exists a homomorphism μ where $\mu(\mathbf{X}) = t$ and $\mu(\Phi(\mathbf{X}, \mathbf{Y})) \in M'$.

Correctness of NeuroLangQA

We now discuss the correctness of NeuroLangQA algorithm with respect to the probabilistic semantics described in Section 2. Without loss of generality, we assume a query of the form

$$Q(\mathbf{X}, \rho_{\mathbf{X}}) = \Phi(\mathbf{X}) \wedge \psi_i(\mathbf{X}, \rho_{\mathbf{X}}),$$

where $\Phi(\mathbf{X})$ is a conjunction of atoms in $\mathcal{R}_D$ and $\psi_i(\mathbf{X}, \rho_{\mathbf{X}})$ is an atom in $\mathcal{T}$.

The result of Step 1 in NeuroLangQA is a special case of a probabilistic ontology (D', Σ'), where Σ' is a set of full TGDs that may contain stratified

negation and recursion. Furthermore, Step 2a removes from Σ' all rules that depend on $C \cup \chi \cup \Phi$ (Baget et al, 2011). Therefore, M computed in Step 2b is unique as neither probabilistic atoms, nor existential rules are involved. Step 3 now considers the probabilistic ontology defined by $\mathcal{O} = (M, C \cup C', \chi)$. Note that atoms in M materialize ontology (D', Aux) and they will hold in every possible world for probabilistic ontology $\mathcal{O}$.

Recall that the purpose of PERs is to incorporate the probability of an atom as an additional term—Step 3 does precisely that: for each PER π, it computes the probability of all ground instantiations of $body(\pi)$ that are entailed by $\mathcal{O}$. For each such instantiation t, set B contains the instantiation itself $(Q_\pi(t))$ and the head of π instantiated by values in t and an extra position with value $Pr^{\mathcal{O}}(body(\pi)(t))$.

Finally, Step 4 considers a deterministic ontology comprised by B (a set of ground atoms) and the set of full TGDs $(\Sigma' - Aux) \cup A$; M' contains all ground atoms that are entailed by such ontology. As in the case of M, M' is unique since neither existential rules nor probabilistic atoms are involved.

Therefore, we can conclude that—by construction—the results computed by the NeuroLangQA algorithm are correct with respect to the probabilistic semantics defined in Section 2 up to Step 3. This means that the probabilities associated with atoms in B correspond to the probability with which they are entailed by the probabilistic ontology. The final two steps simply follow the user-specified rules for establishing personalized views, which may manipulate probability values in an arbitrary fashion. With the framework in place, in the following we show how it can be applied in practice.

4 Evaluation based on Real-World Use Cases in Neuroscience Research

In this section, we illustrate via concrete examples several use cases that appear in real-world tasks carried out by neuroscience researchers. Since all of our analyses are based on meta-analytic components, we first give a brief description of the Neurosynth database we use in our examples. Where extra data is used, it will be clarified in each particular case. The Neurosynth database is composed of 3.228×10^3 terms, 1.4370×10^4 studies (*SelectedStudy*), and 3.3593×10^4 voxels; but this information would not be useful without associations, so we also have $1.049\,299 \times 10^6$ terms reported as present in studies (*TermInStudy*) and $5.078\,91 \times 10^5$ voxels reported as active (*FocusReported*), also with their respective study. Finally, there are 112 brain regions from Destrieux's atlas (Destrieux et al, 2010) associated with brain coordinates through the *VoxelByRegionDestrieux* relation. These data give rise to the following extensional databases:

$$D = \left\{ \begin{array}{l} \mathit{TermInStudy}(\text{“emotion”}, s_1), \\ \vdots \\ \mathit{TermInStudy}(\text{“pain”}, s_{120}), \\ \mathit{FocusReported}(5, -5, 3, s_1), \\ \vdots \\ \mathit{FocusReported}(-10, 5, 1, s_{25}), \\ \mathit{VoxelByRegionDestrieux}(15, 47, 16, \\ \quad \text{'l\_g\_and\_s\_frontomargin'}), \\ \vdots \\ \mathit{VoxelByRegionDestrieux}(16, 46, 15, \\ \quad \text{'l\_g\_and\_s\_frontomargin'}), \end{array} \right\}$$

$$C = \left\{ \begin{array}{l} \mathit{SelectedStudy}(s_i) : \frac{1}{\#studies} \\ \mathit{FocusCoactivates}(\ 5, -5,\ 3, \quad 5, -5,\ 3) : 1 \\ \vdots \\ \mathit{FocusCoactivates}(\ 5, -5,\ 3, \quad -10,\ \ 5,\ 1) : \\ \qquad (2\pi 2)^{-3/2} \exp\left(-\frac{1}{2} \frac{\|(5,-5,3)-(-10,5,1)\|^2}{2^2}\right) \end{array} \right\}$$

where *FocusCoactivates* represents spatial uncertainty in foci reporting, as they encode that the probability that two foci co-activate is mediated by their distance as measured by a 3D Gaussian law with standard deviation 2mm. This dataset has approximately 5 million atoms. Furthermore, the CogAt ontology (Poldrack et al, 2011) is composed of 5.6807×10^4 rules. In the following, examples are written in extended Datalog syntax, as in our implemented tool[1]. We base our examples on versions 1.4.0 of IOBC, 0.3.1 of CogAt, and the Destrieux 2009 atlas (Destrieux et al, 2009) provided by Nilearn software package v0.7.0 (Fischl et al, 2004). In addition, both the software code and other examples can be found on the official NeuroLang repository[1].

4.1 Open world assumption

We now show how we can make use of NeuroLang to solve queries that require taking into account the open world assumption. For that purpose, we use the terms present in the Neurosynth database to associate the studies analyzed with the cognitive processes proposed by CogAt. For this, we make use of a special term included by our ontologies parser, *Entity(t, s)*, that will allow us to associate external data with the internal entities of the ontology.

Each entity that is parsed creates this specific rule, that we can later overload with external information, creating an association between entities and external data. An example of this overloading process can be seen in the first line of listing 2 where we associate the studies of the Neurosynth database with the entities of the ontology, allowing us to perform queries that return these studies, but under the universe modeled by the ontology. All within the same semantics of the NeuroLang program.

[1] https://neurolang.github.io/

Listing 1: Example of rules introduced by our parser when processing ontologies, allowing us to associate internal entities with external datasets.

```
SpatialAttention(X) :- Entity('spatial attention', x)
```

As we can see in the first line of listing 2, we then associate these entities with the Neurosynth studies within the same program. This will allow us to combine both datasets, so that we can use the information structured in the CogAt ontology to ask questions that result in Neurosynth's studies.

Listing 2: Open world assumption. See the description in section 4.1

```
Entity(t, s) :- TermInStudy(t, s)

OpenWorldStudies(s) :- PartOf(t, s), VisualAwareness(s).

ProbMap(x, y, z, PROB) :- FocusReported(x, y, z, s) //
    (SelectedStudy(s) & OpenWorldStudies(s))

ProbabilityImage(create_region_overlay(x, y, z, p)) :-
    ProbMap(x, y, z, p)
```

We focus on solving queries based on some of the ontology's constraints defining open-world knowledge. In particular, we aim at relating the *visual awareness* cognitive process from the CogAt ontology with brain areas reported activate during this process. This can not be done directly through Neurosynth, as the cognitive process is not reported. Therefore, we need a way to associate studies related to this term that do not mention *visual awareness* explicitly. CogAt helps in solving this problem: there is TGD specifying that *spatial attention* is a sub-process of *visual awareness*. Which, expressed as a Datalog+/- rule in CogAt's TGD set, is:

$$\begin{aligned} &\forall X \mathrm{SpatialAttention}(X) \rightarrow \\ &\qquad \exists Y \mathrm{PartOf}(X, Y) \wedge \mathrm{VisualAwareness}(Y) \end{aligned} \in \Sigma_1^{\mathrm{CogAt}}, \tag{3}$$

which has an existentially-quantified variable in the head, hence representing open-world knowledge.

We seamlessly harness this open knowledge to analyse activations related to *visual awareness* using to NeuroLang's built-in capabilities: we write a program (see listing 2) to obtain all studies that, while not mentioning *visual awareness*, mention terms which, according to CogAt, imply that the cognitive process

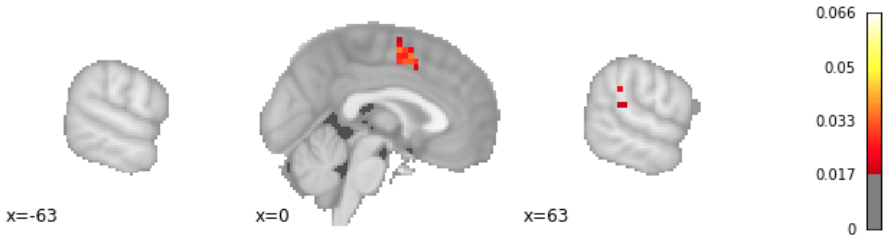


Fig. 2: Resulting thresholded brain image from the NeuroLang use case showing the activations related to spatial attention obtained through the resolution of a query under the open world assumption.

is involved. Importantly, we achieve this by combining an automatically-produced literature database with a expert-produced ontology. The resulting activations can be seen in fig. 2

4.2 Forward inference

In this task, we wish to assess the probability of a voxel being reported as active in a study given that the word "emotion" is present in the specific study.

Note that in order to represent this knowledge we only need the expressive power of full TGDs (no existential rules are needed). In fig. 3 we see that the most important reported activations are concentrated in the amygdala, the region most related to emotions, as generally accepted in the neuroscience field.

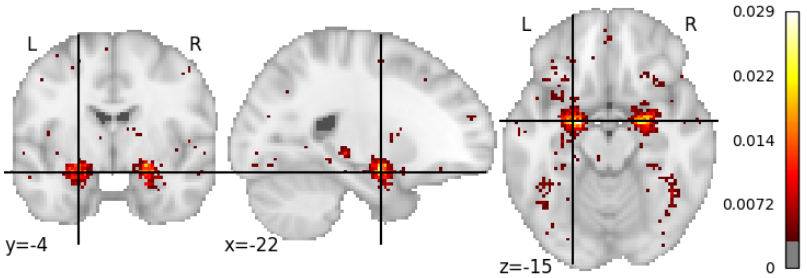


Fig. 3: Resulting thresholded brain image from the NeuroLang use case showing that foci in the amygdala are most probably reported if a study includes the word "emotion". As expected, the main area shown corresponds to the amygdala (Mesulam, 1998).

4.3 Reverse inference over a region of the Destrieux atlas leveraging the CogAt ontology

For this use case, we will use reverse inference techniques to obtain the terms most likely to be associated with the *short insular gyrus* of the Destrieux atlas.

Listing 3: Forward inference

```
TermAssociation(t) :- SelectedStudy(s),
    TermInStudy(t, s).

Activation(i, j, k) :- SelectedStudy(s),
    FocusReported(i1, j1, k1, s),
    FocusCoactivates(i, j, k, i1, j1, k1).

% Probability Encoding Rule: PROB is
% used to encode probability as defined in
% Section 3. The // operator is
% syntactic sugar for conditional
% probability as P(AB) = P(A,B) / P(B).
ProbMap(i, j, k, PROB) :-
    Activation(i, j, k)
    // TermAssociation("emotion").

% Aggregation to build a single image with
% the probability p in each position
% within the top 95% of probability
Percentile_95(compute_percentile(p, 95)) :-
    ProbMap(i, j, k, p).

ProbabilityImage(create_region_overlay(i, j, k, p)) :-
    ProbMap(i, j, k, p),
    Percentile_95(p95), p > p95

Ans(x) :- ProbabilityImage(x)
```

Atlases are parcellations of the brain into distinct areas based on histological, physiological, or other characteristics. In addition, we will also use the information stored in the CogAt ontology to filter the terms from the reverse inference in order to obtain cleaner results, all in the same query. Terms included in the CogAt ontology are characterized by the "label" relation, which we load into our system under the CogAtLabel symbol. The CogAt ontology rewriting adds 4.577×10^3 formulas to our database. The code of this program is presented in listing 4.

We can see in table 1 (right) how, by using the knowledge stored in the CogAt ontology, we can filter out those terms that, being present in most neuroimaging studies, only add noise to the results. Therefore, we obtain a list of much more relevant results that are also more closely related to the general knowledge of the field of neuroscience. Solving this query takes approximately 6 seconds. For another use case leveraging ontological knowledge, please refer to section 4.3.1.

Listing 4: Reverse inference over a region of the Destrieux atlas leveraging the CogAt ontology.

```
FilteredTerms(s, t) :- TermInStudy(s, t), CogAtLabel(uri, t).

RegionActivated(s) :-
    VoxelByRegionDestrieux(i, j, k, "l_g_insular_short"),
    FocusReported(i1, j1, k1, s),
    FocusCoactivates(i, j, k, i1, j1, k1).

RegionActivated(s) :-
    VoxelByRegionDestrieux(i, j, k, "r_g_insular_short"),
    FocusReported(i1, j1, k1, s),
    FocusCoactivates(i, j, k, i1, j1, k1).

TermProbability(t, "unfiltered", PROB) :- TermInStudy(s, t) //
    (RegionActivated(s), SelectedStudy(s)).

TermProbability(t, "filtered", PROB) :- FilteredTerms(s, t) //
    (RegionActivated(s), SelectedStudy(s)).

Percentile_95(is_filtered, compute_percentile(p, 95)) :-
    TermProbability(t, is_filtered, p).

Ans(t, is_filtered, p) :- TermProbability(t, is_filtered, p),
    percentile_95(is_filtered, p95), p > p95.
```

Unfiltered results	
Term	*Prob*
task	0.47
magnetic	0.47
resonance	0.47
magnetic resonance	0.47
functional magnetic	0.43
using	0.38
frontal	0.37
anterior	0.35
network	0.34
prefrontal	0.33

Filtered results	
Term	*Prob*
memory	0.20
attention	0.14
working memory	0.09
perception	0.09
learning	0.08
language	0.08
emotion	0.07

Table 1: Results from section 4.3. *Left*: Results (10 of 161 most relevant terms in the top 0.5% most probable terms) of applying reverse inference on region *short insular gyri* of the Destrieux atlas using Neurosynth term association. Results include irrelevant results in terms of cognitive tasks such as "magnetic resonance". *Right*: Same approach, but filtering of terms based on those present in the CogAt ontology (Nieuwenhuys, 2012).

4.3.1 Retrieving information from related terms via the hierarchical structure of the ontology

We now show how we can leverage the ontological knowledge provided by the International Organization for Biological Control (IOBC) to perform an analysis that includes terms related to our main term (*noxious* and *nociceptive* related to *pain*, in this example) without knowing them beforehand, enriching our analysis automatically. The IOBC ontology rewriting adds 11,102 formulas to our database.

Listing 5: Retrieving information from related terms via the hierarchical structure of the ontology

```
RelatedTerm(term) :- term == "pain".

RelatedTerm(term) :- label(pain_entity, "pain"),
    altLabel(subclass, term),
    related(pain_entity, subclass).

FilteredBySynonym(t, s) :- TermInStudy(t, s), RelatedTerm(t).

Result(i, j, k, PROB) :- FocusReported(i, j, k, s) //
    (SelectedStudy(s), FilteredBySynonym(t, s)).

Percentile_95(compute_percentile(p, 95)) :- Result(i, j, k, p).

VoxelActivationImg(create_region_overlay(i, j, k, p)) :-
    Result(i, j, k, p),
    Percentile_95(p95), p > p95.

ans(img) :- VoxelActivationImg(img).
```

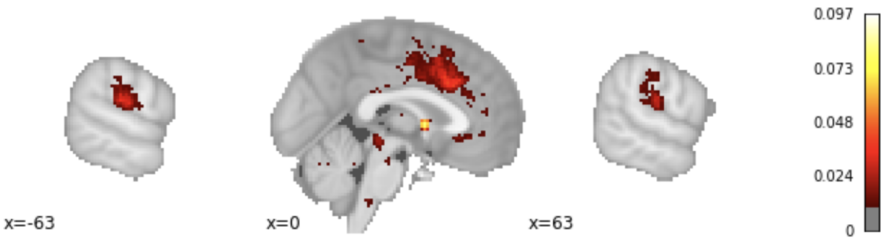


Fig. 4: Resulting thresholded brain image from the NeuroLang use case showing the activations related to pain and its related terms derived from the IOBC ontology (noxious and nociceptive). Dorsal anterior cingulate cortex (x=0) and parietal regions are be active in articles mentioning pain and related words. agreeing with current knowledge in pain location (Lieberman and Eisenberger, 2015).

In fig. 4, we provide a view of the results obtained from this example (see listing 5). In this case, the activations of Noxious and Nociceptive were also automatically included in the result, solving one of the current problems of Neurosynth (the need to know all the terms you want to use beforehand). Solving this query takes approximately 55 seconds.

4.4 Segregation reverse inference query

This final use case shows how we can use negation and existentials to express specificity. We pick the terms present in the CogAt ontology that are mentioned in studies reporting activations within the short insural gyri.

Listing 6: Segregation reverse inference query. See the description in section 4.4.

```
OntologyTerms(t) :- hasTopConcept(u, c), label(u, t)
FilteredTerms(s, t) :- TermInStudy(s, t), OntologyTerms(t)
RegionActivated(s, r) :- VoxelByRegionDestrieux(i, j, k, r),
    FocusReported(i, j, k, s).
SegregatedStudies(s) :- RegionActivated(s, r),
    (DestrieuxLabels(r, 'l_g_insular_short')
    DestrieuxLabels(r, 'l_g_insular_short')),
    ~exists(r2, RegionActivated(s, r2), r != r2)
TermProbability(t, PROB) :- FilteredTerm(s, t)
    // (SegregatedStudies(s)
      SelectedStudy(s)).
Percentile_95(compute_percentile(p, 95)) :- TermProbability(t, p).
Ans(t, p) :- TermProbability(t, p), Percentile_95(p95), p > p95.
```

Processing took 42.45 seconds. Results are shown in table 2.

term	prob
anxiety	0.097819

Table 2: Terms, within the 95th percentile, mentioned in our segregation query in section 4.4. Shows that studies presenting activations only related to the short insula gyrus tend to be associated with anxiety.

4.5 Variance in primary neuroimaging data

In this example, we demonstrate how it's possible, by implementing techniques developed and validated by the scientific community, to account for variance in primary neuroimaging data. In particular, our example focuses on one of the most common algorithms for coordinate-based meta-analyses: activation likelihood estimation, ALE (Turkeltaub et al, 2002; Laird et al, 2005). We will perform a meta-analysis using the modified version of ALE proposed by Eickhoff et al (2009). This modification is based on the idea of using between-subjects and between-templates variance to estimate the size of the modeled Gaussian from which to compute the corresponding FWHM.

For this purpose, we will use the BrainMap database (Laird et al, 2011), composed of 3,112 publications totaling 15,256 experiments, which provides us with information on the number of subjects present in each experiment. Our program will use three different atoms from this database: StimMod, which relates each experiment to its stimulus modality, StimType, which does the same with the type of stimulus, and finally BrainMap, composed of the list of publications and experiments included in the database, the number of participants, and the reported activations. Based on empirical measurements made in 2009 by the BrainMap team, we can calculate the FWHM that includes variation between-subjects and between-templates with the following formula. Given N, the number of subjects in the experiment, the formula is defined as

$$\text{FWHM}(N) : \sqrt{\pi \ln(2) \left(5.7^2 + \frac{11.6^2}{N}\right)} \tag{4}$$

The calculation includes the square root of the inverse of the user-specified number of subjects. For our example, we used 142 studies related to an auditory stimulus modality among one of the following types: "Vocal Sounds", "Nonvocal Sounds", "Sounds (Environmental)", or "Nonverbal Vocal Sounds". Listing 7 presents the program used to calculate the modified ALE. The rule defining the *Activation* atom uses syntactic sugar to define an expression that assigns probabilities to each of the possible values based on the formula for a three-dimensional Gaussian distribution defined in Laird et al (2005). Based on algorithm 1, this rule adds a new probabilistic relation *Activation* to C where the probability is computed according to an expression that can only

contain elements of the rule body belonging to D or Σ, or constants. The variable 'd' is the Euclidean distance between both points (i, j, k) and $(i1, j1, k1)$. Function *sigmaGivenSubjects* calculates, given the number of subjects who participated in the experiments reported by BrainMap, the formula defined in eq. (4). Finally, '*resolution*' is a constant that defines the resolution of the brain image used in the experiment. At the same time, we will present results using the classical ALE variant as a reference, with an FWHM value manually selected of 9. The code for this program can be found at listing 8.

Listing 7: Program code that computes the modified version of ALE

```
StimTypeAuditory(bmapID, expID) :- StimMod('auditory',bmapID,expID),
        StimType('vocal sounds', bmapID, expID)
        ⋮
StimTypeAuditory(bmapID, expID) :- StimMod('auditory',bmapID,expID),
        StimType('nonverbal vocal sounds', bmapID, expID)


Activation(i, j, k) @ max(
        (exp(-(1 / 2) * (d / sigma) ** 2)
        / ((2 * pi) ** (3 / 2) * sigma ** 3))
        * (resolution ** 3)
    ) :- StimTypeAuditory(bmapID, expID),
    BrainMap(bmapID, expID, ..., ..., minSubj, i1, j1, k1),
    Voxels(i, j, k)
    (d == FocusCoactivates(i, j, k, i1, j1, k1)),
    (sigma == sigmaGivenSubjects(minSubj))

Ans(i, j, k, PROB) :- Activation(i, j, k, p)
```

Figure 5 presents a comparison of the results of both algorithms. The ALE scores for each voxel in the reference space were calculated and filtered using the 95th percentile of the modified ALE as the threshold for comparison.

Figure 5a shows a more accurate selection of voxels than Figure 5b concerning the expected results for an auditory stimulus modality. This is because the modified version of ALE allows us to weigh each voxel according to the number of subjects that participated in the experiment. Though Figure 5b tends to show expected results, it is unable to capture the variance and relies on each experiment present in the BrainMap database with the same "weight", leading to noisier results.

5 Discussion and Conclusion

In this paper, we presented a fragment of probabilistic Datalog+/– enriched with negation and aggregation, along with a scalable query resolution algorithm. The main goal of our specific approach is meta-analysis of neuroimaging

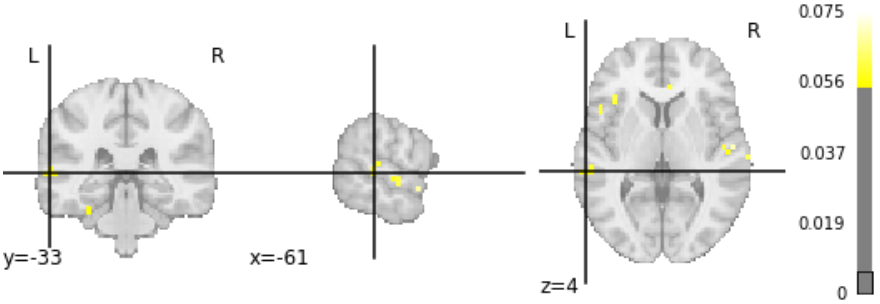
Listing 8: Program code that computes the classic version of ALE

```
StimTypeAuditory(bmapID, expID) :- StimMod('auditory',bmapID,expID),
        StimType('vocal sounds', bmapID, expID)
        ⋮
StimTypeAuditory(bmapID, expID) :- StimMod('auditory',bmapID,expID),
        StimType('nonverbal vocal sounds', bmapID, expID)


Activation(i, j, k) @ max(
        (exp(-(1 / 2) * (d / 9) ** 2)
        / ((2 * pi) ** (3 / 2) * 9 ** 3))
        * (resolution ** 3)
    ) :- StimTypeAuditory(bmapID, expID),
    BrainMap(bmapID, expID, ..., ..., minSubj, i1, j1, k1),
    Voxels(i, j, k),
    (d == FocusCoactivates(i, j, k, i1, j1, k1))

Ans(i, j, k, PROB) :- Activation(i, j, k)
```

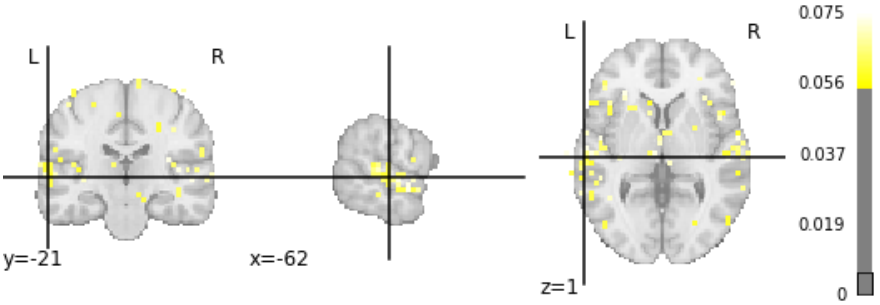
data. Several different approaches to probabilistic Datalog+/– semantics and query resolution exist (Gottlob et al, 2013; Ceylan et al, 2021). Nonetheless, these do not incorporate aggregation, and the possibility of manipulating the probabilistic query results within the same language. These two features, as shown by our use-case analysis in Section 4, are fundamental traits required to provide a probabilistic logic programming language that can encode neuroimaging meta-analysis applications end-to-end.

The possibility of manipulating probabilities within the language comes at a great expense. After our PERs are computed, in Step 4 of Algorithm 1, our language allows handling probabilities as a standard float column. While this allows for analyses required by our target applications, it calls for disciplined programming from the user such that the manipulation of probabilities remains sound. Nonetheless, this gives our language great power; for instance, we can build probabilistic brain images, through aggregation, as shown in Sections 4.2–4.3; and compute the probability differences between two events, which we show in Section 4.4.

All these features allow us to go beyond current tools in meta analyses whose queries are based in propositional logic (Yarkoni et al, 2011; Laird et al, 2011) and harness the full power of the $\text{FO}^{\neg\exists}$ fragment, as well as open-world semantics, to express meta-analysis tasks in a sound, disciplined, and declarative manner. Furthermore, by using, as in Ceylan et al (2021), a lifted query processing approach when possible (see Algorithm 1, Step 3), we are able to process current meta-analytic datasets enriched with ontologies that are of considerable size, as described at the beginning of Section 4. While it is true that there are other works that make possible the resolution of Datalog+/– queries (Ceylan et al (2021); Jha and Suciu (2012a)), the definition of the



(a) Modified ALE, accounting for between-subjects and between-templates variance



(b) Classic ALE, with FWHM = 9

Fig. 5: Comparison of results between ALE (Turkeltaub et al, 2002; Laird et al, 2005) and Modified ALE (Eickhoff et al, 2009) Figure 5a shows a more accurate selection of voxels than Figure 5b concerning the expected results for an auditory stimulus modality. This is because the modified version of ALE allows us to weigh each voxel according to the number of subjects that participated in the experiment. Figure 5b is unable to capture the variance and relies on each experiment present in the BrainMap database with the same weight, leading to noisier results.

problem we wish to solve makes it necessary to have a framework capable of solving probabilistic choice and handling deterministic open-world knowledge. Moreover, we are not aware of any practical implementation of the mentioned works, beyond the provided theory. It's important to highlight that NeuroLang limits the representation of probabilistic atoms as mutually exclusive events or mutually independent events. We are aware of this limitation and of several advances in the field that overcome this limitation, such as MarkoViews (Jha and Suciu, 2012b).

Finally, Neurolang is open-source software, so any member of the community can propose improvements, extensions, or modules. One use case of particular interest is the possibility for researchers/laboratories creating datasets to code their own "connectors" with NeuroLang, making the loading

of these data trivial for the end-user of the tool. As for the core of Neurolang, all contributions are welcome, but it will be the core developers of the project who will be in charge of approving/rejecting modifications, in the spirit of maintaining a reliable tool that guarantees harmonious results among users, as in other popular open-source tools.

To conclude, we have shown that neuroimaging meta-analytic applications are an excellent real-world application for a language such as probabilistic Datalog+/−. By using probabilistic semantics that have recently converged from different probabilistic logic and open-world language approaches (Riguzzi, 2008; Ceylan et al, 2021; Vennekens et al, 2009), with open-world semantics (Calì et al, 2012; Gottlob et al, 2014; Ceylan et al, 2021), and query resolution approaches (Dalvi and Suciu, 2012; Ceylan et al, 2021; Vlasselaer et al, 2016), we have produced a language that is ready to be used in neuroimaging applications.

Statements and Declarations

The authors have no relevant financial or non-financial interests to disclose. The authors declare that they have no competing interest.

Information Sharing Statement

All the datasets and software used in this article are openly available at the following web sites:

- Neurolang: https://neurolang.github.io/
- Nilearn, version 0.7.0: https://nilearn.github.io/
- NeuroSynth database: https://github.com/neurosynth/neurosynth
- CogAt ontology, version 0.3.1: https://bioportal.bioontology.org/ontologies/COGAT
- IOBC ontology, version 1.4.0: https://bioportal.bioontology.org/ontologies/IOBC

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A Probability manipulation

NeuroLang is in charge of complying with the constraints imposed by the laws of probability, as long as the data are handled in this context. Once the rules are translated into PERs (with the use of *PROB* in the head of the rule), the calculated probabilities are exposed to the user. From this moment, it's the responsibility of the users to manipulate this data in the appropriate way, which may vary according to the interpretation required. We provide two NeuroLang programs demonstrating the correct and incorrect uses of this requirement to illustrate both cases.

Let's say that we are interested in computing a forward inference experiment using Meta-analytic data. For example, we could be interested in the probability of a set of voxels being activated given that the terms *pain* or *noxious* are present in the studies. We saw in Section 4.3.1 that these two terms are synonyms and can be derived from the IOBC ontology, but let's do it manually this time, to simplify the program.

Based on the code presented in Listing 3, we could calculate the probability of each voxel for both terms, transform these atoms into a PER and then sum them to obtain our final answer; the code of this program is presented in Listing 9. Of course, this is wrong, since it is easy to see that if the probability of one voxel is higher than 0.5 between both terms, our final answer will sum to more than one. The same will occur if we continue adding more terms to the program.

However, this program is correct in the sense that NeuroLang is not able to stop the user from misusing the probabilities. After being converted to PERs, the probabilities column is exposed to the user and it's their responsibility to use it correctly. Alternatively, we could do the same calculations before converting the atoms with the guarantee that the calculations have been done correctly. Ultimately, it's just a matter of using PERs to extract the results as the final step and use them to build the set of answers (as we saw in the NeuroLang algorithm, probabilistic atoms cannot appear as answers). Listing 10 presents this program.

Listing 9: Breaking the validity of the probabilities obtained after being converted to PERs

```
TermAssociation(t) :- SelectedStudy(s),
    TermInStudy(t, s).

Activation(i, j, k) :- SelectedStudy(s),
    FocusReported(i1, j1, k1, s),
    FocusCoactivates(i, j, k, i1, j1, k1).

ProbMapPain(i, j, k, PROB) :-
    Activation(i, j, k)
    // TermAssociation("pain").

ProbMapNoxious(i, j, k, PROB) :-
    Activation(i, j, k)
    // TermAssociation("noxious").

ProbabilityVoxels(i, j, k, p) :-
    ProbMap(i, j, k, p1),
    ProbMap(i, j, k, p2),
    (p == p1 + p2)

Ans(i, j, k, p) :- ProbabilityVoxels(i, j, k, p)
```

Listing 10: Preserving the validity of the probabilities obtained after being converted to PERs

```
FilteredTerm(t, s) :- TermInStudy(t, s) & (t == 'pain')

FilteredTerm(t, s) :- TermInStudy(t, s) & (t == 'noxious')

TermAssociation(t) :- SelectedStudy(s),
    FilteredTerm(t, s).

Activation(i, j, k) :- SelectedStudy(s),
    FocusReported(i1, j1, k1, s),
    FocusCoactivates(i, j, k, i1, j1, k1).

ProbMap(i, j, k, PROB) :-
    Activation(i, j, k)
    // TermAssociation(t).

Ans(i, j, k, p) :- ProbMap(i, j, k, p)
```

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