Part 2: Machine learning with biomedical ontologies

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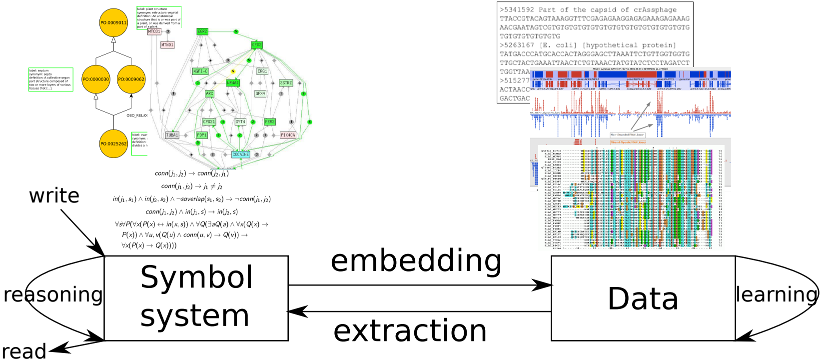
Challenges with semantic similarity

- not data-driven but hand-crafted
- not task-specific
- usually outputs a single value
- hard to chose a similarity measure
- usually graph-based and losing some information

Next: machine learning methods for and with ontologies

Machine learning with ontologies: Overview



phenotype

function

disease

genotype

protein sequence

expression

Embedding formal knowledge

Embedding

An embedding is a map (morphism) from one mathematical structure X into another structure Y:
$f : X \hookrightarrow Y$
such that X is preserved in Y.

- Y may be more suitable than X for some operations/algorithms.
  - similarity
  - gradients, optimization

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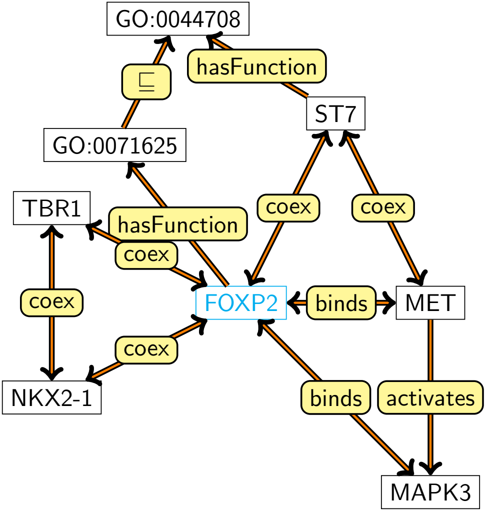
We want to embed *ontologies* in $\Re^n$. Approaches:

- graph-based
- syntactic
- model-theoretic

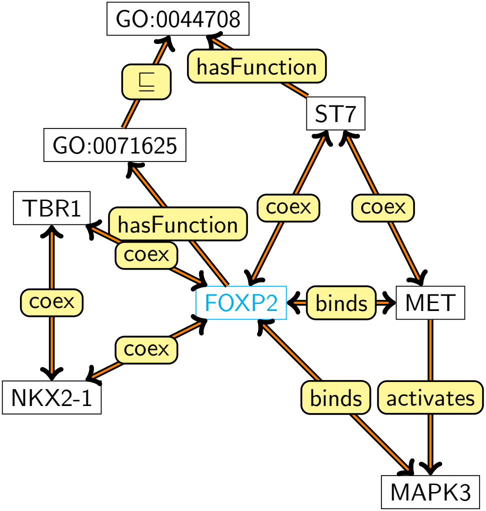
Random walks



FOXP2 is characterized by *adjacent* and close nodes and edges

different edges may "transmit" information differently

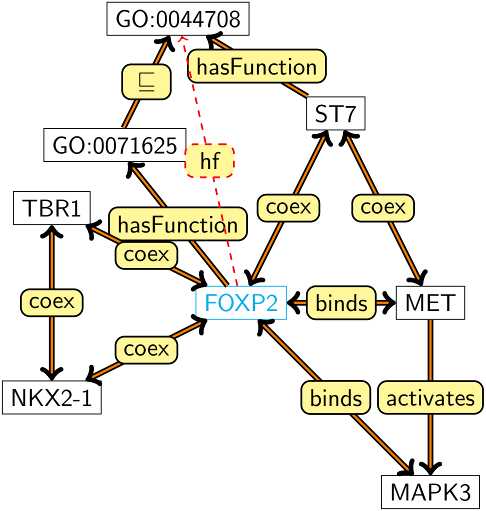
Random walks



precompute the deductive closure:

for all ϕ: if $\mathcal{KG} \models \phi$, add ϕ to $\mathcal{KG}$

Random walks



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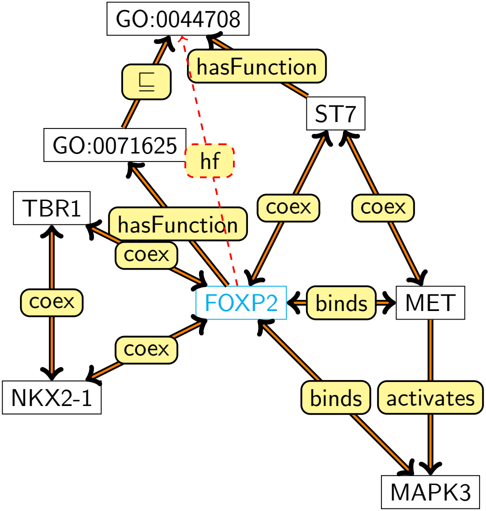
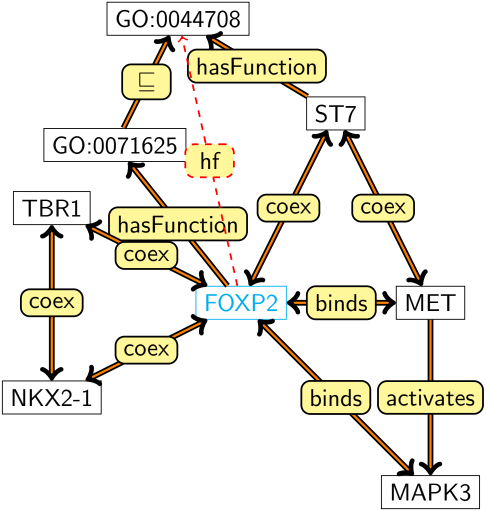


Exploring the graph:

Random walks



Exploring the graph:

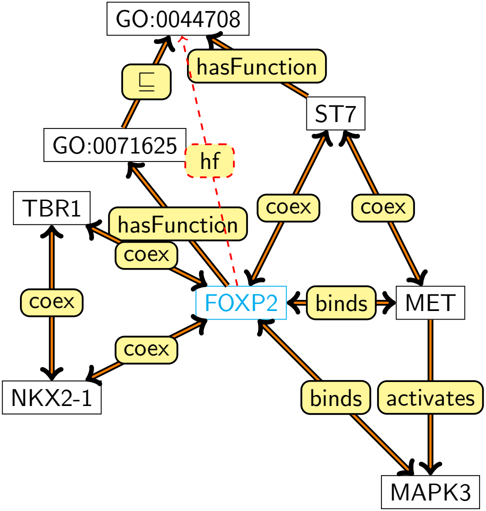
:FOXP2 :binds :MET

:coex :ST7

:hasFunction

GO:0044708

Random walks



Exploring the graph:

:FOXP2 :binds :MET :coex :ST7 :hasFunction GO:0044708

:FOXP2 :hasFunction GO:0071625 subClassOf GO:0044708

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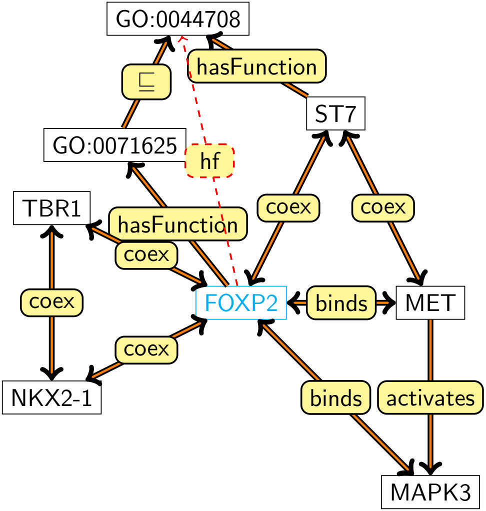

Exploring the graph:

:FOXP2 :binds :MET :coex :ST7 :hasFunction GO:0044708

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:FOXP2 :coex :TBR1 :coex :NKX2-1 :coex :TBR1 :coex ...

Word2Vec

Maximize:

$$\frac{1}{N}\sum_{n=1}^{N}\sum_{-c\leq j\leq c, j\neq 0}\log p(w_{n+j}|w_n) \tag{1}$$

with

$$p(w_o|w_i) = \frac{\exp({v'_{w_o}}^T v_{w_i})}{\sum_{w=1}^{W}\exp({v'_w}^T v_{w_i})} \tag{2}$$

(at least conceptually; different strategies are used to approximate Eqn. 2)

Word2Vec and Random Walks

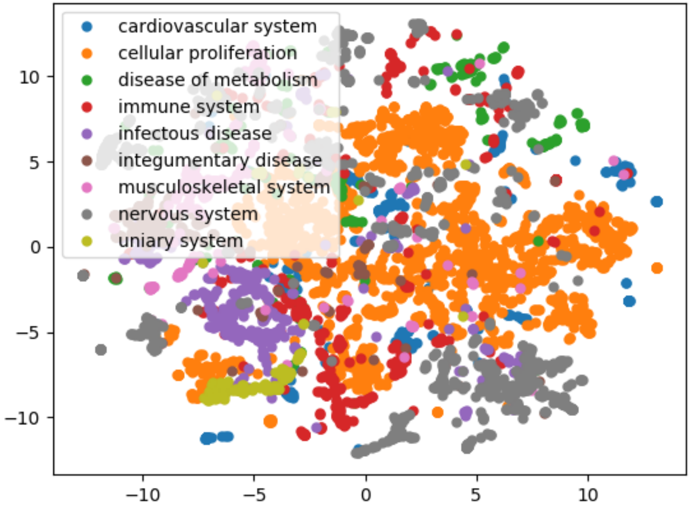
- random walks "flatten" a graph
  - walks capture node neighborhood
  - and generate a "corpus"
- random walks capture graph "structure"
  - hub-nodes, communities, etc.
  - determine "importance" of nodes
- embeddings capture co-occurrence
  - similar graph neighborhood $\Rightarrow$ similar co-occurrence $\Rightarrow$ similar vector
- embeddings generate "feature" vectors
  - functions from symbols (words, labels) into $\Re^n$

What to do with embeddings?

useful for edge prediction, similarity, clustering, as feature vectors

- supervised: edge prediction (e.g., SVM, ANN)
  - e.g.: find a function $f : \Re^n \times \Re^n \mapsto [0, 1]$ s.t. $\sqrt{\frac{\sum_{t=1}^{T}(\hat{y}_t - y_t)^2}{T}}$ (RMSE) is minimized for a set of true labels y_k
- unsupervised: clustering, similarity, visualization
  - cosine similarity (for L2-normalized features)
  - Word2Vec embeddings capture similarity between co-occurrence vectors

Visualizing embeddings



Supervised learning

- feature vectors represent graph neighborhood of nodes
  - adjacent nodes and edges
  - ontology classes (asserted & inferred)
- useful in supervised prediction tasks
- relation prediction:
  - input: two features vectors (from embedding function)
  - output: 0 or 1 (relation or not)
  - training data: positive and negative cases
    - $R(x, y)$ and $\neg R(x, y)$

Features: supervised learning

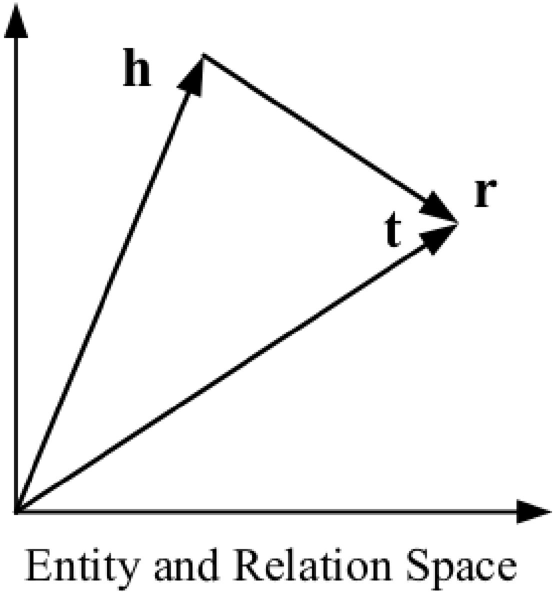
Object property	Source type	Target type	Without reasoning		With reasoning	
			F-measure	AUC	F-measure	AUC
has target	Drug	Gene/Protein	0.94	0.97	0.94	0.98
has disease annotation	Gene/Protein	Disease	0.89	0.95	0.89	0.95
has side-effect*	Drug	Phenotype	0.86	0.93	0.87	0.94
has interaction	Gene/Protein	Gene/Protein	0.82	0.88	0.82	0.88
has function*	Gene/Protein	Function	0.85	0.95	0.83	0.91
has gene phenotype*	Gene/Protein	Phenotype	0.84	0.91	0.82	0.90
has indication	Drug	Disease	0.72	0.79	0.76	0.83
has disease phenotype*	Disease	Phenotype	0.72	0.78	0.70	0.77

Some limitations

"word"-based (Word2Vec):

- semantics is reduced to co-occurrence in the random "walks"
- "disjointWith" vs. "part-of" vs. "subClassOf"

Translating embeddings



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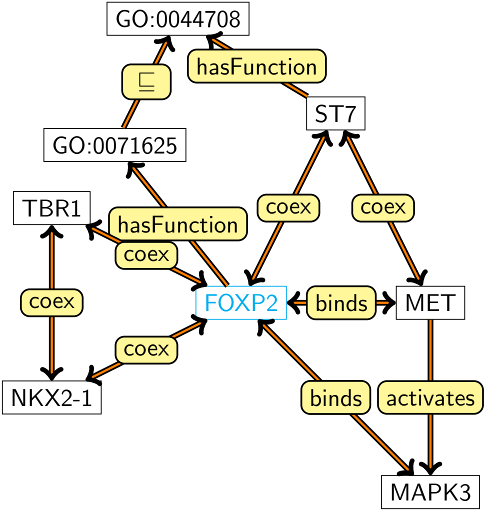

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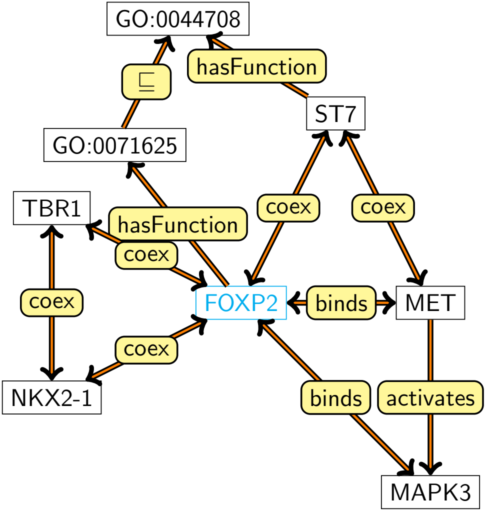
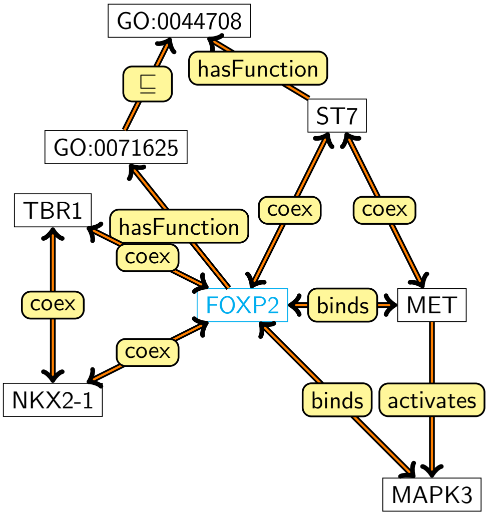


FOXP2 + binds = MET

Translating embeddings



FOXP2 + binds = MET

MAP + activates = MAPK3

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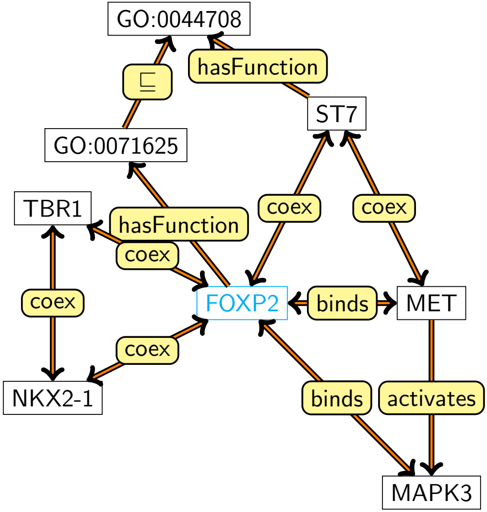

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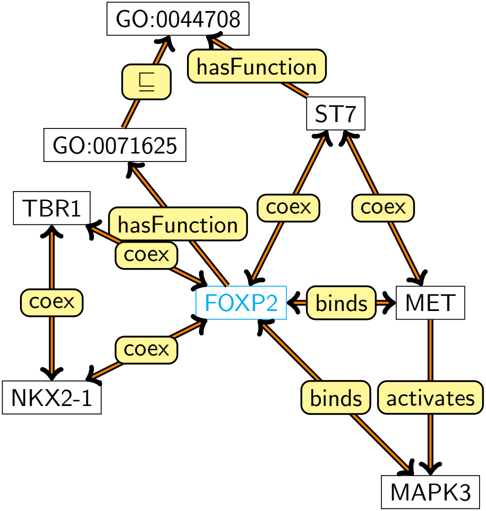

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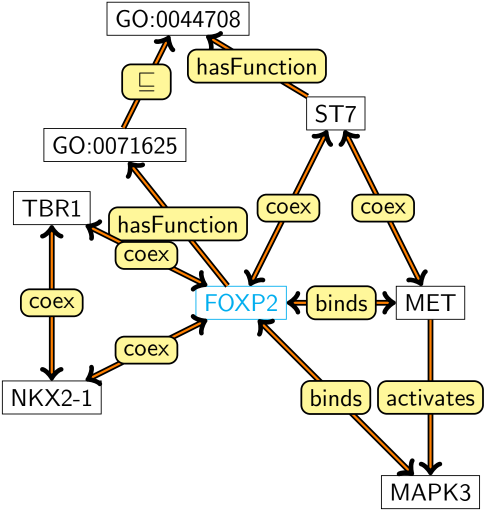

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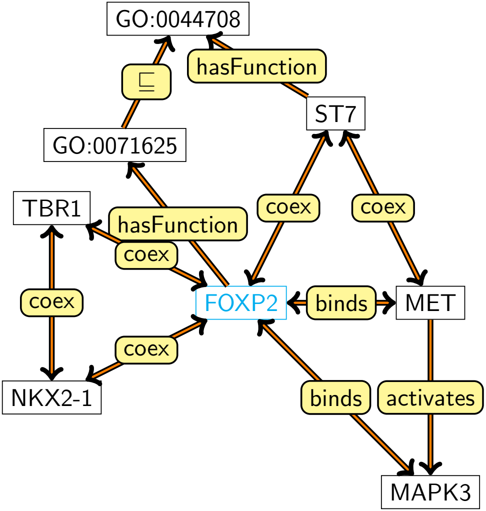


FOXP2 + binds - MET = 0

MAP + activates - MAPK3 = 0

MET + binds - FOXP2 = 0

ST7 + hasFunction - `GO:0044708` = 0

...

Translating embeddings

Algorithm 1 Learning TransE

input Training set $S = \{(h, \ell, t)\}$, entities and rel. sets E and L, margin γ, embeddings dim. k.

initialize $\boldsymbol{\ell} \leftarrow \text{uniform}(-\frac{6}{\sqrt{k}}, \frac{6}{\sqrt{k}})$ for each $\ell \in L$

$\quad\quad\quad\quad \boldsymbol{\ell} \leftarrow \boldsymbol{\ell} / \|\boldsymbol{\ell}\|$ for each $\ell \in L$

$\quad\quad\quad\quad \mathbf{e} \leftarrow \text{uniform}(-\frac{6}{\sqrt{k}}, \frac{6}{\sqrt{k}})$ for each entity $e \in E$

loop

$\quad \mathbf{e} \leftarrow \mathbf{e} / \|\mathbf{e}\|$ for each entity $e \in E$

$\quad S_{batch} \leftarrow$sample$(S, b)$ // sample a minibatch of size b

$\quad T_{batch} \leftarrow \emptyset$ // initialize the set of pairs of triplets

$\quad$ **for** $(h, \ell, t) \in S_{batch}$ **do**

$\quad\quad (h', \ell, t') \leftarrow$sample$(S'_{(h,\ell,t)})$ // sample a corrupted triplet

$\quad\quad T_{batch} \leftarrow T_{batch} \cup \left\{ \left((h, \ell, t), (h', \ell, t') \right) \right\}$

$\quad$ **end for**

$\quad$ Update embeddings w.r.t. $\displaystyle\sum_{\left((h,\ell,t),(h',\ell,t')\right) \in T_{batch}} \nabla \left[\gamma + d(\boldsymbol{h} + \boldsymbol{\ell}, \boldsymbol{t}) - d(\boldsymbol{h'} + \boldsymbol{\ell}, \boldsymbol{t'}) \right]_+$

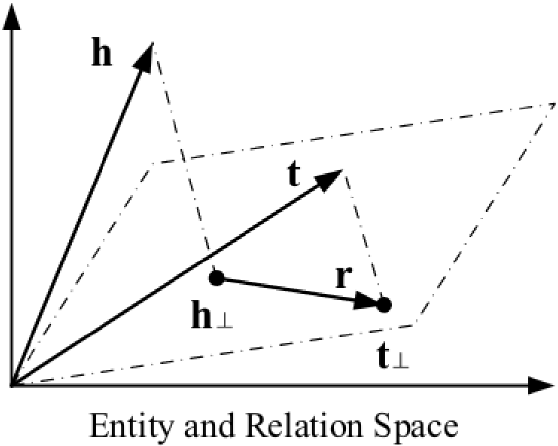
end loop

Bordes et al. (2013). Translating Embeddings for ModelingMulti-relational Data.

Some properties of TransE

- graph-based
  - works well on RDF graphs
  - and ontology graphs
- 1:1 relations only
  - not suitable for hierarchies (1-N relations)
  - not suitable for N-N relations
  - no transitive, symmetric, reflexive relations

Translating embeddings



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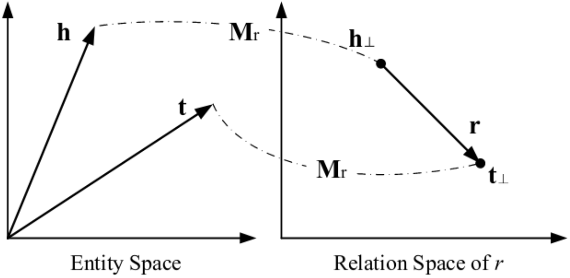


(c) TransR.

Translating embeddings

Method	Ent. embedding	Rel. embedding	Scoring function $f_r(h,t)$	Constraints/Regularization
TransE [14]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^d$	$-\lVert\mathbf{h}+\mathbf{r}-\mathbf{t}\rVert_{1/2}$	$\lVert\mathbf{h}\rVert_2=1, \lVert\mathbf{t}\rVert_2=1$
TransH [15]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r},\mathbf{w}_r\in\mathbb{R}^d$	$-\lVert(\mathbf{h}-\mathbf{w}_r^\top\mathbf{h}\mathbf{w}_r)+\mathbf{r}-(\mathbf{t}-\mathbf{w}_r^\top\mathbf{t}\mathbf{w}_r)\rVert_2^2$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1$ $\lvert\mathbf{w}_r^\top\mathbf{r}\rvert/\lVert\mathbf{r}\rVert_2\le\epsilon, \lVert\mathbf{w}_r\rVert_2=1$
TransR [16]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^k,\mathbf{M}_r\in\mathbb{R}^{k\times d}$	$-\lVert\mathbf{M}_r\mathbf{h}+\mathbf{r}-\mathbf{M}_r\mathbf{t}\rVert_2^2$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1, \lVert\mathbf{r}\rVert_2\le 1$ $\lVert\mathbf{M}_r\mathbf{h}\rVert_2\le 1, \lVert\mathbf{M}_r\mathbf{t}\rVert_2\le 1$
TransD [50]	$\mathbf{h},\mathbf{w}_h\in\mathbb{R}^d$ $\mathbf{t},\mathbf{w}_t\in\mathbb{R}^d$	$\mathbf{r},\mathbf{w}_r\in\mathbb{R}^k$	$-\lVert(\mathbf{w}_r\mathbf{w}_h^\top+\mathbf{I})\mathbf{h}+\mathbf{r}-(\mathbf{w}_r\mathbf{w}_t^\top+\mathbf{I})\mathbf{t}\rVert_2^2$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1, \lVert\mathbf{r}\rVert_2\le 1$ $\lVert(\mathbf{w}_r\mathbf{w}_h^\top+\mathbf{I})\mathbf{h}\rVert_2\le 1$ $\lVert(\mathbf{w}_r\mathbf{w}_t^\top+\mathbf{I})\mathbf{t}\rVert_2\le 1$
TranSparse [51]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^k,\mathbf{M}_r(\theta_r)\in\mathbb{R}^{k\times d}$ $\mathbf{M}_r^1(\theta_r^1),\mathbf{M}_r^2(\theta_r^2)\in\mathbb{R}^{k\times d}$	$-\lVert\mathbf{M}_r(\theta_r)\mathbf{h}+\mathbf{r}-\mathbf{M}_r(\theta_r)\mathbf{t}\rVert_{1/2}^2$ $-\lVert\mathbf{M}_r^1(\theta_r^1)\mathbf{h}+\mathbf{r}-\mathbf{M}_r^2(\theta_r^2)\mathbf{t}\rVert_{1/2}^2$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1, \lVert\mathbf{r}\rVert_2\le 1$ $\lVert\mathbf{M}_r(\theta_r)\mathbf{h}\rVert_2\le 1, \lVert\mathbf{M}_r(\theta_r)\mathbf{t}\rVert_2\le 1$ $\lVert\mathbf{M}_r^1(\theta_r^1)\mathbf{h}\rVert_2\le 1, \lVert\mathbf{M}_r^2(\theta_r^2)\mathbf{t}\rVert_2\le 1$
TransM [52]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^d$	$-\theta_r\lVert\mathbf{h}+\mathbf{r}-\mathbf{t}\rVert_{1/2}$	$\lVert\mathbf{h}\rVert_2=1, \lVert\mathbf{t}\rVert_2=1$
ManifoldE [53]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^d$	$-(\lVert\mathbf{h}+\mathbf{r}-\mathbf{t}\rVert_2^2-\theta_r^2)^2$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1, \lVert\mathbf{r}\rVert_2\le 1$
TransF [54]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^d$	$(\mathbf{h}+\mathbf{r})^\top\mathbf{t}+(\mathbf{t}-\mathbf{r})^\top\mathbf{h}$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1, \lVert\mathbf{r}\rVert_2\le 1$
TransA [55]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{r}\in\mathbb{R}^d,\mathbf{M}_r\in\mathbb{R}^{d\times d}$	$-(\lvert\mathbf{h}+\mathbf{r}-\mathbf{t}\rvert)^\top\mathbf{M}_r(\lvert\mathbf{h}+\mathbf{r}-\mathbf{t}\rvert)$	$\lVert\mathbf{h}\rVert_2\le 1, \lVert\mathbf{t}\rVert_2\le 1, \lVert\mathbf{r}\rVert_2\le 1$ $\lVert\mathbf{M}_r\rVert_F\le 1, [\mathbf{M}_r]_{ij}=[\mathbf{M}_r]_{ji}\ge 0$
KG2E [45]	$\mathbf{h}\sim\mathcal{N}(\boldsymbol{\mu}_h,\boldsymbol{\Sigma}_h)$ $\mathbf{t}\sim\mathcal{N}(\boldsymbol{\mu}_t,\boldsymbol{\Sigma}_t)$ $\boldsymbol{\mu}_h,\boldsymbol{\mu}_t\in\mathbb{R}^d$ $\boldsymbol{\Sigma}_h,\boldsymbol{\Sigma}_t\in\mathbb{R}^{d\times d}$	$\mathbf{r}\sim\mathcal{N}(\boldsymbol{\mu}_r,\boldsymbol{\Sigma}_r)$ $\boldsymbol{\mu}_r\in\mathbb{R}^d,\boldsymbol{\Sigma}_r\in\mathbb{R}^{d\times d}$	$-\mathrm{tr}(\boldsymbol{\Sigma}_r^{-1}(\boldsymbol{\Sigma}_h+\boldsymbol{\Sigma}_t))-\boldsymbol{\mu}^\top\boldsymbol{\Sigma}_r^{-1}\boldsymbol{\mu}-\ln\frac{\det(\boldsymbol{\Sigma}_r)}{\det(\boldsymbol{\Sigma}_h+\boldsymbol{\Sigma}_t)}$ $-\boldsymbol{\mu}^\top\boldsymbol{\Sigma}^{-1}\boldsymbol{\mu}-\ln(\det(\boldsymbol{\Sigma}))$ $\boldsymbol{\mu}=\boldsymbol{\mu}_h+\boldsymbol{\mu}_r-\boldsymbol{\mu}_t$ $\boldsymbol{\Sigma}=\boldsymbol{\Sigma}_h+\boldsymbol{\Sigma}_r+\boldsymbol{\Sigma}_t$	$\lVert\boldsymbol{\mu}_h\rVert_2\le 1, \lVert\boldsymbol{\mu}_t\rVert_2\le 1, \lVert\boldsymbol{\mu}_r\rVert_2\le 1$ $c_{min}\mathbf{I}\le\boldsymbol{\Sigma}_h\le c_{max}\mathbf{I}$ $c_{min}\mathbf{I}\le\boldsymbol{\Sigma}_t\le c_{max}\mathbf{I}$ $c_{min}\mathbf{I}\le\boldsymbol{\Sigma}_r\le c_{max}\mathbf{I}$
TransG [46]	$\mathbf{h}\sim\mathcal{N}(\boldsymbol{\mu}_h,\sigma_h^2\mathbf{I})$ $\mathbf{t}\sim\mathcal{N}(\boldsymbol{\mu}_t,\sigma_t^2\mathbf{I})$ $\boldsymbol{\mu}_h,\boldsymbol{\mu}_t\in\mathbb{R}^d$	$\boldsymbol{\mu}_r^i\sim\mathcal{N}(\boldsymbol{\mu}_t-\boldsymbol{\mu}_h,(\sigma_h^2+\sigma_t^2)\mathbf{I})$ $\mathbf{r}=\sum_i\pi_r^i\boldsymbol{\mu}_r^i\in\mathbb{R}^d$	$\sum_i\pi_r^i\exp\left(-\frac{\lVert\boldsymbol{\mu}_h+\boldsymbol{\mu}_r^i-\boldsymbol{\mu}_t\rVert_2^2}{\sigma_h^2+\sigma_t^2}\right)$	$\lVert\boldsymbol{\mu}_h\rVert_2\le 1, \lVert\boldsymbol{\mu}_t\rVert_2\le 1, \lVert\boldsymbol{\mu}_r^i\rVert_2\le 1$
UM [56]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	——	$-\lVert\mathbf{h}-\mathbf{t}\rVert_2^2$	$\lVert\mathbf{h}\rVert_2=1, \lVert\mathbf{t}\rVert_2=1$
SE [57]	$\mathbf{h},\mathbf{t}\in\mathbb{R}^d$	$\mathbf{M}_r^1,\mathbf{M}_r^2\in\mathbb{R}^{d\times d}$	$-\lVert\mathbf{M}_r^1\mathbf{h}-\mathbf{M}_r^2\mathbf{t}\rVert_1$	$\lVert\mathbf{h}\rVert_2=1, \lVert\mathbf{t}\rVert_2=1$

Wang et al. Knowledge Graph Embedding: A Survey ofApproaches and Applications.

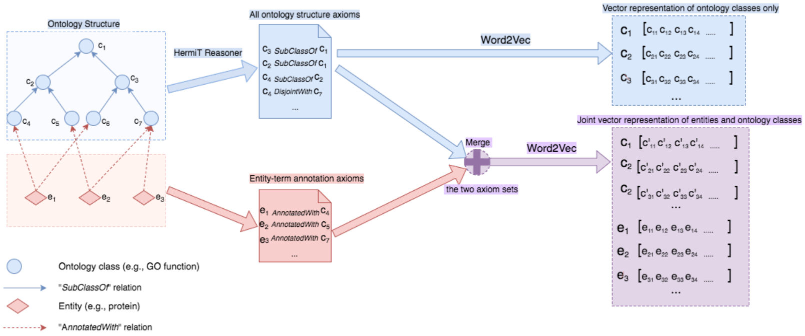
Beyond graphs

so far, all the methods were based on graphs

- ontologies are not graphs!
- converting ontologies to graphs loses information
- no axioms, no definitions

maybe we won't need the graph?

Onto2Vec

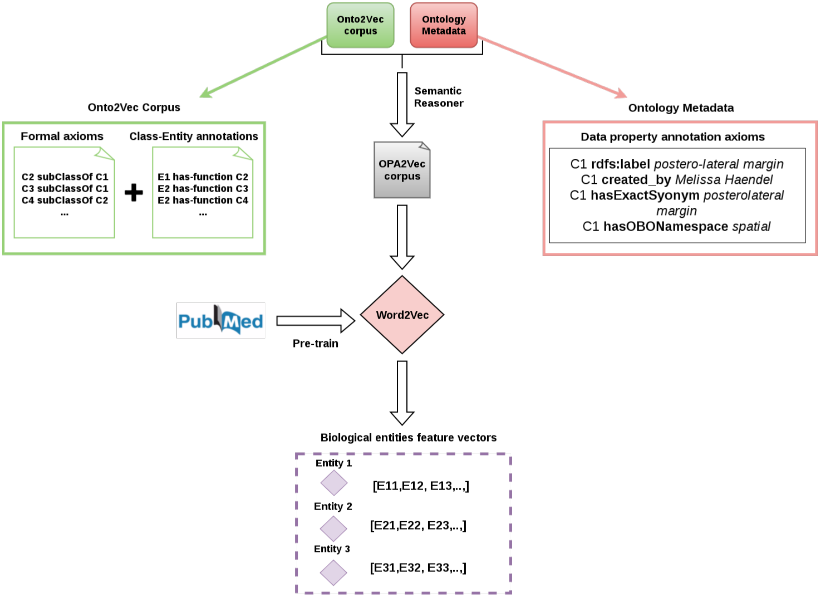


Ontology Structure
HermiT Reasoner
All ontology structure axioms
c3 SubClassOf c1
c2 SubClassOf c1
c4 SubClassOf c2
c4 DisjointWith c7
Word2Vec
Vector representation of ontology classes only
Entity-term annotation axioms
e1 AnnotatedWith c4
e2 AnnotatedWith c5
e3 AnnotatedWith c7
Merge
the two axiom sets
Joint vector representation of entities and ontology classes
Ontology class (e.g., GO function)
"SubClassOf" relation
Entity (e.g., protein)
"AnnotatedWith" relation

Combination with text

- ontologies contain more than axioms:
  - labels, synonyms, definitions, authors, etc.
- Description Logic axioms != natural language
- transfer learning: learn on one domain/task, apply to another
  - e.g.: learn on literature, apply to ontologies
  - words have “meaning” in literature, Description Logic symbols have “meaning” in ontology axioms
- Ontologies Plus Annotations 2 Vec (OPA2Vec) combines both

Ontologies Plus Annotations 2 Vec



Axioms contribute to prediction tasks: GO and GO-PLUS

	Human	Yeast	Arabidopsis
GO_Onto2Vec	0.7660	0.7701	0.7559
GO_Onto2Vec_NN	0.8779	0.8711	0.8364
GO_plus_Onto2Vec	0.7880	0.7943	0.7889
GO_plus_Onto2Vec_NN	**0.9021**	**0.8937**	**0.8834**

How to overcome the semantic gap?

- none of the models discussed above are truly "semantic"
  - all syntactic
  - graph-based or based on axioms

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- what do we actually mean by "semantics"?
  - formal definition of "truth" relies on "models"
  - universal algebra over formal languages (with signature Σ)

Description Logic EL++

Name	Syntax	Semantics
top	$\top$	$\Delta^{\mathcal{I}}$
bottom	$\bot$	$\emptyset$
nominal	$\{a\}$	$\{a^{\mathcal{I}}\}$
conjunction	$C \sqcap D$	$C^{\mathcal{I}} \cap D^{\mathcal{I}}$
existential restriction	$\exists r.C$	$\{x \in \Delta^{\mathcal{I}} \mid \exists y \in \Delta^{\mathcal{I}} : (x, y) \in r^{\mathcal{I}} \wedge y \in C^{\mathcal{I}}\}$
generalized concept inclusion	$C \sqsubseteq D$	$C^{\mathcal{I}} \subseteq D^{\mathcal{I}}$
role inclusion	$r_1 \circ ... \circ r_n \sqsubseteq r$	$r_1^{\mathcal{I}} \circ ... \circ r_n^{\mathcal{I}} \subseteq r^{\mathcal{I}}$

Models

Interpretations and Σ-structures

Model $\mathfrak{A}$ of a formula ϕ: ϕ is true in $\mathfrak{A}$ ($\mathfrak{A} \models \phi$)

Theory T: set of formulas

$\mathfrak{A}$ is a model of T if $\mathfrak{A}$ is a model of all formulas in T

Ontologies are (special kinds of) theories

EL Embeddings

given a theory/ontology T with signature $\Sigma(T)$

aim: find $f_e : \Sigma(T) \mapsto \Re^n$ s.t. $f_e(\Sigma(T))$ is a model of T $(f_e(\Sigma(T)) \models T)$

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more general: find an algorithm that maps symbols (signatures) into $\Re^n$ so that the *semantics* of the symbol (expressed through axioms and explicit in model structures) is preserved

EL Embeddings

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any consistent EL++ theory has infinite models

any consistent EL++ theory has models in $\mathbb{R}^n$ (Loewenheim-Skolem, upwards)

Key idea

for all $r \in \Sigma(T)$ and $C \in \Sigma(T)$, define $f_e(r)$ and $f_e(C)$

$f_e(C)$ maps to points in an open n-ball such that $f_e(C) = C^{\mathcal{I}}$:
$C^{\mathcal{I}} = \{x \in \mathbb{R}^n | \, \|f_e(C) - x\| < r_e(C)\}$

these are the *extension* of a class in $\Re^n$

$f_e(r)$ maps a binary relation r to a vector such that
$r^{\mathcal{I}} = \{(x, y) | x + f_e(r) = y\}$

that's the TransE property for *individuals*

use the axioms in T as constraints

Algorithm

normalize the theory:

- every $\mathcal{EL}^{++}$theory can be expressed using four normal forms (Baader et al., 2005)

eliminate the ABox: replace each individual symbol with a singleton class: a becomes $\{a\}$

rewrite relation assertions $r(a, b)$ and class assertions $C(a)$ as $\{a\} \sqsubseteq \exists r.\{b\}$ and $\{a\} \sqsubseteq C$

- something to remember for the next class-vs-instance discussion?

normalization rules to generate:

- $C \sqsubseteq D$
- $C \sqcap D \sqsubseteq E$
- $C \sqsubseteq \exists R.D$
- $\exists R.C \sqsubseteq D$

Algorithm: loss functions

$$
\begin{aligned}
&loss_{C \sqsubseteq D}(c, d) = \\
&\max(0, \|f_\eta(c) - f_\eta(d)\| + r_\eta(c) - r_\eta(d) - \gamma) \\
&+ |\,\|f_\eta(c)\| - 1| + |\,\|f_\eta(d)\| - 1|
\end{aligned}
\tag{3}
$$

Algorithm: loss functions

Let $h = \frac{r_\eta(c)^2 - r_\eta(d)^2 + \|f_\eta(c) - f_\eta(d)\|^2}{2\|f_\eta(c) - f_\eta(d)\|}$, then the center and radius of the smallest n-ball containing the intersection of $\eta(C)$ and $\eta(D)$ are $f_\eta(c) + \frac{h}{\|f_\eta(c) - f_\eta(d)\|}(f_\eta(d) - f_\eta(c))$ and $\sqrt{r_\eta(c)^2 - h^2}$.

Algorithm: loss functions

$$
\begin{aligned}
& loss_{C \sqsubseteq \exists R.D}(c, d, r) = \\
& \max(0, \|f_\eta(c) + f_\eta(r) - f_\eta(d)\| + r_\eta(c) - r_\eta(d) - \gamma) \qquad (4) \\
& + |\,\|f_\eta(c)\| - 1| + |\,\|f_\eta(d)\| - 1|
\end{aligned}
$$

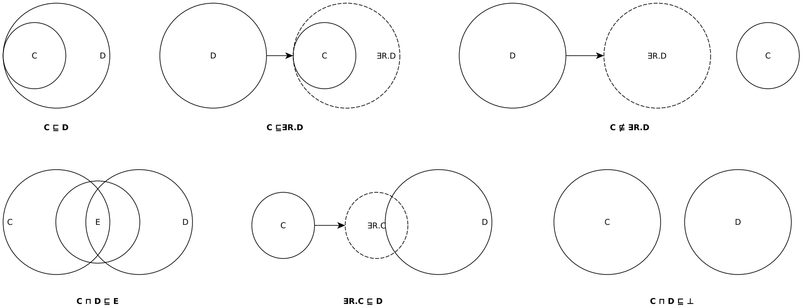
Algorithm: loss functions

$$
\begin{aligned}
&loss_{\exists R.C \sqsubseteq D}(c, d, r) = \\
&\max(0, \|f_\eta(c) - f_\eta(r) - f_\eta(d)\| - r_\eta(c) - r_\eta(d) - \gamma) \qquad (5) \\
&+ |\, \|f_\eta(c)\| - 1| + |\, \|f_\eta(d)\| - 1|
\end{aligned}
$$

Algorithm: loss functions

$$\begin{aligned}
&loss_{C \sqcap D \sqsubseteq \bot}(c, d, e) = \\
&\max(0, r_\eta(c) + r_\eta(d) - \|f_\eta(c) - f_\eta(d)\| + \gamma) \\
&+ |\,\|f_\eta(c)\| - 1| + |\,\|f_\eta(d)\| - 1|
\end{aligned} \tag{6}$$

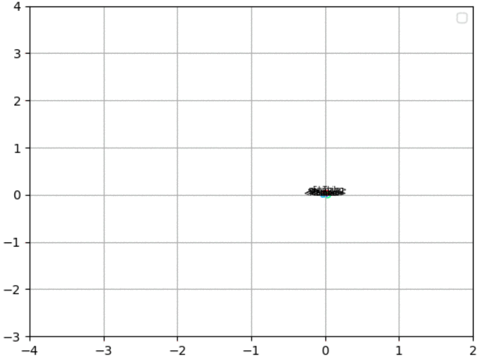
Algorithm: loss functions



EL Embeddings

$$\begin{aligned}
Male &\sqsubseteq Person && (7)\\
Female &\sqsubseteq Person && (8)\\
Father &\sqsubseteq Male && (9)\\
Mother &\sqsubseteq Female && (10)\\
Father &\sqsubseteq Parent && (11)\\
Mother &\sqsubseteq Parent && (12)\\
Female \sqcap Male &\sqsubseteq \bot && (13)\\
Female \sqcap Parent &\sqsubseteq Mother && (14)\\
Male \sqcap Parent &\sqsubseteq Father && (15)\\
\exists hasChild.Person &\sqsubseteq Parent && (16)\\
Parent &\sqsubseteq Person && (17)\\
Parent &\sqsubseteq \exists hasChild.\top && (18)
\end{aligned}$$

EL Embeddings



model with $\Delta = R^n$

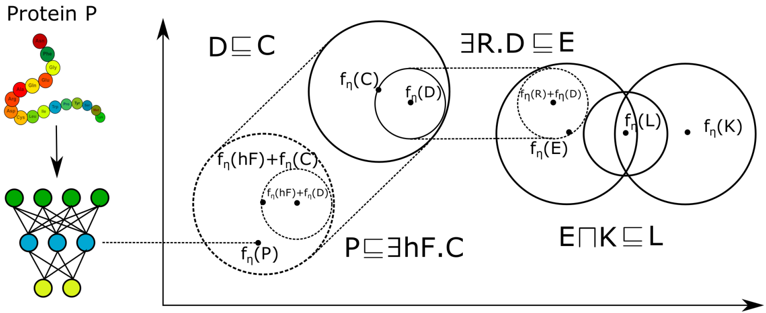
support quantifiers, negation, conjunction,...

IJCAI 2019

Zero-shot prediction with EL Embeddings

- zero-shot prediction:
  - no instance of class C is observed
    - e.g., no protein has *ever* been observed with function C
    - e.g., no individual has *ever* been observed with disease C
  - zero-shot prediction: predict instances of C
    - assumption: C is used in axioms, e.g., $C \sqsubseteq \exists R.D$ or $C \equiv A \sqcap B$
- no training data
  - can we exploit axioms and entailment within the embedding space?

Zero-shot prediction with EL Embeddings



Kulmanov & Hoehndorf, DeepGOZero: Improving protein function prediction from sequence and zero-shot learning based on ontology axioms. ISMB, 2022.

Zero-shot prediction: more general

Embedding

An embedding is a map (morphism) from one mathematical structure X into another structure Y:
$f : X \hookrightarrow Y$
such that X is preserved in Y.

Zero-shot prediction: more general

Embedding

An embedding is a map (morphism) from one mathematical structure X into another structure Y:

$f : X \hookrightarrow Y$

such that X is preserved in Y.

- existence of f^{-1}
  - inverse embedding
  - allows "extraction" of X from Y
- formulation of the prediction problem in X
  - e.g., classification: $X \sqsubseteq \exists R.Y$
  - loss expressed in terms of f^{-1}
- joint embedding of X and Z in Y
  - Z is a third structure providing external information

mOWL

- high-performance software library for machine learning with Semantic Web (OWL) ontologies
- ontology embeddings, zero-shot, constrained optimization
- contains
  - graph generation (DL2Vec, OWL2Vec*, Taxonomy)
  - graph embedding (random walk + word2vec, node2vec, various knowledge graph embedding methods from PyKEEN)
  - model-based embeddings (ELEm, EMEI, ELBE)
  - category-theoretical embeddings
  - FuzzFuzzFuzz ALC embeddings
- Algorithms written in Python + Scala (OWLAPI), tuned for performance

https://github.com/bio-ontology-research-group/mowl

Hands-on part

There is a notebook available that shows how to use mOWL with all the methods introduced here. Run the code in the Notebook. When complete, change the task from prediction of PPIs to the prediction of gene–disease associations as in the Semantic Similarity notebook.

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