Node Embeddings and Application in Biomedical Ontology

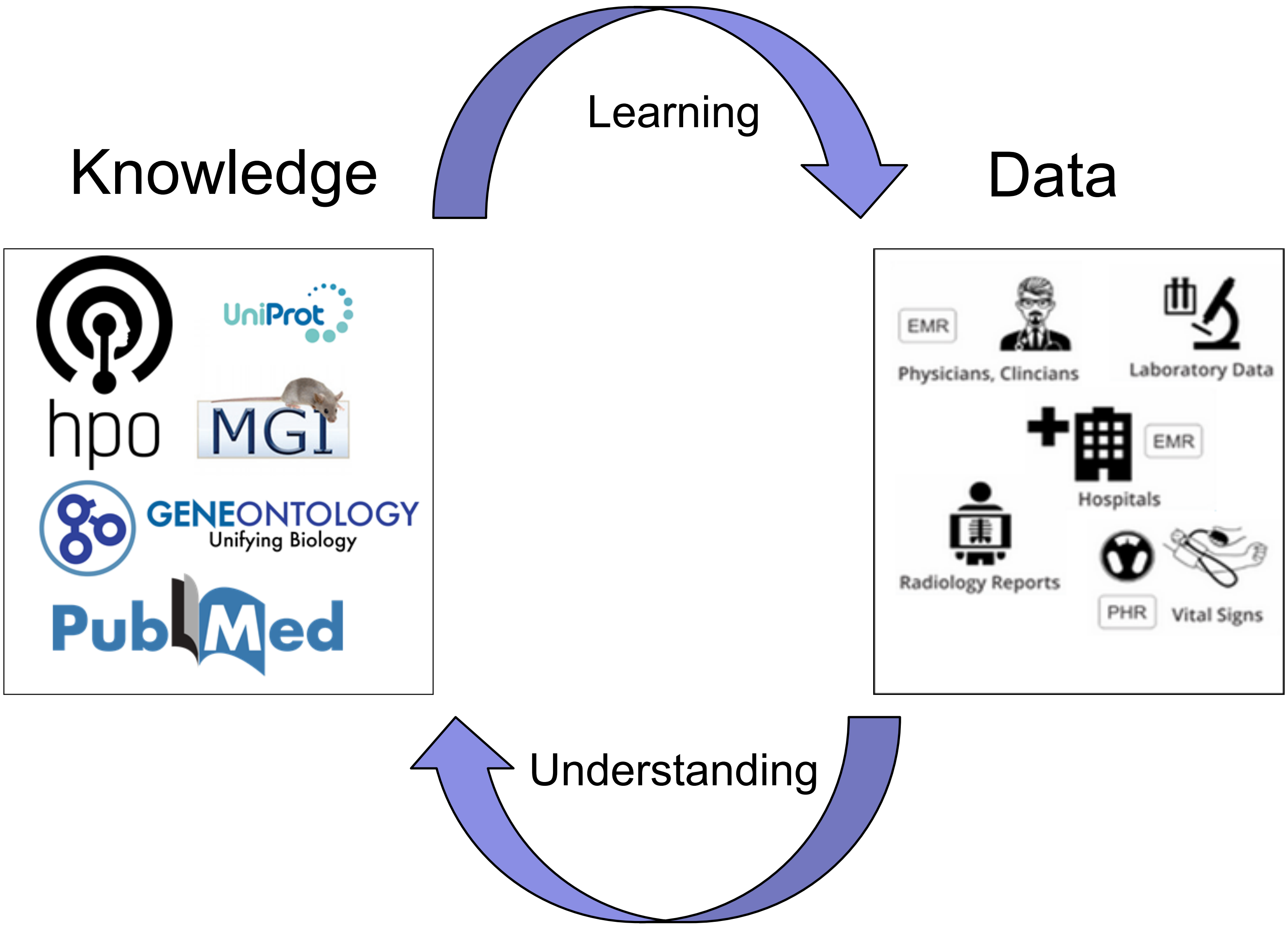
Feichen Shen, PhD
Mayo Clinic, Division of Digital Health Sciences
Shen.feichen@mayo.edu

OUTLINES

- Introduction
- Word representation
- Node representation
- Application of constructing node embeddings for a biomedical ontology
- Implementation details

MAYO CLINIC

INTRODUCTION



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WORD REPRESENTATION

WORD REPRESENTATION

- Representing words using a vocabulary of words
- V = [a, apple, bee, …, zoo]
- Assume |V| = 10,000
- one-hot encoding

$$
\begin{array}{cccccc}
\text{Man} & \text{Woman} & \text{King} & \text{Queen} & \text{Apple} & \text{Orange} \\
(5391) & (9853) & (4914) & (7157) & (456) & (6257) \\
\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \\ 0 \end{bmatrix} &
\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \end{bmatrix} &
\begin{bmatrix} 0 \\ 0 \\ 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \\ 0 \\ 0 \end{bmatrix} &
\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \end{bmatrix} &
\begin{bmatrix} 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} &
\begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ \vdots \\ 1 \\ \vdots \\ 0 \end{bmatrix}
\end{array}
$$

Deeplearning.ai. Sequence Model. Andrew Ng

Word Representation

- Using one-hot encoding, it is hard to identify semantic relationship between two vectors.
- Apple and orange are much more similar than king and orange.
- Better to have a featurized representation for each of these words

WORD REPRESENTATION

	Gender	Royal	Food	Cost	…
King	-1	0.93	0.02	0	…
Queen	1	0.95	0.01	0	…
Apple	0	-0.01	0.95	0.93	…
Orange	0.01	0	0.97	0.91	…

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Deeplearning.ai. Sequence Model. Andrew Ng

WORD EMBEDDINGS

Distributed representations of text in an n-dimensional space

WORD2VEC

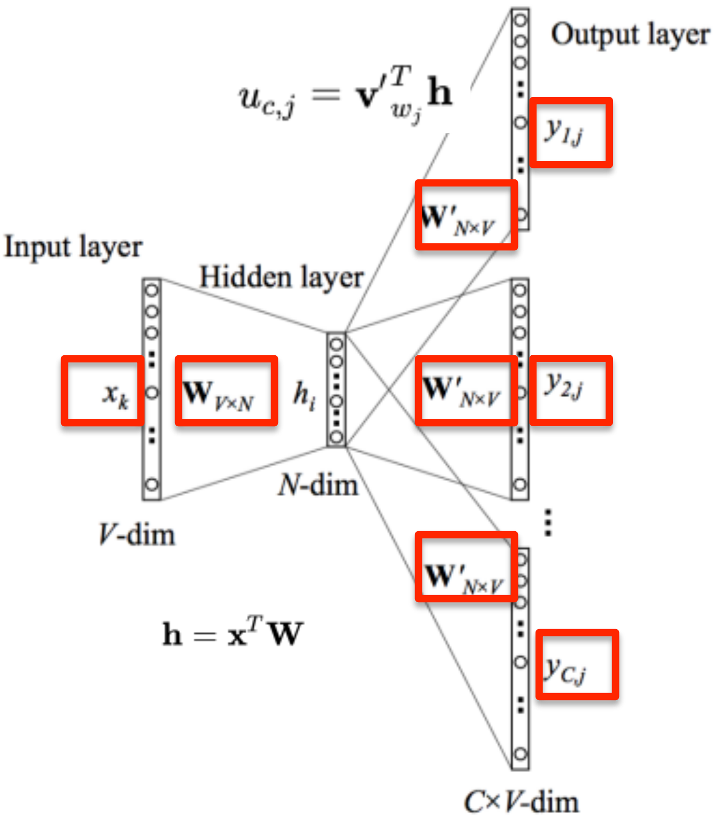
- One of the models used to learn word embeddings
- Mikolov T, Sutskever I, Chen K, Corrado GS, Dean J. Distributed representations of words and phrases and their compositionality. In Advances in neural information processing systems 2013 (pp. 3111-3119).

Word2vec

Skip-Gram

$$\frac{exp(u_{c,j})}{\sum_{j'=1}^{V} exp(u_{j'})}$$

$$u_{c,j} = \mathbf{v}'^{T}_{w_j}\mathbf{h}$$



$$\mathbf{h} = \mathbf{x}^T\mathbf{W}$$

Predict context words given an input word

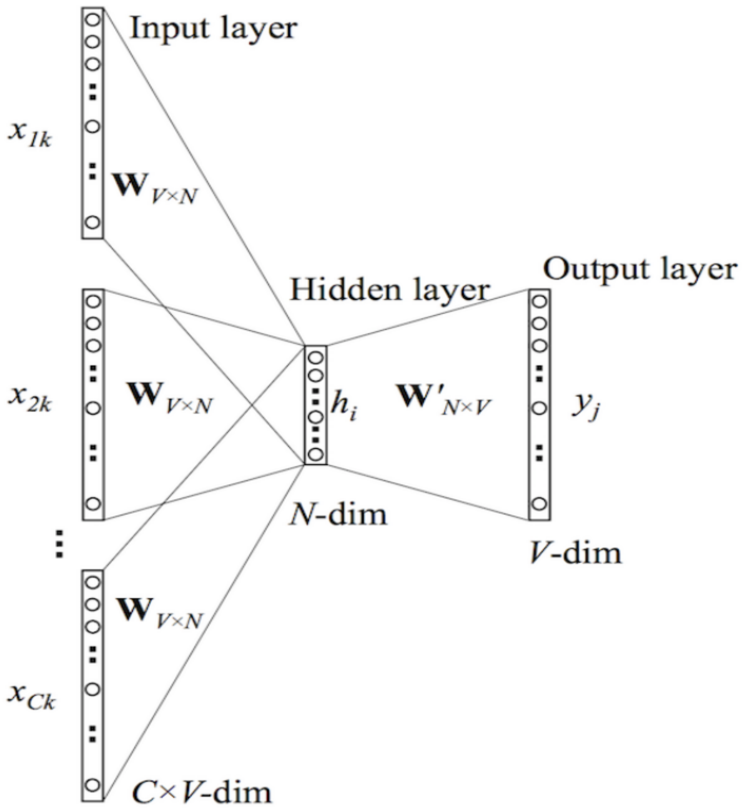
Loss function

$$\begin{aligned} E &= -\log p(w_{O,1}, w_{O,2}, \ldots, w_{O,C} | w_I) \\ &= -\log \prod_{c=1}^{C} \frac{exp(u_{c,j_c^*})}{\sum_{j'=1}^{V} exp(u'_j)} \\ &= -\sum_{c=1}^{C} u_{j_c^*} + C \cdot \log \sum_{j'=1}^{V} exp(u_{j'}) \end{aligned}$$

Learn the weights with Backpropagation

WORD2VEC

Continuous Bag-of-Words (CBOW)



Input: Context words with window size C

Output: A single word

Loss function

$$
\begin{aligned}
E &= -\log p(w_O|w_I) \\
&= -u_{j*} - \log \sum_{j'=1}^{V} \exp(u_{j'}) \\
&= -\mathbf{v_{w_O}}^T \cdot \mathbf{h} - \log \sum_{j'=1}^{V} \exp(\mathbf{v_{w_{j'}}}^T \cdot \mathbf{h})
\end{aligned}
$$

Learn the weights with Backpropagation

NODE EMBEDDINGS

- Similar to word embeddings
- Node→Word, Neighborhood→Context
- However, sliding window for text is not suitable for non-linear graph
- One solution is to use random walk to select “context” in graph

NODE EMBEDDINGS

Node Embeddings with Random Walk

GE Algorithm	Ransom Walk Methods	Preserved Proximity	DL Model
DeepWalk[17]	truncated random walk	2^{nd}	
[34]	truncated random walk	2^{nd} (word-image)	
GenVector [66]	truncated random walk	2^{nd} (user-user & concept-concept)	SkipGram with
Constrained DeepWalk [25]	sampling with edge weight	2^{nd}	hierarchical softmax (Eq. (11))
DDRW [47]	truncated random walk	2^{nd} + class identity	
TriDNR [73]	truncated random walk	2^{nd} (among node, word & label)	
node2vec [28]	BFS + DFS	2^{nd}	
UPP-SNE [113]	truncated random walk	2^{nd} (user-user & profile-profile)	SkipGram with
Planetoid [62]	sampling node pairs by labels and structure	2^{nd} + label identity	negative sampling
NBNE [19]	sampling direct neighbours of a node	2^{nd}	(Eq. (12))
DGK [93]	graphlet kernel: Random sampling [114]	2^{nd} (by graphlet)	SkipGram (Eqs. (11)–(12))
metapath2vec [46]	meta-path based random walk	2^{nd}	heterogeneous SkipGram
ProxEmbed [44]	truncate random walk	node ranking tuples	
HSNL [29]	truncate random walk	2^{nd} + QA ranking tuples	LSTM
RMNL [30]	truncated random walk	2^{nd} + user-question quality ranking	
DeepCas [63]	Markov chain based random walk	information cascade sequence	GRU
MRW-MN [36]	truncated random walk	2^{nd} + cross-modal feature difference	DCNN+ SkipGram

https://ieeexplore.ieee.org/stamp/stamp.jsp?tp=&arnumber=8294302

NODE REPRESENTATION: NODE2VEC

NODE2VEC

- Scalable feature learning for networks.
- Grover A, Leskovec J.
- In Proceedings of the 22nd ACM SIGKDD international conference on Knowledge discovery and data mining 2016 Aug 13 (pp. 855-864). ACM.

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Node2vec

2 steps

- ❑ Sampling strategy

Apply random walk on graph to prepare input data

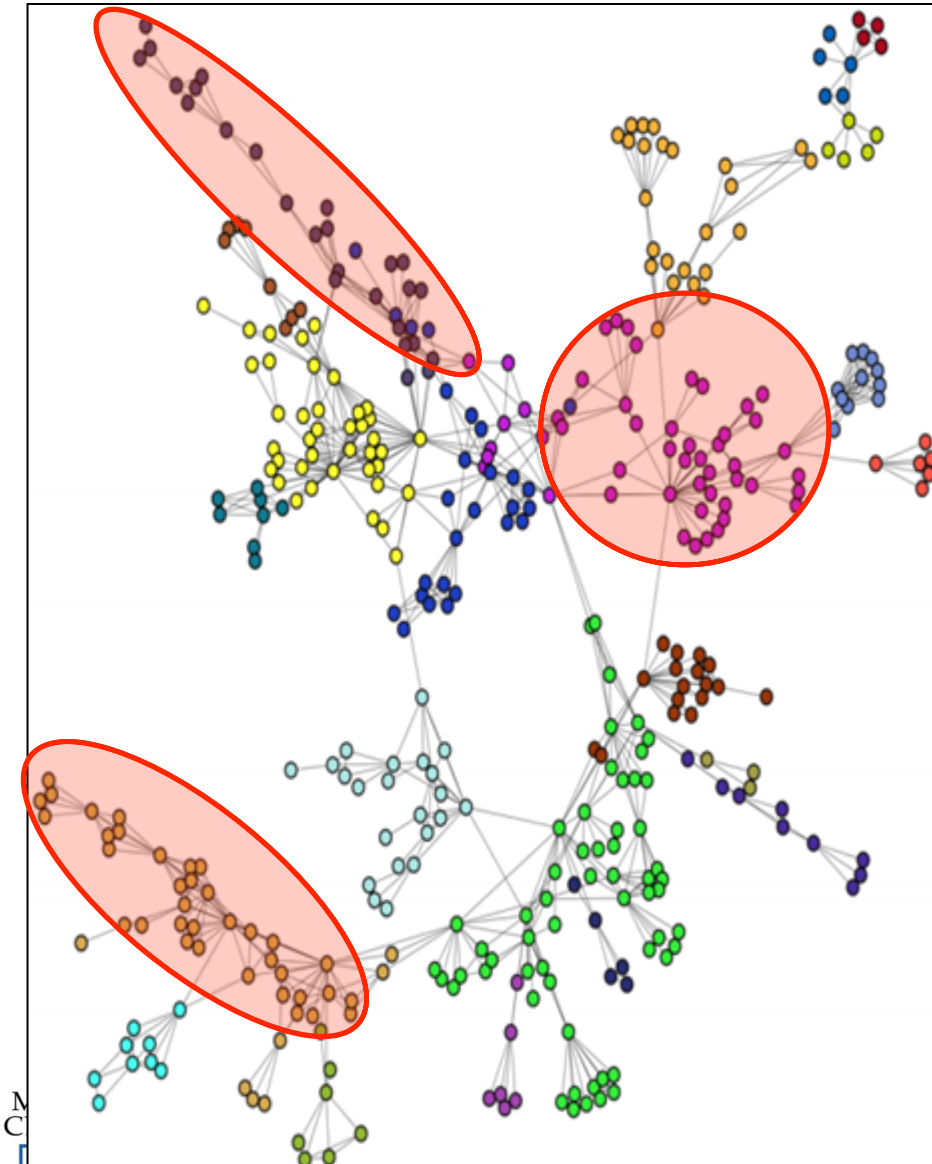
- ❑ Node embeddings

Apply word2vec on prepared input data to generate embeddings for node

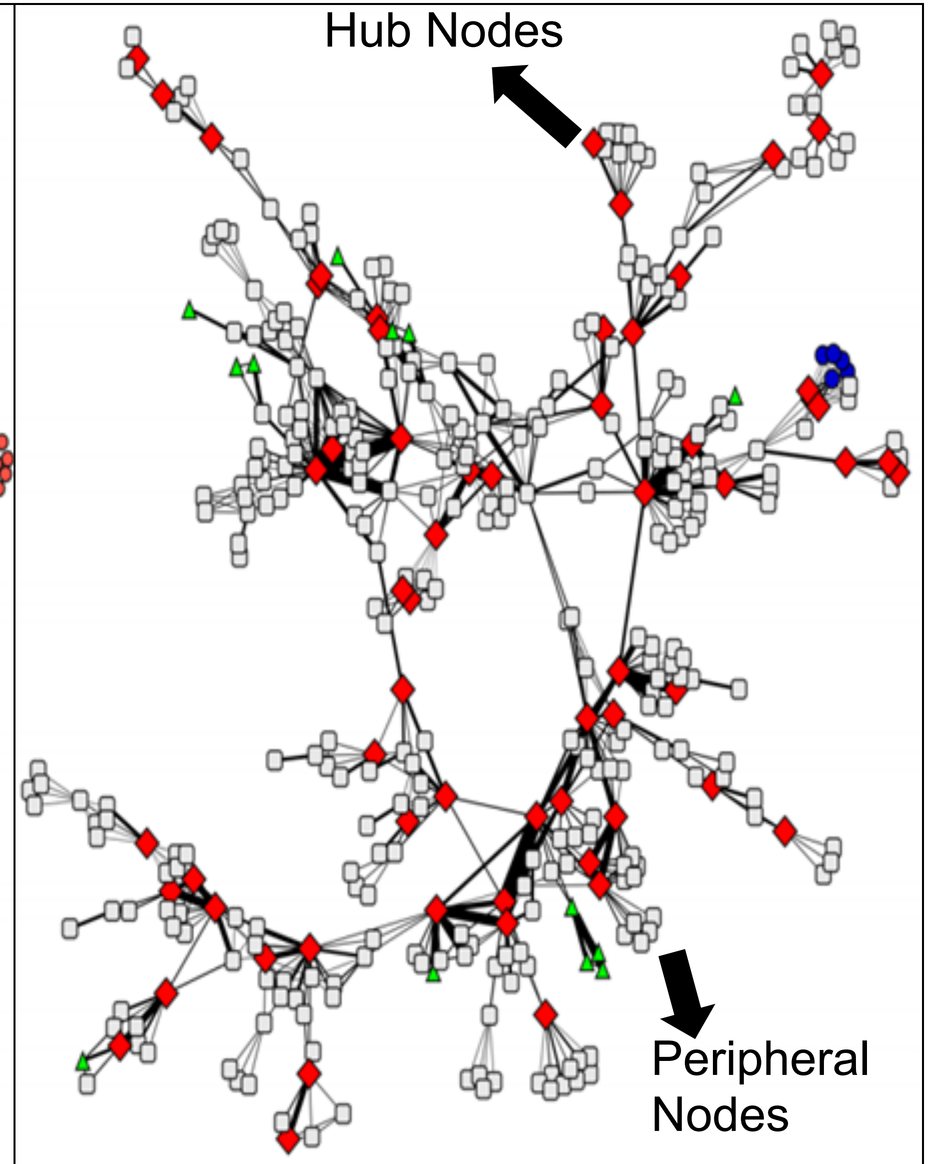
Approach
-1. Sampling strategy

- 1. **Homophily equivalence**: embed nodes from the same network community closely together
- 2. **Structural equivalence**: nodes share similar roles have similar embeddings

Homophily equivalence



Structural equivalence



Approach
-1. Sampling strategy

- Classic search strategies
  - Breadth-first sampling (BFS)
  - Depth-first sampling (DFS)

APPROACH
-1. SAMPLING STRATEGY

Breadth-first sampling (BFS)

- The goal is to traverse all nodes in the graph.
- Starts at the top level of a graph and explores the neighbor nodes first before moving to the next level neighbors.
- Iterative, FIFO queue

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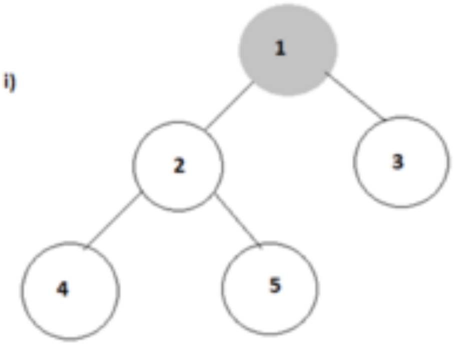
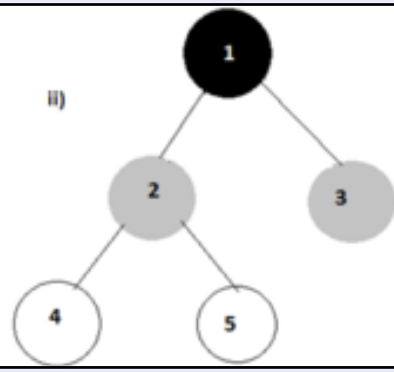
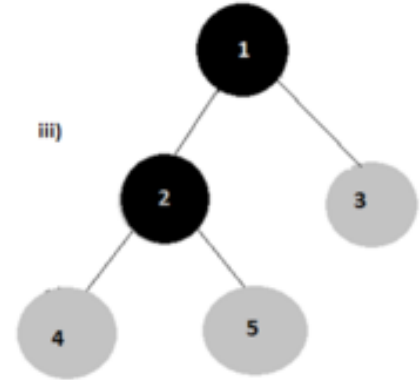
1. Start from node 1



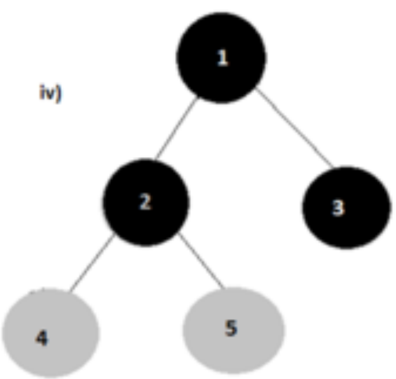
2. Find node 1 and continue to look at node 1's neighbor 2 and 3, now 2 and 3 has the highest priority to be searched



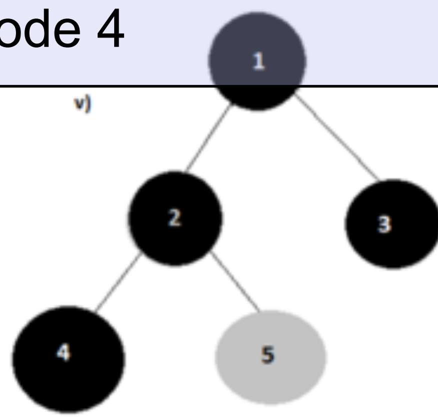
3. Find node 2



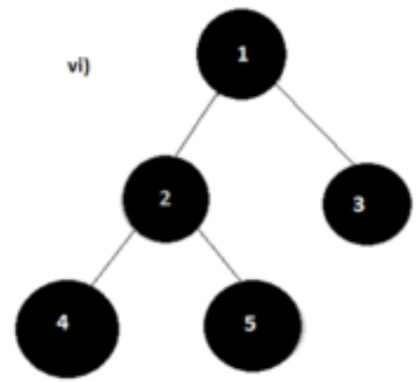
4. Find node 3



5. Check 2's neighbor 4 and 5, find node 4



6. Find node 5



APPROACH
-1. SAMPLING STRATEGY

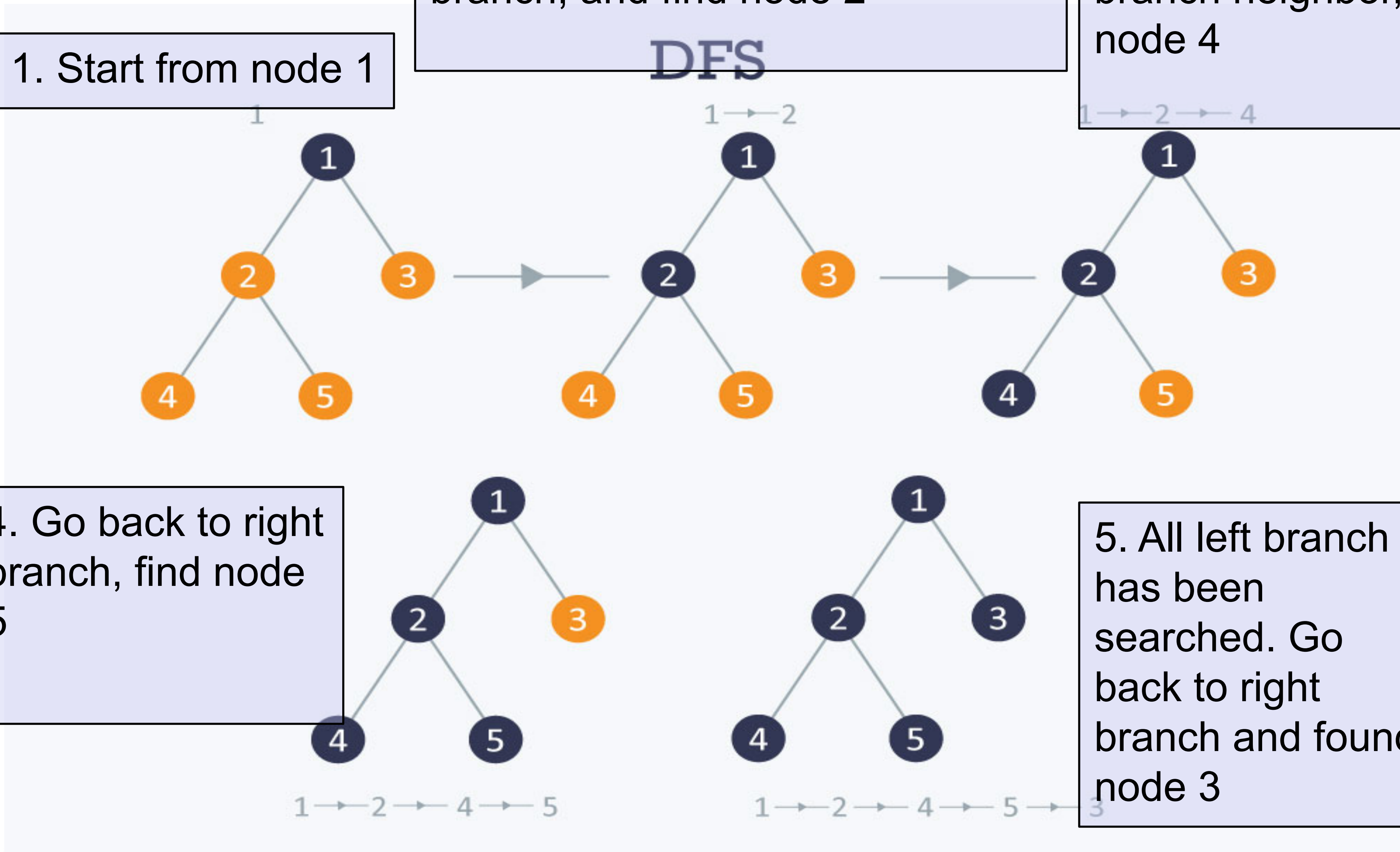
Depth-first sampling (DFS)

- It starts from the top level and explores as far as possible along each branch before backtracking
- Recursive, LIFO stack

1. Start from node 1

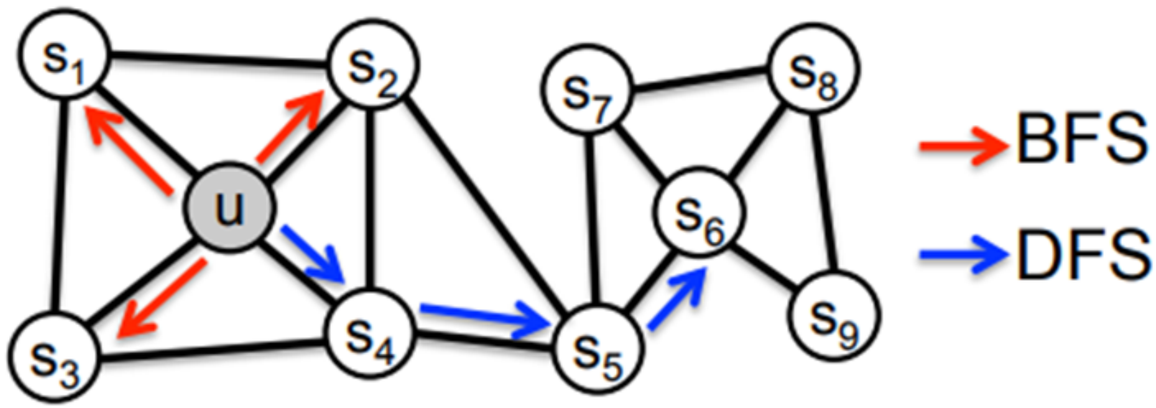
2. Look at 1's neighbor in the left branch, and find node 2

3. Find 2's left branch neighbor, node 4



4. Go back to right branch, find node 5

5. All left branch has been searched. Go back to right branch and found node 3



- **BFS: structural analysis**, **microscopic view** of neighborhood of every node
- **DFS: homophily analysis**, **macro-view** of the neighborhood among different communities
- Real-world network has a lot of such mixture of BFS and DFS

Approach
-1. Sampling Strategy

- Flexible neighborhood sampling strategy to smoothly interpolate between BFS and DFS

$$P(c_i = x | c_{i-1} = v) = \begin{cases} \frac{\pi_{vx}}{Z} & if\,(v,x) \in E \\ 0 & otherwise \end{cases}$$

Random Walk

$$\pi_{vx} = \alpha_{pq}(t,x) \cdot w_{vx}$$

Transition Probability

$$\alpha_{pq}(t,x) = \begin{cases} \frac{1}{p} & if\ d_{tx} = 0 \\ 1 & if\ d_{tx} = 1 \\ \frac{1}{q} & if\ d_{tx} = 2 \end{cases}$$

Bias Term

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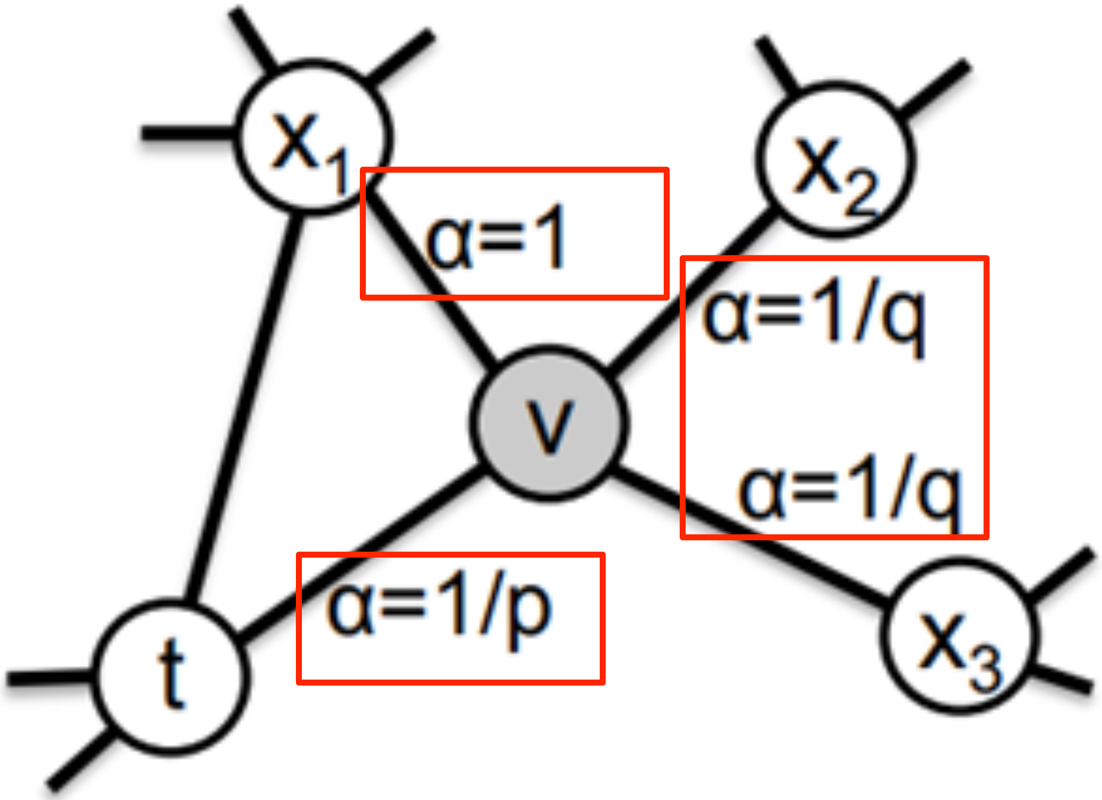
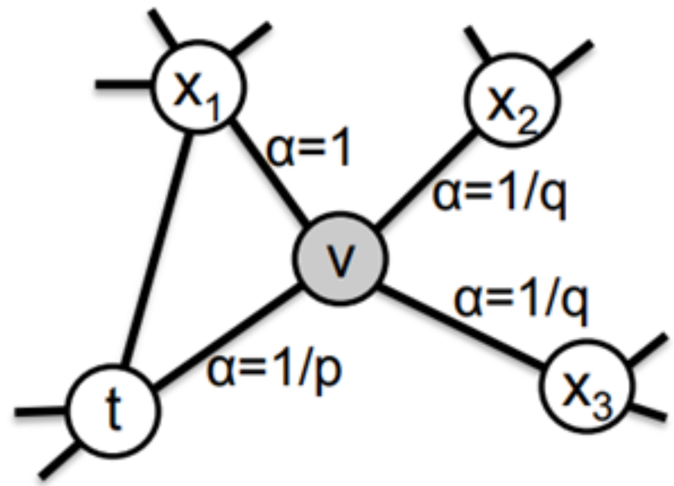
$$\alpha_{pq}(t,x) = \begin{cases} \frac{1}{p} & if\ d_{tx} = 0 \\ 1 & if\ d_{tx} = 1 \\ \frac{1}{q} & if\ d_{tx} = 2 \end{cases}$$



the current scenario is that the walk just transitioned from t to v and is now evaluating its next step out of node v.

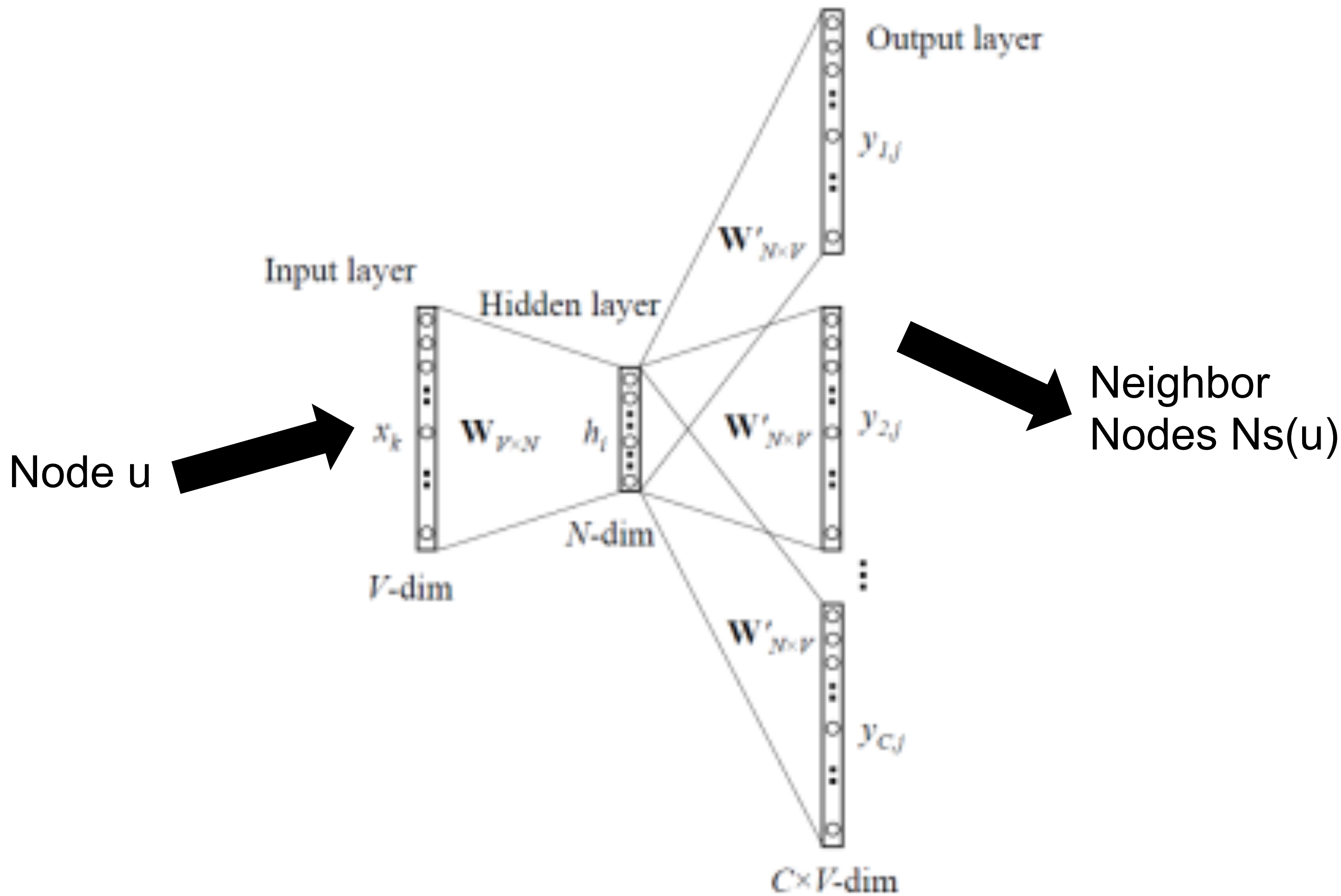
APPROACH
-1. SAMPLING STRATEGY



- p controls the return step, and q controls the step of walk to outside world
- p: return parameter. Control the likelihood of revisit. Large p ensure less revisit. Small p lead a back step
- q: in-out parameter. BFS while q>1 and DFS while q<1
- p and q are controller to balance between BFS and DFS

APPROACH
-2. WORD2VEC

Skip-gram



APPROACH
-2. WORD2VEC

- The purpose is to maximize the log-probability of Ns(u) given the input – feature representation of node u

$$\max_{f} \sum_{u \in V} \log \Pr(N_s(u) | f(u))$$

- Optimize weight matrix with SGD

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CLINIC

Apply Node2vec on Biomedical Ontology

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Ontology

Representation, formal naming, and definition of the categories, properties, and relations between concepts, data and entities within one domain

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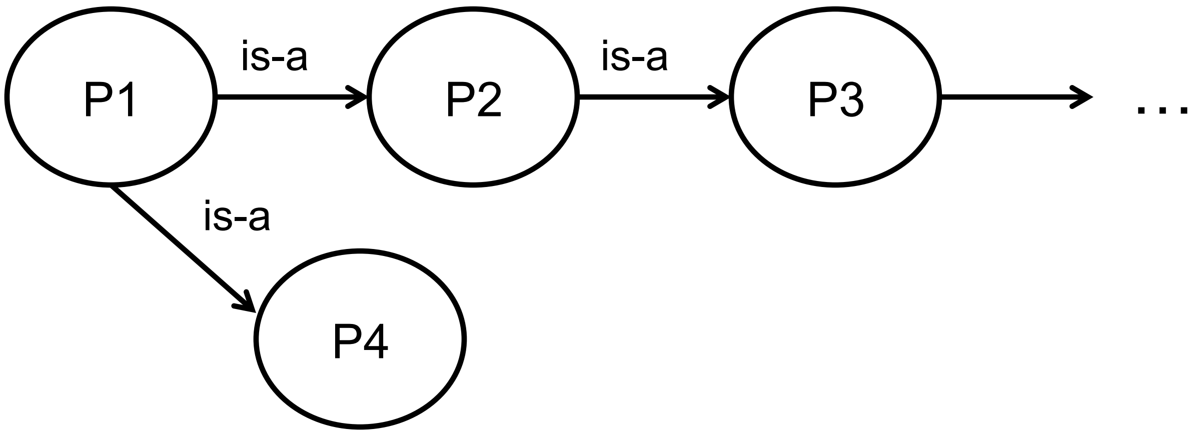
https://en.wikipedia.org/wiki/Ontology_(information_science)

Ontology

Resource Description Framework (RDF)

- {Subject, Predict, Object} triplet is the smallest unit to build the RDF graph



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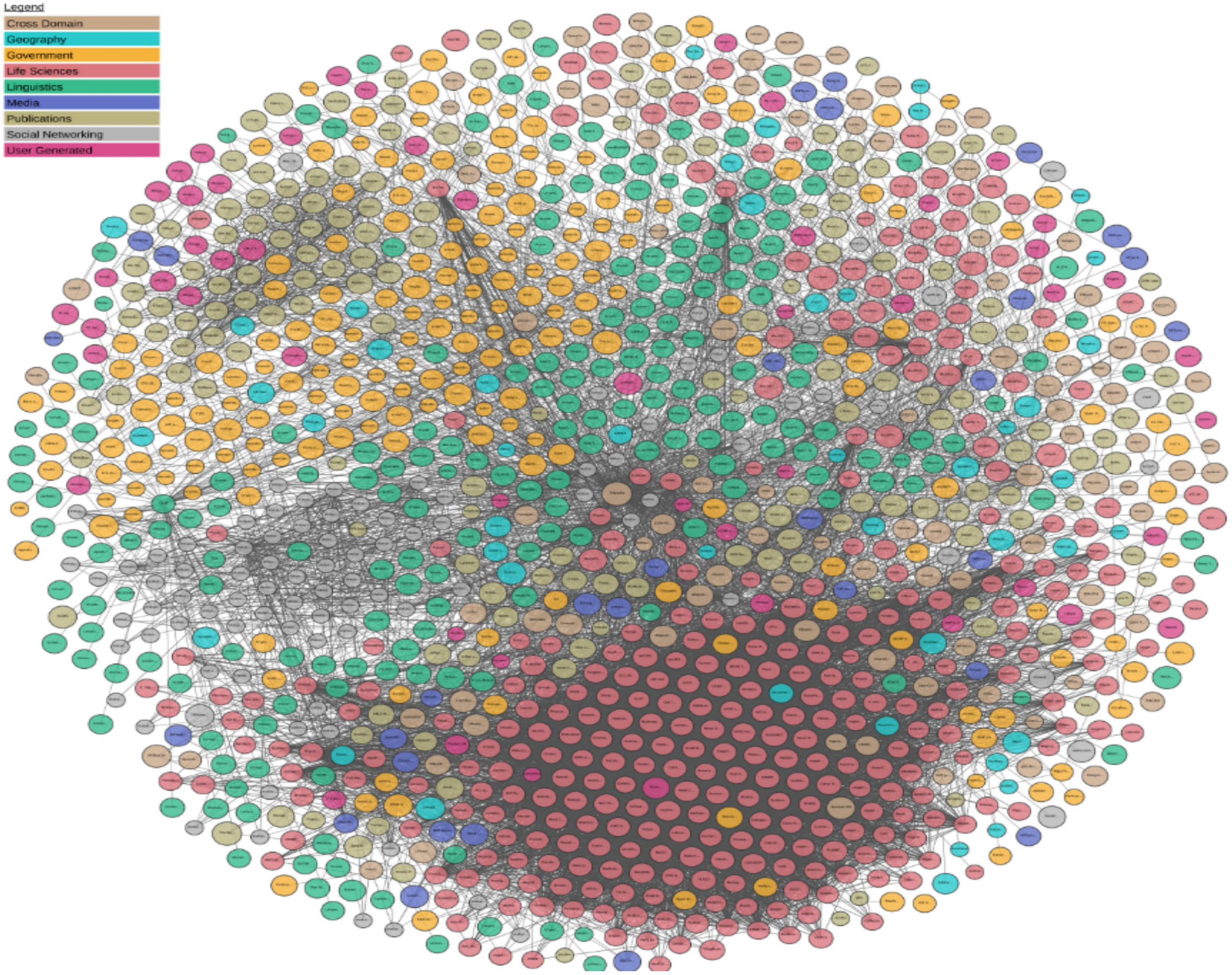
ONTOLOGY



http://linkeddata.org/

Ontology

- The Web Ontology Language (OWL) is used to describe ontology

.owl format


```xml
<?xml version="1.0"?>
<rdf:RDF xmlns="http://purl.obolibrary.org/obo/hp.owl#"
     xml:base="http://purl.obolibrary.org/obo/hp.owl"
     xmlns:rdf="http://www.w3.org/1999/02/22-rdf-syntax-ns#"
     xmlns:owl="http://www.w3.org/2002/07/owl#"
     xmlns:oboInOwl="http://www.geneontology.org/formats/oboInOwl#"
     xmlns:hsapdv="http://purl.obolibrary.org/obo/hsapdv#"
     xmlns:hp="http://purl.obolibrary.org/obo/hp#"
     xmlns:xsd="http://www.w3.org/2001/XMLSchema#"
     xmlns:rdfs="http://www.w3.org/2000/01/rdf-schema#"
     xmlns:hp2="http://purl.obolibrary.org/obo/hp.owl#"
     xmlns:obo="http://purl.obolibrary.org/obo/"
     xmlns:dc="http://purl.org/dc/elements/1.1/">
    <owl:Ontology rdf:about="http://purl.obolibrary.org/obo/hp.owl">
        <oboInOwl:saved-by rdf:datatype="http://www.w3.org/2001/XMLSchema#string">Peter Robinson, Sebastian Koehler, Sandra Doelken, Chris Mungall, Melissa Haendel,
        <rdfs:comment rdf:datatype="http://www.w3.org/2001/XMLSchema#string">Please see license of HPO at http://www.human-phenotype-ontology.org</rdfs:comment>
        <oboInOwl:logical-definition-view-relation rdf:datatype="http://www.w3.org/2001/XMLSchema#string">has_part</oboInOwl:logical-definition-view-relation>
        <oboInOwl:default-namespace rdf:datatype="http://www.w3.org/2001/XMLSchema#string">human_phenotype</oboInOwl:default-namespace>
        <dc:creator>Peter N Robinson</dc:creator>
        <dc:contributor>Mark Engelstad</dc:contributor>
        <dc:contributor>Sandra Doelken</dc:contributor>
        <dc:rights>Peter Robinson, Sebastian Koehler, The Human Phenotype Ontology Consortium, and The Monarch Initiative</dc:rights>
        <dc:creator>Sebastian Koehler</dc:creator>
        <dc:contributor>Chris Mungall</dc:contributor>
        <dc:subject>Phenotypic abnormalities encountered in human disease</dc:subject>
        <dc:contributor>Joie Davis</dc:contributor>
        <dc:contributor>Courtney Hum</dc:contributor>
        <dc:contributor>Melissa Haendel</dc:contributor>
        <dc:contributor>Nicole Vasilevsky</dc:contributor>
        <dc:creator>The Monarch Initiative</dc:creator>
        <dc:creator>The Human Phenotype Ontology Consortium</dc:creator>
        <dc:license>see http://www.human-phenotype-ontology.org</dc:license>
```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ONTOLOGY

.nt format

Subject	Predicate	Object
<http://www.skeim.org#002>	<http://www.skeim.org#hasLevel>	<http://www.skeim.org#Secondary>
<http://www.skeim.org#0021>	<http://www.w3.org/1999/02/22-rdf-syntax-ns#type>	<http://www.skeim.org#School>.
<http://www.skeim.org#0021>	< http://www.w3.org/2000/01/rdf-schema#Comment>	"About High School Institutions@en".
<http://www.skeim.org#0021>	< http://www.w3.org/2000/01/rdf-schema#subClassOf>	<http://www.skeim.org#002>.
<http://www.skeim.org#0021105770>	< http://www.w3.org/ns/org#memberOf>	"http://www.skeim.org#0021".
<http://www.skeim.org#0021105770>	< http://www.skeim.org#hasEIIN>	"105770@en".
<http://www.skeim.org#0021105770>	<http://www.w3.org/2000/01/rdf-schema#label>	"Comilla Zilla School@en".
<http://www.skeim.org#0021105770>	< http://www.skeim.org#division>	"Chittagong @en".
<http://www.skeim.org#0021105770>	<http://www.skeim.org#district>	"Comilla@en".
<http://www.skeim.org#0021105770>	< http://www.skeim.org#thana>	"Adarsha Sadar @en".
<http://www.skeim.org#0021105770>	<http://www.skeim.org#postOffice>	"Comilla@en".
<http://www.skeim.org#0021105770>	< http://www.w3.org/ns/org#site>	"Kandirpar@en".

https://www.researchgate.net/figure/Machine-understandable-educational-institutions-data-of-Bangladesh-in-N-TRIPLE-format_fig7_293808026

ONTOLOGY

.ttl format

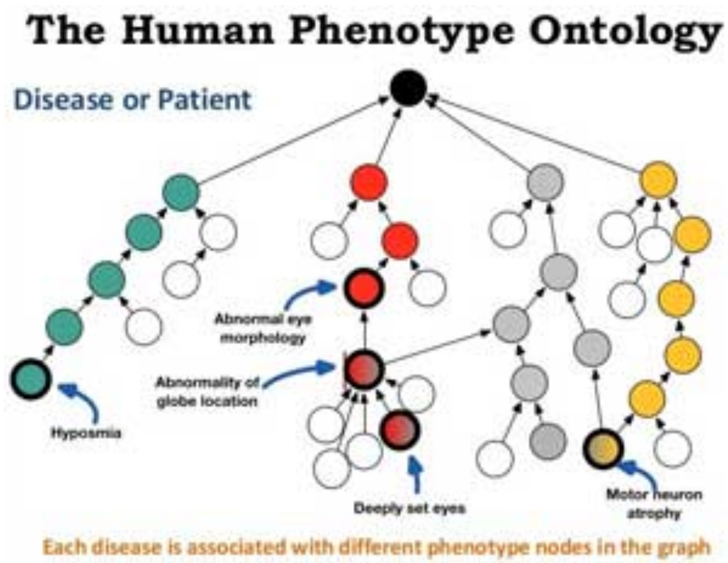
```
@prefix rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#> .
@prefix dc: <http://purl.org/dc/elements/1.1/> .
@prefix ex: <http://example.org/stuff/1.0/> .

<http://www.w3.org/TR/rdf-syntax-grammar>
  dc:title "RDF/XML Syntax Specification (Revised)" ;
  ex:editor [
    ex:fullname "Dave Beckett";
    ex:homePage <http://purl.org/net/dajobe/>
  ] .
```


https://en.wikipedia.org/wiki/Turtle_(syntax)

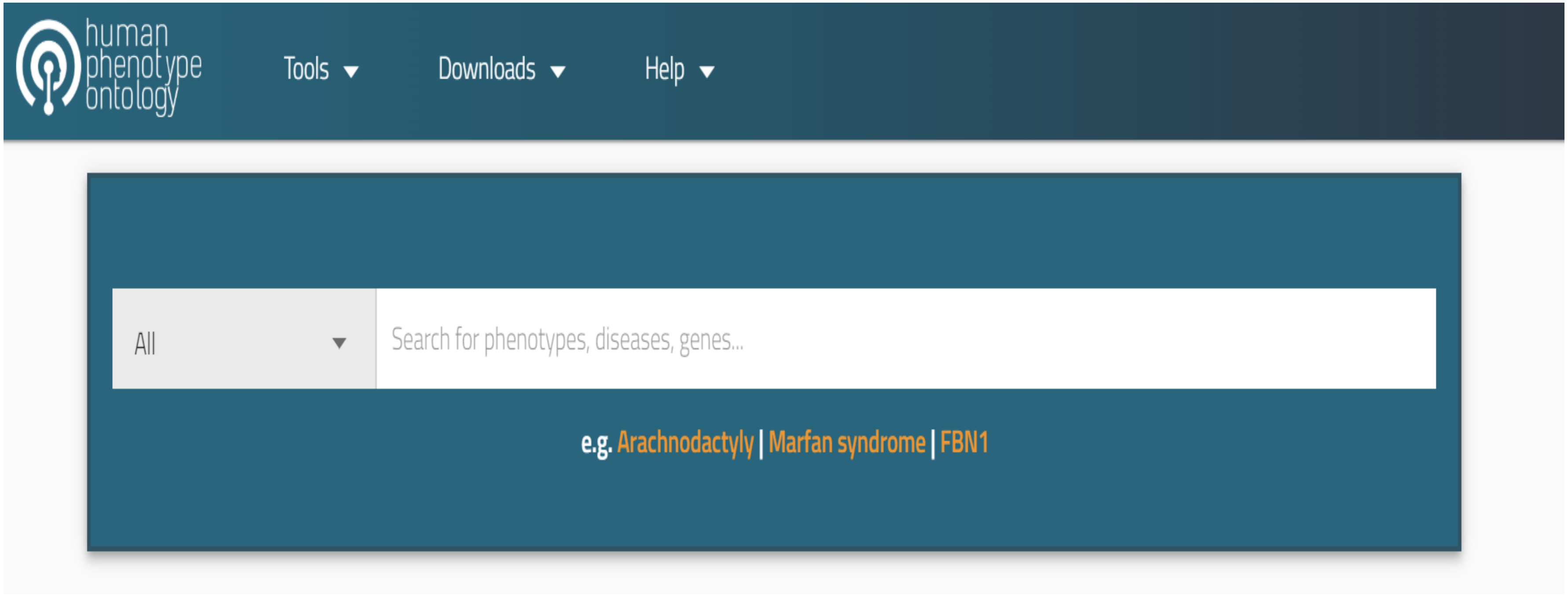
HUMAN PHENOTYPE ONTOLOGY (HPO)

- A standardized vocabulary of phenotypic abnormalities encountered in human disease
- The HPO has been used in many different tools and algorithms for clinical diagnostics, phenotype-driven genomic diagnostics, translational bioinformatics, and more
- The HPO is currently being developed using the medical literature, Orphanet, DECIPHER, and OMIM.
- Over 13,000 terms in total, maintained in a hierarchical structure



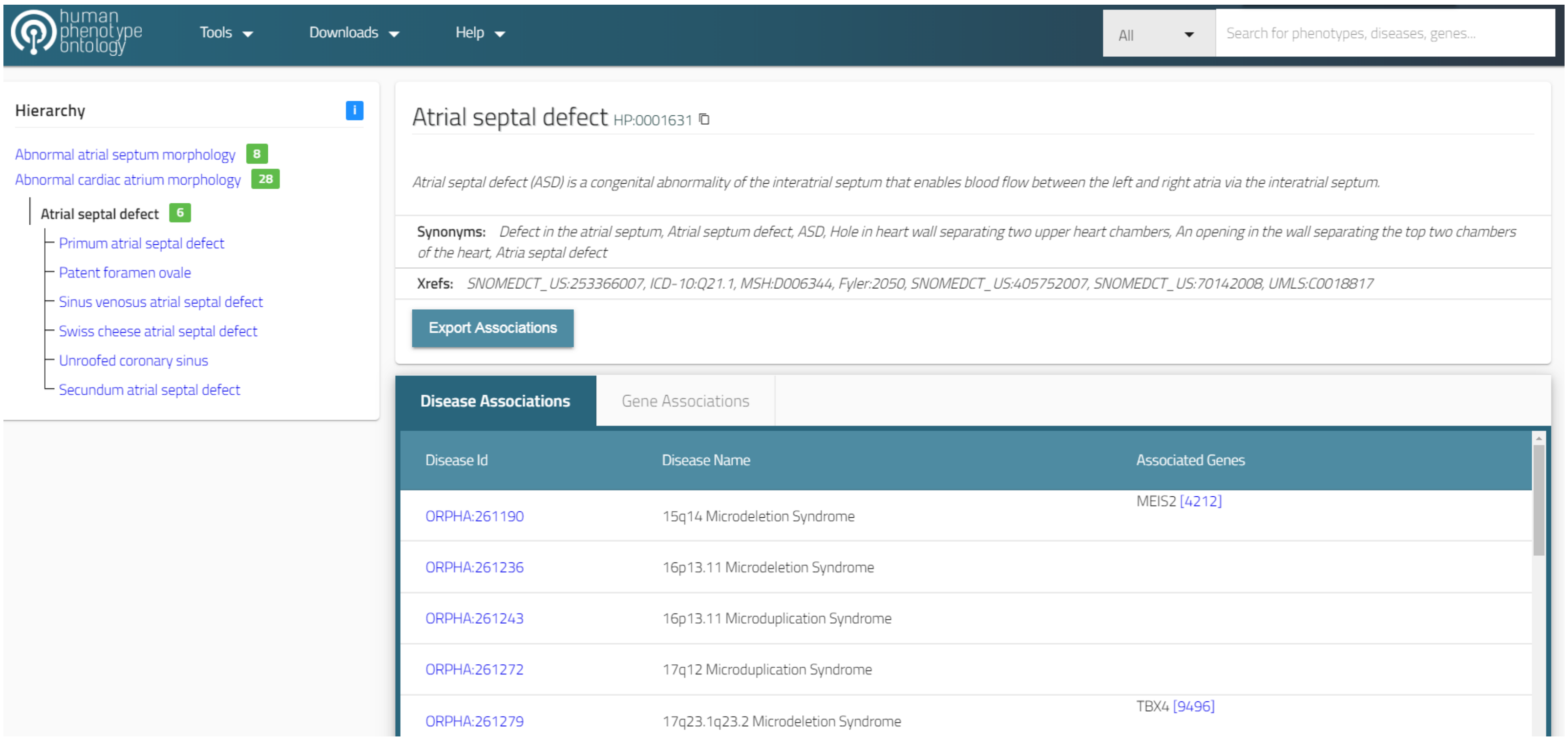
https://hpo.jax.org/app/

Human Phenotype Ontology (HPO)



https://hpo.jax.org/app/

HUMAN PHENOTYPE ONTOLOGY (HPO)



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https://hpo.jax.org/app/

HUMAN PHENOTYPE ONTOLOGY (HPO)

Download Ontology

hp.obo

The OBO flat file format is a simple way of representing an ontology that models represent a subset of the concepts in the OWL description logic language. The OBO format was designed to maximize human readability and has been widely used in the field of bio-ontologies and was probably one of the many factors responsible for the success of the Gene Ontology. The HPO file in OBO format can be downloaded here:

- http://purl.obolibrary.org/obo/hp.obo

hp.owl

OWL, which stands for *Web Ontology Language*, is an ontology language for the semantic web. The OWL version of the HPO (which is the primary version) contains some features that the OBO version does not, including the logical definitions of HPO classes. Consider for instance the following definition of the HPO term for Astigmatism.

```
'has part' some
  ('asymmetrically curved'
     and ('inheres in' some cornea)
     and ('has modifier' some abnormal))
```

The logical makes use of terms from the PATO Phenotype And Trait Ontology as well as the UBERON cross-species anatomy ontology in order to define *Astigmatism* as an abnormal asymmetric curvature of the cornea. A number of HPO-based algorithms make use of these definitions to link to definitions of mouse phenotypes at the Mouse Genome Informatics resource, for quality control, and other purposes. For many of the HPO algorithms that are primarily intended for clinical phenotype matching, these features are not relevant and either the OBO or the OWL format are suitable. The HPO file in OWL format can be downloaded here:

- http://purl.obolibrary.org/obo/hp.owl

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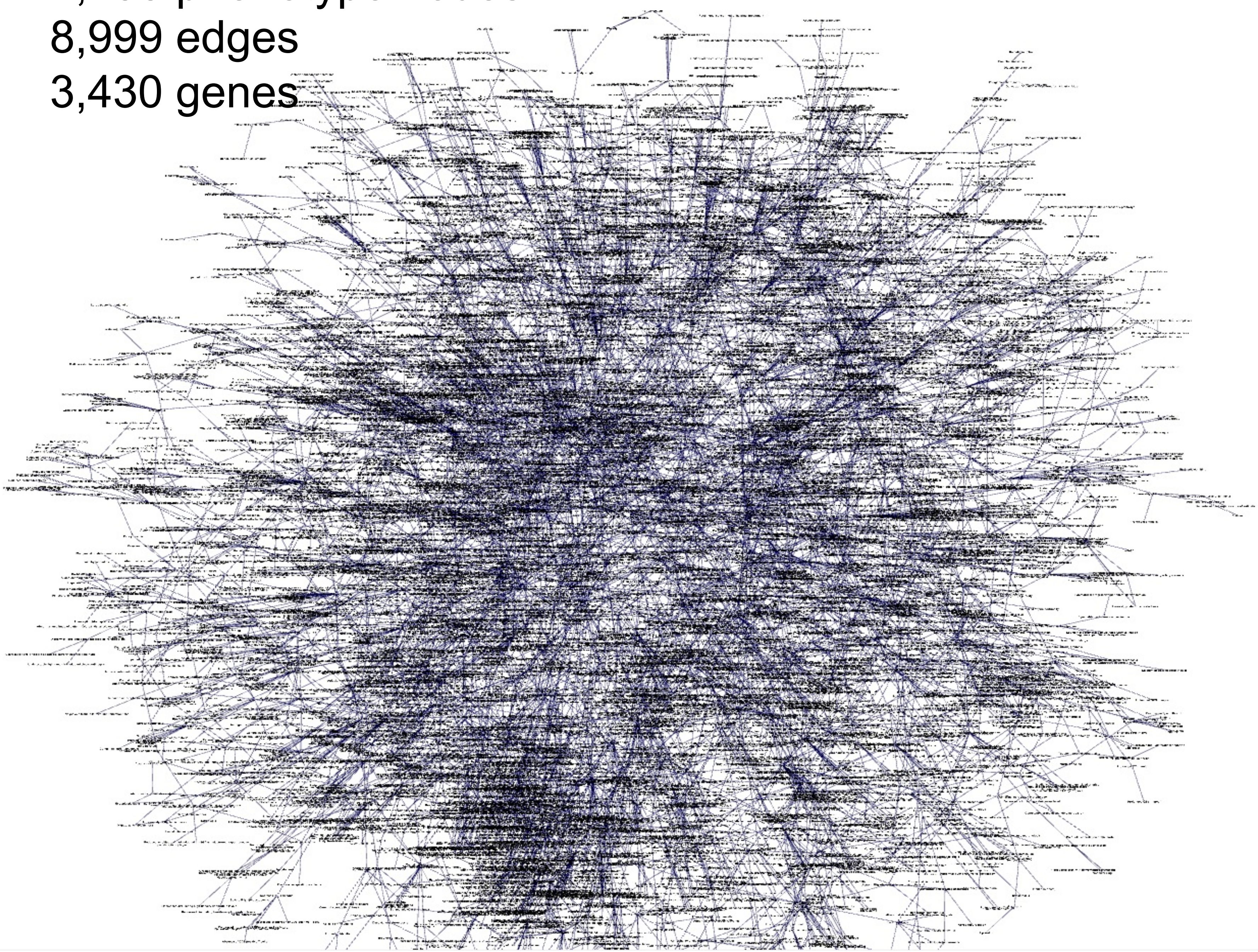
https://hpo.jax.org/app/download/ontology

EXPERIMENTS

Human Phenotype Ontology

- ❑Annotate 7,280 phenotypes with gene information (entrez ID)
- ❑Sub-graph, nodes with annotated gene information
- ❑Prune isolated nodes to make all nodes connected

7,258 phenotype nodes
8,999 edges
3,430 genes



RESULTS

Link prediction

- Prepare positive examples:
  - ❑ Randomly used 60%, 10%, and 30% of entire edges for training, validation, and testing purposes.
- Prepare negative examples:
  - ❑ Randomly used 60%, 10%, and 30% of entire edges for training, validation, and testing purpose

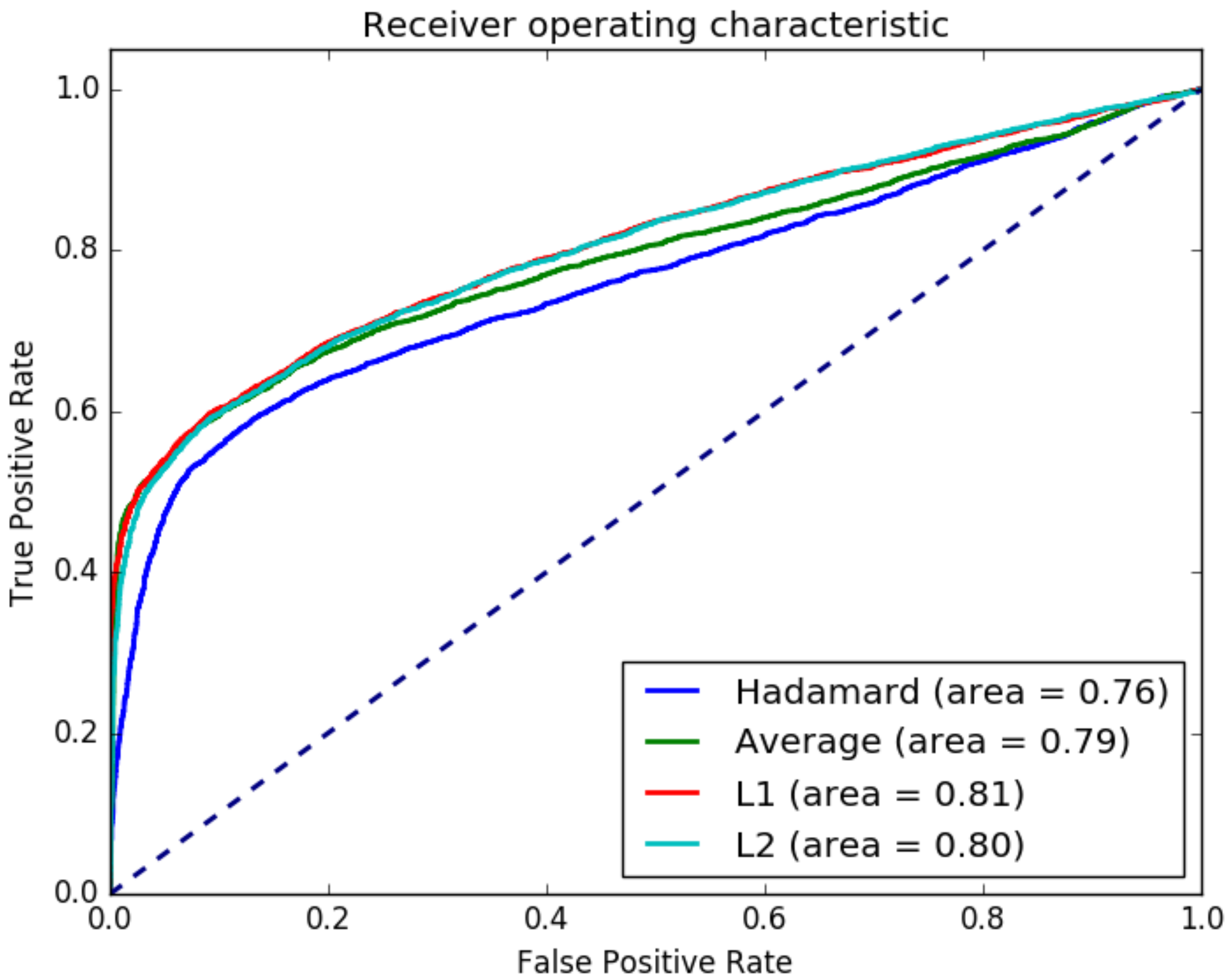
RESULTS

- Generate edge embedding based on node embedding
- Given nodes u and v, f(u) and f(v) denotes their feature representations
  - LogisticRegression(edge_emb, edge_label)

Operator	Definition
Average	$\frac{f(u)+f(v)}{2}$
Hadamard	$f(u) * f(v)$
Weighted-L1	$\lvert f(u)-f(v)\rvert$
Weighted-L2	$\lvert f(u)-f(v)\rvert^{2}$

Results

p=1, q=0.05
neighbor_size=10
num_walks=10
walk_length=5
dimension=128



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RESULTS

Operator	Precision	Recall	F-measure
Average	0.76	0.75	0.74
Hadamard	0.74	0.73	0.72
Weighted-L1	0.76	0.75	0.75
Weighted-L2	0.78	0.75	0.74

Results

- Comparing with baseline scoring methods:

Scores	Definition
Jaccard's Coefficient	$\frac{N(u) \cap N(v)}{N(u) \cup N(v)}$
Adamic-Adar Score	$\sum_{t \in N(u) \cap N(v)} \frac{1}{\log \lvert N(t) \rvert}$

N(u): direct neighbor of node u
N(v): direct neighbor of node v
N(t): direct neighbor of node t

RESULTS

Methods	AUROC	Average Precision
Node2vec (L1)	0.81	0.85
Adamic-Adar	0.63	0.67
Jaccard	0.5	0.46

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Results

- **HPOEmbedding_V0.1**
- (7258, 128)

```
0 -0.240330 0.058522 0.153959 -0.002036 -0.064240 0.235507 -0.186960 -0.338655 -0.119517 0.175563 0.391702 -0.066000 -0.124363 -0.063367 0.
3098 -0.272518 0.076228 0.161163 0.021788 -0.076025 0.278918 -0.195849 -0.394783 -0.128165 0.200492 0.445066 -0.061802 -0.165236 -0.087852
1369 -0.266067 0.057190 0.168280 0.006649 -0.070766 0.245432 -0.184228 -0.374658 -0.125654 0.183740 0.413518 -0.069982 -0.153400 -0.066426
1033 -0.259970 0.057397 0.163549 -0.002428 -0.077161 0.241342 -0.191172 -0.370289 -0.126249 0.182140 0.415996 -0.066236 -0.137282 -0.070804
989 -0.250128 0.055444 0.166569 0.014121 -0.078800 0.240832 -0.191375 -0.365271 -0.127956 0.181881 0.414304 -0.058934 -0.137044 -0.058468 0
2081 -0.246176 0.047528 0.161245 0.009027 -0.060807 0.230705 -0.185488 -0.356683 -0.124391 0.176036 0.388074 -0.061950 -0.130584 -0.059033
830 -0.224584 0.049370 0.152805 0.004360 -0.063052 0.225471 -0.169435 -0.322209 -0.111722 0.172882 0.371441 -0.056873 -0.126904 -0.056810 0
1872 -0.223858 0.028879 0.134200 0.009756 -0.053364 0.234226 -0.187693 -0.329627 -0.123021 0.177479 0.365998 -0.049611 -0.123004 -0.062653
327 -0.226755 0.054007 0.141038 0.012875 -0.058397 0.198548 -0.155008 -0.317698 -0.105430 0.162329 0.344005 -0.057285 -0.122505 -0.063517 0
92 -0.225669 0.050669 0.132185 0.000865 -0.052302 0.219648 -0.157705 -0.317097 -0.104145 0.161302 0.355088 -0.054497 -0.118933 -0.052913 0.
496 -0.211478 0.042819 0.136933 0.004403 -0.050679 0.208560 -0.158854 -0.306980 -0.100467 0.150951 0.343334 -0.057042 -0.113162 -0.047319 0
1759 -0.215291 0.050190 0.135453 0.005083 -0.062060 0.205241 -0.160292 -0.308093 -0.111927 0.162504 0.351751 -0.060556 -0.115892 -0.058769
2150 -0.224865 0.041183 0.145084 0.005946 -0.057137 0.219195 -0.160681 -0.338186 -0.102507 0.167785 0.370981 -0.058028 -0.129208 -0.059591
1461 -0.222304 0.053975 0.132621 0.014579 -0.057800 0.215194 -0.163410 -0.313907 -0.101367 0.158752 0.352470 -0.061913 -0.116908 -0.056670
1026 -0.234396 0.045661 0.148524 0.007663 -0.052798 0.224044 -0.171789 -0.334390 -0.112462 0.170467 0.378480 -0.064150 -0.127602 -0.059090
3039 -0.217818 0.050422 0.134099 0.012842 -0.066442 0.205347 -0.155844 -0.310195 -0.110612 0.159405 0.345328 -0.054990 -0.113828 -0.047740
1115 -0.223488 0.052431 0.148303 0.002554 -0.063774 0.206668 -0.162822 -0.321313 -0.111940 0.155479 0.353809 -0.053989 -0.120905 -0.055936
190 -0.237800 0.055537 0.145510 0.002572 -0.054028 0.230477 -0.169945 -0.331388 -0.111711 0.167688 0.379870 -0.063387 -0.129694 -0.052272 0
677 -0.214353 0.052189 0.134712 0.010339 -0.052341 0.208794 -0.155401 -0.303248 -0.106807 0.160090 0.344848 -0.055918 -0.114665 -0.057178 0
987 -0.197369 0.045039 0.125478 0.009690 -0.046102 0.184292 -0.136240 -0.272959 -0.097918 0.140693 0.304756 -0.043673 -0.105947 -0.043855 0
323 -0.215443 0.051718 0.145657 0.010977 -0.059549 0.210862 -0.160736 -0.313210 -0.103026 0.156158 0.346836 -0.060588 -0.122748 -0.051498 0
259 -0.212490 0.049053 0.139140 0.001940 -0.061963 0.199641 -0.158844 -0.317382 -0.105923 0.149482 0.346885 -0.060574 -0.123020 -0.050471 0
880 -0.214039 0.048417 0.130425 0.009720 -0.056724 0.203819 -0.158062 -0.312044 -0.109439 0.150580 0.346755 -0.062049 -0.113490 -0.045735 0
4307 -0.213021 0.045414 0.135402 0.010044 -0.059401 0.206574 -0.154959 -0.313658 -0.106180 0.154264 0.345726 -0.061927 -0.113313 -0.052572
1008 -0.207112 0.050631 0.133816 0.002981 -0.050075 0.196813 -0.148940 -0.285359 -0.104198 0.141817 0.330695 -0.046988 -0.112498 -0.048617
996 -0.215358 0.041260 0.132543 0.012829 -0.050389 0.203927 -0.155883 -0.305718 -0.108328 0.155589 0.339067 -0.054132 -0.116024 -0.046225 0
1224 -0.217495 0.048022 0.140306 0.011062 -0.056477 0.209850 -0.168410 -0.310982 -0.104730 0.159963 0.355919 -0.061271 -0.119244 -0.056927
2002 -0.216393 0.052970 0.141161 0.004912 -0.056215 0.209660 -0.162081 -0.310780 -0.102078 0.147595 0.344340 -0.059995 -0.109240 -0.057045
332 -0.209703 0.039071 0.131613 0.009140 -0.048731 0.206831 -0.162645 -0.304422 -0.100736 0.156964 0.345549 -0.056915 -0.110919 -0.048142 0
2955 -0.205782 0.045253 0.129652 0.010800 -0.048560 0.199658 -0.152954 -0.287979 -0.099875 0.152010 0.323420 -0.048287 -0.113029 -0.050371
804 -0.203928 0.039433 0.129529 0.012169 -0.051414 0.198383 -0.144608 -0.287990 -0.096271 0.146931 0.320889 -0.050625 -0.108652 -0.047109 0
1020 -0.205594 0.051070 0.136965 0.000829 -0.056967 0.198051 -0.151474 -0.300690 -0.108494 0.142082 0.335021 -0.052939 -0.108617 -0.047203
1361 -0.199030 0.036256 0.135451 0.010022 -0.056347 0.200584 -0.157369 -0.295043 -0.100084 0.156233 0.331045 -0.050897 -0.110129 -0.055913
1765 -0.207103 0.041020 0.132277 0.009502 -0.056525 0.196352 -0.156987 -0.291991 -0.095114 0.152518 0.336234 -0.051432 -0.111460 -0.053085
1625 -0.205050 0.041435 0.137897 0.005170 -0.059694 0.199951 -0.160806 -0.297397 -0.099223 0.157134 0.337223 -0.057472 -0.116203 -0.056040
```

IPF-related Phenotype	Similar Phenotypes	Similarity Score
cough	Neonatal breathing dysregulation	0.93
	Abnormal breath sound	0.92
	Snoring	0.92
	Abnormal blood gas level	0.92
	Restrictive ventilatory defect	0.91

IPF-related Phenotype	Similar Phenotypes	Similarity Score
gastroesophageal reflux (GERD)	Prominent interphalangeal joints	0.56
	Abnormality of body height	0.53
	Depigmented fundus	0.52
	Wrist swelling	0.52
	Facial wrinkling	0.51

IPF-related Phenotype	Similar Phenotypes	Similarity Score
pulmonary fibrosis	Atelectasis	0.9
	Pulmonary hypoplasia	0.89
	Abnormal lung morphology	0.89
	Alveolar proteinosis	0.88
	Unilateral primary pulmonary dysgenesis	0.88

IPF-related Phenotype	Similar Phenotypes	Similarity Score
exertional dyspnea	Dyspnea	0.98
	Respiratory distress	0.94
	Hypoplastic distal radial epiphyses	0.47
	Spastic dysarthria	0.46
	Nonketotic hyperglycinemia	0.45

IPF-related Phenotype	Similar Phenotypes	Similarity Score
bronchiectasis	Abnormal bronchus morphology	0.96
	Bronchomalacia	0.93
	Recurrent bronchitis	0.89
	Recurrent upper respiratory tract infections	0.79
	Recurrent lower respiratory tract infections	0.77

IPF-related Phenotype	Similar Phenotypes	Similarity Score
pulmonary insufficiency	Abnormal pulmonary valve physiology	0.97
	Pulmonic stenosis	0.93
	Renal steatosis	0.5
	Calf muscle hypertrophy	0.48
	Prominent coccyx	0.47

IMPLEMENTATION

Tools

- Python 3.6
- Jupyter Notebook
- Anaconda 3.7

1. Install Anaconda 3.7 version
2. Create a running env with necessary libaries

```
conda create --name NEEnv python=3.6 networkx pandas scipy scikit-learn gensim matplotlib
```

3. install ontospy

```
pip install ontospy
```

4. Activate your running env

```
conda activate NEEnv
```

5. Run the Jupyter Notebook

```
jupyter notebook
```

Notice:

For Mac, if you face some troubles opening NEEnv in you jupyter notebook, you explicitly install the new kernel using the following command in terminal

```
ipython kernel install --user --name=NEEnv
```

After this, the system will create a new kernel directory under "/Users/you_account/Library/Jupyter/kernels/NEEnv. You can then open notebook and select NEEnv as the enviornment

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Sources

- *Reference implementation of Ontospy. http://lambdamusic.github.io/Ontospy/*
- *Reference implementation of node2vec. Author: Aditya Grover For more details, refer to the paper: node2vec: Scalable Feature Learning for Networks Aditya Grover and Jure Leskovec Knowledge Discovery and Data Mining (KDD), 2016. https://github.com/aditya-grover/node2vec*
- *Reference implementation of link prediction task using fb data: Lucas Hu https://github.com/lucashu1*

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STEPS

- Ontology exploration
- Graph generation
- Node embeddings generation
- t-Distributed Stochastic Neighbor Embedding (t-SNE) visualization
- Similarity measurement
- Edge embeddings generation
- Link prediction evaluation

Ontology exploration

OntologyPractice.ipynb

```
import ontospy
```

```
model = ontospy.Ontospy("http://xmlns.com/foaf/0.1/", verbose=True)
```

```
Reading: <http://xmlns.com/foaf/0.1/>
.. trying rdf serialization: <xml>
..... success!
----------
Loaded 631 triples.
----------
RDF sources loaded successfully: 1 of 1.
..... 'http://xmlns.com/foaf/0.1/'
----------
```

```
Scanning entities...
----------
Ontologies.........: 1
Classes............: 15
Properties.........: 67
..annotation.......: 7
..datatype.........: 26
..object...........: 34
Concepts (SKOS)....: 0
Shapes (SHACL).....: 0
----------
```

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Ontology exploration

```
model.all_classes
```

```
[<Class *http://xmlns.com/foaf/0.1/Agent*>,
 <Class *http://xmlns.com/foaf/0.1/Document*>,
 <Class *http://xmlns.com/foaf/0.1/Group*>,
 <Class *http://xmlns.com/foaf/0.1/Image*>,
 <Class *http://xmlns.com/foaf/0.1/LabelProperty*>,
 <Class *http://xmlns.com/foaf/0.1/OnlineAccount*>,
 <Class *http://xmlns.com/foaf/0.1/OnlineChatAccount*>,
 <Class *http://xmlns.com/foaf/0.1/OnlineEcommerceAccount*>,
 <Class *http://xmlns.com/foaf/0.1/OnlineGamingAccount*>,
 <Class *http://xmlns.com/foaf/0.1/Organization*>,
 <Class *http://xmlns.com/foaf/0.1/Person*>,
 <Class *http://xmlns.com/foaf/0.1/PersonalProfileDocument*>,
 <Class *http://xmlns.com/foaf/0.1/Project*>,
 <Class *http://www.w3.org/2003/01/geo/wgs84_pos#SpatialThing*>,
 <Class *http://www.w3.org/2004/02/skos/core#Concept*>]
```

ONTOLOGY EXPLORATION

```
model.all_properties_object
```

```
[<Property *http://xmlns.com/foaf/0.1/account*>,
 <Property *http://xmlns.com/foaf/0.1/accountServiceHomepage*>,
 <Property *http://xmlns.com/foaf/0.1/based_near*>,
 <Property *http://xmlns.com/foaf/0.1/currentProject*>,
 <Property *http://xmlns.com/foaf/0.1/depiction*>,
 <Property *http://xmlns.com/foaf/0.1/depicts*>,
 <Property *http://xmlns.com/foaf/0.1/focus*>,
 <Property *http://xmlns.com/foaf/0.1/fundedBy*>,
 <Property *http://xmlns.com/foaf/0.1/holdsAccount*>,
 <Property *http://xmlns.com/foaf/0.1/homepage*>,
 <Property *http://xmlns.com/foaf/0.1/img*>,
 <Property *http://xmlns.com/foaf/0.1/interest*>,
 <Property *http://xmlns.com/foaf/0.1/isPrimaryTopicOf*>,
 <Property *http://xmlns.com/foaf/0.1/knows*>,
 <Property *http://xmlns.com/foaf/0.1/logo*>,
 <Property *http://xmlns.com/foaf/0.1/made*>,
 <Property *http://xmlns.com/foaf/0.1/maker*>,
```

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ONTOLOGY EXPLORATION

```
model.printClassTree()
```

```
foaf:Agent
----foaf:Group
----foaf:Organization
----foaf:Person
foaf:Document
----foaf:Image
----foaf:PersonalProfileDocument
foaf:LabelProperty
foaf:OnlineAccount
----foaf:OnlineChatAccount
----foaf:OnlineEcommerceAccount
----foaf:OnlineGamingAccount
foaf:Project
http://www.w3.org/2003/01/geo/wgs84_pos#SpatialThing
----foaf:Person
skos:Concept
```

MAYO CLINIC

ONTOLOGY EXPLORATION

```
model.toplayer_classes
```

```
[<Class *http://xmlns.com/foaf/0.1/Agent*>,
 <Class *http://xmlns.com/foaf/0.1/Document*>,
 <Class *http://xmlns.com/foaf/0.1/LabelProperty*>,
 <Class *http://xmlns.com/foaf/0.1/OnlineAccount*>,
 <Class *http://xmlns.com/foaf/0.1/Project*>,
 <Class *http://www.w3.org/2003/01/geo/wgs84_pos#SpatialThing*>,
 <Class *http://www.w3.org/2004/02/skos/core#Concept*>]
```

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Ontology exploration

```
model.get_class('document')
```

```
[<Class *http://xmlns.com/foaf/0.1/Document*>,
 <Class *http://xmlns.com/foaf/0.1/PersonalProfileDocument*>]
```

```
c1 = _[1]
```

```
print(c1.rdf_source())
```

```
@prefix dc: <http://purl.org/dc/elements/1.1/> .
@prefix foaf: <http://xmlns.com/foaf/0.1/> .
@prefix owl: <http://www.w3.org/2002/07/owl#> .
@prefix rdf: <http://www.w3.org/1999/02/22-rdf-syntax-ns#> .
@prefix rdfs: <http://www.w3.org/2000/01/rdf-schema#> .
@prefix sh: <http://www.w3.org/ns/shacl#> .
@prefix skos: <http://www.w3.org/2004/02/skos/core#> .
```

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ONTOLOGY EXPLORATION

```
c1.parents()
```

```
[<Class *http://xmlns.com/foaf/0.1/Document*>]
```

```
c1.children()
```

```
[]
```

DATASET INFORMATION

Facebook anonymous user data

- This dataset consists of 'circles' (or 'friends lists') from Facebook. The dataset includes node features (profiles), circles, and ego networks.
- A small network with annotated features will be demonstrated

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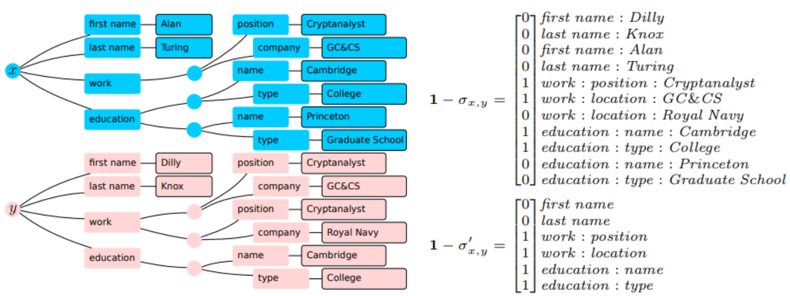
http://i.stanford.edu/~julian/pdfs/nips2012.pdf

http://snap.stanford.edu/data/egonets-Facebook.html

DATASET INFORMATION

- Feature matrix




```
0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 1 0 1 1 1 1 0 0 0 0 0 0 0 0 0 0 0 0
1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
2 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 1 0 1 0 0 0 0 0 0 0 0 0 0
3 0 0 0 0 0 0 0 1 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 1 0 1 0 0 0 1 0 0 0 0 0 1 0 0
4 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 1 0 1 1 0 0 0 0 0 0 0 0 0 0 0
5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 1 0 0 1 1 0 0 0 0 0 0 0 0 0 0 1 0 0
6 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 1 0 0 0 0 0 0 1 0 0 0 0 0
7 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 0 0 0 1 0 0 1 1 1 0 0 0 1 0 0 0 0 0 0 0 0
8 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0
```

- Edges data, represented by source-target pair

```
236 186
122 285
24 346
271 304
176 9
```

http://i.stanford.edu/~julian/pdfs/nips2012.pdf

http://snap.stanford.edu/data/egonets-Facebook.html

MAYO CLINIC

GRAPH GENERATION - READ INPUT DATA

graphGeneration.ipynb

```
import networkx as nx
import pandas as pd
import numpy as np
import pickle
```

```
edges_dir = 'testData/0.edges'
feats_dir = 'testData/0.allfeat'
```

```
# Read edge list
g = nx.read_edgelist(edges_dir,nodetype=int)
```

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GRAPH GENERATION
- READ INPUT DATA

```
# Read feature list
df = pd.read_csv(feats_dir, sep=' ', header=None, index_col=0)
```

```
g.node[node_index]['features'] = features_series.values
```

```
# Make sure the graph is connected
nx.is_connected(g)
```

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GRAPH GENERATION
-DUMP TO PICKLE FILE

```
# Save adj, features in pickle file
network_tuple = (adj, features)
```

```
with open("test-adj-feat.pkl", "wb") as f:
        pickle.dump(network_tuple, f)
```

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GRAPH GENERATION

- Some upgrades from Python 2 to Python 3

1.

```
f = open(edges_dir)
g = nx.read_edgelist(f, nodetype=int)
```

→

```
g = nx.read_edgelist(edges_dir,nodetype=int)
```

2.

features_series.as_matrix() → features_series.values

3.

pd.read_table → pd.read_csv

GRAPH LOADING

```python
# Load pickled (adj, feat) tuple
network_dir = 'test-adj-feat.pkl'
with open(network_dir, 'rb') as f:
    adj, features = pickle.load(f)

g = nx.Graph(adj)
```

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Graph visualization

```
# visualize network
#plt.figure(figsize=(16,16)) # set up canvas size
nx.draw_networkx(g, alpha=0.5,with_labels=True, node_size=50, node_color='r')
plt.show()
```

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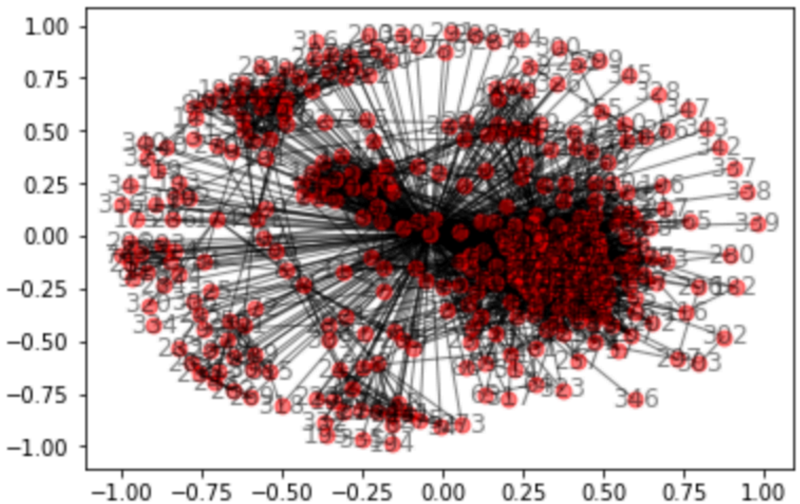
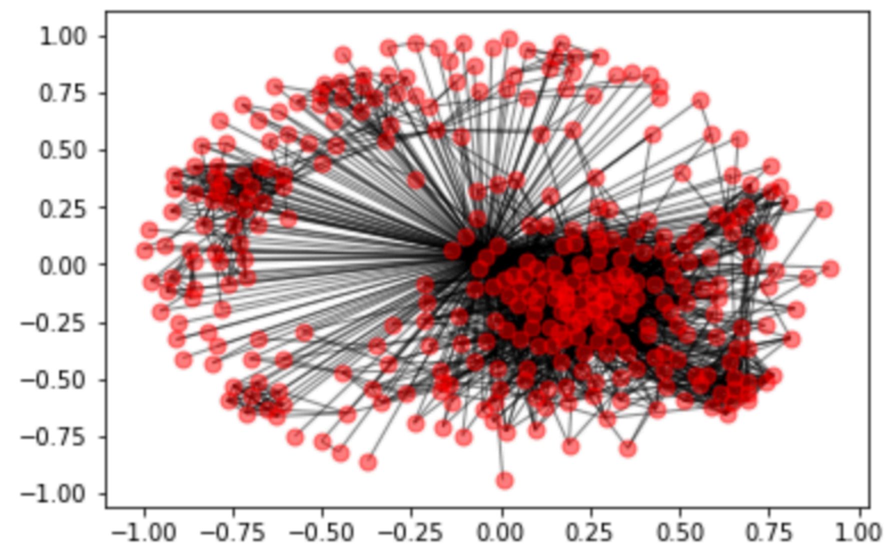
GRAPH VISUALIZATION





Node embeddings generation -Train and test split

Node2vecTest.ipynb

```
adj_sparse = nx.to_scipy_sparse_matrix(g)

adj_train, train_edges, train_edges_false, val_edges, val_edges_false, \
    test_edges, test_edges_false = mask_test_edges(adj_sparse, test_frac=.3, val_frac=.1)

g_train = nx.from_scipy_sparse_matrix(adj_train)
```

Node embeddings generation -Hyperparameters

```
P = 1 # Return hyperparameter
Q = 0.25 # In-out hyperparameter
WINDOW_SIZE = 10 # Context size for optimization
NUM_WALKS = 10 # Number of walks per source
WALK_LENGTH = 80 # Length of walk per source
DIMENSIONS = 128 # Embedding dimension
DIRECTED = False # Graph directed/undirected
WORKERS = 8 # Num. parallel workers
ITER = 1 # SGD epochs
```

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Node embeddings generation -Random walk

```python
import node2vec
```

```python
# Preprocessing, generate walks
g_n2v = node2vec.Graph(g_train, DIRECTED, P, Q)
g_n2v.preprocess_transition_probs()
walks = g_n2v.simulate_walks(NUM_WALKS, WALK_LENGTH)
walks = [list(map(str, walk)) for walk in walks]
```

NODE EMBEDDINGS GENERATION -RANDOM WALK

```
# Preprocessing, generate walks
g_n2v = node2vec.Graph(g_train, DIRECTED, P, Q)
g_n2v.preprocess_transition_probs()
walks = g_n2v.simulate_walks(NUM_WALKS, WALK_LENGTH)
walks = [list(map(str, walk)) for walk in walks]
```

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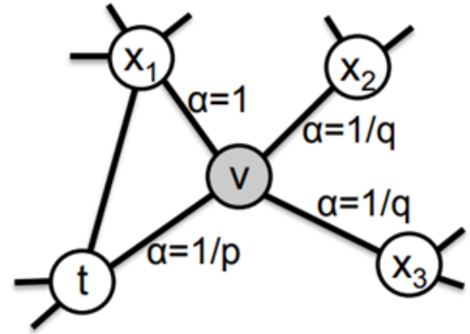
NODE EMBEDDINGS GENERATION -RANDOM WALK

$$\alpha_{pq}(t,x) = \begin{cases} \frac{1}{p} & if\ d_{tx} = 0 \\ 1 & if\ d_{tx} = 1 \\ \frac{1}{q} & if\ d_{tx} = 2 \end{cases}$$

Node2vec.py

- Preprocessing_transition_probs:




```
for dst_nbr in sorted(G.neighbors(dst)):
        if dst_nbr == src:
                unnormalized_probs.append(G[dst][dst_nbr]['weight']/p)
        elif G.has_edge(dst_nbr, src):
                unnormalized_probs.append(G[dst][dst_nbr]['weight'])
        else:
                unnormalized_probs.append(G[dst][dst_nbr]['weight']/q)
```

```
norm_const = sum(unnormalized_probs)
normalized_probs =  [float(u_prob)/norm_const for u_prob in unnormalized_probs]
```

Node embeddings generation -Random walk

```
# Preprocessing, generate walks
g_n2v = node2vec.Graph(g_train, DIRECTED, P, Q)
g_n2v.preprocess_transition_probs()
walks = g_n2v.simulate_walks(NUM_WALKS, WALK_LENGTH)
walks = [list(map(str, walk)) for walk in walks]
```

Node embeddings generation -Word2vec

```
from gensim.models import Word2Vec
from gensim.models import KeyedVectors
```

```
# Train skip-gram model
model = Word2Vec(walks, size=DIMENSIONS, window=WINDOW_SIZE,
                 min_count=0, sg=1, workers=WORKERS, iter=ITER)

# Store embeddings mapping
emb_mappings = model.wv

model.wv.save_word2vec_format('fb_test.emd')
```

NODE EMBEDDINGS VISUALIZATION

```python
# Open embedding file
with open('fb_test.emd') as f:
    next(f)
    for line in f:
        splits = line.strip().split()
        label = splits[0]
        vec = [float(v) for v in splits[1:]]

        X.append(vec)
        y.append(label)
```

MAYO CLINIC

NODE EMBEDDINGS VISUALIZATION

```
from sklearn.manifold import TSNE
```

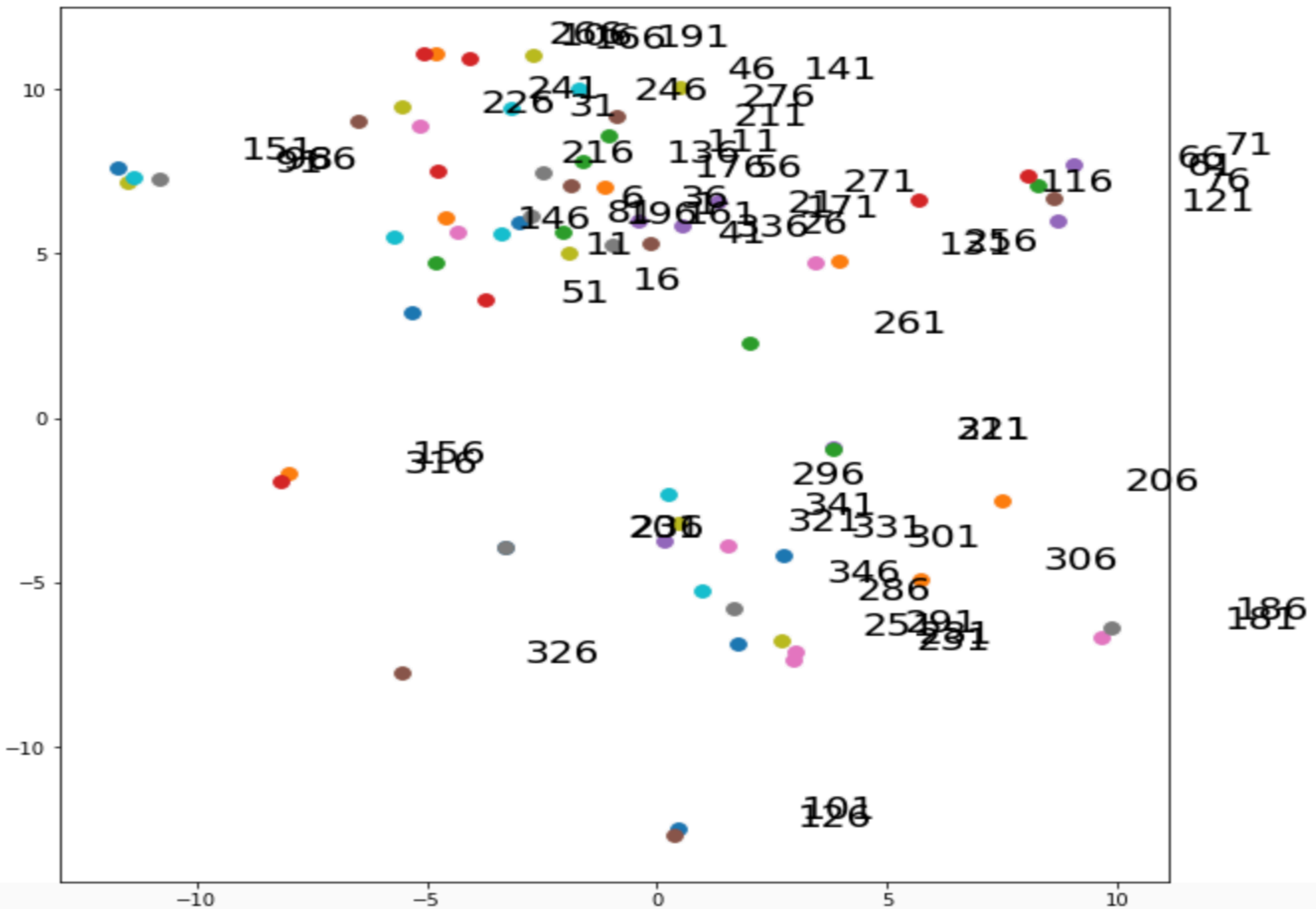
```
tsne = TSNE(n_components=2,perplexity=50.0)
X_tsne = tsne.fit_transform(X)

plt.figure(figsize=(10,10))

for i in range(1, len(X), 5):
        plt.scatter(X_tsne[i, 0], X_tsne[i, 1],s=60)
        plt.annotate(str(i),
                     xy=(X_tsne[i, 0], X_tsne[i, 1]),
                     xytext=(100, 2),
                     textcoords='offset points',
                     ha='right',
                     va='bottom',fontsize=20)

plt.show()
```

Node embeddings visualization



MAYO CLINIC

Similarity measurement

```
s1 = emb_mappings.similarity('156', '316')
print(s1)
```

```
s2 = emb_mappings.most_similar('156')
print(s2)
```

MAYO
CLINIC

GENERATE EDGE EMBEDDINGS

```
func_list = [lambda x1, x2: np.multiply(x1, x2),
             lambda x1, x2: (x1 + x2) / 2,
             lambda x1, x2: np.absolute(x1 - x2),
             lambda x1, x2: np.square(x1 - x2),
             ]
```

Operator	Definition
Average	$\frac{f(u)+f(v)}{2}$
Hadamard	$f(u) * f(v)$
Weighted-L1	$\|f(u) - f(v)\|$
Weighted-L2	$\|f(u) - f(v)\|^2$

MAYO CLINIC

Evaluate link prediction performance

```
train_edge_embs = np.concatenate([pos_train_edge_embs[i], neg_train_edge_embs[i]])
train_edge_labels = np.concatenate([np.ones(len(train_edges)), np.zeros(len(train_edges_false))])

test_edge_embs = np.concatenate([pos_test_edge_embs[i], neg_test_edge_embs[i]])
test_edge_labels = np.concatenate([np.ones(len(test_edges)), np.zeros(len(test_edges_false))])

edge_classifier = LogisticRegression(random_state=0,solver='lbfgs')
edge_classifier.fit(train_edge_embs, train_edge_labels)
```

MAYO CLINIC

Evaluate link prediction performance

```
test_preds = edge_classifier.predict_proba(test_edge_embs)[:, 1]
test_roc = roc_auc_score(test_edge_labels, test_preds)
test_ap = average_precision_score(test_edge_labels, test_preds)
```

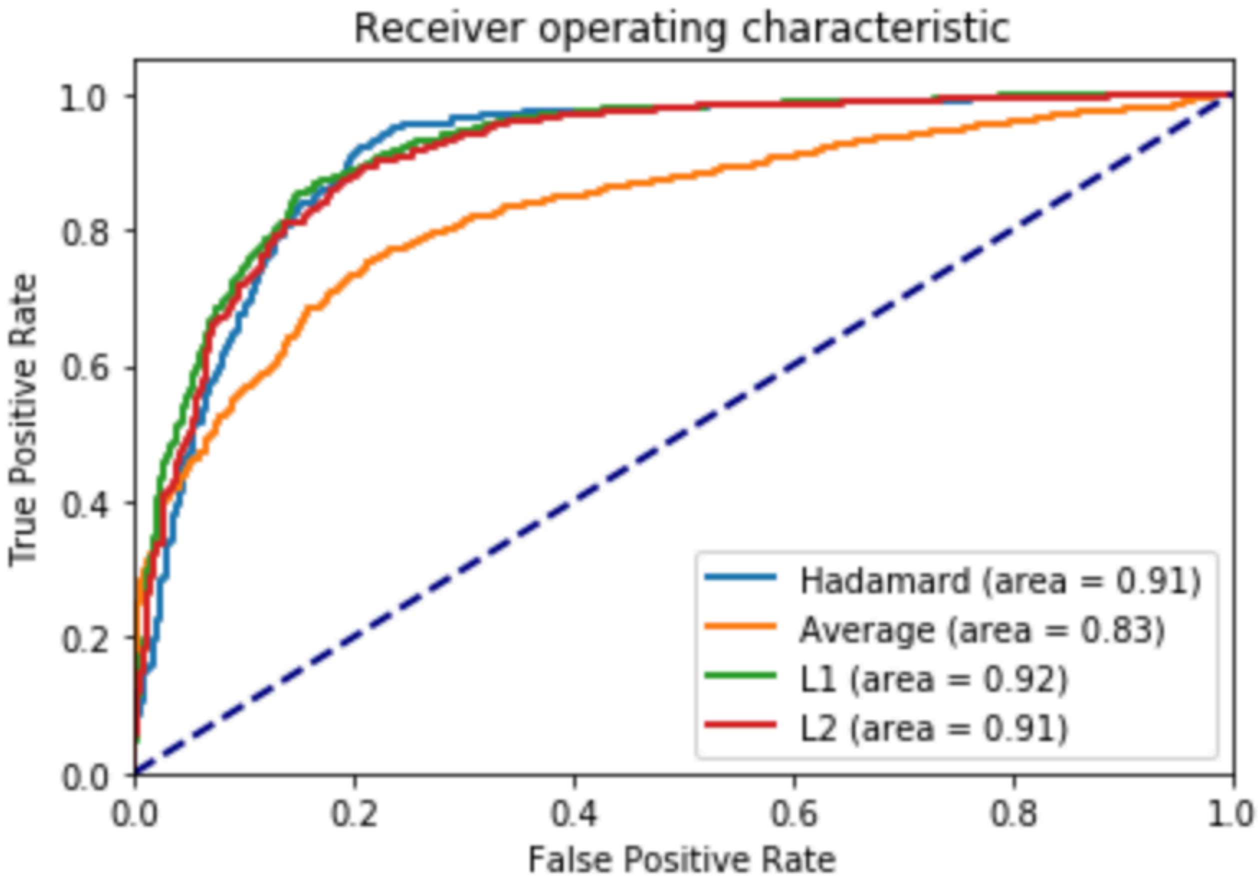
EVALUATE LINK PREDICTION PERFORMANCE

```
fpr = dict()
tpr = dict()
roc_auc = dict()
fpr, tpr, _ = roc_curve(test_edge_labels, test_preds)
roc_auc = auc(fpr, tpr)
lw = 2

plt.plot(fpr, tpr,
         lw=lw, label='%s (area = %0.2f)' % (labels[i], roc_auc))
```

MAYO
CLINIC

EVALUATE LINK PREDICTION PERFORMANCE



Thank you!