Hierarchical Data Analysis

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Questions

- A typical format of hierarchical data?
- Any example of hierarchical data?

Ontology

- **Ontology in Philosophy**
  - The study of the nature of being or existence including their categories and their relations (wikipedia)
- **Ontology in Computer Science**
  - The specification of a conceptualization: description of the concepts and relationships that exist for an agent or a community of agents (Gruber)
  - A set of representational primitives (i.e., classes, attributes, and relationships) for modeling a domain of knowledge
- **Ontology in Biology**
  - A formal way of representing biological knowledge which is described by the concepts and their relationships to each other (Bard and Rhee)

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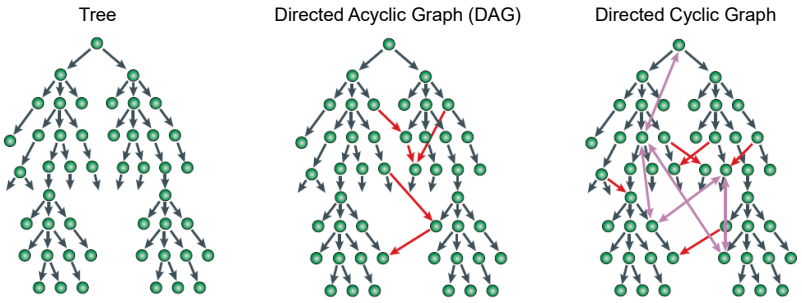
Representation of Ontology

- **Components**
  - Concepts and Relationships
- **Representation**
  - Graph (concepts → nodes, relationships → edges)



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Relationships in Ontology

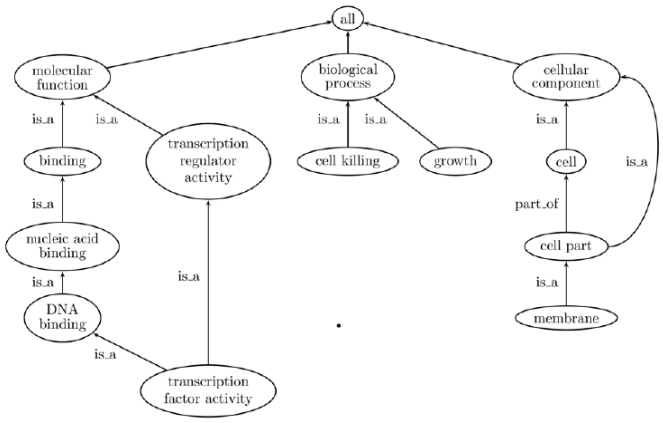
- **Directions**
  - Relationships are generally directed
  - Concepts have parent-child relationships
- **Properties** (in tree or DAG)
  - Antisymmetric
  - Transitivity
- **Examples**
  - "is-a" relationship
  - "part-of" relationship

Ontology Example 1

- **Gene Ontology (GO)**
  - Organized by GO Consortium
  - A repository of bio-ontology (controlled vocabularies) databases - consistent descriptions across different organisms
  - Nodes represent GO terms structured in 3 main categories: biological processes, molecular functions, and cellular components
  - DAG for the relationships between GO terms
  - Provides annotation of genes and gene products
  - Created by any published evidence (mostly, from high-throughput data)
  - Data curation, e.g., redundant annotation elimination
  - http://www.geneontology.org/index.shtml

Ontology Structure

- **Example of GO DAG structure**



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Ontology Example 2

- **Human Phenotype Ontology (HPO)**
  - A repository of phenotypic information of human
  - Nodes represent the HPO terms describing phenotypic features
  - DAG for the relationships between HPO terms
  - Provides annotation of human genes and gene products
  - Based on OMIM, a catalog of human genes and genetic disorders
  - Data manual curation

  - http://human-phenotype-ontology.github.io/

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Questions

- How to measure similarity (or distance) between data objects in a hierarchy?

Research Topic 1. Semantic Similarity Analysis

- Definition of Semantic Similarity
  - Ontological relatedness between two concepts
  - In Gene Ontology, similarity between two terms
- Categories
  - Ontology structure-based methods
    - Edge-based methods
    - Node-based methods
  - Information theoretic methods
  - Integrative methods

Edge-Based Measures

- Path length between two terms
  - $sim(C_1, C_2) = \frac{1}{len(C_1, C_2) + 1}$
- Normalized path length between two terms by GO depth
  - $sim(C_1, C_2) = -\log\left(\frac{len(C_1, C_2)}{2 \times depth}\right)$
- Depth to the most specific common ancestor
- Normalized depth to the most specific common ancestor by average depth to two terms
  - $sim(C_1, C_2) = \frac{2 \times len(C_{root}, C_0)}{len(C_0, C_1) + len(C_0, C_2) + 2 \times len(C_{root}, C_0)}$

    where C_0 is the most specific common ancestor term

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Node-Based Measures

- Number of common ancestors
  - $sim(C_1, C_2) = |Pt(C_1) \cap Pt(C_2)|$

    where $Pt(C)$ is the set of ancestors of the term C
- Normalized number of common ancestors
  - Jaccard index $sim(C_1, C_2) = \frac{|Pt(C_1) \cap Pt(C_2)|}{|Pt(C_1) \cup Pt(C_2)|}$
  - Dice index $sim(C_1, C_2) = \frac{2 \times |Pt(C_1) \cap Pt(C_2)|}{|Pt(C_1)| + |Pt(C_2)|}$
  - Min normalization $sim(C_1, C_2) = \frac{|Pt(C_1) \cap Pt(C_2)|}{\min(|Pt(C_1)|, |Pt(C_2)|)}$

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Information Contents

- Formulation
  - In Information Theory, the information content of a concept *C* is defined as –log P(*C*)
- Transitivity Property of Annotations
  - If a gene *g* is annotated to a term *C*, then it is also annotated to all the ancestor terms of *C* towards the root
  - The likelihood of *C* can be defined by the annotation on *C*

$$P(C) = \frac{\text{the number of genes annotated to } C}{\text{the number of all genes annotated to the ontology}}$$

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Information Theoretic Measures

- Information content of the most specific common ancestor
  - $sim(C_1, C_2) = -\log P(C_0)$

    where C_0 is the most specific common ancestor
- Normalized information content of the most specific common ancestor by average information content of two terms
  - $sim(C_1, C_2) = \frac{2 \times \log P(C_0)}{\log P(C_1) + \log P(C_2)}$
- Sum of differences between information content of the most specific common ancestor and information content of two terms
  - $sim(C_1, C_2) = \frac{1}{2 \times \log P(C_0) - \log P(C_1) - \log P(C_2) + 1}$

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Integrative Methods

- Combination of an edge-based measure and a node-based measure
  - $sim(C_1, C_2) = \sum_{C_0 \in (Pt(C_1) \cap Pt(C_2))} len(C_{root}, C_0)$
- Combination of a node-based measure and an information theoretic measure
  - $sim(C_1, C_2) = \frac{\sum_{C_i \in (Pt(C_1) \cap Pt(C_2))} \log P(C_i)}{\sum_{C_j \in (Pt(C_1) \cup Pt(C_2))} \log P(C_j)}$
- Combination of two information theoretic measures

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Problems of Semantic Similarity

- Node-Based Methods
  - Assumes that all GO terms are meaningful
    (Terms have been randomly created based on evidence.)
- Edge-Based Methods
  - Assumes that all relationships represents the same quantity of similarity
    (Relationships have been randomly created based on evidence.)
- Information Theoretic Methods
  - Applicable only if genes are fully annotated

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Questions

- How to measure similarity between labels from a labeled tree?
  - Group-wise vs. Pairwise
- How to measure similarity between labels from a labeled tree if each node in tree can have multiple labels?

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Applications of Semantic Similarity

- Applications
  - Functional prediction of incompletely annotating genes
  - Semantic similarity between terms (concepts)
    - → Functional similarity between genes
- Challenges
  - A single gene performs multiple functions
  - A single gene is annotated on multiple terms
    - $X=\{X_1, X_2, \ldots, X_m\}$ are the most specific terms having a gene g_1
    - $Y=\{Y_1, Y_2, \ldots, Y_n\}$ are the most specific terms having a gene g_2

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Implementation of Functional Similarity

- Functional Similarity between Genes
  - Measuring semantic similarity between two sets of terms
- Pairwise Methods
  - Measuring semantic similarity between terms
  - Aggregating term-to-term semantic similarities
  - Ex, edge-based semantic similarity methods
- Group-wise Methods
  - Measuring semantic similarity directly between two sets of terms
  - Ex, node-based semantic similarity methods

Aggregation of Semantic Similarities

- Pairwise Averaging
  - Average of semantic similarity scores between X_i and Y_i

$$sim(g_1, g_2) = \frac{\sum_{i,j} sim(X_i, Y_j)}{|X| \times |Y|}$$

- Best Matching
  - Maximum semantic similarity score between X_i and Y_i

$$sim(g_1, g_2) = \max_{i,j} sim(X_i, Y_j)$$

- Best-Match Averaging

$$sim(g_1, g_2) = \frac{\sum_i \max_j sim(X_i, Y_j) + \sum_j \max_i sim(X_i, Y_j)}{|X| + |Y|}$$

Questions?

- Lecture Slides are found on the Course Website, web.ecs.baylor.edu/faculty/cho/5V93