From terminology integration
to information integration

Unified Medical Language System (UMLS)

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Outline

- Overview through an example
- UMLS components
  - Lexical resources
  - Metathesaurus
  - Semantic Network
- UMLS and information integration
What does UMLS stand for?

- **Unified**
- **Medical**
- **Language**
- **System**

UMLS®
Unified Medical Language System®
UMLS Metathesaurus®
Motivation

- Started in 1986
- National Library of Medicine
- “Long-term R&D project”

“[…] the UMLS project is an effort to overcome two significant barriers to effective retrieval of machine-readable information.

- The first is the variety of ways the same concepts are expressed in different machine-readable sources and by different people.
- The second is the distribution of useful information among many disparate databases and systems.”
Overview through an example
Addison’s disease

- Addison's disease is a rare endocrine disorder
- Addison's disease occurs when the adrenal glands do not produce enough of the hormone cortisol
- For this reason, the disease is sometimes called chronic adrenal insufficiency, or hypocortisolism
Adrenal insufficiency  Clinical variants

◆ Primary / Secondary
  ● Primary: lesion of the adrenal glands themselves
  ● Secondary: inadequate secretion of ACTH by the pituitary gland

◆ Acute / Chronic

◆ Isolated / Polyendocrine deficiency syndrome
Addison’s disease: Symptoms

- Fatigue
- Weakness
- Low blood pressure
- Pigmentation of the skin (exposed and non-exposed parts of the body)
- …
AD in medical vocabularies

◆ Synonyms: different terms
  - Addisonian syndrome
  - Bronzed disease
  - Addison melanoderma
  - Asthenia pigmentosa
  - Primary adrenal deficiency
  - Primary adrenal insufficiency
  - Primary adrenocortical insufficiency
  - Chronic adrenocortical insufficiency

◆ Contexts: different hierarchies
  - Symptoms
  - Clinical
  - Variants
  - Eponym
Organize terms

- Synonymous terms clustered into a concept
- Preferred term
- Unique identifier (CUI)

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Addison's disease
Diseases of the endocrine system
diseases of the adrenal glands
Addison’s disease
MeSH

Diseases

Endocrine Diseases

Adrenal Gland Diseases

Adrenal Gland Hypofunction

Addison’s Disease
Endocrine disorder

Disorder of adrenal gland

Hypoadrenalism

Adrenal Hypofunction

Corticoadrenal insufficiency

Addison’s Disease
Primary adrenocortical insufficiency

Other disorders of adrenal gland

Disorders of other endocrine gland

ICD-10
Organize concepts

- Inter-concept relationships: hierarchies from the source vocabularies
- Redundancy: multiple paths
- One graph instead of multiple trees (multiple inheritance)
Adrenal Cortex Diseases

Hypoadrenalism

Adrenal Gland Hypofunction

Adrenal cortical hypofunction

Addison’s Disease

Endocrine Diseases

SNOMED
MeSH
AOD
Read Codes

UMLS
Relate to other concepts

- Additional hierarchical relationships
  - link to other trees
  - make relationships explicit
- Non-hierarchical relationships
- Co-occurring concepts
- Mapping relationships
Endocrine Diseases

Adrenal Gland Diseases

Adrenal Cortex Diseases

Hypoadrenalism

Adrenal Gland Hypofunction

Adrenal cortical hypofunction

Secondary hypocortisolism

Addison’s Disease

Addison’s disease due to autoimmunity

relate to other concepts
Categorize concepts

- High-level categories (semantic types)
- Assigned by the Metathesaurus editors
- Independently of the hierarchies in which these concepts are located

Disease or Syndrome
\[\text{Diseases} \rightarrow \text{Endocrine Diseases} \rightarrow \text{Adrenal Gland Diseases} \rightarrow \text{Adrenal Gland Hypofunction} \rightarrow \text{Addison’s Disease}\]
How do they do that?

- Lexical knowledge
- Semantic pre-processing
- UMLS editors
Lexical knowledge

- Adrenal gland diseases
- Adrenal disorder
- Disorder of adrenal gland
- Diseases of the adrenal glands
- C0001621
Semantic pre-processing

- Metadata in the source vocabularies
- Tentative categorization
- Positive (or negative) evidence for tentative synonymy relations based on lexical features
Adrenal Gland Diseases

Adrenal Cortex Diseases

Adrenal Cortex Dysfunction

Hypoadrenalism

Adrenal Gland Hypofunction

Addison’s Disease

Other disorders of adrenal gland

Adrenal cortical hypofunction
UMLS: 3 components

◆ SPECIALIST Lexicon
  ● 200,000 lexical items
  ● Part of speech and variant information

◆ Metathesaurus
  ● 5M names from over 100 terminologies
  ● 1M concepts
  ● 16M relations

◆ Semantic Network
  ● 135 high-level categories
  ● 7000 relations among them
UMLS Metathesaurus
Source Vocabularies

◆ 139 source vocabularies
  ● 17 languages

◆ Broad coverage of biomedicine
  ● 5.1M names
  ● 1.3M concepts
  ● 16M relations

◆ Common presentation
Addison’s Disease: Concept

A disease characterized by hypotension, weight loss, anorexia, weakness, and sometimes a bronze-like melanotic hyperpigmentation of the skin. It is due to tuberculosis- or autoimmune-induced disease (hypofunction) of the adrenal glands that results in deficiency of aldosterone and cortisol. In the absence of replacement therapy, it is usually fatal.
Metathesaurus Concepts (2006AB)

- **Concept** (> 1.3M) CUI
  - Set of synonymous concept names
- **Term** (> 4.6M) LUI
  - Set of normalized names
- **String** (> 5.1M) SUI
  - Distinct concept name
- **Atom** (> 6.2M) AUI
  - Concept name in a given source

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Metathesaurus  Evolution over time

- Concepts never die (in principle)
  - CUIs are permanent identifiers
- What happens when they do die (in reality)?
  - Concepts can merge or split
  - Resulting in new concepts and deletions

Addison's disease
C0001403

Addison's disease, NOS
C0271735

Metathesaurus Relationships

- Symbolic relations: ~9 M pairs of concepts
- Statistical relations: ~7 M pairs of concepts (co-occurring concepts)
- Mapping relations: 100,000 pairs of concepts

Categorization: Relationships between concepts and semantic types from the Semantic Network
Symbolic relations

◆ Relation
  ● Pair of “atom” identifiers
  ● Type
  ● Attribute (if any)
  ● List of sources (for type and attribute)

◆ Semantics of the relationship:
  defined by its type [and attribute]

Source transparency: the information is recorded at the “atom” level
Symbolic relationships

- **Hierarchical**
  - Parent / Child
  - Broader / Narrower than

- **Derived from hierarchies**
  - Siblings (children of parents)

- **Associative**
  - Other

- **Various flavors of near-synonymy**
  - Similar
  - Source asserted synonymy
  - Possible synonymy
Symbolic relationships

- Hierarchical
  - isa (is-a-kind-of)
  - part-of
- Associative
  - location-of
  - caused-by
  - treats
  - ...
- Cross-references (mapping)
UMLS Semantic Network
Semantic Network

- Semantic types (135)
  - tree structure
  - 2 major hierarchies
    - Entity
      - Physical Object
      - Conceptual Entity
    - Event
      - Activity
      - Phenomenon or Process
Semantic Network

Semantic network relationships (54)

- hierarchical (isa = is a kind of)
  - among types
    - Animal isa Organism
    - Enzyme isa Biologically Active Substance
  - among relations
    - treats isa affects

- non-hierarchical
  - Sign or Symptom diagnoses Pathologic Function
  - Pharmacologic Substance treats Pathologic Function
“Biologic Function” hierarchy (isa)
Why a semantic network?

- Semantic Types serve as high level categories assigned to Metathesaurus concepts, independently of their position in a hierarchy.

- A relationship between 2 Semantic Types (ST) is a possible link between 2 concepts that have been assigned to those STs:
  - The relationship may or may not hold at the concept level.
  - Other relationships may apply at the concept level.
Relationships can inherit semantics

Semantic Network

- Fully Formed Anatomical Structure
- Biologic Function
- Pathologic Function
- Disease or Syndrome
- Body Part, Organ, or Organ Component
- Adrenal Cortex
- Adrenal Cortical hypofunction

Metathesaurus

location of

isa
UMLS Summary

- Synonymous terms clustered into concepts
- Unique identifier
- Finer granularity
- Broader scope
- Additional hierarchical relationships
- Semantic categorization
Integrating subdomains

- Clinical repositories
- Genetic knowledge bases
- Other subdomains
- SNOMED
- OMM
- Biomedical literature
- MeSH
- Genome annotations
- NCBi Taxonomy
- Model organisms
- UWDA
- Anatomy
- GO
Integrating subdomains

- Clinical repositories
- Genetic knowledge bases
- Biomedical literature
- Genome annotations
- Anatomy
- Model organisms
- Other subdomains
Information integration

Genomics as an example
Neurofibromatosis 2 is an autosomal dominant disease characterized by tumors called schwannomas involving the acoustic nerve, as well as other features. The disorder is caused by mutations of the NF2 gene resulting in absence or inactivation of the protein product. The protein product of NF2 is commonly called merlin (but also neurofibromin 2 and schwannomin) and functions as a tumor suppressor.
Schwannoma (acoustic neuroma)

http://www.mayoclinic.com
NF2 gene

http://staff.washington.edu/timk/cyto/human/

Merlin

- **Synonyms**
  - Neurofibromin 2
  - Schwannomin
  - Schwannomerlin
  - Neurofibromatosis-2

- **10 isoforms**

- **Annotations**
  - Negative regulation of cell proliferation
  - Cytoskeleton
  - Plasma membrane
Neurofibromatosis 2 (Type II neurofibromatosis, Bilateral acoustic neurofibromatosis)  
**C0027832**

NF2 (Neurofibromin 2 gene)  
**C0085114**

Merlin (Schwannomin, Neurofibromin 2)  
**C0254123**

UMLS Metathesaurus (Concepts and relations)  
**U49724**

External resources  
OMIM #101000
Limitations

- **Genes not systematically represented**
  - Most gene products and diseases are

- **Gene/Gene product-Disease relations**
  - Not systematically represented
  - Not explicitly represented (e.g., co-occurrence)

- **Cross-references not systematically represented**

- **Naming conventions (genes)**
References

- UMLS
  umlsinfo.nlm.nih.gov

- UMLS browsers
  (free, but UMLS license required)
    - Semantic Navigator:
    - RRF browser
      (standalone application distributed with the UMLS)
Recent overviews


References

◆ UMLS as a research project


References

◆ Technical papers


Medical Ontology Research

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