Division of Biomedical Informatics
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NLM Resources for Mining Biomedical Text

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Overview

- An example
- Types of resources for mining biomedical text
- Three types of resources
  - Lexical resources
  - Terminological resources
  - Ontological resources

An example

Neurofibromatosis 2

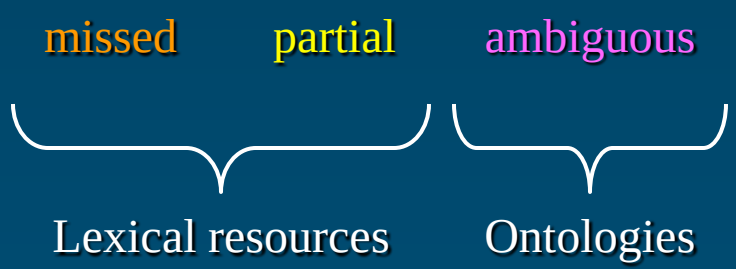
Neurofibromatosis 2

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin, located on chromosome 22.

[Uppal, S., and A. P. Coatesworth. "Neurofibromatosis Type 2." *Int J Clin Pract*, 57, no. 8, 2003, pp. 698-703.]

Entity recognition

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin, located on chromosome 22.



Relation extraction

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin, located on chromosome 22.

- vestibular schwannomas *manifestation of* neurofibromatosis 2
- neurofibromatosis 2 *associated with* mutation of NF2 gene
- NF2 gene *located on* chromosome 22

Ontologies

Types of resources for mining biomedical text

Types of resources

- Lexical resources
  - Collections of lexical items
  - Additional information
    - Part of speech
    - Spelling variants
  - Useful for entity recognition
  - UMLS SPECIALIST Lexicon, WordNet
- Ontological resources
  - Collections of
    - kinds of entities (substances, qualities, processes)
    - relations among them
  - Useful for relation extraction
  - UMLS Semantic Network, BioTop

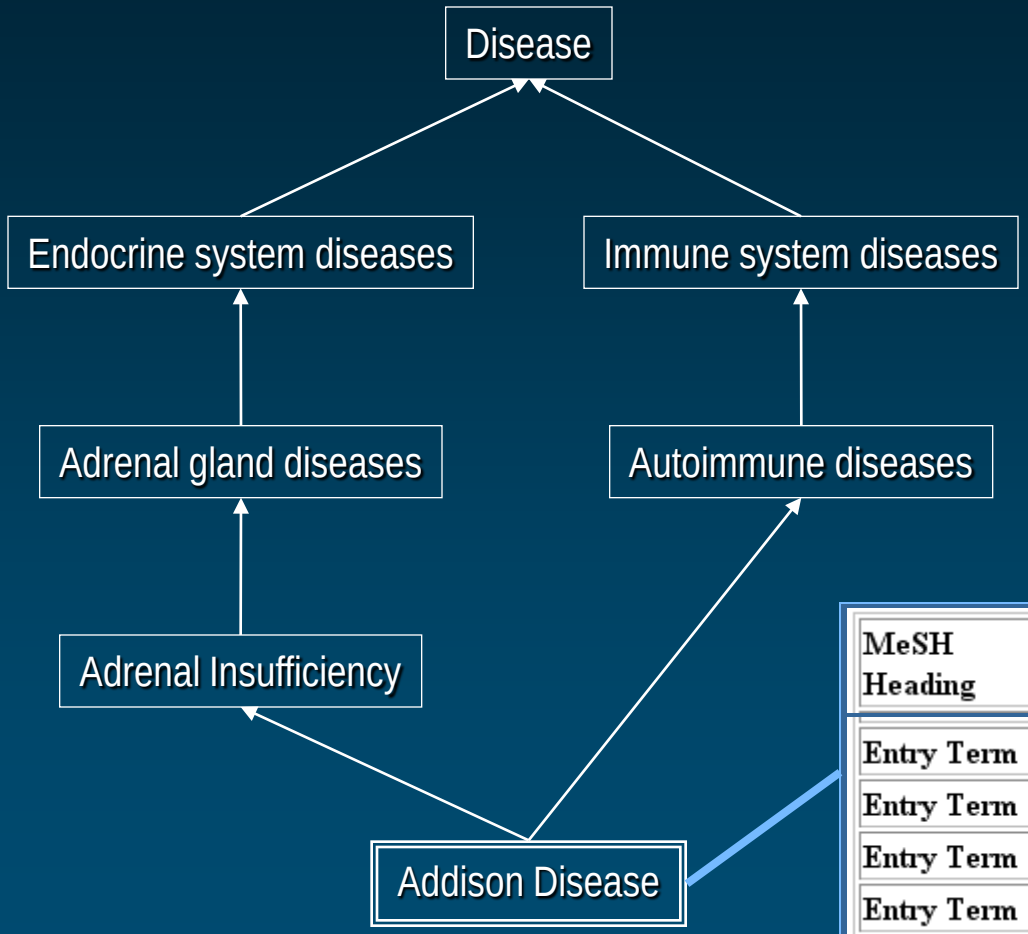
- Terminological resources
  - Collections lexical items + identifiers
  - Useful for entity resolution
  - UMLS Metathesaurus

Types of resources (revisited)

- Lexical and terminological resources
  - Mostly collections of names for biomedical entities
  - Often have some kind or hierarchical organization (e.g., relations)
- Ontological resources
  - Mostly collections of relations among biomedical entities
  - Sometimes also collect names

Lexical / Ontological MeSH

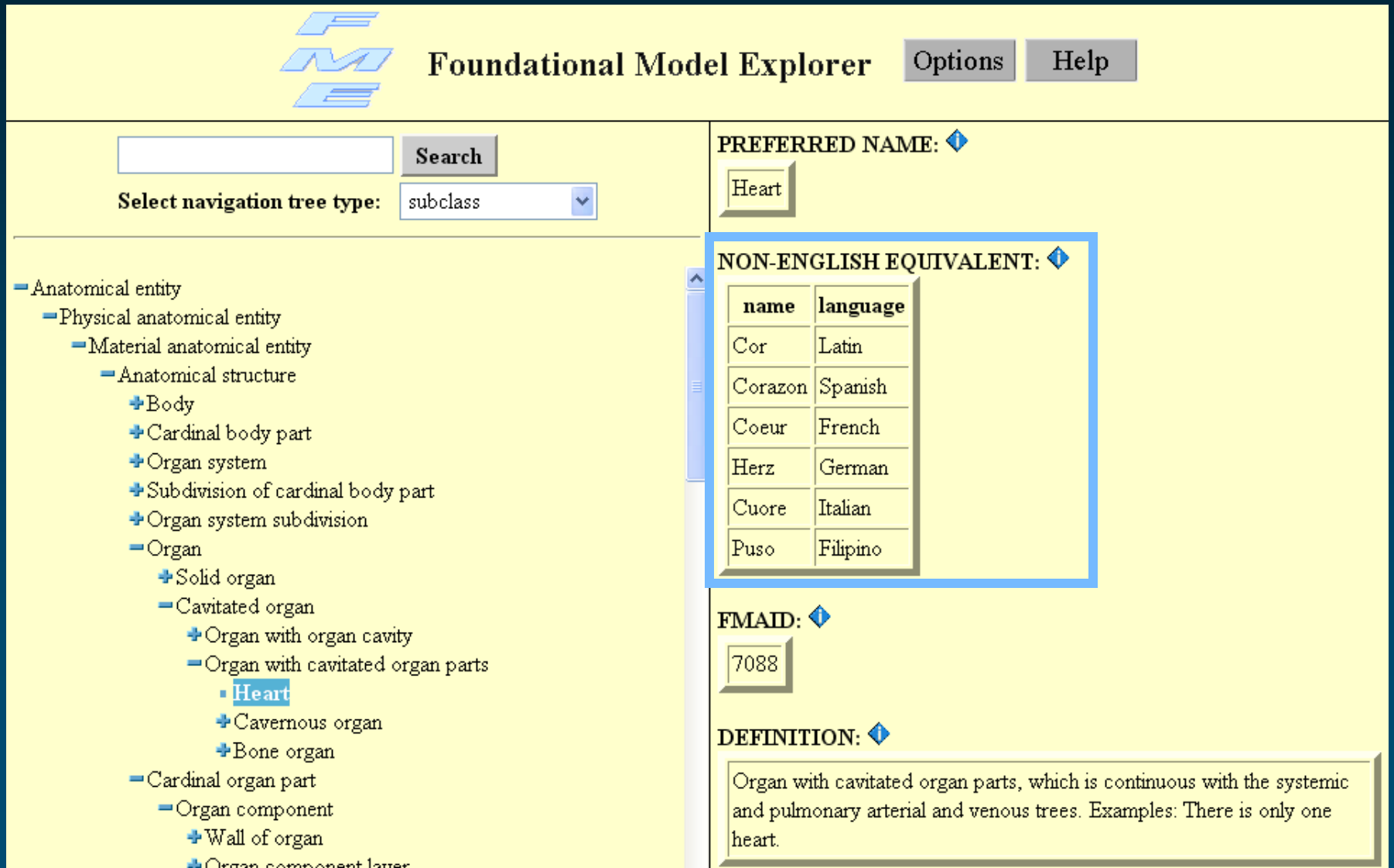
http://www.nlm.nih.gov/mesh/MBrowser.html



MeSH Heading	Addison Disease
Entry Term	Addison's Disease
Entry Term	Primary Adrenal Insufficiency
Entry Term	Primary Adrenocortical Insufficiency
Entry Term	Primary Hypoadrenalism

Lexical / Ontological FMA

http://fme.biostr.washington.edu/index.html



Unified Medical Language System

- SPECIALIST Lexicon
  - 465,000 lexical items
  - Part of speech and variant information
- Metathesaurus
  - 8.7M names from over 100 terminologies
  - 2.6M concepts
  - >10M relations
- Semantic Network
  - 133 high-level categories
  - 7000 relations among them

Lexical resources

LVG / Norm

Terminological resources

MetaMap

Ontological resources

SemRep

Lexical resources

SPECIALIST Lexicon and lexical tools

Lexical Systems Group

http://umlslex.nlm.nih.gov/

SPECIALIST Lexicon

- Content
  - English lexicon
  - Many words from the biomedical domain
- 465,000 lexical items
- Word properties
  - morphology
  - orthography
  - syntax
- Used by the lexical tools

Morphology

- Inflection
  - noun — nucleus, nuclei
  - verb — cauterize, cauterizes, cauterized, cauterizing
  - adjective — red, redder, reddest
- Derivation
  - verb ⟺ noun — cauterize -- cauterization
  - adjective ⟺ noun — red -- redness

Orthography

- Spelling variants
  - oe/e — oesophagus - esophagus
  - ae/e — anaemia - anemia
  - ise/ize — cauterise - cauterize
  - genitive mark — Addison's disease
Addison disease
Addisons disease

Syntax

- Complementation
  - verbs
    - intransitive — I'll treat.
    - transitive — He treated the patient.
    - ditransitive — He treated the patient with a drug.
  - nouns
    - prepositional phrase

      Valve of coronary sinus
- Position for adjectives

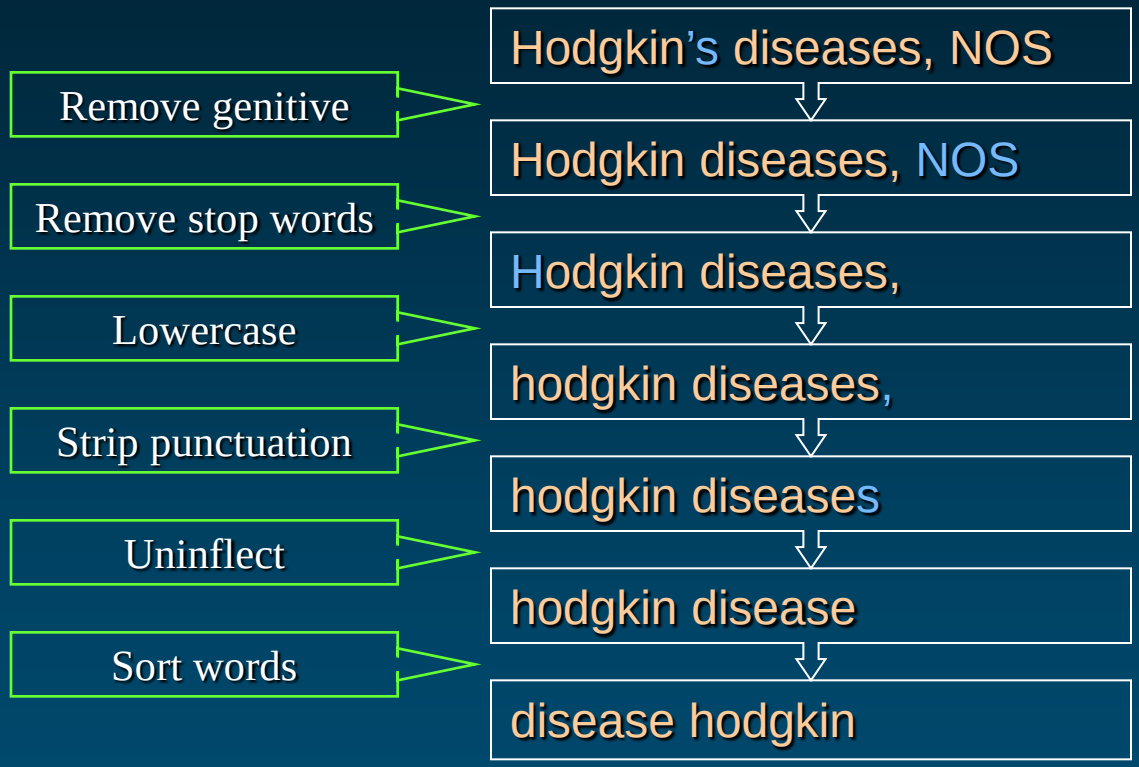
SPECIALIST Lexicon record

```
{
  base=hemoglobin      (base form)
  spelling_variant=haemoglobin
  entry=E0031208       (identifier)
  cat=noun             (part of speech)
  variants=uncount     (no plural)
  variants=reg         (plural: hemoglobins, hemoglobins)
}
```

Lexical tools

- To manage lexical variation in biomedical terminologies
- Major tools
  - Normalization
  - Indexes
  - Lexical Variant Generation program (lvg)
- Based on the SPECIALIST Lexicon
- Used by noun phrase extractors, search engines

Normalization



Normalization: Example

Hodgkin Disease
HODGKINS DISEASE
Hodgkin's Disease
Disease, Hodgkin's
Hodgkin's, disease
HODGKIN'S DISEASE
Hodgkin's disease
Hodgkins Disease
Hodgkin's disease NOS
Hodgkin's disease, NOS
Disease, Hodgkins
Diseases, Hodgkins
Hodgkins Diseases
Hodgkins disease
hodgkin's disease
Disease, Hodgkin

Normalization Applications

- Model for lexical resemblance
- Help find lexical variants for a term
  - Terms that normalize the same usually share the same LUI
- Help find candidates to synonymy among terms
- Help map input terms to UMLS concepts

Indexes

- Word index
  - word to Metathesaurus strings
  - one word index per language
- Normalized word index
  - normalized word to Metathesaurus strings
  - English only
- Normalized string index
  - normalized term to Metathesaurus strings
  - English only

Lexical Variant Generation program

- Tool for specialists (linguists)
- Performs atomic lexical transformations
  - generating inflectional variants
  - lowercase
  - …
- Performs sequences of atomic transformations
  - a specialized sequence of transformations provides the normalized form of a term (the *norm* program)

Related NLM tools

http://umlslex.nlm.nih.gov/

Public Projects

- SPECIALIST Lexicon
- LexAccess
- Lexical Tools
- Text Tools
- Text Categorization
- GSpell
- dTagger

The SPECIALIST Text Tools includes tokenizers that analyze text into word, term, phrase, sentence and section pieces. The tools also include a variant lookup module that retrieves variant ways of expressing the phrases found in the text. The tools are intended to analyze documents into instances of document objects.

The tools are written in Java. These tools include the following:

- a word/Sentence/section Tokenizer
- a term tokenizer
- a phrase tokenizer
- a term variant lookup
- a part-of-speech tagger (client)
- a document index maker
- a tool to create the textTool indexes

The SPECIALIST spelling resources include two programs GSpell a spelling suggestion tool and BagOwordsPlus a phrase retrieval tool.

GSpell uses several word similarity algorithms to suggest correct spellings for misspelled words. Unlike other spelling suggestion programs GSpell treats space as it would any other letter so that GSpell can correct errors in word compounding. GSpell also be used in word similarity tasks that do not involve misspelling.

BagOWordsPlus uses the word similarity algorithms of GSpell to perform word similarity based phrase level information retrieval.

The dTagger is a Part of Speech (POS) tagger. A POS tagger assigns part of speech tags such as noun, adjective, adverb to sentences. Such tag assignments are a needed component to determining phrase boundaries and head assignment. The dTagger includes the following features: It can tokenize text into single or multi-word terms. It is built specifically for use with the SPECIALIST Lexicion. A default trained model is included, trained on a set of annotated MEDLINE abstracts in the genomics field, (the MedPost corpus). The trainer and updater programs are included to allow the creation of new trained models. Models can be updated with lots of untagged text. Can be trained with just untagged text, if need be. The dTagger is an open source resource and is freely available subject to these terms and conditions.

Lexical resources

Other resources

Similar resources

- BioLexicon
  - Developed as part of the EU project BOOTStrep
  - Focus on biological entities (genes, proteins, chemical entities, organisms) in support of the extraction of gene regulation events
- BioThesaurus
  - Developed as part of the Protein Information Resource
  - Focus on proteins

Need for additional resources

- More generic
  - WordNet
- More specific
  - Lexical items specific to specialized subdomains
    - Not listed in biolexicons
    - Not amenable to normalization
  - Examples
    - Genes, proteins
      - MAPK3 / Mapk3 / mapk3
    - Chemicals
      - 5’-3’ exonuclease / 3’-5’ exonuclease
    - Drugs
    - Acronyms

Gene and protein names

- Additional resources

Genew	http://www.gene.ucl.ac.uk/nomenclature/
Entrez Gene	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene
UniProt	http://www.ebi.uniprot.org/index.shtml

- Additional identification methods
  - e.g., ABGene (Tanabe & Wilbur, NCBI)
  - BioCreAtIvE
    - Gene mention identification
    - Gene normalization

Chemical names

- Additional resources

PubChem	http://pubchem.ncbi.nlm.nih.gov/
ChemIDplus	http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp
ChEBI	http://www.ebi.ac.uk/chebi/

Drug names

- Covered by UMLS
- Specialized resource: RxNorm
  - Branded names / generic names
  - Various levels of aggregation
    - Ingredient
    - Ingredient + dose
    - Ingredient + form
    - Ingredient + dose + form
  - Codes in various reference systems
- Mostly US drugs, no “over-the-counter” drugs

Acronyms

- Many resources available
  - AcroMine
    http://www.nactem.ac.uk/software/acromine/
  - ARGH: Biomedical Acronym Resolver
    http://lethargy.swmed.edu/ARGH/argh.asp
  - Stanford Biomedical Abbreviation Server
    http://bionlp.stanford.edu/abbreviation/
  - AcroMed
    http://medstract.med.tufts.edu/acro1.1/index.htm
  - SaRAD
    http://www.hpl.hp.com/research/idl/projects/abbrev.html

Terminological resources

UMLS Metathesaurus

http://www.nlm.nih.gov/research/umls/

Source Vocabularies (2011AB)

- 161 source vocabularies
- 21 languages
- Broad coverage of biomedicine
  - 8.7M distinct names
  - 2.6M concepts
  - >10M relations
- Common presentation

Organize terms

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

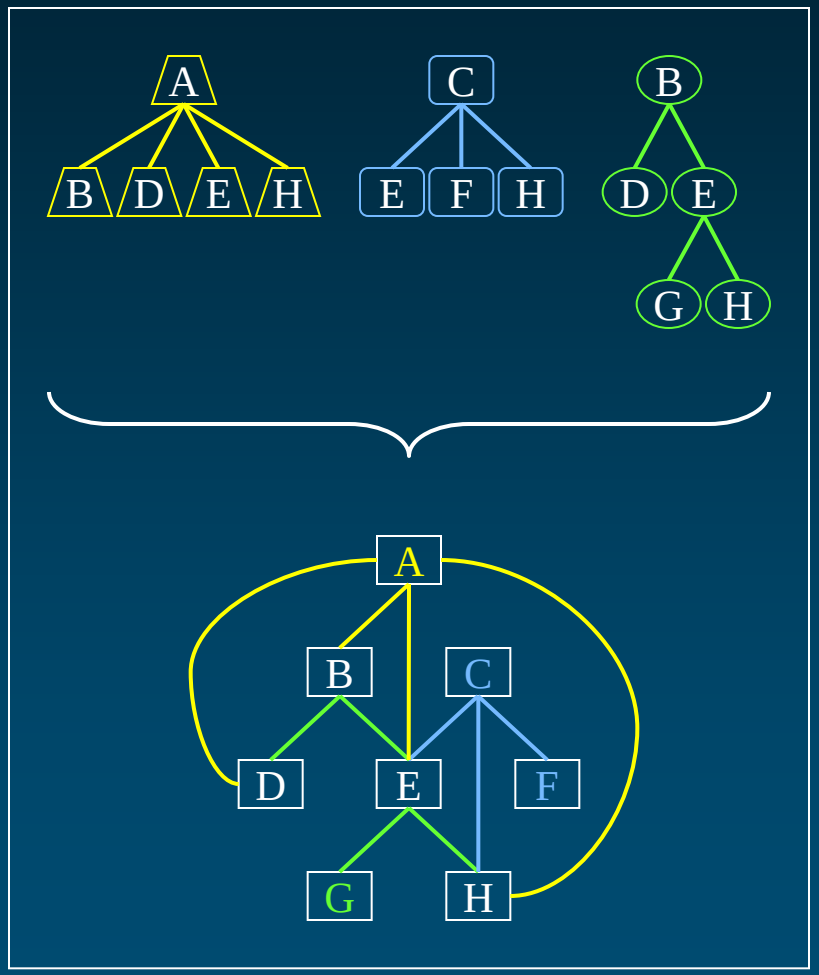
Addison Disease	MeSH	D000224
Primary hypoadrenalism	MedDRA	10036696
Primary adrenocortical insufficiency	ICD-10	E27.1
Addison's disease (disorder)	SNOMED CT	363732003

C0001403

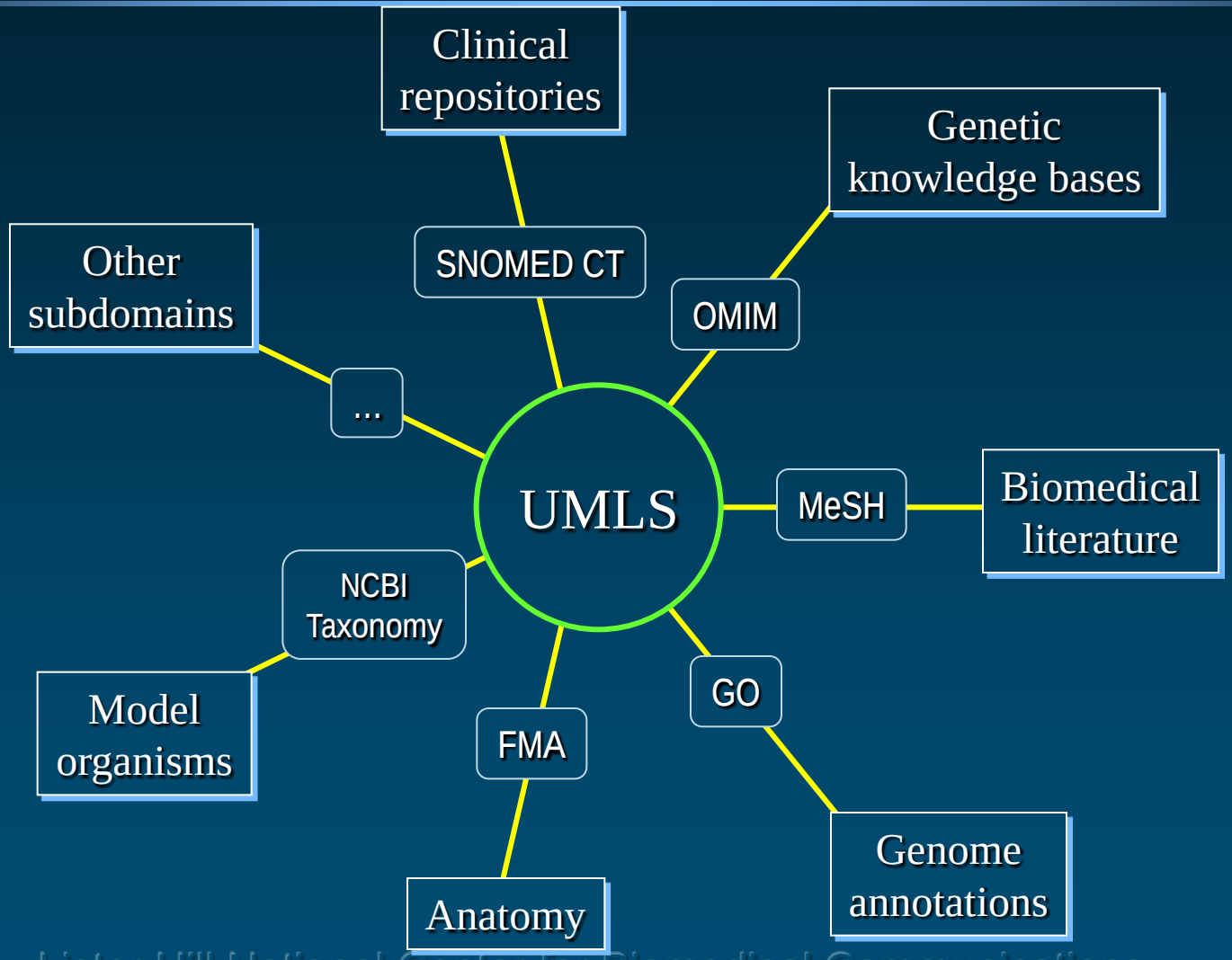
Addison's disease

Organize concepts

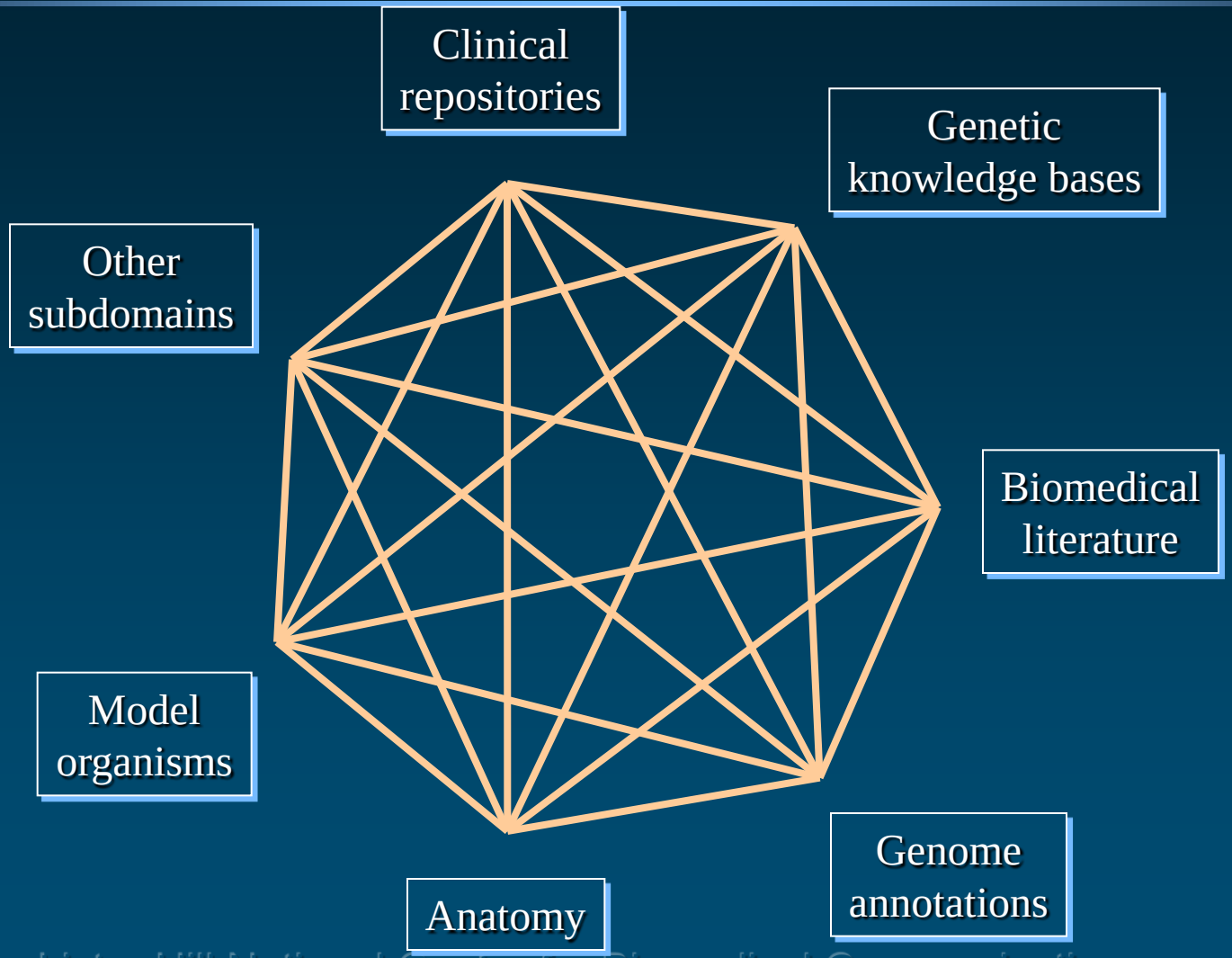
- Inter-concept relationships: hierarchies from the source vocabularies
- Redundancy: multiple paths
- One graph instead of multiple trees (multiple inheritance)



Integrating subdomains



Integrating subdomains



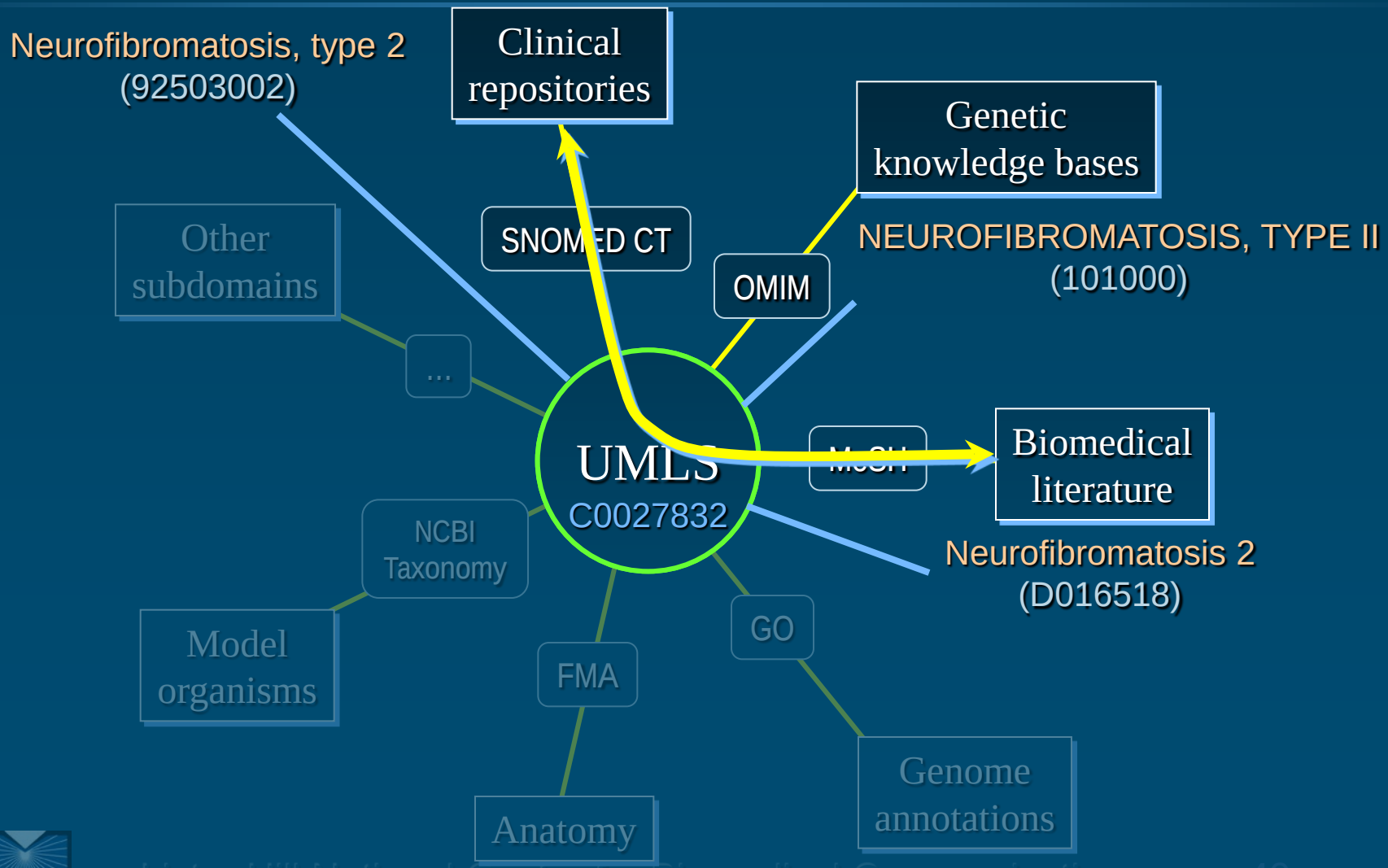
Entity mention vs. resolution

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin, located on chromosome 22.

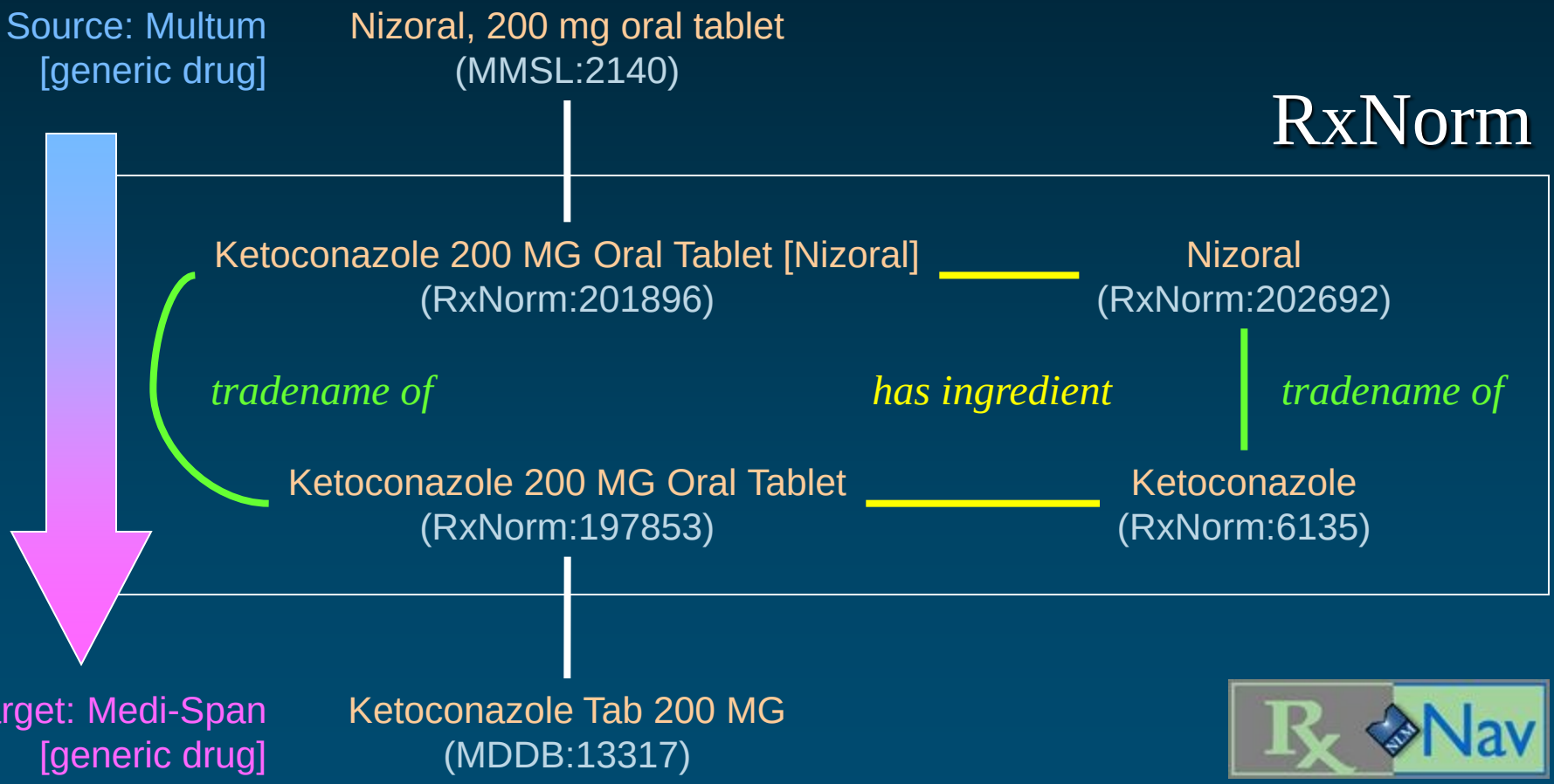
UMLS:C0027832
MeSH:D016518
SNOMEDCT:92503002
OMIM:101000

UMLS:C0254123
EG:4771
HGNC:7773
UniProt:P35240

Trans-namespace resolution (1)



Trans-namespace resolution (2)



http://mor.nlm.nih.gov/download/rxnav/

Terminological resources

MetaMap

INDEXING INITIATIVE

http://ii.nlm.nih.gov/

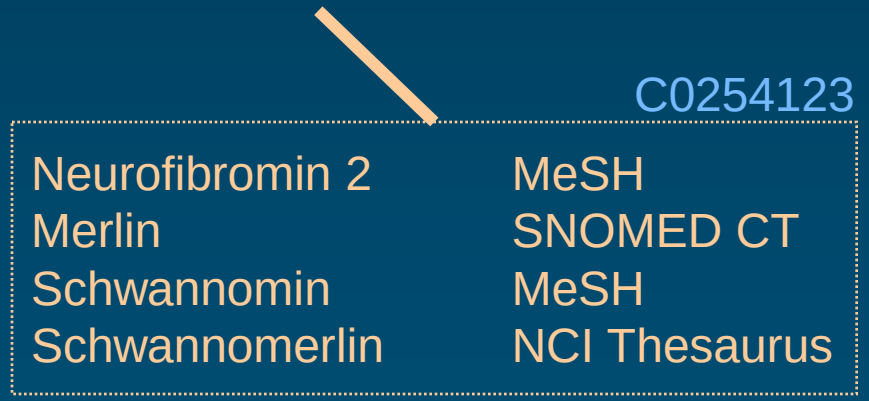
MetaMap

- UMLS-based entity recognition system
  - Linguistically motivated
  - Exploits both the SPECIALIST lexicon and Metathesaurus
- In practice, used to identify UMLS concepts in biomedical text
- Freely available (UMLS license)
- Two versions
  - Web-based
  - Standalone (MMTx)

MetaMap Example

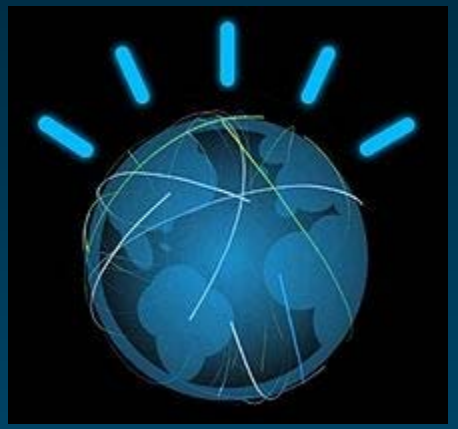
Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin, located on chromosome 22.

C0027832 C0027832 C0027831 C0027832 C0027859 C0027832 C0026882 C0254123 C0008665



MetaMap Recent developments

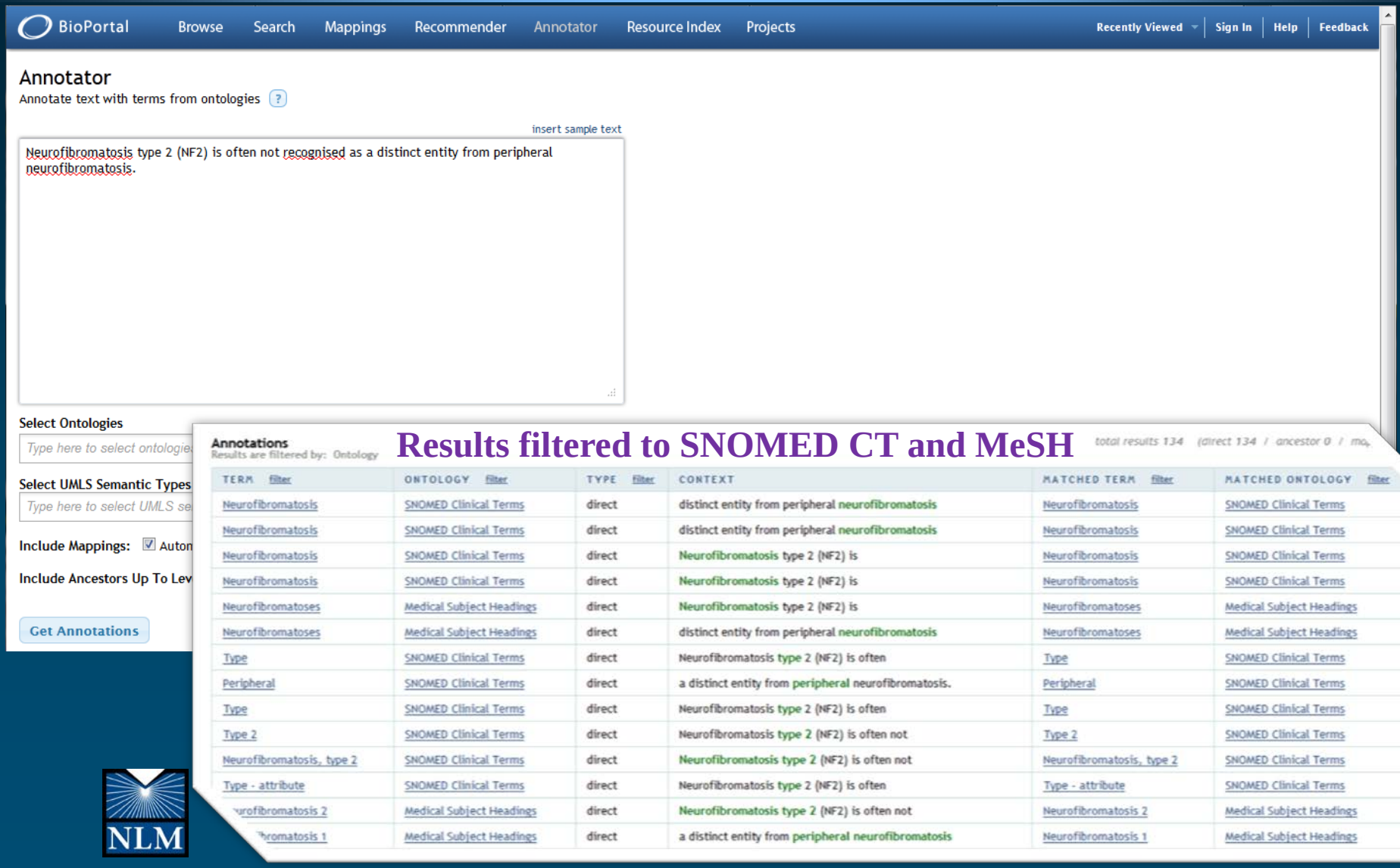
- Negation processing (NegEx)
- Word sense disambiguation
- Integration in NLP pipelines
  - UIMA wrapper
- Performance improvements
- User-defined acronyms
- Applications
  - MetaMap is a key component of the Medical Text Indexer (MEDLINE indexing)
    - From indexing support to “first-line indexing”



Terminological resources

Other NER systems

BioPortal Annotator



NLM

TerMine

TerMine (C-value) analysis

Service questionnaire

Found **5** terms in 2.2 seconds - all terms (in table) (in text) - threshold: 0 Apply

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin , located on chromosome 22.

Thank you for using TerMine. Please now complete a questionnaire to let us know your views about this service.

Whatizit

Whatizit

3 Select a pipeline:

whatizitEBIMedDiseaseChemicals

Resulting tagged text

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis . NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas . NF2 results from a mutation in the gene named merlin, located on chromosome 22 .

Ontological resources

Ontological resources

- Provide background knowledge
  - For resolving ambiguity in entity recognition
    - Merlin: Protein or Bird?
  - For relation extraction
    - Template relations between high-level concepts
    - Used in combination with clues from linguistic phenomena in text

Ontological resources

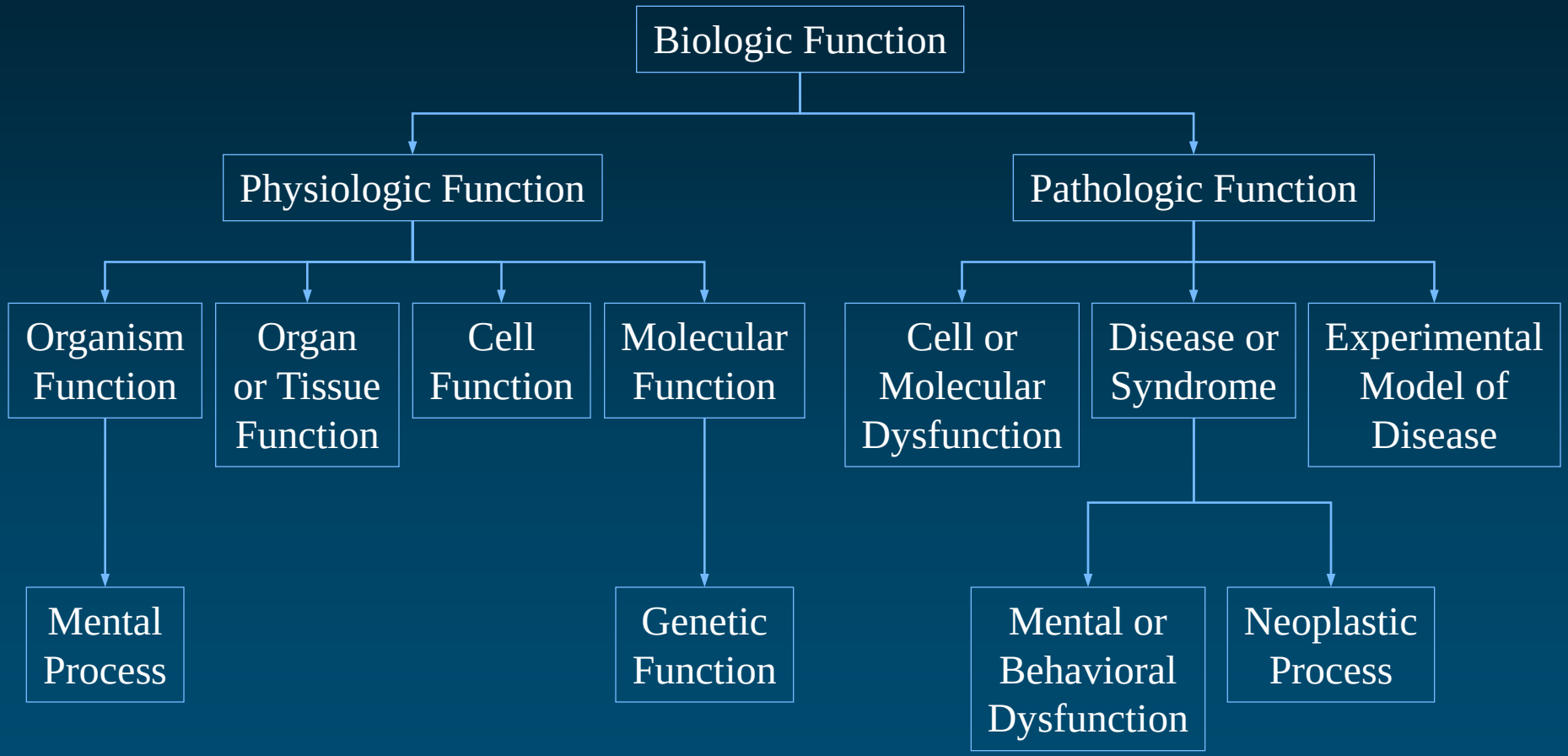
- Various level of formality
  - Formal top-level ontologies (e.g., BioTop)
  - Informal top-level ontologies (e.g., UMLS Semantic Network)
  - Domain-Range constraints for roles in DL-based terminologies (e.g., SNOMED CT, NCI Thesaurus)
  - Relations in terminologies
- Various level of granularity
  - UMLS Semantic Network: 133 types
  - Foundational Model of Anatomy: 70,000 classes

Ontological resources

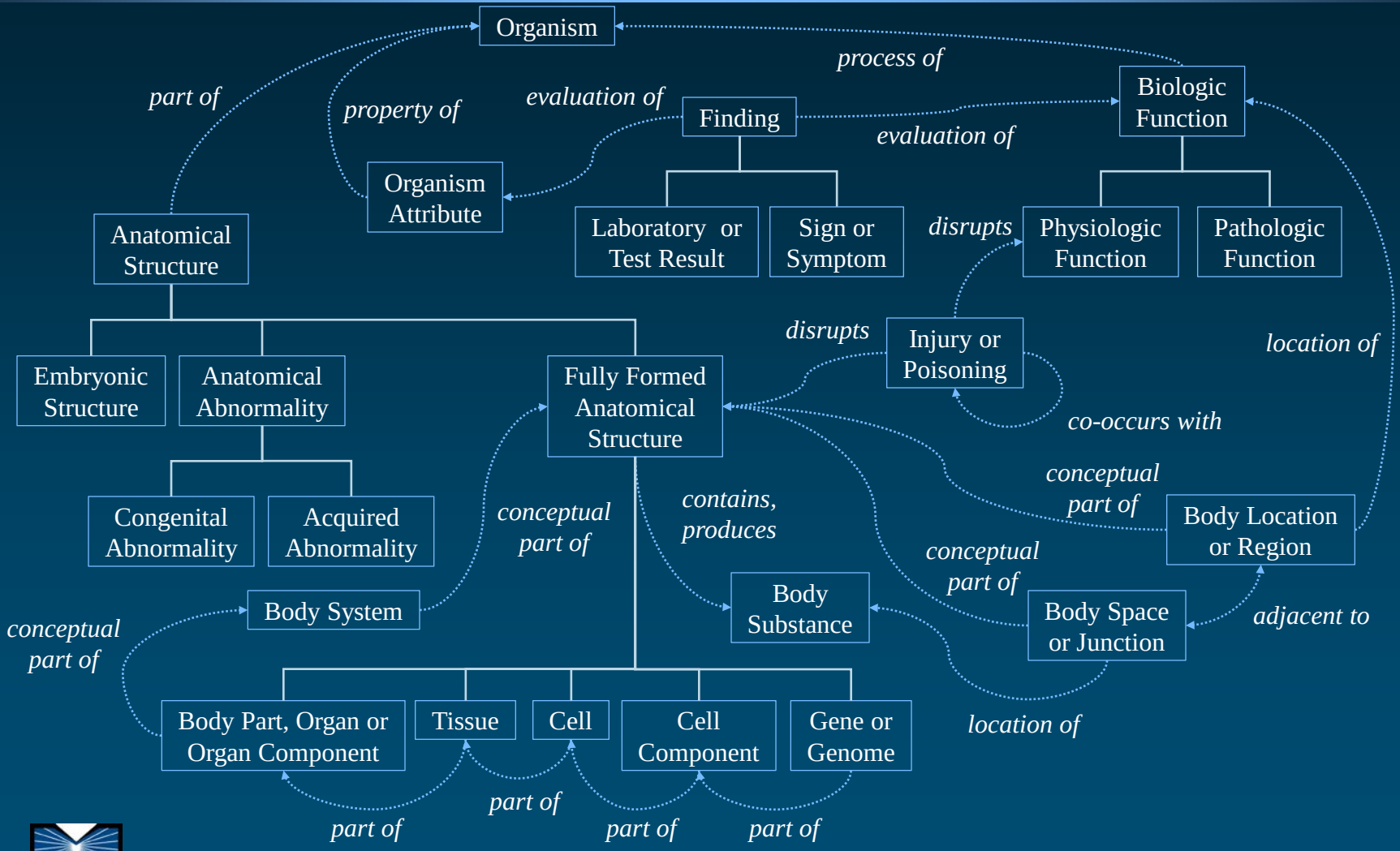
UMLS Semantic Network

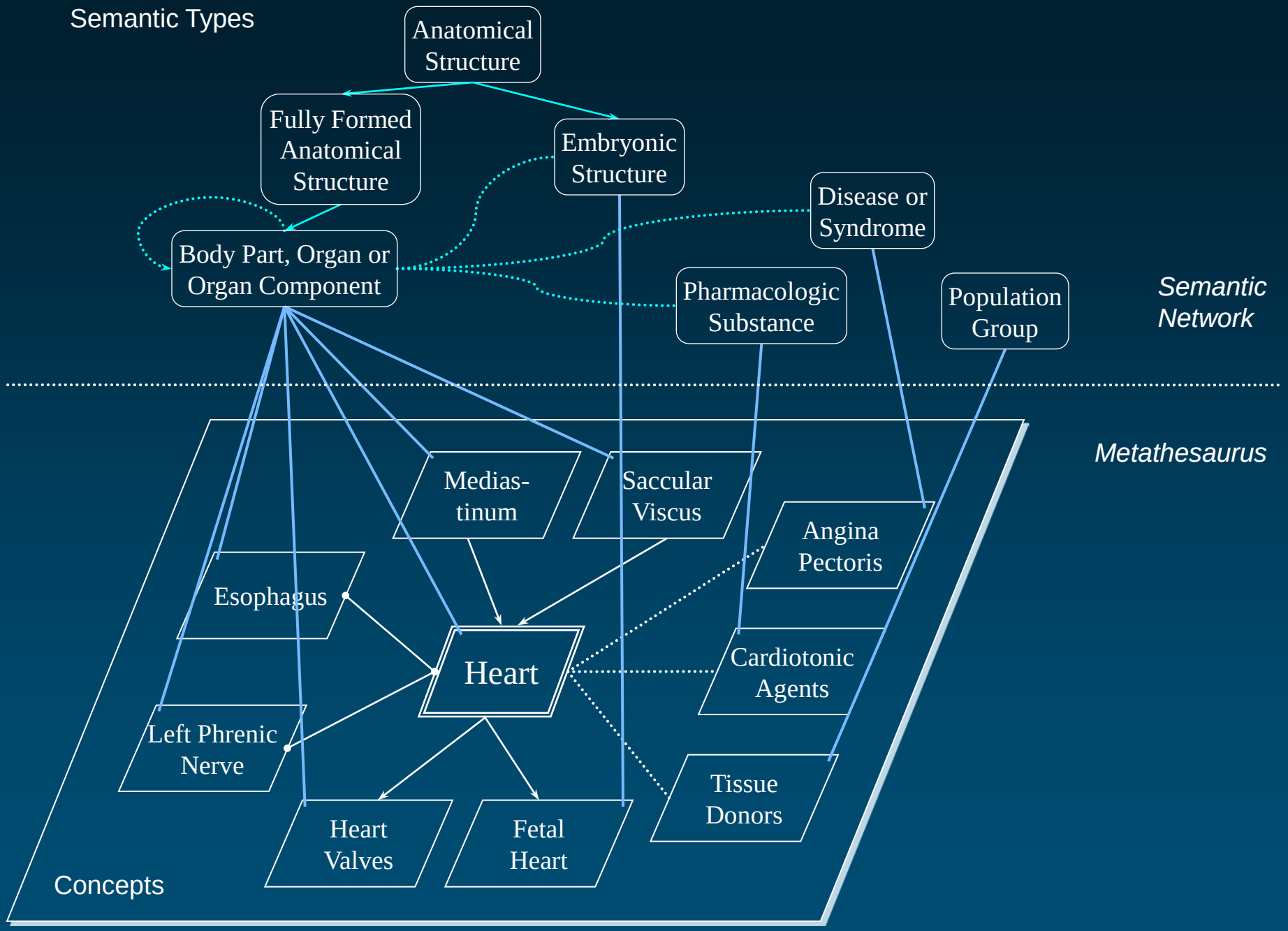
http://semanticnetwork.nlm.nih.gov/

“Biologic Function” hierarchy (isa)



Associative (non-isa) relationships



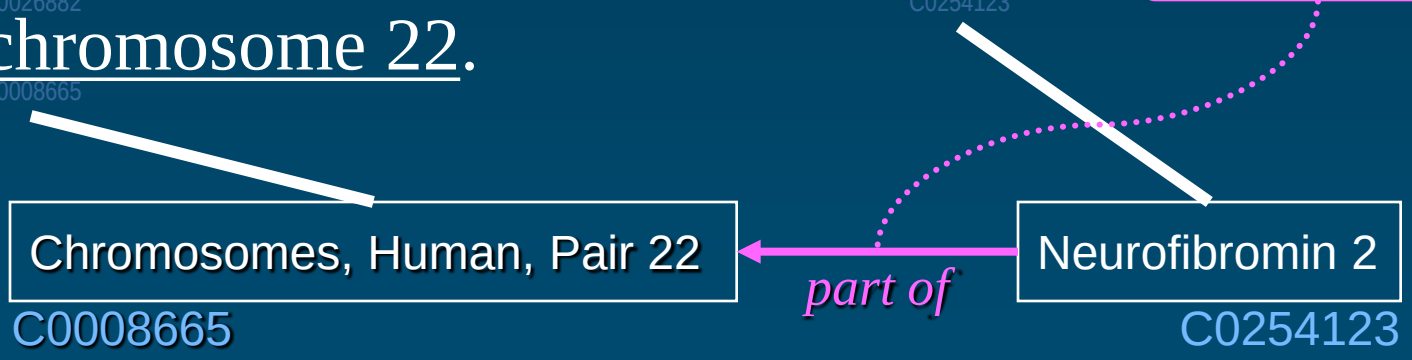

Semantic Types
Anatomical Structure
Fully Formed Anatomical Structure
Embryonic Structure
Disease or Syndrome
Body Part, Organ or Organ Component
Pharmacologic Substance
Population Group
Semantic Network
Metathesaurus
Medias-tinum
Saccular Viscus
Angina Pectoris
Esophagus
Heart
Cardiotonic Agents
Left Phrenic Nerve
Tissue Donors
Heart Valves
Fetal Heart
Concepts

Ontological resources

SemRep

SemRep Relation extraction

Neurofibromatosis type 2 (NF2) is often not recognised as a distinct entity from peripheral neurofibromatosis. NF2 is a predominantly intracranial condition whose hallmark is bilateral vestibular schwannomas. NF2 results from a mutation in the gene named merlin, located on chromosome 22.



SemRep Recent developments

- All of MEDLINE processed
  - 60M predications
- Use of graph theory principles for selecting salient associations
- Applications
  - Literature-based discovery
    - Relationship between testosterone, cortisol and sleep quality in aging men
  - Automatic summarization
    - Semantic MEDLINE http://skr3.nlm.nih.gov/SemMedDemo/

Ontological resources

Other resources

Other ontological resources

- Ontology integration systems
  - NCBO BioPortal
    http://www.bioontology.org/BioPortal
- Ontologies
  - Top-level ontologies (e.g., BioTop)
  - Domain ontologies (e.g., FMA, SNOMED CT, NCI Thesaurus)

Other relation extraction systems

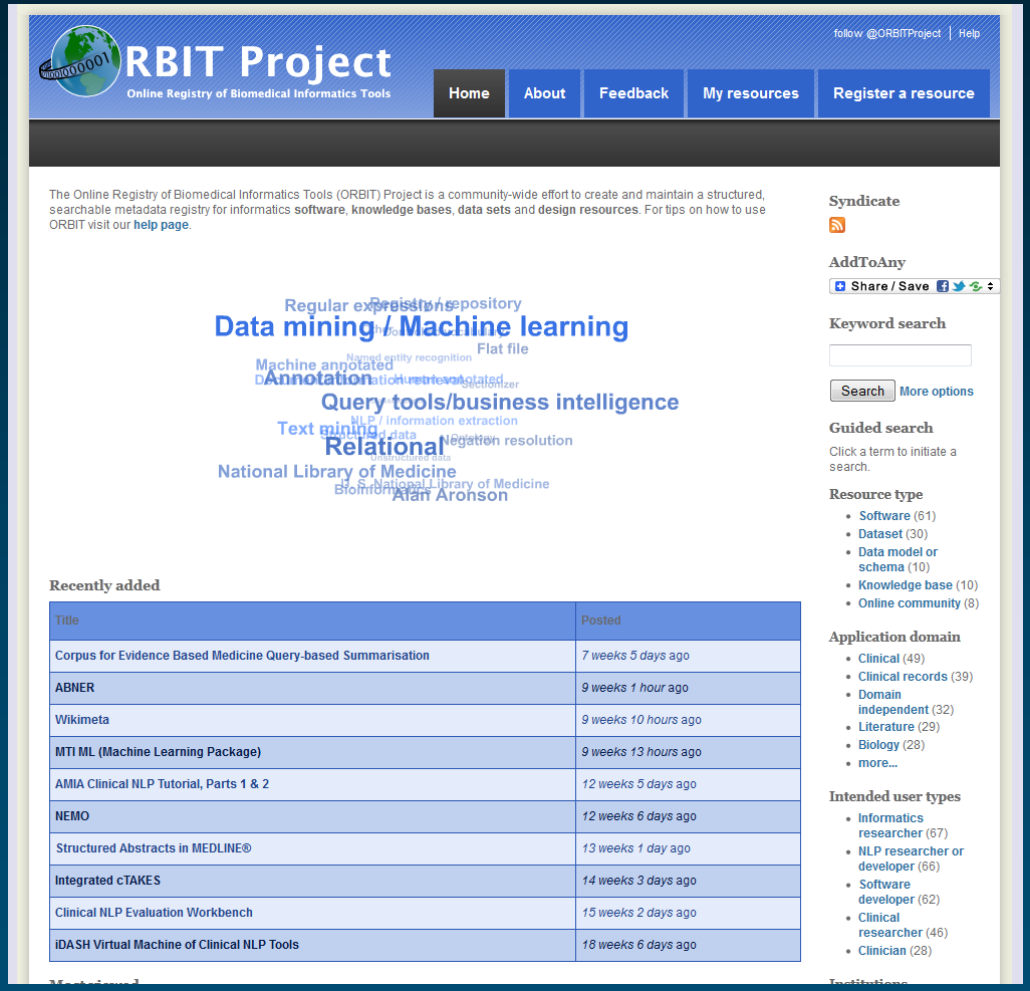
- Many relation extraction systems available
  - Specialized
    - Protein-protein interaction (e.g., Info-PubMed, TextPresso, …)
    - BioCreAtIvE (task 2)
  - More generic (e.g., MedLEE / BioMedLEE)
  - Commercial systems (TeSSI, Linguamatics, …)

Future directions

- Evolution of existing resources
  - Modularization
  - Compatibility with NLP pipelines (UIMA, GATES)
  - Services (web services, CTS2)
- Clinical text
  - Limited availability to non-clinical institutions
  - Opportunity to develop new tools (e.g., de-identification)
  - Integration with knowledge bases
    - Definitional vs. assertional knowledge
- Collaborative development

ORBIT project

http://orbit.nlm.nih.gov/



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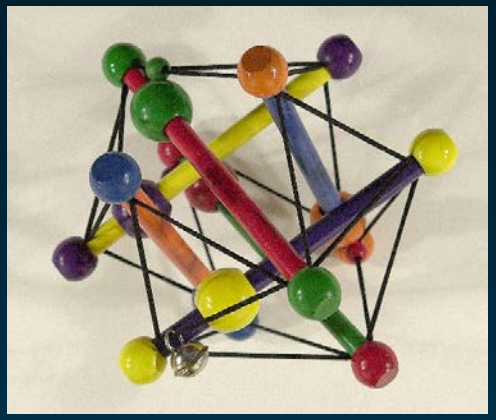
- Bodenreider O.
  Lexical, terminological and ontological resources for biological text mining.
  In: Ananiadou S, McNaught J, editors. Text mining for biology and biomedicine: Artech House; 2006. p. 43-66.



Medical Ontology Research

Contact: olivier@nlm.nih.gov
Web: mor.nlm.nih.gov

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