Text Mining Hands-on Course and Training Seminar

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# Medical terminologies and medical literature analysis

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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*

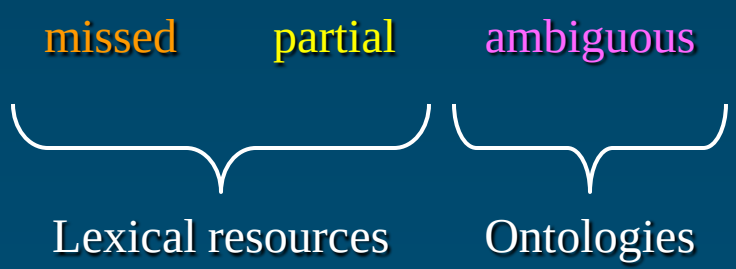
# Neurofibromatosis 2

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

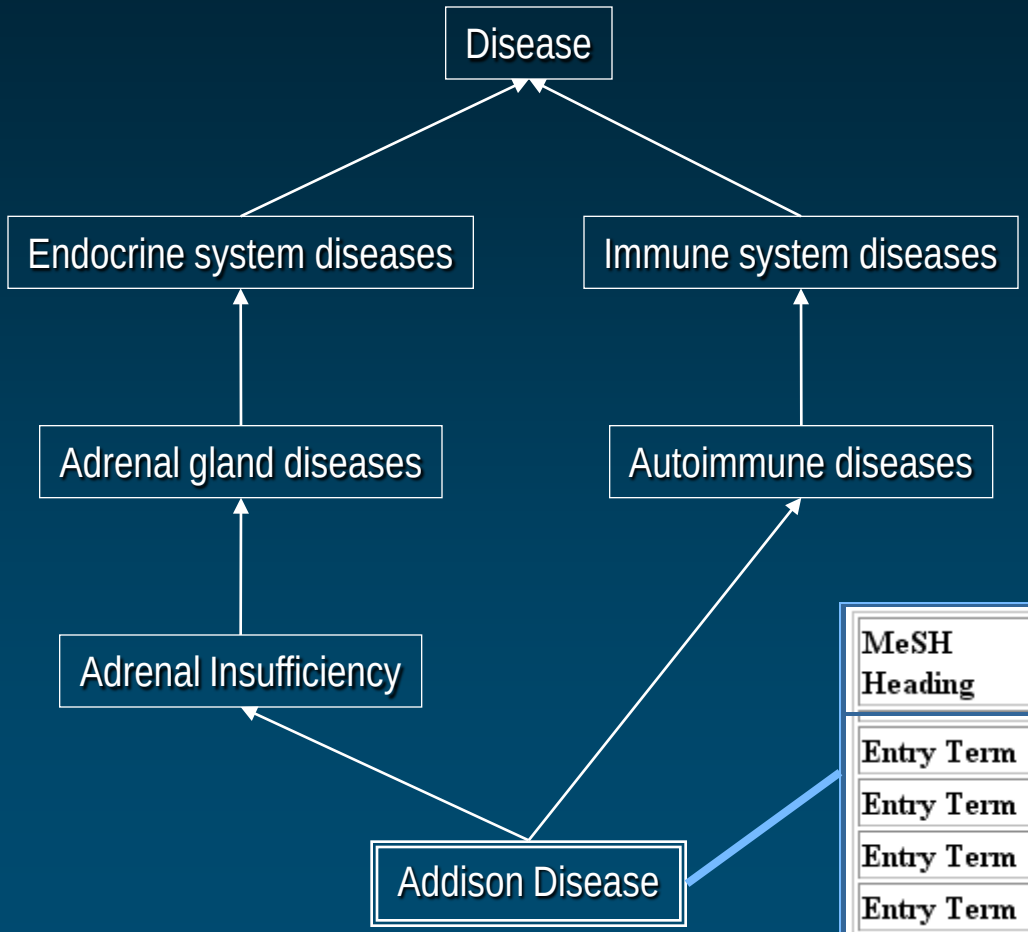
- Terminological resources
  - Collections lexical items + identifiers
  - Useful for entity resolution
  - UMLS Metathesaurus

# 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

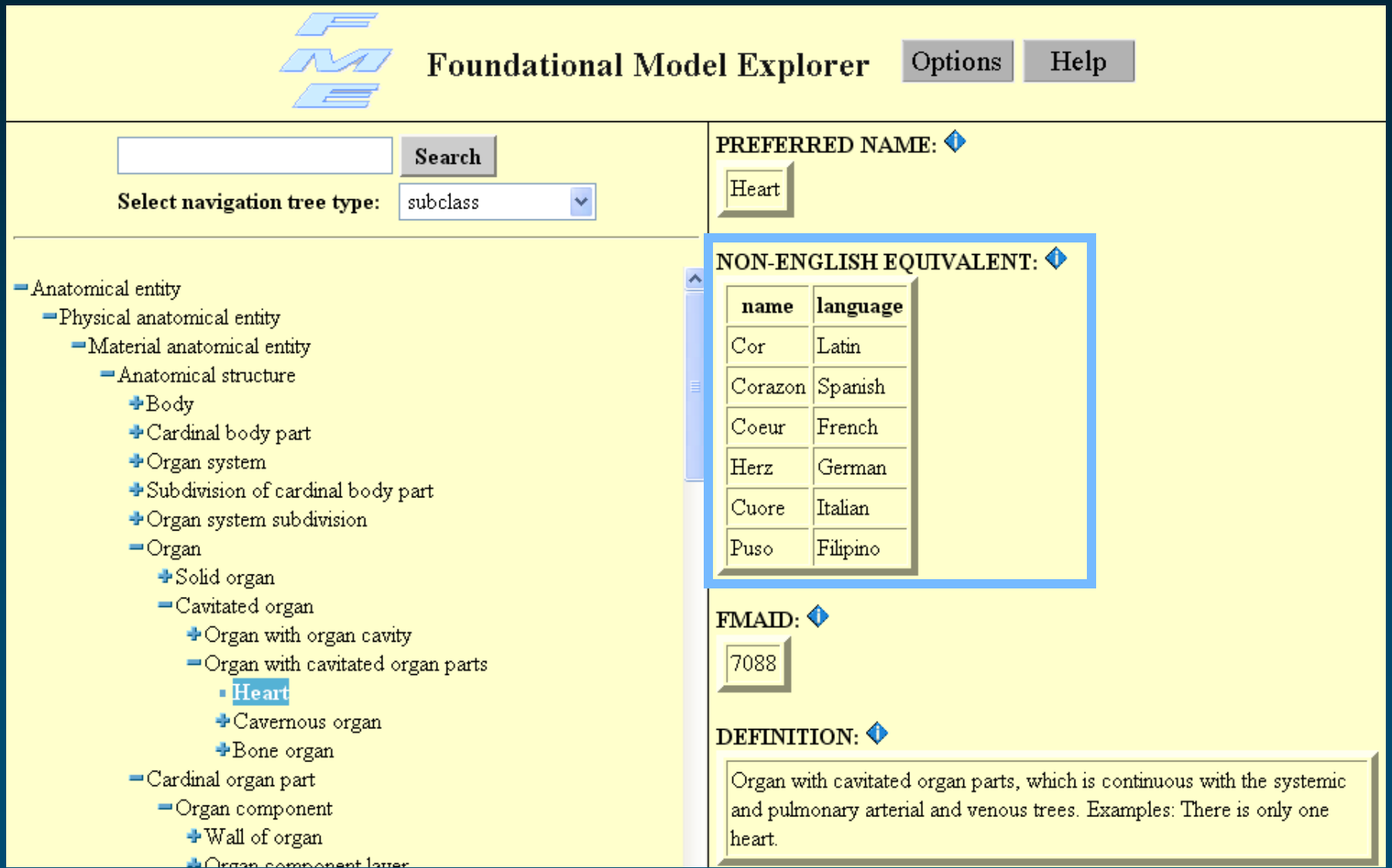
http://www.nlm.nih.gov/mesh/2007/MBrowser.html




| 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
  - 450,000 lexical items
  - Part of speech and variant information
- Metathesaurus
  - 10M names from over 100 terminologies
  - 2.2M 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
- 450,000 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<br>Addison disease<br>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

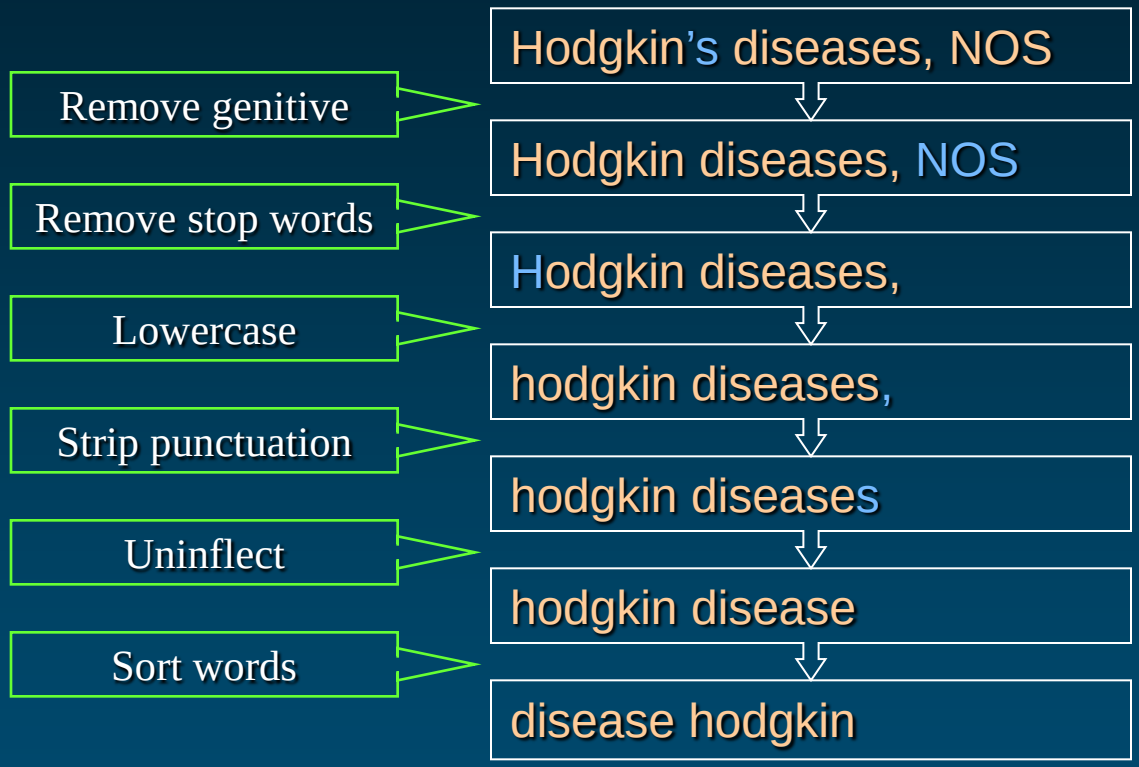
# SPECIALIST Lexicon record

```
{
  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*

# 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 (2010AA)

- 156 source vocabularies
- 20 languages
- Broad coverage of biomedicine
  - 10M names
  - 2.2M concepts
  - >10M relations
- Common presentation

# Organize terms

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

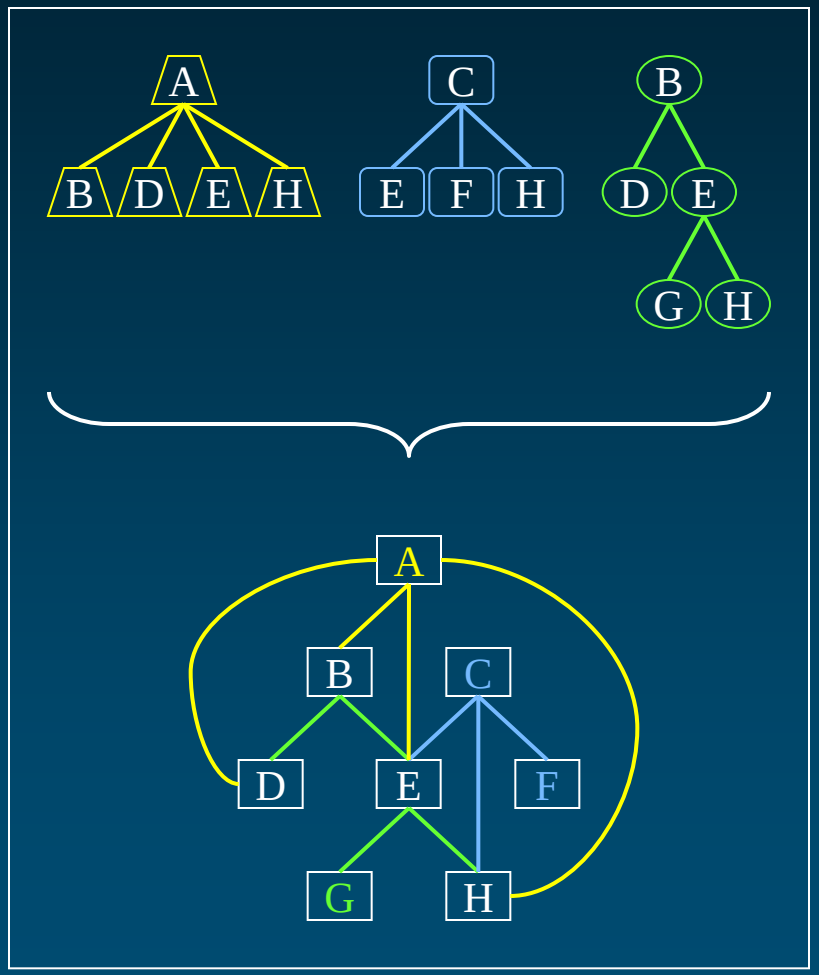
| | | |
|---|---|---|
| Addison Disease | MeSH | D000224 |
| Primary hypoadrenalism | MedDRA | 10036696 |
| Primary adrenocortical insufficiency | ICD-10 | E27.1 |
| Addison's disease (disorder) | SNOMED CT | 363732003 |

C0001403

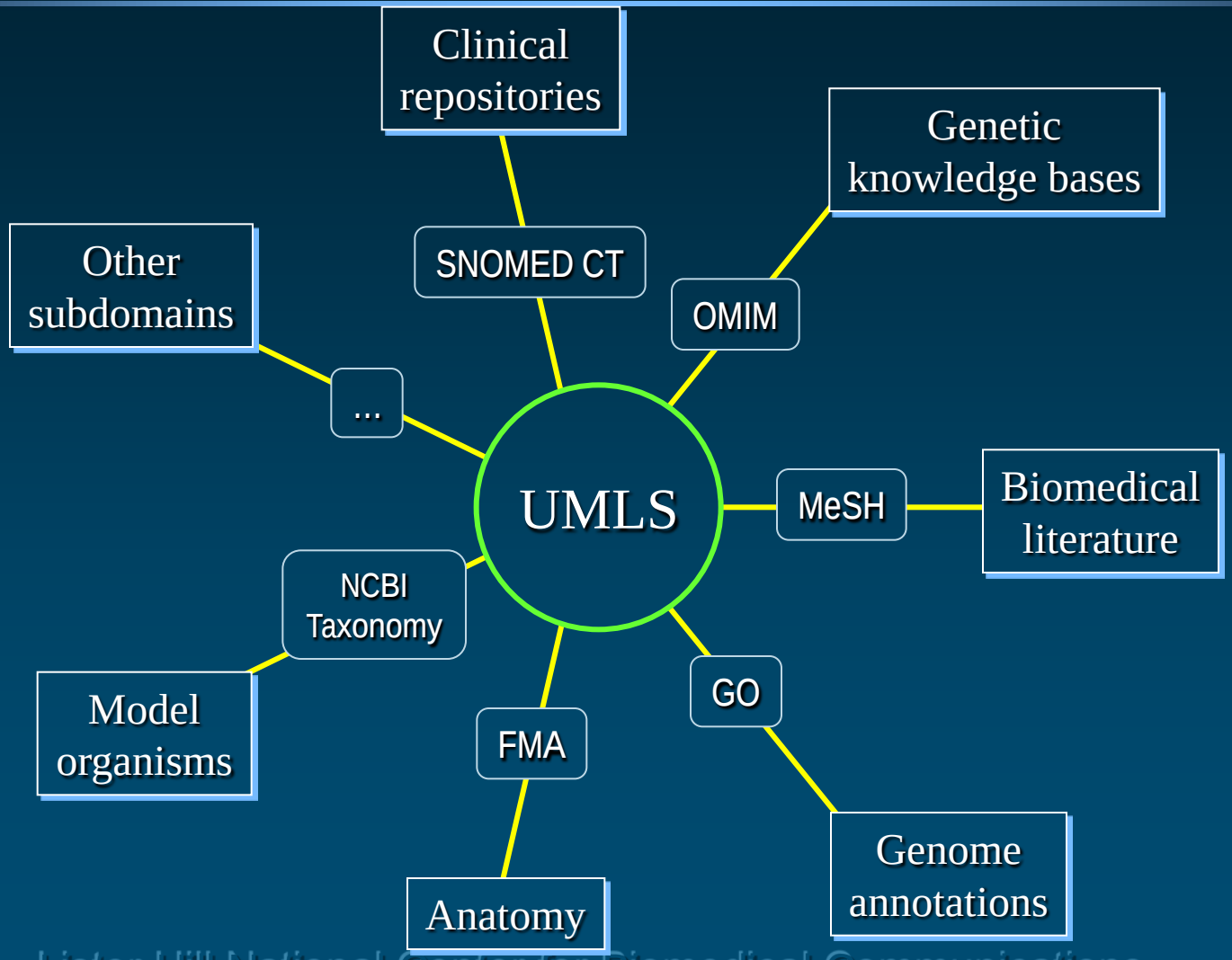
Addison's disease

# Organize concepts

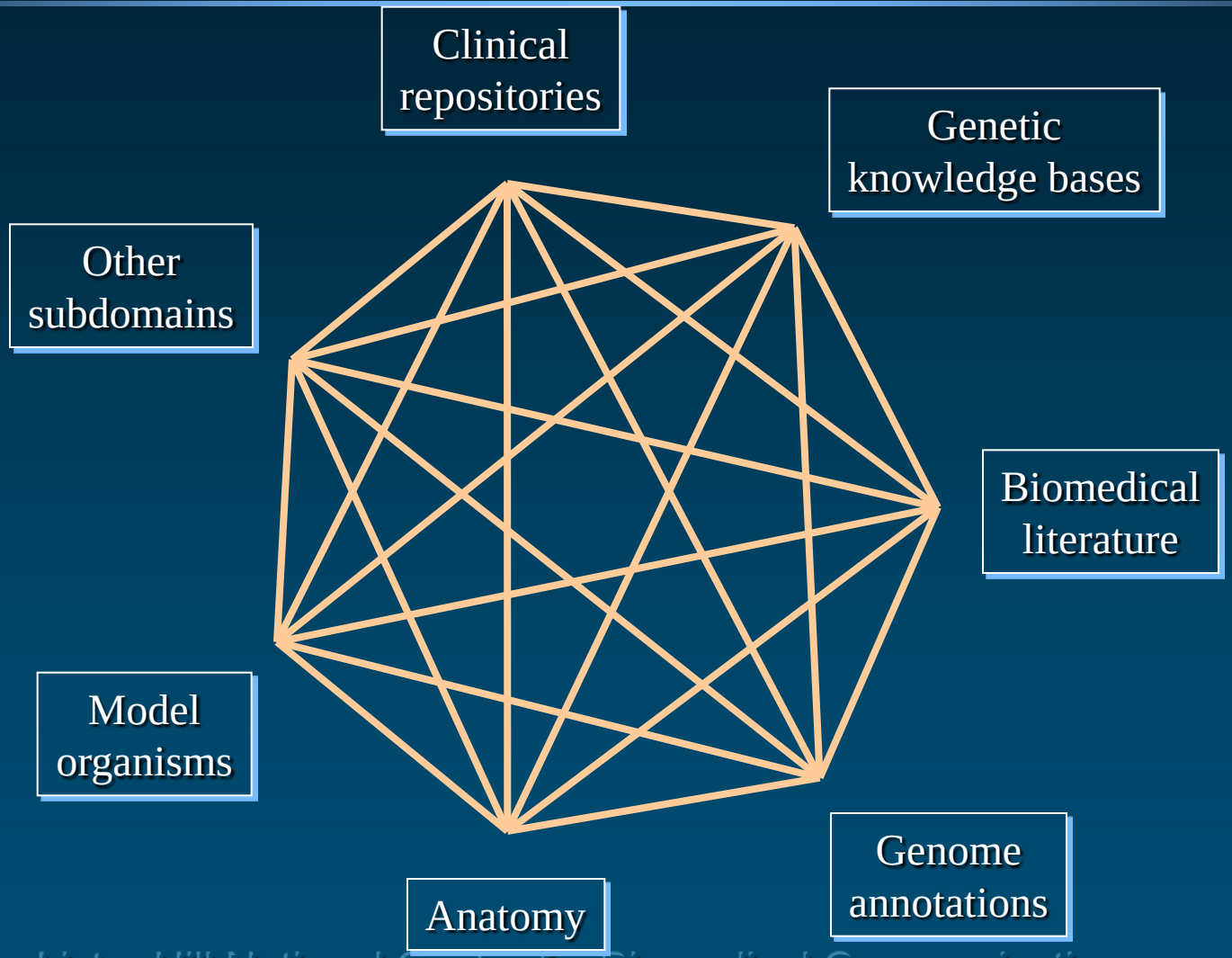
- Inter-concept relationships: hierarchies from the source vocabularies
- Redundancy: multiple paths
- One graph instead of multiple trees (multiple inheritance)



# Integrating subdomains



# Integrating subdomains



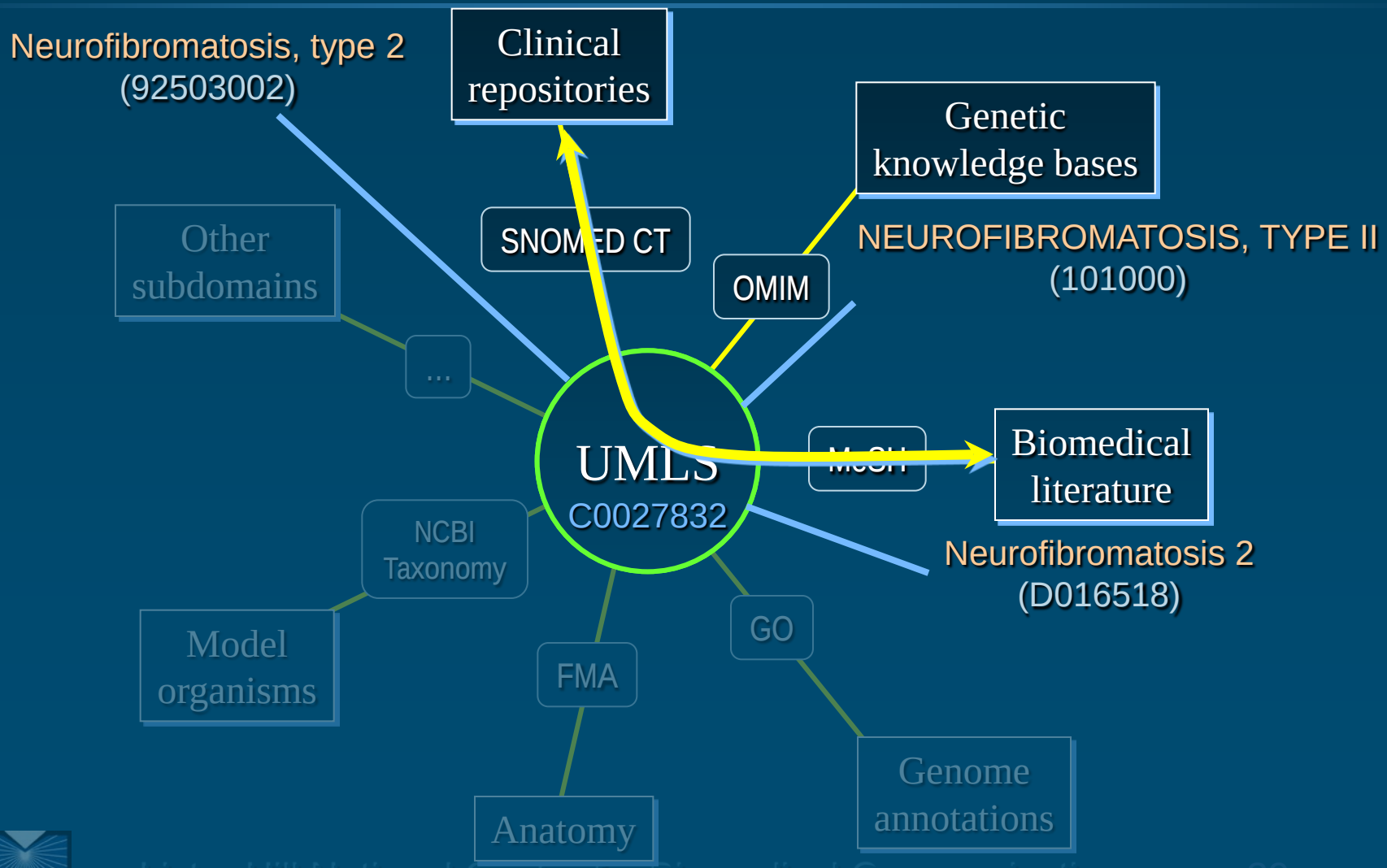
# Entity mention vs. resolution

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.

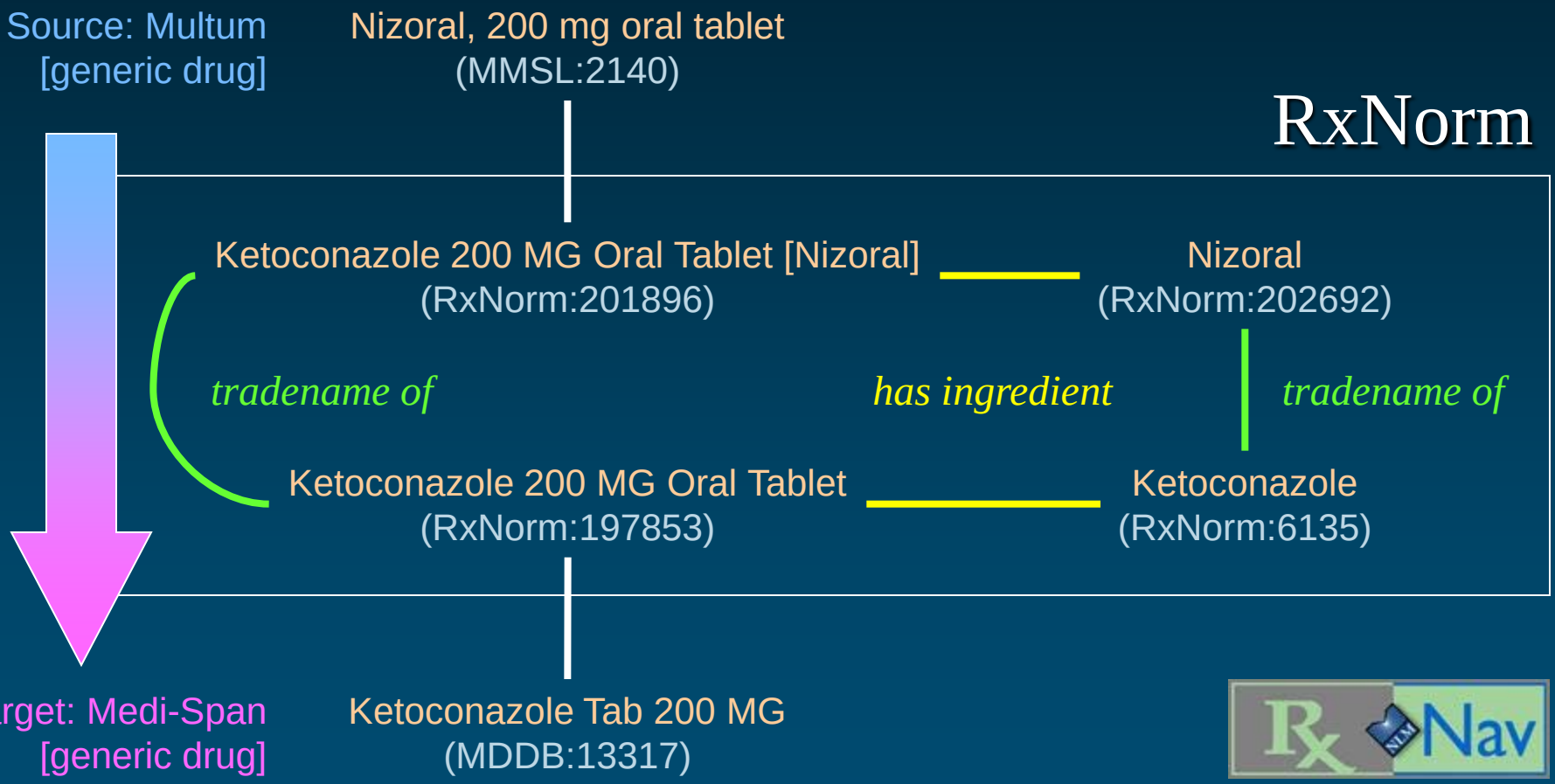
UMLS:C0027832
MeSH:D016518
SNOMEDCT:92503002
OMIM:101000

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/

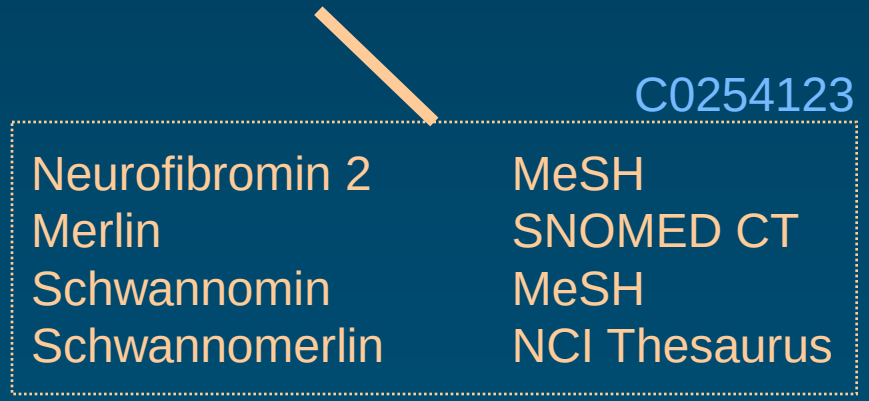
# MetaMap

- 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.

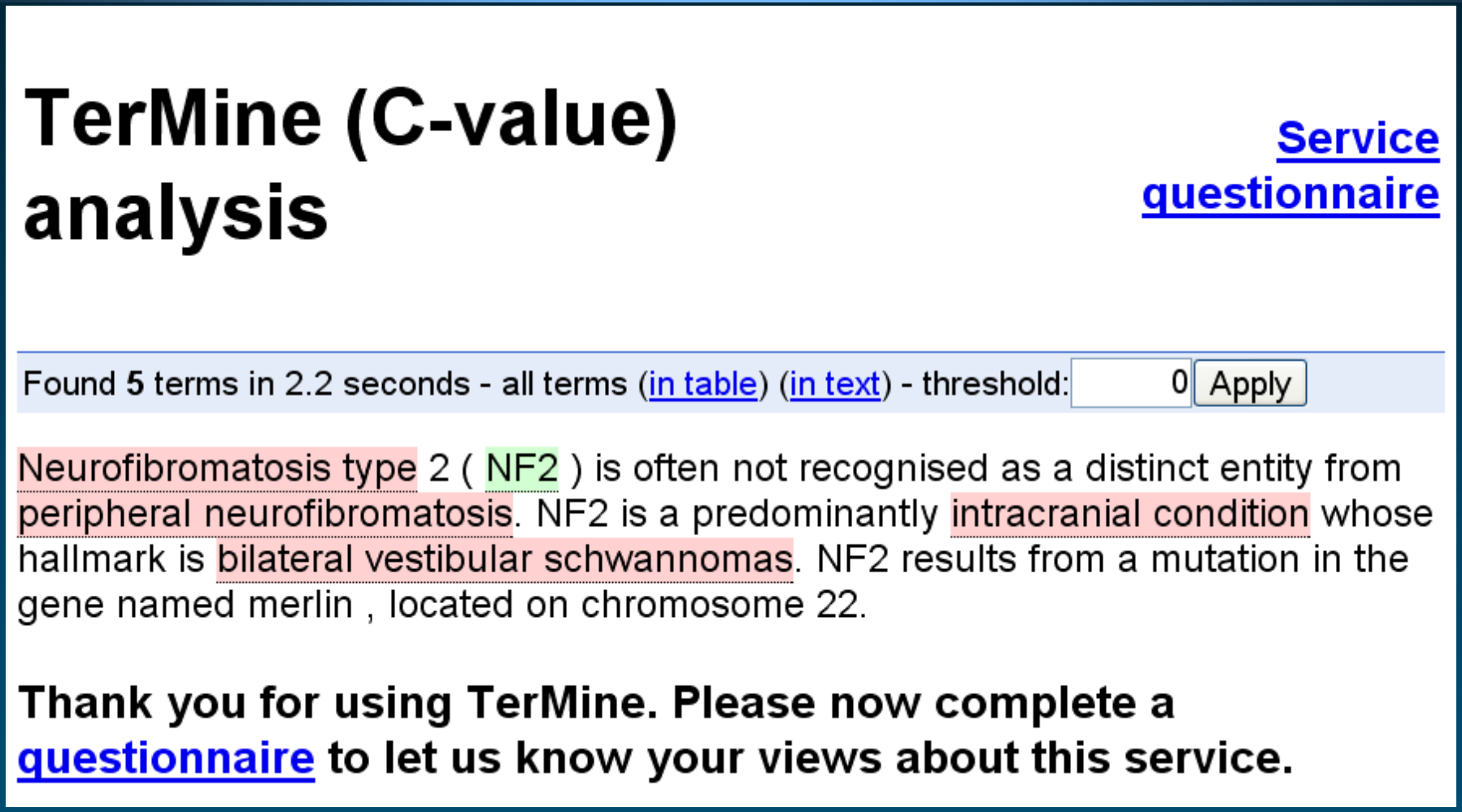
C0027832 C0027832 C0027832 C0027831 C0027832 C0027859 C0027832 C0026882 C0254123 C0008665



# Terminological resources

*Other resources*

# Other NER systems TerMine



## TerMine (C-value) analysis

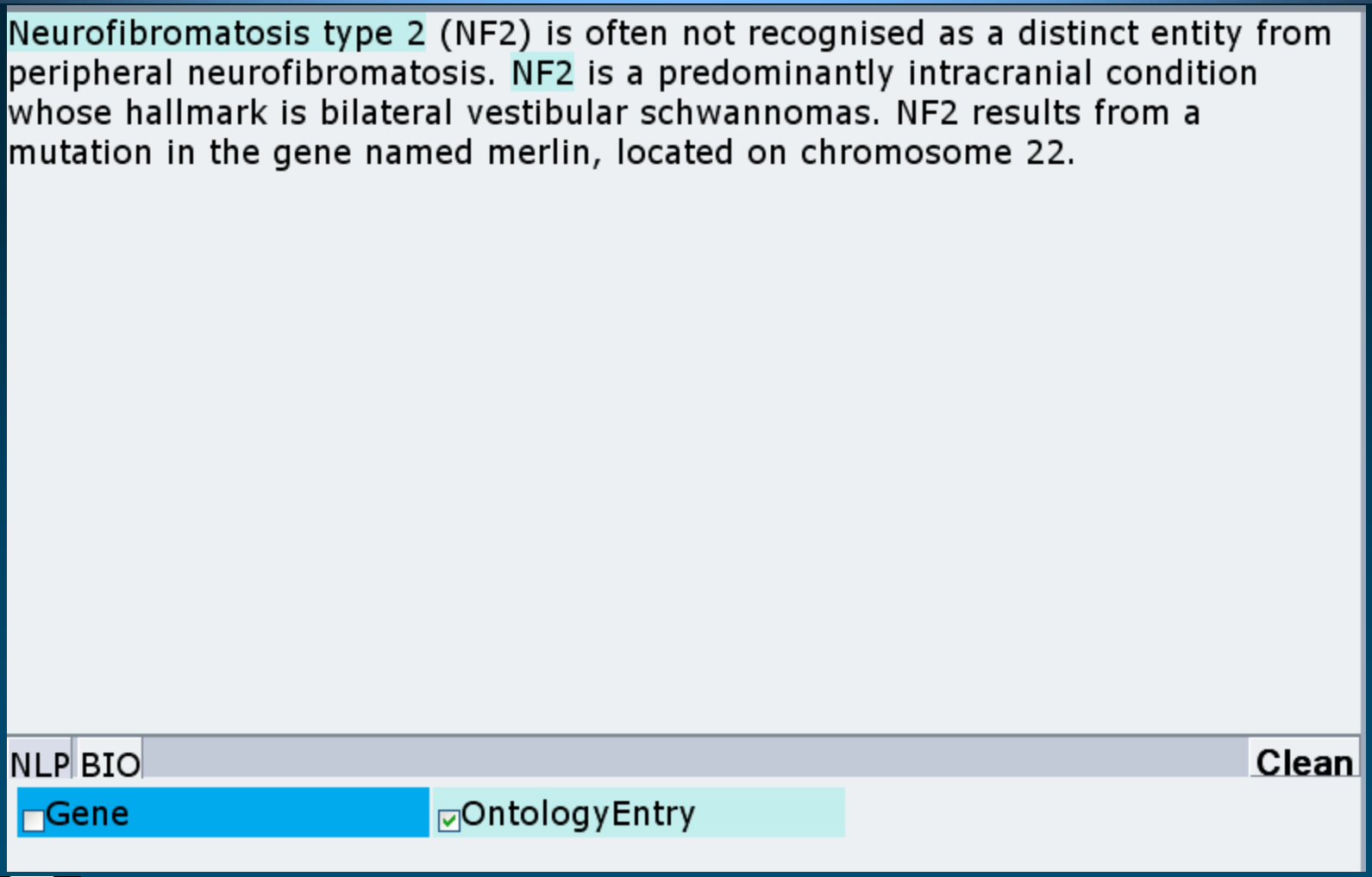
Service questionnaire

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.**

# Other NER systems DocProWI (Beta)



# Other NER systems 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

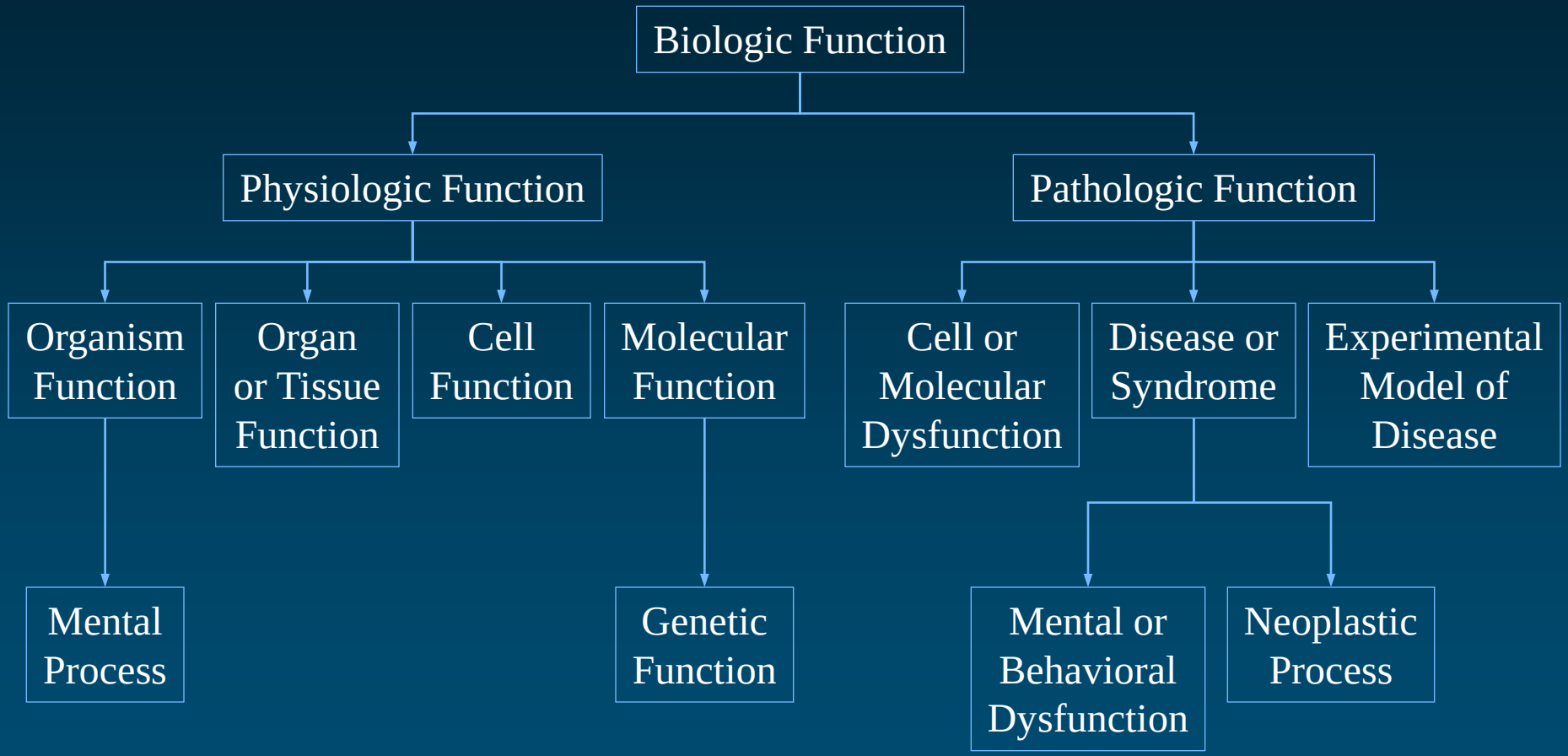
# Ontological resources

- 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 Smeantic Network: 133 types
  - Foundational Model of Anatomy: 70,000 classes

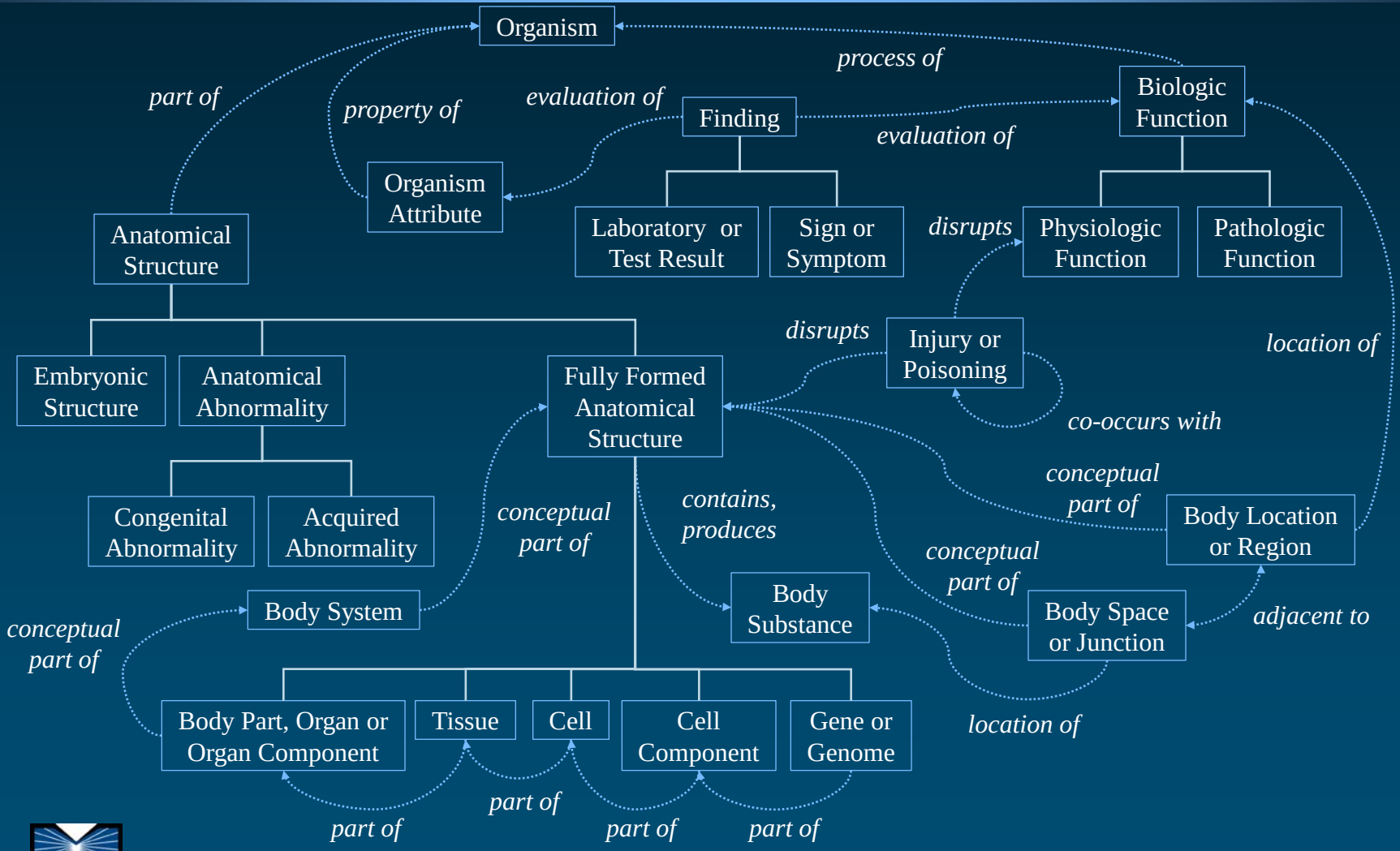
# Ontological resources

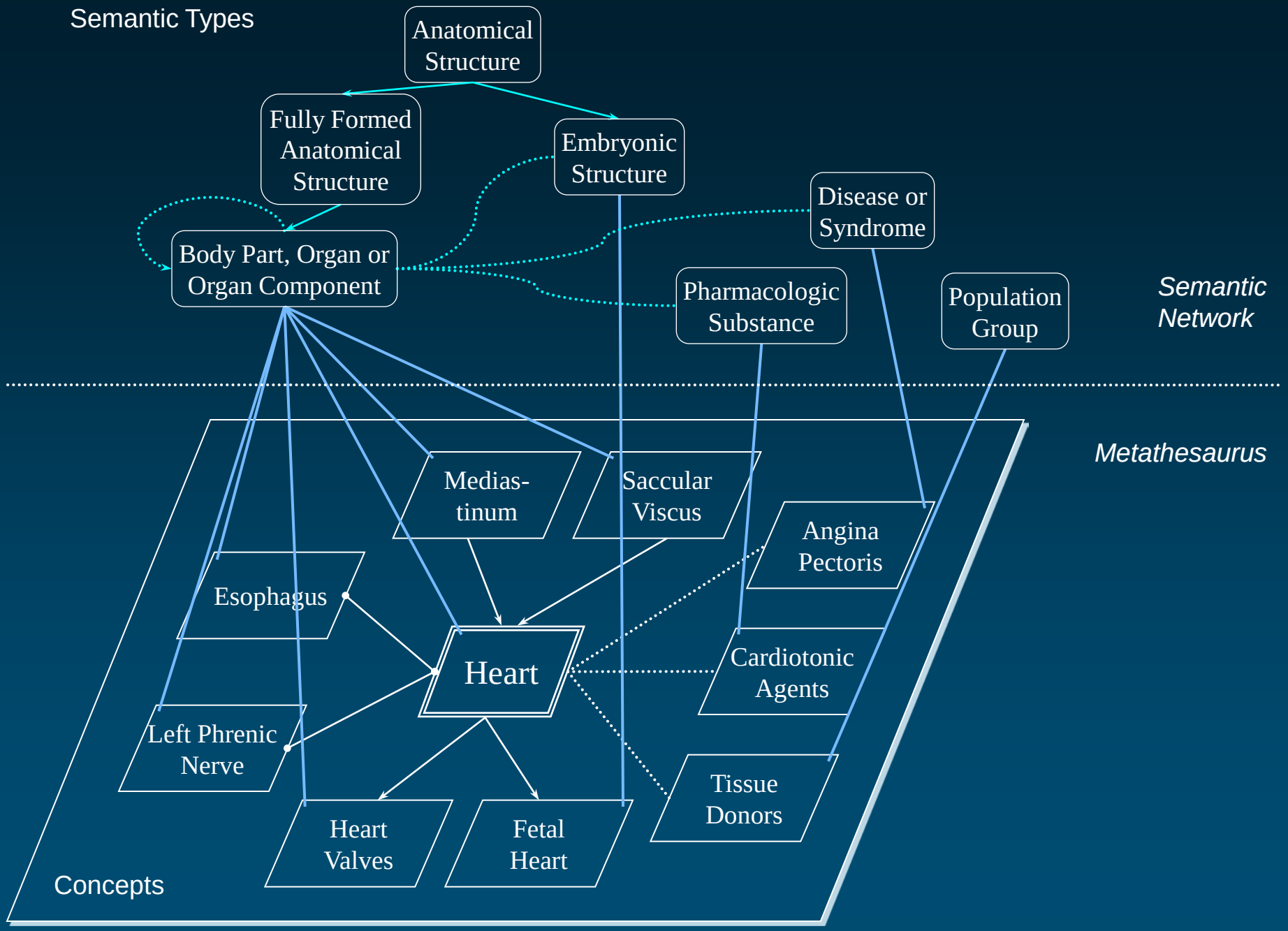
*UMLS Semantic Network*

# “Biologic Function” hierarchy (isa)



# Associative (non-isa) relationships



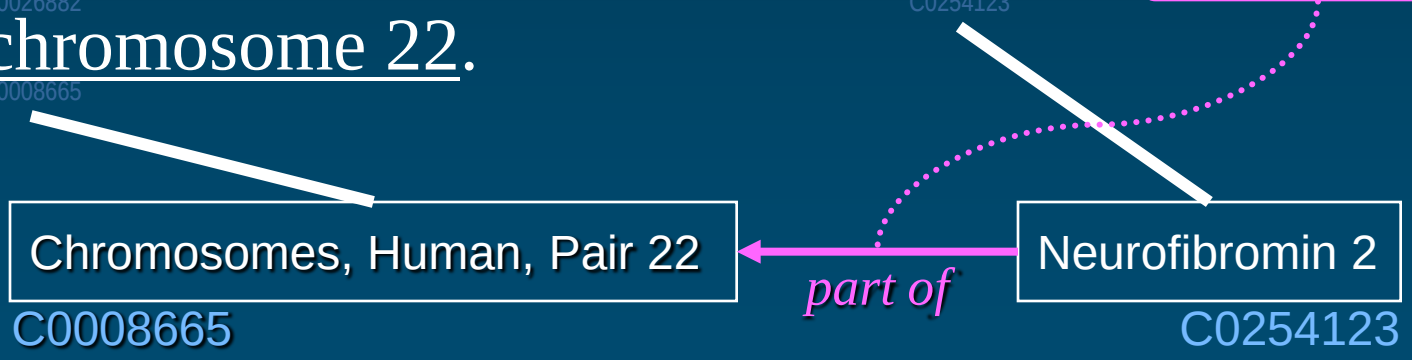

Semantic Types
Anatomical Structure
Fully Formed Anatomical Structure
Embryonic Structure
Disease or Syndrome
Body Part, Organ or Organ Component
Pharmacologic Substance
Population Group
Semantic Network
Metathesaurus
Medias-tinum
Saccular Viscus
Angina Pectoris
Esophagus
Heart
Cardiotonic Agents
Left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



# Ontological resources

*Other resources*

# Other ontological resources

- Ontologies
  - Top-level ontologies (e.g., BioTop)
  - Domain ontologies (e.g., FMA, SNOMED CT, NCI Thesaurus)
- Many information 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, …)

# Conclusions

# Conclusions

- Lexical and terminological resources enable entity recognition
  - Terminological resources enable entity *resolution*
- Terminological and ontological resources enable relation extraction

But…

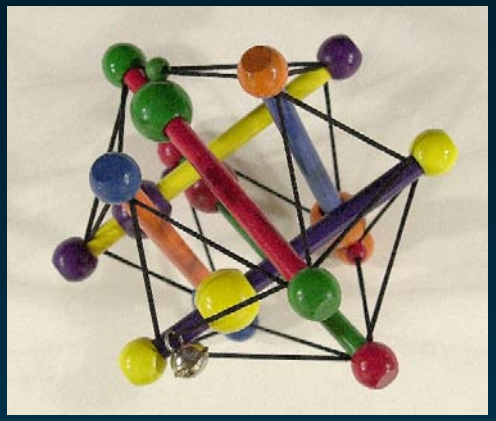
- Text mining techniques can also benefit
  - Specialized lexicons: NER based on machine learning techniques
  - Terminologies: term extraction / computational terminology
  - Ontologies: ontology population

# Future directions

- Information integration
  - Knowledge extracted from text
  - Knowledge in structured knowledge bases
- Ontologies for relations
  - In complement to ontologies for entities
  - To support reasoning
- W3C Health Care and Life Sciences Interest Group (Semantic Web)
  - http://www.w3.org/2001/sw/hcls/

# References


- 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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Web: mor.nlm.nih.gov

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