

# The NLM Indexing Initiative: Current Status and Role in Improving Access to Biomedical Information

*A Report to the Board of Scientific Counselors*

April 5, 2012

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# Outline

- **Introduction [Lan]**
- MetaMap [François]
- The NLM Medical Text Indexer (MTI) [Jim]
- Availability of Indexing Initiative Tools [Willie]
- Research and Outreach Efforts [Antonio, Caitlin, Lan]
- Summary and Future Plans [Lan]
- Questions



# MEDLINE Citation Example

NCBI Resources How To

PubMed

US National Library of Medicine  
National Institutes of Health

Display Settings:  Abstract

Clin Lab Haematol. 1992;14(4):281-7.

**Cigarette smoking increases factors for atherosclerosis.**

Kario K, Matsuo T, Nakao K.  
Department of Internal Medicine, Hyogo Prefectural A

**Abstract**  
To study the effects of cigarette smoking on platelet volume (MPV) and other platelet parameters in 142 subjects. The MPV and the platelet count were higher (MPV = 10.54, P < 0.05) when compared with the normal values in 8 smoking subjects in the atherosclerotic group. These results suggest that smoking may increase platelet activation and that megakaryocytes are activated to produce large platelets. Smoking may also contribute to the acceleration of atherosclerotic disease.

**Publication Types, MeSH Terms**

**Publication Types**  
Comparative Study  
Research Support, Non-U.S. Gov't

**MeSH Terms**  
Aged  
Aged, 80 and over  
Arteriosclerosis/blood\*  
Blood Platelets/ultrastructure\*  
Cell Size  
Female  
Hematopoiesis  
Humans  
Male  
Megakaryocytes/cytology  
Platelet Count  
Risk Factors  
Smoking/blood\*

Advanced

Send to:

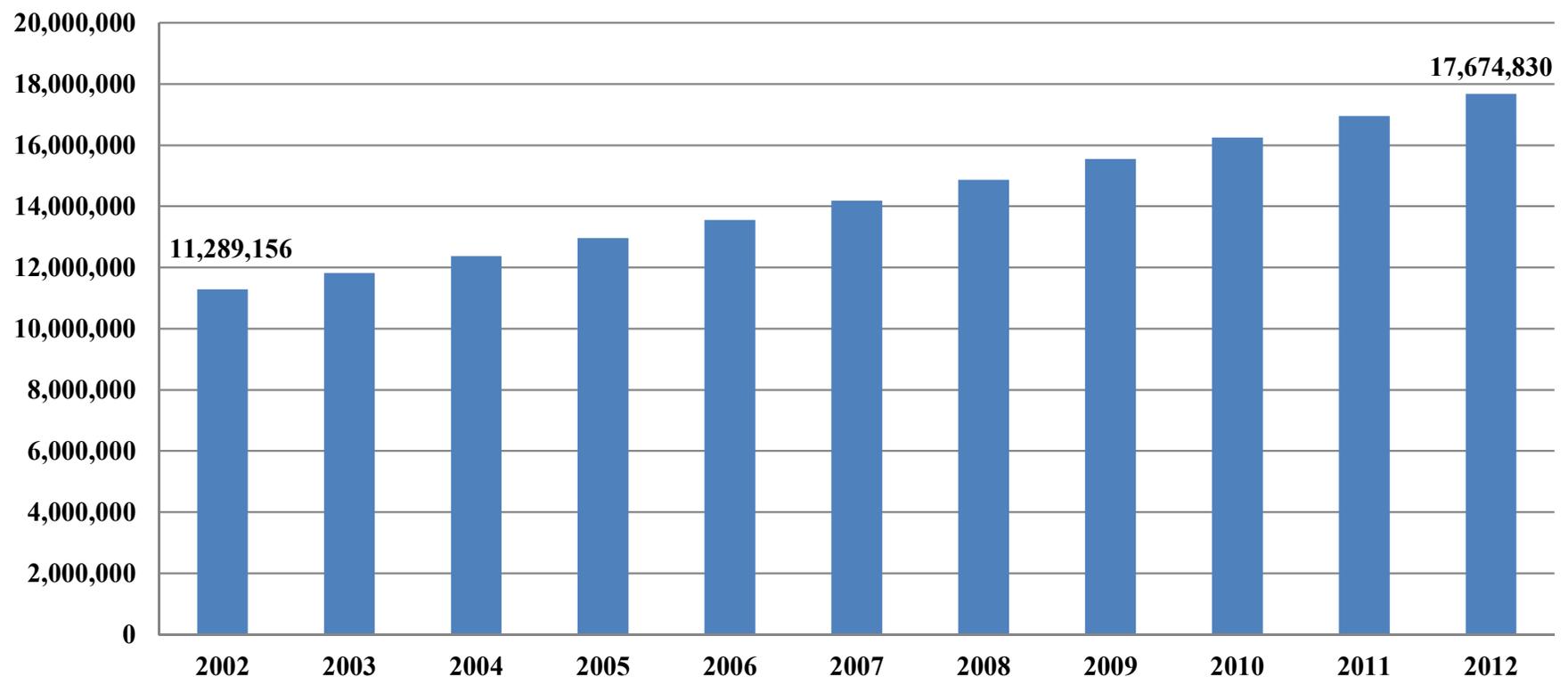
**Elderly patients with risk**

measured the mean platelet volume without atherosclerotic risk factors. The MPV was significantly lower in the atherosclerotic smokers (r = -0.54, P < 0.05). A 10% decrease of MPV was found in the atherosclerotic smokers (P < 0.05). These results suggest that subsequently an increase in MPV due to smoking may be considered as a risk factor for



# Introduction - Growth in MEDLINE

Indexed MEDLINE Sizes\* (2002 - 2012)



\* MEDLINE Baseline less OLDMEDLINE and PubMed-not-MEDLINE

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# The NLM Indexing Initiative (II)

- The need for MEDLINE indexing support
  - Increasing demand/costs for indexing in light of
  - Flat budgets
- One solution: creation of the NLM Indexing Initiative in 1996 resulting in NLM Medical Text Indexer (MTI)
- The Indexing Initiative today:
  - Identification of problems or needs followed by subsequent research
  - Production of MTI recommendations and other indexing
  - Opportunities for training and collaboration



# Medical Informatics Training Program Fellows

- **Antonio J. Jimeno-Yepes**, Postdoctoral Fellow: 2010-
- **J. Caitlin Sticco**, Library Associate Fellow: 2011-
- **Bridget T. McInnes**, Postgraduate Fellow: 2008  
PhD in 2009  
Current affiliation: Securboration
- **Aurélie Névéol**, Postdoctoral Fellow: 2006-2008  
Current affiliation: NCBI
- **Marc Weeber**, Postgraduate Fellow: 2000  
PhD in 2001  
Current affiliation: Personalized Media



## II Highlights from 2008

- Subheading attachment (Aurélie Névéol)
- Full text experiments (Cliff Gay)
- Initial Word Sense Disambiguation (WSD) method based on Journal Descriptor (JD) Indexing (Susanne Humphrey)
  - The *Journal of Cardiac Surgery* has JDs
  - ‘Cardiology’ and
  - ‘General Surgery’



## II Accomplishments since 2008

- The inauguration of MTI as a first-line indexer (MTIFL)
- Downloadable releases of MetaMap, most recently for Windows XP/7
- Significant improvement in MTI's performance due to
  - Technical improvements to MetaMap and MTI, but even more to
  - Close collaboration with LO Index Section
- More WSD methods with better performance
- The development of Gene Indexing Assistant (GIA)



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# MetaMap - Overview

- Purpose
- Foundations
- Complexity
- Processing Example
- Challenge of UMLS Metathesaurus Growth
- Significant New Features

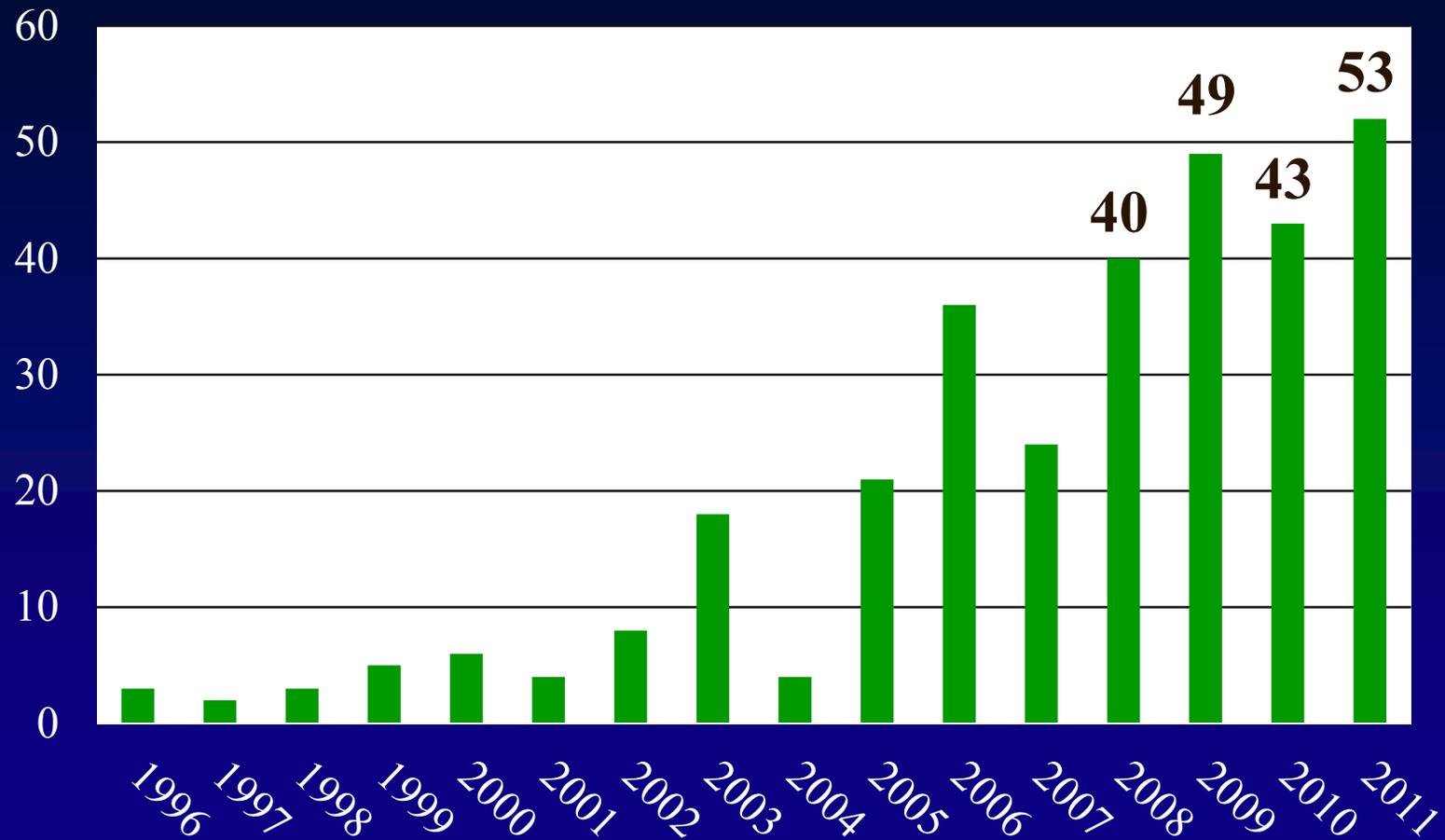


# MetaMap - Purpose

- Named-entity recognition
- Identify UMLS Metathesaurus concepts in text
- Important and difficult problem
- MetaMap's dual role:
  - Local: Critical component of NLM's Medical Text Indexer (MTI)
  - Global: Pre-eminent biomedical concept-identification application



# “MetaMap” in PubMed Central



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# MetaMap - Foundations

- Knowledge-intensive approach
- Natural Language Processing (NLP)
- Emphasize thoroughness over efficiency
- However...efficiency is still important!



# Complexity of Language - Synonymy

*Heart Attack*

*Myocardial infarction*

*Attack coronary*

*Heart infarction*

*Myocardial necrosis*

*Infarction of heart*

*AMI*

*MI*

C0027051: Myocardial Infarction



# Complexity of Language - Ambiguity

*cold*



C0009264: Cold Temperature

C0234192: Cold Sensation

C0009443: Common Cold

Ambiguity resolved by Word Sense Disambiguation



C0180860: Filters [mnob]  
 C0581406: Optical filter [medd]  
 C1522664: filter information process [inpr]  
 C1704449: Filter (function) [cnce]  
 C1704684: Filter Device Component [medd]

## Meta] Metathesa] Metathesauru UMLS Semantic Type

909	C0080306:	Inferior Vena Cava Filter	[medd]
804	C0180860:	Filter	[mnob]
804	C0581406:	Filter	[medd]
804	C1522664:	Filter	[inpr]
804	C1704449:	Filter	[cnce]
804	C1704684:	Filter	[medd]
	C0038257:	Stent, device	[medd]
	C1705817:	Stent Device Component	[medd]
673	C0042460:	Vena caval	[bpoc]
637	C0038257:	Stent	[medd]
637	C1705817:	Stent	[medd]
637	C0447122:	Vena	[bpoc]



# MetaMap - Processing Example

## *Inferior vena caval stent filter*

Final Mappings (subsets of candidate sets):

### Meta Mapping (911)

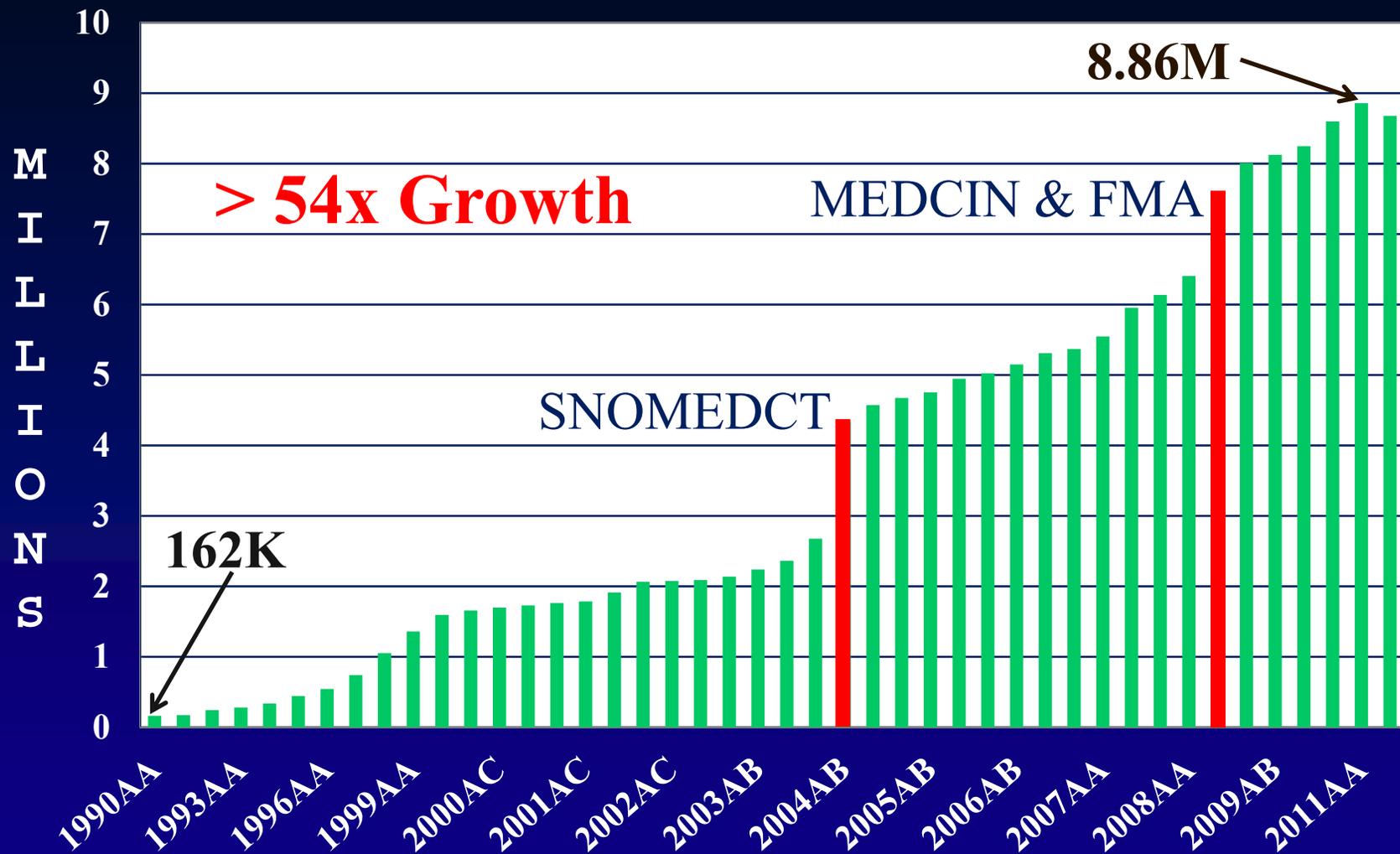
909 C0080306: Inferior Vena Cava Filter [medd]  
637 C1705817: Stent [medd]

### Meta Mapping (911):

909 C0080306: Inferior Vena Cava Filter [medd]  
637 C0038257: Stent [medd]



# Metathesaurus String Growth 1990-2011



# An Especially Egregious Example

- Phrase from PMID 10931555

*protein-4 FN3 fibronectin type III domain GSH glutathione GST glutathione S-transferase hIL-6 human interleukin-6 HSA human serum albumin IC(50) half-maximal inhibitory concentration Ig immunoglobulin IMAC immobilized metal affinity chromatography K(D) equilibrium constant*

- Extreme, but not atypical
- MetaMap identifies 99 concepts
- Mappings are subsets of candidates: Up to  $2^{99}$  mappings
- Would require  $10^{21}$  TB of memory!
- **Algorithmic Solutions**



# Solution - Pruning the Candidate Set

## *Inferior vena caval stent filter*

909	C0080306:	Inferior Vena Cava Filter	[medd]
804	C0180860:	Filter	[mnob]
804	C0581406:	Filter	[medd]
804	C1522664:	Filter	[inpr]
804	C1704449:	Filter	[cnce]
804	C1704684:	Filter	[medd]
804	C1875155:	FILTER	[medd]
717	C0521360:	Inferior vena caval	[blor]
673	C0042460:	Vena caval	[bpoc]
637	C0038257:	Stent	[medd]
637	C1705817:	stent	[medd]
637	C0447122:	Vena	[bpoc]



# Results of Algorithmic Improvements

- 2010 MEDLINE baseline: 146 troublesome citations
- Original runtime > 12 hours per citation
- Improved runtime ~ 12.3 seconds per citation
- **350,000%** improvement for problematic citations

Efficiency improvements across MEDLINE baseline:

- 2004 MEDLINE Baseline (12.5M citations): 6 months
- 2012 MEDLINE Baseline (20.5M citations): 8 days



# Significant New MetaMap Features

## Solutions for problems

- Default output difficult to post-process:
  - XML output
- MetaMap originally developed for literature, not clinical:
  - Wendy Chapman's NegEx (negation detection)
  - User-Defined Acronyms



# Literature: Author-Defined Acronyms

Acronyms often defined by authors in literature:

- *Trimethyl cetyl ammonium pentachlorophenate* (TCAP) and fatty acids as antifungal agents.
- *Reticulo-endothelial immune serum* (REIS) in a globulin fraction
- The bacteriostatic action of *isonicotinic acid hydrazid* (INAH) on tubercle bacilli
- the *interstitial latero-dorsal hypothalamic nucleus* (ILDHN) of the female guinea pig
- The *adrenocorticotropic hormone* (ACTH) of the anterior pituitary.

MetaMap replaces acronyms' short form with their long form



# Clinical Text: Undefined Acronyms

Acronyms rarely defined in clinical text:

- He underwent a **CABG** and **PTCA** in 2008.
- EKGs show a **RBBB** with **LAFB** with 1st **AV** block
- Sequential **LIMA** to the diagonal and **LAD** and sequential **SVG** to the **PLB** and **PDA** and **SVG** to **IM** grafts were placed

**post-transplantation lymphoproliferative disorder** **LAD** and **SVG** to **D1** patent

- treatment for **PTLD** with Rituxan versus **CHOP**

MetaMap **cyclophosphamide, hydroxydaunomycin, Oncovin, and prednisone**

Allows customizations tailored to specific needs



# User-Defined Acronyms (UDAs)

Customize UDAs for radio

- **CAT** | Computerized A
- **PET** | Positron Emiss

Otherwise.....

- C0031268: Pet (Pet Ani
- C1456682: Pets (Pet He
- C0007450: Cat (Felis c
- C0325090: Cat (Felis s
- C0524517: Cat (Genus F
- C0325089: cats (Family



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# The NLM Medical Text Indexer (MTI)

- Overview
- Uses
- MTI as First-Line Indexer (MTIFL)
- Performance



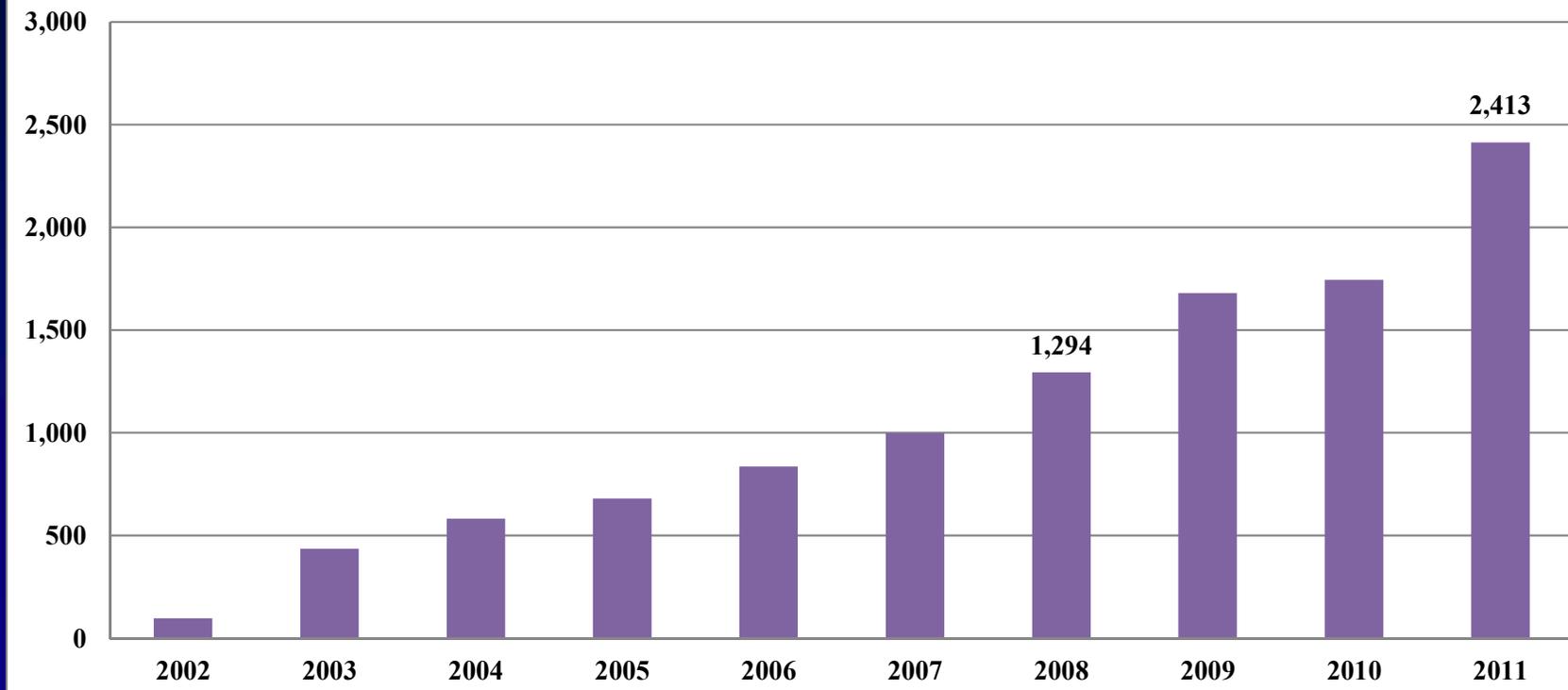
# MTI - Overview

- Summarizes input text into an ordered list of MeSH Headings
- In use since mid-2002
- Developed with continued Index Section collaboration
- Uses article Title and Abstract
- Provides recommendations for **96%** of indexed articles
- Indexer consulted for **50%** of indexed articles



# MTI Usage

Average Daily Indexer Requests to MTI (2002 - 2011)



# MTI - Uses

- Assisted indexing of Index Section journal articles
- Assisted indexing of Cataloging and History of Medicine Division records
- Automatic indexing of NLM Gateway meeting abstracts
- First-line indexing (MTIFL) since February 2011
- Also available to the Community
  - 45,000 requests (2011)



# Data Creation and Management System

DCMS IssueList ArticleList Article Index Gene View Help Manual Logoff

Indexing

<< >> 1 of 1 in: Neuron. 2007 Feb 15;53(4) PubMed

Climbing the scaffolds of Parkinson's disease

\* 5 MeSH / 0 IM QuickEdit

JOURNAL ARTICLE (PT)

- Parkinson Disease/GENET/PATHOL
- alpha-Synuclein/GENET/METAB
- Neurodegenerative Disorders/ETIOL/PATHOL
- Lewy Bodies/METAB/PATHOL
- Protein Folding

- Parkinson Disease /  COMPL /  GENET /  PATHOL
- alpha-Synuclein /  GENET /  METAB
- Neurodegenerative Disorders /  ETIOL /  METAB /  PATHOL
- Lewy Bodies /  METAB /  PATHOL
- Alzheimer's Disease /  COMPL /  PATHOL
- Parkinsonian Disorders /  COMPL
- Ubiquitin-Protein Ligases /  METAB /  PHYSIOL
- Dementia /  COMPL
- Nitroquinolines
- Dopamine Plasma Membrane Transport Proteins /  METAB
- Brain Diseases /  COMPL
- tau Proteins /  METAB
- Proteins /  METAB
- Protein Folding

ags

SAP

Proteins /  METAB

Protein Folding



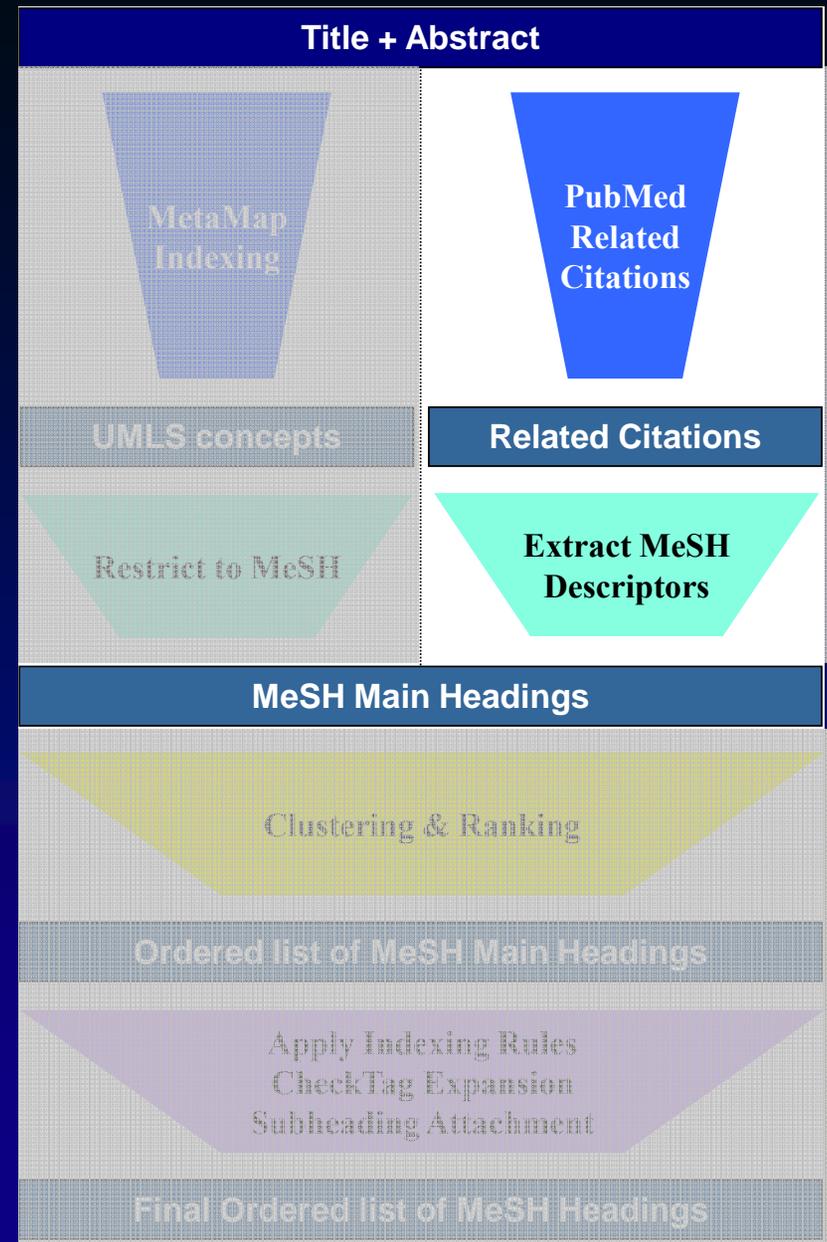
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# MTI

- MetaMap Indexing – Actually found in text
- Restrict to MeSH – Maps UMLS Concepts to MeSH
- PubMed Related Citations – Not necessarily found in text



# PubMed Query Example

NCBI Resources How To My NCBI Sign In

PubMed.gov  
US National Library of Medicine  
National Institutes of Health

PubMed 1478007[uid] Search

RSS Save search Limits Advanced Help

Display Settings: Abstract Send to:

Clin Lab Haematol. 1992;14(4):281-7.

**Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for atherosclerosis.**

Kario K, Matsuo T, Nakao K.  
Department of Internal Medicine, Hyogo Prefectural Awaji Hospital, Japan.

**Abstract**  
To study the effects of cigarette smoking and atherosclerosis on platelet size, we measured the mean platelet volume (MPV) and other platelet parameters in 142 elderly smokers and nonsmokers with or without atherosclerotic risk factors. The MPV and the platelet count were highest and their inverse correlation was strongest in the atherosclerotic smokers ( $r = 0.54$ ,  $P < 0.05$ ) when compared with the nonsmoking and non-atherosclerotic groups. A 10% decrease of MPV was found in 8 smoking subjects in the atherosclerotic group, who successfully discontinued smoking ( $P < 0.05$ ). These results suggest that smoking may increase platelet consumption in atherosclerotic vessels and that subsequently megakaryocytes are activated to produce larger platelets, which are more active. Thus, an increase in MPV due to smoking may also contribute to the acceleration of atherosclerosis and should be considered as a risk factor for atherosclerotic disease.

PMID: 1478007 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms

LinkOut - more resources

**Related citations**

- Could mean platelet volume be a predictive marker? [Med Sci Monit. 2005]
- [The effect of smoking on mean platelet volume an [Anadolu Kardiyol Derg. 2008]
- Platelet activation in patients with Familial Mediterranean [Platelets. 2008]
- Review Passive smoking, platelet function a [Wien Klin Wochenschr. 1996]
- Review From precursor to product: how do megakaryo [Prog Clin Biol Res. 1986]

See review s...  
See all...

**Search details**

1478007 [uid]



# MTI

- MetaMap Indexing – Actually found in text

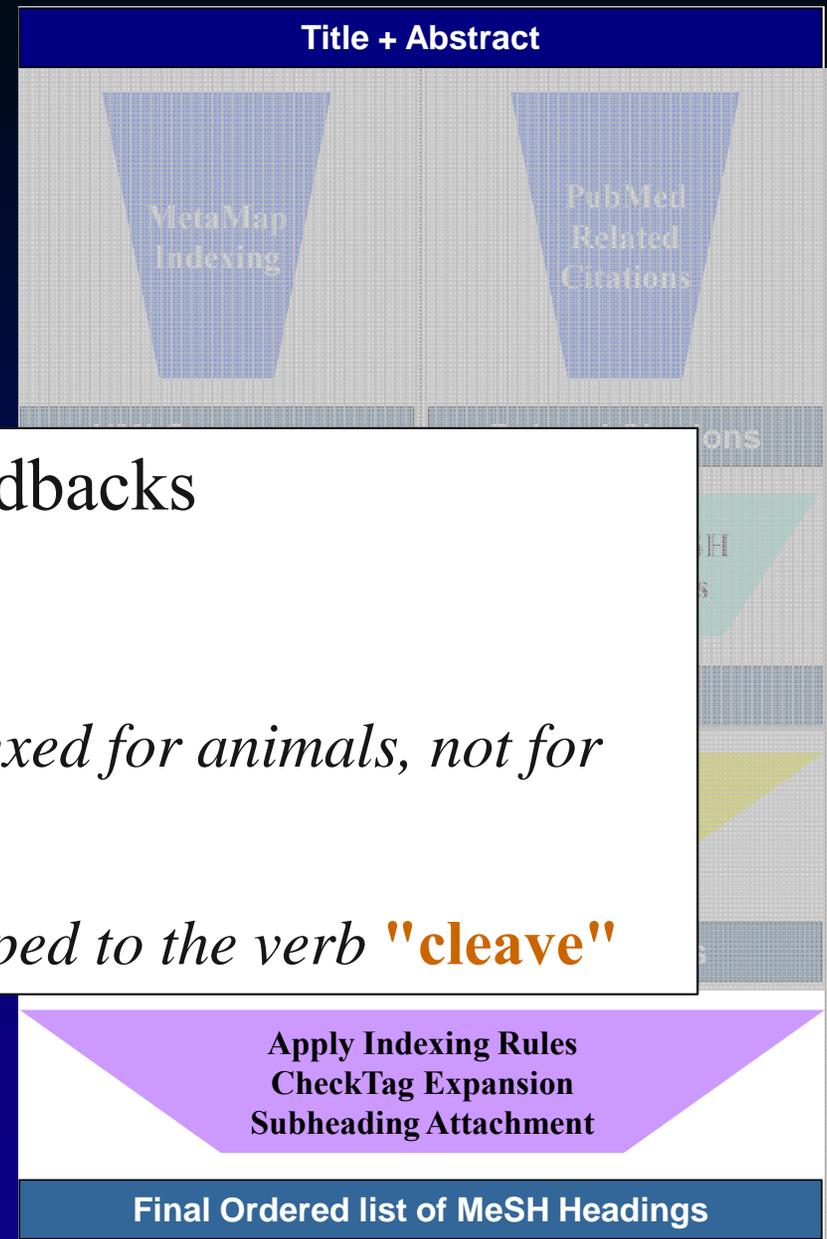
Received **2,330** Indexer Feedbacks

- Incorporated **40%** into MTI

March 20, 2012

- **Hibernation** *should only be indexed for animals, not for "stem cell hibernation"*

**Clove** (*spice*) *should not be mapped to the verb "cleave"*



M

TI - Cigaret

AB - To study the effects of cigarette smoking and atherosclerosis on platelet size, we measured the mean platelet volume (MPV) and other platelet parameters in 142 elderly smokers and nonsmokers with or without atherosclerotic risk factors. The MPV and the platelet count were

TI - Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for atherosclerosis.

AB - To study the effects of cigarette smoking and atherosclerosis on platelet size, we measured the mean platelet volume (MPV) and other platelet parameters in 142 elderly smokers and nonsmokers with or without atherosclerotic risk factors. The MPV and the platelet count were

osis.

platelet  
therosclerotic risk  
therosclerotic  
decrease of  
(05).  
ntly

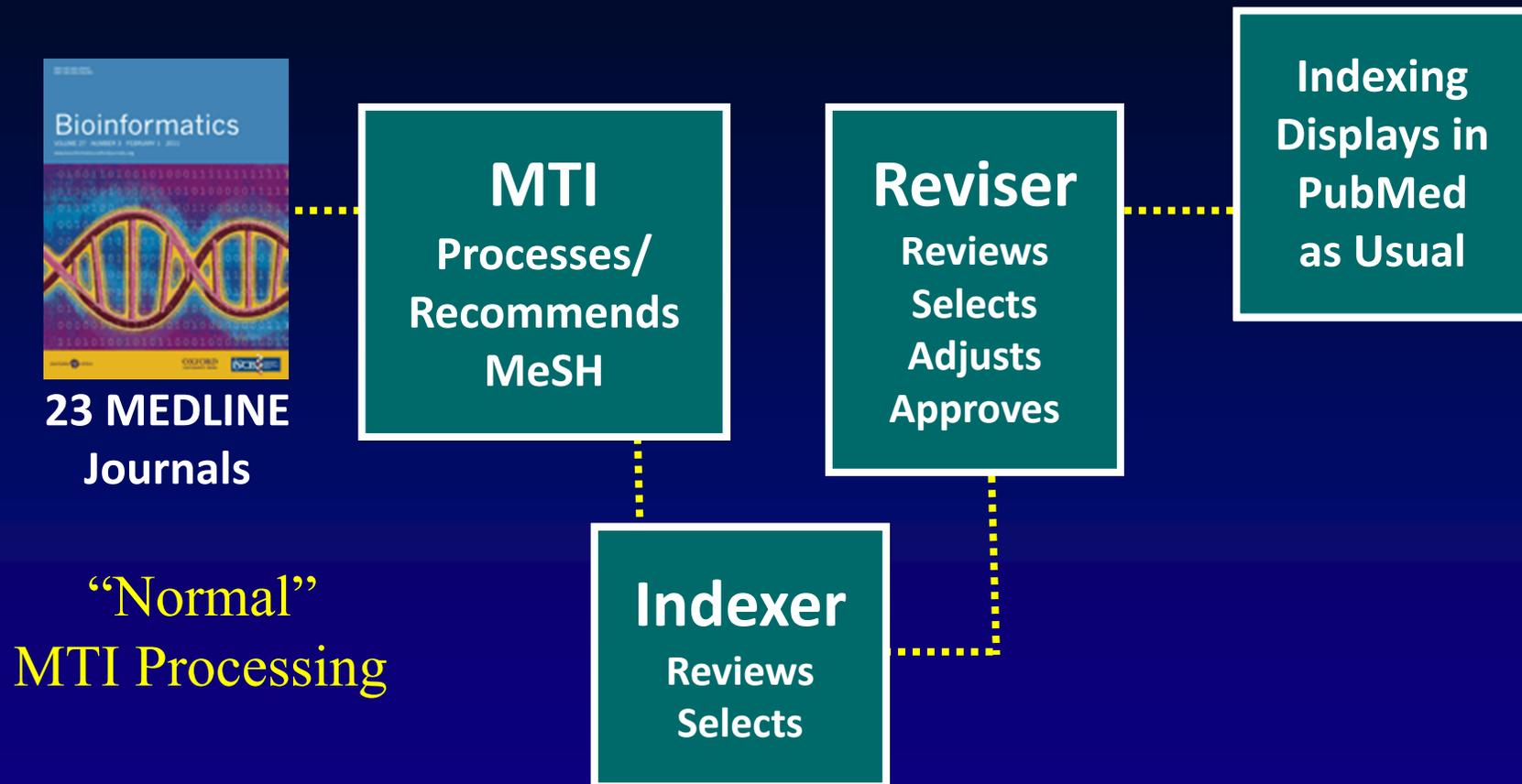
Aged  
Aged, 80 and over  
Arteriosclerosis/blood\*  
Blood Platelets/ultrastructure\*  
Cell Size  
Female  
Hematopoiesis  
Humans  
Male  
Megakaryocytes/cytology  
Platelet Count  
Risk Factors  
Smoking/blood\*

Indexed	MTI
Aged	Aged
Aged, 80 and over	Humans
Arteriosclerosis/blood*	Platelet (ET for Blood Platelets)
Blood Platelets/ultrastructure*	Platelet Count
Cell Size	Atherosclerosis
Female	Risk Factors
Hematopoiesis	Platelet Activation
Humans	Megakaryocytes
Male	Cigarette Smoking (ET for Smoking)
Megakaryocytes/cytology	Erythrocytes
Platelet Count	Blood Cell Count
Risk Factors	Cell Size (PRC Only)
Smoking/blood*	

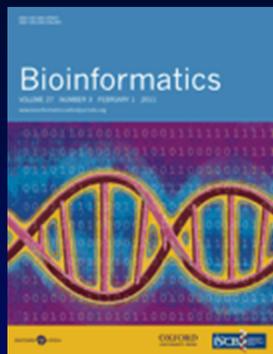
PMID: 147



# MTI as First-Line Indexer (MTIFL)



# MTI as First-Line Indexer (MTIFL)



23 MEDLINE  
Journals

MTIFL  
MTI Processing

**MTI**  
Processes/  
Indexes  
MeSH

**Reviser**  
Reviews  
Selects  
Adjusts  
Approves

Indexing  
Displays in  
PubMed  
as Usual

Index  
Section  
Compares  
MTI and  
Reviser  
Indexing

**Indexer**  
Reviews  
Selects



# MTIFL

- Experiments in 2010 led by Marina Rappaport
  - Microbiology, Anatomy, Botany, and Medical Informatics journals
- Initial experiment involved both Indexers and MTI
  - Provided baseline timings and performance

	Indexer	MTIFL	Diff
Number of Articles	609	668	
Average Total Minutes	12.05	14.37	+2.32
Average MHs	11.12	24.75	+13.63

- Identified challenges (and opportunities)
    - Publication Types
    - Chemical Flags
    - Functional annotation of genes
- } Manually added by indexer



# MTIFL

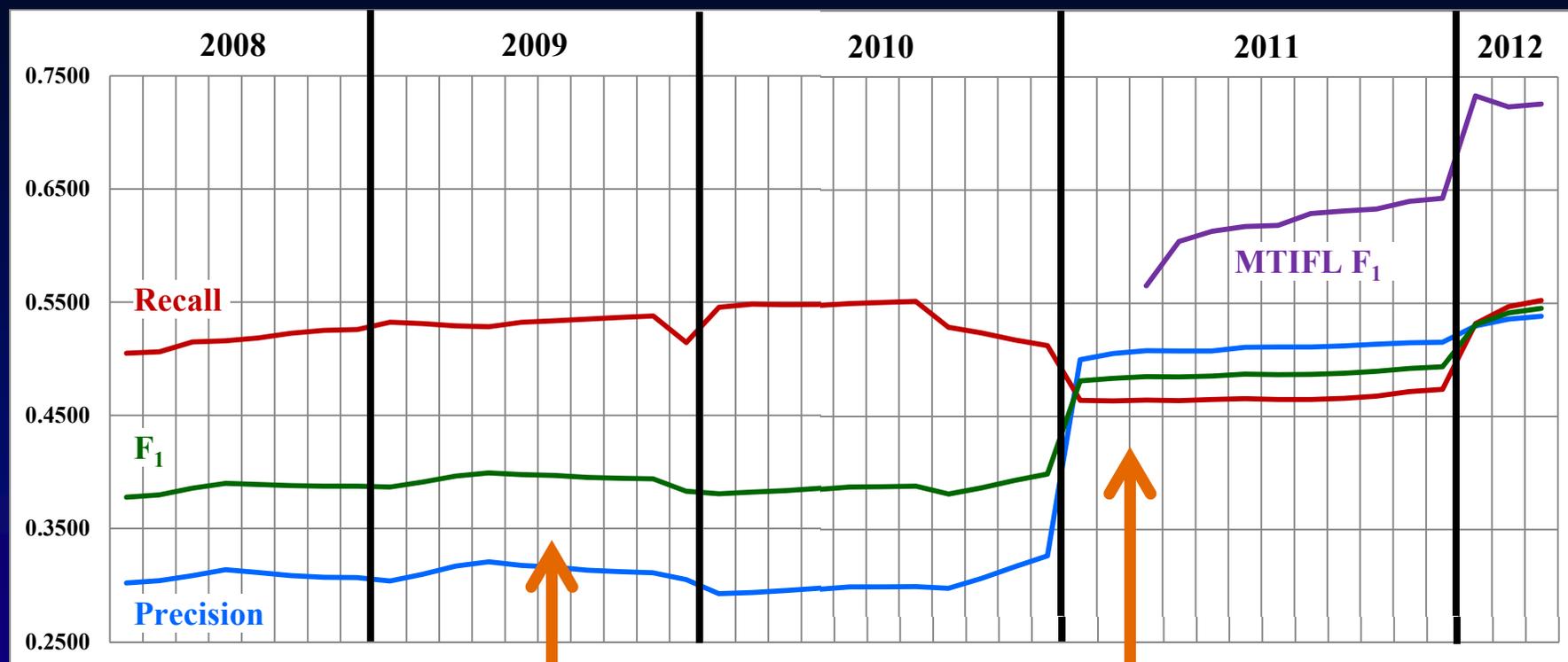
- Follow-on experiments focused on reducing MTI revision time:
  - Reduce the number of MTI indexing terms
  - Focus on journals with few/no Gene Annotation or Chemical Flags

	Initial		Final	MTIFL Diff
	Indexer	MTIFL	MTIFL	
Average Total Minutes	12.05	14.37	10.01	-4.36
Average MHs	11.12	24.75	8.58	-16.17

- MTI revision time **2.04 minutes faster** than Indexer revised time (**10.01 minutes** vs **12.05 minutes**)
- Pilot project started with 14 journals, expanded to 23 in 2011



# MTI - How are we doing?



Fruition of 2011 Changes Precision versus Recall



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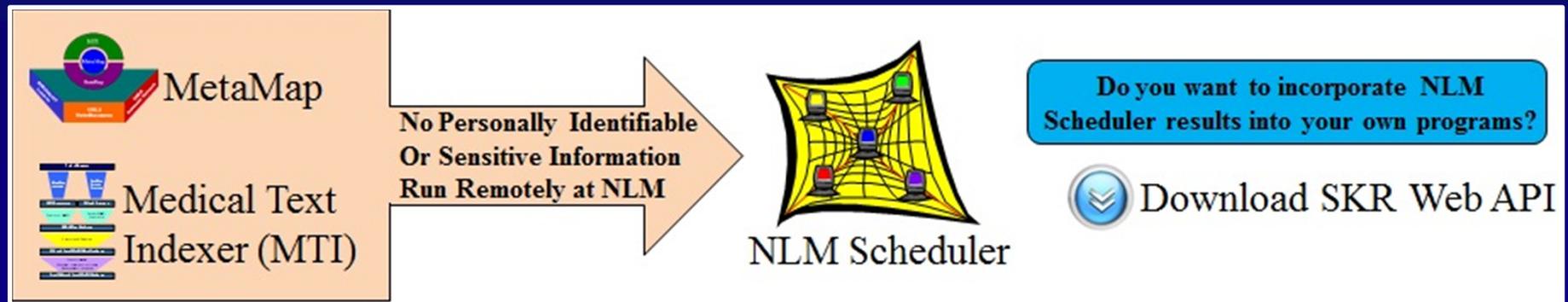
# Availability of Indexing Initiative Tools

- Remote Access
  - Web
  - API
- Local Installation
  - Linux
  - Mac OS/X
  - Windows XP/7



# Remote Access

- Interactive
  - Small input data (for testing, etc.), immediate results
- Batch
  - Large input data processed using a large pool of computing resources



# Interactive MetaMap

Users are responsible for compliance with the [UMLS Copyright Restrictions](#)

User: wjrogers: NLM » LHNCBC » SKR

## Text to be Processed:

Cigarette smoking increases patients with risk factors

To study the effects of cigarette smoking and atherosclerosis on platelet size, we measured the mean platelet volume (MPV) and other platelet parameters in 142 elderly smokers and nonsmokers with or without atherosclerotic risk factors. The MPV and the platelet count were highest and their inverse correlation was strongest in the atherosclerotic smokers ( $r = 0.54$ ,  $P < 0.05$ ) when compared with the nonsmoking and non-atherosclerotic groups. A 10% decrease of MPV was found in 8 smoking subjects in the atherosclerotic group, who

Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for atherosclerosis.

To study the effects of cigarette smoking and atherosclerosis on platelet size, we measured the mean platelet volume (MPV) and other platelet parameters in 142 elderly smokers and nonsmokers with or without atherosclerotic risk factors. The MPV and the platelet count were highest and their inverse correlation was strongest in the atherosclerotic smokers ( $r = 0.54$ ,  $P < 0.05$ ) when compared with the nonsmoking and non-atherosclerotic groups. A 10% decrease of MPV was found in 8 smoking subjects in the atherosclerotic group, who

User Defined Acronyms File (--UDA) [Optional]: 

Browse...

Knowledge Source (-Z): 1112 (11/12 Transiti

## Output Display

- Tagger Output (-T)
- Hide Header Info 
- Variants (-v)
- Hide Plain Syntax (-p)
- Syntax (-x)
- Hide Candidates (-c)
- Number Candidates (-n)
- Number Mappings (-f) 
- Hide Semantic Types (-s)
- Show CUIs (-l)
- Hide Mappings (-m)

## Output Display

- Tagger Output (-T)
- Hide Header Info 
- Variants (-v)
- Hide Plain Syntax (-p)
- Syntax (-x)
- Hide Candidates (-c)
- Number Candidates (-n)
- Number Mappings (-f) 
- Hide Semantic Types (-s)
- Show CUIs (-l)

- Unique Acronym/Abbreviation Variants Only (-u)

Strict Model (-A) 

## Browse Mode Options

Term Processing (-z)  
Allow Overmatches (-o)

## Misc. Options

Allow Concept Gaps (-g)  
Display Phrases Only  
Dynamic Variant Generation



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# Interactive MetaMap Results

## User Information:

Run Time: 03/26/2012 10:09:01

```
M >>>> Mappings
M Meta Mapping (1000):
L   1000 C0239059:cigarette smoking (Cigarette smoke (substance)) [Hazardous or Poisonous Substance]
L Meta Mapping (1000):
L   1000 C0700219:Cigarette Smoking (Cigarette smoking behavior) [Individual Behavior]
L <<<< Mappings
L >>>> Mappings
L Meta Mapping (1000):
L   1000 C0442805:increases (Increase) [Functional Concept]
L <<<< Mappings
L >>>> Mappings
L Meta Mapping (1000):
L   1000 C0200665:Mean platelet volume (Platelet mean volume determination (procedure)) [Laboratory Procedure]
L Meta Mapping (1000):
L   1000 C0344388:Mean platelet volume (Platelet mean volume finding) [Finding]
L <<<< Mappings
```

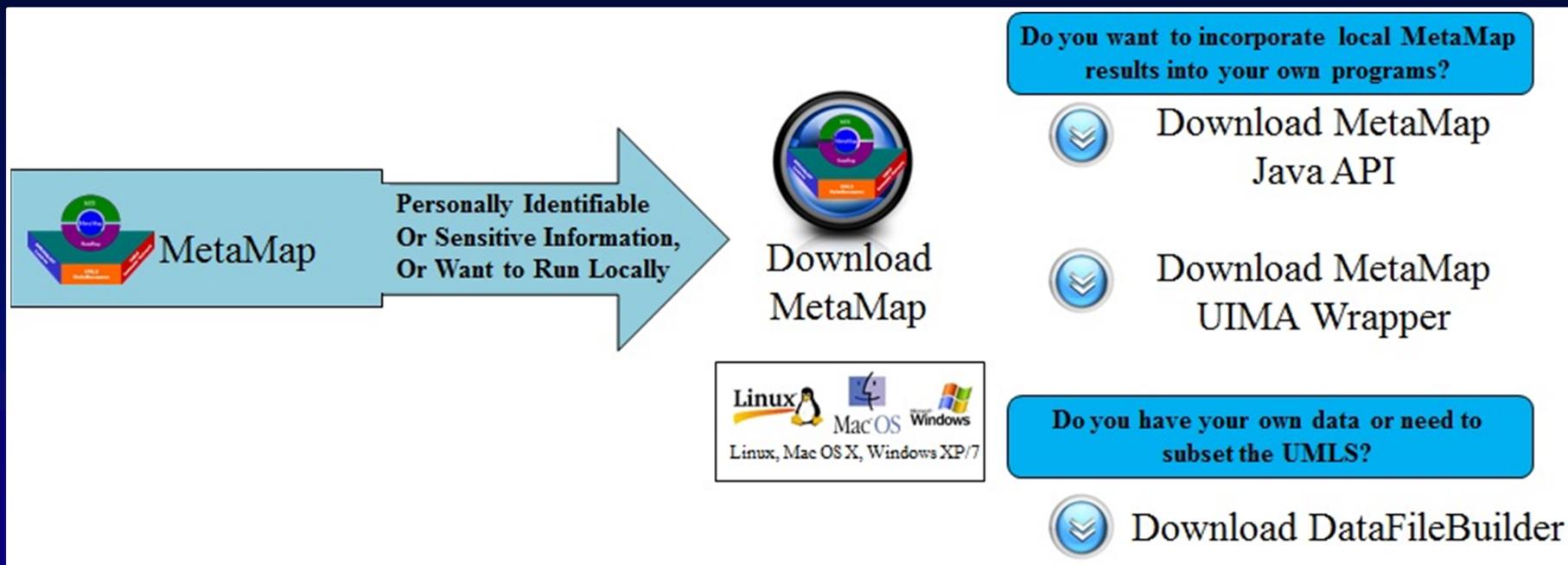
vessels and that subsequently megakaryocytes are activated to produce larger platelets, which are more active. Thus, an increase in MPV due to smoking may also contribute to the acceleration of atherosclerosis and should be considered as a risk factor for atherosclerotic disease.

## Results:

```
WARNING: Option V overridden by option V.
##### WARNING: Overriding default model 2011AA with 2011AB.
Processing 00000000.tx.1: Cigarette smoking increases the mean platelet volume in elderly patients with risk factors for
```



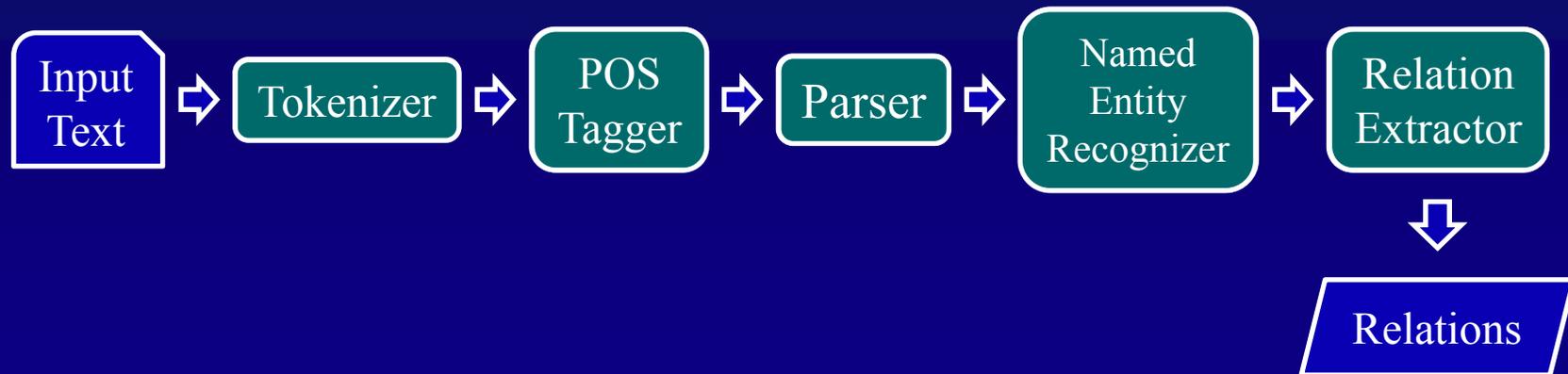
# Local Installation of MetaMap



# MetaMap as a UIMA Component

- Allows MetaMap to be used as an UIMA “annotator” component.
- UIMA - Unstructured Information Management Architecture

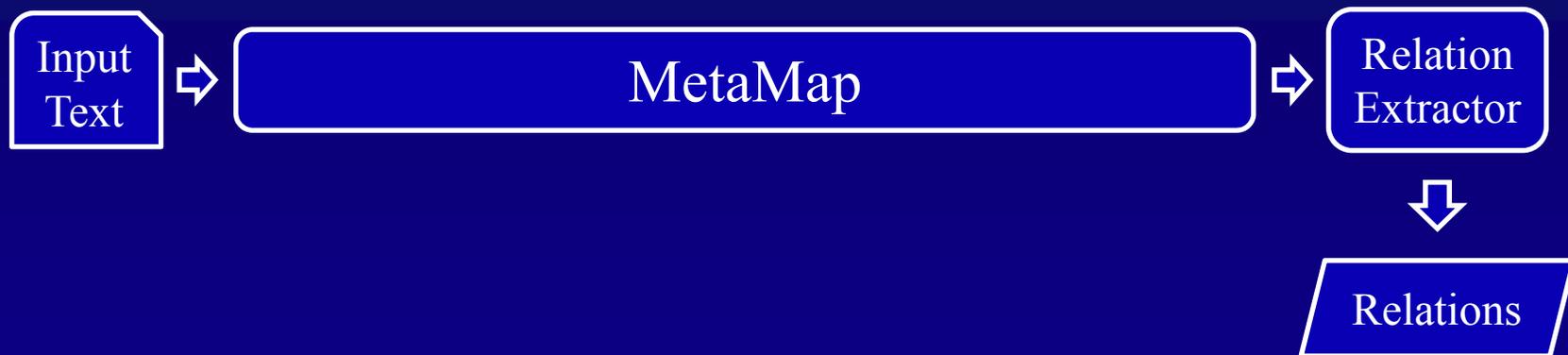
a component-based software for the analysis of unstructured information.



# MetaMap as a UIMA Component

- Allows MetaMap to be used as an UIMA “annotator” component.
- UIMA - Unstructured Information Management Architecture

a component-based software for the analysis of unstructured information.



# UIMA-compliant NLP Toolkits

- A number of NLP toolkits that are UIMA compliant
  - OpenNLP
  - clinical Text Analysis and Knowledge Extraction System (cTAKES)
  - OpenPipeline



# Data File Builder

Provides the ability to create specialized data models for MetaMap:

- UMLS augmented with user data
- UMLS subsets
- Independent knowledge sources
  - Should have notion of concept, synonymy
  - Ontologies
  - Local Thesauri
  - Other Knowledge Sources



# Web Access Statistics (2011)

- Remote Access:
  - 7,500 unique visits - 124 different countries
  - 70,000 Interactive Requests
  - 87,000 Batch Requests
- MetaMap Downloads:
  - 1,050 for MetaMap program
    - 570 Linux, 200 Mac/OS, 280 Windows
  - 41 for Data File Builder



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# Enhancing MetaMap and MTI Performance

- MetaMap precision enhancement through knowledge-based Word Sense Disambiguation
- MTI enhancement based on Machine Learning



# Word Sense Disambiguation (WSD)

- Kids with *colds* may also have a sore throat, cough, headache, mild fever, fatigue, muscle aches, and loss of appetite.
- Candidate MetaMap mappings for *cold*

C0234192: Cold (Cold sensation)

C0009264: Cold (Cold temperature)

C0009443: Cold (Common cold)



# Knowledge-based WSD

- Compare UMLS candidate concept profile vectors to context of ambiguous word
- Concept profile vectors' words from definition, synonyms and related concepts

Common cold	
Weight	Word
265	infect
126	disease
41	fever
40	cough

Cold temperature	
Weight	Word
258	temperature
86	hypothermia
72	effect
48	hot

- Candidate concept with highest similarity is predicted



# Knowledge-based WSD

- Kids with *colds* may also have a sore throat, *cough*, headache, mild *fever*, fatigue, muscle aches, and loss of appetite.

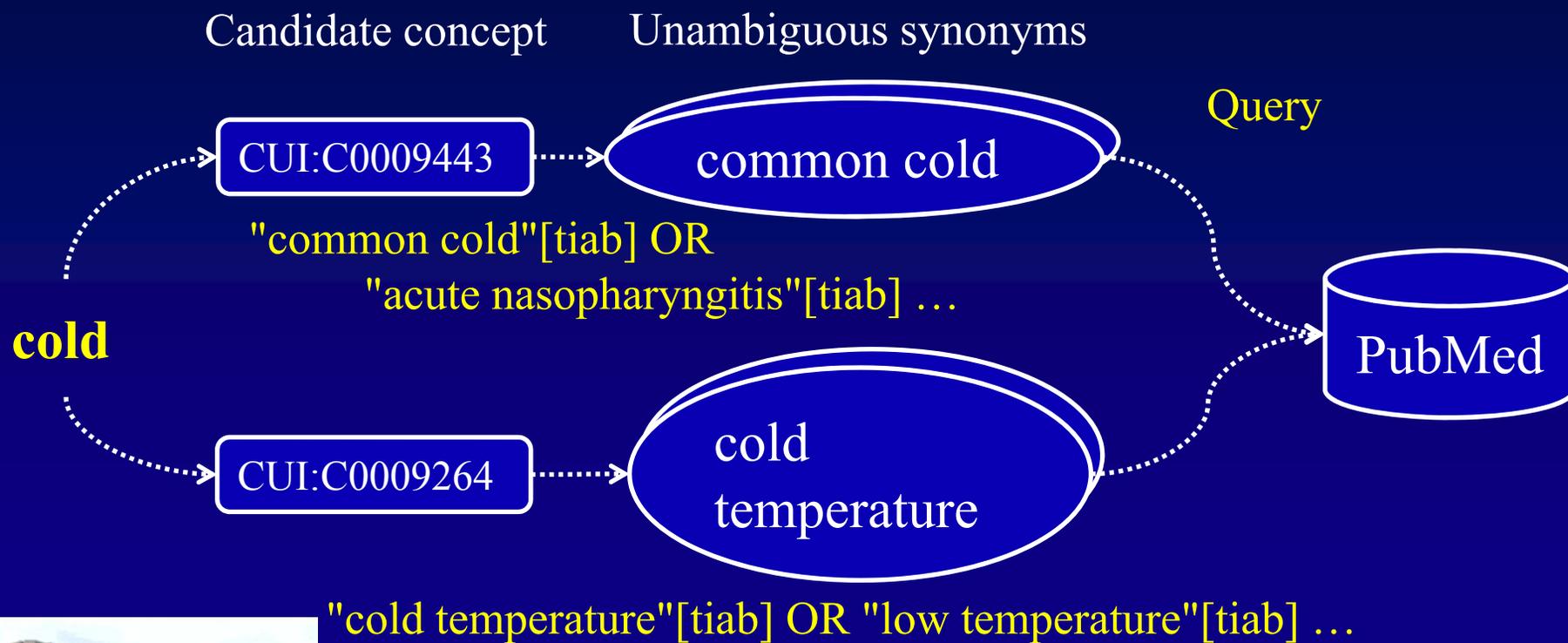
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Cold temperature	
Weight	Word
258	temperature
86	hypothermia
72	effect
48	hot



# Automatically Extracted Corpus WSD

- MEDLINE contains numerous examples of ambiguous words context, though not disambiguated



# WSD Method Results

- Corpus method has better accuracy than UMLS method

	UMLS	Corpus
NLM WSD	0.65	<b>0.69</b>
MSH WSD	0.81	<b>0.84</b>

- MSH WSD data set created using MeSH indexing
  - 203 ambiguous words
  - 81 semantic types
  - 37,888 ambiguity cases
- Indirect evaluation with summarization and MTI correlates with direct evaluation



# Citation indexed w/Female, Humans and Male

## TI -Documenting the symptom experience of cancer patients

**AB** - Cancer patients experience symptoms associated with their disease, treatment, and comorbidities. Symptom experience is complicated, reflecting symptom prevalence, frequency, and severity. Symptom burden is associated with treatment tolerance as well as patients' quality of life (QOL). A convenience sample of patients with the five most common cancers at a comprehensive cancer center completed surveys assessing symptom experience (Memorial Symptom Assessment Survey) and QOL (Functional Assessment of Cancer Therapy). Patients completed surveys at baseline and at 3, 6, 9, and 12 months thereafter. Surveys were completed by 558 cancer patients with breast, colorectal, gynecologic, lung, or prostate cancer. Patients reported an average of 9.1 symptoms, with symptom experience varying by cancer type. The mean overall QOL for the total sample was 85.1, with results differing by cancer type. Prostate cancer patients reported the lowest symptom burden and the highest QOL. The symptom experience of cancer patients varies widely depending on cancer type. Nevertheless, most patients report symptoms, regardless of whether or not they are currently receiving treatment.



# MTI enhancement with Machine Learning

- Large number of indexing examples available from MEDLINE
- Two approaches
  - Semi-automatic generation of indexing rules
  - Indexing algorithm selection through meta-learning



# Bottom-up Indexing Approach

- Automatic analysis of citations
  - selection of terms
  - production of candidate annotation rules
- Manual examination and processing
- Post-filtering based on machine learning
- Works well with some MeSH headings; e.g. ‘Carbohydrate Sequence’



# MTI Meta-Learning

- No single method performs better than all evaluated indexing methods
- Manual selection of best performing indexing methods becomes tedious with a large number of MHs
- Select indexing methods automatically based on meta-learning



# CheckTags Machine Learning Results

- 200k citations for training and 100k citations for testing

CheckTag	F <sub>1</sub> before ML	F <sub>1</sub> with ML	Improvement
Middle Aged	1.01%	59.50%	+58.49
Aged	11.72%	54.67%	+42.95
Child, Preschool	6.11%	45.40%	+39.29
Adult	19.49%	56.84%	+37.35
Male	38.47%	71.14%	+32.67
Aged, 80 and over	1.50%	30.89%	+29.39
Young Adult	2.83%	31.63%	+28.80
Female	46.06%	73.84%	+27.78
Adolescent	24.75%	42.36%	+17.61
Humans	79.98%	91.33%	+11.35
Infant	34.39%	44.69%	+10.30
Swine	71.04%	74.75%	+3.71



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Aged, 80 and over	1.50%	30.89%	+29.39
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# Research - J. Caitlin Sticco

- Introduction to Gene Indexing
- The Gene Indexing Assistant



## FLNA filamin A, alpha [ *Homo sapiens* ]

Gene ID: 2316, updated on 10-Mar-2012

### Summary

<b>Official Symbol</b>	FLNA provided by <a href="#">HGNC</a>
<b>Official Full Name</b>	filamin A, alpha provided by <a href="#">HGNC</a>
<b>Primary source</b>	<a href="#">HGNC:3754</a>
<b>Locus tag</b>	XX-FW83128A1.1
<b>See related</b>	<a href="#">Ensembl:ENSG00000196924</a> ; <a href="#">HPRD:02060</a> ; <a href="#">MIM:300017</a> ; <a href="#">Vega:OTTHUMG00000022712</a>
<b>Gene type</b>	protein coding
<b>RefSeq status</b>	REVIEWED
<b>Organism</b>	<a href="#">Homo sapiens</a>
<b>Lineage</b>	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo
<b>Also known as</b>	FLN; FMD; MNS; OPD; ABPX; CVD1; FLN1; NHBP; OPD1; OPD2; XLVD; XMVD; FLN-A; ABP-280
<b>Summary</b>	The protein encoded by this gene is an actin-binding protein that crosslinks actin filaments and links actin filaments to membrane glycoproteins. The encoded protein is involved in remodeling the cytoskeleton to effect changes in cell shape and migration. This protein interacts with integrins, transmembrane receptor complexes, and second messengers. Defects in this gene are a cause of several syndromes, including periventricular nodular heterotopias (PVNH1, PVNH4),

### GeneRIFs: Gene References Into Functions [What's a GeneRIF?](#)

- [These results demonstrate that FLNA is prone to pathogenic rearrangements](#)
- [mutations in FLNA may represent an unrecognized cause of macrothrombocytopenia with an altered platelet production and a modified platelet-vessel wall interaction](#)
- [study reports on two brothers with X-linked cardiac valvular dystrophy and a hemizygous FLNA mutation and review previously described cases from the literature](#)
- [Consistent with structural predictions, strain increases beta-integrin binding to FLNA, whereas it causes FilGAP to dissociate from FLNA, providing a direct and specific molecular basis for cellular mechanotransduction](#)
- [Hepatitis C virus nonstructural \(NS\) 3 and NS5A proteins were associated with filamin A, while core protein partially with filamin A and vimentin.](#)
- [regulates actin-linked caveolae dynamics following loss of cell adhesion](#)
- [Adapter protein SH2B1beta binds filamin A to regulate prolactin-dependent cytoskeletal reorganization and cell motility](#)
- [crystal structure of FlnA-Ig10 determined at 2.44 A resolution provides insight into the perturbations caused by these mutations](#)
- [The presence of these clinical findings in a mutation-confirmed case of OPD2 supports the notion that corneal clouding, bifid tongue, and DWM are part of the constellation of](#)



# The Gene Indexing Assistant

- An automated tool to assist the indexer in identifying and creating GeneRIFs
  - Evaluate the article
  - Identify genes
  - Make links to Entrez Gene
  - Suggest geneRIF annotation
- Anticipated Benefits:
  - Increase in speed
  - Increase in comprehensiveness

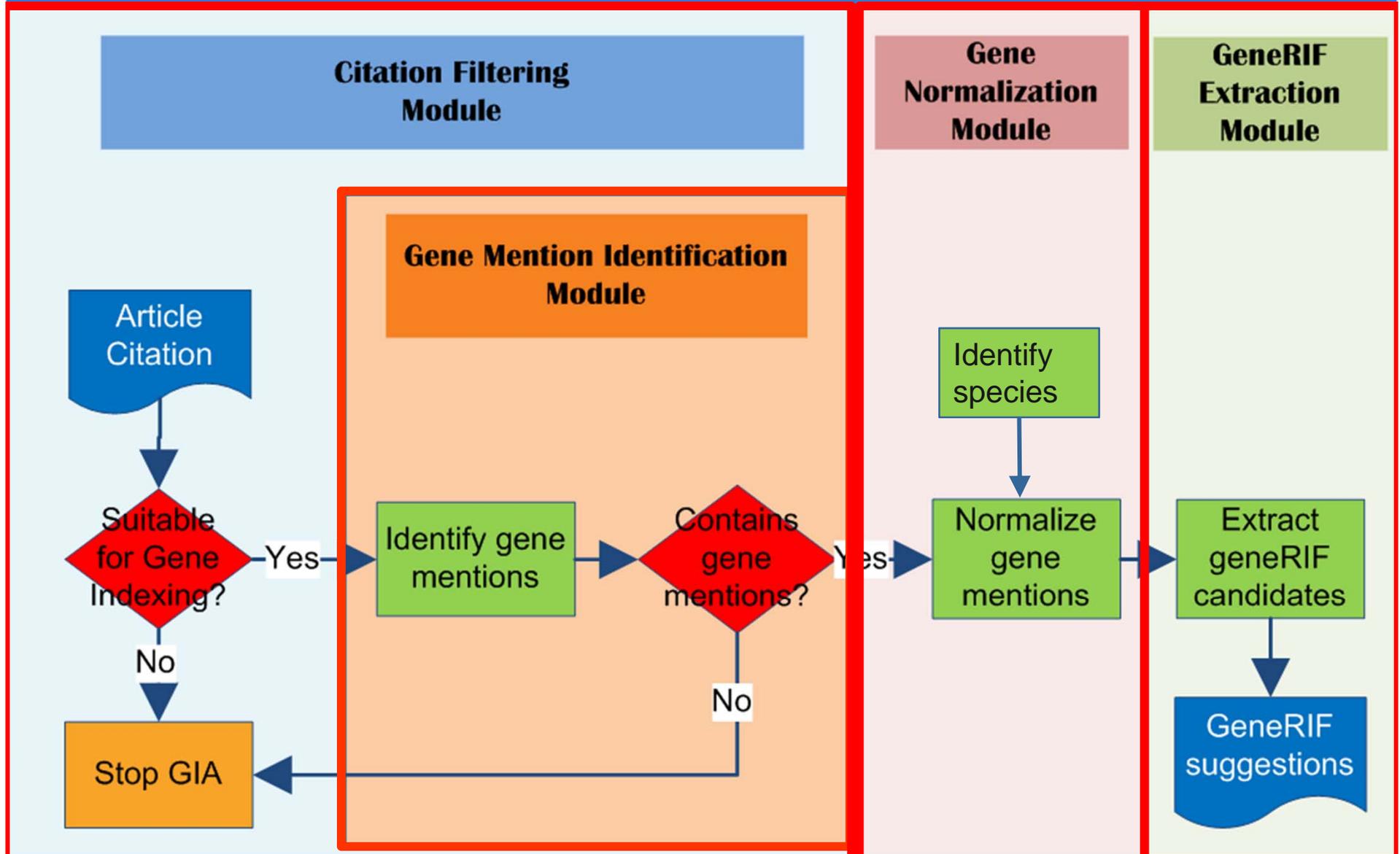


# Corpus Creation

- **Gene mentions**
  - tagged by manually correcting the automated program
- **GeneRIF classes**
  - Non-geneRIF, Structure, Function, Expression, Isolation, Reference, and Other
- **Claims classes**
  - Putative, Established, or Non-claim
- **Discourse classes**
  - Title, Background, Purpose, Methods, Results, Conclusions
  - Alternate dataset of 600,000 structured abstracts with similar labels



# Gene Indexing Assistant Structure



# Software Origins

## Integrated External Software

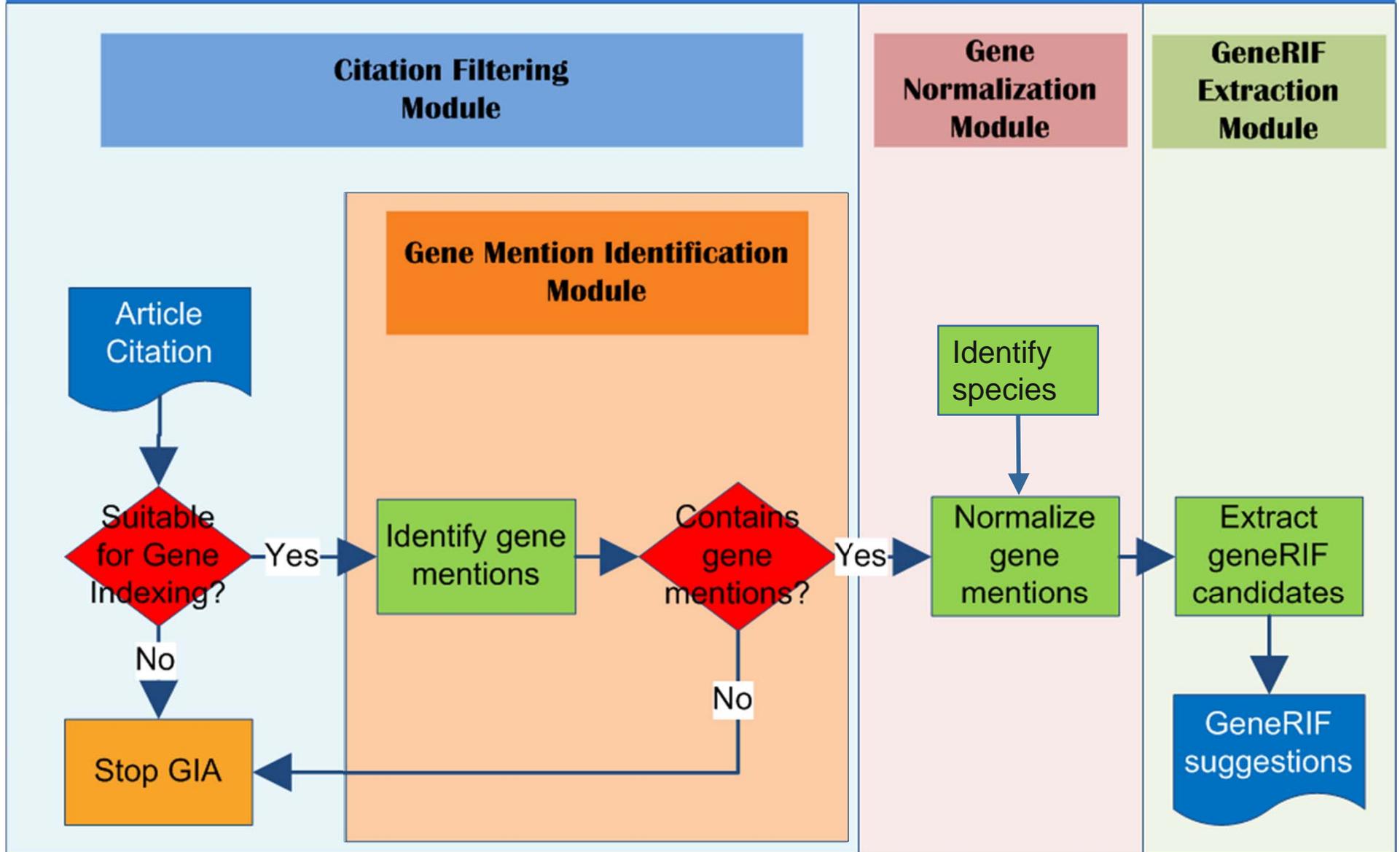
- GNAT from Jorg Hakenberg
  - Include BANNER for gene identification
- Linnaeus from Gerner, Nenadic, and Bergman
- Organism Tagger from Naderi et al.

## Components Developed In-house

- Framework
- Hand-curated dictionary
- In-house modules for human gene identification, normalization, and geneRIF extraction



# Gene Indexing Assistant Structure



# Gene Mention Identification

**Filamin a mediates HGF/c-MET signaling in tumor cell migration.**

Deregulated hepatocyte growth factor (HGF)/c-MET axis has been correlated with poor clinical outcome and drug resistance in many human cancers. In our study, we show that multiple human cancer tissues and cells express filamin A (FLNA), a large cytoskeletal actin-binding protein, and expression of c-MET is significantly reduced in human tumor cells deficient for FLNA.



# Gene Mention Identification

**Filamin a** mediates **HGF/c-MET** signaling in tumor cell migration.

Deregulated **hepatocyte growth factor (HGF)/c-MET** axis has been correlated with poor clinical outcome and drug resistance in many human cancers. In our study, we show that multiple human cancer tissues and cells express **filamin A (FLNA)**, a large cytoskeletal actin-binding protein, and expression of **c-MET** is significantly reduced in human tumor cells deficient for **FLNA**.

**filamin a, flna, hepatocyte growth factor, c-met**



# Gene Mention Identification

## In-House Components

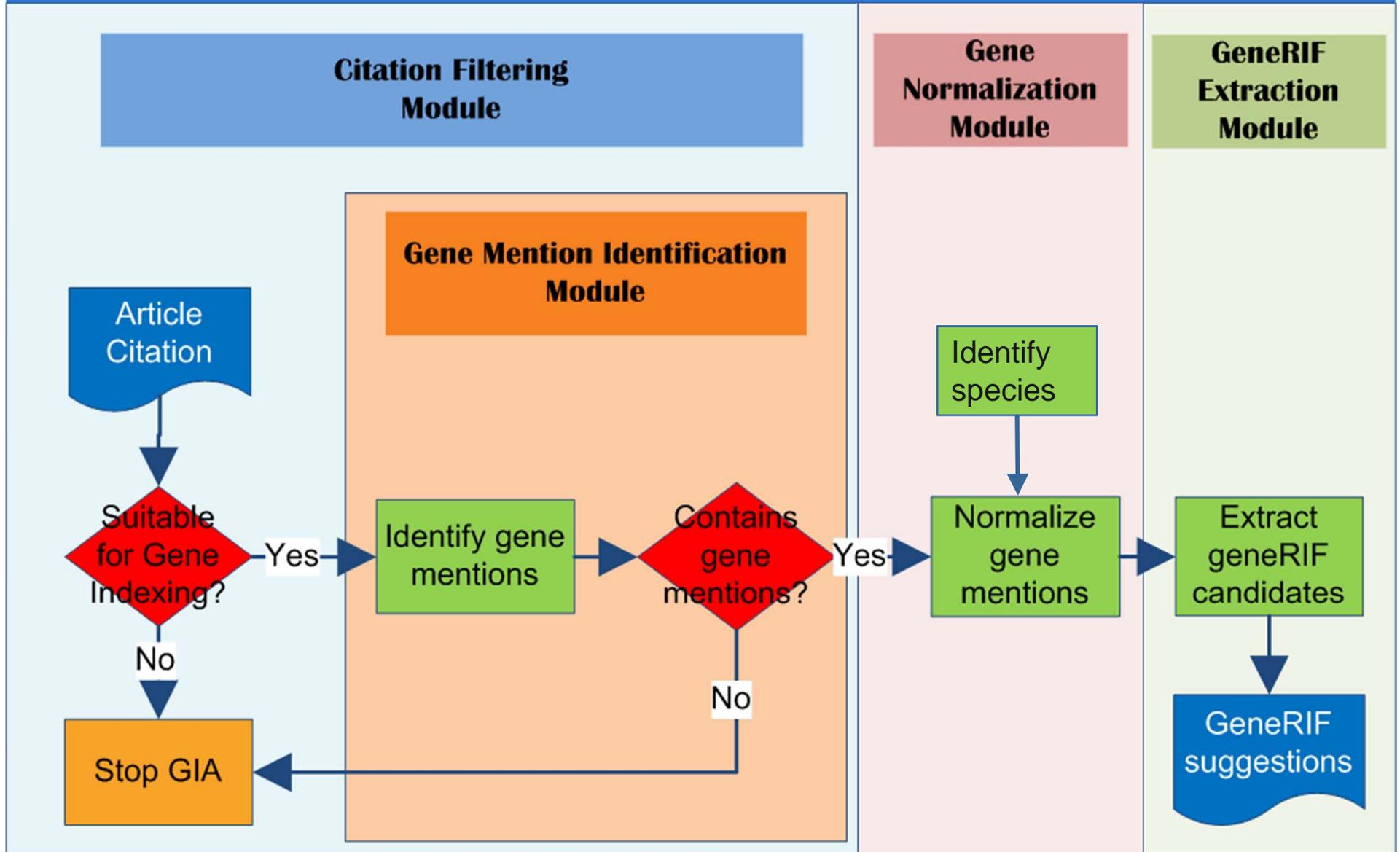
- Hand curated dictionary
  - Derived from Entrez Gene
  - Filtering for problem synonyms
  - Variant creation (reductive tokenization?)
- Strict Dictionary Mapping

## External Components

- GNAT: Conditional Random Fields (CRF) from BANNER



# Gene Indexing Assistant Structure



# Species Identification and Assignment

## External Components

- Identification
  - Linnaeus: includes common names and maps stand alone genera to most likely species
  - Organism Tagger: includes cell lines and microbial strains
- Assigning genes to species
  - GNAT: Proximity heuristic



# Gene Mention Normalization

**c-met**



ID: 4233, MET

**hepatocyte  
growth  
factor**



ID: 3082, HGF

Official Name

cell migration, cytokine, tumor

ID: 4233, MET

Synonym

Oncogene, renal, cancer, tyrosine

Cancer, tumor, cytokine, cell migration



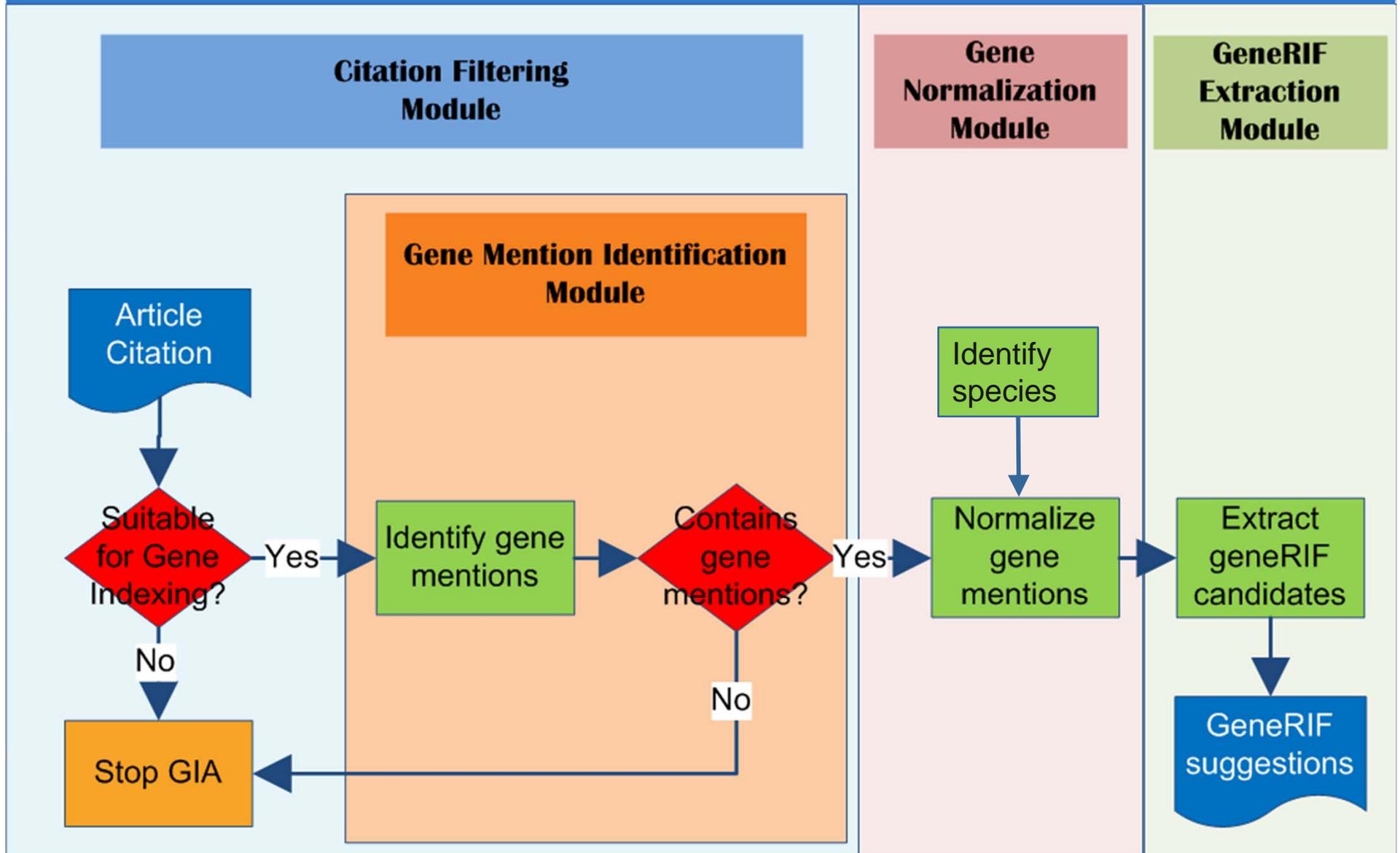
# Gene Mention Normalization

## Identification and Normalization Results

Species	Recall	Precision	F <sub>1</sub>
<b>Human</b>	<b>83%</b>	<b>80%</b>	<b>81%</b>



# Gene Indexing Assistant Structure



# Classifier Results

Features	Precision	Recall	F <sub>1</sub>
Position (pos)	72%	73%	72%
Text (word features)	63%	64%	63%
Gene Names	55%	70%	62%
Discourse (Structured Ab. Labels)	70%	80%	75%
pos + discourse	70%	86%	76.89%
★ pos + discourse + GO	70%	86%	77.07%



# Future Improvements and Research Areas

- Additional preprocessing
  - Expand certain anaphora
- Extracting interaction data
- Expanding the dictionaries
- Improved abbreviation resolution
- Additional training for low-performing species
- Integration of additional identification or normalization software



# Research and Outreach Efforts (concl.)

- External Collaboration
  - IBM DeepQA group: applying Watson to health care
- Data Dissemination
  - MEDLINE Baseline Repository
  - WSD test collections
- Biomedical NLP/IR Challenges
  - Text Retrieval Conference (TREC)
    - Genomics track
    - Medical Records track
  - Informatics for Integrating Biology & the Bedside (i2b2)
  - Medical NLP Challenge



# Outline

- Introduction [Lan]
- MetaMap [François]
- The NLM Medical Text Indexer (MTI) [Jim]
- Availability of Indexing Initiative Tools [Willie]
- Research and Outreach Efforts [Antonio, Caitlin, Lan]
- **Summary and Future Plans [Lan]**
- Questions



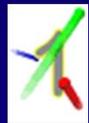
# Indexing Initiative Top 10 (1/2)

10. 'MTI Why' explanation facility
9. Application of MTI to Cataloging and History of Medicine records
8. The MetaMap UIMA wrapper, increasing MetaMap's availability
7. Significant speedup of MetaMap
6. Collaboration with IBM DeepQA group applying Watson to health care



# Indexing Initiative Top 10 (2/2)

5. The development of Gene Indexing Assistant (GIA)
4. More WSD methods with better results
3. Improvement in MTI's performance due to technical enhancements and close collaboration with Index Section
2. Downloadable releases of MetaMap, especially for Windows



**Inauguration of MTI as a first-line indexer (MTIFL)!**



# Future Plans

- Continued collaboration with
  - The NLM Index Section
  - IBM and other external organizations
- Planned improvements to MetaMap and MTI such as
  - Expansion/improvement of MTIFL capability
  - Add species detection to MTI for disambiguation and for GIA
  - Further MTI research with Antonio Jimeno-Yepes and Caitlin Sticco
  - Possible high-level MetaMap modularization to facilitate plug and play strategies





Extra slides in case of questions



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# Candidate Pruning: Output Example

*protein-4 FN3 fibronectin type III domain GSH glutathione  
GST glutathione S-transferase hIL-6 human interleukin-6  
HSA human serum albumin IC(50) half-maximal inhibitory  
concentration Ig immunoglobulin IMAC immobilized metal  
affinity chromatography K(D) equilibrium constant*



# Candidate Pruning: Output Example

(Total=99; Excluded=13; Pruned=50; Remaining=36)

783 equilibrium constant [npop]

780 P Equilibrium [orgf]

780 P Kind of quantity - Equilibrium [qnco]

780 P Constant (qualifier) [qlco]

713 protein K [aapp]

691 Protein concentration [lbpr]

671 protein serum [aapp,bacs]

671 Protein.serum [lbtr]

656 P serum K+ [lbpr]

656 protein human [aapp,bacs]

653 Human immunoglobulin [aapp,imft,phsu]



# User-Defined Acronyms (UDAs)

Simply create a text file with UDA definitions:

<b>CABG</b>		coronary artery bypass graft
<b>PTCA</b>		percutaneous transluminal coronary angioplasty
<b>RBBB</b>		right bundle branch block
<b>LAFB</b>		left anterior fascicular block
<b>AV</b>		aortic valve
<b>PTLD</b>		post-transplantation lymphoproliferative disorder
<b>CHOP</b>		cyclophosphamide, hydroxydaunomycin, Oncovin, and prednisone
<b>LIMA</b>		left internal mammary artery
<b>LAD</b>		left anterior descending coronary artery
<b>SVG</b>		saphenous vein graft
<b>PLB</b>		posterolateral bundle
<b>PDA</b>		posterior descending artery
<b>IM</b>		internal mammary



# Complexity - Composite Phrases

*Pain on the left side of the chest*

Left sided chest pain (C0541828)

Linguistic variants

Syntactic processing

Word order



# $10^{21}$ Terabytes of Memory?!

$$10^{21} = 10^{10} * 10^{11}$$

$$= (10 \text{ billion}) * (100 \text{ billion})$$

150% of world  
population

Required  
terabytes/person

Oak Ridge National Lab's Cray Jaguar: 300TB

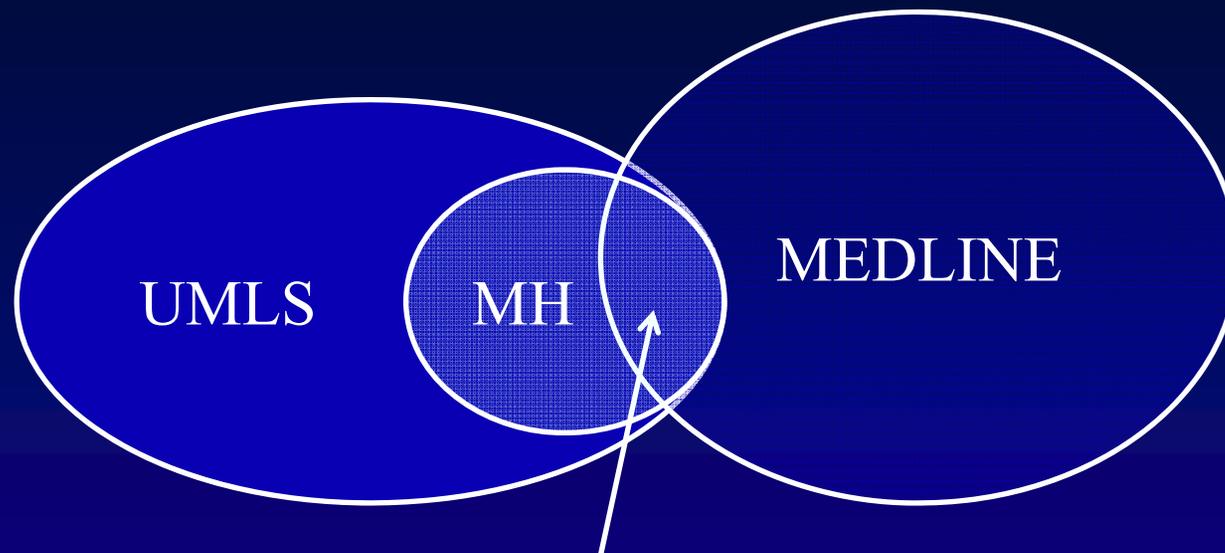


# Concepts with at least 300 Synonyms

- 349: C1163679 | Water 1000 MG/ML Injectable Solution
- 327: C0874083 | Triclosan 3 MG/ML Medicated Liquid Soap
- 312: C0980221 | Sodium Chloride 0.154 MEQ/ML Injectable Solution



# MSH WSD corpus



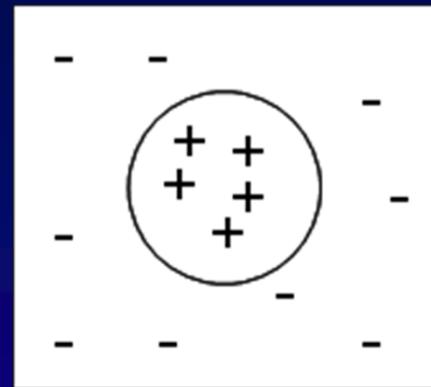
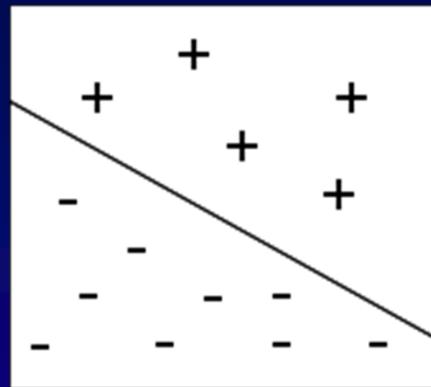
Disambiguation corpus



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# Meta-learning



# ML: Human MeSH heading

Method	Average F-measure
MTI	0.72
Naïve Bayes	0.85
Support vector machine	0.88
AdaBoostM1	0.92



# Accuracy

- Accuracy is how close a measured value is to the **actual (true) value**

$$\textit{accuracy} = \frac{TP + TN}{TP + FP + FN + TN}$$

- Precision, proportion of relevant predictions

$$\textit{precision} = \frac{TP}{TP + FP}$$



# Micro/macro averaging

- Macro averaging takes into account the category (MH)
- Micro averaging does not consider MH

MH	True Pos	False Pos	Positive	Precision	Recall	F-measure
Humans	66,429	5,985	71,484	0.9174	0.9293	0.9233
Male	24,664	7,107	34,463	0.7763	0.7157	0.7448
Female	25,824	6,718	35,501	0.7936	0.7274	0.7590
Macro				0.8291	0.7908	0.8090

Micro	116,917	19,810	141,448	0.8551	0.8266	0.8406
-------	---------	--------	---------	--------	--------	--------



# MetaMap Indexing (MMI)

- Summarizes and scores what is found within a citation
- Location - Title given more emphasis
- Frequency of occurrence
- Relevancy:
  - MeSH Tree Depth
  - MetaMap score
- Provides a scored and ordered list of UMLS concepts describing the citation
- Provides our best indicator of MeSH Headings



# Restrict to MeSH

- Allows us to map UMLS concepts to MeSH Headings
- Maps nomenclature to MeSH

## Encephalitis Virus, California

ET: Jamestown Canyon virus

ET: Tahyna virus

Inkoo virus

Jerry Slough virus

Keystone virus

Melao virus

San Angelo virus

Serra do Navio virus

Snowshoe hare virus

Trivittatus virus

Lumbo virus

South River virus

California Group Viruses

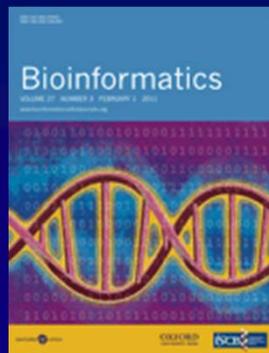


# PubMed Related Citations (PRC)

- Uses PubMed pre-calculated related articles, same as DCMS Related Articles tab
- Provides terms not available in title/abstract
- Used to filter and support MeSH Headings identified by MetaMap Indexing
- Only use MeSH Headings, no CheckTags, no Subheadings, no Supplemental Concepts
- Can provide non-related terms, so heavily filtered



# MTI – Initial MTIFL Journals (Feb 18, 2011)



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# MTI – Added MTIFL Journals

Added June 1, 2011



(17)

Added August 18, 2011



Added September 5, 2011

(19)

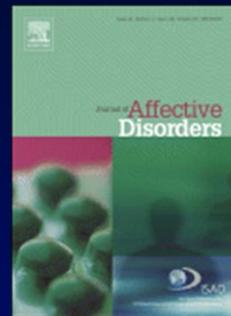


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# MTI – Added MTIFL Journals

Added October 5, 2011



(23)



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# MTIFL Journal Performance

Journal	Current MTIFL Statistics						Previous Results							
	2012				Diff 2011	Diff 2010	2010				2011			
	Articles	Recall	Precision	F <sub>1</sub>			Articles	Recall	Precision	F <sub>1</sub>	Articles	Recall	Precision	F <sub>1</sub>
Arch Microbiol	15	57.24%	58.78%	58.00%	-1.15%	4.67%	103	71.50%	44.01%	54.48%	69	55.97%	62.71%	59.15%
Bioinformatics	113	57.98%	64.65%	61.13%	2.38%	15.75%	820	76.61%	29.89%	43.01%	433	53.66%	64.91%	58.75%
BMC Bioinformatics	126	63.84%	70.80%	67.14%	5.33%	19.69%	851	77.83%	28.87%	42.12%	403	57.13%	67.33%	61.81%
Can J Microbiol	22	60.53%	61.69%	61.10%	-1.37%	16.22%	131	67.07%	35.29%	46.25%	59	61.07%	63.94%	62.47%
Curr Opin Biotechnol	29	73.81%	79.15%	76.39%	7.99%	38.45%	99	53.86%	20.73%	29.94%	25	59.73%	80.00%	68.39%
Curr Opin Cell Biol	0	0.00%	0.00%	0.00%	0.00%	33.39%	97	54.38%	26.60%	35.72%	31	70.94%	67.38%	69.12%
Ecotoxicol Environ Saf	42	69.91%	79.74%	74.50%	2.81%	27.96%	122	68.92%	32.03%	43.73%	199	65.42%	79.30%	71.69%
Environ Int	11	68.21%	77.44%	72.54%	7.47%	22.33%	92	55.94%	34.57%	42.73%	54	57.20%	75.44%	65.06%
Environ Microbiol	58	60.92%	71.62%	65.84%	3.55%	13.98%	256	63.68%	38.91%	48.31%	183	58.54%	66.56%	62.29%
Environ Toxicol	15	75.26%	76.88%	76.06%	5.98%	25.44%	49	68.25%	33.17%	44.65%	24	63.73%	77.85%	70.08%
Environ Toxicol Chem	54	68.00%	72.27%	70.07%	1.87%	22.42%	287	66.24%	34.98%	45.78%	111	62.44%	75.13%	68.20%
FEMS Microbiol Ecol	0	0.00%	0.00%	0.00%	0.00%	8.60%	178	68.62%	44.11%	53.70%	157	58.32%	66.87%	62.30%
Genomics Proteomics Bioinformatics	0	0.00%	0.00%	0.00%	0.00%	7.29%	30	77.30%	35.80%	48.93%	15	50.36%	63.64%	56.22%
Health Psychol	20	80.36%	74.75%	77.45%	8.06%	30.29%	93	45.06%	34.54%	39.11%	18	67.08%	71.88%	69.40%
Int J Food Microbiol	12	81.89%	74.82%	78.20%	14.82%	14.57%	305	69.95%	37.48%	48.81%	272	62.48%	64.31%	63.38%
ISME J	34	64.02%	62.69%	63.35%	1.80%	15.78%	122	65.03%	35.31%	45.77%	120	58.00%	65.56%	61.55%
J Affect Disord	130	82.60%	91.44%	86.80%	50.47%	New	338	45.32%	30.32%	36.33%	0	0.00%	0.00%	0.00%
J Appl Microbiol	49	59.33%	65.36%	62.20%	-0.16%	16.19%	562	71.73%	34.04%	46.17%	489	60.38%	64.48%	62.36%
J Ind Microbiol Biotechnol	26	71.21%	81.31%	75.93%	10.35%	19.66%	107	66.90%	34.95%	45.92%	82	64.23%	66.98%	65.58%
J Morphol	30	76.34%	62.31%	68.61%	-1.22%	28.91%	131	65.02%	29.85%	40.92%	64	76.85%	63.98%	69.83%
Lett Appl Microbiol	60	64.14%	69.27%	66.61%	-0.06%	15.00%	188	71.46%	40.46%	51.67%	116	65.13%	68.28%	66.67%
Nord J Psychiatry	19	79.32%	72.76%	75.90%	-4.61%	42.83%	55	43.37%	33.30%	37.68%	9	79.17%	81.90%	80.51%
Vet Microbiol	25	79.69%	72.73%	76.05%	10.01%	18.82%	285	71.54%	35.24%	47.22%	278	64.54%	67.61%	66.04%
<b>Totals</b>	<b>890</b>	<b>69.99%</b>	<b>74.85%</b>	<b>72.34%</b>	<b>8.35%</b>	<b>19.67%</b>	<b>5,301</b>	<b>66.64%</b>	<b>33.19%</b>	<b>44.31%</b>	<b>3,211</b>	<b>60.74%</b>	<b>67.60%</b>	<b>63.99%</b>



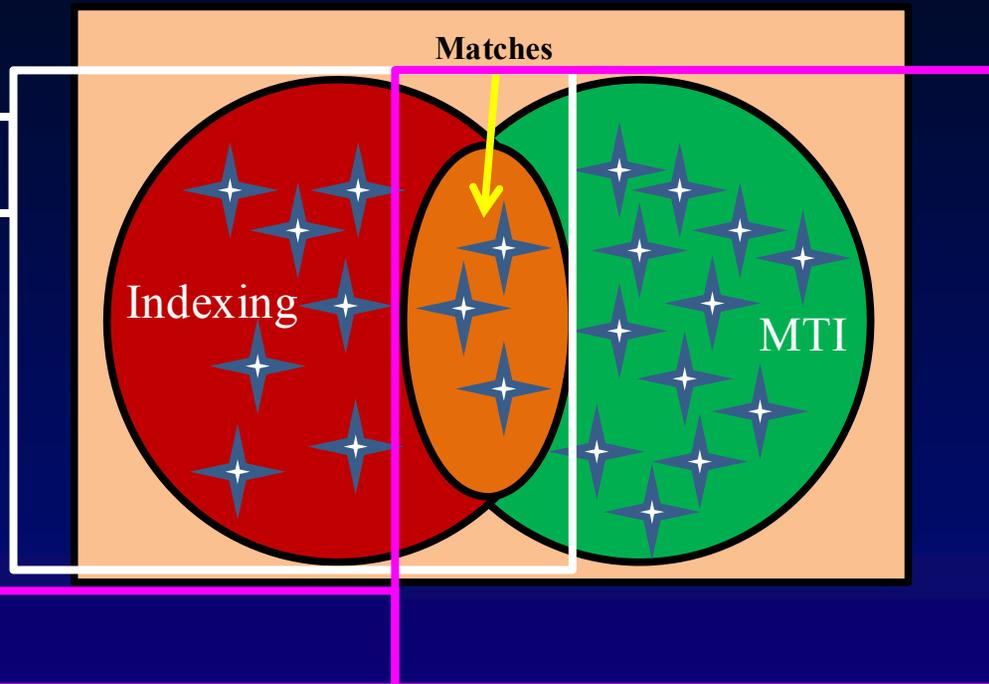
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# Precision, Recall, F-Measure

Recall:  $3/10 = 0.3$

10 Indexing  
15 MTI  
3 Matches



Precision:  $3/15 = 0.2$

F<sub>1</sub>-Measure:  $(2 * 0.2 * 0.3) / (0.2 + 0.3) = 0.24$



# MTIWhy

## MTI Recommendation Information

Processed On: Wednesday, September 22, 2010  
MeSH: 2010 Batch: medline10n0876  
PRC From: PubMed Related Articles

[-]  
FEEDBACK



MTI Request:

Submit MTI Request

- Adult
- Humans
- Vena Cava, Inferior
- Venous Thrombosis**
- Thrombophlebitis
- Thrombus

Select for

Received **2,330** Indexer Feedbacks

Incorporated **40%** into MTI

March 20, 2012

*Why did MTI pick up the term "Crow" in this health services article?  
This is definitely wrong and needs to be looked into.*

*Polypeptide aptamer should be indexed as Peptide aptamer (instead  
of Peptides and Oligonucleotides).*

### Venous

Type: MeSH Heading (MH)  
Recommended by: Both Meta  
Location: Found in Abstract C

### MTI Triggering Information

The following words/phrases w  
-- "DVT"  
-- "DVTs"

### Details:

Text "DVT"  
--> MetaMap Mapped to: "DVT (Deep Vein Thrombosis)"  
--> Restrict to MeSH gave us: "Venous Thrombosis"

19631870 [ PRC Rank: 10 ]

Management of pregnancy in women with previous left ilio-caval stenting.  
J Vasc Surg. 2009 Aug;50(2):355-9.



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110

# Questions

Alan (Lan) R. Aronson

James G. Mork

François-Michel Lang

Willie J. Rogers

Antonio J. Jimeno-Yepes

J. Caitlin Sticco



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