

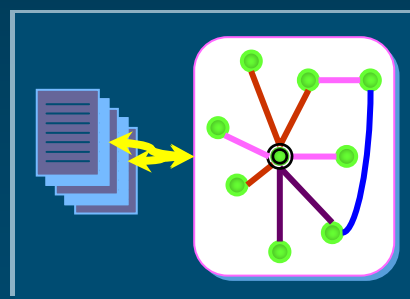


NCICB Operations meeting
April 13, 2007



Advanced Library Services

*Developing a Biomedical Knowledge Repository
to Support Advanced Information Management Applications*

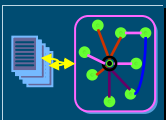


Olivier Bodenreider, M.D., Ph.D.
Thomas C. Rindflesch, Ph.D.

Context

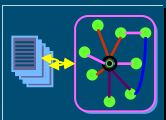
- ◆ Provide biomedical information to health care professionals and consumers
 - Exploit NLM resources
 - Maintain NLM's cutting edge

- ◆ Proposal overview
 - *Advanced Library Services*
 - *Biomedical Knowledge Repository*
- ◆ Pilot projects



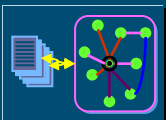
Why additional services?

- ◆ Biomedical information is growing at an increasingly faster pace
 - High-throughput approach to knowledge processing
- ◆ Information retrieval is the starting point, not the end of the journey for the researcher
 - Towards “computable” knowledge
- ◆ Integration between literature and other resources is insufficient
 - Adequate for navigation purposes
 - Insufficient for knowledge processing



What additional services?

- ◆ Refined information retrieval
 - Indexing on relations in addition to concepts
 - *Find articles asserting that **IL-13 inhibits COX-2***
- ◆ Multi-document summarization
 - Extract and visualize facts from the literature
 - *Summarize the top 300 papers on **panic disorder***
- ◆ Question answering
 - Clinical and biological questions
 - *What drugs **interact** with **imipramine**?*
- ◆ Knowledge discovery
 - Reasoning with facts from heterogeneous resources
 - *From MEDLINE and UMLS together*



Normalized and integrated knowledge

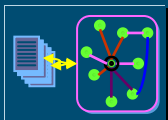
◆ Normalized knowledge

- Common format
- Common identification mechanism

◆ Integrated knowledge

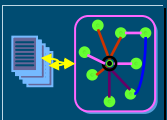
- Single repository
- Seamless environment
- *Phenotype and genotype information together*

Biomedical Knowledge Repository

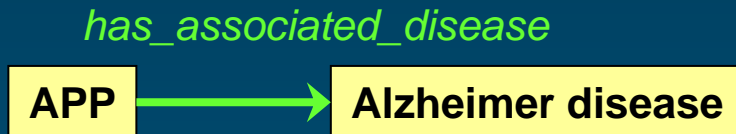


Sources of knowledge

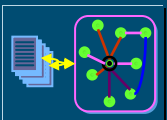
- ◆ Biomedical literature
 - Predications extracted from **MEDLINE** abstracts and full-text publicly available articles using text mining techniques
 - Other corpora (e.g., **ClinicalTrials.gov**)
- ◆ Terminological knowledge
 - **UMLS**
- ◆ Structured knowledge bases
 - NCBI resources (e.g., **Entrez Gene**)
 - Functional annotations from model organism databases
 - ...
- ◆ Contributed knowledge
 - The repository is open to collaborators outside NLM



Formalism Triples

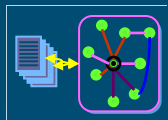


- ◆ Facts
- ◆ Assertions
- ◆ Relations
- ◆ Semantic predications
- ◆ RDF triples



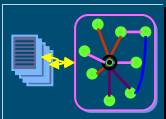
Annotated knowledge

- ◆ Provenance information
 - Source (e.g., PMID)
 - Extraction mechanism
 - Timestamp
- ◆ Frequency information
 - Redundancy
- ◆ Collaborative annotation
 - “Was this information useful?”
 - Context of use/usefulness

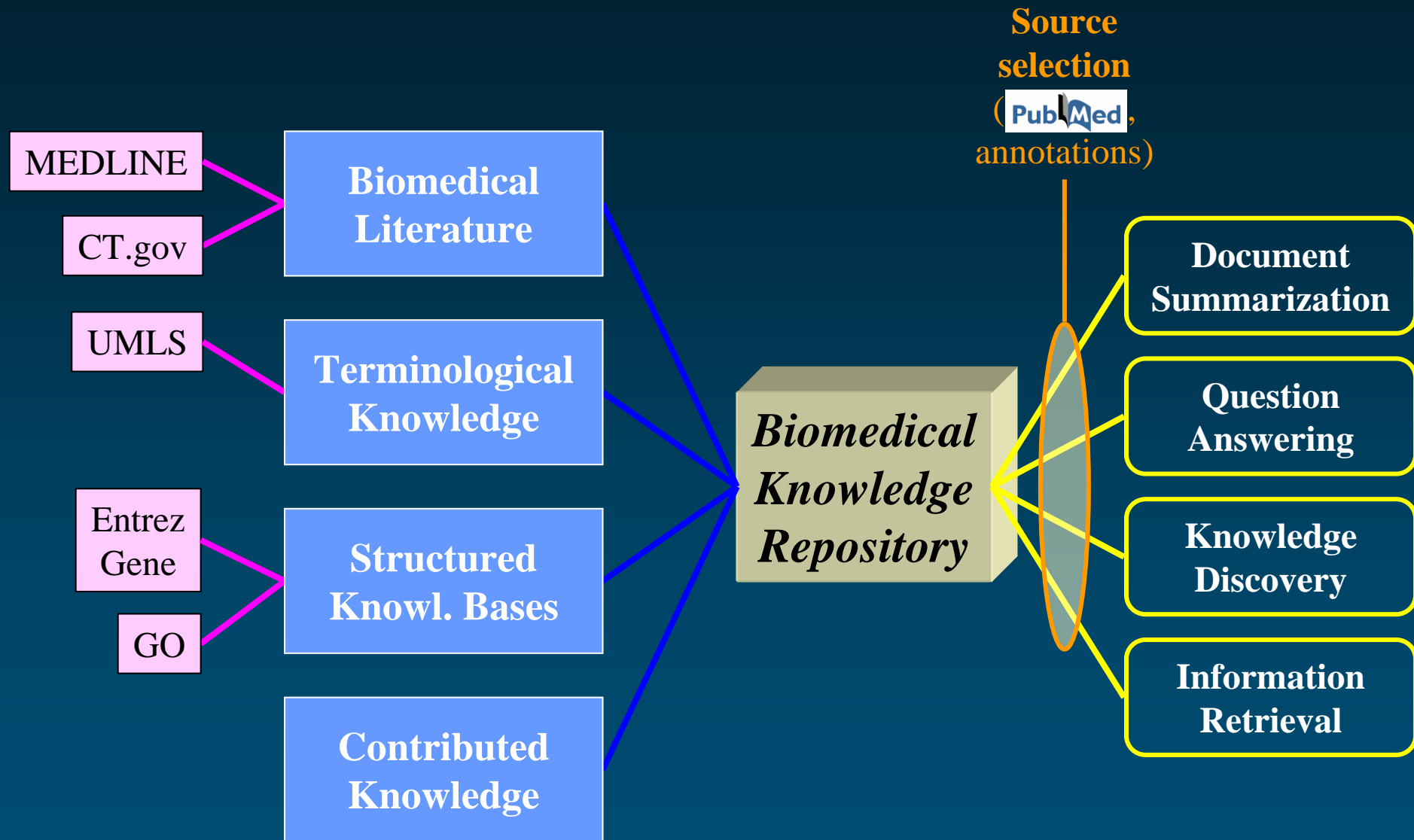


Semantic Web perspective

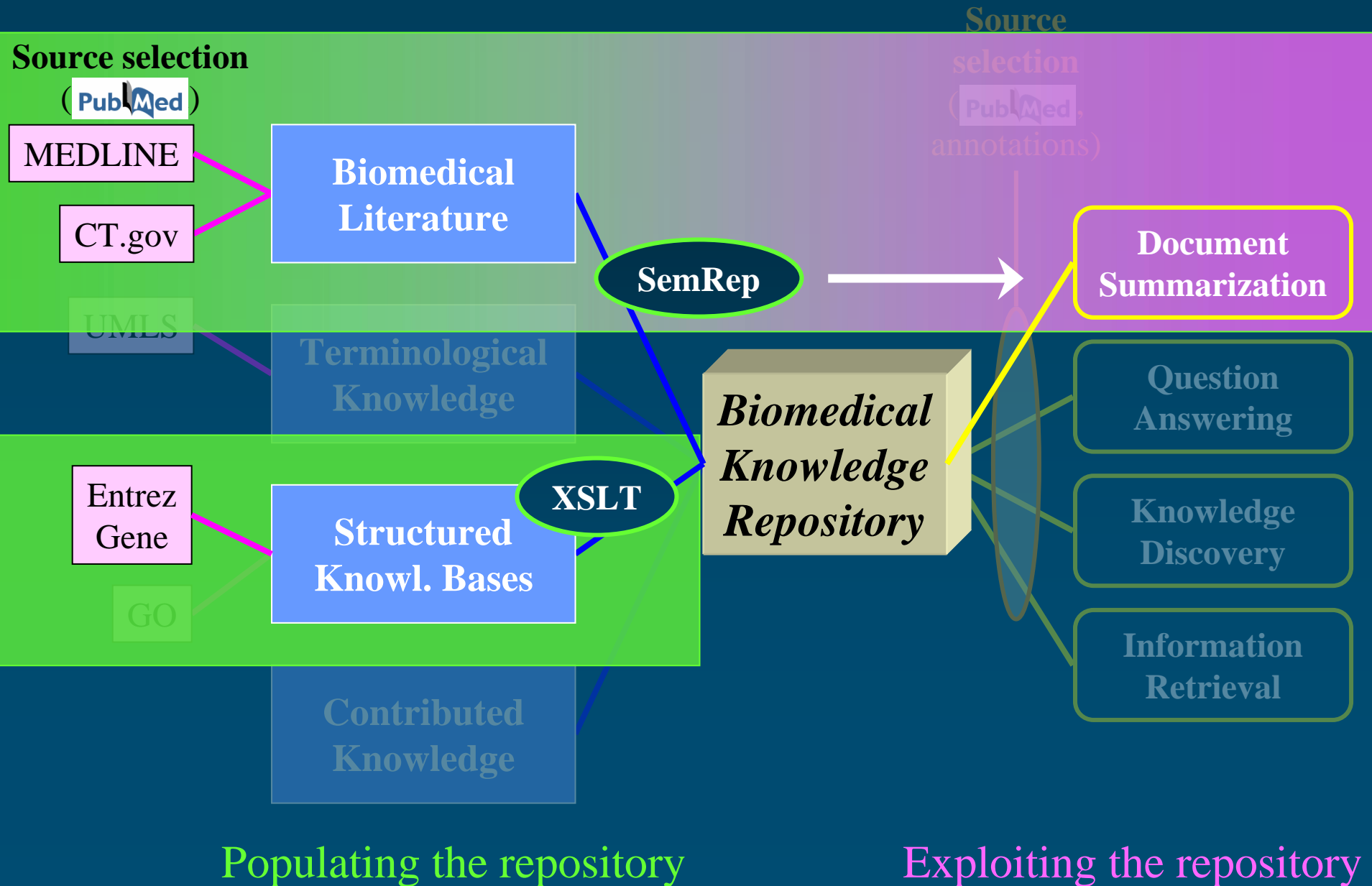
- ◆ Common format for knowledge
 - Resource Description Format (RDF)
- ◆ Common identification scheme
 - Unified Resource Identifier (URI)
- ◆ Standard tools
 - RDF browsers
 - RDF “reasoners”
- ◆ High level of interest for biomedicine in the SW community
 - Health Care and Life Sciences Interest Group



Advanced Library Services Summary



Advanced Library Services Pilot projects



Pilot #1

Populating and exploiting the Biomedical Knowledge Repository

Converting Entrez Gene into RDF

With Satya Sahoo (U. Georgia)
and Kelly Zeng (LHC)

Search for

Display Show Send to

All: 1 Current Only: 1 Genes Genomes: 1 SNP GeneView: 1

1: **APP amyloid beta (A4) precursor protein (peptidase nexin-II, Alzheimer disease)** [*Homo sapiens*]
 GeneID: 351 Primary source: [HGNC:620](#) updated 26-Jul-2006

[Entrez Gene Home](#)

- [Table Of Contents](#)
- [Summary](#)
- [Genomic regions, transcripts...](#)
- [Genomic context](#)
- [Bibliography](#)
- [HIV-1 protein interactions](#)
- [Interactions](#)
- [General gene information](#)
- [General protein information](#)
- [Reference Sequences](#)
- [Related Sequences](#)
- [Additional Links](#)
- [Links](#)

Summary

Official Symbol: APP **and Name:** amyloid beta (A4) precursor protein (peptidase nexin-II, Alzheimer disease) **provided by** [HUGO Gene Nomenclature Committee](#)

See related: [HPRD:00100](#), [MIM:104760](#)

Gene type: protein coding

Gene name: APP

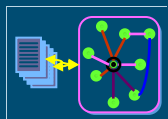
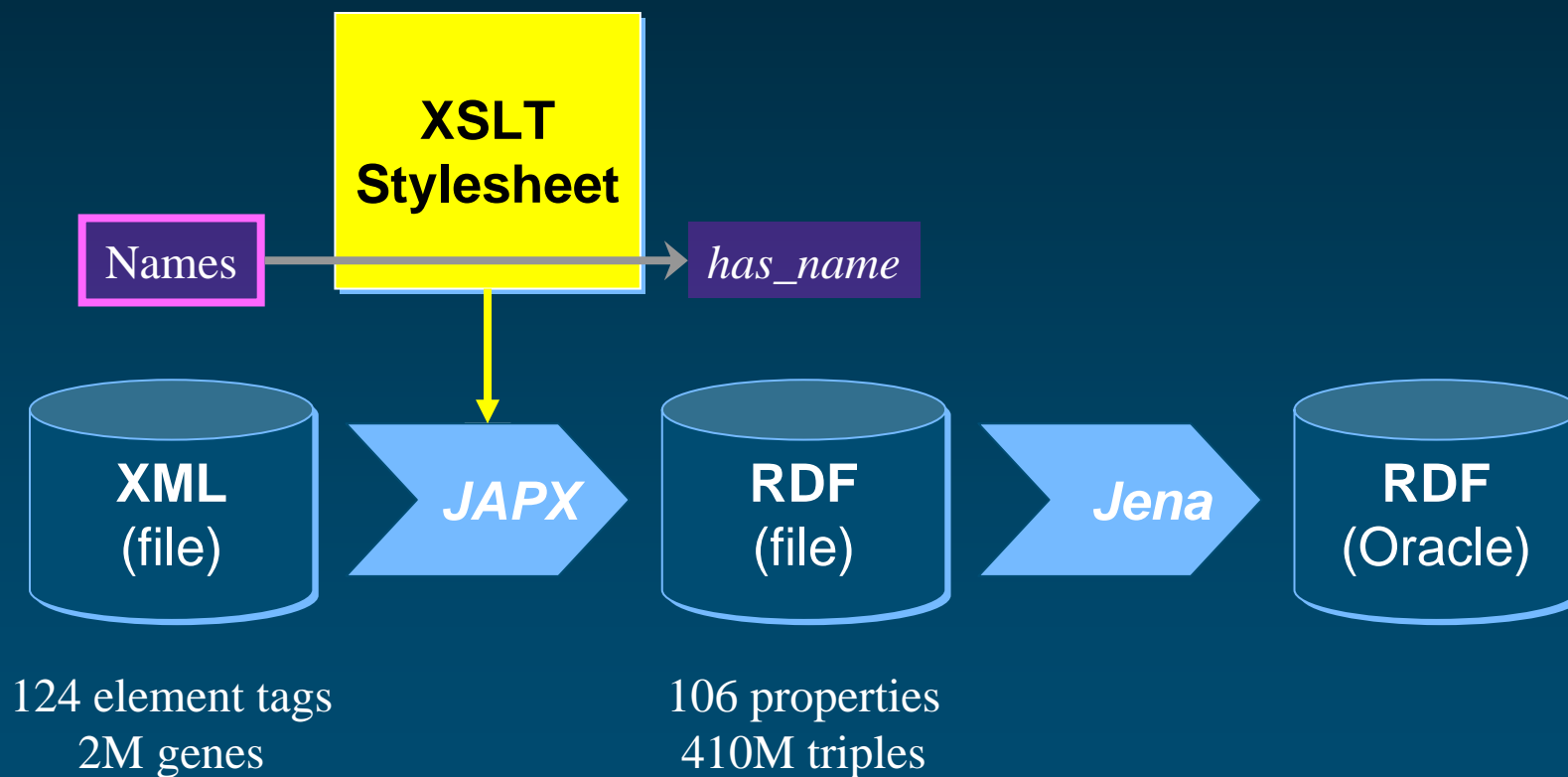
Gene description: amyloid beta (A4) precursor protein (peptidase nexin-II, Alzheimer disease)

General protein information

Names: amyloid beta A4 protein

protease nexin-II; A4 amyloid protein; amyloid-beta protein; beta-amyloid peptide; cerebral vascular amyloid peptide; amyloid beta (A4) precursor protein (protease nexin-II, Alzheimer disease)

Overview



Search Gene for APP amyloid beta (A4) precursor protein (peptidase nexin-II, Alzheimer disease) Go Clear

Limits Preview/Index History Clipboard Details

Display Full Report Show 5 Send to

All: 1 Current Only: 1 Genes Genomes: 1 SNP GeneView: 1

APP
(GeneID: 351)

1: APP amyloid beta (A4) precursor protein (peptidase nexin-II, Alzheimer disease) [Homo sapiens]
GeneID: 351 Primary source: [HGNC:620](#) updated 26-Jul-2006

Summary

has_protein_name

amyloid beta A4 protein

Official Symbol: APP and **Name:** amyloid beta (A4) precursor protein (peptidase nexin-II, Alzheimer disease) provided by [HUGO Gene Nomenclature Committee](#)
See related: [HPRD:00100](#), [MIM:104760](#)
Gene type: protein coding
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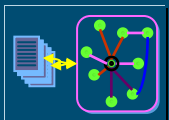
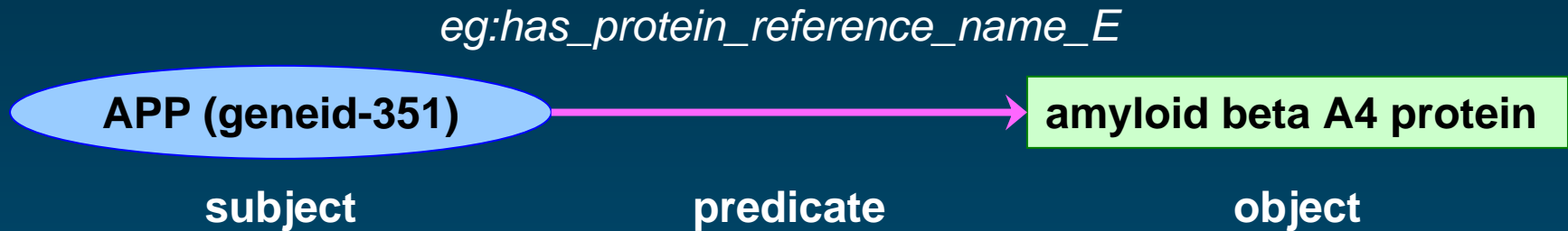
Entrez Gene Home

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- Interactions
- General gene information
- General protein information
- Reference Sequences
- Related Sequences
- Additional Links
- Links

General protein information

Names: amyloid beta A4 protein
protease nexin-II; A4 amyloid protein; amyloid-beta protein; beta-amyloid peptide; cerebral vascular amyloid peptide; amyloid beta (A4) precursor protein (protease nexin-II, Alzheimer disease)

RDF triple Gene property



RDF graph Connecting several genes

MAPT → Parkinson disease

MAPT → Pick disease

PARK1 → Parkinson disease

TBP → Parkinson disease

TBP → Spinocerebellar ataxia

has_associated_disease

MAPT → Parkinson disease

MAPT → Pick disease

PARK1 → Parkinson disease

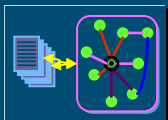
TBP → Parkinson disease

TBP → Spinocerebellar ataxia

MAPT → Pick disease

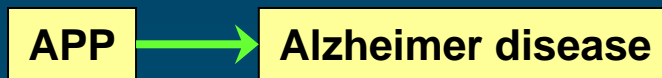
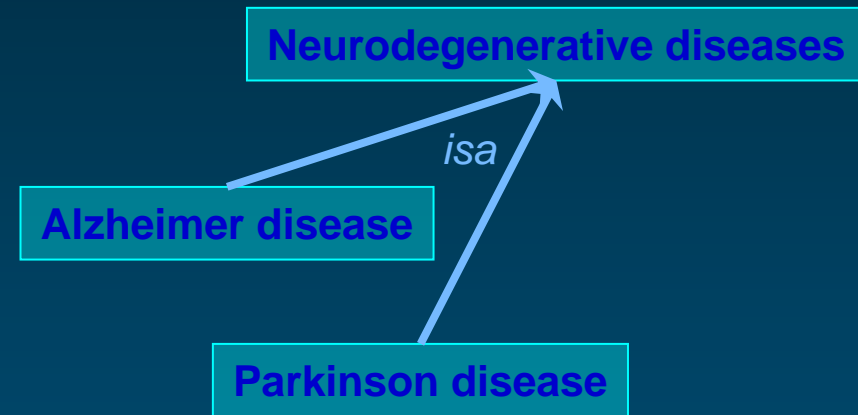
PARK1 → Parkinson disease

TBP → Spinocerebellar ataxia

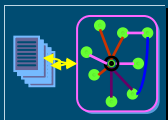
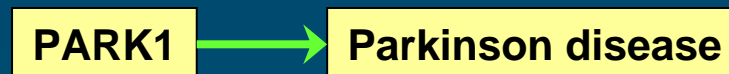


Future work

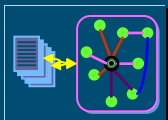
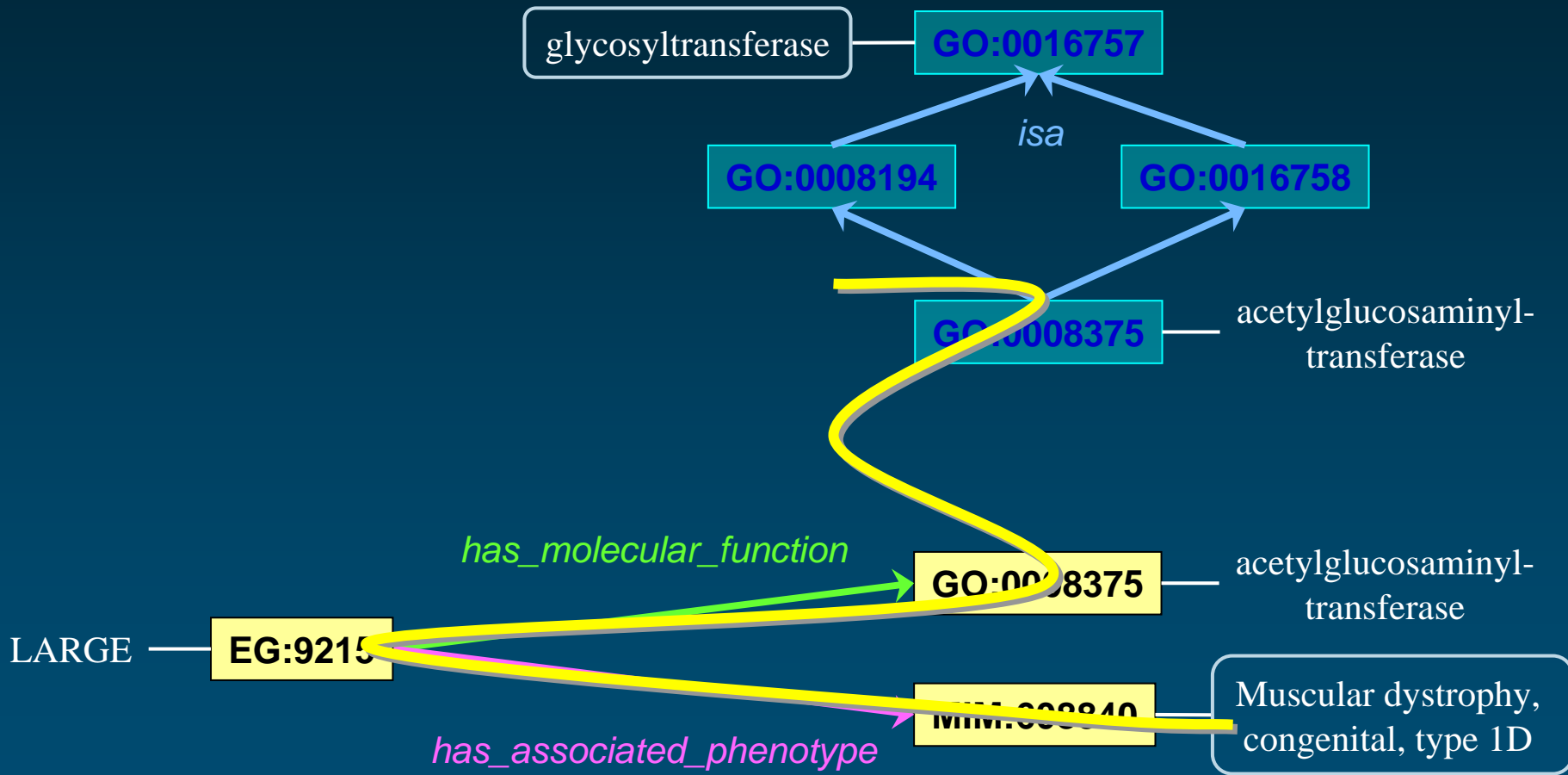
- ◆ Transform additional resources into RDF
 - UMLS Metathesaurus
 - Other NCBI databases
 - Drug knowledge bases
 - ...
- ◆ Integrate resources
 - Query across resources



has_associated_disease



From *glycosyltransferase* to congenital muscular dystrophy



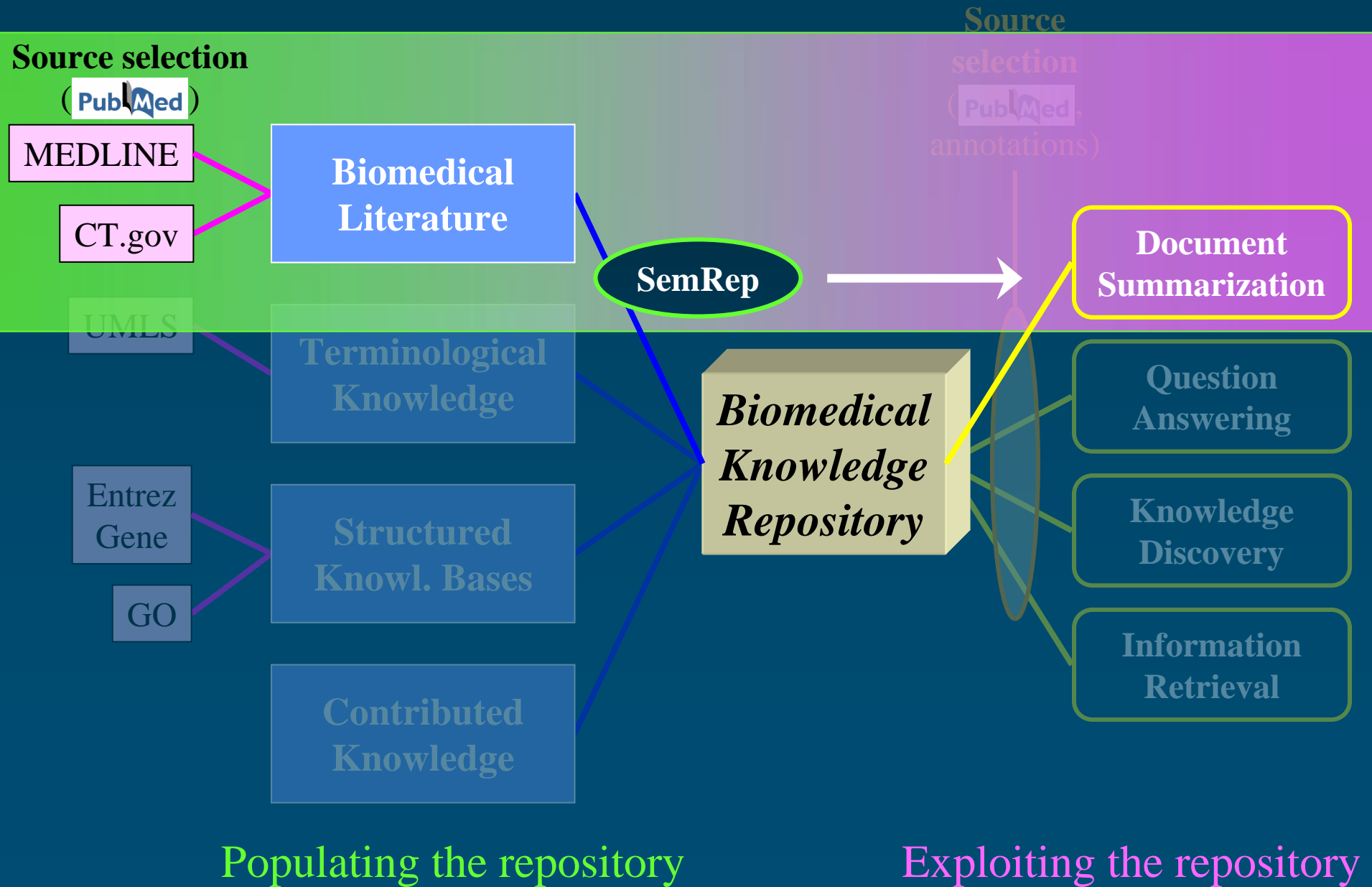
Pilot #2

Populating and exploiting the Biomedical Knowledge Repository

*Semantic Medline:
Multi-document summarization
and visualization*

With Marcelo Fiszman, M.D., Ph.D.
and Halil Kilicoglu, M.S.

Advanced Library Services Pilot projects

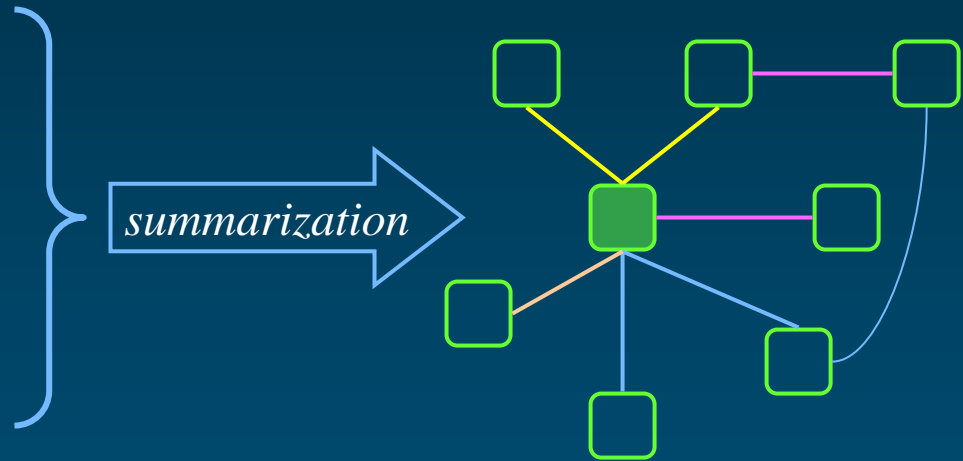


Managing retrieval results



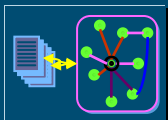
500 citations

Information retrieval

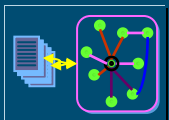
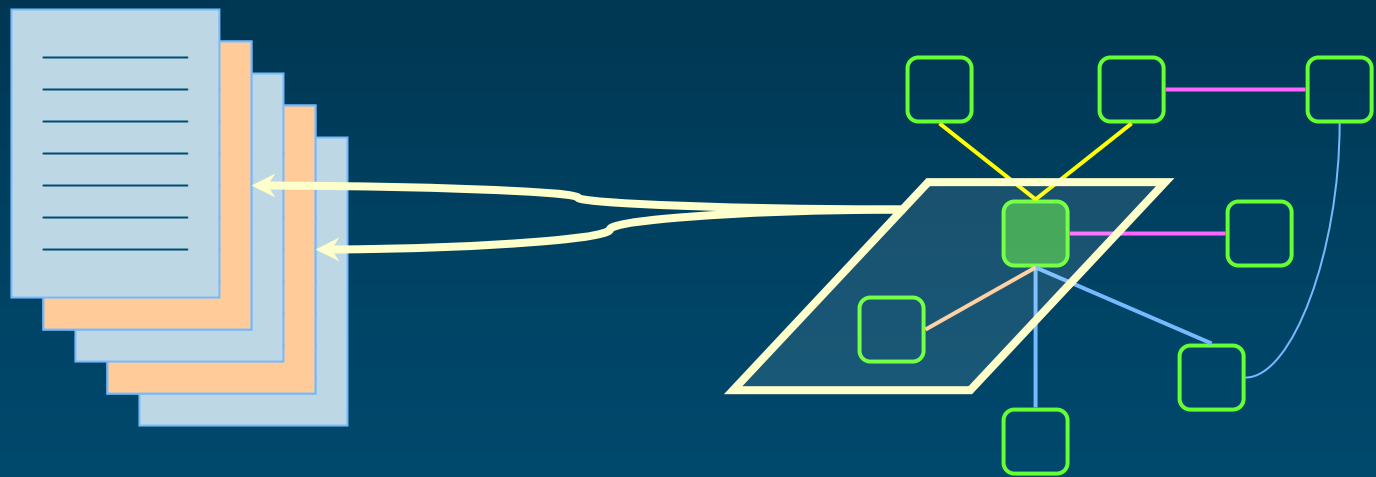


Network of relations

Semantic Medline

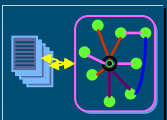


Managing retrieval results



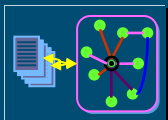
Guiding principles

- ◆ Visualization
 - Overview first [Shneiderman 1996]
 - Details on demand
- ◆ Integration of knowledge content [BoSC, April, 2006]
- ◆ Automated management of knowledge from text
- ◆ Seamless application interfaces

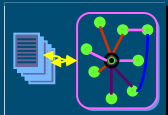
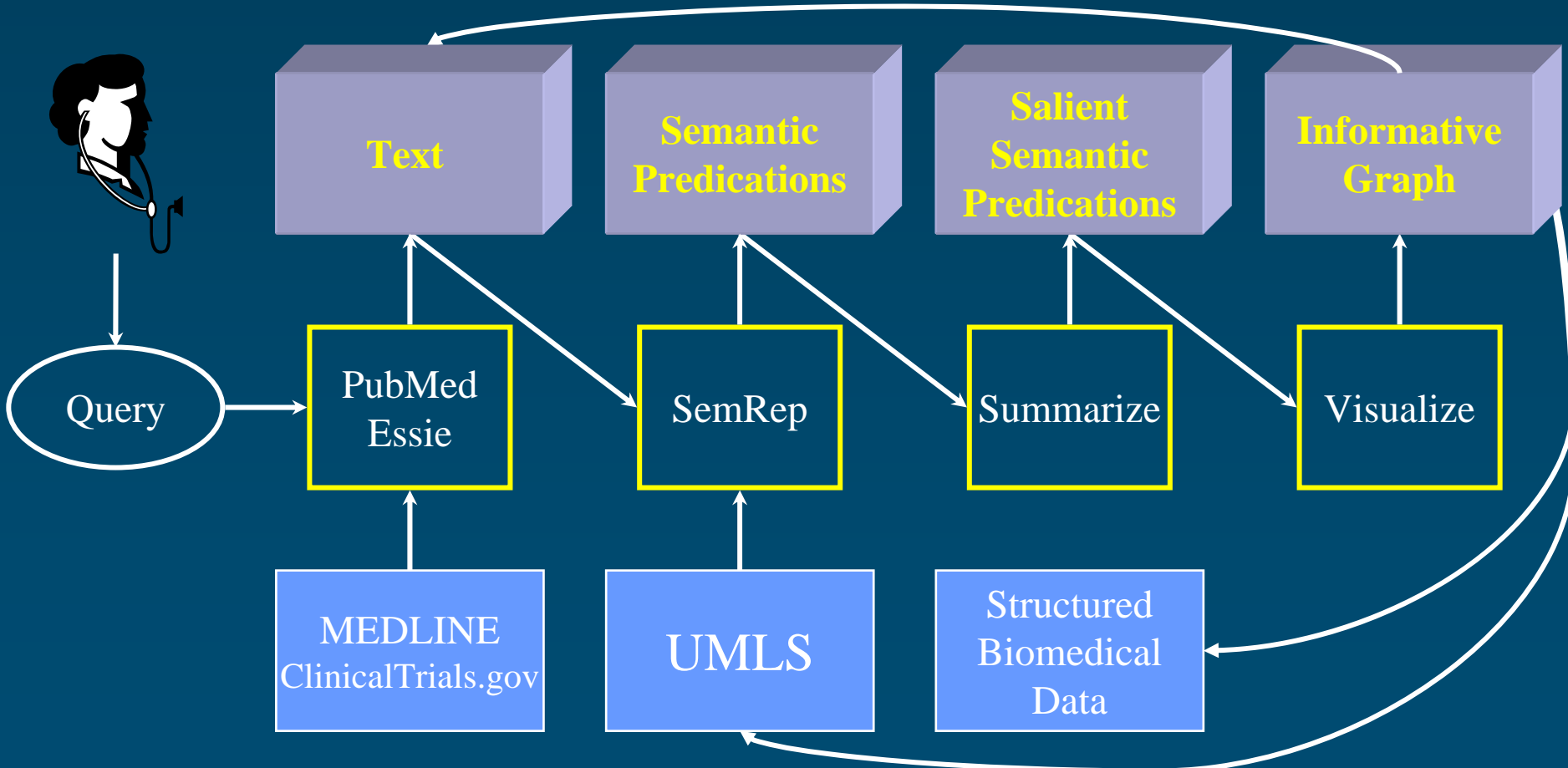


Seamless integration of technologies

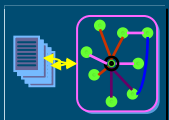
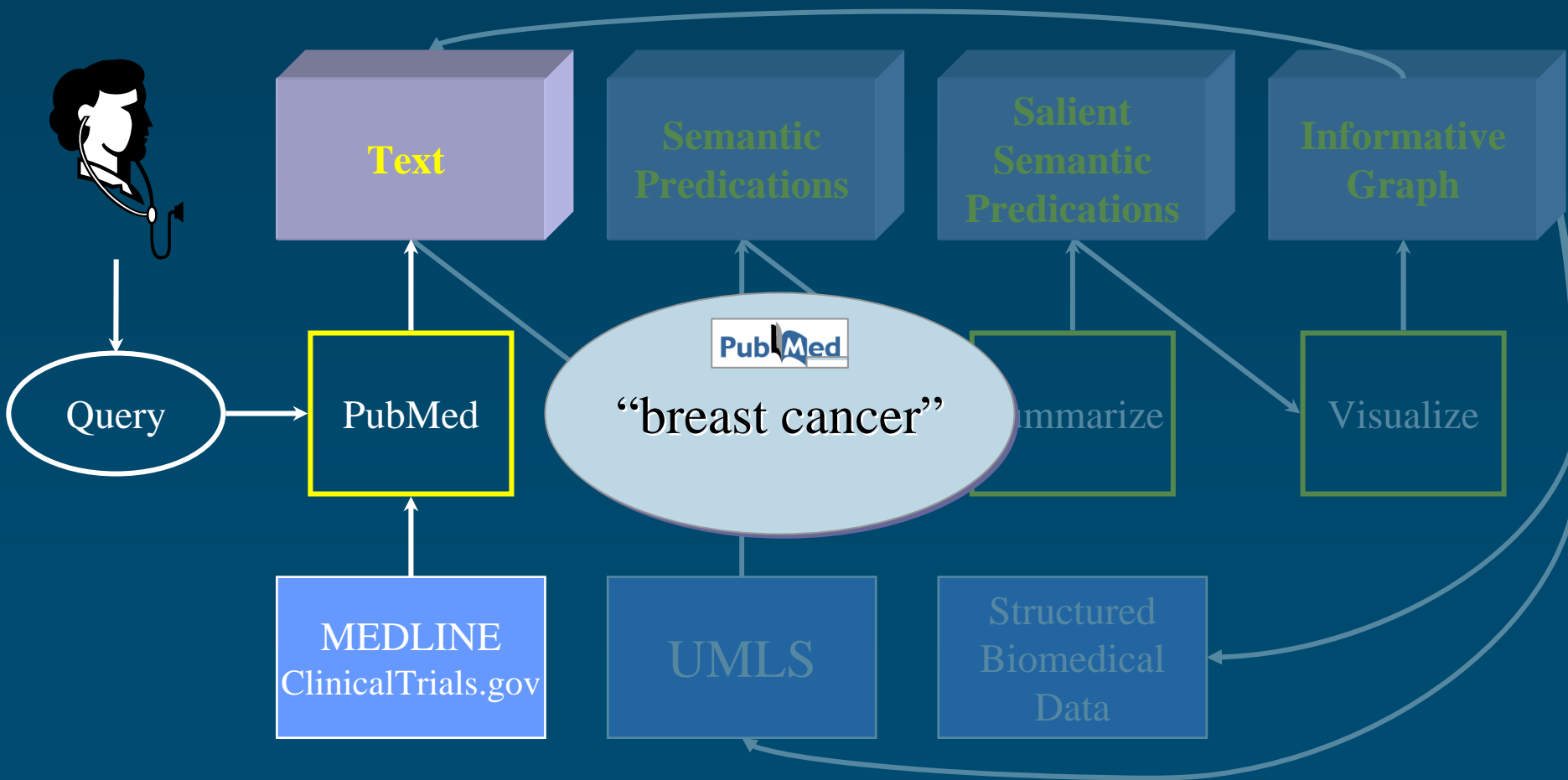
- ◆ Information retrieval
 - PubMed - MEDLINE
 - Essie - ClinicalTrials.gov
- ◆ Natural language processing: [SemRep](#)
 - Represent content of text with semantic predications
- ◆ Abstraction summarization
 - Informative: Overview of most salient information
- ◆ Visualization
 - Indicative: Links to source text and additional information



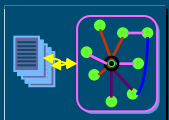
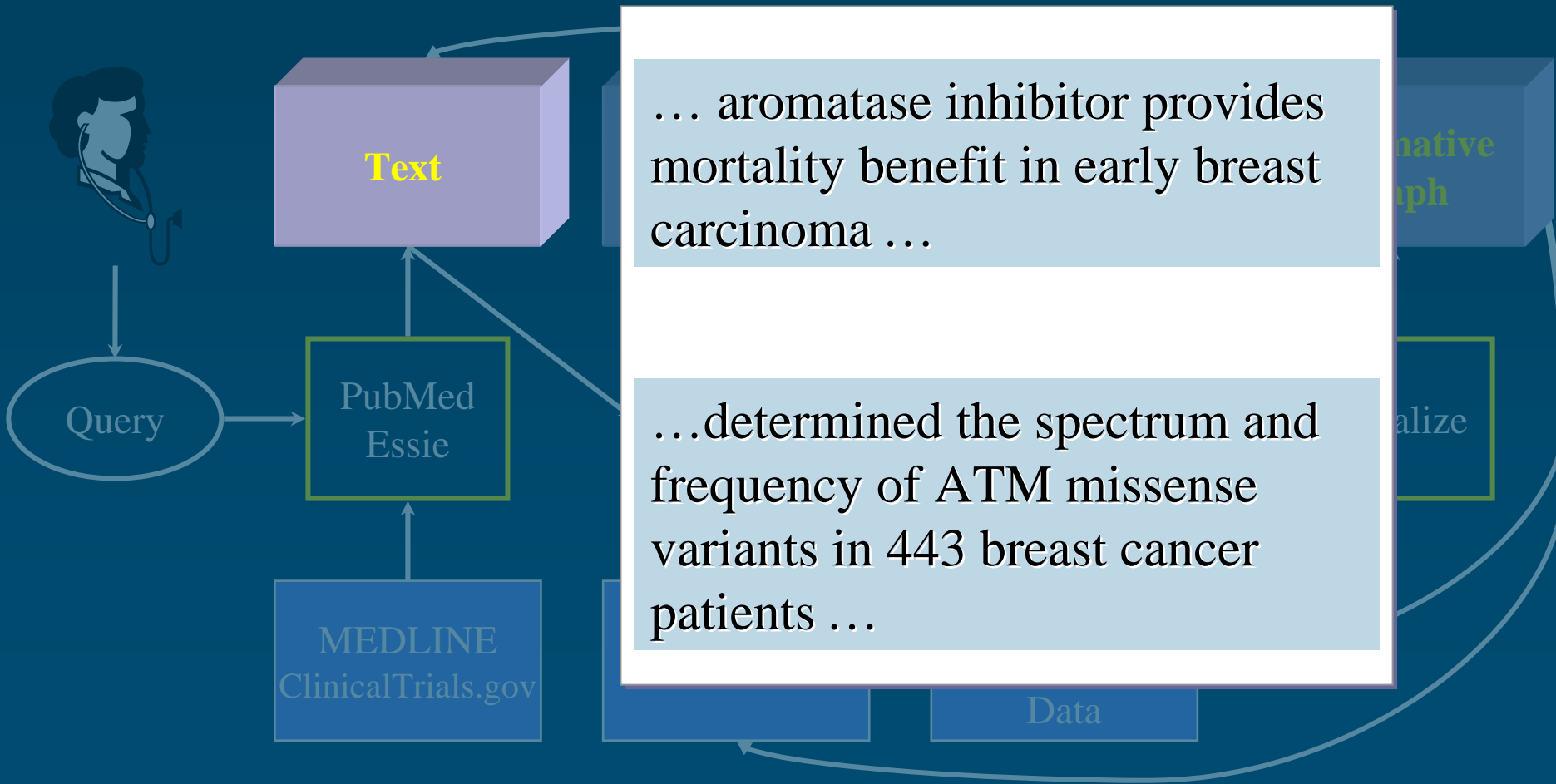
Semantic Medline Overview



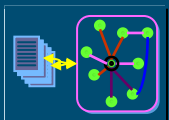
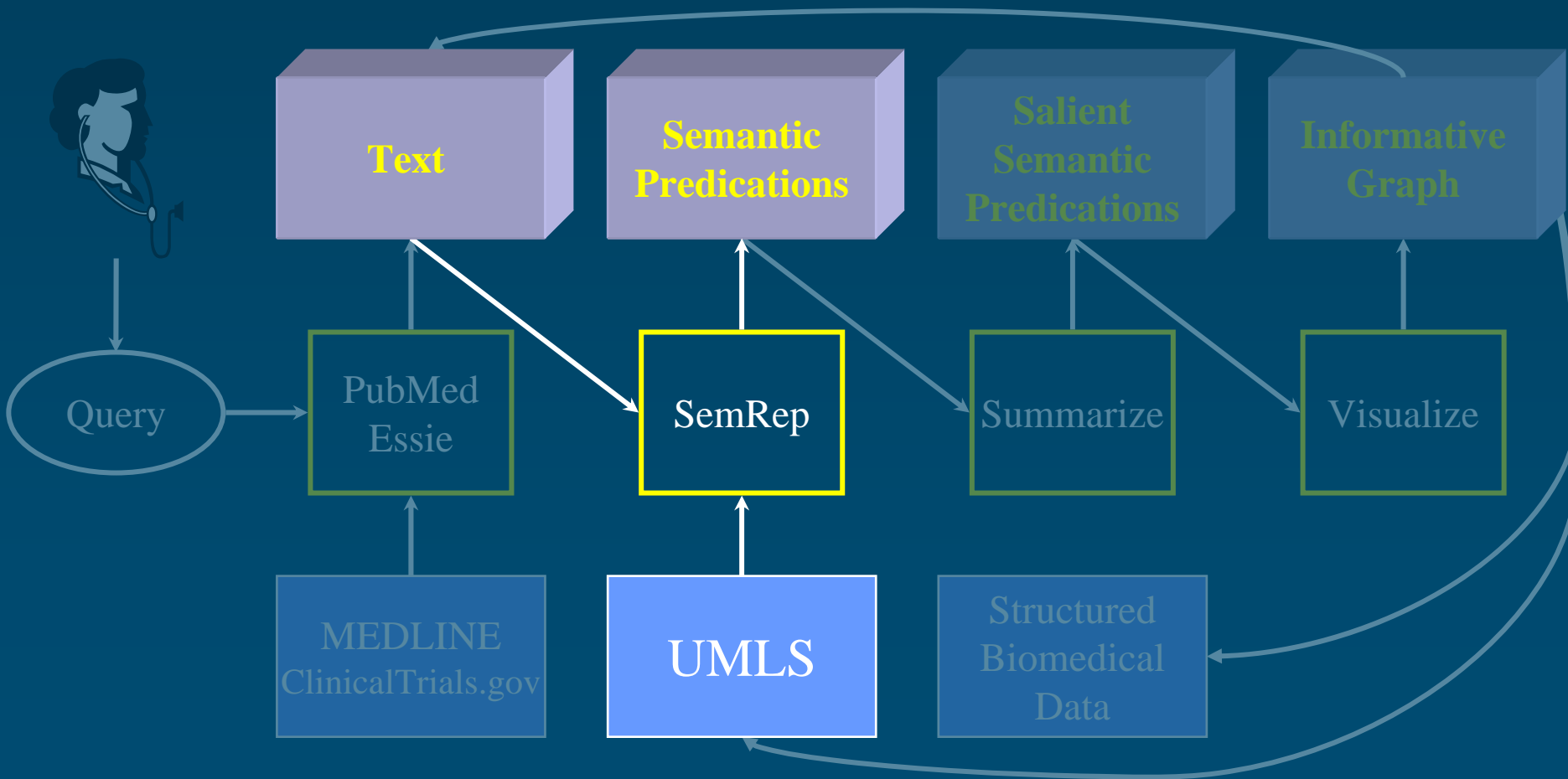
Document selection



MEDLINE citations



Semantic interpretation

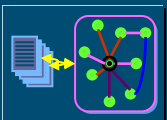


Semantic interpretation

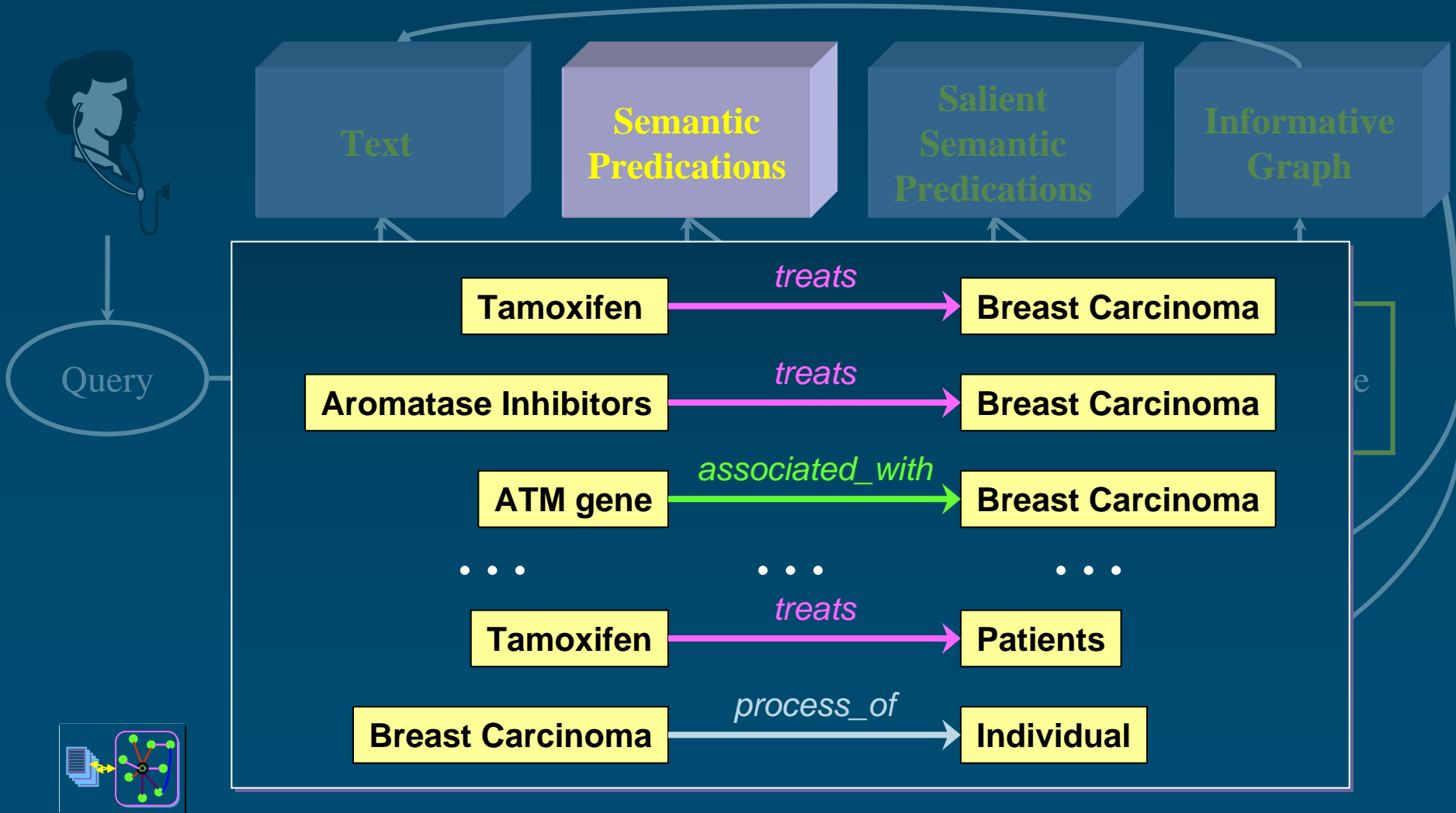
... aromatase inhibitor provides mortality benefit in early breast carcinoma ...



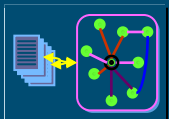
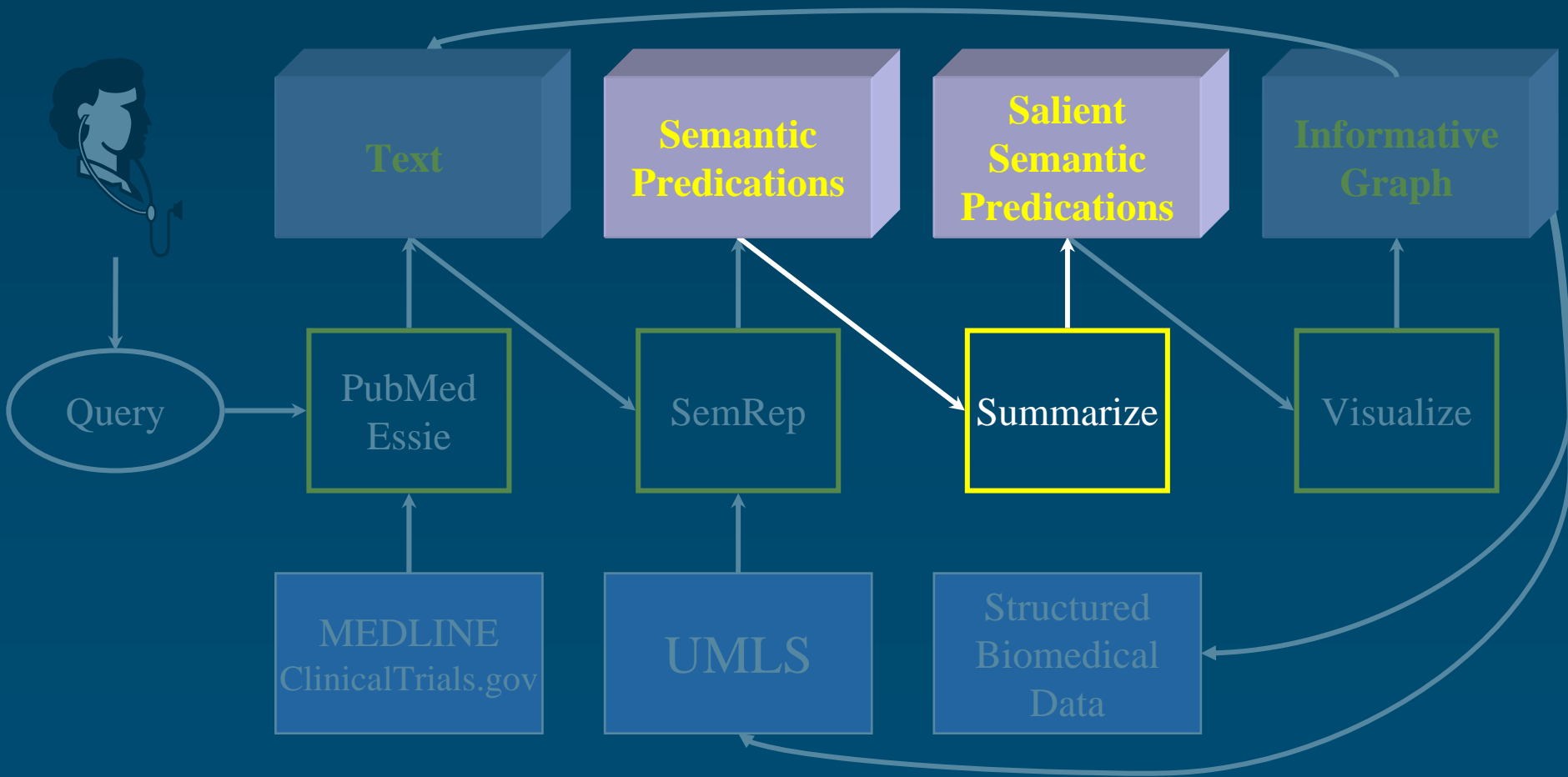
... determined the spectrum and frequency of ATM missense variants in 443 breast cancer patients ...



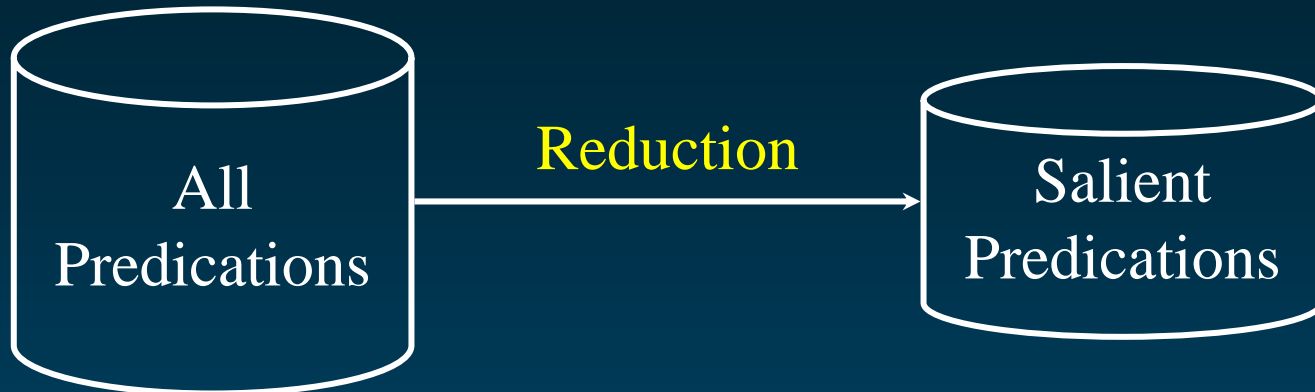
Semantic predications



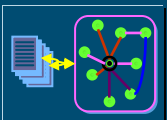
Summarization



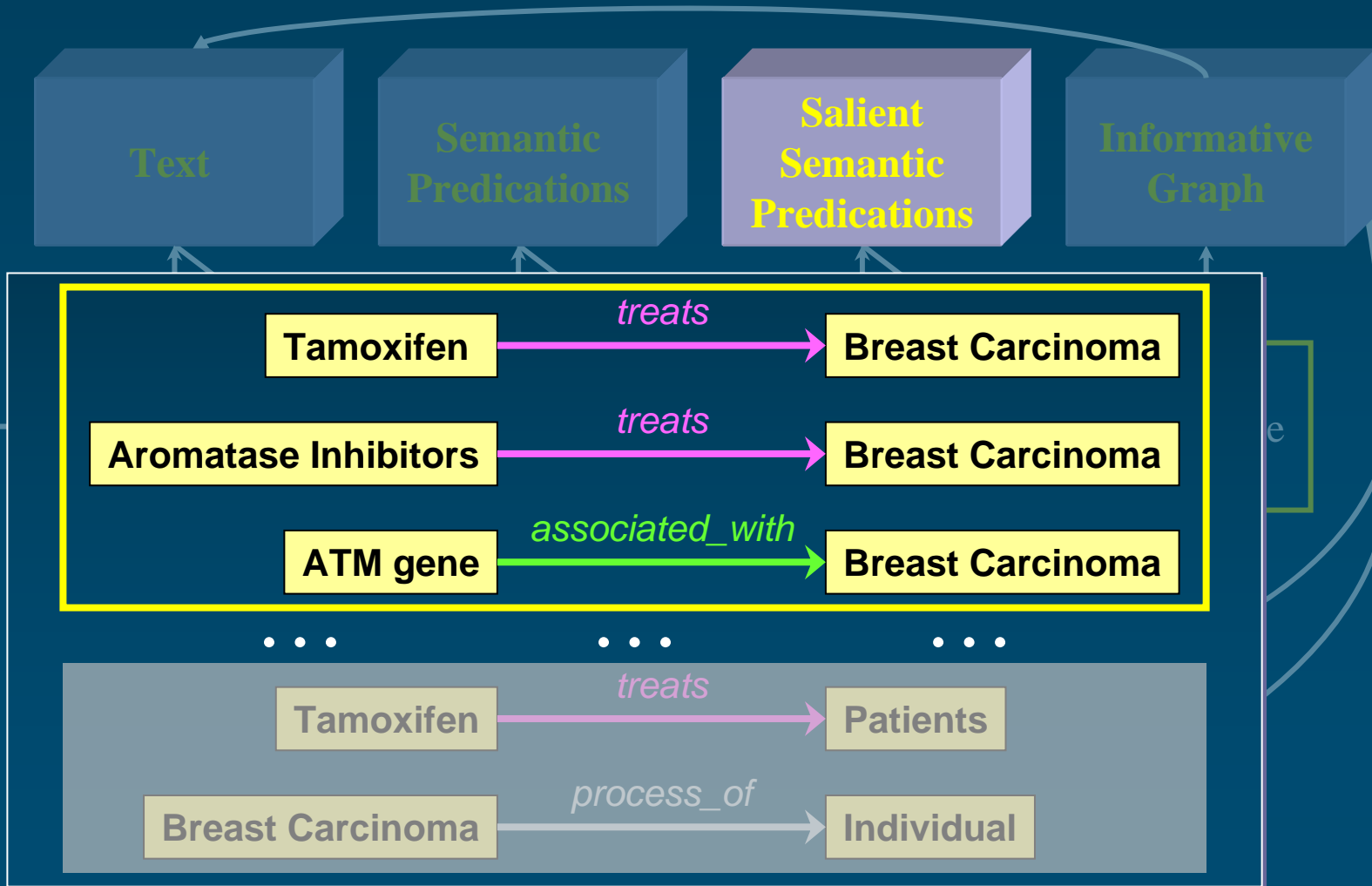
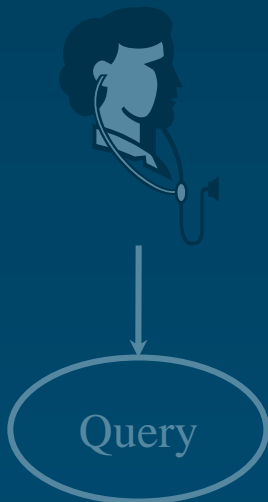
Abstraction summarization



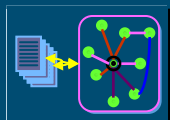
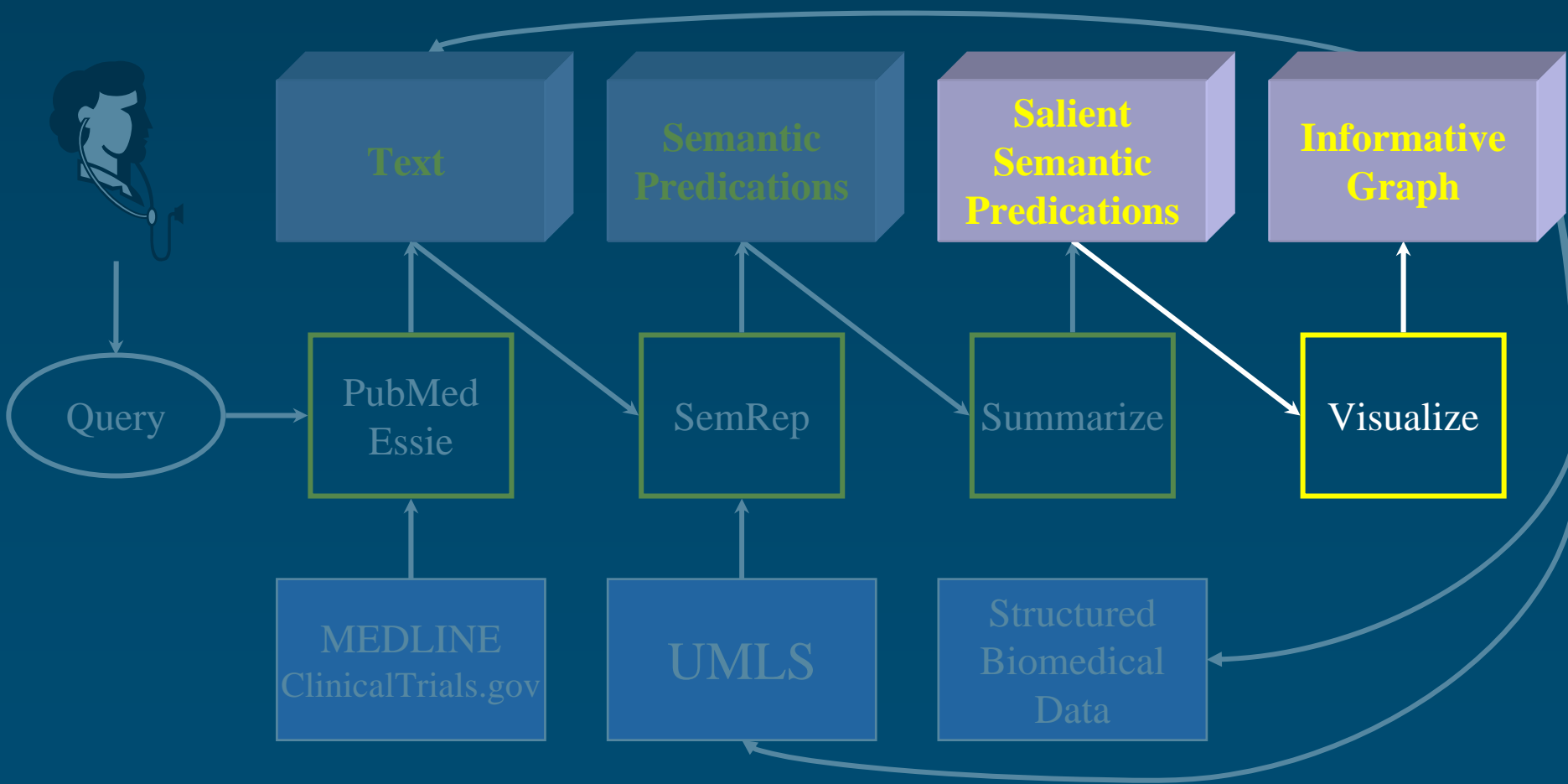
- ◆ Specify a topic
- ◆ Retain predications on the topic
- ◆ Eliminate uninformative predications
- ◆ Retain most frequent predications



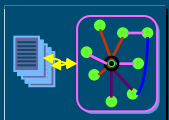
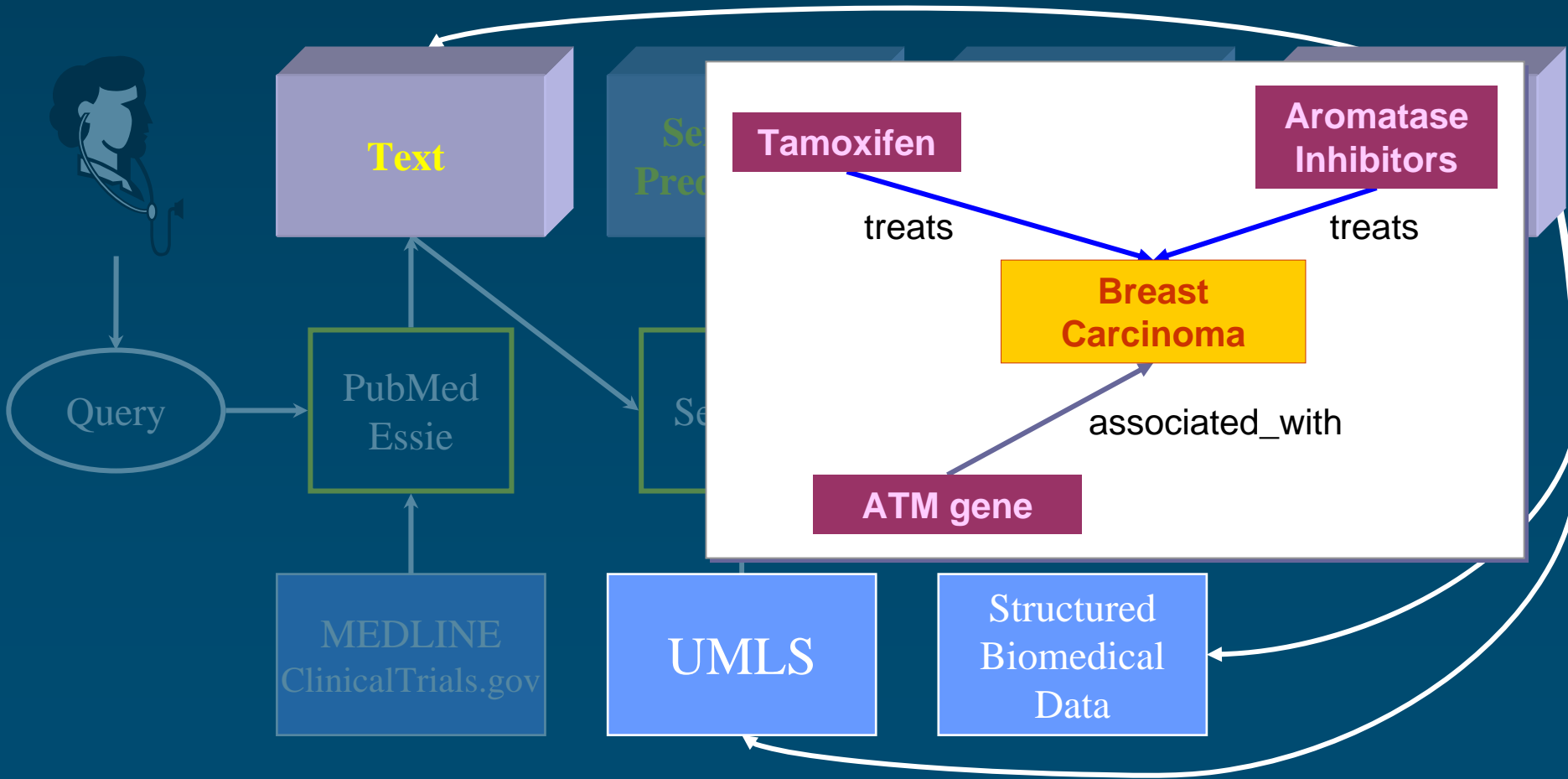
Salient semantic predications



Visualization



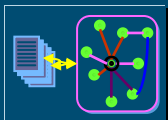
Informative graph



Semantic Medline Live

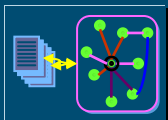
The screenshot displays the Semantic MEDLINE Prototype interface in a Mozilla Firefox browser window. The main area features a network graph with 'Breast Carcinoma' as the central node, connected to various related concepts such as 'ERBB2 gene', 'Herceptin', 'Estrogens', 'rastuzumab', 'Immunologic Adjuvants', 'BRCA1 Protein', 'BRCA2 Protein', 'Aromatase Inhibitors', 'BCL-2 Protein', 'Lignans', 'Hormones', 'Adiponectin', 'Neoplasms', 'cohort', 'Mice, Nude', 'Mammary Neoplasms', 'Breast cancer invasive NOS', 'BRCA1 Mutation', 'cancer regression', 'woman', 'cancer metastatic', 'Neoplasm Metastasis', 'DUSP22 gene', 'ESR1 protein, human', 'Carbon', 'Eld', 'Anthracycline Antibiotics', 'Untranslated Regions', 'Protein p53', 'Psychologist - Health', 'Estradiol', 'Tamoxifen', 'cyclooxygenase 2', '17q23', and 'Neoplasm progres'. A right-hand sidebar lists relationship types: ASSOCIATED_WITH, CAUSES, COEXISTS_WITH, DISRUPTS, INHIBITS, INTERACTS_WITH, ISA, LOCATION_OF, and PART_OF. Below the graph, the following text is displayed:

PMID- 17393301
DP - 2007 Mar 28
T1 - The spectrum of ATM missense variants and their contribution to contralateral breast cancer.
AB - Heterozygous carriers of ATM mutations are at increased risk of breast cancer. In this case-control study, we evaluated the significance of germline ATM missense variants to the risk of contralateral breast cancer (CBC). We have determined the spectrum and frequency of ATM missense variants in 443 breast cancer patients diagnosed before age 50, including 247 patients who subsequently developed CBC. Twenty-one per cent of the women with



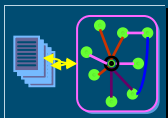
Related research Visualizing relations

- ◆ Maps of linked concepts among document
[Fuller et al. 2004]
- ◆ Literature network of co-occurring genes
[Jensen et al. 2001]
- ◆ Associative concept space for discovery
[van der Eijk et al. 2004]
- ◆ Genomic information across structured and textual databases
[Tao et al. 2005]



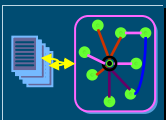
Future work

- ◆ Process all of MEDLINE/PubMed
 - With SemRep
- ◆ Incrementally integrate structured knowledge sources
 - Entrez databases
 - UMLS
 - Genetics Home Reference
- ◆ Implementation
 - Efficiency
 - Large amount of data



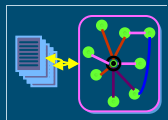
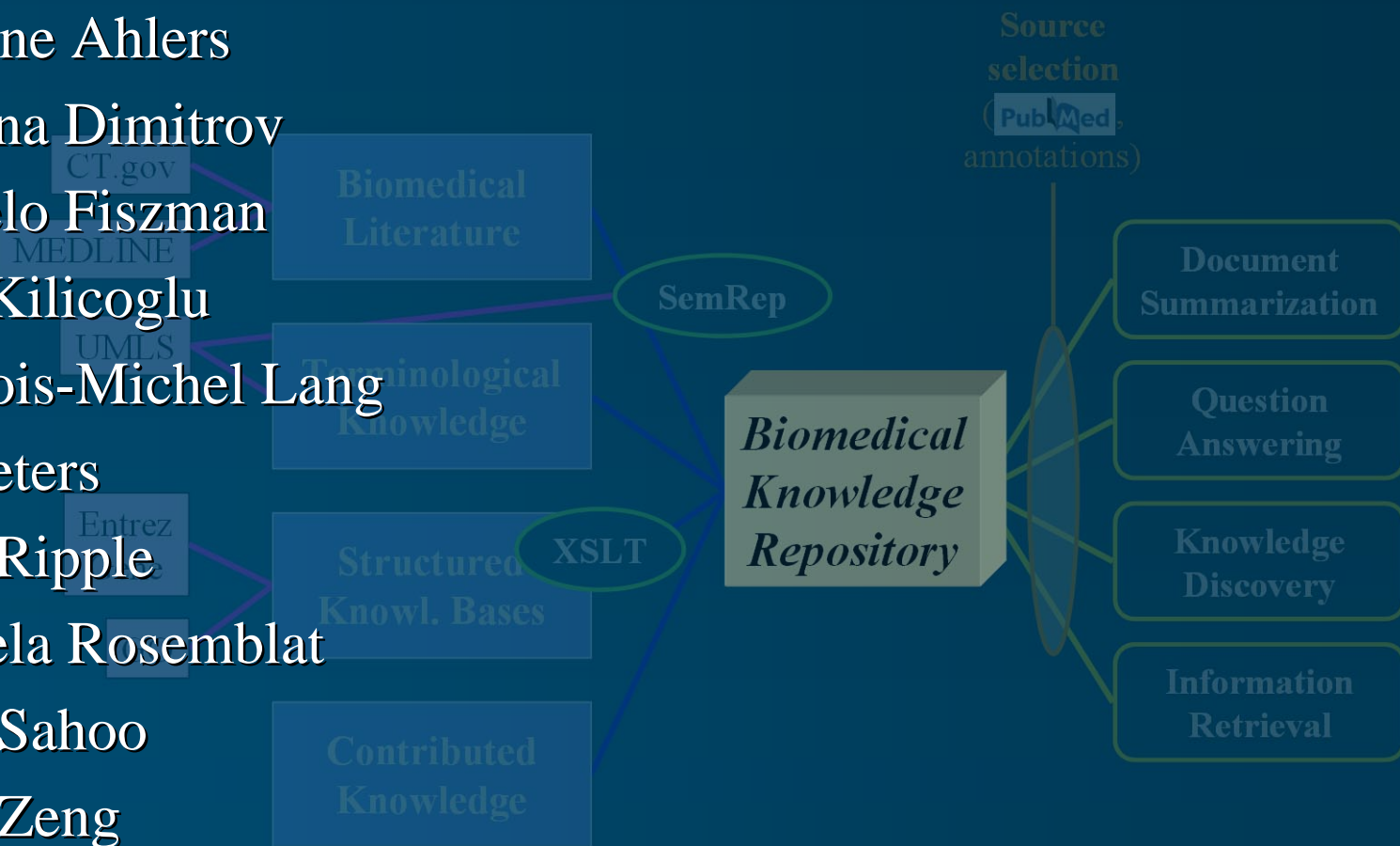
Summary

- ◆ Deliver health information
 - Biomedical Knowledge Repository
 - Advanced Library Services
- ◆ Exploit
 - Current Library resources
 - Advanced information technology
- ◆ Support timely translation
 - Of biomedical research
 - Into improvements in patient care and public health



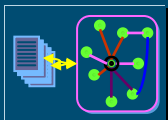
Acknowledgments

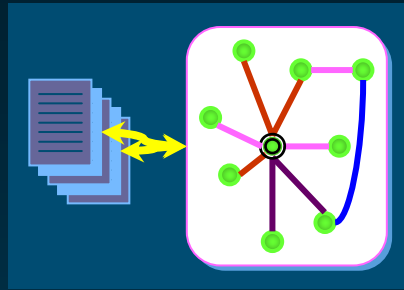
- ◆ Caroline Ahlers
- ◆ Mariana Dimitrov
- ◆ Marcelo Fiszman
- ◆ Halil Kilicoglu
- ◆ François-Michel Lang
- ◆ Lee Peters
- ◆ Anna Ripple
- ◆ Graciela Roseblat
- ◆ Satya Sahoo
- ◆ Kelly Zeng



References

- ◆ Bodenreider O, Rindflesch TC. *Advanced library services: Developing a biomedical knowledge repository to support advanced information management applications*. Technical report. Bethesda, Maryland: Lister Hill National Center for Biomedical Communications, National Library of Medicine; September 14, 2006.
<http://lhncbc.nlm.nih.gov/lhc/docs/reports/2006/tr2006001.pdf>





Advanced Library Services

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