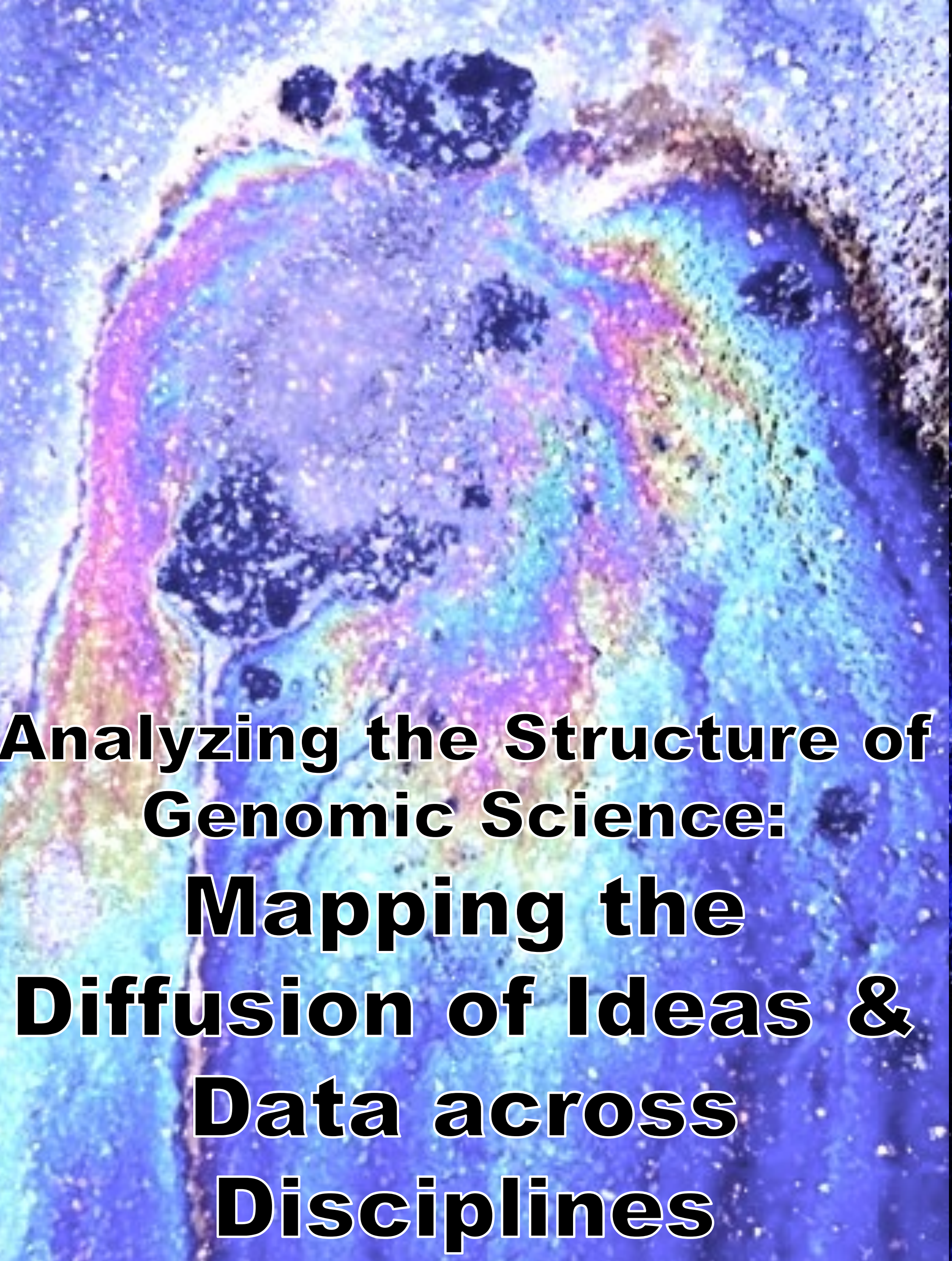
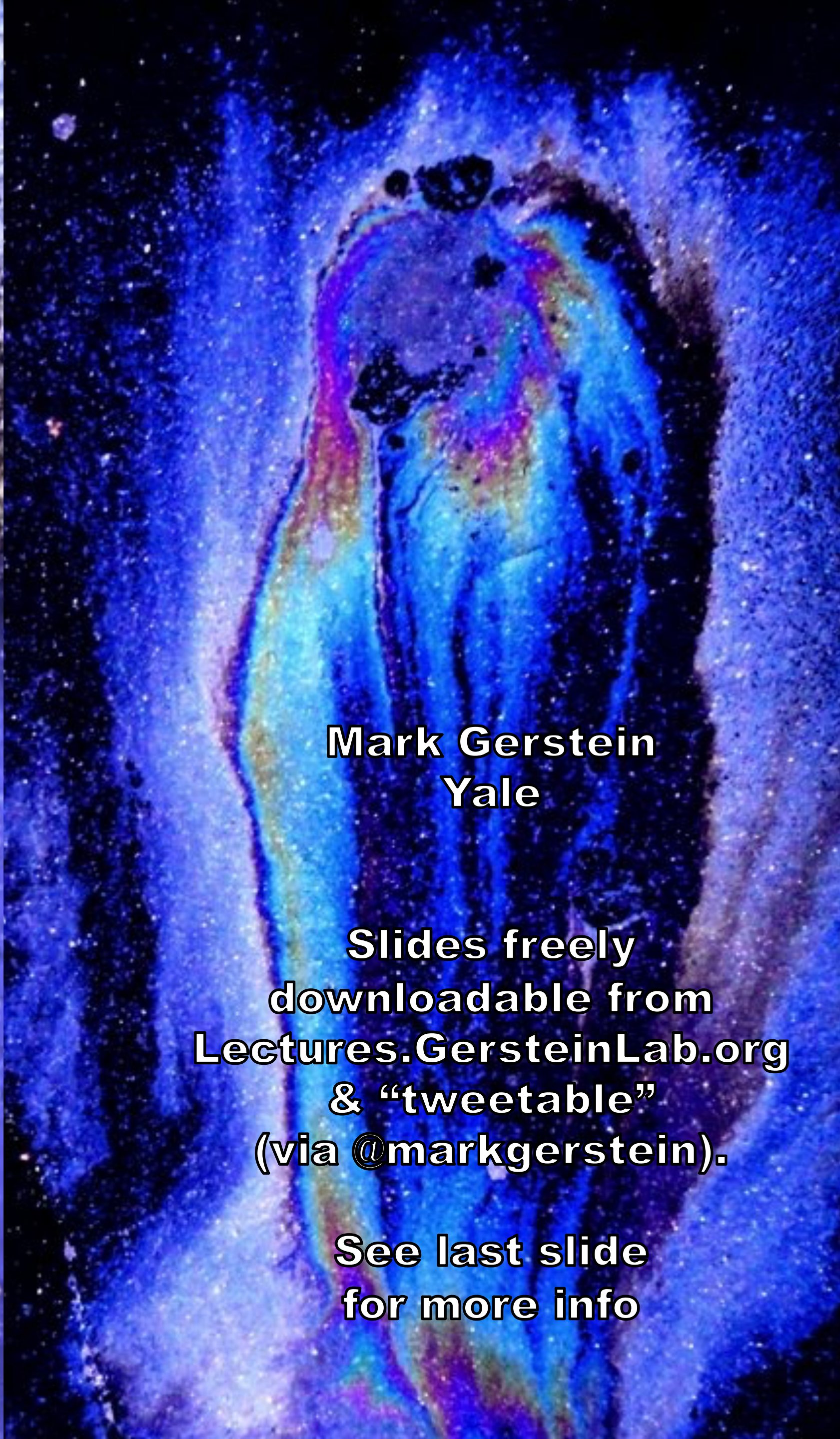


# Analyzing the Structure of Genomic Science: Mapping the Diffusion of Ideas & Data across Disciplines

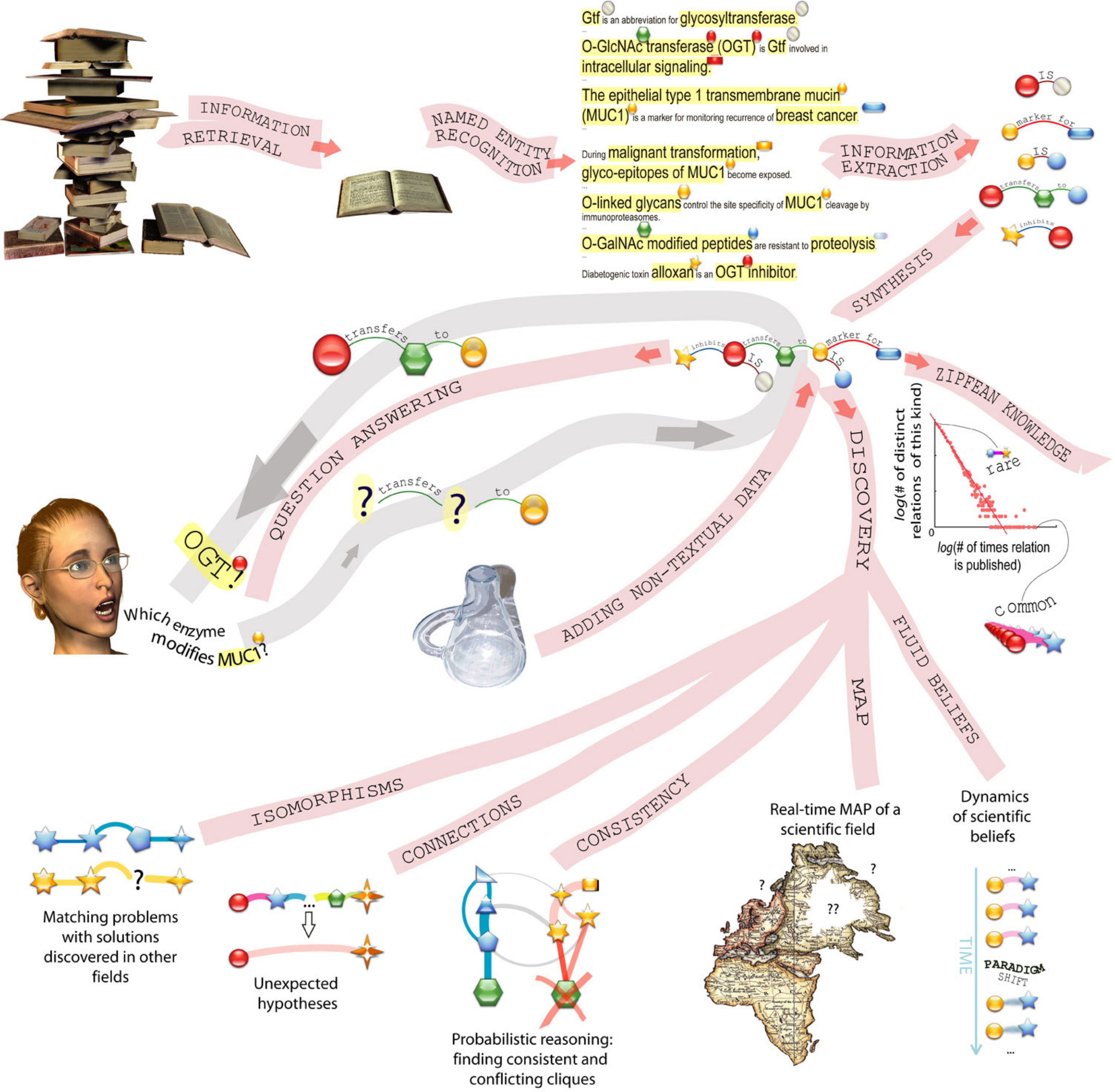


Mark Gerstein
Yale

Slides freely downloadable from Lectures.GersteinLab.org & “tweetable” (via @markgerstein).

See last slide for more info

# Vision for Mining Large-scale Structured Literature



Gtf is an abbreviation for glycosyltransferase

O-GlcNAc transferase (OGT) is Gtf involved in intracellular signaling.

The epithelial type 1 transmembrane mucin (MUC1) is a marker for monitoring recurrence of breast cancer.

During malignant transformation, glyco-epitopes of MUC1 become exposed.

O-linked glycans control the site specificity of MUC1 cleavage by immunoproteasomes.

O-GalNAc modified peptides are resistant to proteolysis.

Diabetogenic toxin alloxan is an OGT inhibitor.

Which enzyme modifies MUC1?

Matching problems with solutions discovered in other fields

Unexpected hypotheses

Probabilistic reasoning: finding consistent and conflicting cliques

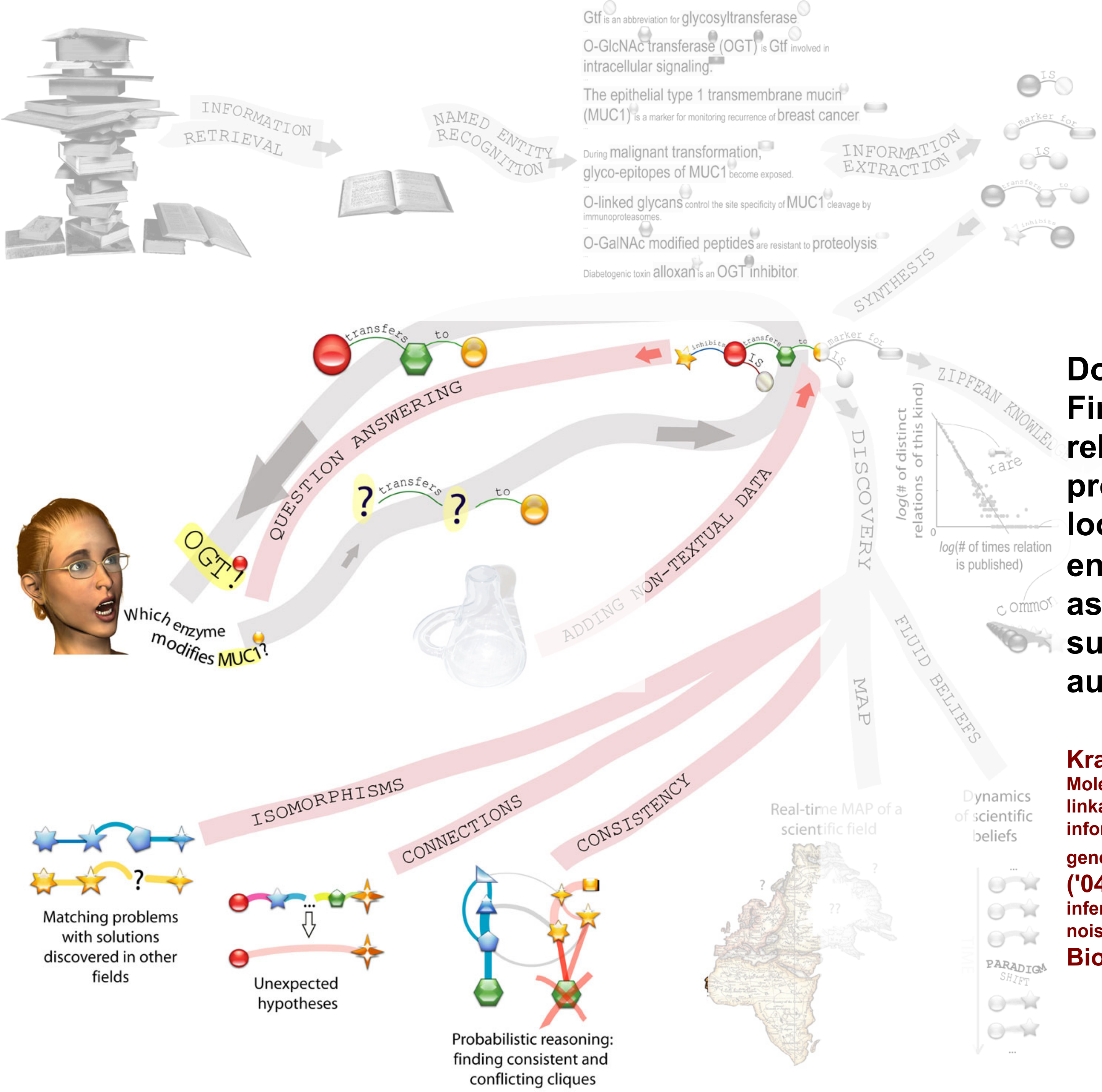
Real-time MAP of a scientific field

Dynamics of scientific beliefs

Harnessing the “Data Exhaust” from large-scale efforts

[Rzhetsky et al, Cell ('08), PLOS CB ('09); Bourne et al. PLOS CB '08]

# Vision for Mining Large-scale Structured Literature


INFORMATION RETRIEVAL
NAMED ENTITY RECOGNITION
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INFORMATION EXTRACTION
IS
marker for
IS
transfers to
inhibits
SYNTHESIS
transfers to
inhibits transfers to
marker for
IS
ZIPFEAN KNOWLED
log(# of distinct relations of this kind)
0
rare
log(# of times relation is published)
common
QUESTION ANSWERING
? transfers ? to
OGT?
Which enzyme modifies MUC1?
ADDING NON-TEXTUAL DATA
DISCOVERY
MAP
FLUID BELIEFS
ISOMORPHISMS
CONNECTIONS
CONSISTENCY
?
Matching problems with solutions discovered in other fields
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?
??
?
Dynamics of scientific beliefs
...
TIME
PARADIGM SHIFT
...

**Doing better science: Finding new protein relationships (e.g. protein interactions), looking for inconsistencies in arguments, assembling consensus definitions automatically**

**Krauthammer et al. Molecular triangulation: bridging linkage and molecular-network information for identifying candidate genes in Alzheimer's disease. PNAS ('04); Iossifov et al. Probabilistic inference of molecular networks from noisy data sources. Bioinformatics ('04)**

[Rzhetsky et al, Cell ('08), PLOS CB ('09); Bourne et al. PLOS CB '08]

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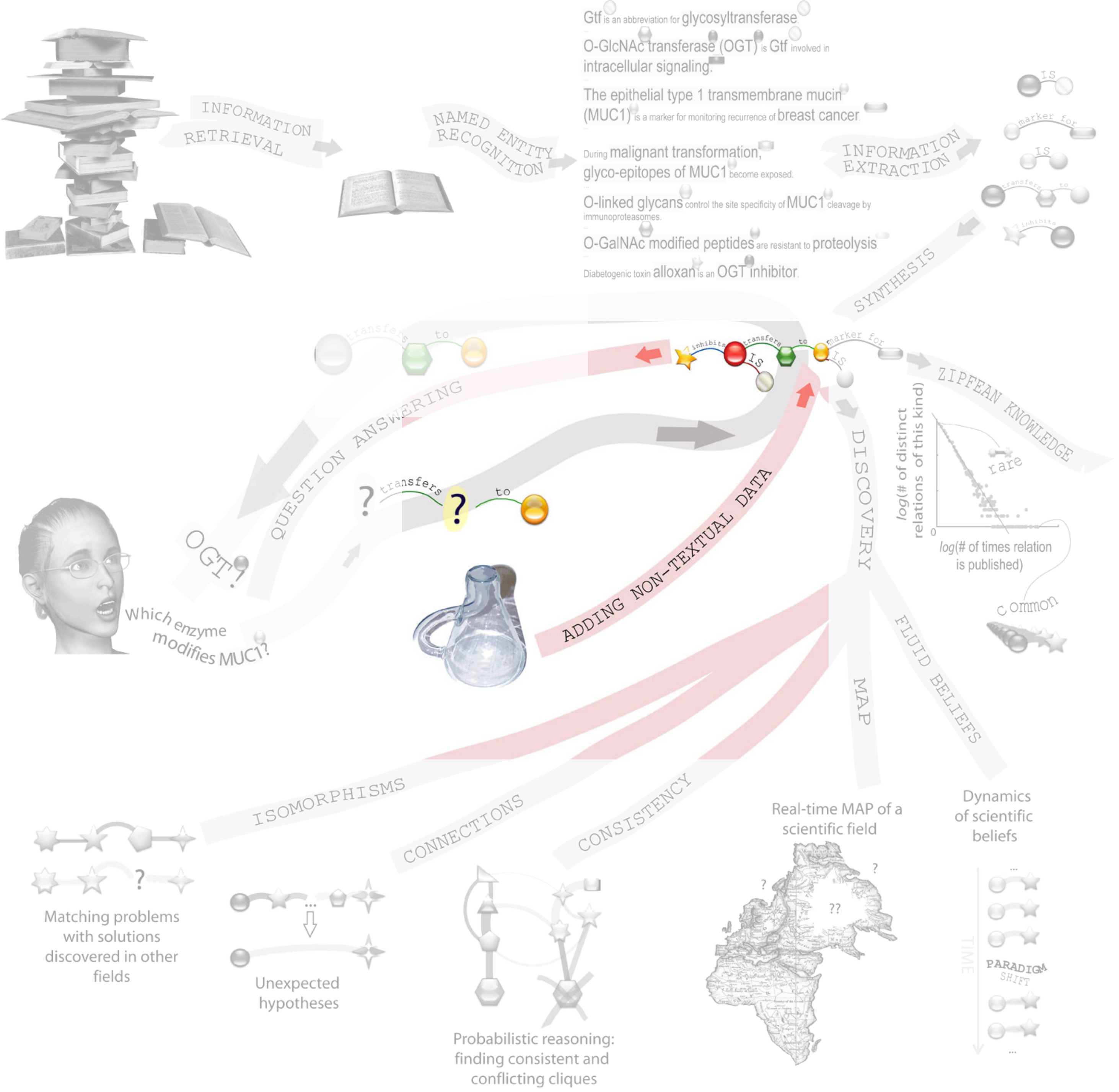

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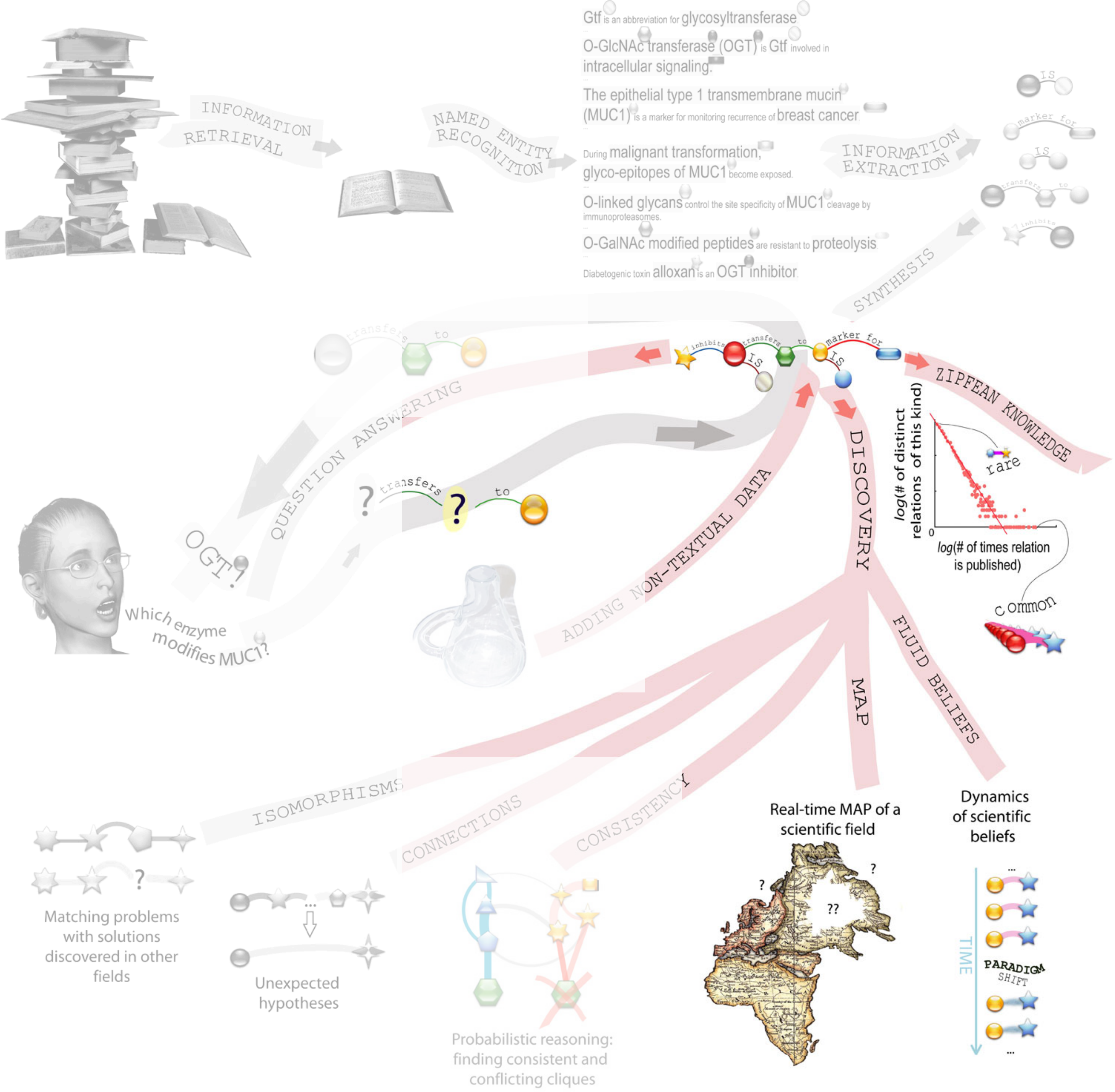
**Making it understand-able (through “mashup”)**

**SciVee, podcasts**

[Rzhetsky et al, Cell ('08), PLOS CB ('09); Bourne et al. PLOS CB '08]

# Vision for Mining Large-scale Structured Literature



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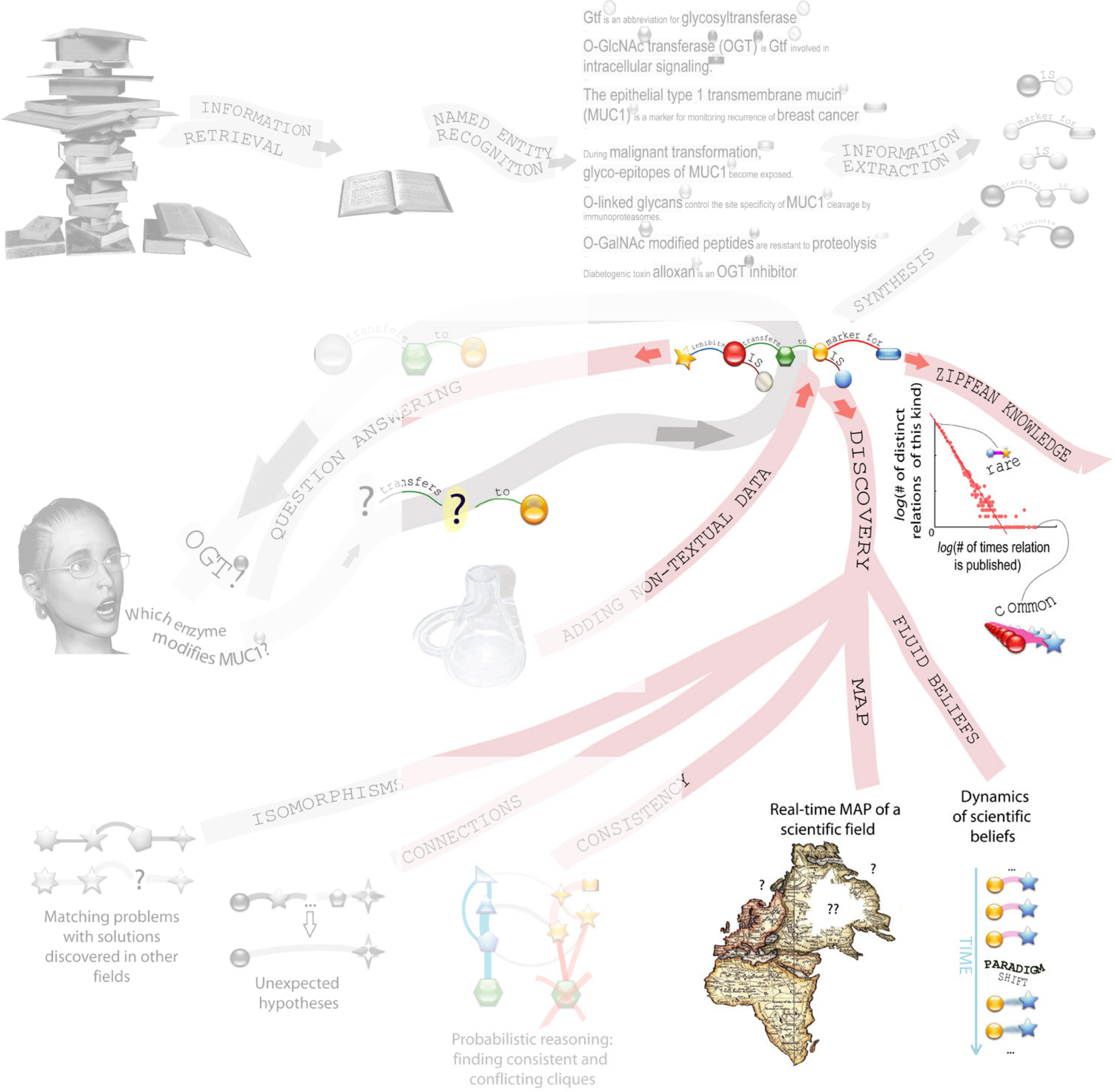
**Mapping Science**

**+**

**Studying its Dynamics & Evolution**

[Rzhetsky et al, Cell ('08), PLOS CB ('09); Bourne et al. PLOS CB '08]



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# Vision for Mining Large-scale Structured Literature

- Revealing patterns of collaboration
- Understanding basis of terms & nomenclature
- Tracking the evolution of ideas
- Models for the evolution of science;
- Helping set policy & research directions

[Rzhetsky et al, Cell ('08), PLOS CB ('09); Bourne et al. PLOS CB '08]

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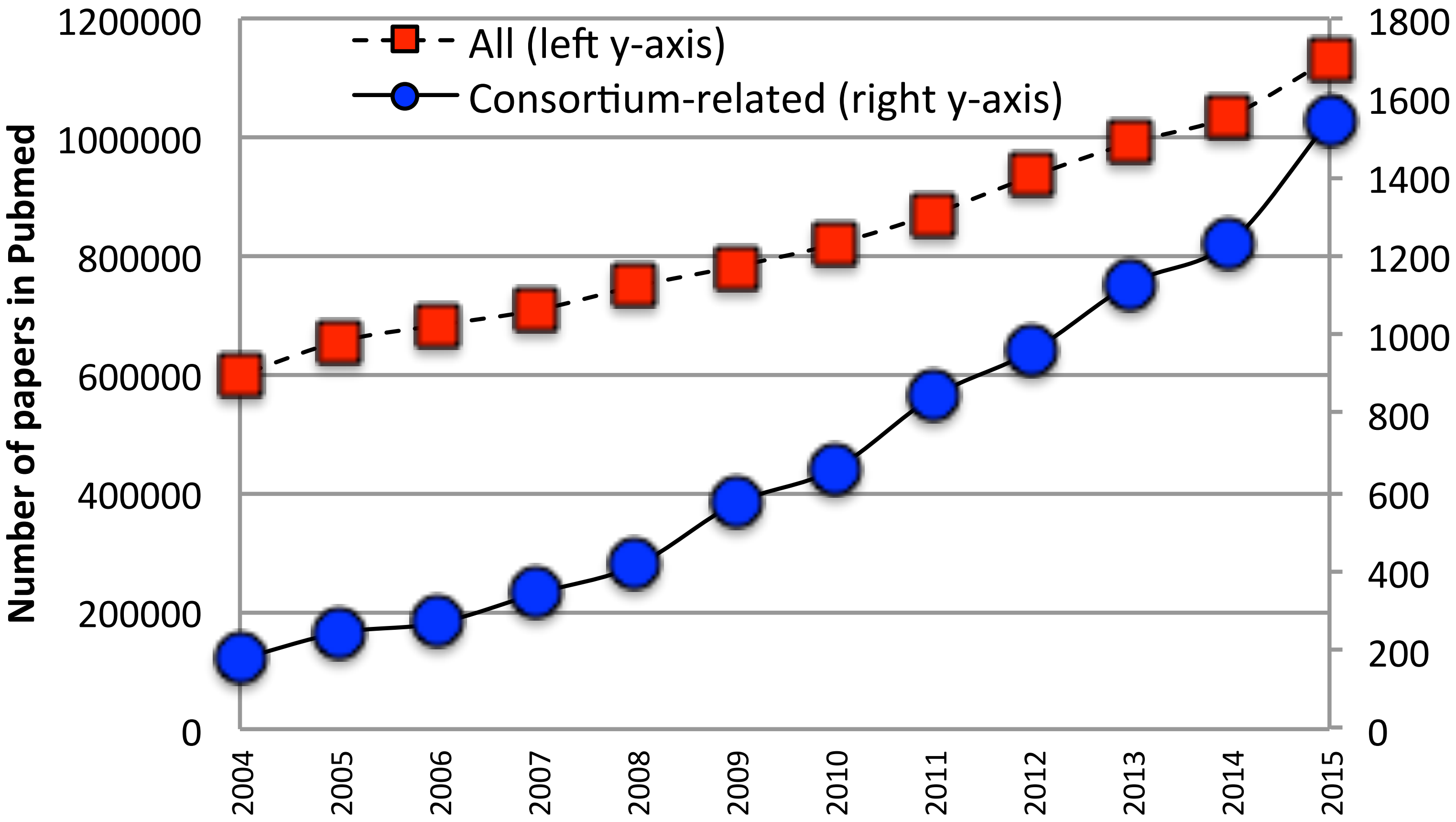
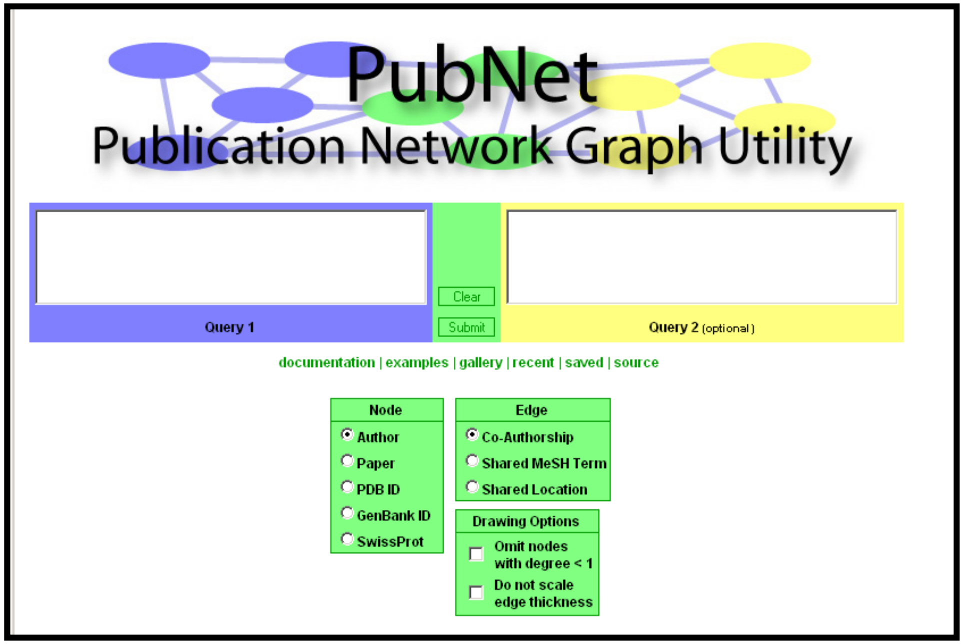
# Increase in Consortium Science



## Examples Illuminating Current State of Affairs:

# Using Network Representations to Make Maps of Science -- Studying the Publication Patterns of Genomics Consortia



PubNet

Publication Network Graph Utility

Clear

Submit

Query 1

Query 2 (optional)

documentation | examples | gallery | recent | saved | source

Node

● Author

○ Paper

○ PDB ID

○ GenBank ID

○ SwissProt

Edge

● Co-Authorship

○ Shared MeSH Term

○ Shared Location

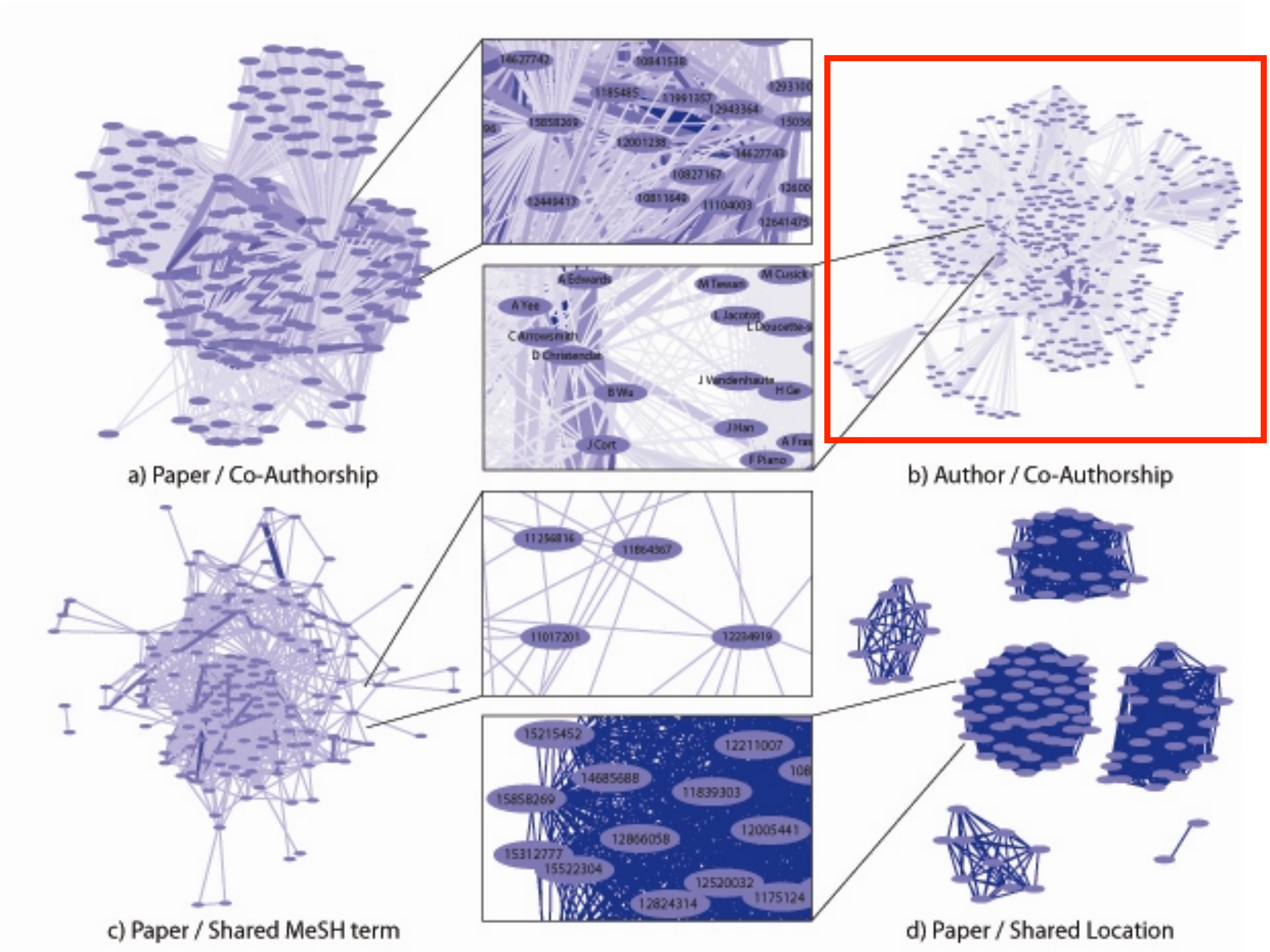
Drawing Options

□ Omit nodes with degree < 1

□ Do not scale edge thickness

[Douglas et al. GenomeBiol. ('05), pubnet.gersteinlab.org]

# Different Representations of the Publication Network of a Structural Genomics Center (NESG)



a) Paper / Co-Authorship

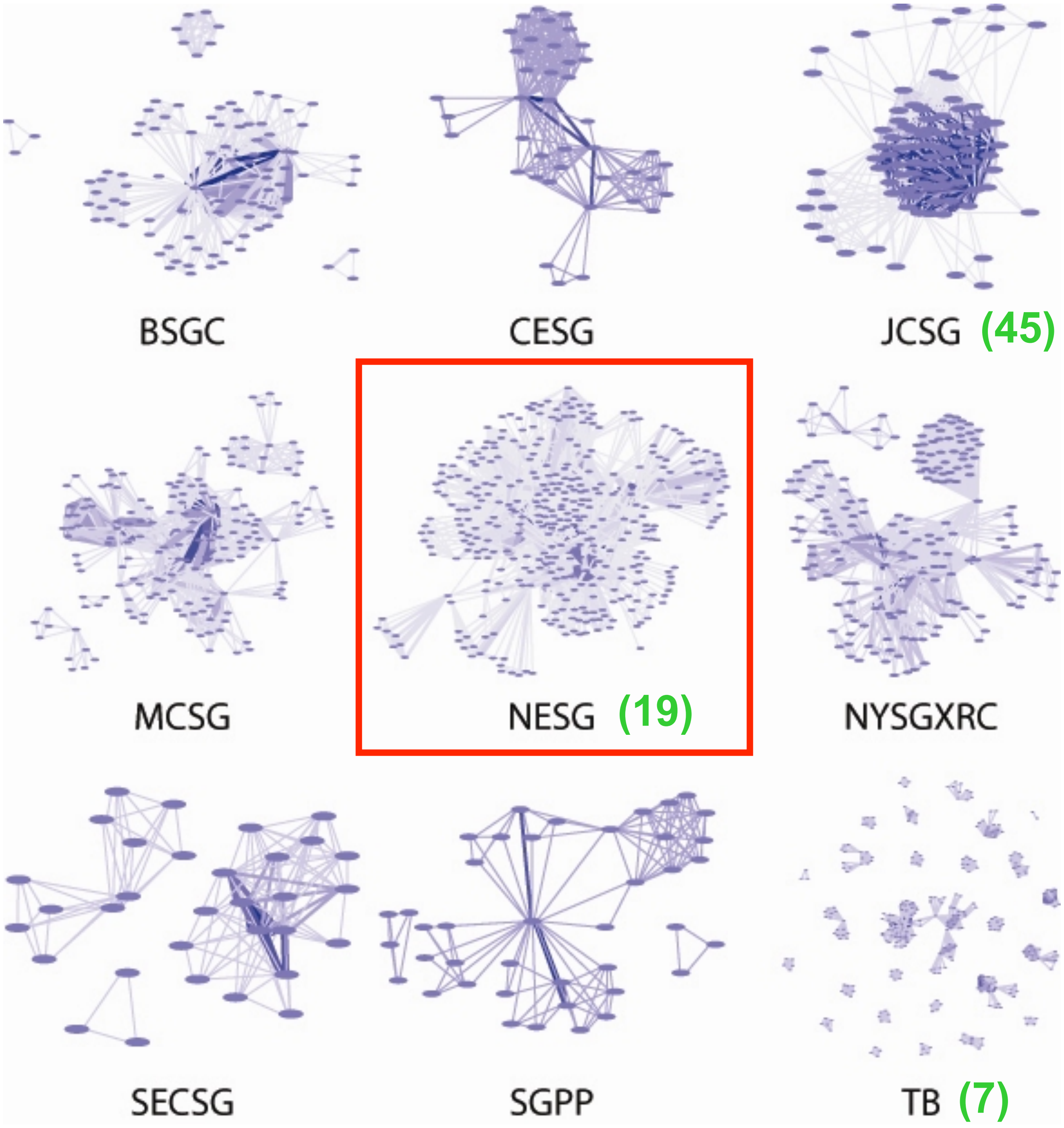
b) Author / Co-Authorship

c) Paper / Shared MeSH term

d) Paper / Shared Location

[Douglas et al. GenomeBiol. ('05), pubnet.gersteinlab.org]

# Co-authorship Networks comparing the 9 NIH Structural Genomics Centers



**Average Degree**

[Douglas et al.
GenomeBiol. ('05),
pubnet.gersteinlab.org]

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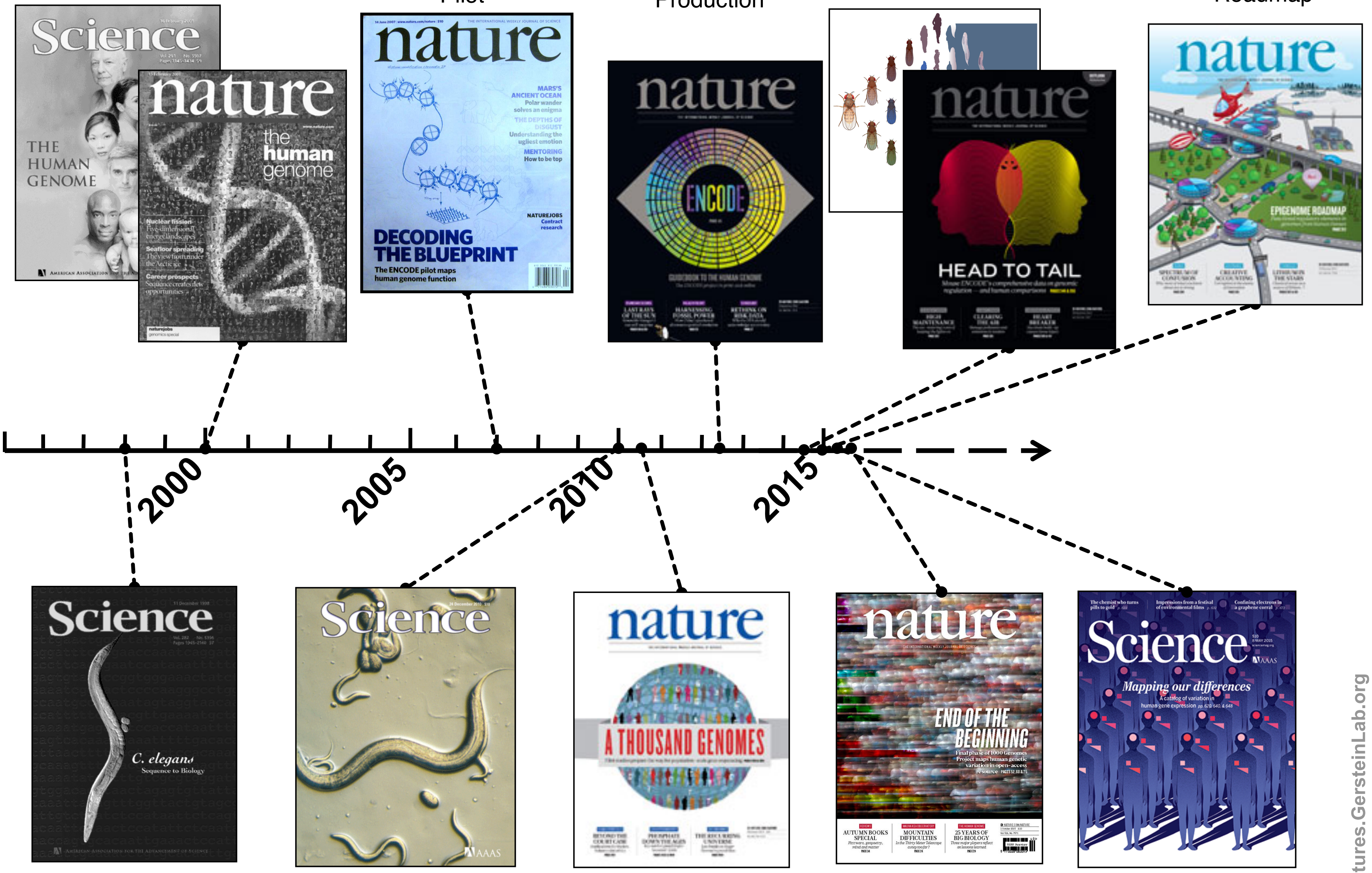


HumanGenome Project

ENCODE Pilot

ENCODE Production

ComparativeENCODE

Epigenome Roadmap

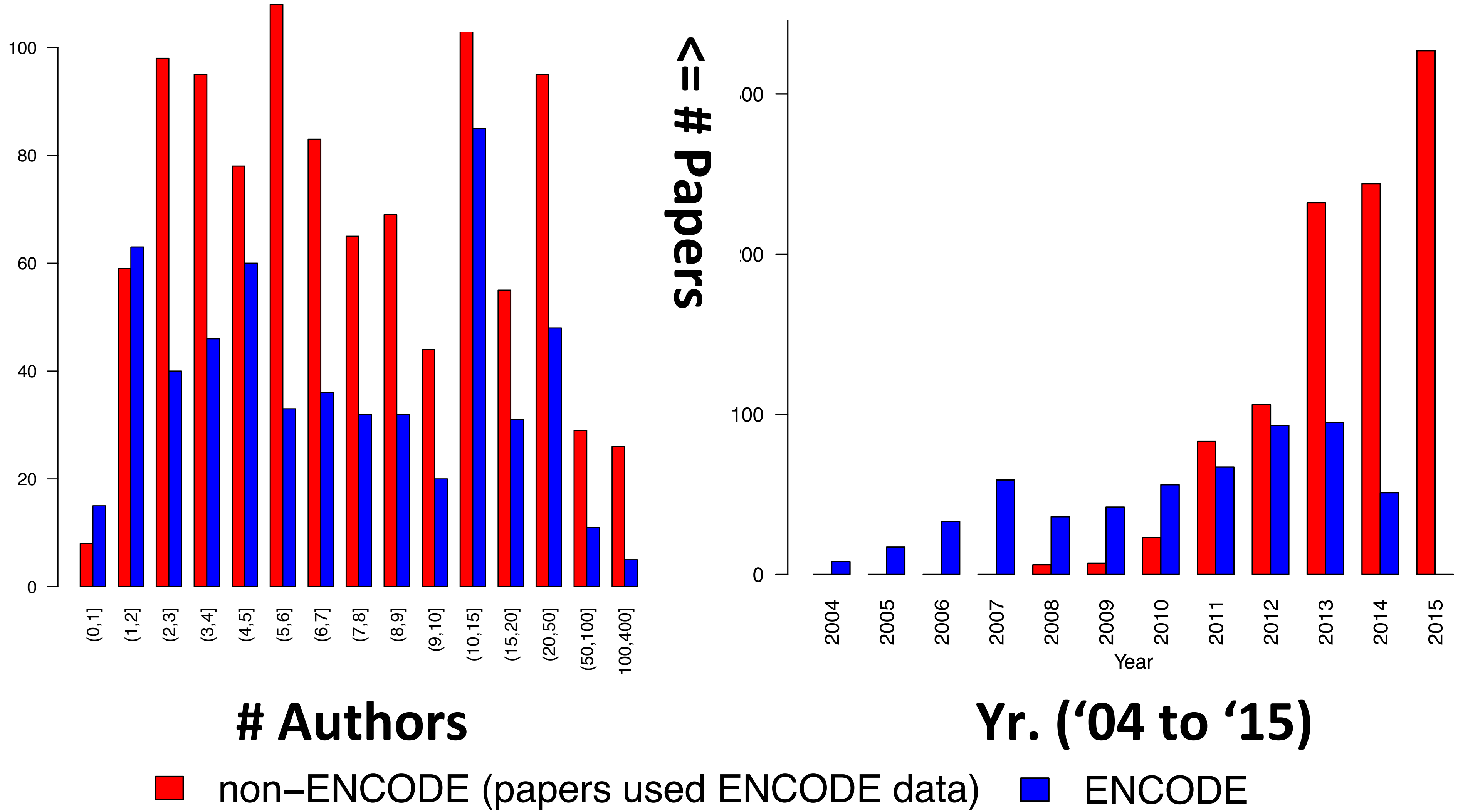
Worm Genome

modENCODE

1000 Genomes Pilot

1000 Genomes Phase 3

GTEx



With help of NHGRI, identified:

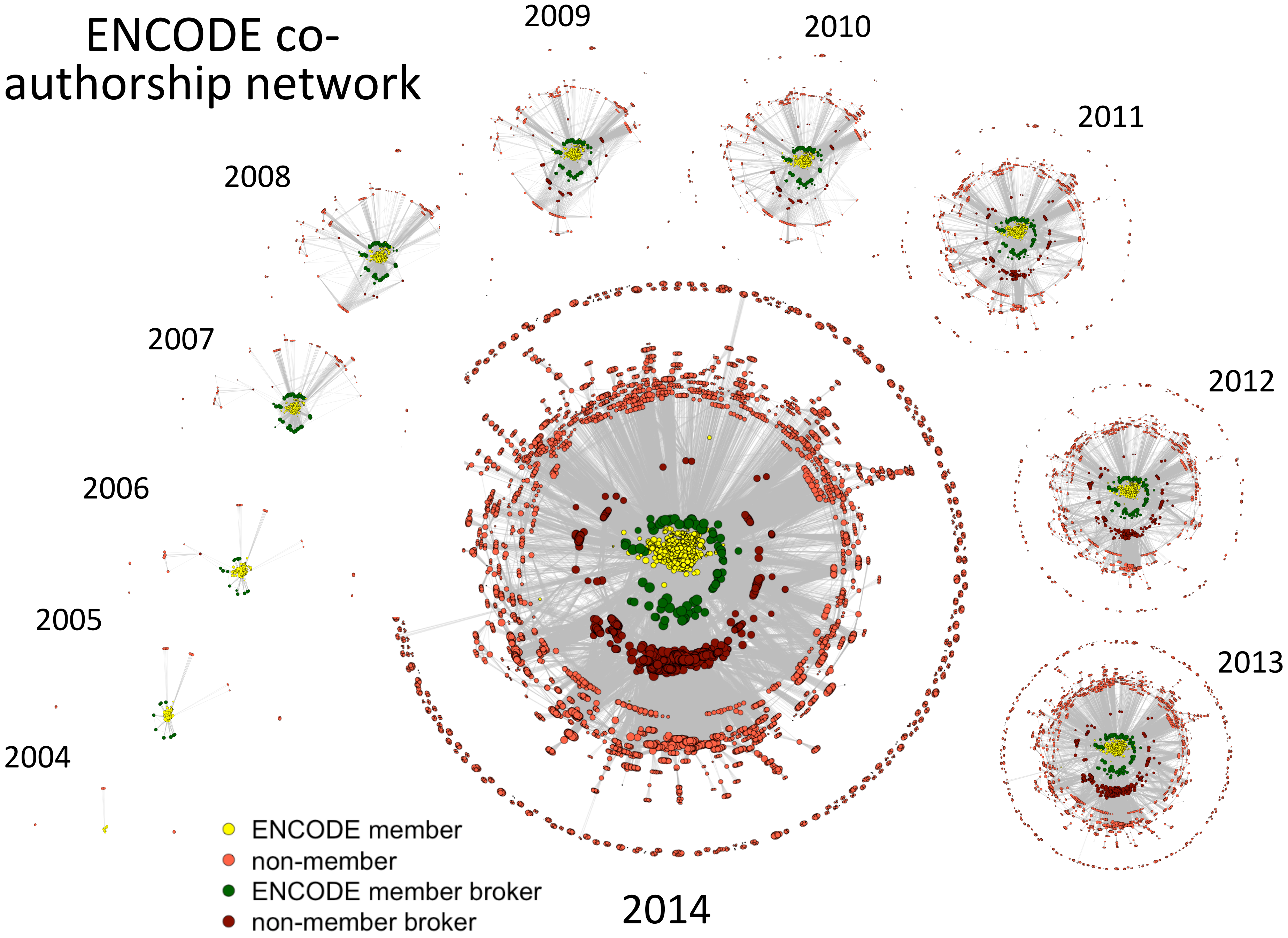
1,786 ENCODE members & 8,263 non-members

from 558 consortium papers supported by ENCODE funding &

702 community papers that used ENCODE data but were not supported by ENCODE funding

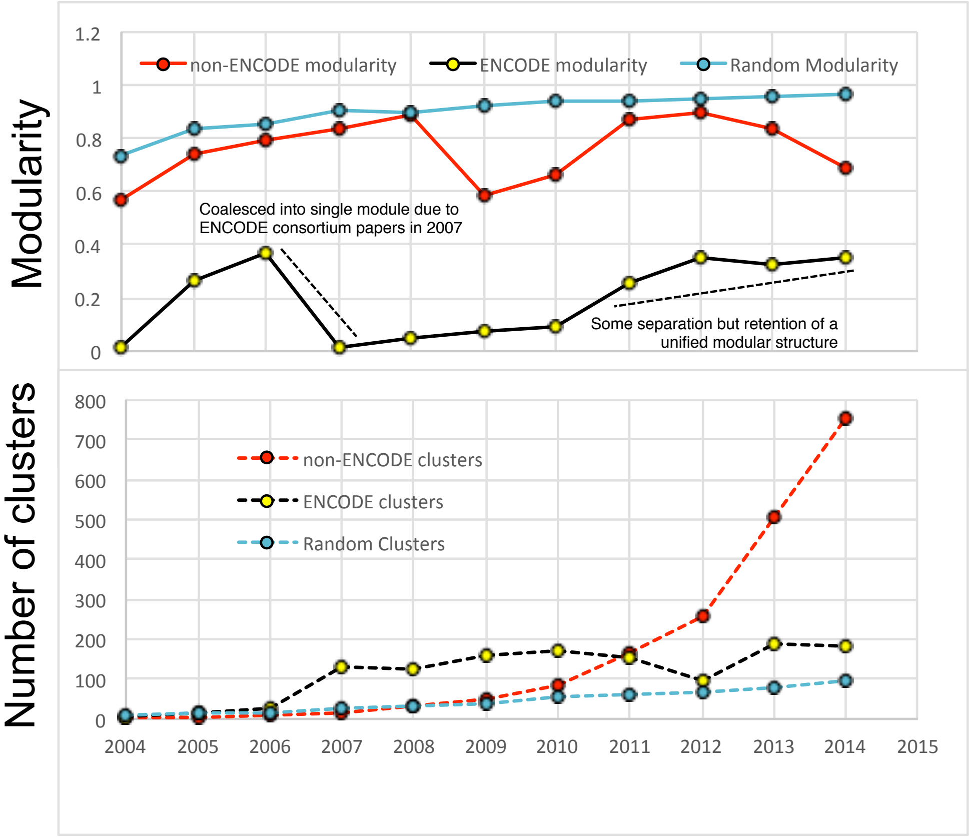
[Wang et al., TIG ('16)]

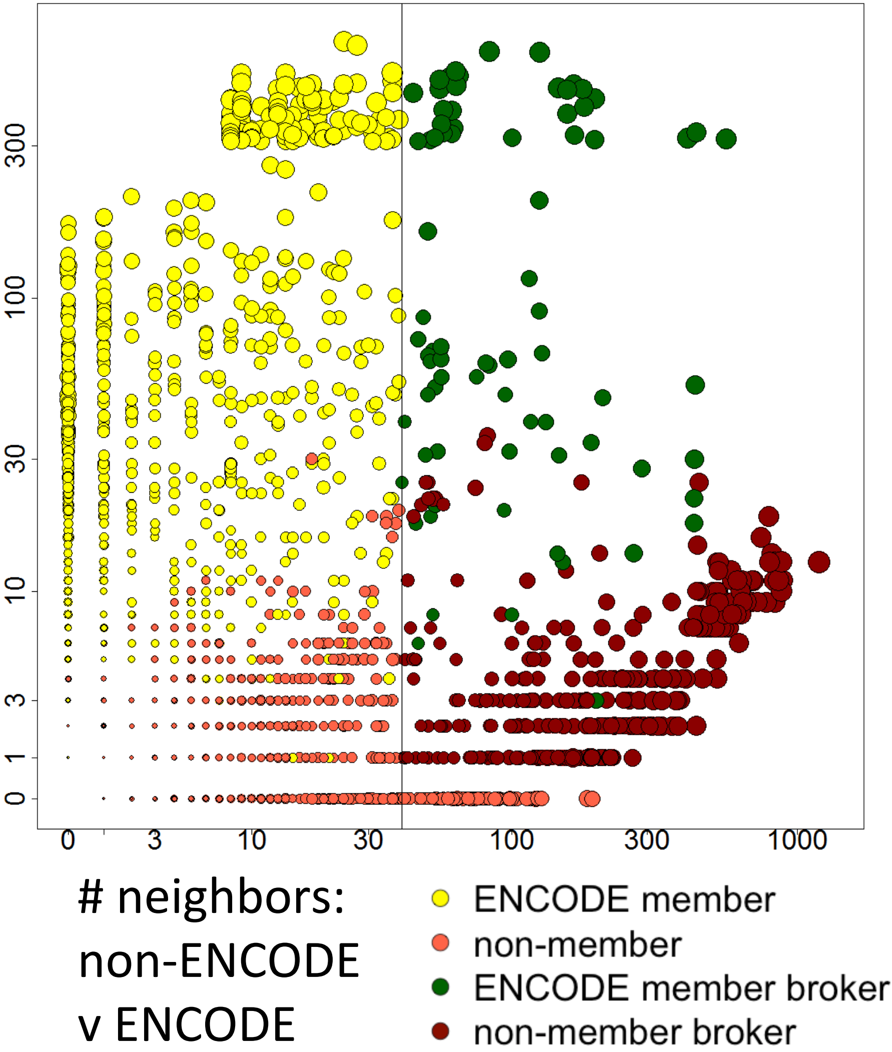
# ENCODE co-authorship network



[Wang et al., TIG ('16)]

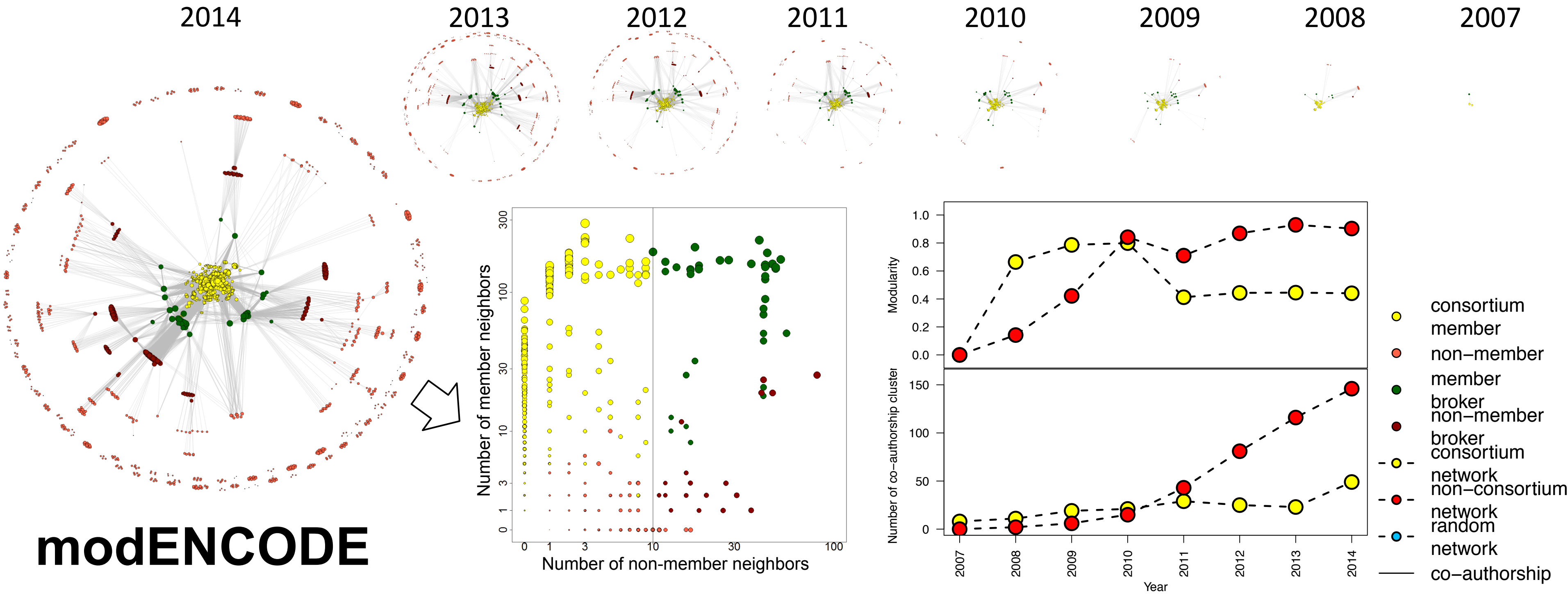
# Network statistics highlight change in modularity with consortium rollouts (L) & importance of broker role (R)





[Wang et al., TIG ('16)]

# Similar Findings in terms of modularity & broker scientists in the modENCODE consortium as for ENCODE



modENCODE

[Wang et al., TIG ('16)]

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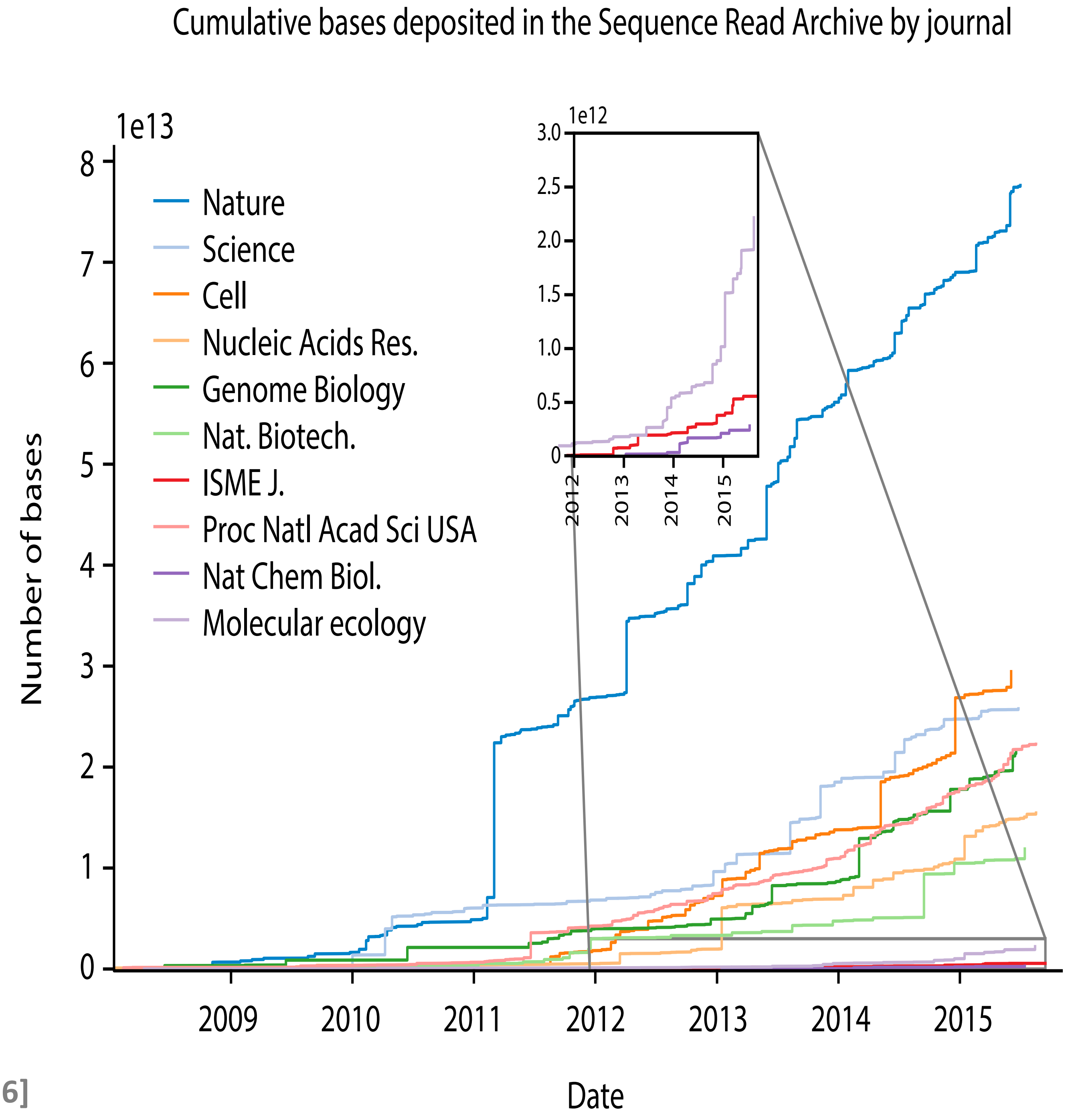
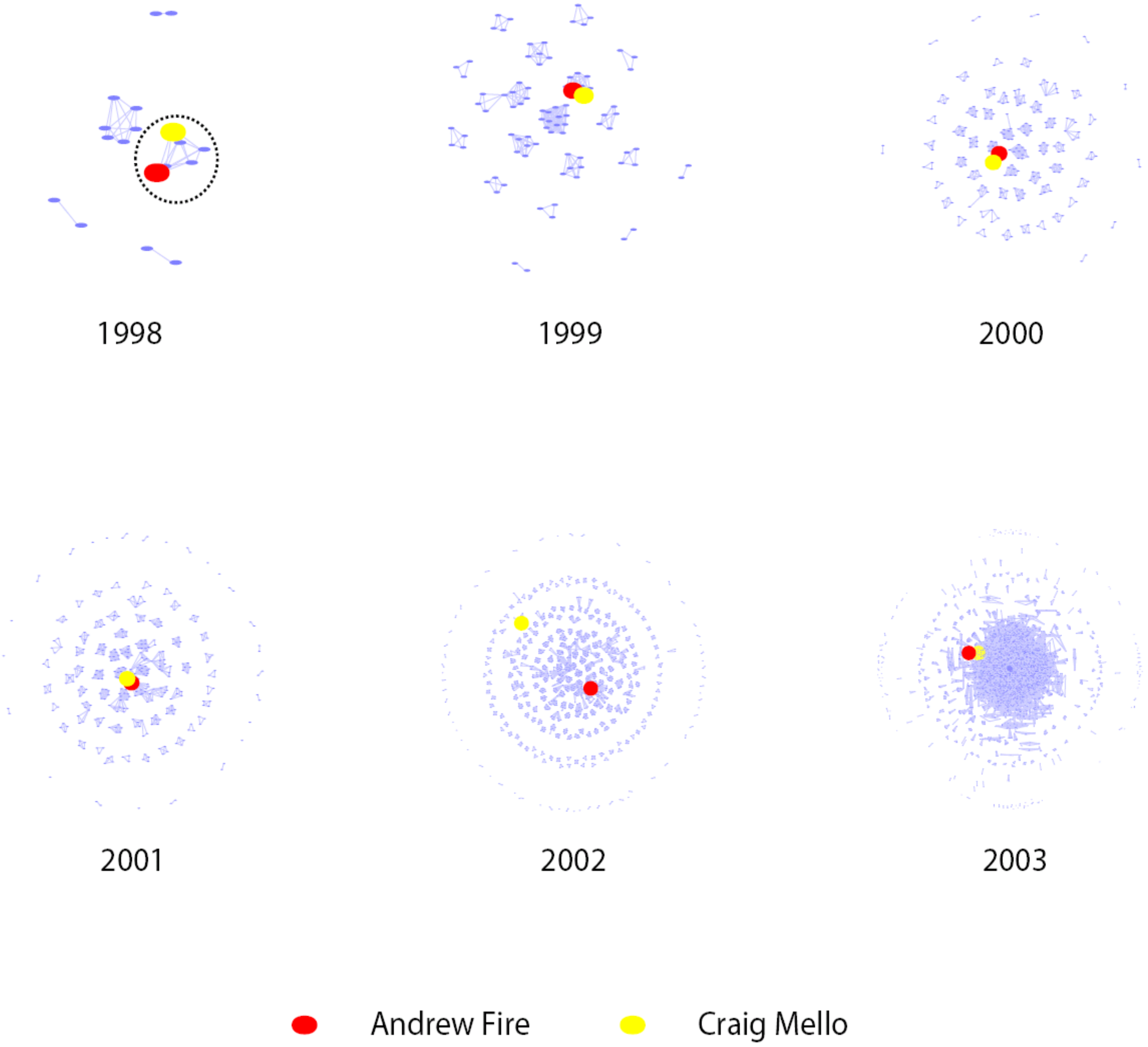
# Diffusion of a data type (sequenced bases) measured by occurrence in specialty journals



[Muir et al. GenomeBiol. '16]

# RNAi: Birth of a Field in the Literature Culminating in the 2006 Nobel



Source:
Gerstein & Douglas. PLoS Comp. Bio. 3:e80 (2007)
PubNet.GersteinLab.org

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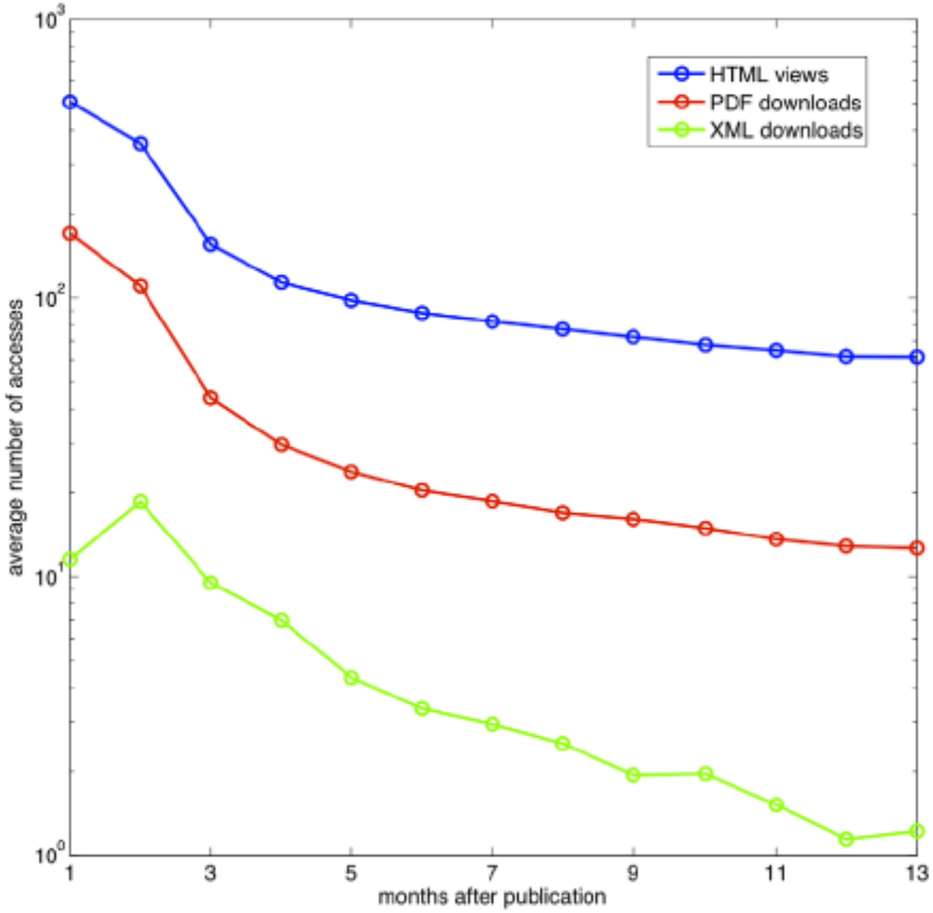
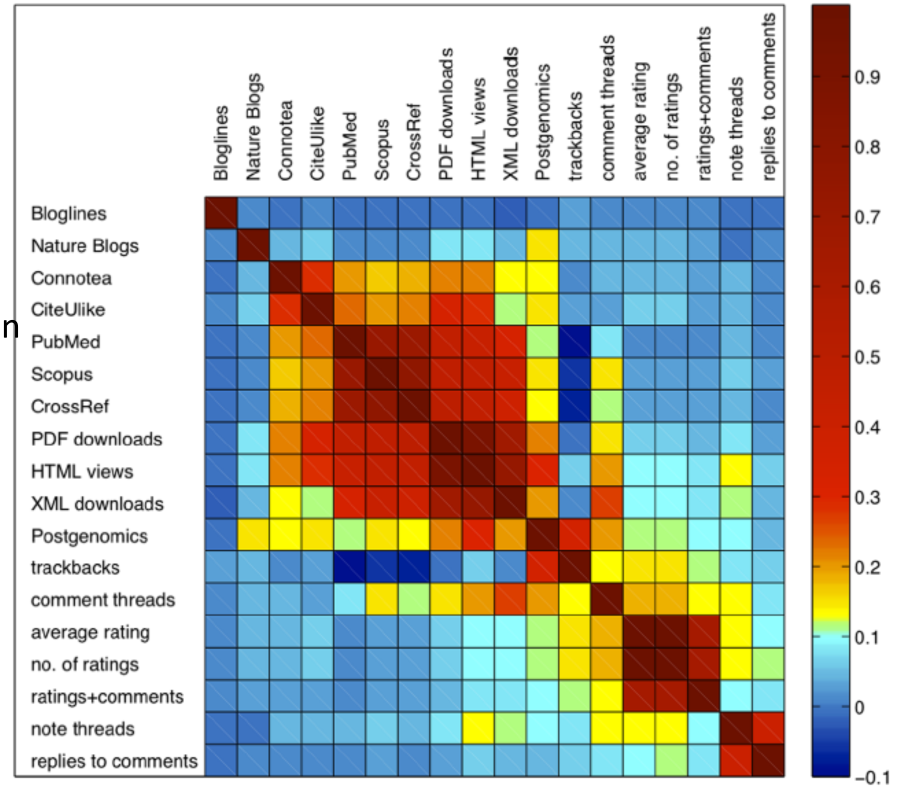
# Spread of information as a diffusion process

The knowledge of a scientific publication is a piece of information





Based on PLOS ALM data for ~7000 papers

the access of different articles follows a log-normal distribution

Yan and Gerstein PLoS One 2011.

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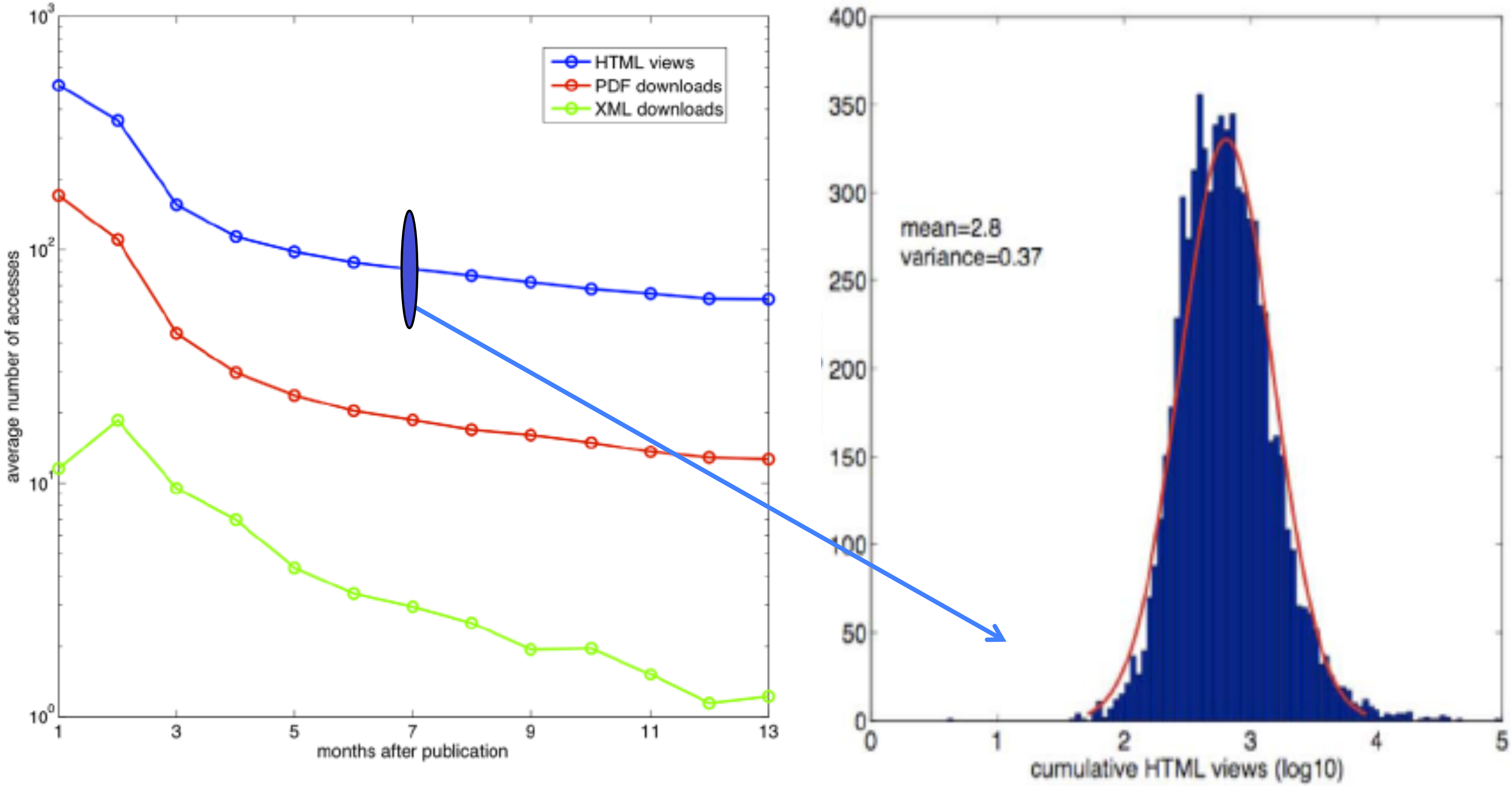

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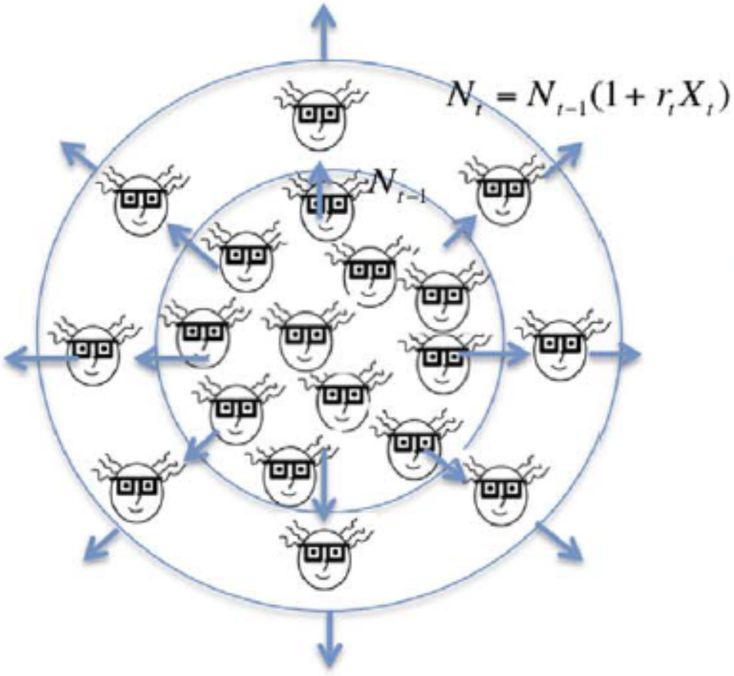
Yan and Gerstein PLoS One 2011.

# Modeling Information diffusion

share the information with friends?



log-normal distribution suggests a simple model,
random multiplicative process for a given paper p:

$$N_t(p) = N_{t-1}(p)\,(\,1 + r_t\,X_t(p)\,)$$

$N_t$=cumulative number of accesses for a given paper up to time t

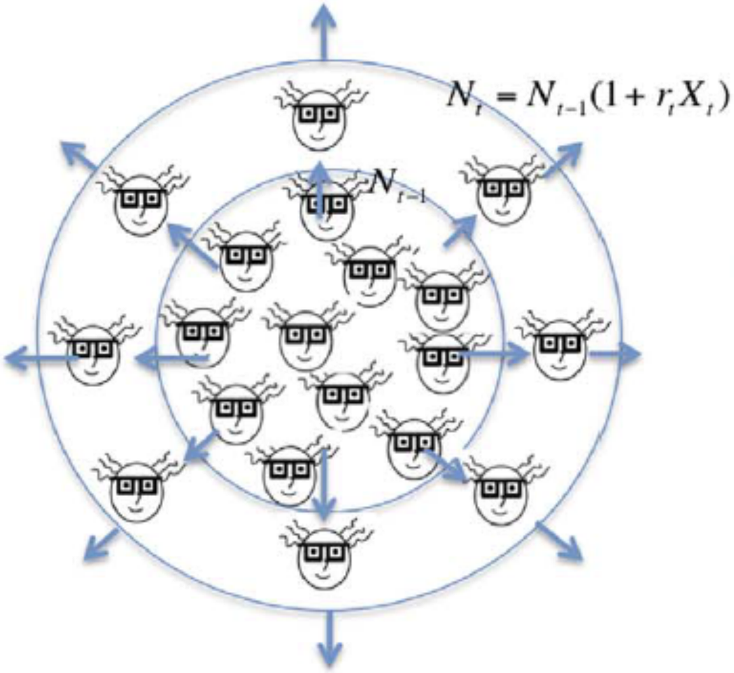
$X_t$ = iid random variable whose mean represents avg. fraction of scientists willing to "spread" the paper at t

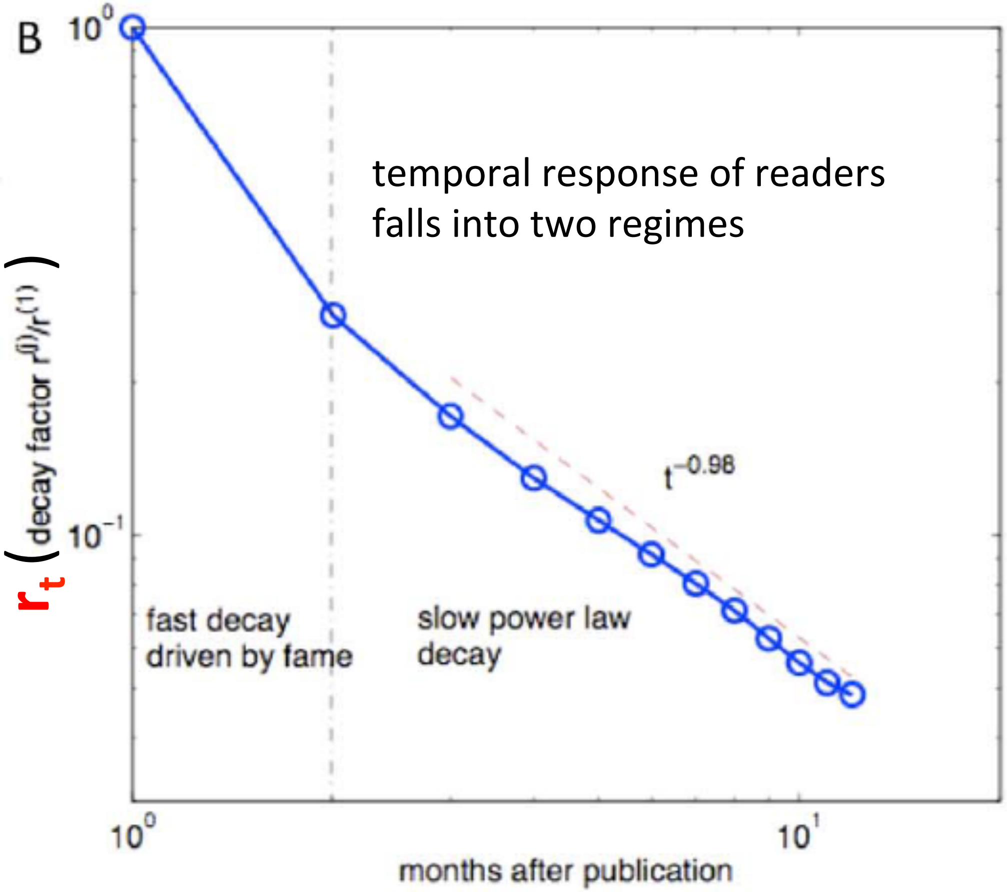
$r_t$ = moderating parameter on how the "spreading" changes over time

Yan and Gerstein PLoS One 2011.

# Modeling Information diffusion

## Refine values of $r_t$ for different times





temporal response of readers falls into two regimes

Yan and Gerstein PLoS One 2011.

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# Acknowledgments

"Encode authors"

**D Wang**,

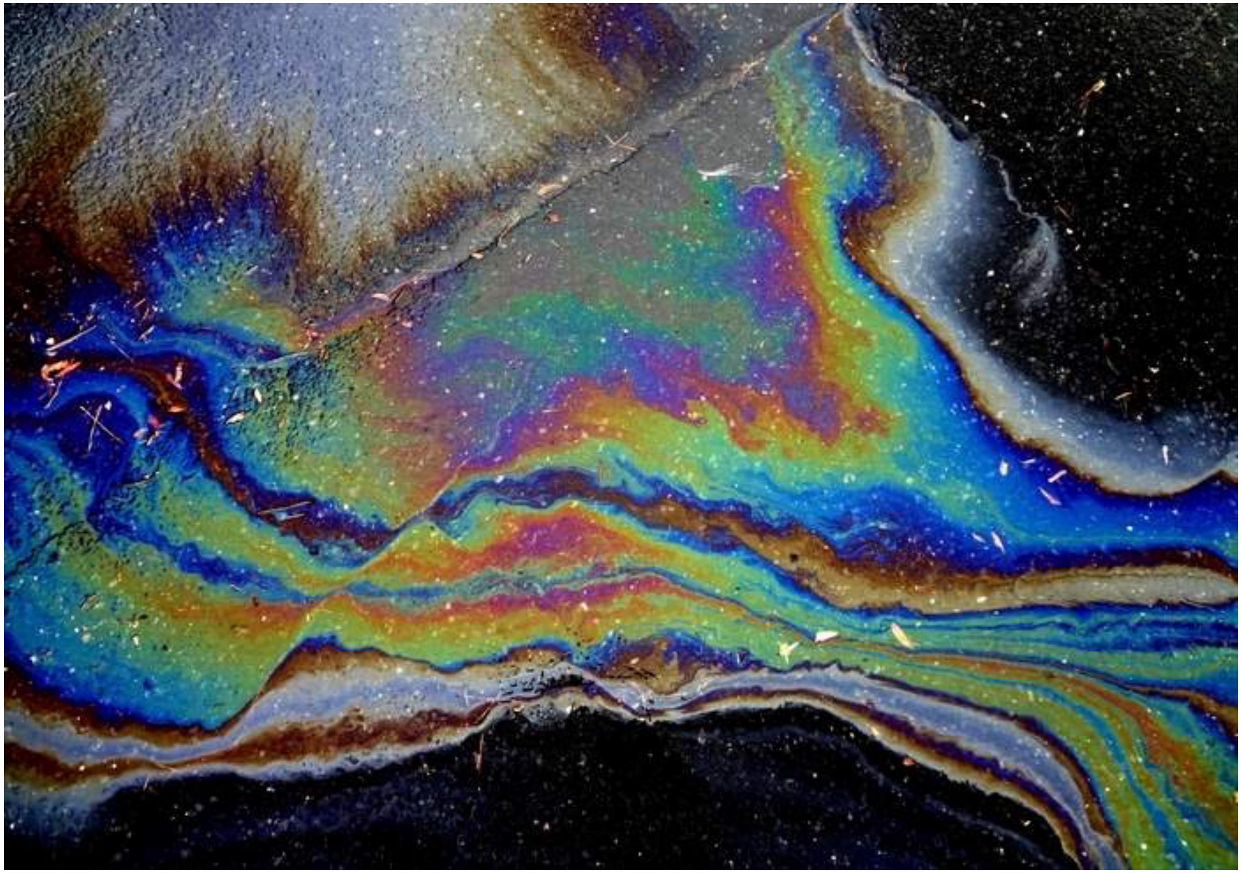
KK Yan,

J Rozowsky,

E Pan

"Info Flow"

**KK Yan**



Cost of Seq. & SRA bases

P Muir, S Li, S Lou, D Wang, DJ Spakowicz, L Salichos, J Zhang, GM Weinstock, F Isaacs, J Rozowsky

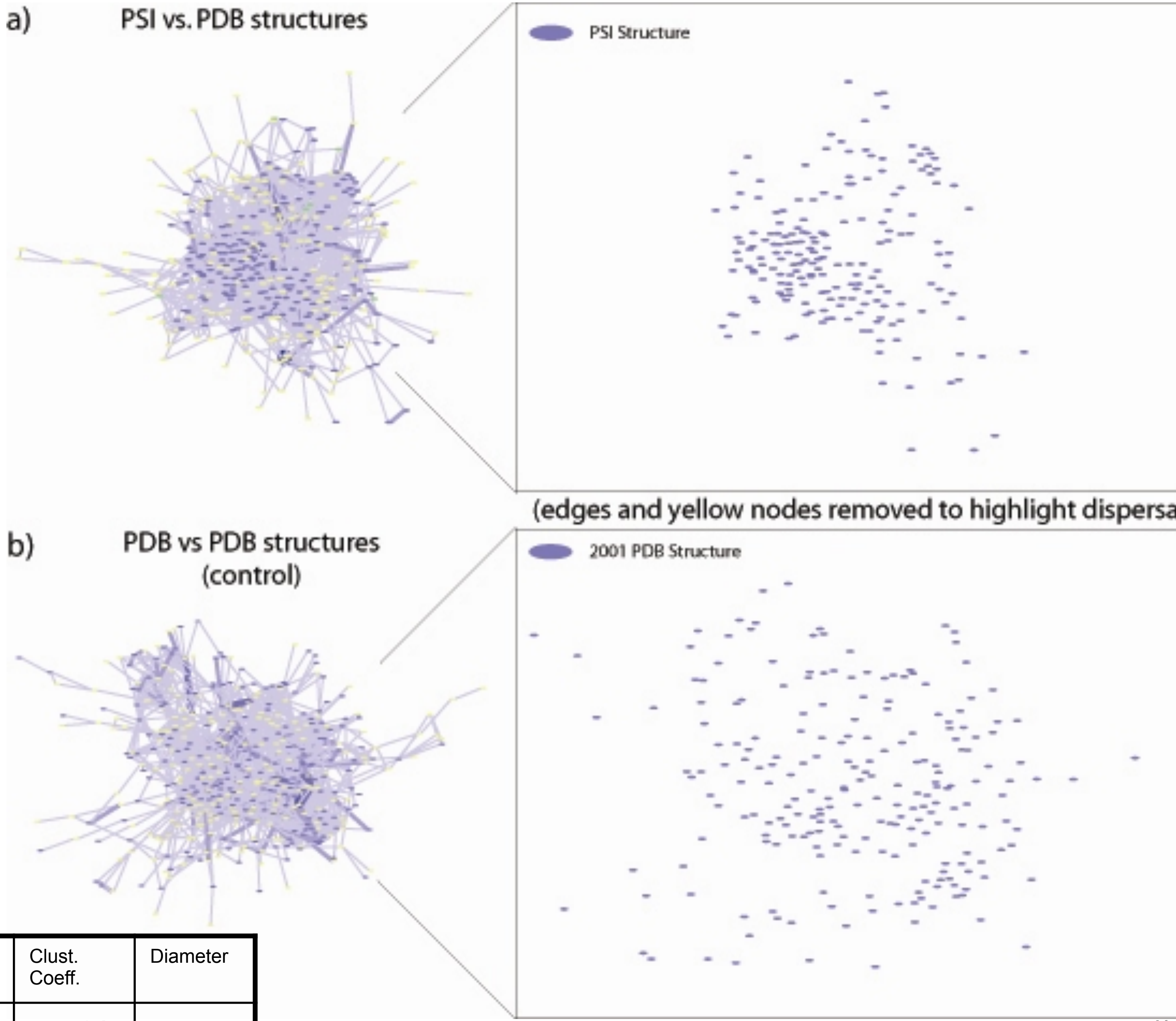
PubNet.gersteinlab.org & RNAi -- SM Douglas

Vision for "Text Mining" -- A Rzhetsky, M Seringhaus

Hiring Postdocs. See gersteinlab.org/jobs

# Extra

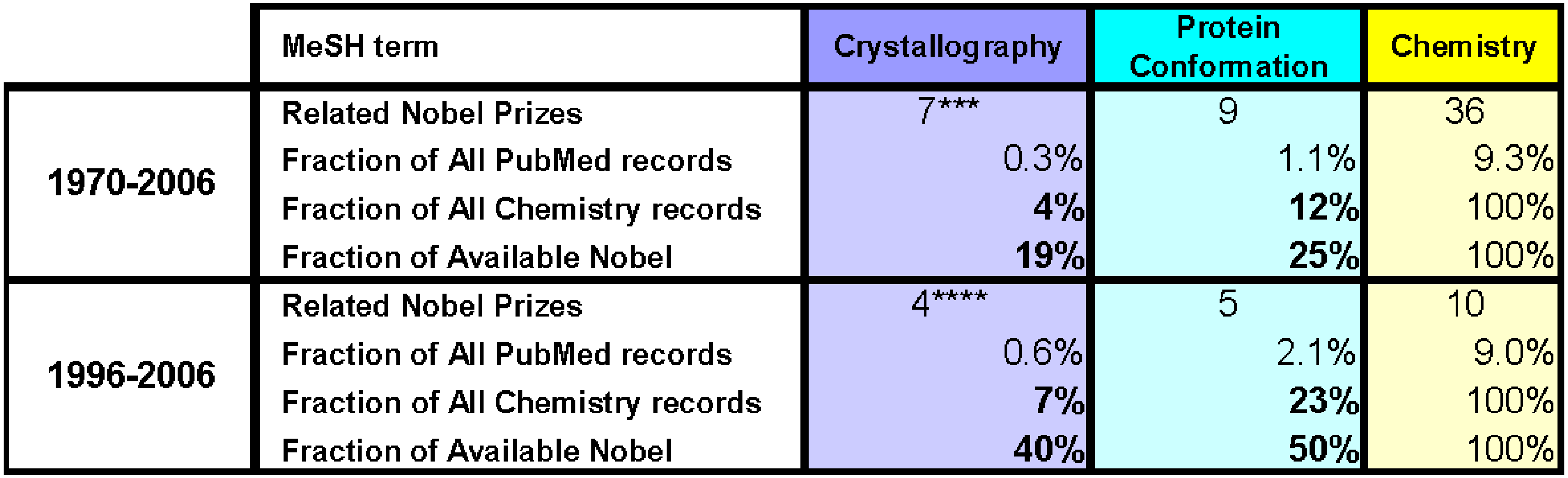
# Clustering structures determined by struc. genomics consortia according to functional similarity: Is there a functional bias in consortia structures?



| | Avg. Degree | Avg. Path | Clust. Coeff. | Diameter |
|---|---|---|---|---|
| PSI | 24 | 2.6 | 37% | 7 |
| PDB | 6 | 3.9 | 31% | 9 |

[Douglas et al. GenomeBiol. ('05), pubnet.gersteinlab.org]

# Over-representation of crystallography among the Nobel Prizes, highlighted by the 2006 Nobels



| | MeSH term | Crystallography | Protein Conformation | Chemistry |
|---|---|---|---|---|
| **1970-2006** | Related Nobel Prizes | 7*** | 9 | 36 |
| | Fraction of All PubMed records | 0.3% | 1.1% | 9.3% |
| | Fraction of All Chemistry records | **4%** | **12%** | 100% |
| | Fraction of Available Nobel | **19%** | **25%** | 100% |
| **1996-2006** | Related Nobel Prizes | 4**** | 5 | 10 |
| | Fraction of All PubMed records | 0.6% | 2.1% | 9.0% |
| | Fraction of All Chemistry records | **7%** | **23%** | 100% |
| | Fraction of Available Nobel | **40%** | **50%** | 100% |

[Seringhaus & Gerstein, Science (2007)

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