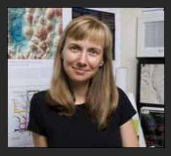
Cyberinfrastructures in Service of Health

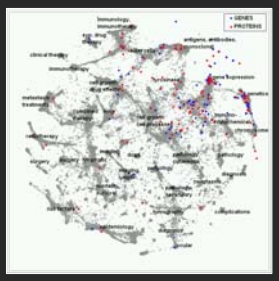



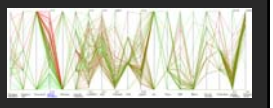
Dr. Katy Börner & Ketan Mane
Cyberinfrastructure for Network Science Center, Director
Information Visualization Laboratory, Director
School of Library and Information Science
Indiana University, Bloomington, IN
katy@indiana.edu

Cancer Institute's (NCI) speaker series Informatics in Action, Bethesda, Maryland, July 20, 2006.

CIShell

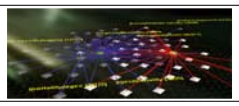
NetworkWorkbench





This Talk has Three Parts:

1. **Why do we need Cyberinfrastructures (CI)?**
2. CI applied to map 'melanoma' related literature, genes, and proteins.
3. CI applied to support computational diagnostics of Acute Lymphoblastic leukemia patients



Why Do we Need Cyberinfrastructures?

Problem

- There are too many and too complex datasets that need to be correlated and understood to arrive at the best possible decisions.
- There are too many different data formats, different algorithms, different implementations of the same algorithm, different programming languages, different research purposes (modeling, analysis, visualization), different communities and practices.
- The analysis, modeling, and visualization of large datasets requires powerful computing infrastructures.
- Managing 1000+ of different data sets and 100+ of different algorithms requires a means to quickly select the best dataset(s)/algorithm(s).

Needed is a socio-technical cyberinfrastructure that supports

Easy access to datasets and algorithms, computer resources, their descriptions, and associated learning modules and access to expertise.

Katy Börner, Cyberinfrastructures in Service of Health, NCI Speaker Service, July 20, 2006.

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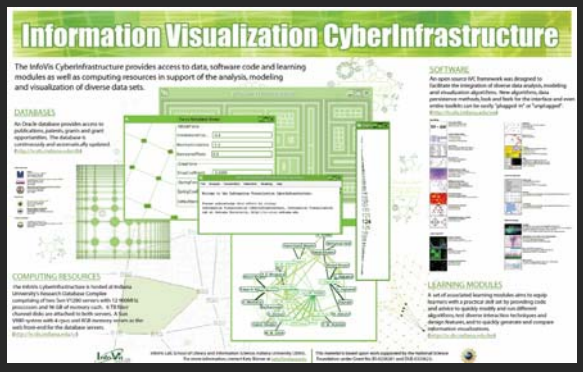
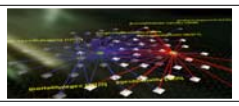


CAREER: Visualizing Knowledge Domains. NSF IIS-0238261 award (Katy Börner, $451,000) Sept. 03-Aug. 08.
http://iv.slis.indiana.edu/

NetworkWorkbench
A Workbench for Network Scientists

SEI: Network Workbench: A Large-Scale Network Analysis, Modeling and Visualization Toolkit for Biomedical, Social Science and Physics Research. NSF IIS-0513650 award (Katy Börner, Albert-Laszlo Barabasi, Santiago Schnell, Alessandro Vespignani & Stanley Wasserman, Eric Wernert (Senior Personnel), $1,120,926) Sept. 05 - Aug. 08.
http://nwb.slis.indiana.edu

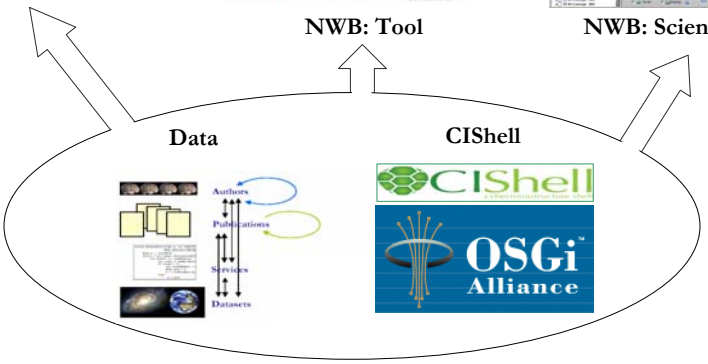


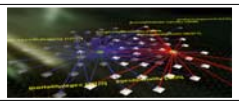
CIShell in Support of IV and NWB CIs & Tools

InfoVis CI

NWB: Tool

NWB: Science Map





CIShell in Support of IV and NWB CIs & Tools

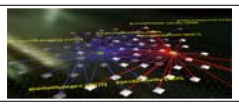
InfoVis CI

NWB: Tool

NWB: Science Map

CIShell Framework: http://sourceforge.net/projects/cishell

InfoVis Cyberinfrastructure: http://iv.slis.indiana.edu
Network Workbench: http://nwb.slis.indiana.edu
SciMaps.org: http://www.SciMaps.org



Cyberinfrastructure Shell (CIShell)

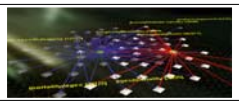
CIShell is an 'empty shell' that supports

- Easy integration of new datasets and algorithms by algorithm developers and
- Easy usage of algorithms by algorithm users.

Its plug-and-play architecture supports the integration and utilization of diverse

- Datasets, e.g., stored in files, databases, steaming data.
- Algorithms, e.g., data processing, analysis, modeling, visualization.
- Interfaces, e.g., remote services, scripting engines, peer-to-peer clients.
- Services, e.g., workflow support, scheduler.

Hence, it can be used for custom UI/Toolkit development.



CIShell – Technical Details

CIShell is built upon the Open Services Gateway Initiative (OSGi) Framework.

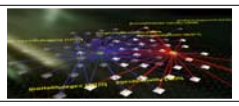
OSGi (http://www.osgi.org) is

- A standardized, component oriented, computing environment for networked services.
- Successfully used in the industry from high-end servers to embedded mobile devices since 7 years.
- Alliance members include IBM (Eclipse), Sun, Intel, Oracle, Motorola, NEC and many others.
- Widely adopted in open source realm, especially since Eclipse 3.0 that uses OSGi R4 for its plugin model.

Advantages of Using OSGi

- Any CIShell algorithm is a service that can be used in any OSGi-framework based system.
- Using OSGi, running CIShells/tools can connected via RPC/RMI supporting peer-to-peer sharing of data, algorithms, and computing power.

Ideally, CIShell becomes a standard for creating OSGi Services for algorithms. Developed Tools/CI, e.g., IVC & NWB, provide a reference GUI for underlying services.



Serve Algorithms Developers & Users

CIShell

Developers

Users

CIShell Wizards

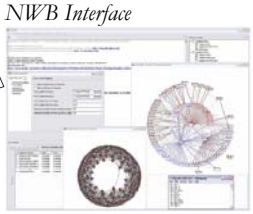
CIShell

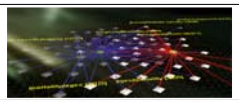
CIShell

OSGi Alliance

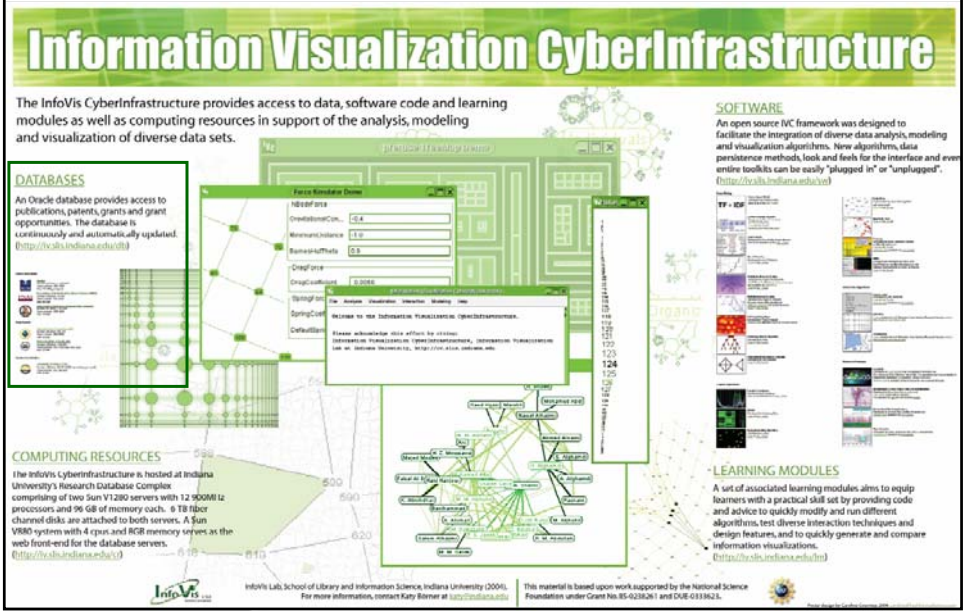
IVC Interface

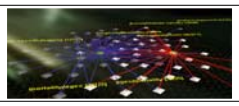
NWB Interface





InfoVis Cyberinfrastructure





IVC Database (http://iv.slis.indiana.edu/db)

Papers and Patents

Medline
Number of Entries: 11,693,477
Years covered: 1963-2002
Size: 135 MB (gunzipped)

Proceedings of the Natioanl Academy of Science (PNAS)
Number of Entries: 16,169
Years covered: 1997-2002
Size: 583 MB

United States Patent and Trademark Office (Patents)
Number of Entries: 2,582,647
Years covered: 1976-2003
Size: 350 MB

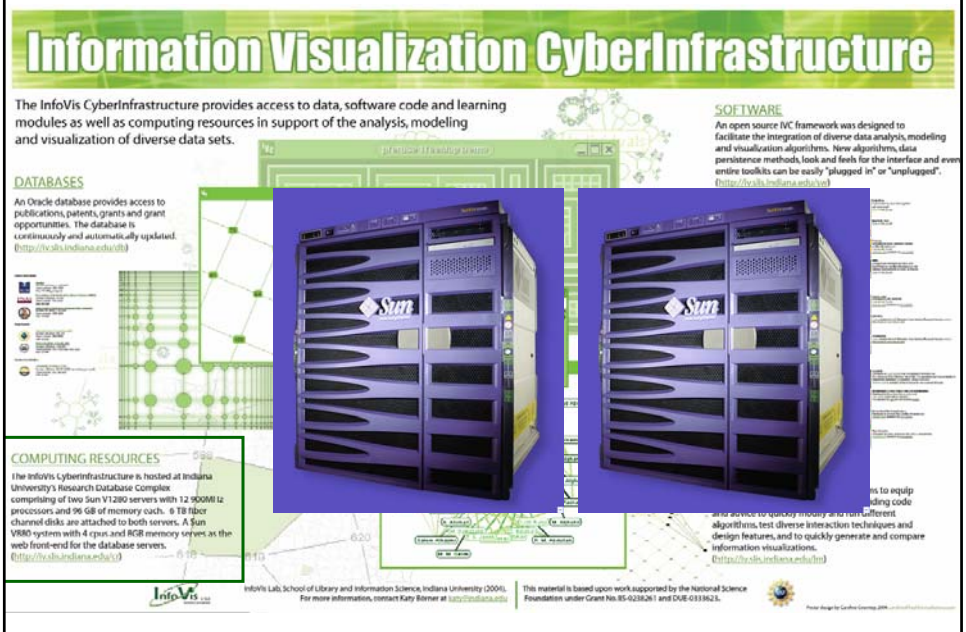
Grant Awards

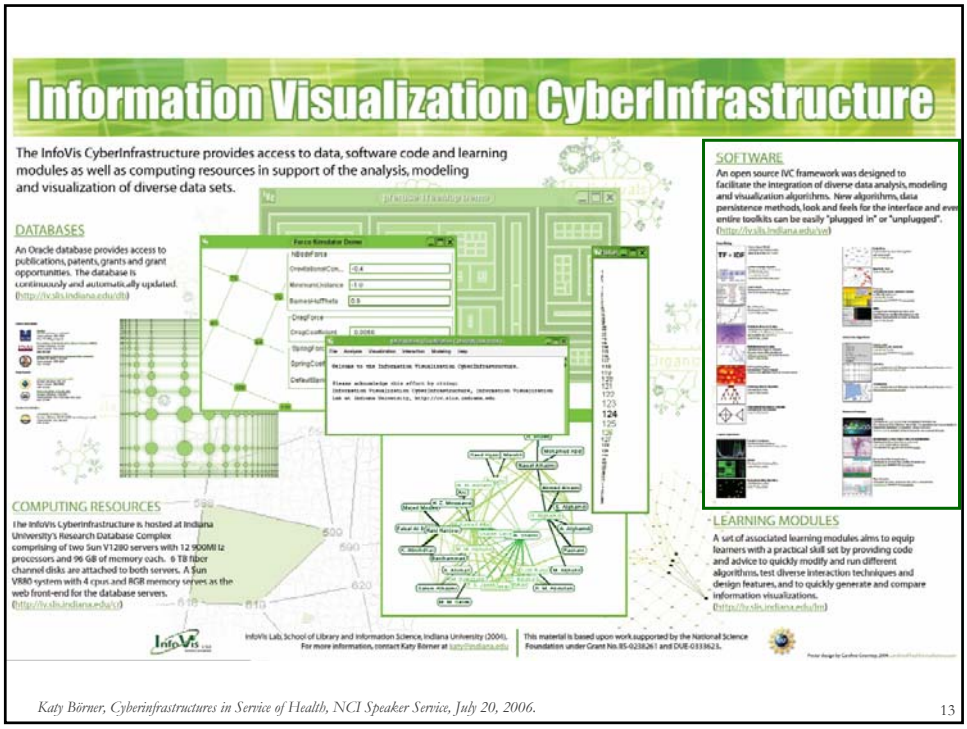
National Science Foundation (NSF)
Number of Entries: 181,132
Years covered: 1985-2002
Size: 400 MB

National Institute of Health (NIH)
Number of Entries: 1,003,521
Years covered: 1972-1992 and 1994-2002
Size: 2.3 GB

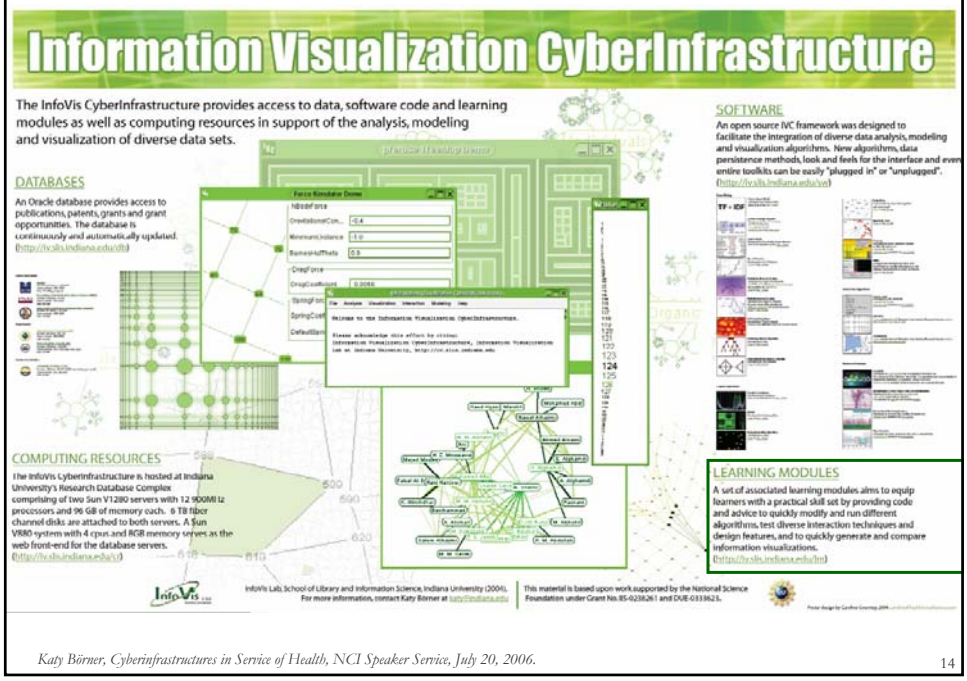
Funding Opportunities

Community of Science (COS)
Number of Entries: 38,154 (6,000 new entries per month)
Years covered: 2001-present
Size: 60 MB

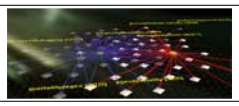




Katy Börner, Cyberinfrastructures in Service of Health, NCI Speaker Service, July 20, 2006. 13



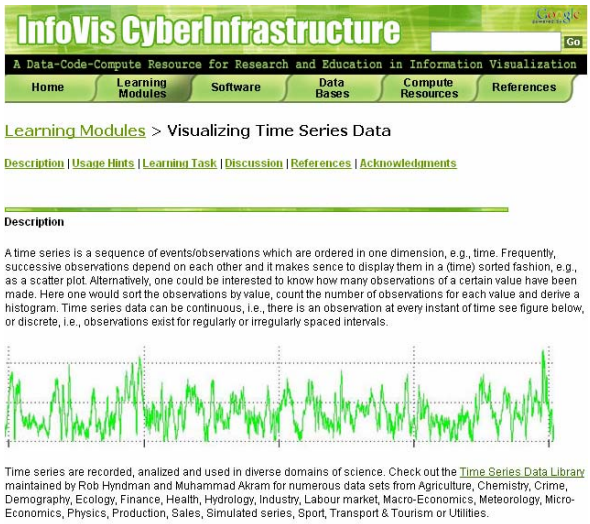
Katy Börner, Cyberinfrastructures in Service of Health, NCI Speaker Service, July 20, 2006. 14

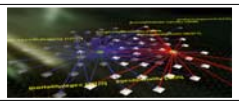


Time Series Analysis

Learning Module

http://iv.slis.indiana.edu/lm/lm-time-series.html

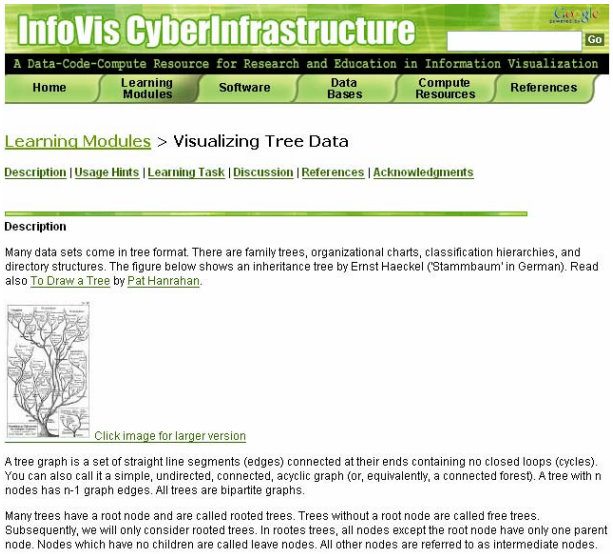


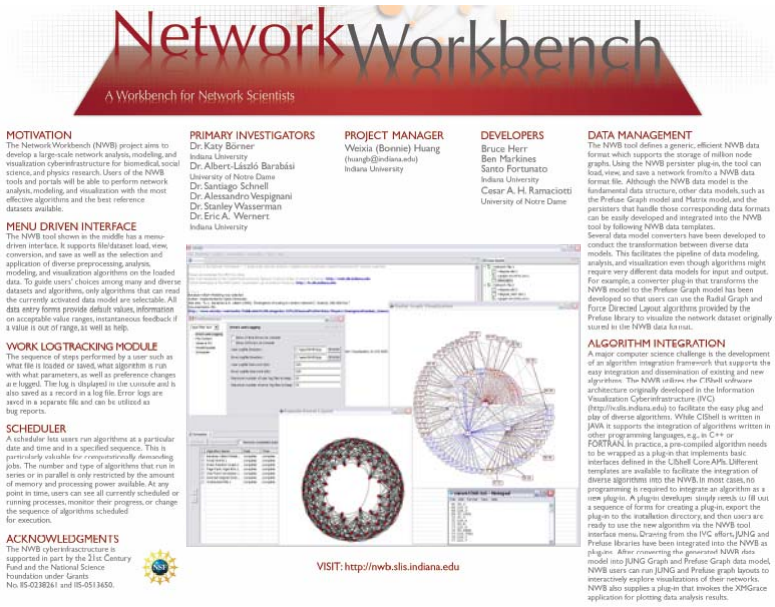


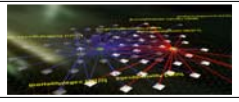
Visualizing Tree Data

Learning Module

http://iv.slis.indiana.edu/lm/lm-trees.html







Network Workbench

Investigators: Katy Börner, Albert-Laszlo Barabasi, Santiago Schnell, Alessandro Vespignani & Stanley Wasserman, Eric Wernert

Software Team: **Team Lead: Weixia (Bonnie) Huang**
Software Developers: Bruce Herr & Ben Markines
Algorithm Developers: Santo Fortunato & Cesar Hidalgo

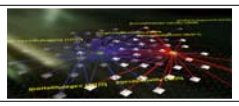
Goal: Develop a large-scale network analysis, modeling and visualization toolkit for biomedical, social science and physics research.

Amount: $1,120,926 NSF IIS-0513650 award.

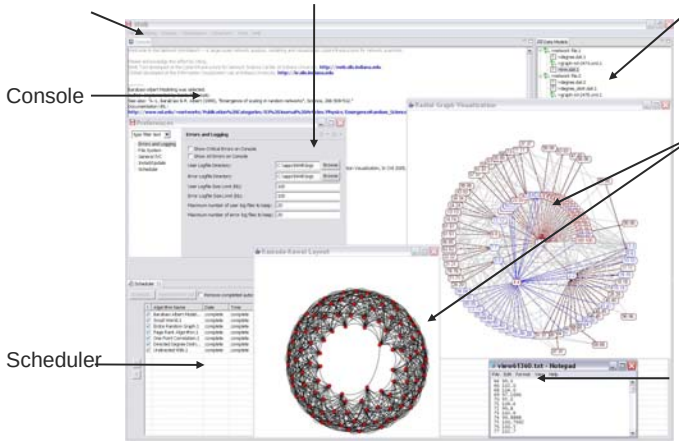
Duration: Sept. 2005 - Aug. 2008

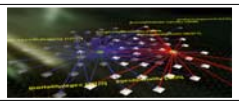
Website: http://nwb.slis.indiana.edu

Katy Börner, Cyberinfrastructures in Service of Health, NCI Speaker Service, July 20, 2006. 18



NWB Tool: Interface Elements





List of Algorithms (partially implemented)

Modeling
Random Network Model
Random

Preferential Attachment Algorithms
Barabasi-Albert Model
Dorogovtsev-Mendes-Samukhin
Fitness
Vertices/edges deletion
Copying strategy
Finite vertex capacity
TARL

Rewiring algorithms
Rewiring based on degree distribution
Watts Strogatz Small World Model

Peer-to-Peer Models

Structured
CAN Model
Chord Model

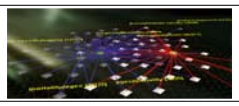
Unstructured
PRU Model
Hypergrid Model

Measurement
Edge/Node level
node degree
BC value of nodes/edges
Max flow edge
Hub/Authority value for nodes
Distribution of node distances (Hop plot)

Local (directed and weighted versions)
Clustering Coefficient (Watts Strogatz)
Clustering Coefficient (Newman)
k-Core Count
Distributions (Plot and gamma, and R^2)
Degree Distributions (in, out, total) (Directed/Total Degree Distribution)
Degree Correlations (in-out, out-out, out-in, in-in, total-total)
Clustering Coefficient over k
Coherence for weighted graphs
Distribution of weights
Probability of degree distribution

Global
Density
Square of Adjacency Matrix
Giant Component
Strongly Connected Component
Betweenness Centrality
Diameter
Shortest Path = Geodesic Distance
Average Path Length

Motif Identification
Page Rank
Closeness centrality
Reach centrality
Eigenvector centrality
Minimum Spanning Tree



List of Algorithms (partially implemented)

Basic Processes on Networks
Search
k Random-Walk Search
Depth First Search
p-rand Breadth-First Search
P2P
CAN Search
Chord Search

Epidemics Spreading
SIR
SIS

Graph Matching
Simple Match
Similarity Flooding
ABSURDIST

Clustering
Based on Attributes
Hierarchical Clustering
Single Link
Complete Link
Average Link
Ward's Algorithm

Based on Network Structure
Newman Girvan
Clauset-Newman-Moore
Newman
Cecconi-Parisi
Simulated annealing of modularity
Caldarelli
Weak Component Clustering
vanDongen (random walk)
Cfinder (Clique percolation method)
Reichardt, Bornholdt (q-potts model)

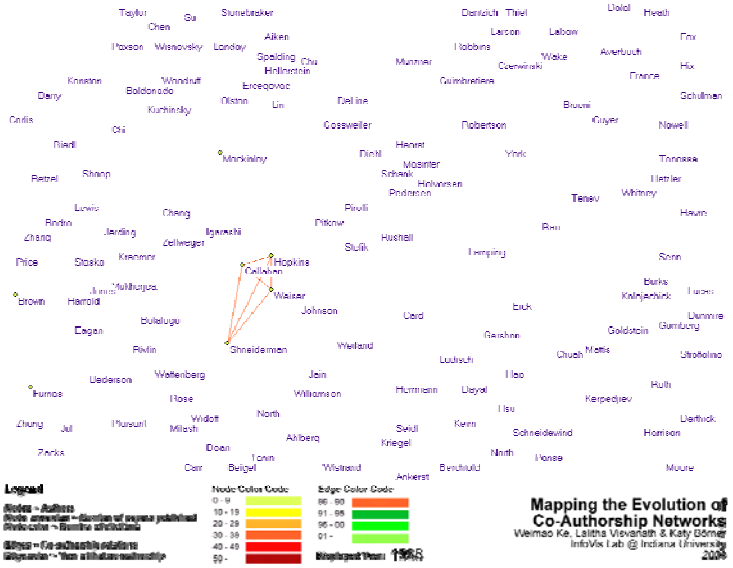
Visualization
Distribution
Scatterplot
Histogram
Geospatial
Circle layout
Grid-based
Dendrogram
Treemap
Hyperbolic tree
Radial Tree
Sparse Matrix Visualization
Kamada-Kawaii
Fruchterman-Rheingold
Orthogonal Layout
k-core visualization

This Talk has Three Parts:

1. Why do we need Cyberinfrastructures (CI)?
2. **CI applied to map 'melanoma' related literature, genes, and proteins.**
3. CI applied to support computational diagnostics of Acute Lymphoblastic leukemia patients

Mapping the Evolution of Co-Authorship Networks in Information Visualization, 1988 - 2004

Ke, Visvanath & Börner, (2004) Won 1st price at the IEEE InfoVis Contest.



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Mapping the Evolution of Co-Authorship Networks

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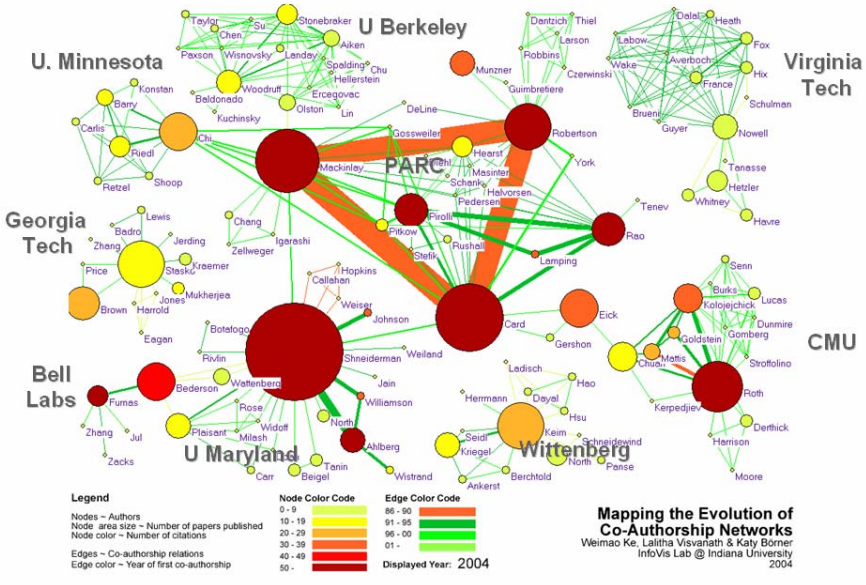

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Analyzing, Modeling, and Mapping Science

- *Shiffrin, Richard M. and Börner, Katy (Eds.) (2004).* ***Mapping Knowledge Domains.*** *Proceedings of the National Academy of Sciences of the United States of America, 101(Suppl_1).*
- *Börner, Katy, Chen, Chaomei, and Boyack, Kevin. (2003).* ***Visualizing Knowledge Domains.*** *In Blaise Cronin (Ed.), Annual Review of Information Science & Technology, Volume 37, Medford, NJ: Information Today, Inc./American Society for Information Science and Technology, chapter 5, pp. 179-255.*
- *Börner, Katy, Sanyal, Soma and Vespignani, Alessandro (in press).* ***Network Science.*** *In Blaise Cronin (Ed.), Annual Review of Information Science & Technology, Information Today, Inc./American Society for Information Science and Technology, Medford, NJ.*

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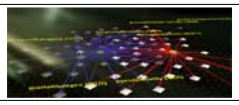


Process of Analyzing and Mapping Science

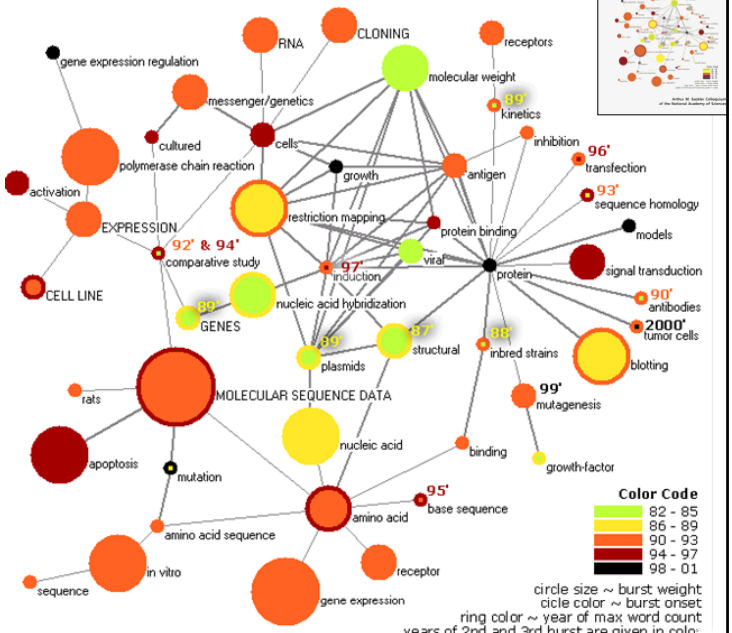
DATA EXTRACTION	UNIT OF ANALYSIS	MEASURES	LAYOUT (often one code does both similarity and ordination steps)		DISPLAY
			SIMILARITY	ORDINATION	
SEARCHES ISI INSPEC Eng Index Medline ResearchIndex Patents etc. BROADENING By citation By terms	COMMON CHOICES Journal Document Author Term	COUNTS/FREQUENCIES Attributes (e.g. terms) Author citations Co-citations By year THRESHOLDS By counts	SCALAR (unit by unit matrix) Direct citation Co-citation Combined linkage Co-word / co-term Co-classification VECTOR (unit by attribute matrix) Vector space model (words/terms) Latent Semantic Analysis (words/terms) incl. Singular Value Decomp (SVD) CORRELATION (if desired) Pearson's R on any of above	DIMENSIONALITY REDUCTION Eigenvector/ Eigenvalue solutions Factor Analysis (FA) and Principal Components Analysis (PCA) Multi-dimensional scaling (MDS) LSA, **Topics** Pathfinder networks (PFNet) Self-organizing maps (SOM) includes SOM, ET-maps, etc. CLUSTER ANALYSIS SCALAR Triangulation Force-directed placement (FDP)	INTERACTION Browse Pan Zoom Filter Query Detail on demand ANALYSIS

Börner, Chen & Boyack.. (2003) Visualizing Knowledge Domains. In Blaise Cronin (Ed.), Annual Review of Information Science & Technology, Volume 37, Medford, NJ: Information Today, Inc./American Society for Information Science and Technology, chapter 5, pp. 179-255.

Mapping Topic Bursts

Co-word space of the top 50 highly frequent and bursty words used in the top 10% most highly cited PNAS publications in 1982-2001.

Mane & Börner. (2004) PNAS, 101(Suppl. 1): 5287-5290.



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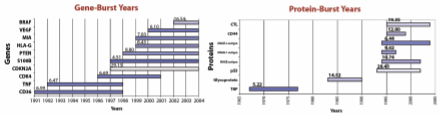
Mapping Medline Papers, Genes, and Proteins Related to Melanoma Research

GOAL

To provide researchers, practitioners and students with a global map of a research domain, to help them answer questions such as: What are the major research areas, experts, institutions, regions, nations, grants, publications, journals in a certain area of research? Which areas are most insular? What are the main connections for each area? What is the relative speed of areas? What new research areas are evolving? How are the objects of study (e.g., genes, proteins) interconnected via papers?

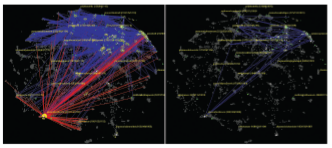
TOP-RESEARCHED GENES & PROTEINS

Identification of sudden interests in research/published papers on certain genes and proteins using Kleinberg's burst detection algorithm. The diagrams show the amount and the time spans of major burst for genes and proteins.



ASSOCIATION MAPS

A gene-gene, gene-paper, gene-protein, protein-paper and protein-protein map was generated. The figure shows the gene-paper (left) and gene-gene (right) network. Highlighted in red is a single gene (CMM) and all its connections within the given network.



DATASETS

- 53804 Medline publication (1960 – Feb 2004)
- 299 Genes downloaded from Entrez-Gene
- 367 Proteins downloaded from Uniprot

Kevin W. Boyack, Ketan K. Mane, Katy Börner (in press) *Mapping Medline Papers, Genes, and Proteins Related to Melanoma Research.* Accepted for the Information Visualization Conference 2004.

For more information, contact Katy Börner at katy@indiana.edu.

This material is based upon work supported by the National Science Foundation under Grants No. IIS-0238261 and DUE-0333623.

PAPER-GENE-PROTEIN MAP

Shown here is the melanoma research area over the last 40 years. Gray dots represent papers, red dots denote proteins, blue dots indicate genes. Experts classified the shown research areas into two main categories:

- Applied Medical Sciences (left side) where research work occurs at organism level.
- Basic Molecular Sciences (right side) with studies related to genes and proteins.

TIME SERIES ANALYSIS

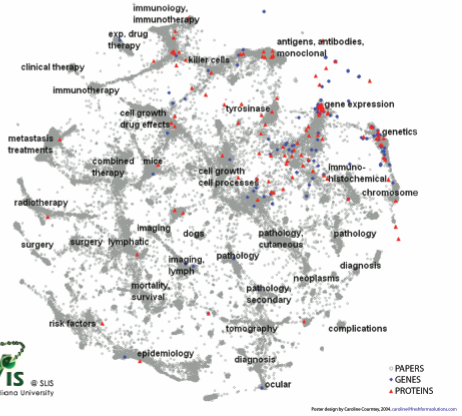
The structure & dynamics of melanoma research was examined:

1964-1973: Diagnostic and immunity based approaches dominate. Chemotherapy emerges as a new area for cancer treatment.

1974-1983: Chemotherapy gains popularity as viable treatment. Monoclonal studies involving tagging cancerous cells using antigens start.

1984-1993: Research on metastasis behavior of cancer dominates.

1994-2003: Gene-expression and mutation related studies gain popularity.



Boyack, Kevin W., Mane, Ketan and Börner, Katy. (2004). Mapping Medline Papers, Genes, and Proteins Related to Melanoma Research. IV2004 Conference, London, UK, pp. 965-971.

SRS Browser: A Visual Interface to The Sequence Retrieval System

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Abstract

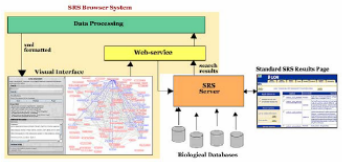
The sequential retrieval system (SRS) facilitates retrieval of information from a large number of biological, biochemical and biomedical databases. Currently not supported by SRS is the navigation of associations to answer questions such as: What relation exists between genes that are known to cause melanoma? Which proteins are associated with a particular disease? What is the most well researched gene in cancer research? What papers refer to many genes and/or proteins related to a melanoma?

The 'SRS Browser' system helps researchers to find answers to these questions via association identification in SRS query results. The associations among genes, proteins and papers are presented to the user as highly interactive, navigable visualizations.

System Architecture

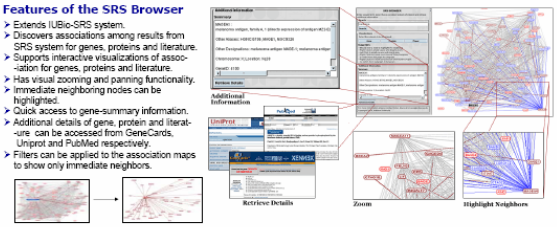
The SRS Browser consists of four components:

- **SRS System**
  The IUBio-SRS system at Indiana University is queried through the web service program.
- **SRS Visual Interface**
  Client-side interface to query the SRS system and to visualize data associations.
- **Web Service**
  An interface used to access SRS system via SOAP.
- **Data-Processing Module**
  Query results are obtained in xml format. Association among genes, proteins and literature are identified. Underlying assumption is that genes/proteins co-occuring in the same paper are related. In the case of literature, if two papers are related if they refer to the same gene or protein.



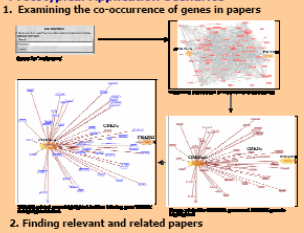
Features of the SRS Browser

- Extends IUBio-SRS system.
- Discovers associations among results from SRS system for genes, proteins and literature.
- Supports interactive visualizations of association for genes, proteins and literature.
- Has visual zooming and panning functionality.
- Immediate neighboring nodes can be highlighted.
- Quick access to gene-summary information.
- Additional details of gene, protein and literature can be accessed from GeneCards, Uniprot and PubMed respectively.
- Filters can be applied to the association maps to show only immediate neighbors.

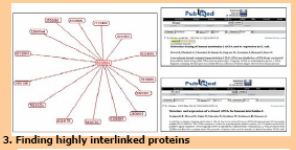


Prototypical Application Scenarios

1. Examining the co-occurrence of genes in papers



2. Finding relevant and related papers



3. Finding highly interlinked proteins

Acknowledgements: We would like to thank Shashikant Penumarthy, Josh Goodman, Don Gilbert, Santiago Schnell and Kranthi Varala for their valuable input throughout the project. This work is supported by National Science Foundation grant DUE-0333623.

Mane, Ketan & Börner, Katy. (2006). SRS Browser: A visual interface to Sequence Retrieval System Visualization and Data Analysis, San Jose, CA, SPIE-IS&T, Jan 15-19, 2006.

This Talk has Three Parts:

1. Why do we need Cyberinfrastructures (CI)?
2. CI applied to map 'melanoma' related literature, genes, and proteins.
3. **CI applied to support computational diagnostics of Acute Lymphoblastic Leukemia patients**

Center of Excellence for Computational Diagnostics

21st Century Grant, Sept. 04 - Aug. 06, $1,994,951.

Investigators: Susanne Ragg (PI), David Clemmer, Sven Rahmann, and Ilka Ott, Terry Vik, R Clement McDonald, Nunroe Pecock, Zina Ben Miled & Katy Börner.

Visualization Subproject:

Aims to develop visualizations that help identify factors which cause relapse in Acute Lymphoblastic Leukemia (ALL) patients.

Current visualizations provide a

- Global overview of medical condition and diagnostic variable(s) of all patients in the dataset.
- Means to identify patients with best or worst phenotype/prognosis data values.
- Ability to compare patients or patient groups that share similar medical/diagnostic variables.

Visualization Team:


Dr. Susanne Raggs


Julie Haydon


Jada Pane


Ketan Mane

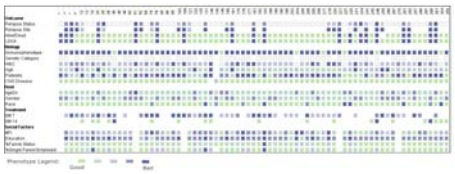

Dr. Katy Börner

Computational Diagnostics – Interactive Visualizations

Coupling of different interactive visualizations such as

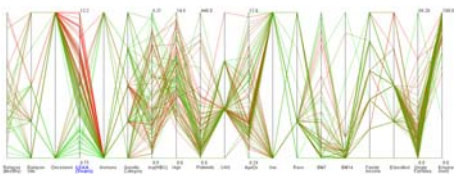
Matrix Visualization

phenotype, prognosis, combined view.

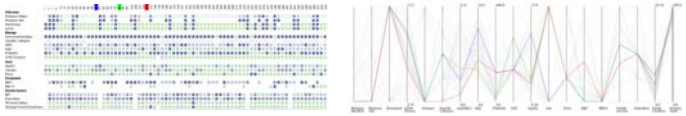


Parallel Coordinate Visualization

phenotype view.

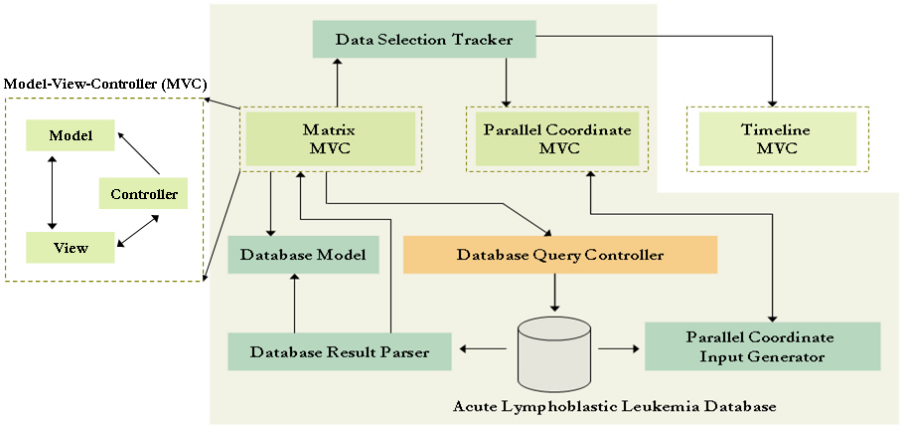


Coupled Windows



Computational Diagnostics – Interactive Visualizations

System Architecture



Computational Diagnostics - Dataset Details

Diagnostic data variables from medical records for Acute Lymphoblastic Leukemia (ALL) patients are grouped into

a. Outcome
Patient Variables: relapse, relapse site, alive/death status, and LDKA.

b. Biology
Patient Variables: immunophenotype, genetic condition, WBC, Hgb, platelets, and CNS.

c. Host
Patient Variables: diagnostic age (ageDx), gender, and race.

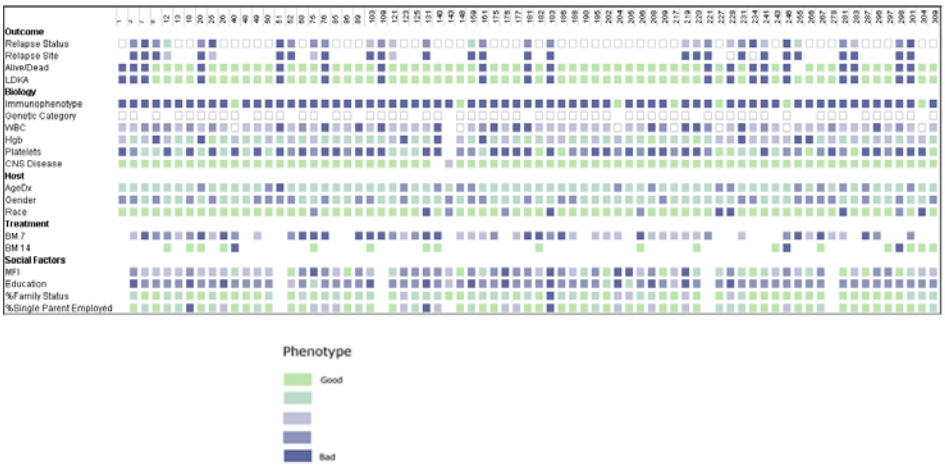
d. Treatment
Patient Variables: BM 7 and BM 14.

e. Social Factors
Patient Variables: MFI-class, education level, %single family members. and % family employment.

All data was provided by Dr. Susanne Raggs, Julie Haydon and Jada Pane.

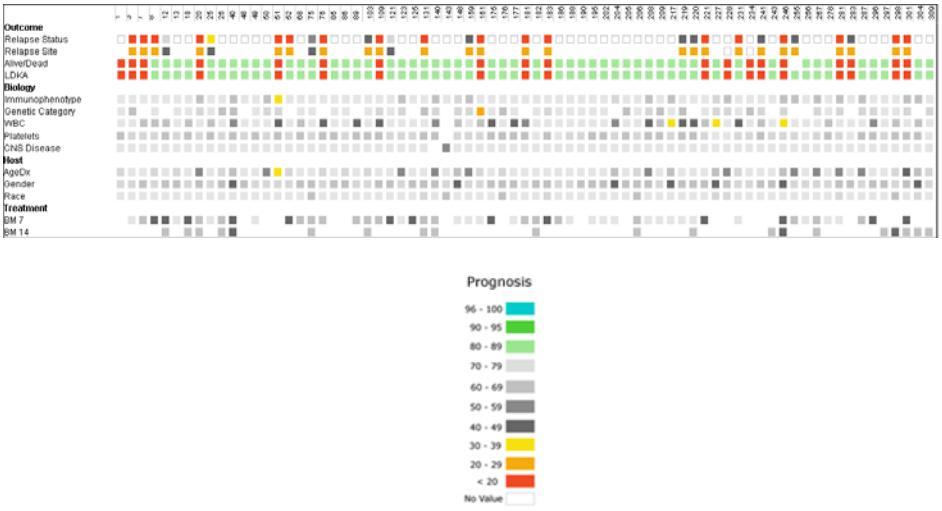
Matrix Visualization – Phenotype View

- Data (vertical axis) - patient (horizontal axis) matrix.
- Data values are color coded according to their severity.



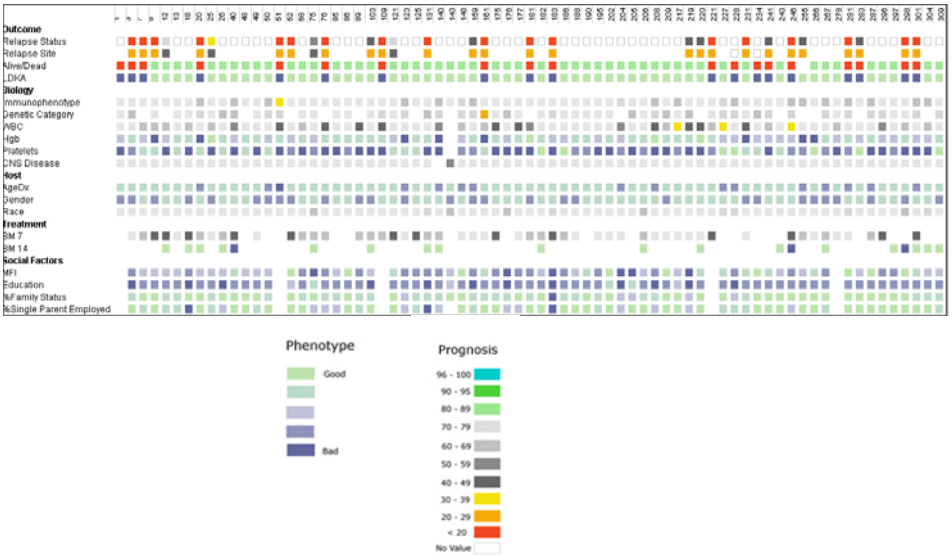
Matrix Visualization – Prognosis View

- Data (vertical axis) - patient (horizontal axis) matrix.
- Color codes indicate event free survival in percent (%EFS).



Matrix Visualization – Combined View

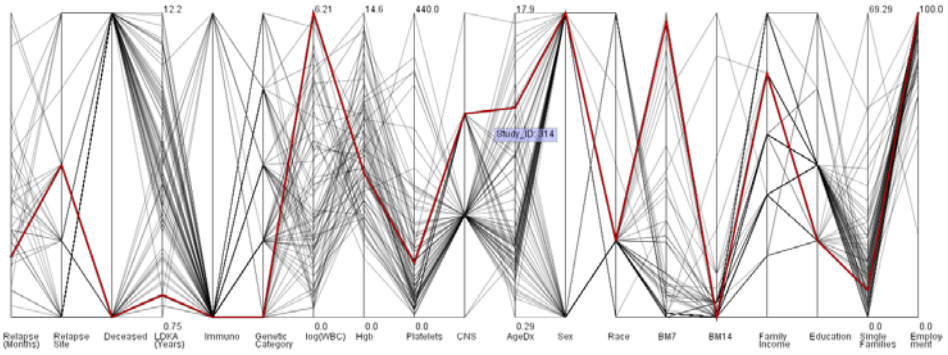
- Facilitates selection of phenotype/prognosis view for individual diagnostic variables.



Parallel Coordinates Visualization

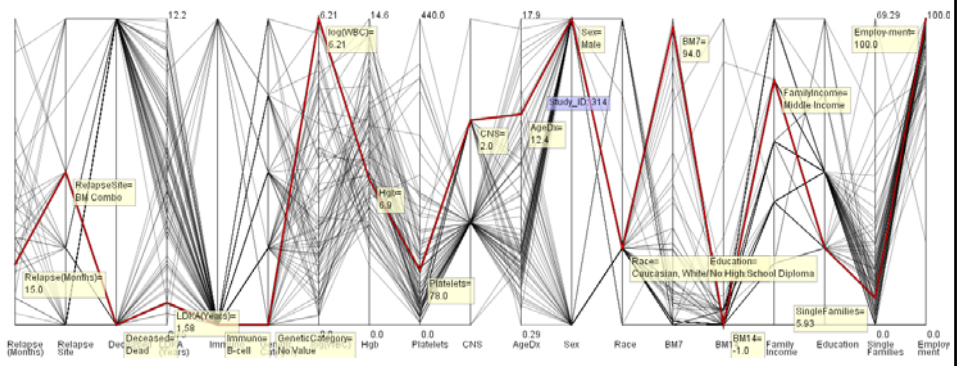
- Uses one axis for each data variable.
- For each patient, all data values on the different parallel axes are connected.
- All patent graphs are shown here.

Single or multiple patients can be selected and studied in detail.



Parallel Coordinates Visualization

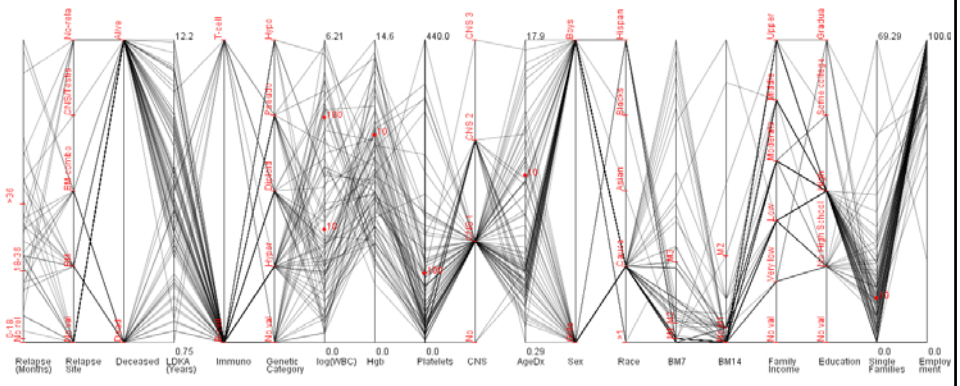
Tool-tip display to show diagnostic values of selected patient.



Parallel Coordinates Visualization – User Interactions

Display axes-labels to mark different regions/values along axes

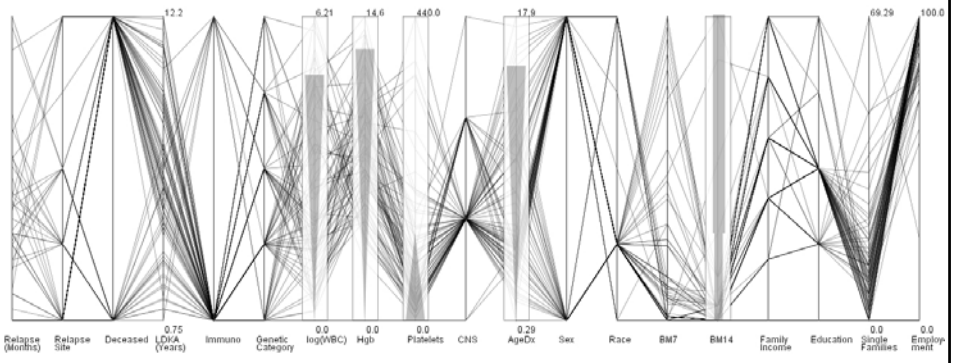
- Numerical landmarks along axes showing values for quantitative variables.
- Category labels along axes show values for nominal variables.



Parallel Coordinates Visualization – User Interactions

Display zones to show severity values for different variables

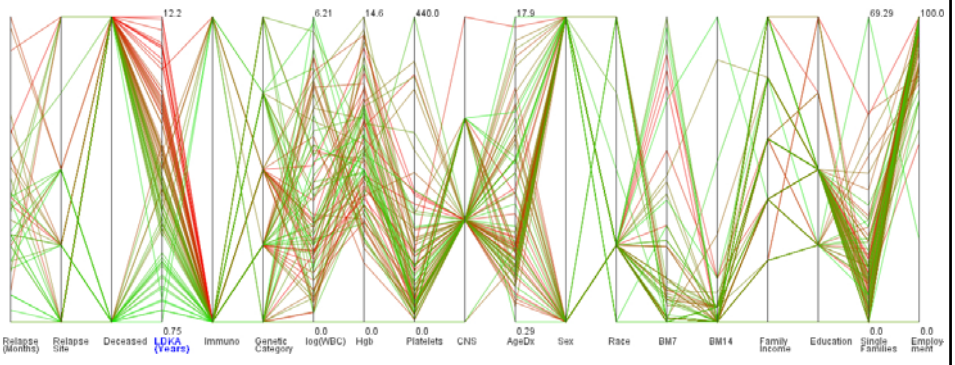
- Triangular zones indicate variables with quantitative values.
- Rectangular zones are used for variables with nominal values.



Parallel Coordinates Visualization – User Interactions

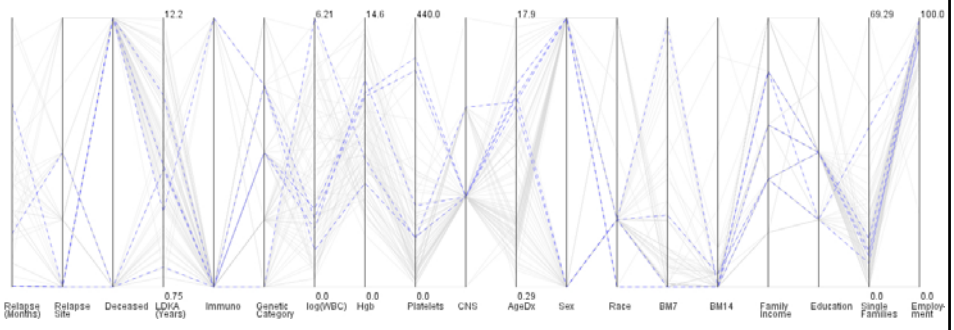
Axis selection to study global variations in patient values

- Single axis can be selected to study the trend in patient values.
- Red-to-green gradient used to indicate values along the selected axis.
  [Red = High value, Green = Low value]



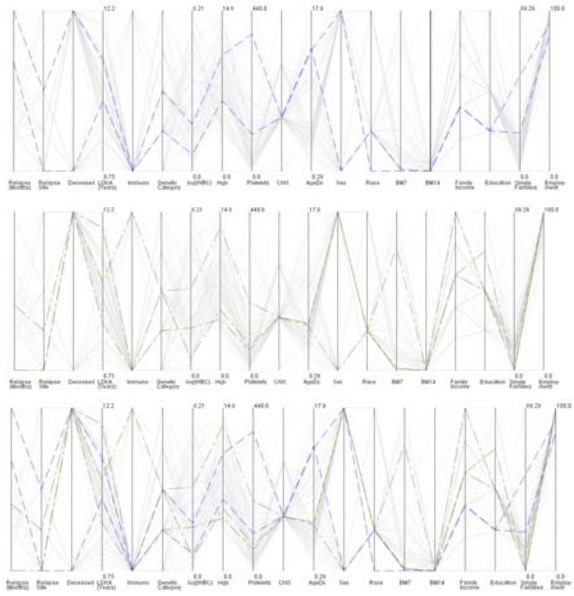
Parallel Coordinates Visualization

A subset of patents can be selected and examined as a group.



Parallel Coordinates Visualization

Simultaneous display of patient groups to study differences.



Patient Group 1

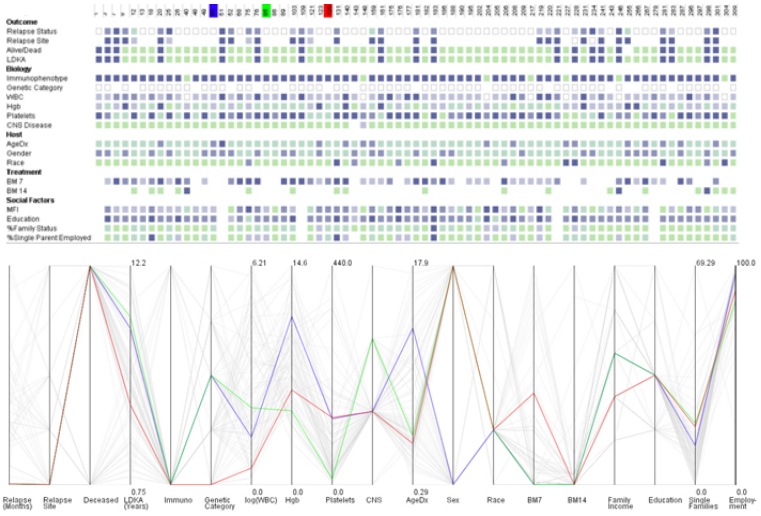
Patient Group 2

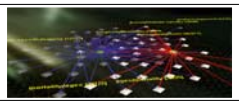
Patient Group 1 & 2

Parallel Coordinates Visualization

Multiple Coordinated Views

- Patient can be selected and color coded in matrix view.
- Corresponding patient lines are highlighted in parallel coordinate view.





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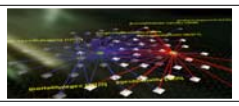

Thank you.

Please feel free to attend demonstrations of the diverse tools by Ketan Mane.