Systematic Annotation

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4/5/2012

Review

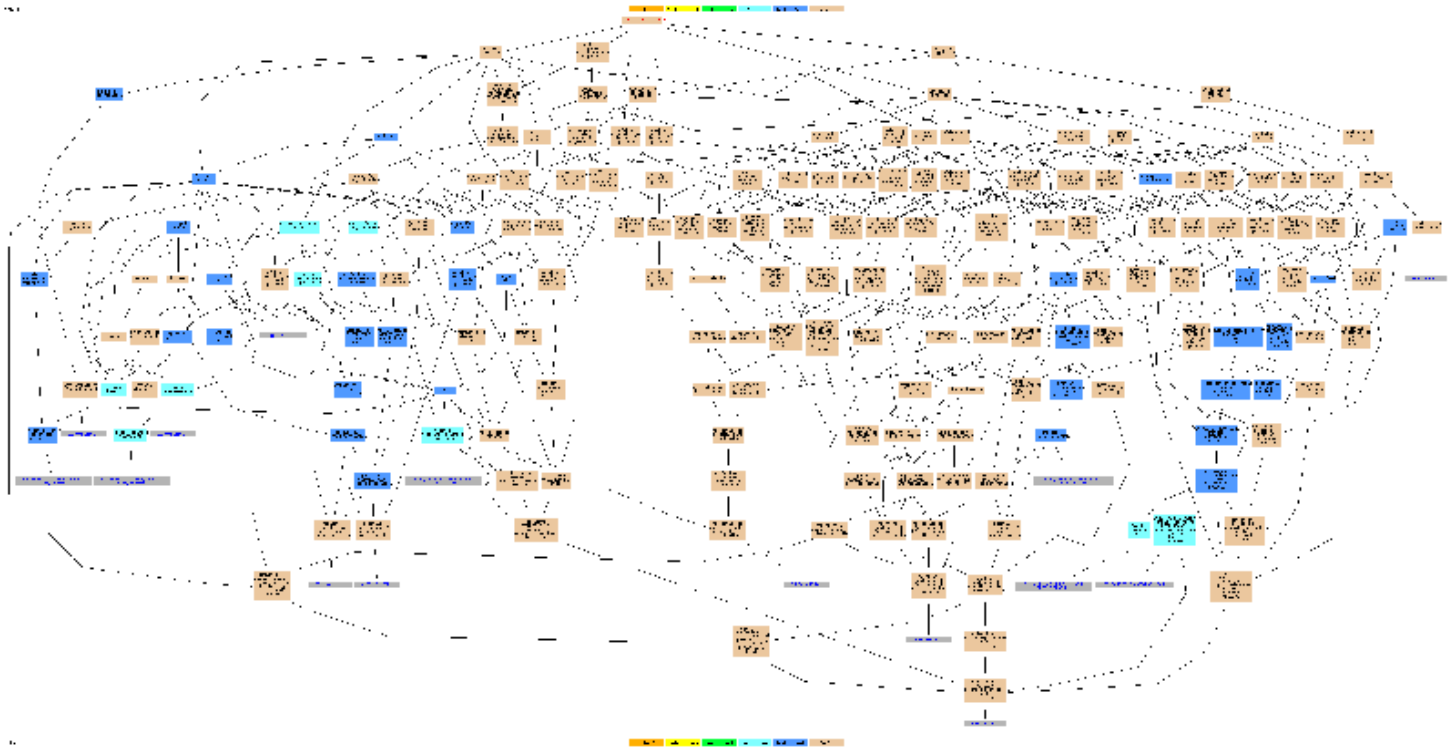
- RTFM
- PNAS 95:14863

The Gene Ontology

Three directed acyclic graphs (aspects):

- Biological Process
- Molecular Function
- Subcellular Component

The Gene Ontology



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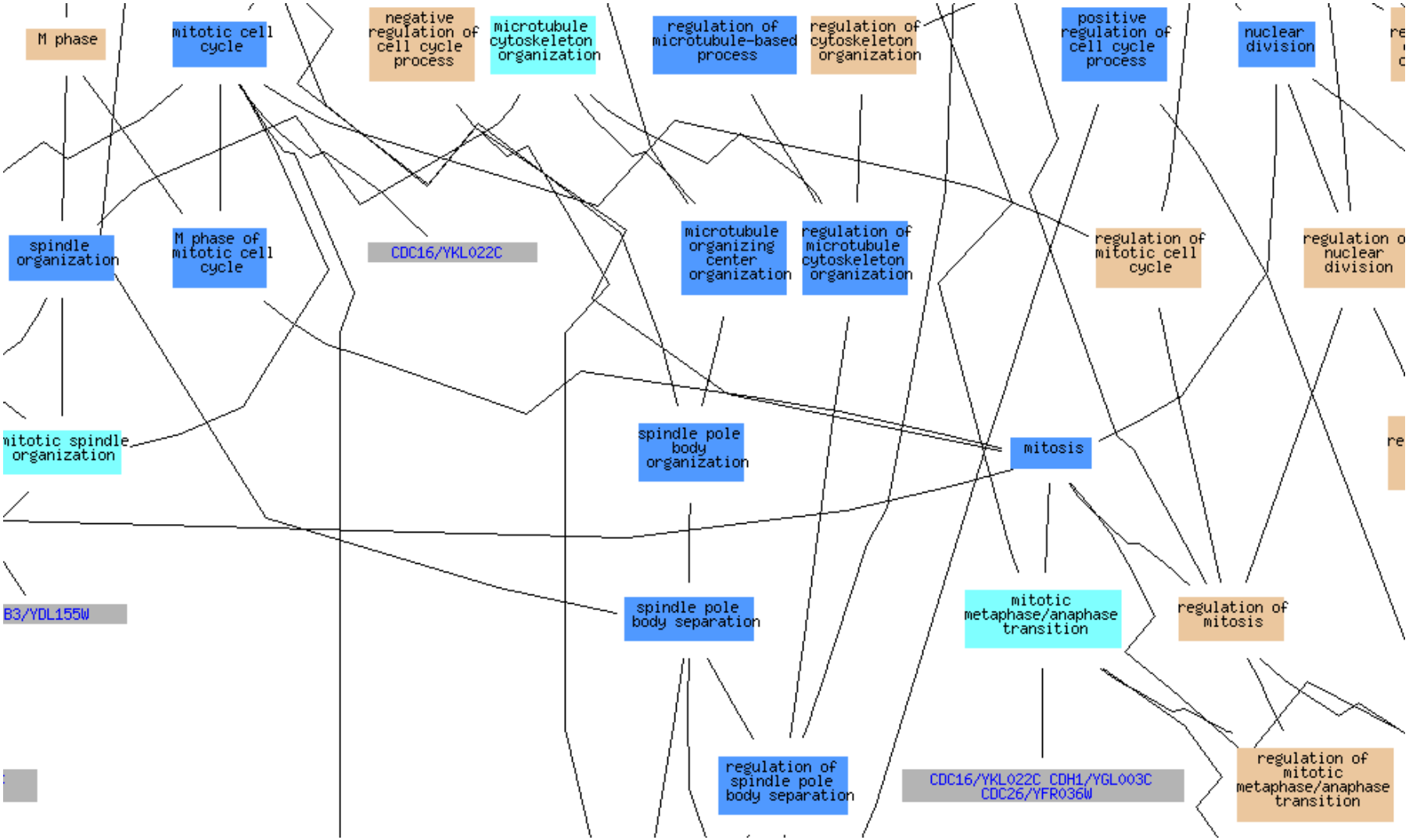
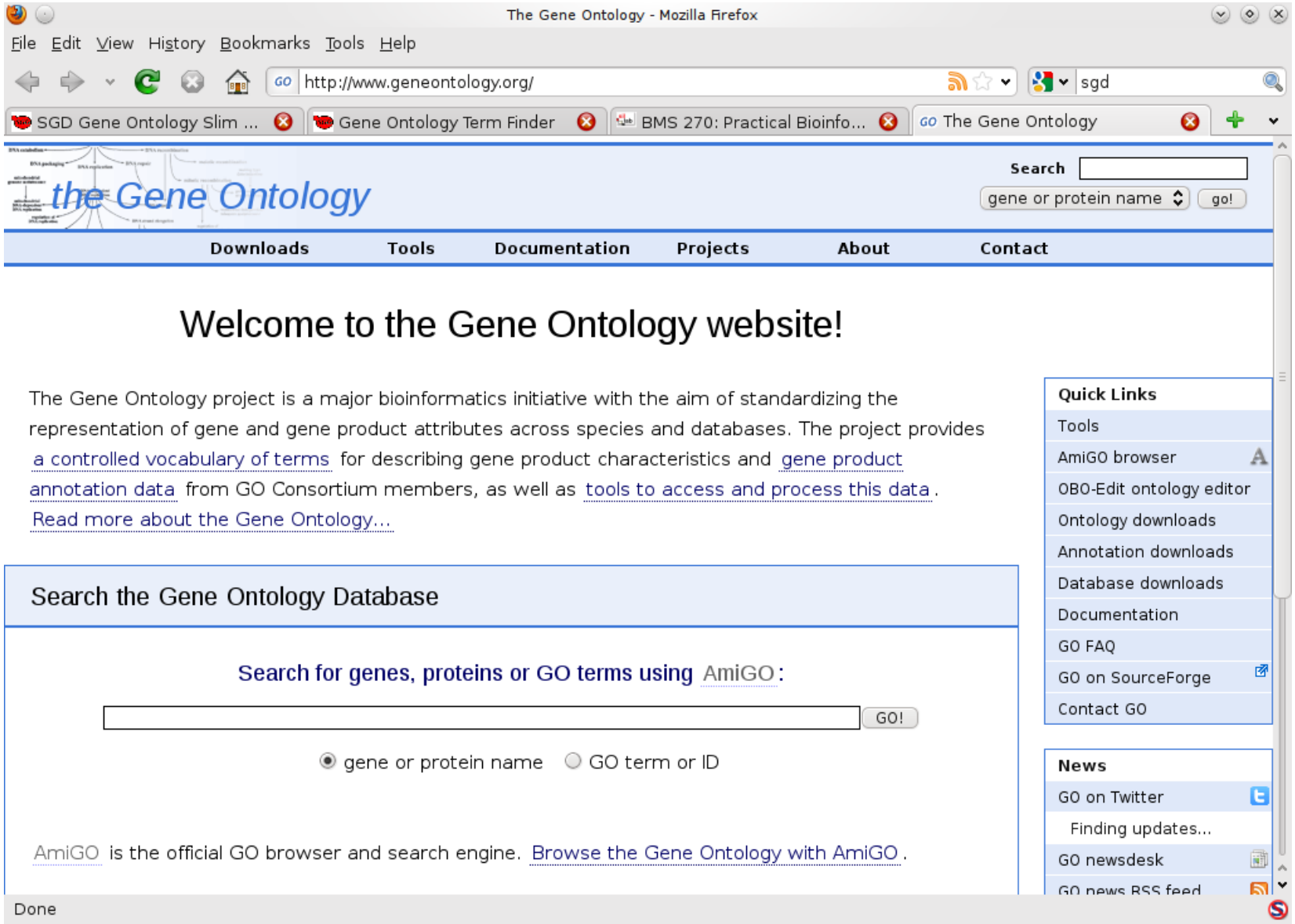


The AmiGO browser



The Gene Ontology

- How might we annotate genes with GO terms?
- How do we calculate the significance of the GO terms associated with a particular group of genes?

Associating GO terms

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- By sequence homology (*e.g.*, BLAST)
- By domain homology (*e.g.*, InterProScan)
- Mapping from an annotated relative (*e.g.*, INPARANOID)
- Human curation of the literature (*e.g.*, SGD)

Associating GO terms: Evidence codes

- Experimental
  - EXP: Inferred from Experiment
  - IDA: Inferred from Direct Assay
  - IPI: Inferred from Physical Interaction
  - IMP: Inferred from Mutant Phenotype
  - IGI: Inferred from Genetic Interaction
  - IEP: Inferred from Expression Pattern
- Computational Analysis
  - ISS: Inferred from Sequence or Structural Similarity
  - ISO: Inferred from Sequence Orthology
  - ISA: Inferred from Sequence Alignment
  - ISM: Inferred from Sequence Model
  - IGC: Inferred from Genomic Context
  - RCA: inferred from Reviewed Computational Analysis
- Author Statement
  - TAS: Traceable Author Statement
  - NAS: Non-traceable Author Statement
  - Curator Statement Evidence Codes
  - IC: Inferred by Curator
  - ND: No biological Data available
- Automatically-assigned
  - IEA: Inferred from Electronic Annotation
- Obsolete
  - NR: Not Recorded

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This is also the expected genome coverage.

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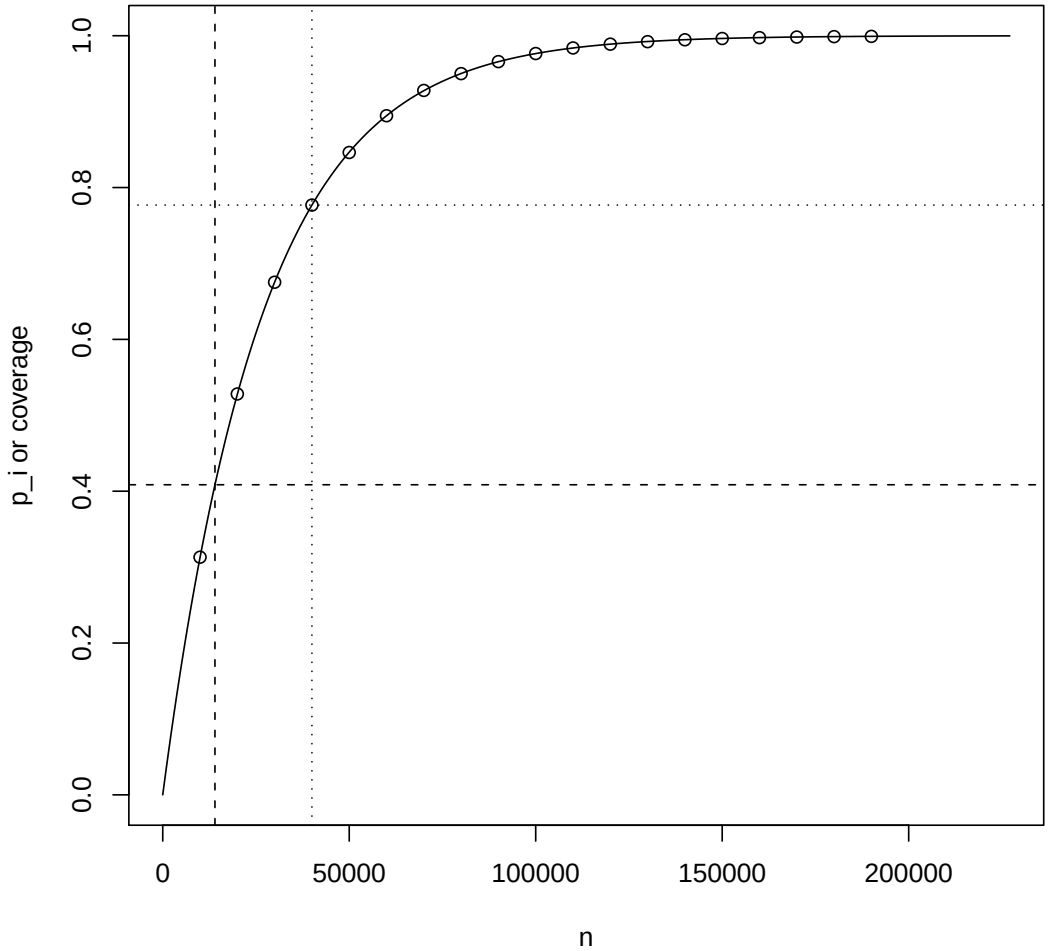

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What if there is more than one type of event?
Multinomial distribution:

$$p_{k_1,k_2,\ldots,n} = \frac{n!}{\prod k_i!} \prod p_i^{k_i} \tag{8}$$

Sampling without replacement: GO Annotation

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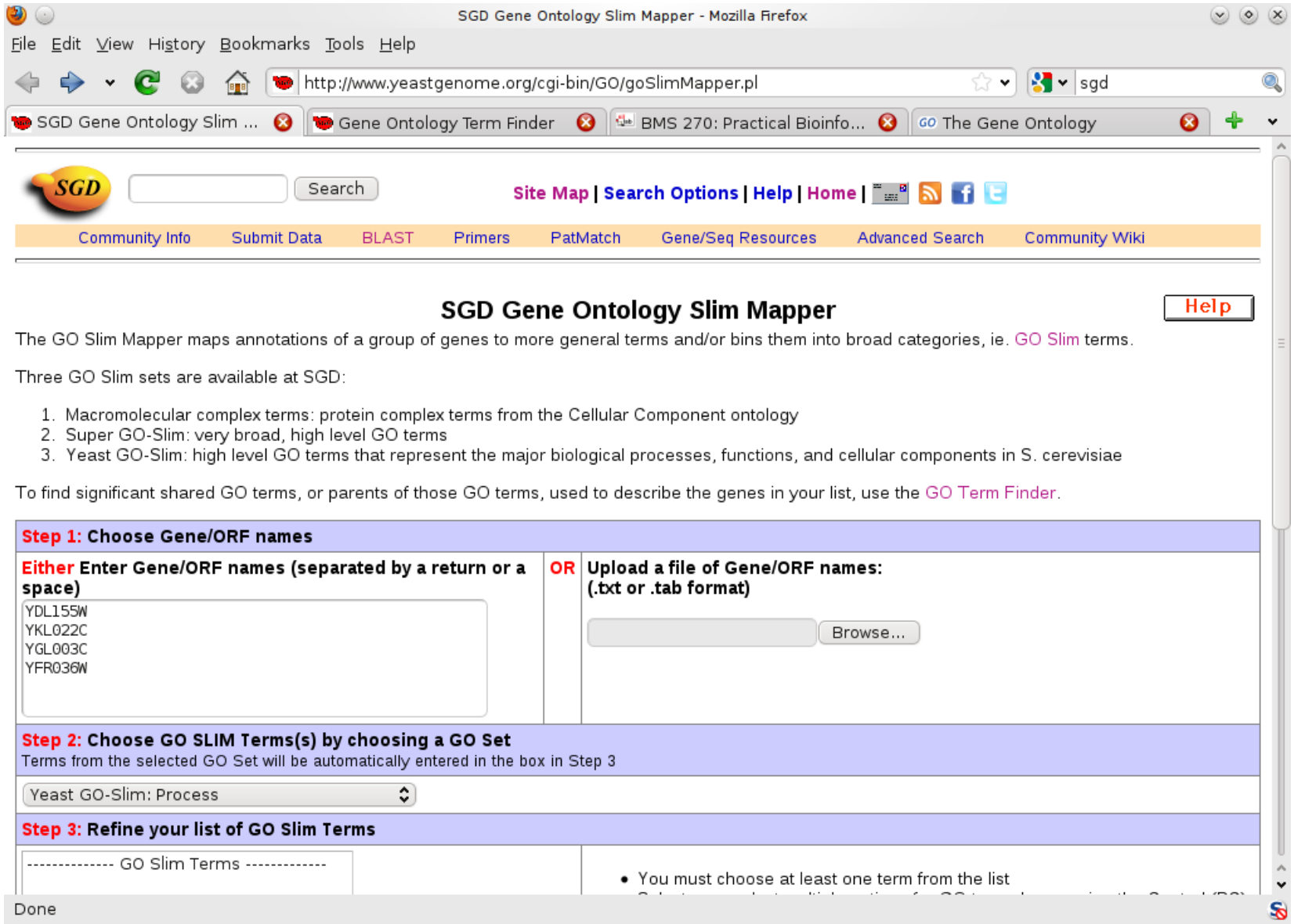
More than one *disjoint* type of label:

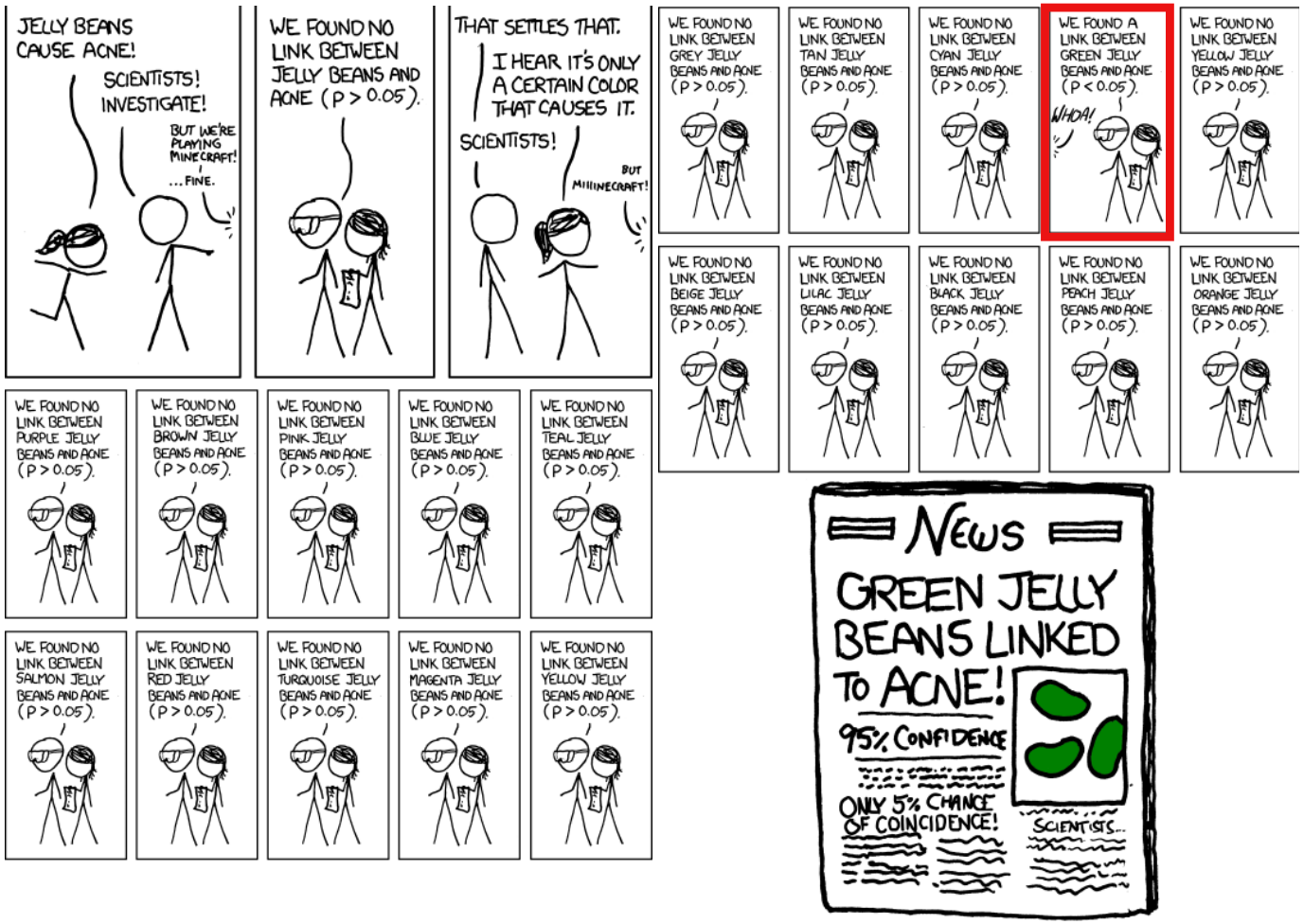
$$p_{k_1,k_2,\ldots,m_1,m_2,\ldots,n} = \frac{\prod \binom{m_i}{k_i}}{\binom{N}{n}} \tag{11}$$

Extracting gene lists from JavaTreeView

The SGD GO Slim Mapper



Multiple Hypothesis Testing



http://xkcd.com/882/

Alternatives to Hierarchical Clustering

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- Pre-calling number of clusters: k-means and k-medians

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- Principal Component Analysis (PCA)

Homework

- Download PyMol