TOOLS FOR EXPLORING BIOLOGICAL NETWORKS

- Pathway information page
  - Each pathway shows a detailed mini-review from MetaCyc
  - Search pathways by name, substrates, length
- Reaction information page
- Metabolite information page
  - Search metabolites by name, accession numbers, substructure, mass, monoisotopic mass, element composition
- Customize pathway diagrams for figures in publications (add/remove gene names, enzyme names, chemical structures, omics data)
- Create personalized pathway diagrams – pathway collages – by assembling groups of pathways into one diagram, moving pathways relative to one another, customizing display styles, and adding omics data.
- Cellular Overview diagrams (Figure 1) are organism-specific depictions of metabolic and transporter networks that are zoomable and searchable.
- Route Search tool finds minimum-cost paths between metabolites in the metabolic network (Figure 6). Route Search paths maximize the number of atoms conserved from feedstock to target by using an extensive library of reaction atom mappings.
- Regulatory Overview (Figure 2) presents the genetic regulatory network stored in a PGDB.
- Dead-end metabolite identification algorithm.
- Identify anti-microbial drug targets using a tool that computes metabolic choke points.

ANALYSIS TOOLS FOR GENE EXPRESSION AND METABOLOMICS DATA

- SmartTables store lists of genes or metabolites. Browse database attributes, share with colleagues, transform to pathway lists, perform enrichment analysis.
- Cellular Omics Viewer (Figure 1) enables the user to paint omics datasets onto the Cellular Overview diagram. Scientists can interpret gene expression, proteomics, and metabolomics datasets in a pathway context, including animation of time-course or comparative datasets (example animation at http://biocyc.org/ov-expr.shtml).
- Paint omics data onto individual pathways and pathway collages.
- Regulatory Omics Viewer paints omics datasets onto the regulatory network to enable comparisons of expression measurements with regulatory mechanisms.
- Genome-browser tracks facility (Figure 5) allows user datasets to be plotted against the genome.

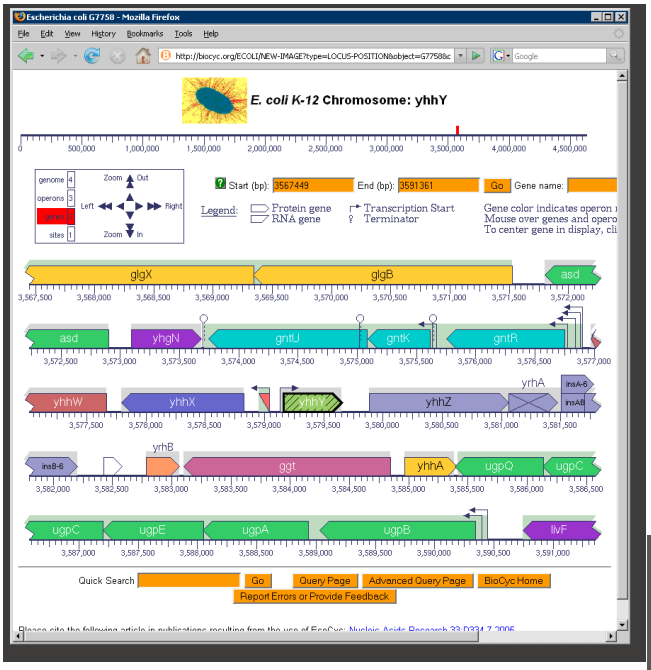
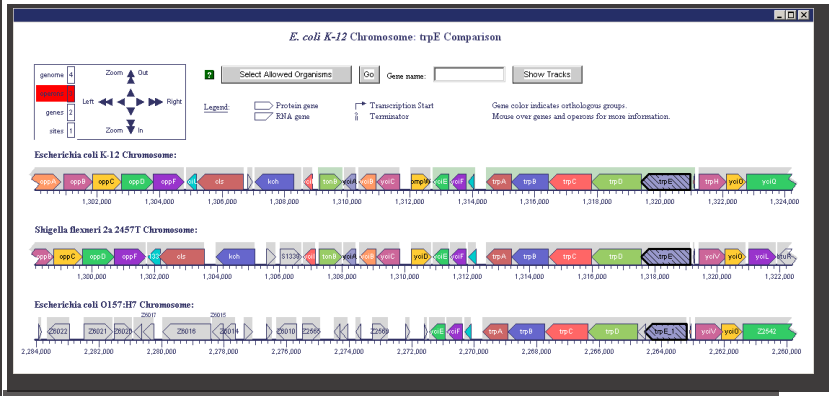
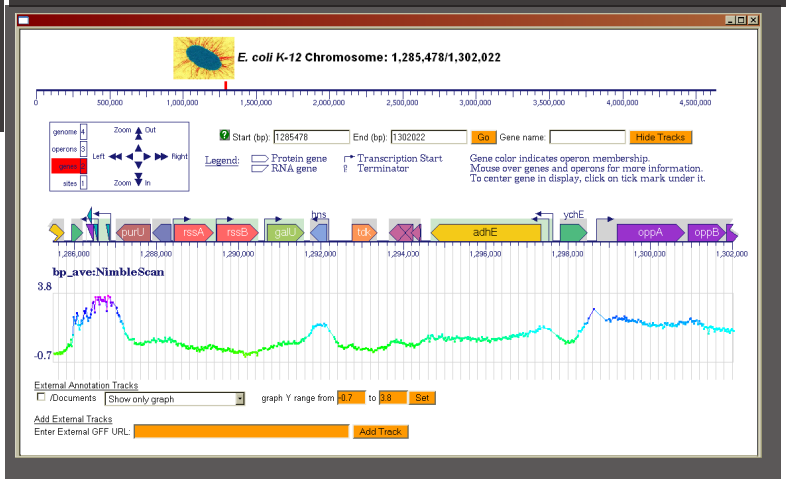


Figure 5: Genome browser with tracks display enabled. The single track shown here was generated from a data file containing ChIP-chip data for RNA polymerase binding. This facility allows the user to compare the frequency of protein binding from ChIP-chip experiments against curated promoters within a PGDB.

Figure 4. Left: Genome browser depiction of a region of the E. coli chromosome. Gene colors indicate operon organization. Promoters and terminators are depicted when known. Pseudogenes are marked with X's. Below: Comparative genome browser showing alignments with respect to the trpE gene of two E. coli genomes and the Shigella flexneri genome. Colors indicate orthologs.





Generate an organism-specific metabolic wall chart from a PGDB.

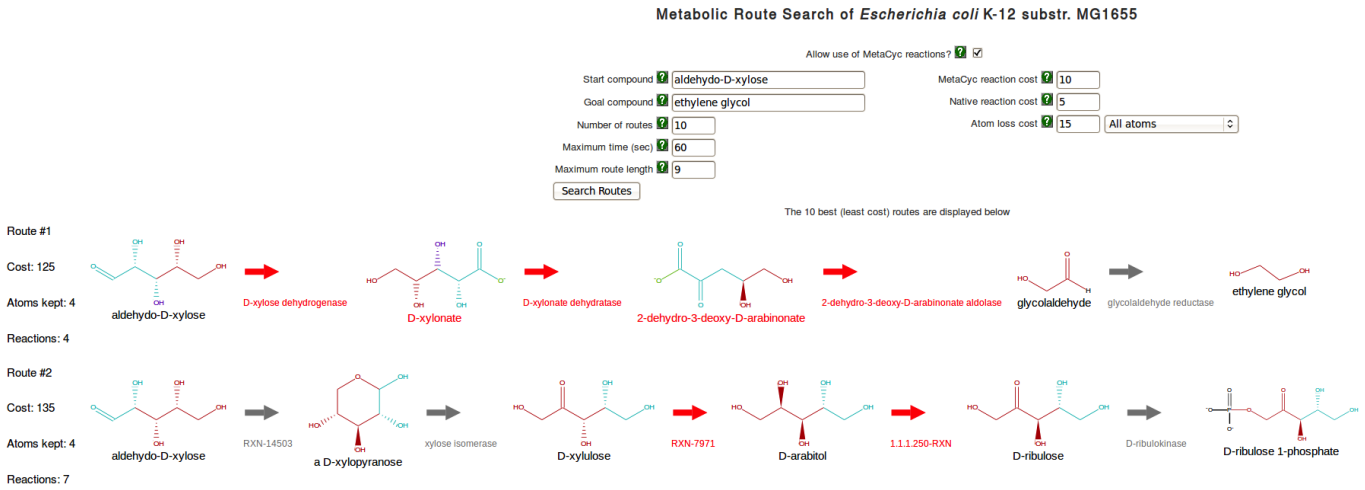


Figure 6: Output from the RouteSearch tool for metabolic path searching. The tool was asked to find paths from aldehyde-D-xylose to ethylene glycol in E. coli. The two lowest-cost paths are shown; the second path is truncated. Coloring of the chemical structures indicates conservation of atoms along the pathways. Red arrows indicate reactions added from MetaCyc.

COMPARATIVE GENOMICS TOOLS

- Comparative genome browser (Figure 4, Right) aligns chromosomal regions from multiple genomes at orthologous genes
- Sequence alignments
- Compare pathway, reaction, metabolite, and protein complements of specified organisms
- Quick navigation between corresponding entities (e.g., genes, pathways, metabolites) in different organisms.
- Cross-organism search finds genes, metabolites, pathways across BioCyc organisms

WEB EXECUTION OF METABOLIC MODELS

- Execute steady-state metabolic flux models using flux-balance analysis
- Specify organism nutrients, secreted metabolites, and biomass metabolites synthesized by metabolic network
- Predict reaction flux rates, cellular growth rates
- Visualize reaction fluxes on metabolic network diagram
- Initial models available for *Escherichia coli, Eubacterium rectale, Bacteroides thetaiotamicron*; additional organisms to come

ADVANCED DATABASE ACCESS

- Users can define genes, pathways, and Gene Ontology terms in their areas of interest to receive automated notifications of curation updates for these entities.
- Extensive web service API provided.
- Author advanced queries: The Structured Advanced Query Form enables intuitive construction of database queries of SQL power using a Web-based interface.

ABOUT SRI'S BIOINFORMATICS RESEARCH GROUP

SRI International, an independent research institute, is a key player in the field of computational biology, which uses computer science principles and powerful computing capabilities to understand complex biological systems. SRI's Bioinformatics Research Group is a leader in the development of database content and software tools for bioinformatics.

REFERENCES

[1] The EcoCyc Database. EcoSal Plus. 2014. http://www.asmscience.org/content/journal/ecosalplus/10.1128/ecosalplus.ESP-0009-2013ecosalplus.ESP-0009-2013

[2] MetaCyc: Nucleic Acids Research 444: D471-80 2016 http://nar.oxfordjournals.org/content/44/D1/D471.long

[3] "Pathway Tools version 19.0: Software for Pathway/Genome Informatics and Systems Biology," *Briefings in Bioinformatics* 2015. http://arxiv.org/abs/1510.03964

[4] "The Pathway Tools Software and Its Role in Anti-Microbial Drug Discovery," Microbial Genomics and Drug Discovery, T.J. Dougherty and S.J. Projan eds., Marcel Dekker Inc., New York, 2003

Additional publications: http://biocyc.org/publications.shtml

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SRI International

333 Ravenswood Avenue
Menlo Park, CA 94025-3493
650.859.2000

www.sri.com