The analysis and expansion of regulatory binding site data in a wide range of bacteria through the use of a semi-automatic system - RegTransBase

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Overview

RegTransBase (RTB) is a database of regulatory sequences and regulatory interactions in prokaryotic genomes. RTB is based on journal articles devoted to transcriptional and post-transcriptional regulation of gene expression.

Annotation of each article in RTB contains a list of experiments (with a short description) and a list of structural elements of genomes involved in regulatory interactions (genes, sites, transcripts, operons, loci, regulons, regulators, effectors).

RTB brings together these interactions in a user-friendly interface, allowing the user to explore and compare their genomes of interest, as well as view all experiments on a given element in one place.

RTB provides more then just a collection of articles, experiments and elements, it also provides tools for the analysis of regulation within one organism, as well as a comparison between multiple organisms. Using the combination of previous knowledge from published experiments along with computational prediction tools, a user can make informed decisions on the analysis of regulatory sites throughout genomes.

RTB contains modules for simple text searching (such as gene name, function, or experiment description), sequence based searching (BLAST), and searching using motifs or alignments (MAST).

RegTransBase is available at http://regtransbase.lbl.gov

Figure 1. Main page of RegTransBase.

Data

In the studies on bacterial regulation the final decision of whether to include each putative site in a particular regulon is made after detailed inspection and consultation with relevant scientific literature by a human expert. RegTransBase (RTB), a manually curated database of regulatory interactions, captures the knowledge in published scientific literature using a controlled vocabulary. RTB describes a large number of regulatory interactions reported in many organisms and contains the following types of experimental data:

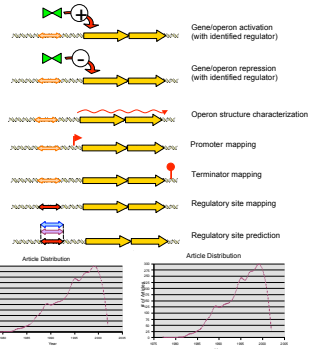


Table 1. Distribution of the number of elements based on organisms.

Table 2. Listing of the number of entries of different experiment types in RegTransBase.

Figure 2. Number of articles annotated per year published.

Information

RegTransBase contains structured information obtained directly from experiments explained in **published literature**. **Articles** contain multiple experiments.

Each **experiment** contains multiple elements that make up that experiment. **Elements** themselves can have a hierarchical relationship (operons->genes). Elements may be **linked** to other elements (**sites** are linked to **regulators**). We provide the **tools** to view this experiment, and then

- obtain a **global** view of the genomic region
- view features/elements in that region
- list **effectors** that act on these elements
- Provide tools for the **comparisons** between species.

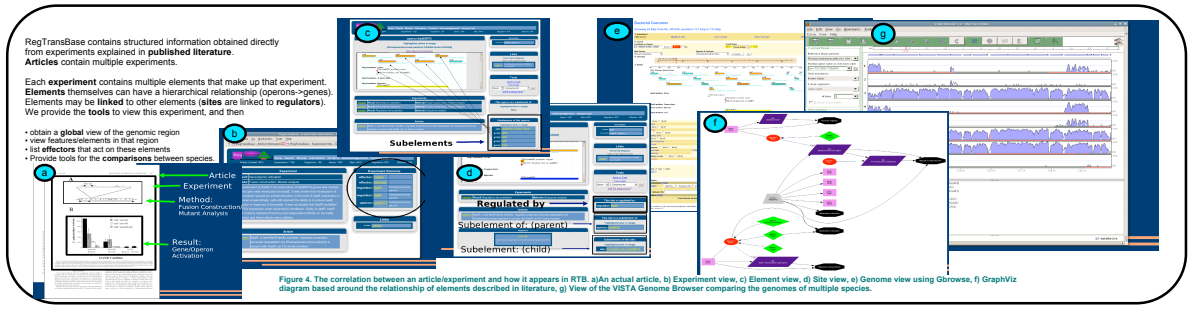
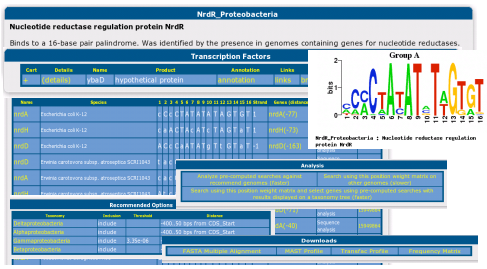


Figure 4. The correlation between an article/experiment and how it appears in RTB. a)An actual article, b) Experiment view, c) Element view, d) Site view, e) Genome view using Gbrowse, f) GraphViz diagram based around the relationship of elements described in literature, g) View of the VISTA Genome Browser comparing the genomes of multiple species.

Alignments of Binding Sites



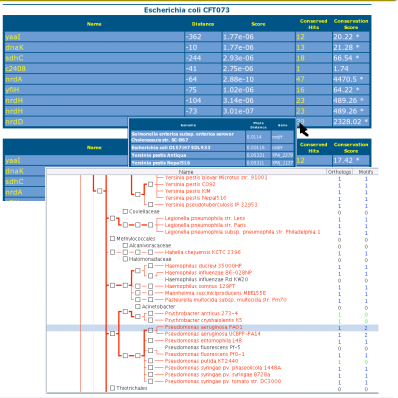
In addition to publication data, RTB provides its users with a growing collection of curated binding site alignments. Each alignment was created by an expert curator who provided descriptions explaining all alignments, specific sequence locations referenced to NCBI RefSeq genomes, available publications, and recommended options for using this alignment to search new genomes. This data is available for download

Comparison

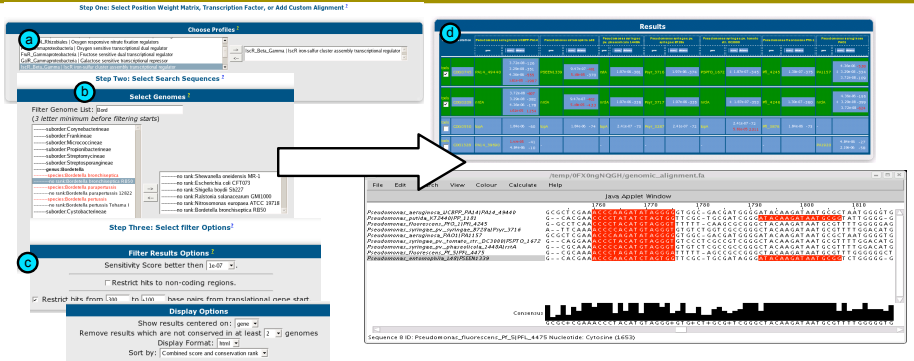
We currently have a manually curated collection of over 100 position weight matrices and alignments (with plans for more in the future). We provide the ability to search sequenced genomes using these matrices or the user can supply their own alignment. Using a collection of interfaces we aim to provide a tool for the following situations:

- One matrix + one genome of interest
  - Show predicted binding sites which match this matrix, while providing additional information.
- One gene + multiple genomes
  - Predict binding sites for orthologus genes using certified matrices.
- One matrix + multiple genomes
  - Compare the predicted binding sites across genomes for a particular matrix, highlighting orthologus similarities.
- Multiple matrices + multiple genomes
  - Compare the predicted binding sites across genomes for a set of matrices.

These tools allow a person to be guided through a semi-automated process which will highlight conserved transcription factor binding sites.



Prediction



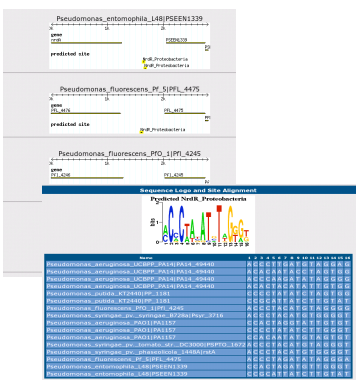


Figure 5. The process for comparing hits of a particular motif against multiple genomes is shown here. a) A predefined alignment is chosen to create a position weight matrix from (custom alignment option is available also), b) Genomes to compare are selected, c) Results will be filtered by the options given, d) The result is a table with rows being orthologus genes, and hits specified within each row. For each orthologus row, additional analysis tools may be accessed, such as graphical alignments, sequence logos, text alignments, phylogenetic trees and the ability to view the alignment in the feature rich application JalView.