Available online at www.sciencedirect.com

ScienceDirect

Journal of Biotechnology 129 (2007) 279–289

Journal of BIOTECHNOLOGY

www.elsevier.com/locate/jbiotec

CoryneRegNet 3.0—An interactive systems biology platform for the analysis of gene regulatory networks in corynebacteria and *Escherichia coli*

Jan Baumbach[a,b], Tobias Wittkop[a], Katrin Rademacher[a], Sven Rahmann[a,b], Karina Brinkrolf[b,c], Andreas Tauch[b,c,*]

[a] *Algorithms and Statistics for Systems Biology Group, Genominformatik, Technische Fakultät, Universität Bielefeld, Universitätsstraße 25, D-33615 Bielefeld, Germany*
[b] *International NRW Graduate School in Bioinformatics and Genome Research, Centrum für Biotechnologie, Universität Bielefeld, Universitätsstraße 25, D-33615 Bielefeld, Germany*
[c] *Institut für Genomforschung, Centrum für Biotechnologie, Universität Bielefeld, Universitätsstraße 25, D-33615 Bielefeld, Germany*

Received 30 August 2006; received in revised form 22 November 2006; accepted 4 December 2006

Abstract

CoryneRegNet is an ontology-based data warehouse for the reconstruction and visualization of transcriptional regulatory interactions in prokaryotes. To extend the biological content of CoryneRegNet, we added comprehensive data on transcriptional regulations in the model organism *Escherichia coli* K-12, originally deposited in the international reference database RegulonDB. The enhanced web interface of CoryneRegNet offers several types of search options. The results of a search are displayed in a table-based style and include a visualization of the genetic organization of the respective gene region. Information on DNA binding sites of transcriptional regulators is depicted by sequence logos. The results can also be displayed by several layouters implemented in the graphical user interface GraphVis, allowing, for instance, the visualization of genome-wide network reconstructions and the homology-based inter-species comparison of reconstructed gene regulatory networks. In an application example, we compare the composition of the gene regulatory networks involved in the SOS response of *E. coli* and *Corynebacterium glutamicum*. CoryneRegNet is available at the following URL: http://www.cebitec.uni-bielefeld.de/groups/gi/software/coryneregnet/.

© 2006 Elsevier B.V. All rights reserved.

Keywords: *Corynebacterium glutamicum*; *Escherichia coli*; Transcriptional regulation; Regulatory network; SOS response; Systems biology

1. Introduction

Information on molecular interactions, such as those involved in protein–DNA interactions during transcriptional regulation of gene expression, has

---

* Corresponding author at: Institut für Genomforschung, Centrum für Biotechnologie, Universität Bielefeld, Universitätsstraße 25, D-33615 Bielefeld, Germany. Fax: +49 521 106 5626.
E-mail address: andreas.tauch@genetik.uni-bielefeld.de (A. Tauch).

0168-1656/$ – see front matter © 2006 Elsevier B.V. All rights reserved.
doi:10.1016/j.jbiotec.2006.12.012

greatly increased with the recent advances in high-throughput technologies (Herrgård et al., 2004). As a consequence of this development, systems biology, whose goal is to comprehend a microorganism as a complex system of interactions between its multiple entities, becomes a tangible field of research (Mori, 2004; Covert et al., 2004). Mathematical modeling of molecular interactions and subsequent computer simulations are promising tools for a better understanding of the bacterial cell (Reed and Palsson, 2003). Apparently, computer-assisted approaches will have a great impact on biological and medical sciences and the biotechnological industry (Adrio and Demain, 2006).

CoryneRegNet is a systems biology platform originally designed to facilitate the genome-wide reconstruction of transcriptional regulatory interactions in corynebacteria relevant in biotechnology and human medicine (Baumbach et al., 2006a,b). The database contains comprehensive information on transcriptional regulation of gene expression derived from experimental studies, computational predictions and accumulating literature knowledge. CoryneRegNet was implemented with the relational database management system MySQL and an ontology-based data structure that combines the features of semantic database integration with methods for graph-based analysis (Baumbach et al., 2006a; Köhler et al., 2006). During the data import and integration process, CoryneRegNet generates links to the corresponding genome annotations, transcriptional regulators and cognate DNA binding sites. Graphical reconstruction of gene regulatory networks is supported by the yFiles JAVA graph library.

Our previous publications explain in detail the ontology-based design of CoryneRegNet (Baumbach et al., 2006a,b) that allows a continuing development according to the expansion of the type of information that is integrated into the database. This publication describes the main changes in the biological content and computational infrastructure of CoryneRegNet 3.0 that, most notably, includes information on transcriptional regulation of the gram-negative model organism *Escherichia coli* K-12. These data were adopted from the international reference database RegulonDB that is constantly updated to provide a comprehensive overview on transcriptional regulation in *E. coli* K-12 (Huerta et al., 1998; Salgado et al., 2006).

2. Materials and methods

2.1. Ontology-based design of CoryneRegNet

CoryneRegNet is a data warehouse that performs all time-consuming operations during data import. It integrates all available information on transcriptional regulation of gene expression in corynebacteria and *E. coli* K-12 into a MySQL database back-end. To overcome semantic heterogeneity and other data integration problems, we use an ontology-based data structure that consists of typed concepts and relations (Köhler et al., 2006). A concept is a biological entity, for instance, a gene or a protein, while a relation connects two concepts. All concepts and relations are linked to concept classes and relation types to specify their semantic meanings. Concept classes used in CoryneRegNet to specify the types of imported concepts (biological entities) are: organism, gene, operon, module, protein, transcription factor (TF) and sigma factor (SF). The concept classes “TF” and “SF” are specializations of “protein”, which is modeled by using an additional tree-like data structure that stores all specializations (Baumbach et al., 2006a). The concept class “module” defines parts of a network structure that perform a common physiological function and may be linked by regulatory interactions (Aderem, 2005). Table 1 summarizes the relation types used in CoryneRegNet to specify linkages between two concepts.

2.2. Computational infrastructure of CoryneRegNet

CoryneRegNet is designed as a web-based software environment that is publicly available. For the web-based front-end PHP 5 (http://www.php.net) is used. CoryneRegNet runs on an Apache server 2.0.49 (http://www.apache.org), which queries the database management system MySQL 4.1.9 (http://www.mysql.org). In version 3.0 of CoryneRegNet, diagram graphics are created with JpGraph 1.20.3 (http://www.aditus.nu/jpgraph) and GD Graphics Library 2.0 (http://www.boutell.com/gd). Operon information for corynebacterial genomes is based on the VIMSS operon prediction (Price et al., 2005). The sequence logo painter is implemented in Java 5 (http://java.sun.com), as is the graph-based network visualization tool GraphVis that uses an academic

Download English Version:

https://daneshyari.com/en/article/25466

Download Persian Version:

https://daneshyari.com/article/25466

Daneshyari.com