Gene Regulation and Metabolism: Post-Genomic Computational Approaches (Computational Molecular Biology)

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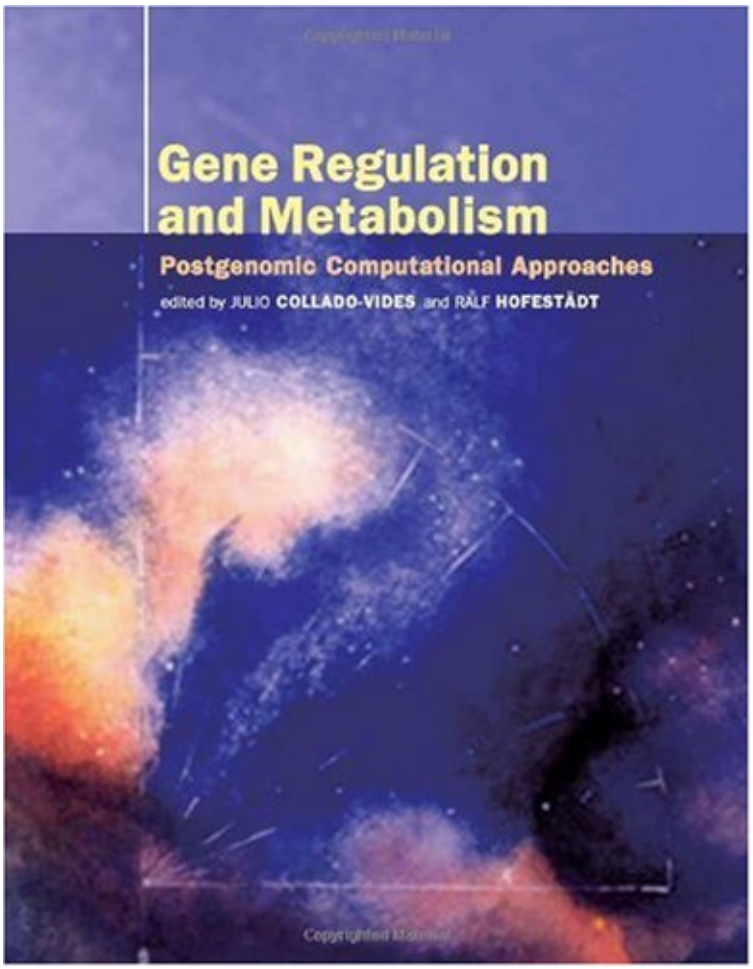

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From A Bradford Book : Gene Regulation and Metabolism: Post-Genomic Computational Approaches (Computational Molecular Biology) before purchasing it in order to gage whether or not it would be worth my time, and all praised Gene Regulation and Metabolism: Post-Genomic Computational Approaches (Computational Molecular Biology):

0 of 0 people found the following review helpful. Good overview and literature survey of modern developmentsBy Dr. Lee D. CarlsonThe determination of the genome of organisms is quite an achievement, and one that is taking place with incredible rapidity at the present time. But in order to completely understand the life processes of an organism one needs to understand how the genes are expressed and the consequent effects on the metabolism. As is pointed out

in this book, even for the bacterial organism Escherichia coli, whose genome is the most understood in the biosphere, only about six hundred promoters have been determined experimentally. If genome determination is to have practical applications to human and animal health, it will become necessary to have a much better understanding of how the metabolism of an organism is regulated by its genes. This is an enormously difficult undertaking due to the magnitude of the information involved. It is therefore no surprise that computing machines and algorithms have been used to sort through and organize this information. Whether it goes by the name of computational biology or computational genomics, the use of these machines has assisted greatly in the understanding of the life processes. This book outlines a few of the approaches that have been taken. It is directed towards experts, but it could be read by anyone who has an interest in genetic and metabolic engineering from an information-theoretic, computational perspective. The book was first published four years ago, and so it is somewhat out of date, due to the increases in CPU processing speeds and new algorithms that have been developed since then.Of particular interest is the article by Collado-Vides et al and which concerns the use of software to translate a DNA sequence into all possible proteins so as to compare them against a database of proteins that were determined by experiment. The authors discuss how this can be done for the case of E. coli and for a database called RegulonDB, which can be accessed on the Web, and which contains information on transcription initiation and operon organization in the K-12 strain of E. coli. The goal of the authors is to understand the structure of gene regulatory networks, both from a purely computational point of view and using experimentally determined transcription profiles. The article is broken down into four parts, with the first one concentrating on the prediction of gene regulatory networks using sequence information, followed by one discussing the use of Bayesian networks to assist in these predictions. The third part gives examples on how to use the database information to analyze transcription experiments and the last puts all of this analysis in the context of evolutionary origins of transcriptional regulation.The authors are very interested in the process of transcription, particularly the initiation phase. As is well known, gene transcription is catalyzed by the RNA polymerase (RNAP) proteins. In particular, the RNAP `holoenzyme' contains the `sigma factor' that guides RNAP to specific sequences on the genomic DNA (the promoter). The RNAP holoenzyme with the sigma factor thus recognizes the precise site where transcription is initiated. Having located a promoter and binding to it, the RNAP holoenzyme and the bound DNA then undergo a series of conformational changes that allow RNA synthesis to be initiated. For the case of E. coli, the study of the formation of RNAP contacts at these specific sites on the promoter DNA has been the subject of intense experimental investigation, the challenge being the measurement of the formation of these contacts in real time. In this context the author's goal is find computational schemes that will predict the promoters and other protein-binding sites. This has traditionally been done with the use of weight matrices, but as the authors point out this method (and others) results in a large number of false positives. To improve on this method, they first obtain a population of potential candidates using a low enough threshold that weaker sites can be identified. The next step is to select a collection of promoters by comparing them with all candidates within the regulatory region. The candidates are split into groups separated by the distance to the beginning of the gene, and each group contributes one best candidate. This method, the authors claim, leads to one true promoter out of six candidates on the average.The authors though do not end the analysis here, as they believe that the prediction of promoters is not reliable enough to search for sites for operator sites for specific transcriptional regulators (the information content of the promoter sites is too low). They therefore make use of a `dyad-detector' algorithm that has the ability to identify oligonucleotides up to seven bases long that are overrepresented in a given family of upstream regions. The dyad-detector can also find words with internal symmetry, such as palindromes. Also of interest to the authors is the identification of transcriptional activators and repressors that affect transcription initiation. Their goal is to identify which protein binds to which set of sites, assuming that a collection of protein-binding motifs has been identified and that the number in this collection is equal to the number of transcriptional regulators.

As exciting as the new field of genomics is, it has not yet produced a basic conceptual change in biology. The fundamental problems remain: the origin of life, cell organization, the pathways of differentiation, aging, and the molecular and cellular capabilities of the brain. What has occurred is an explosion of molecular information obtained by genomic sequences, which will soon be followed by exhaustive catalogs of protein interactions and protein function. This wealth of information can be analyzed and manipulated only with the help of computers. The rapidly expanding role of computers in biology may usher in a profound conceptual change in how we study living systems in the laboratory.This book focuses on current computational approaches to understanding the complex networks of metabolic and gene regulatory capabilities of the cell. The contributors look well beyond the state of the art in computational biology to anticipate what biological research will be like in a post-genomic world.

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