

Inferring the experimental design for accurate gene regulatory network inference

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Abstract

Motivation: Accurate inference of gene regulatory interactions is of importance for understanding the mechanisms of underlying biological processes. For gene expression data gathered from targeted perturbations, gene regulatory network (GRN) inference methods that use the perturbation design are the top performing methods. However, the connection between the perturbation design and gene expression can be obfuscated due to problems, such as experimental noise or off-target effects, limiting the methods' ability to reconstruct the true GRN.

Results: In this study, we propose an algorithm, IDEMAX, to infer the effective perturbation design from gene expression data in order to eliminate the potential risk of fitting a disconnected perturbation design to gene expression. We applied IDEMAX to synthetic data from two different data generation tools, GeneNetWeaver and GeneSPIDER, and assessed its effect on the experiment design matrix as well as the accuracy of the GRN inference, followed by application to a real dataset. The results show that our approach consistently improves the accuracy of GRN inference compared to using the intended perturbation design when much of the signal is hidden by noise, which is often the case for real data.

Availability and implementation: https://bitbucket.org/sonnhammergmi/idemax.

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Supplementary information: Supplementary data are available at Bioinformatics online.

1 Introduction

Gene regulatory interactions control many of the av trico biochemical mechanisms, and thus play a key role in most processes in living organisms. Interruptions of these mechanisms can result in several diseases including cancers (Emmert-Streib et al., 2014; Price et al., 2010; Sonawane et al., 2019). Therefore, identification of these regulatory interactions speatheads the way to understand the nature of the genetic diseases and ultimately care there. The interactions berequilatory network (GRN), and the underlying mechanism of the system can be revealed by the accurate inference of these GRNs. For this reason, GRNs can be considered as a key factor in understanding and separating the pathological mechanisms from physiological. Through this understanding, GRNs can also be used to directly propose targets for potential treatments.

Inference of GRNs can be performed from gone expression data where each gene's expression is altered by knockdown or overexpression experiments, such as via shRNAs, siRNAs or small molecules i.e. drugs. Such experiments are generally referred to as gene perturbations. There exists a variety of GRN inference methods, some of which require knowledge of the targets of the perturbations as input, and some that do not. The most popular examples of the first type, requiring known perturbations, include LASSO (Friedman et al., 2010; Tibshirani, 1996), least squares with out-off (Takesberg et al., 2013) and ridge regression (Friedman et al., 2010). Popular examples of the latter type, not needing known perturbamons, include GENIEJ (Huyeh-Thu et al., 2010), ARACNe-(Margolin et al., 2006) and Context Likelihood of Relatedness (CLR) (Faith et al., 2007). It has previously been shown that methods of the first type are able to achieve perfect GRN inference accuracy under good conditions (Turmberg et al., 2017, 2015), which is an advantage over the latter type whose performance remained limited in previous boochmarks (Gerenfield et al., 2010; Guo et al., 2016; Marbach et al., 2012; Schaffter et al., 2011). However, a

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Problems in Experimental Design and Inference Benton J. Underwood,1966 Philosophical Problems of Statistical <u>Inference</u> T. Seidenfeld, 1979-08-31 Probability and inverse inference Neyman Pearson theory Fisherian significance testing The fiducial argument one parameter The fiducial argument several parameters Ian hacking s theory Henry Kyburg s theory Relevance and experimental design **Experimental Political Science and the Study of Causality Rebecca B.** Morton, Kenneth C. Williams, 2010-08-06 Increasingly political scientists use the term experiment or experimental to describe their empirical research One of the primary reasons for doing so is the advantage of experiments in establishing causal inferences In this book Rebecca B Morton and Kenneth C Williams discuss in detail how experiments and experimental reasoning with observational data can help researchers determine causality They explore how control and random assignment mechanisms work examining both the Rubin causal model and the formal theory approaches to causality They also cover general topics in experimentation such as the history of experimentation in political science internal and external validity of experimental research types of experiments field laboratory virtual and survey and how to choose recruit and motivate subjects in experiments They investigate ethical issues in experimentation the process of securing approval from institutional review boards for human subject research and the use of deception in experimentation Error and Inference Deborah G. Mayo, Aris Spanos, 2011 Explores the nature of error and inference drawing on exchanges on experimental reasoning reliability and the objectivity of science Using Propensity Scores in Quasi-Experimental Designs William M. Holmes, 2013-06-10 Using an accessible approach perfect for social and behavioral science students requiring minimal use of matrix and vector algebra Holmes examines how propensity scores can be used to both reduce bias with different kinds of quasi experimental designs and fix or improve broken experiments This unique book covers the causal assumptions of propensity score estimates and their many uses linking these uses with analysis appropriate for different designs Thorough coverage of bias assessment propensity score estimation and estimate improvement is provided along with graphical and statistical methods for this process Applications are included for analysis of variance and covariance maximum likelihood and logistic regression two stage least squares generalized linear regression and general estimation equations The examples use public data sets that have policy and programmatic relevance across a variety of social and behavioral science disciplines

Experimental Design Roger E. Kirk,2012-06-12 This classic text with a reputuation for accessibility and readability has been revised and updated to make learning design concepts even easier Roger E Kirk shows how three simple experimental designs can be combined to form a variety of complex designs He provides diagrams illustrating how subjects are assigned to treatments and treatment combinations New terms are emphasized in boldface type there are summaries of the advantages and disadvantages of each design and real life examples show how the designs are used **Research Methodology in Plant Science** P.S. Narayana,D. Varalakshmi,T. Pullaiah,2016-11-01 The book comprises of different chapters associated

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world applications of experimental design and reliability The authors utilize R and JMP software throughout as appropriate and a supplemental website contains the related data sets Written by internationally known experts in the fields of experimental design methodology and reliability data analysis sample topics covered in the book include An introduction to reliability lifetime distributions censoring and inference for parameter of lifetime distributions Design of experiments optimal design and robust design Lifetime regression parametric regression models and the Cox Proportional Hazard Model Design strategies for reliability achievement Accelerated testing models for acceleration and design of experiments for accelerated testing The text features an accessible approach to reliability for readers with various levels of technical expertise This book is a key reference for statistical researchers reliability engineers quality engineers and professionals in applied statistics and engineering It is a comprehensive textbook for upper undergraduate and graduate level courses in statistics and engineering

Error and the Growth of Experimental Knowledge Deborah G. Mayo, 1996-07-17 We may learn from our mistakes but Deborah Mayo argues that where experimental knowledge is concerned we haven t begun to learn enough Error and the Growth of Experimental Knowledge launches a vigorous critique of the subjective Bayesian view of statistical inference and proposes Mayo s own error statistical approach as a more robust framework for the epistemology of experiment Mayo genuinely addresses the needs of researchers who work with statistical analysis and simultaneously engages the basic philosophical problems of objectivity and rationality Mayo has long argued for an account of learning from error that goes far beyond detecting logical inconsistencies In this book she presents her complete program for how we learn about the world by being shrewd inquisitors of error white gloves off Her tough practical approach will be important to philosophers historians and sociologists of science and will be welcomed by researchers in the physical biological and social sciences whose work depends upon statistical analysis The Routledge Handbook of Philosophy of Public Health Sridhar Venkatapuram, Alex Broadbent, 2022-10-07 In comparison to medicine the professional field of public health is far less familiar What is public health and perhaps as importantly what should public health be or become How do causal concepts shape the public health agenda How do study designs either promote or demote the environmental causal factors or health inequalities How is risk understood expressed and communicated Who is public health research centered on How can we develop technologies so the benefits are more fairly distributed Do people have a right to public health How should we integrate ethics into public health practice The Routledge Handbook of Philosophy of Public Health addresses these questions and more and is the first collection of its kind Comprising 26 chapters by an international and interdisciplinary team of contributors the handbook is divided into four clear parts Concepts and distinctions Reasons and actions Distribution and inequalities Rights and duties The Routledge Handbook of Philosophy of Public Health is a field defining and sustained reflection on the various ethical political methodological and conceptual aspects of global public health As such it is an essential reference source for students and scholars working in political philosophy bioethics public health ethics and the

philosophy of medicine as well as for professionals and researchers in related fields such as public health health economics and epidemiology **Complex Problem Solving** Robert J. Sternberg, Peter A. Frensch, 2014-01-14 Although complex problem solving has emerged as a field of psychology in its own right the literature is for the most part widely scattered and often so technical that it is inaccessible to non experts This unique book provides a comprehensive in depth and accessible introduction to the field of complex problem solving Chapter authors experts in their selected domains deliver systematic thought provoking analyses generally written from an information processing point of view Areas addressed include politics electronics and computers

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