



A Bayesian Semiparametric Regression Model for Joint Analysis of Microbiome Data

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The successional dynamics of microbial communities are influenced by the synergistic interactions of physical and biological factors. In our motivating data, ocean microbiome samples were collected from the Santa Cruz Municipal Wharf, Monterey Bay at multiple time points and then 16S ribosomal RNA (rRNA) sequenced. We develop a Bayesian semiparametric regression model to investigate how microbial abundance and succession change with covarying physical and biological factors including algal bloom and domoic acid concentration level using 16S rRNA sequencing data. A generalized linear regression model is built using the Laplace prior, a sparse inducing prior, to improve estimation of covariate effects on mean abundances of microbial species represented by operational taxonomic units (OTUs). A nonparametric prior model is used to facilitate borrowing strength across OTUs, across samples and across time points. It flexibly estimates baseline mean abundances of OTUs and provides the basis for improved quantification of covariate effects. The proposed method does not require prior normalization of OTU counts to adjust differences in sample total counts. Instead, the normalization and estimation of covariate effects on OTU abundance are simultaneously carried out for joint analysis of all OTUs. Using simulation studies and a real data analysis, we demonstrate improved inference compared to an existing method.

Keywords: count data, Laplace prior, metagenomics, microbiome, regularizing prior, process convolution, negative binomial model, 16S ribosomal RNA sequencing

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1. INTRODUCTION

Microbial communities are influenced by several factors whether they live in the host's guts or other occupied niches. Their successional dynamics could further change in response to perturbations of the host or of the surrounding environments (Turnbaugh et al., 2009; Needham and Fuhrman, 2016). Understanding how abiotic and biotic factors influence the dynamics of microbial communities is of great interest in the field of microbiome studies. Recent revolutionary advances in next-generation sequencing (NGS) technologies along with rapidly decreasing costs, have facilitated the accumulation of large datasets of 16S ribosomal RNA (rRNA) amplicon sequences across various disciplines such as medicine, biology, ecology, and environmental sciences (Woo et al., 2008). Sequencing data is usually pre-treated for quality filtering, noise removal and chimera checking through bioinformatics algorithms and the filtered sequences are clustered into Operational Taxonomic Units (OTUs), which represent similar organisms (microbial species) based on sequence homology (called OTU picking). An OTU abundance table is generated,

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Beom Seuk Hwang



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Joint Modeling of Longitudinal and Time-to-Event Data Robert Elashoff, Gang li, Ning Li, 2016-10-04 Longitudinal studies often incur several problems that challenge standard statistical methods for data analysis These problems include non ignorable missing data in longitudinal measurements of one or more response variables informative observation times of longitudinal data and survival analysis with intermittently measured time dependent covariates that are subject to measurement error and or substantial biological variation Joint modeling of longitudinal and time to event data has emerged as a novel approach to handle these issues Joint Modeling of Longitudinal and Time to Event Data provides a systematic introduction and review of state of the art statistical methodology in this active research field The methods are illustrated by real data examples from a wide range of clinical research topics A collection of data sets and software for practical implementation of the joint modeling methodologies are available through the book website This book serves as a reference book for scientific investigators who need to analyze longitudinal and or survival data as well as researchers developing methodology in this field It may also be used as a textbook for a graduate level course in biostatistics or statistics

Bayesian Semiparametric Joint Modeling of Longitudinal Predictors and Discrete Outcomes Woobeen Lim, 2021 Many prospective biomedical studies collect data on longitudinal variables that are predictive of a discrete outcome and oftentimes primary interest lies in the association between the outcome and the values of the longitudinal measurements at a specific time point A common problem in these longitudinal studies is inconsistency in timing of measurements and missing follow ups since few subjects have values close to the time of interest Another difficulty arises from the fact that numerous studies collect longitudinal measurements with different scales as there is no known multivariate distribution that is capable of accommodating variables of mixed scale simultaneously These challenges are well demonstrated in our motivating data example the Life and Longevity After Cancer LILAC a cohort study of cancer survivors who participated in the Women s Health Initiative WHI One research area of interest in these studies is to determine the relationship between lifestyle or health measures recorded in the WHI with treatment related outcomes measured in LILAC For instance a researcher may want to examine if sleep related factors measured prior to initial cancer treatment such as insomnia rating scale a continuous variable sleep duration ordinal and depression binary imputed at the time of cancer diagnosis can predict the incidence of adverse effects of cancer treatment Despite the multitude of such applications in biostatistical areas no previous methods exist that are able to tackle these challenges In this work we propose a new class of Bayesian joint models for a discrete outcome and longitudinal predictors of mixed scale Our model consists of two submodels 1 a longitudinal submodel which uses a latent normal random variable construction with regression splines to model time dependent trends with a Dirichlet Process prior assigned to random effects to relax distribution assumptions and 2 an outcome submodel which standardizes timing of the predictors by relating the discrete outcome to the imputed longitudinal values at a set time point We present

two outcome models that will accommodate either a binary or count outcome which will be used to model the incidence of insomnia and the number of symptoms after initial cancer treatment in LILAC respectively The proposed models will be evaluated via simulation studies to demonstrate their performance in comparison with other competing models

Joint Models for Longitudinal and Time-to-Event Data Dimitris Rizopoulos, 2012-06-22 In longitudinal studies it is often of interest to investigate how a marker that is repeatedly measured in time is associated with a time to an event of interest e.g prostate cancer studies where longitudinal PSA level measurements are collected in conjunction with the time to recurrence Joint Models for Longitudinal and Time to Event Data With Applications in R provides a full treatment of random effects joint models for longitudinal and time to event outcomes that can be utilized to analyze such data The content is primarily explanatory focusing on applications of joint modeling but sufficient mathematical details are provided to facilitate understanding of the key features of these models All illustrations put forward can be implemented in the R programming language via the freely available package JM written by the author All the R code used in the book is available at <http://jmr.r-project.org>

Applied Statistics in Biomedicine and Clinical Trials Design Zhen Chen, Aiyi Liu, Yongming Qu, Larry Tang, Naitee Ting, Yi Tsong, 2015-05-04 This volume is a unique combination of papers that cover critical topics in biostatistics from academic government and industry perspectives The 6 sections cover Bayesian methods in biomedical research Diagnostic medicine and classification Innovative Clinical Trials Design Modelling and Data Analysis Personalized Medicine and Statistical Genomics The real world applications are in clinical trials diagnostic medicine and genetics The peer reviewed contributions were solicited and selected from some 400 presentations at the annual meeting of the International Chinese Statistical Association ICSA held with the International Society for Biopharmaceutical Statistics ISBS The conference was held in Bethesda in June 2013 and the material has been subsequently edited and expanded to cover the most recent developments

The Mathematics of the Uncertain Eduardo Gil, Eva Gil, Juan Gil, María Ángeles Gil, 2018-02-28 This book is a tribute to Professor Pedro Gil who created the Department of Statistics OR and TM at the University of Oviedo and a former President of the Spanish Society of Statistics and OR SEIO In more than eighty original contributions it illustrates the extent to which Mathematics can help manage uncertainty a factor that is inherent to real life Today it goes without saying that in order to model experiments and systems and to analyze related outcomes and data it is necessary to consider formal ideas and develop scientific approaches and techniques for dealing with uncertainty Mathematics is crucial in this endeavor as this book demonstrates As Professor Pedro Gil highlighted twenty years ago there are several well known mathematical branches for this purpose including Mathematics of chance Probability and Statistics Mathematics of communication Information Theory and Mathematics of imprecision Fuzzy Sets Theory and others These branches often intertwine since different sources of uncertainty can coexist and they are not exhaustive While most of the papers presented here address the three aforementioned fields some hail from other Mathematical disciplines such as Operations Research others in turn put

the spotlight on real world studies and applications The intended audience of this book is mainly statisticians mathematicians and computer scientists but practitioners in these areas will certainly also find the book a very interesting read

Novel Approaches in Microbiome Analyses and Data Visualization Jessica Galloway-Peña,Michele Guindani,2019-02-06 High throughput sequencing technologies are widely used to study microbial ecology across species and habitats in order to understand the impacts of microbial communities on host health metabolism and the environment Due to the dynamic nature of microbial communities longitudinal microbiome analyses play an essential role in these types of investigations Key questions in microbiome studies aim at identifying specific microbial taxa enterotypes genes or metabolites associated with specific outcomes as well as potential factors that influence microbial communities However the characteristics of microbiome data such as sparsity and skewedness combined with the nature of data collection reflected often as uneven sampling or missing data make commonly employed statistical approaches to handle repeated measures in longitudinal studies inadequate Therefore many researchers have begun to investigate methods that could improve incorporating these features when studying clinical host metabolic or environmental associations with longitudinal microbiome data In addition to the inferential aspect it is also becoming apparent that visualization of high dimensional data in a way which is both intelligible and comprehensive is another difficult challenge that microbiome researchers face Visualization is crucial in both the analysis and understanding of metagenomic data Researchers must create clear graphic representations that give biological insight without being overly complicated Thus this Research Topic seeks to both review and provide novels approaches that are being developed to integrate microbiome data and complex metadata into meaningful mathematical statistical and computational models We believe this topic is fundamental to understanding the importance of microbial communities and provides a useful reference for other investigators approaching the field

Frontiers of Biostatistical Methods and Applications in Clinical Oncology Shigeyuki Matsui,John Crowley,2017-10-03 This book presents the state of the art of biostatistical methods and their applications in clinical oncology Many methodologies established today in biostatistics have been brought about through its applications to the design and analysis of oncology clinical studies This field of oncology now in the midst of evolution owing to rapid advances in biotechnologies and cancer genomics is becoming one of the most promising disease fields in the shift toward personalized medicine Modern developments of diagnosis and therapeutics of cancer have also been continuously fueled by recent progress in establishing the infrastructure for conducting more complex large scale clinical trials and observational studies The field of cancer clinical studies therefore will continue to provide many new statistical challenges that warrant further progress in the methodology and practice of biostatistics This book provides a systematic coverage of various stages of cancer clinical studies Topics from modern cancer clinical trials include phase I clinical trials for combination therapies exploratory phase II trials with multiple endpoints treatments and confirmative biomarker based phase III trials with interim monitoring and adaptation It also covers important areas of cancer screening

prognostic analysis and the analysis of large scale molecular data in the era of big data *Semiparametric Bayesian Joint Modeling with Applications in Toxicological Risk Assessment* Beom Seuk Hwang, 2013 Abstract Many dose response studies collect data on correlated outcomes For example in developmental toxicity studies uterine weight and presence of malformed pups are measured on the same dam Joint modeling can result in more efficient inferences than independent models for each outcome Most methods for joint modeling assume standard parametric response distributions However in toxicity studies it is possible that response distributions vary in location and shape with dose which may not be easily captured by standard models To address this issue we propose a semiparametric Bayesian joint model for a binary and continuous response In our model a kernel stick breaking process KSBP prior is assigned to the distribution of a random effect shared across outcomes which allows flexible changes in distribution shape with dose shared across outcomes The model also includes outcome specific fixed effects to allow different location effects Joint Longitudinal-survival-cure Model with Application in Prostate Cancer Studies Menggang Yu, 2004 *A General Joint Model for Longitudinal Measurements and Competing Risks Survival Data with Heterogenous Random Effects* Xin Huang, 2008 *Journal of the American Statistical Association*, 2009 Joint Analysis of Longitudinal Data and Competing Risks Failure Time Data Wenhua Hu, 2007 **Bayesian Nonparametric Methods for Emulation, Sensitivity Analysis, and Calibration of Computer Simulators** Marian Farah, 2011 **Joint Modelling of Time-to-event and Longitudinal Data** Yi-Kuan Tseng, 2005 *Statistica*, 2006 *Statistica Sinica*, 2004

Bayesian Statistics and Its Applications Satyanshu K. Upadhyay, Umesh Singh, Dipak Dey, 2007 In the last two decades Bayesian Statistics has acquired immense importance and has penetrated almost every area including those where the application of statistics appeared to be a remote possibility This volume provides both theoretical and practical insights into the subject with detailed up to date material on various aspects It serves two important objectives to offer a thorough background material for theoreticians and gives a variety of applications for applied statisticians and practitioners Consisting of 33 chapters it covers topics on biostatistics econometrics reliability image analysis Bayesian computation neural networks prior elicitation objective Bayesian methodologies role of randomisation in Bayesian analysis spatial data analysis nonparametrics and a lot more The book will serve as an excellent reference work for updating knowledge and for developing new methodologies in a wide variety of areas It will become an invaluable tool for statisticians and the practitioners of Bayesian paradigm **A New Class of Bayesian Semi-Parametric Joint Longitudinal-Survival Models for Biomarker Discovery** Sepehr Akhavan Masouleh, 2016 In studying the progression of a disease and to better predict time to death survival data investigators often collect repeated measures over time longitudinal data and are interested in testing the association between risk factors including collected repeated measures and time to death One such example is testing the association between the biomarker serum albumin that is measured repeatedly on end stage renal disease ESRD patients A modeling framework that is capable of modeling longitudinal and survival outcomes simultaneously is called a joint

longitudinal survival model Joint longitudinal survival models have received a great deal of attention over the past years where many different joint models have been proposed Joint models commonly make parametric assumptions on either the functional form of the repeated measures or on the distribution of survival times In this dissertation we are interested in joint models that are robust to common parametric and semi parameteric survival and longitudinal assumptions We propose a flexible Bayesian joint longitudinal survival framework that avoids common parametric and semi parameteric assumptions More specifically our modeling framework incorporates a flexible longitudinal component by utilizing Gaussian process GP technique This technique avoids any explicit functional assumption on the trajectory of the repeated measures Our modeling framework also uses Dirichlet process DP prior to avoid explicit distributional assumptions on survival times We further extend our framework to modeling multiple longitudinal processes simultaneously We propose a multivariate joint longitudinal survival technique to jointly model the association between multiple longitudinal processes with survival outcomes Our proposed technique is capable of taking correlation between longitudinal processes into account This is particularly useful when observed measures from different longitudinal processes are taken at different frequencies That means some longitudinal processes are observed less frequently compared to other longitudinal processes By jointly modeling these processes one can take the correlation between the processes into account and hence better estimate the trajectory of the processes including those less frequent ones Our proposed joint modeling frameworks use Dirichlet process techniques Therefore understanding parameter estimation in these models is vital Using synthetic longitudinal and survival data we compare parameter estimation under DPM models as opposed to commonly used parametric techniques We are particularly interested in evaluation of the performance of the model in parameter estimation when a population consists of sub populations with latent features that are different across subgroups We propose a Dirichlet process mixture survival model that is capable of detecting latent subpopulations characterized by differing baseline risks for mortality Our proposed technique is particularly useful when interest lies in estimation of the conditional effect of covariates as opposed to estimates that are marginalized across all subpopulations Throughout our work is motivated by data on patients with end stage renal disease ESRD a condition where the kidneys are no longer capable of cleaning blood sufficiently enough to sustain life In this context a modeling framework capable of finding mortality related biomarkers which are measured longitudinally over time can significantly help physicians and practitioners to lower mortality among these patients

A New Framework for Bayesian Analysis of Dose-response Studies Through Dependent Nonparametric Modeling for Categorical Responses Cassandra M. Fronczyk,2011 [Bayesian Nonparametric Analysis of Conditional Distributions and Inference for Poisson Point Processes](#) Matthew Alan Taddy,2008

Bayesian Semiparametric Methods For Joint Modeling Book Review: Unveiling the Magic of Language

In an electronic digital era where connections and knowledge reign supreme, the enchanting power of language has are more apparent than ever. Its ability to stir emotions, provoke thought, and instigate transformation is really remarkable. This extraordinary book, aptly titled "**Bayesian Semiparametric Methods For Joint Modeling**," written by a very acclaimed author, immerses readers in a captivating exploration of the significance of language and its profound impact on our existence. Throughout this critique, we will delve into the book is central themes, evaluate its unique writing style, and assess its overall influence on its readership.

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