

EFFICIENT PARTIALLY OBSERVABLE MARKOV DECISION PROCESS
BASED FORMULATION OF GENE REGULATORY NETWORK CONTROL
PROBLEM

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UTKU ERDOĞDU

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**EFFICIENT PARTIALLY OBSERVABLE MARKOV DECISION PROCESS
BASED FORMULATION OF GENE REGULATORY NETWORK
CONTROL PROBLEM**

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I hereby declare that all information in this document has been obtained and presented in accordance with academic rules and ethical conduct. I also declare that, as required by these rules and conduct, I have fully cited and referenced all material and results that are not original to this work.

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ABSTRACT

EFFICIENT PARTIALLY OBSERVABLE MARKOV DECISION PROCESS BASED FORMULATION OF GENE REGULATORY NETWORK CONTROL PROBLEM

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The need to analyze and closely study the gene related mechanisms motivated the research on the modeling and control of gene regulatory networks (GRN). Different approaches exist to model GRNs; they are mostly simulated as mathematical models that represent relationships between genes. Though it turns into a more challenging problem, we argue that partial observability would be a more natural and realistic method for handling the control of GRNs. Partial observability is a fundamental aspect of the problem; it is mostly ignored and substituted by the assumption that states of GRN are known precisely, prescribed as full observability. On the other hand, current works addressing partially observability focus on formulating algorithms for the finite horizon GRN control problem. So, in this work we explore the feasibility of realizing the problem in a partially observable setting, mainly with Partially Observable Markov Decision Processes (POMDP). We proposed a POMDP formulation for the infinite horizon version of the problem. Knowing the fact that POMDP problems suffer from the curse of dimensionality, we also proposed a POMDP solution method

that automatically decomposes the problem by isolating different unrelated parts of the problem, and then solves the reduced subproblems. We also proposed a method to enrich gene expression data sets given as input to POMDP control task, because in available data sets there are thousands of genes but only tens or rarely hundreds of samples. The method is based on the idea of generating more than one model using the available data sets, and then sampling data from each of the models and finally filtering the generated samples with the help of metrics that measure compatibility, diversity and coverage of the newly generated samples.

Keywords: Gene Regulatory Networks, Partially Observable Markov Decision Process, Control of GRN, Gene Expression Data, Data Enrichment

ÖZ

GEN AĞLARININ KISMİ GÖZLEMLENEBİLİR MARKOV SÜREÇLERİ İLE MODELLENEREK ETKİN OLARAK KONTROLÜ

Erdoğan, Utku

Doktora, Bilgisayar Mühendisliği Bölümü

Tez Yöneticisi : Prof. Dr. Faruk Polat

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Nisan 2012 , 6 sayfa

Genlerin çalışma prensiplerini inceleme gereksinimi gen düzenleyici ağların (GDA) modellenmesi ve kontrolü üzerine bilimsel çalışmalar yapılmasına yol açmıştır. GDA'ları modellemek için değişik yaklaşımlar mevcuttur ve bu yaklaşımların çoğu genler arasındaki ilişkileri matematiksel modeller vasıtasıyla modellemektedir. Problemi daha zorlaştırmasına rağmen, GDA kontrol problemlerinin daha doğal ve gerçekçi çözülebilmesi için kısmi gözlemlenebilirliğin önerilmesi gerektiğini savunuyoruz. Kısmi gözlemlenebilirlik bu problemin temel bir bileşeni olmasına rağmen çoğunlukla gözardı edilmiş ve problemin çözümünde GDA'nın tüm durumlarının mükemmel olarak bilinebileceği varsayımı yapılmıştır, yani problem tam gözlemlenebilir kabul edilmiştir. Bir yandan da literatürdeki kısmi gözlemlenebilirliği dikkate alan yöntemler sınırlı adımdan oluşan bir problem tanımı ile GDA kontrol problemini çözen algoritmalar üretmeye çalışmaktadır. Bu çalışmada problemin kısmi gözlemlenebilir bir kurgu ile tanımlanması üzerinde çalışılmakta ve Kısmi Gözlemlenebilir Markov Karar Süreçleri (POMDP) bu kurguda kullanılmaktadır. Bu çalışmada problemin sonsuz adımdan oluşan bir hali problem

POMDP modeline uygun bir şekilde tanımlanarak sunulmaktadır. POMDP problemlerinin boyutlardan kaynaklanan problemler yaşamasından dolayı POMDP problemlerin birbirinden bağımsız parçalarını ayırıp problemi otomatik olarak parçalayan ve bu parçaları çözerek problemin çözümünü bulan bir çözüm yaklaşımı da bu çalışmada sunulmuştur. Bu çalışmada ayrıca POMDP kontrol problemine girdi olarak verilen gen ifade verisini zenginleştirmek için de bir metot sunulmaktadır. Gen ifade verilerinde binlerce gen olmasına rağmen genelde onlarca, nadir olarak da yüz mertebesinde örneklem bulunduğundan böyle bir metot gerekli ve faydalıdır. Sunulan metot varolan veri kümesini kullanarak birden fazla model oluşturur; her modelden yeni veri noktaları üretikten sonra üretilen veri noktalarını veri kümesinin uygunluğunu, farklılığını ve genişliğini ölçen metrikler yardımıyla filtreyerek kullanıma hazır bir veri kümesi oluşturur.

Anahtar Kelimeler: Gen Düzenleyici Ağlar, Kısmi Gözlemlenebilir Markov Karar Süreçleri, GDA'ların Kontrolü, Gen İfade Verisi, Veri Zenginleştirme

To my grandparents

Hatice Oruç, İbrahim Oruç, Necibe Erdoğan, Şehmus Erdoğan

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TABLE OF CONTENTS

ABSTRACT	iv
ÖZ	vi
ACKNOWLEDGMENTS	ix
TABLE OF CONTENTS	xi
LIST OF TABLES	xii
LIST OF FIGURES	xiii
LIST OF ABBREVIATIONS	xiv
CHAPTERS	
1 INTRODUCTION	1
2 NEXT ONE	2
REFERENCES	3
APPENDICES	
A PROOF OF SOME THEOREM	4
CURRICULUM VITAE	5

LIST OF TABLES

TABLES

LIST OF FIGURES

FIGURES

LIST OF ABBREVIATIONS

A	An abbreviation
AA	Another abbreviation
LONGESTABBRV	Longest Abbreviation is used to balance the columns of list of abbreviations

CHAPTER 1

INTRODUCTION

This is the introductory chapter.

CHAPTER 2

NEXT ONE

This is another chapter. All these chapters can go into seperate .tex files and you can include them with `\input{chapter1.tex}`. This is a citation [1].

REFERENCES

- [1] U. Erdoğan. Sample reference article. *METU Thesis Journal*, 2(2):1–2, 2012.

APPENDIX A

PROOF OF SOME THEOREM

This is appendix text.

CURRICULUM VITAE

PERSONAL INFORMATION

Surname, Name: Surname, Name

Nationality: Turkish (TC)

Date and Place of Birth: Birthday, Birthplace

Marital Status: Marital Status

Phone: Phone Number

Fax: Fax Number

EDUCATION

Degree	Institution	Year of Graduation
M.S.	M.S. Institute	M.S. Year
B.S.	B.S. Institute	B.S. Year
High School	High School Name	High School Graduating Year

PROFESSIONAL EXPERIENCE

Year	Place	Enrollment
Duration 1	Institute/Company 1	Role/Position/Experience 1
Duration 2	Institute/Company 2	Role/Position/Experience 2

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