## Contents

1 **Introduction** 1  
   1.1 Background and Motivation 1  
   1.1.1 HIV Epidemic 3  
   1.1.2 HIV Dynamics 4  
   1.2 Modeling HIV Dynamics 5  
   1.2.1 Phylogenetic Analysis 6  
   1.2.2 Agent-based Models 7  
   1.2.3 Complex Network Models 7  
   1.3 Thesis Overview 9  

2 **Modeling HIV-1 Intracellular Replication** 11  
   2.1 Introduction 12  
   2.2 Modeling HIV-1 intracellular replication 13  
   2.2.1 Cell infection 14  
   2.2.2 Cell states and transitions 16  
   2.3 Model Implementation: Two different approaches 17  
   2.3.1 Stochastic Rate-Based Approach 17  
   2.3.2 Stochastic diffusion-based Approach 22  
   2.4 Simulation Results 26  
   2.5 Conclusions 29
3 Combining Epidemiological and Genetic Networks Signifies the Importance of Early Treatment in HIV-1 Transmission 33
3.1 Introduction ................................................. 34
3.2 Results ..................................................... 36
  3.2.1 Characteristics of the study population ............. 36
  3.2.2 Filter-reduction method and network construction 37
  3.2.3 Analyzing characteristics of the contact network 38
  3.2.4 Constructing the hypothetical transmission net-
       works .................................................... 47
  3.2.5 Transmission network and phylogenetic clusters 53
  3.2.6 Factors associated with super-spreaders .......... 53
  3.2.7 Comparison with random networks ................. 56
3.3 Discussion ................................................ 57
3.4 Materials and Methods .................................... 59
  3.4.1 The Data ............................................. 60
  3.4.2 Phylogenetic analysis ................................ 61
  3.4.3 Filtering process in the filter-reduction method .. 63
  3.4.4 Network visualization ............................... 64
3.A Appendix Chapter 3 ....................................... 65
  3.A.1 Tables ................................................. 65
  3.A.2 Figures ................................................ 67

4 Combining Social and Genetic Networks to Study HIV trans-
mission in Mixed Risk Groups 73
4.1 Introduction ................................................ 74
4.2 Combining Social and Genetic Networks ............... 75
  4.2.1 Filter-Reduction Method ............................ 76
  4.2.2 Overlaying Networks ................................ 80
4.3 Transmission Between Risk Groups ..................... 82
4.4 Conclusions and Future Directions ..................... 86

5 Complex Agent Networks: An Emerging approach for Mod-
eling Complex Systems 89
5.1 Introduction ............................................... 90
5.2 Formal definition of CANs ............................... 94
  5.2.1 The agent node model ............................. 95
  5.2.2 Networks of agent interactions ................... 98