Contents

1 Introduction ................................................................. 1
  1.1 Historical Background of HIV/AIDS ................................. 1
  1.2 Global Scenario of HIV Pandemic ..................................... 2
  1.3 Disease Transmission ................................................. 3
  1.4 Drug Therapy Used in HIV/AIDS Treatment ......................... 6
  1.5 Aims of the Book ..................................................... 9
  1.6 Organization of the Book ............................................. 10
References ........................................................................... 11

Part I Dynamics of Immune System Against HIV

2 Role of CTL in Restricting Virus ........................................ 19
  2.1 Suppression of CTL Responses ........................................ 19
    2.1.1 Equilibria ....................................................... 20
    2.1.2 Existence Condition ............................................ 20
    2.1.3 Stability Analysis .............................................. 21
    2.1.4 Numerical Simulation and Discussion ......................... 22
  2.2 Reduction of HIV Infection with Cure Rate ......................... 24
    2.2.1 Equilibria and Local Stability ................................ 24
    2.2.2 Boundedness and Permanence of the System ................. 26
    2.2.3 Global Stability of the System ............................... 27
    2.2.4 Discussion .................................................... 27
  2.3 Antiviral Drug Treatment along with IL-2 .......................... 28
    2.3.1 Existence Condition and Stability Analysis ................. 29
    2.3.2 Numerical Simulation with Discussion ....................... 30
  2.4 IL-2 based Immune Therapy on T Cell .............................. 32
    2.4.1 General Analysis of the Mathematical Model ............... 33
    2.4.2 Discussion .................................................... 35
  2.5 Saturation Effects for CTL-Mediated Control ...................... 35
    2.5.1 Theoretical Study of the System ............................. 35
    2.5.2 Existence Condition and Biological Interpretation ........ 36
2.5.3 Stability Analysis ............................................. 36
2.5.4 Numerical Simulation ........................................ 38
2.5.5 Discussion .................................................. 38
2.6 Impact for Antigenic Stimulation on T Cell Homeostasis ....... 39
  2.6.1 Equilibrium Points and their Stability Analysis ............ 40
  2.6.2 Numerical Illustration and Discussion ....................... 40
References .......................................................... 42

3 T Cell Proliferation ................................................. 43
  3.1 CTL Activity through HIV Infection .......................... 43
    3.1.1 Formulation of HIV Model ................................. 43
    3.1.2 Equilibria and Local Stability ............................. 44
    3.1.3 Boundedness and Permanence of the System ............... 46
    3.1.4 Global Stability of System ............................... 47
    3.1.5 Numerical Analysis and Discussion ......................... 47
  3.2 Effect of HAART on CTL-Mediated Immune Cells ............... 49
    3.2.1 Equilibria ............................................... 50
    3.2.2 Stability Analysis ....................................... 50
    3.2.3 Numerical Solutions of the Model Equations ............... 53
  3.3 CTL-Mediated Control of HIV Infection ....................... 53
    3.3.1 Theoretical Study of the System .......................... 54
    3.3.2 Numerical Simulation ..................................... 56
References .......................................................... 58

4 Feedback Effect towards HIV Infection ........................... 59
  4.1 Immune Cell Response to Negative Feedback Effect in HIV .... 59
    4.1.1 Theoretical Analysis ..................................... 60
    4.1.2 Stability of the System ................................... 61
    4.1.3 Numerical Analysis ....................................... 62
    4.1.4 Discussion ............................................... 64
  4.2 Negative Feedback Effect in HIV Progression .................. 65
    4.2.1 Steady-State Analysis .................................... 66
    4.2.2 Numerical Analysis ....................................... 67
References .......................................................... 69

Part II Control-Based Therapeutic Approach

5 Insight of Delay Dynamics ........................................ 79
  5.1 Delay Effect during Long-Term HIV Infection .................. 79
    5.1.1 Local Stability Analysis ................................... 81
    5.1.2 Sufficient Conditions for Delay-Induced Instability ........ 82
    5.1.3 Stability, Instability, and Bifurcation Results ........... 83
    5.1.4 Numerical Simulations: Results and Discussions ............ 86
    5.1.5 Delay in Different Variants ................................ 89
5.2 Delay-Induced System in Presence of Cure Rate ......................... 91
  5.2.1 Analysis ................................................. 91
  5.2.2 Numerical Simulation ..................................... 94
5.3 Delay Effect during Early Stage of Infection ................................. 95
  5.3.1 General Mathematical Model ................................ 96
  5.3.2 Numerical Simulation ...................................... 100
5.4 Effect of Delay in Presence of Positive Feedback Control............... 102
  5.4.1 Numerical Analysis of the Delayed System .................... 106
5.5 Effect of Delay during Combination of Drug Therapy ...................... 107
  5.5.1 Stability Analysis of the Delay-Induced System ............... 108
5.6 Delay-Induced System in Presence of Saturation Effect .................. 113
References .............................................................. 117
6 Optimal Control Theory ................................................... 119
  6.1 Optimal Control Theoretic Approach of the Implicit Model ............. 119
    6.1.1 Numerical Simulation of the Implicit Model ................ 122
  6.2 The Optimal Control Problem on Chemotherapy for (3.15) ............ 125
    6.2.1 Existence Condition of an Optimal Control ................ 126
    6.2.2 Characterization of an Optimal Control .................... 126
    6.2.3 Numerical Solutions of the Model Equations ................. 128
  6.3 The Optimal Control Problem for the System (4.1) ..................... 131
    6.3.1 Numerical Analysis ..................................... 134
  6.4 The Optimal Control Problem of the System (4.5) ..................... 134
    6.4.1 Numerical Analysis ..................................... 137
  6.5 Optimization of the System (3.22) ................................ 138
    6.5.1 Numerical Simulation .................................... 140
  6.6 The Optimal Control Problem (2.11) ................................ 140
    6.6.1 Discussion ........................................... 144
  6.7 Optimal Control Strategy ........................................ 144
    6.7.1 Numerical Experiment of Optimal Control Strategy ............ 147
  6.8 The Optimal Control Problem in case of Recovery of Infected
      Cells in HIV Model ........................................... 148
    6.8.1 Numerical Simulation and Discussion ....................... 151
References .............................................................. 152
7 Perfect Drug Adherence .................................................... 155
  7.1 Drug Therapy with Perfect Adherence in Explicit Form ................. 155
    7.1.1 Analysis of the Model .................................. 156
    7.1.2 Dynamics of the Drug ................................... 157
    7.1.3 Numerical Simulation of the Explicit Model ............... 160
  7.2 Enfuviritide-IL-2 Administration for HIV-1 Treatment ................ 162
    7.2.1 Combining T Cell Population with Virus and Drugs .......... 162
    7.2.2 Analysis of the Model ................................... 163
    7.2.3 Dynamics of the Drug ................................... 164
    7.2.4 Numerical Simulation .................................... 166
7.3 Effect of Chemokine Analog through Perfect Adherence
    7.3.1 Analysis of the Model
    7.3.2 Drug Dynamics
    7.3.3 Cell Count in Extreme Cases
    7.3.4 Numerical Simulation

References

8 Mathematical Models in Stochastic Approach
    8.1 Impact for Antigenic Stimulation on T Cell Homeostasis
        8.1.1 Formulation of the Kolmogorov’s Forward Equation
        8.1.2 Finding the Time to Extinction of Infected Cells
        8.1.3 The Distribution of the Time to Extinction
        8.1.4 Diffusion Approximation
        8.1.5 Numerical Illustration
        8.1.6 Discussion
    8.2 Expected Time to Extinction of the Disease
        8.2.1 Stochastic Version of the Model
        8.2.2 The Stochastic Model Formulation
        8.2.3 Description of the Transition States
        8.2.4 Diffusion Approximation
        8.2.5 Expected Time to Extinction
        8.2.6 Numerical Simulation
        8.2.7 Discussion
    8.3 Insight of T Cell Proliferation in the Expected Time
        to Extinction
        8.3.1 The Deterministic Model
        8.3.2 The Stochastic Model Formulation
        8.3.3 Description of the Transition States
        8.3.4 Kolmogorov’s Forward Equation
        8.3.5 Time to Extinction of Infected T Cells
        8.3.6 The Distribution of the Time to Extinction
        8.3.7 Diffusion Approximation
        8.3.8 The Expected Time to Extinction
        8.3.9 Numerical Illustration
        8.3.10 Discussion and Conclusion

References
Mathematical Models for Therapeutic Approaches to Control HIV Disease Transmission
Roy, P.K.
2015, XIX, 213 p. 67 illus., 4 illus. in color., Hardcover