

Title: “Mathematical Modelling to Control Psoriatic Inflammation Introducing Stem Cell Therapy”

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Abstract

Stem cell therapy is gaining attention in autoimmune disease treatment and is emerging as a promising field of regenerative medicine. Psoriasis, a chronic autoimmune skin disorder, remains a major challenge due to its complex immune pathways and multifactorial nature. Existing therapies often provide only temporary relief, with relapse occurring after discontinuation, and complete remission is rarely achieved. This thesis studies the progression and control of psoriasis from mathematical points of view through modelling. The aim is to understand the underlying biological mechanisms and to evaluate the effects of control strategies, mainly biologic drugs and stem cell-based therapies. Special focus is given to stem cell therapy as a possible future alternative where conventional approaches fail. Each chapter combines theoretical analysis with numerical simulations to maintain biological relevance and clinical applicability. Methods such as optimal control theory and impulsive differential equations are applied to design and evaluate different control interventions. The overall goal is to provide a mathematical framework that may guide the development of more effective treatment strategies for psoriasis in the future.

Chapter wise Contributions

- **Chapter 2** provides a nonlinear ODE-based model including Th_1 , Th_{17} cells, keratinocytes, and mesenchymal stem cells (MSCs). The effects of pulsed MSC transplantation are studied, showing their potential in immune modulation.
- **Chapter 3** introduces simplified mathematical model with T cells, dendritic cells, keratinocytes, and MSCs. The role of anti-TNF- α biologics is examined introducing optimal control. Further, pulsed MSC therapy is introduced as an adjunct in resistant cases, demonstrating the combined therapeutic benefits of the biologic TNF- α inhibitor and MSCs.
- **Chapter 4** extends the model of Chapter 3 to fractional-order systems to include the memory effects. Three operators, namely Caputo, Caputo-Fabrizio, and Atangana-Baleanu-Caputo operators, are used for the fractional-order models. Theoretical analysis is carried out for the ABC operator with a non-singular Mittag-Leffler kernel, and biologic control strategies are tested using the Forward-Backward Sweep Method with respect to all considered fractional operators.
- **Chapter 5** incorporates two intracellular time delays in T cell-dendritic cell interactions. Hopf bifurcation analysis is carried out, and a dual-biologic strategy (TNF- α and IL-17 inhibitors) is proposed to regulate oscillatory disease behavior, highlighting the role of delayed immune signaling.
- **Chapter 6** provides a model with stem cell maturation stages and uses impulsive differential equations to study the effect of stem cell administrations. The results show that periodic impulses, given at proper intervals, can control T cell and keratinocyte over-activity effectively.
- **Chapter 7** integrates five key cytokines with T cells, dendritic cells, keratinocytes, and stem cells with differentiation lineages. Quasi-steady-state approximations simplify cytokine interactions. Hopf bifurcation analysis and numerical simulations confirm that impulsive stem cell therapy can restore cytokine balance and control keratinocyte overgrowth.
- **Chapter 8** outlines future directions of research and presents a model as part of ongoing work.



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