

**Mathematical Methods and Models in Biosciences**

June 15–20, 2025, Sofia, Bulgaria

<https://biomath.math.bas.bg/biomath/index.php/bmcs>

## Optimal breast cancer hormone therapy strategy under uncertainty in clients behavior: A $H_2 - H_\infty$ robust control approach

V. Kumar Murty, Mortaza Baky Haskuee

Department of Mathematics,  
University of Toronto, Canada  
[murty@math.toronto.edu](mailto:murty@math.toronto.edu)  
[m.baky@utoronto.ca](mailto:m.baky@utoronto.ca)

Many cancers require extended, multi-stage treatments which may span several years. Hormonal therapies, such as tamoxifen, are prescribed for 5-10 years. Effective cancer treatment must balance tumor reduction against the preservation of healthy cells, while patient adherence and variable responses to treatment and drug regimens introduce significant uncertainties. Cancer treatment is a multi-player framework in which the efficacy requires cooperation between physicians and patients. Patient adherence is critical for treatment success, reducing recurrence, and improving survival. Evidence from scientific research highlights the challenges and importance of adherence in specific cancer types. Studies show that non-adherence to hormonal therapy significantly increased the risk of recurrence and mortality in breast cancer patients.

This paper proposes a robust control framework that integrates  $H_2 - H_\infty$  optimal control and non-cooperative differential games (NCDG) to develop adaptive, patient-centered treatment strategies. By modeling tumor and healthy cell populations within a nonlinear stochastic system and using a control input for hormone therapy and external disturbance to capture patient-specific adherence uncertainty, one can derive a feedback law that minimizes worst-case treatment impacts. While  $H_2$  performance index evaluates the transition behavior of the system,  $H_\infty$  performance index can measure the robustness of system against the external uncertainties.

*Keywords: breast cancer, hormonal therapy, robust control, optimal strategies*

*MSC2020: 93A16, 91A16, 34A34, 92B10*

### References

- [1] D. H. Moore II, M. L. Mendelsohn, Optimal treatment levels in cancer therapy, *Cancer*, 30:97–106, 1972.
- [2] U. Ledzewicz, H. Schättler, A. Friedman, E. Kashdan, *Mathematical Methods and Models in Biomedicine*, Springer Science & Business Media, 2012.