Mathematical Modeling of Personalized Androgen Ablation Therapy for Advanced Metastatic Prostate Cancer

Model Aims and Scope

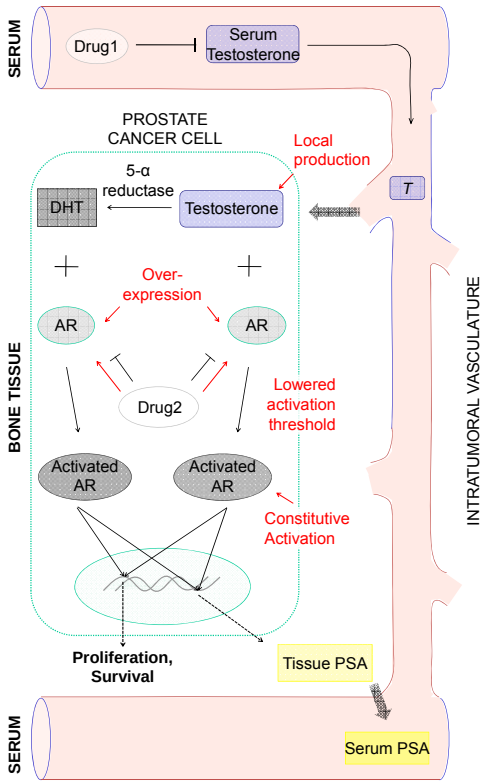
A biochemically motivated model of prostate cancer progression is developed, to conduct a *postscriptive* analysis of available patient data, for testing the impact of **Intermittent** versus **Continuous Androgen Ablation** therapy on the emergence of castrate resistance.

Model predictions are based on fits to Prostate Specific Antigen (PSA) time course data in response to treatment already provided. This results in the identification of new potential biomarkers of disease significance, namely:
(i) PSA Velocity; (ii) Cancer cell growth rates; (iii) Cancer cell PSA expression

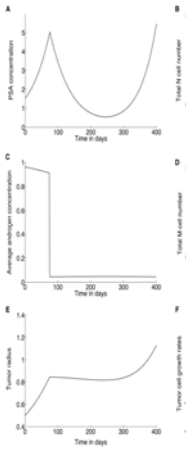
Key Predictions

- If castration-resistant cancer cells are **androgen-independent** (positive growth rate irrespective of androgen ablation), both continuous and intermittent therapy will eventually fail.
- Ignoring side-effects, Continuous therapy is preferable to (any) intermittent schedule in general. Intermittent therapy induces earlier onset of castration-resistance.
- Intermittent therapy outperforms continuous scheduling if androgen-independent cells are out competed by androgen-dependent cells.
- If castration-resistant cells are **androgen-repressed** (negative growth rate in the presence of androgens), intermittent scheduling may delay or prevent the onset of castration-resistance.
- In this case, intermittent scheduling with fixed times on/off androgen ablation outperforms scheduling based on target PSA levels.

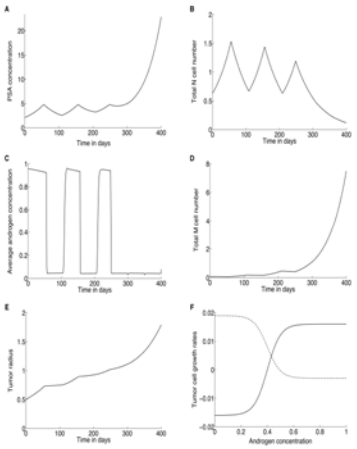
Model Schematic



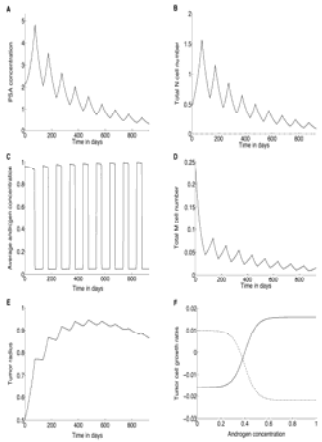
Continuous Therapy



Intermittent Therapy, schedule 1



Intermittent Therapy, schedule 2



Intermittent Schedule 1: Therapy switched 'on' if PSA rises above a predetermined threshold, and is then administered for a preset period of time.

Intermittent Schedule 2: The times therapy is 'on' and 'off' are fixed, with their ratio determined by cancer cell proliferation and death rates.

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