Industrial Mathematics: One Canadian Perspective (Part 3)

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Canada-China Workshop in Industrial Math,
BIRS, August 2007

Range of Projects with industrial collaborators

- Property & Casualty Insurance Compensation Corporation (started 2006, ongoing)
- **Princess Margaret Hospital (started 2005, ongoing)**
- Department of National Defence (Navy) (started 2005, ongoing)
- Environment Canada (started 2007, ongoing)
- IBM Toronto software Lab (started 2004, ongoing)
- Bank of Canada (started 2006, ongoing)
- Ontario Power Generation (2000-2002)
- Dydex Ltd (2003)
- Canadian Energy Wholesalers Inc (Jan-Feb 2007)
- Waterloo Maple Inc (2006)

Moving away from Money

- Radiation Physics

H Keller, M Couillard, MD, D Moseley, and D Jaffray (2005), “Novel Geometric and Dosimetric On-Line Correction Strategies: Can Chance Work in Your Favor?” *Medical Physics* **32**(6),1892- 1893

H Keller & MD (2007). “Optimal Dose-Per-Fraction Schedules for Simple Drug Radiosensization Schedules”, *Proceedings of International Conference on Computers in Radiotherapy 2007*.

Introduction

- Radiation Therapies of the future will be guided and adaptive through the use of anatomical, functional and molecular imaging.
- Adaptation today: managing changes of geometry. Adaptation tomorrow: managing changes of biology?
- Investigate fractionation schedules for altered repair capability of tumor.

Medical Research

Static LQ Model

- Slow proliferation, no explicit time dependency
- Surviving fraction of tumor cells:

$$SF_T(d_1, d_2, \ldots, d_N) = \exp\left[-\sum_{j=1}^{N}\left(\alpha^T d_j + \beta^T d_j^2\right)\right]$$

- Surviving fraction of sensitive structure cells:

$$SF_S(d_1, d_2, \ldots, d_N) = \exp\left[-\sum_{j=1}^{N}\left(\alpha^S \omega d_j + \beta^S \omega^2 d_j^2\right)\right]$$

- "sparing factor" $\omega = \dfrac{\text{Dose to sensitive structure}}{\text{Dose to tumor}}$

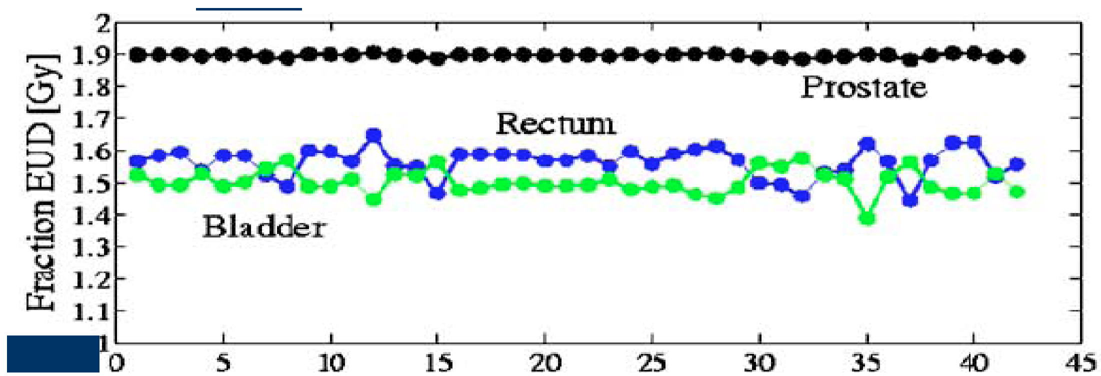
Optimization Problem

- Maximize cell kill: $$\max_{\{d_1, d_2, \ldots, d_N\}} \sum_{j=1}^{N} \left(\alpha_j^T d_j + \beta_j^T d_j^2 \right)$$
- Subject to: $$\sum_{j=1}^{N} \left(\alpha^S \omega d_j + \beta^S \omega^2 d_j^2 \right) = \Omega$$
- Dynamic Programming

Medical Research

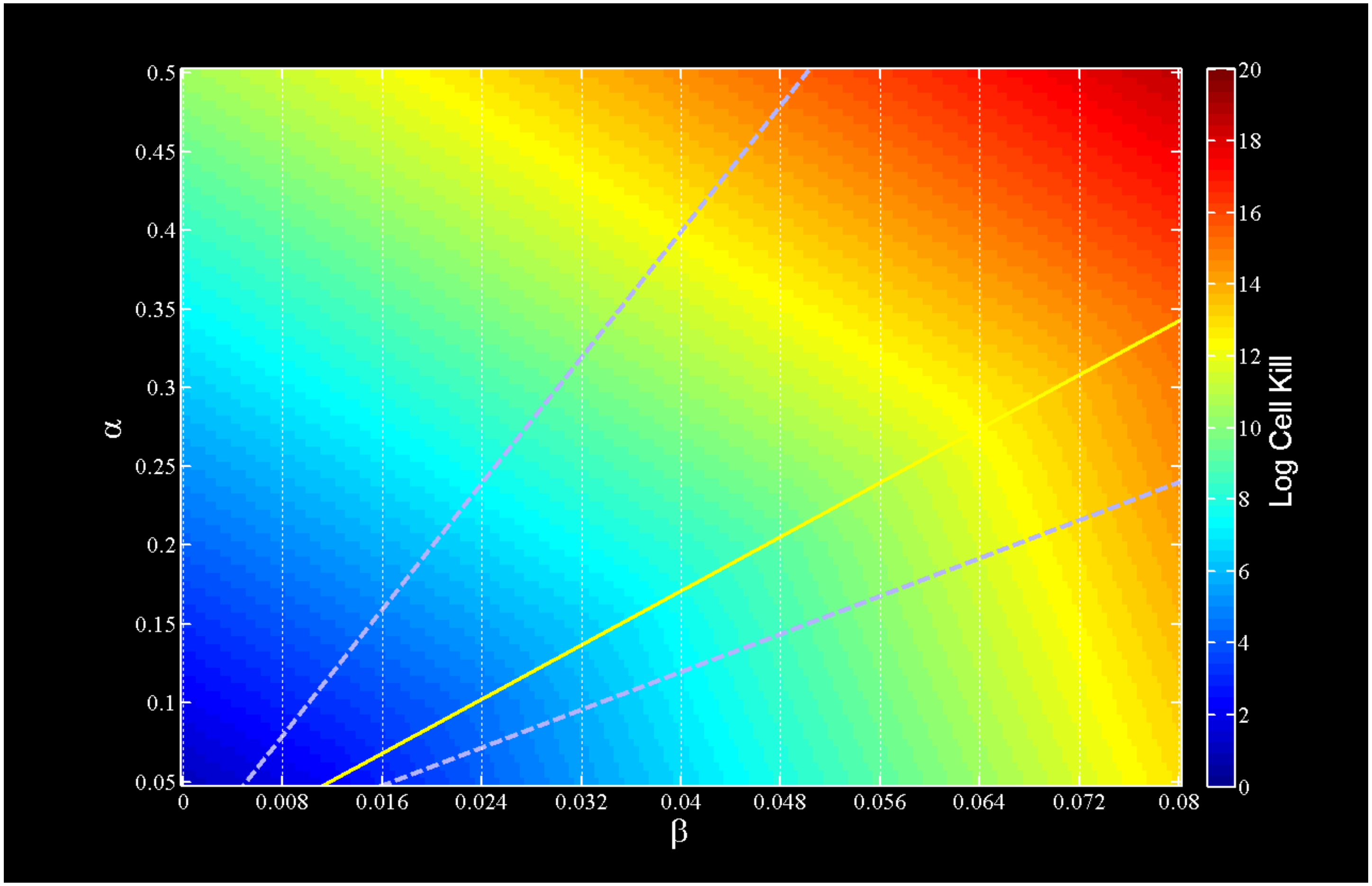
Sparing Factor ω

- For a typical prostate patient: ω = 0.7-0.8.

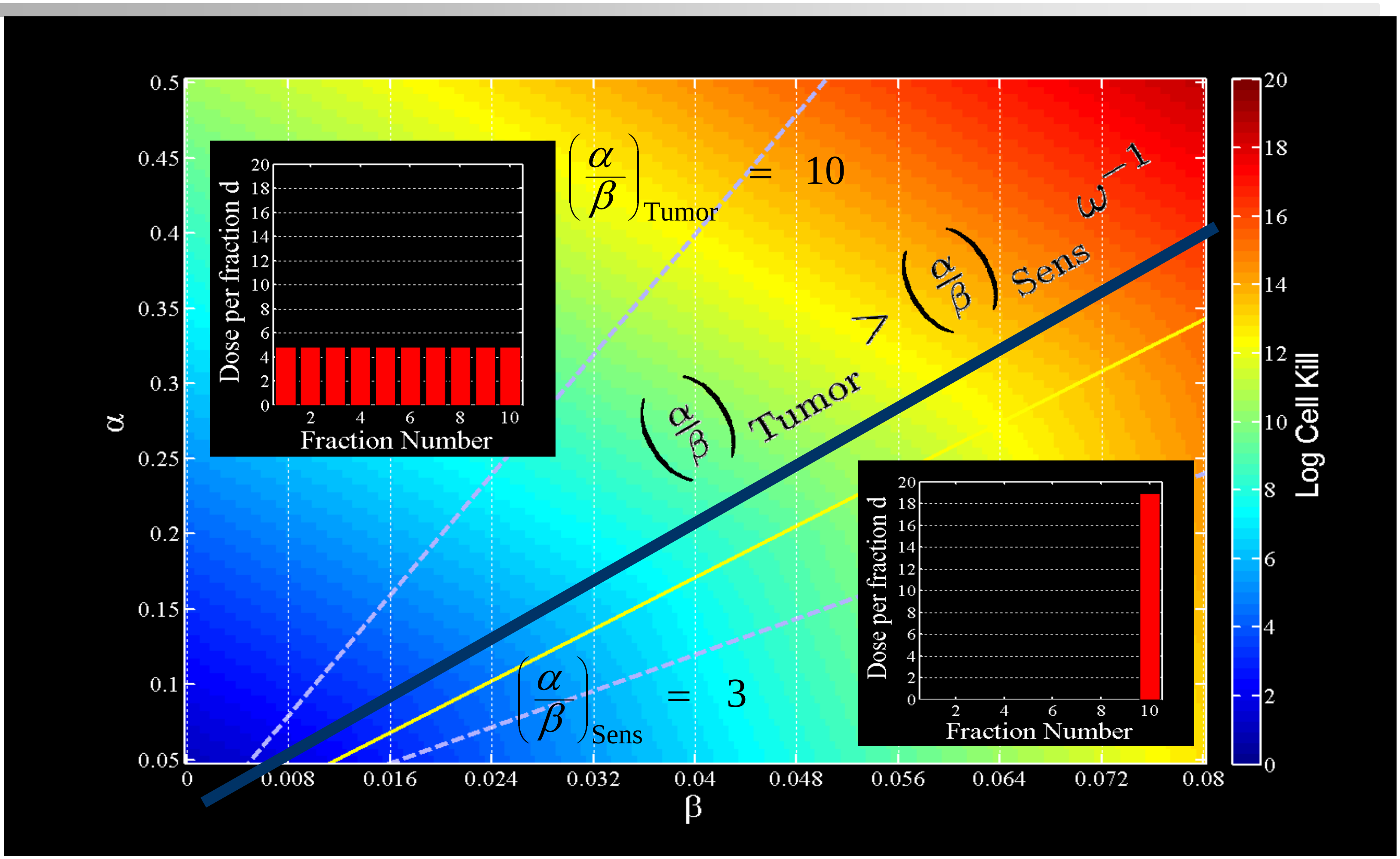


[Keller, Med. Phys., 2006]

Static LQ model: 10 fractions



Static LQ model: 10 fractions



Dynamic LQ model

$$SF_T(d_1, d_2, ..., d_N) = \exp\left[-\sum_{j=1}^{N}\left(\alpha^T(t)d_j + \beta^T(t)d_j^2\right)\right]$$

Drug

Action of the drug

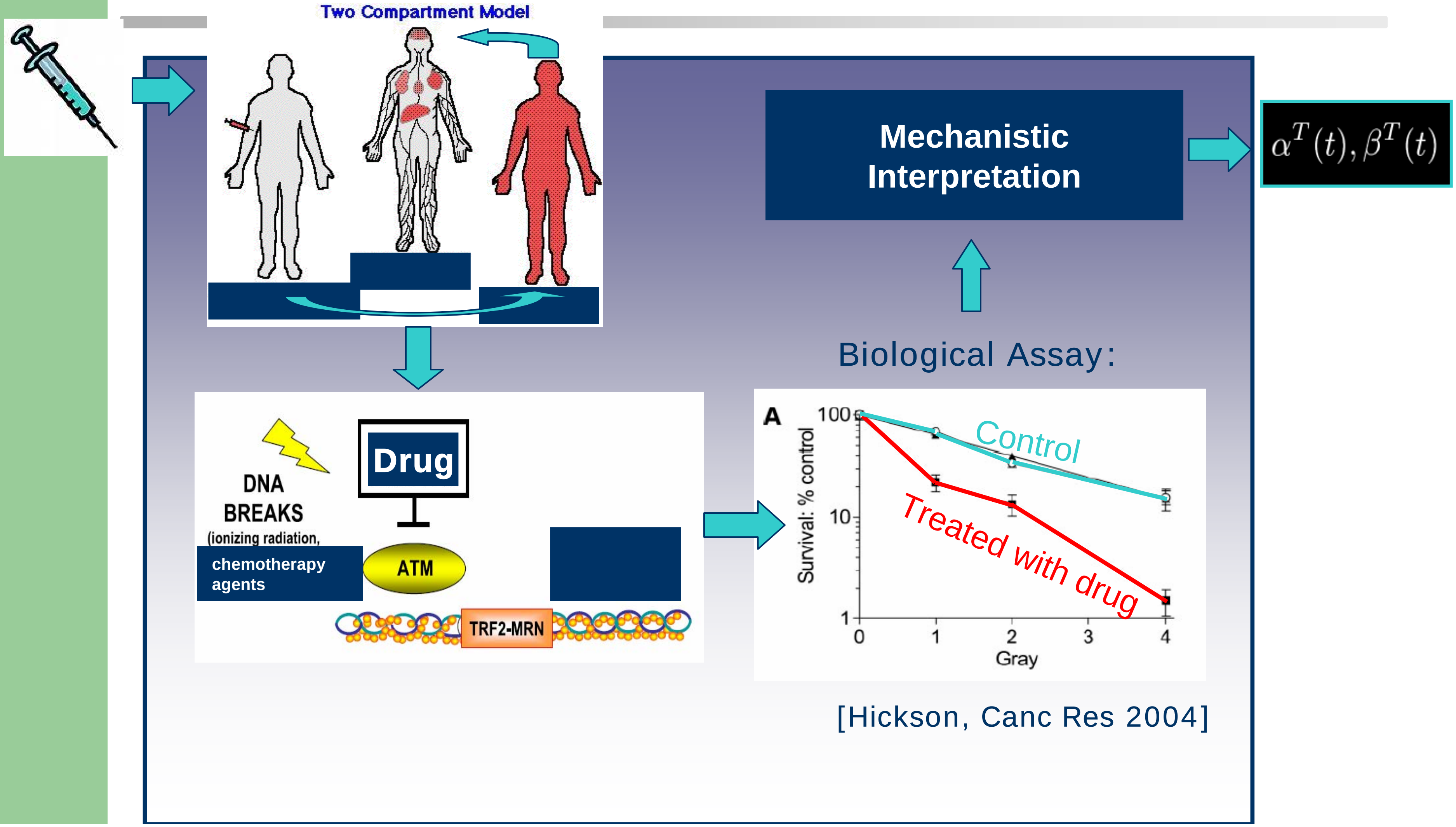
$\alpha^T(t), \beta^T(t)$

Hypoxia

Some other mechanism

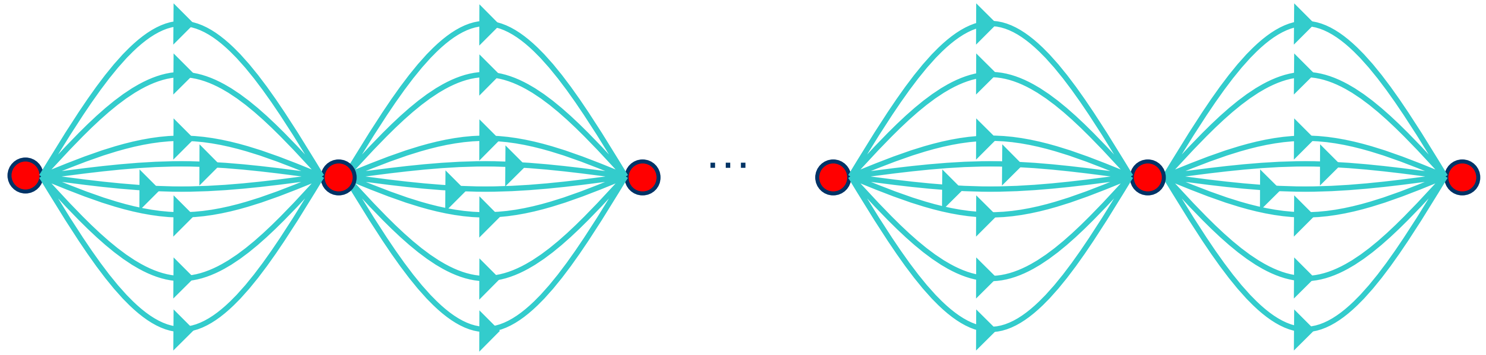
$\alpha^T(t), \beta^T(t)$

Dynamic LQ model



Dynamic Programming

- Ideal for solving multistage optimization problems

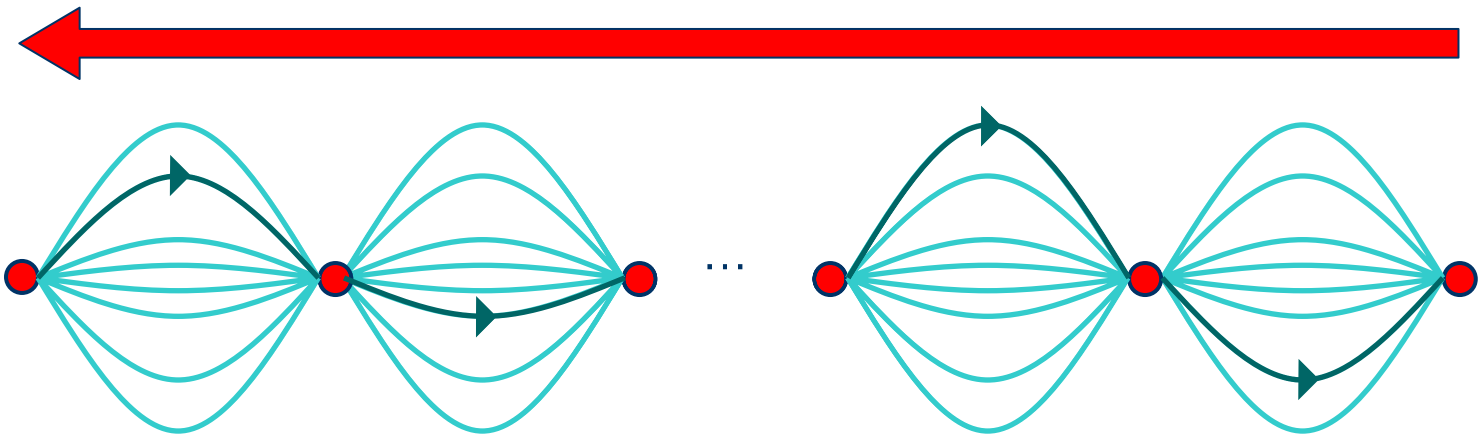


Fraction 1 2 ... N-1 N

Dynamic Programming

Principle of Optimality:

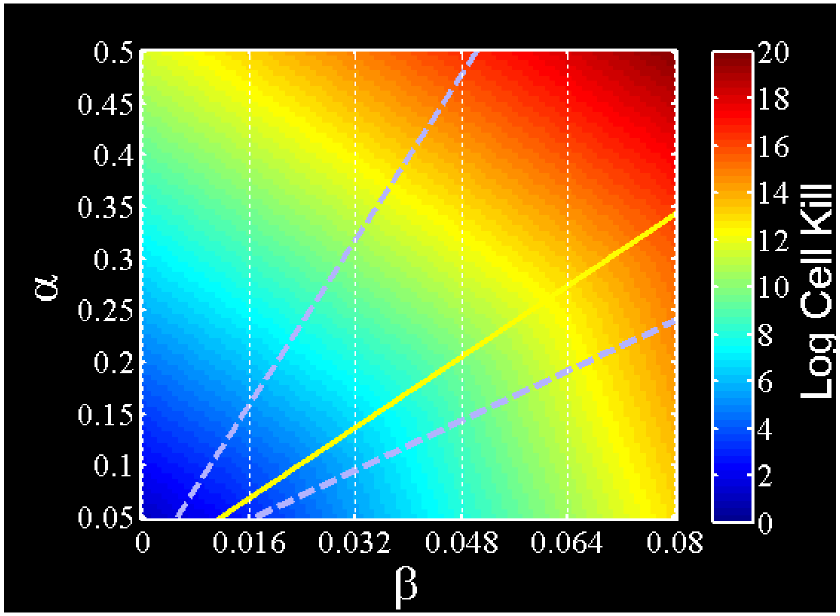
"The tail portion of an optimal solution is optimal for the tail problem."



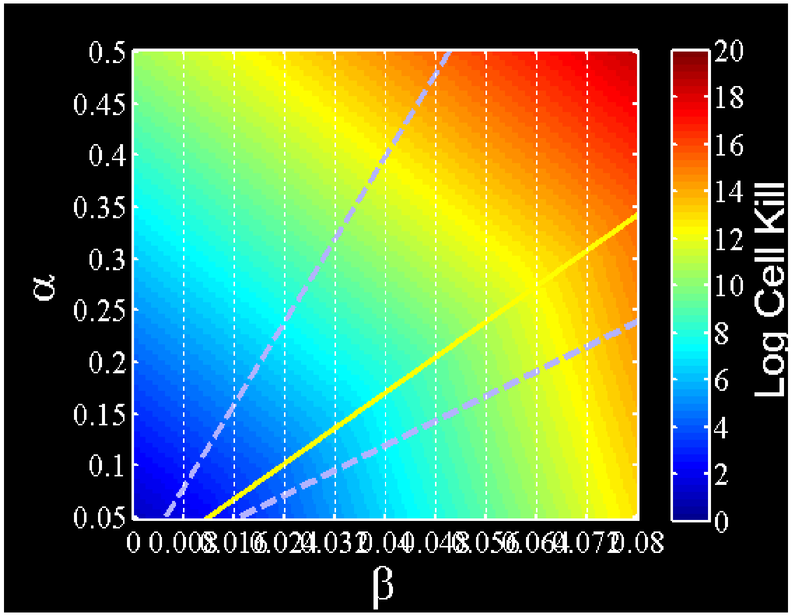
Fraction 1 2 ... N-1 N

Scenario 1: Linearly changing α^T

- Drug effect is equivalent to linear increase in α^T by 20%.

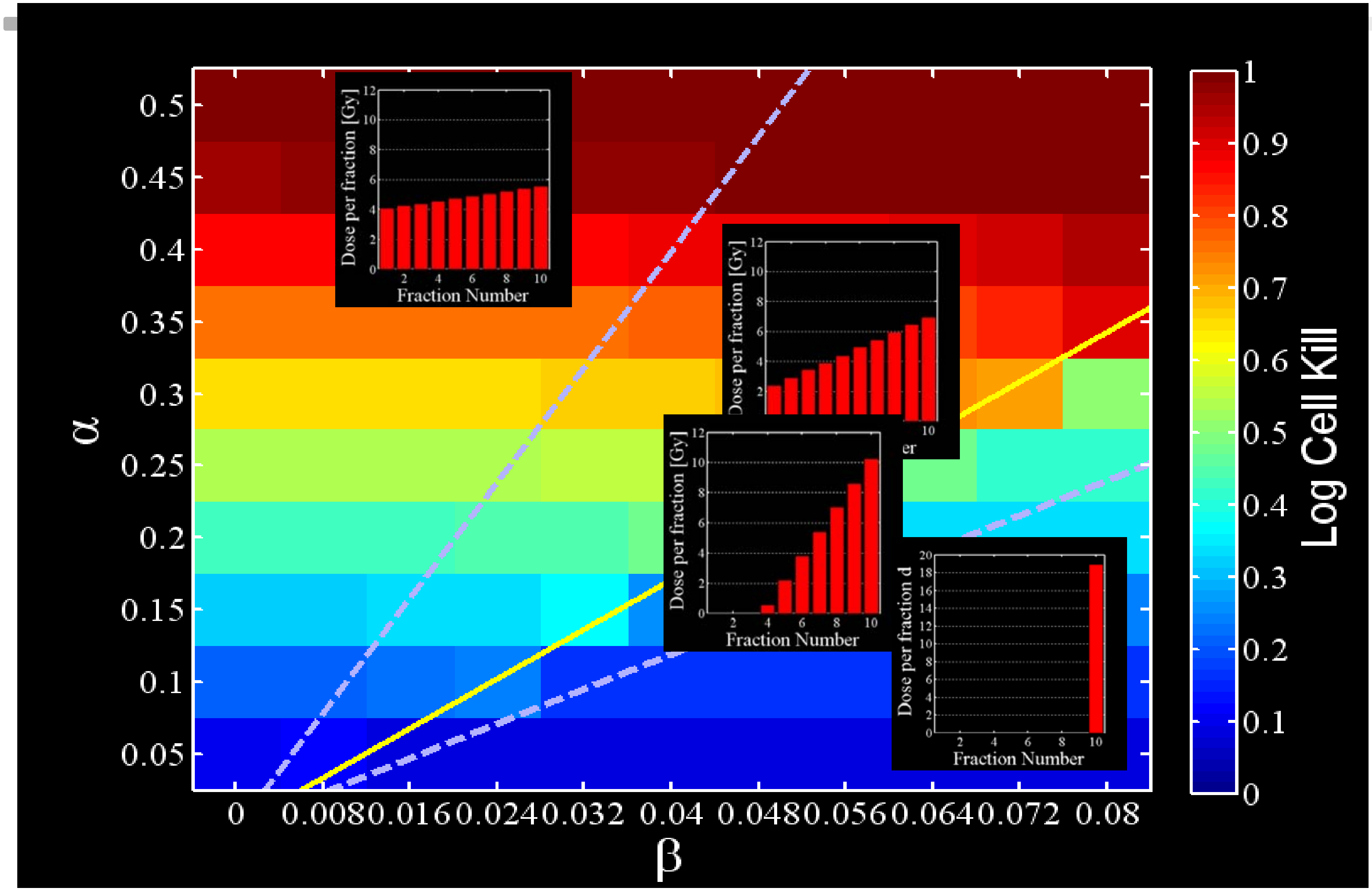


$\Delta\alpha$ = +20%



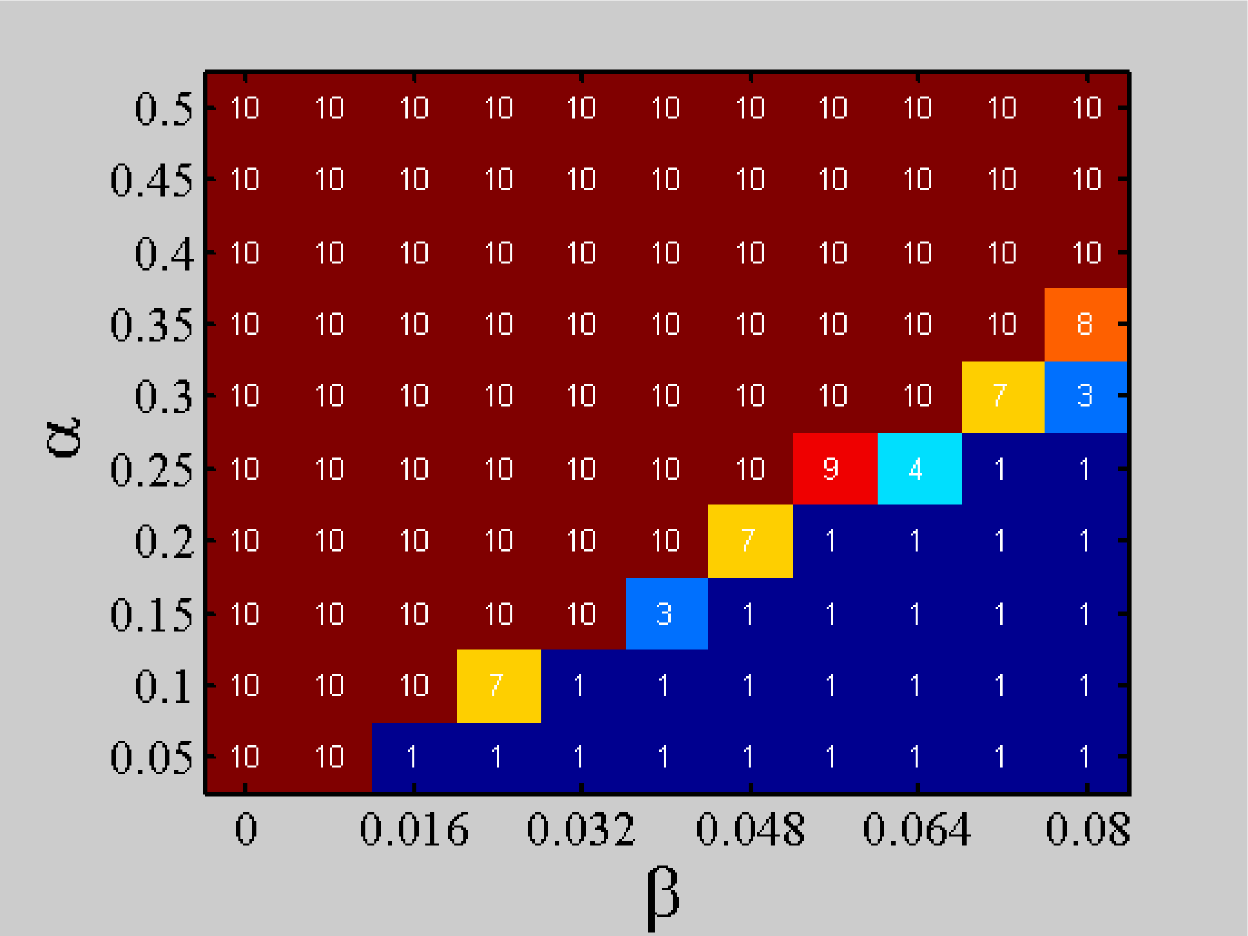
$\Delta\alpha$ = 0

Scenario 1: Linearly changing α^T

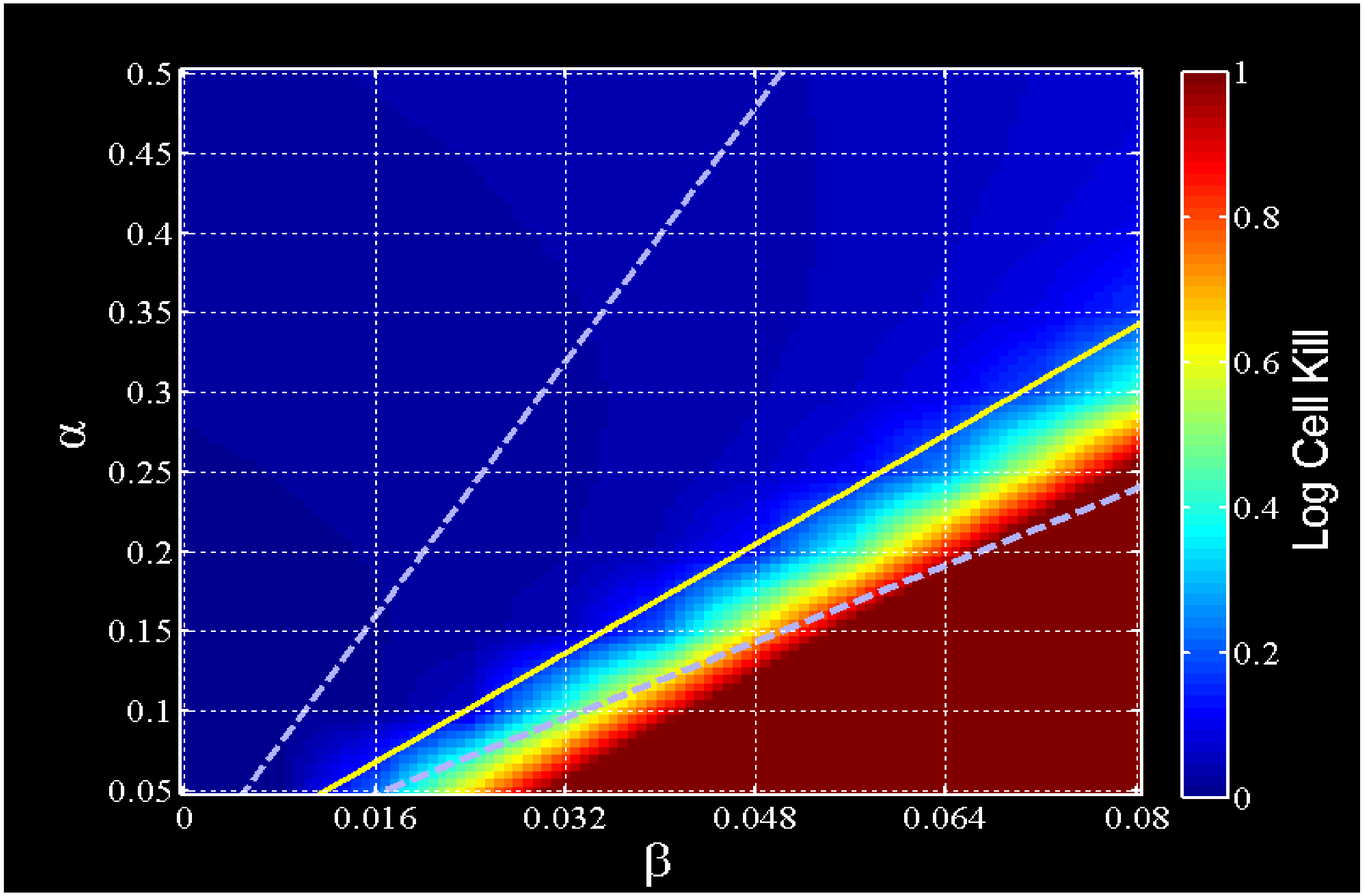


Medical Research

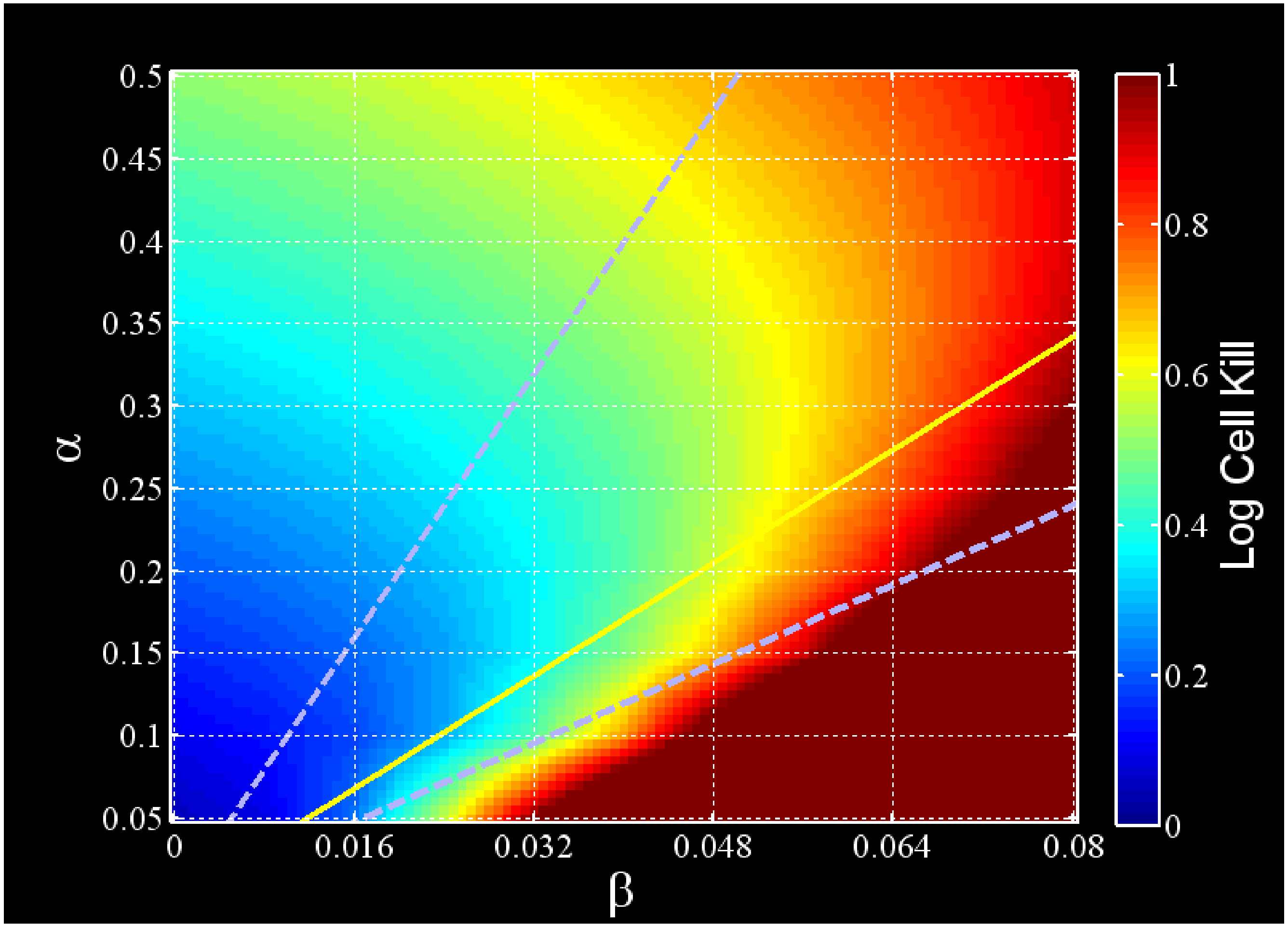
Scenario 1: Linearly changing α^T



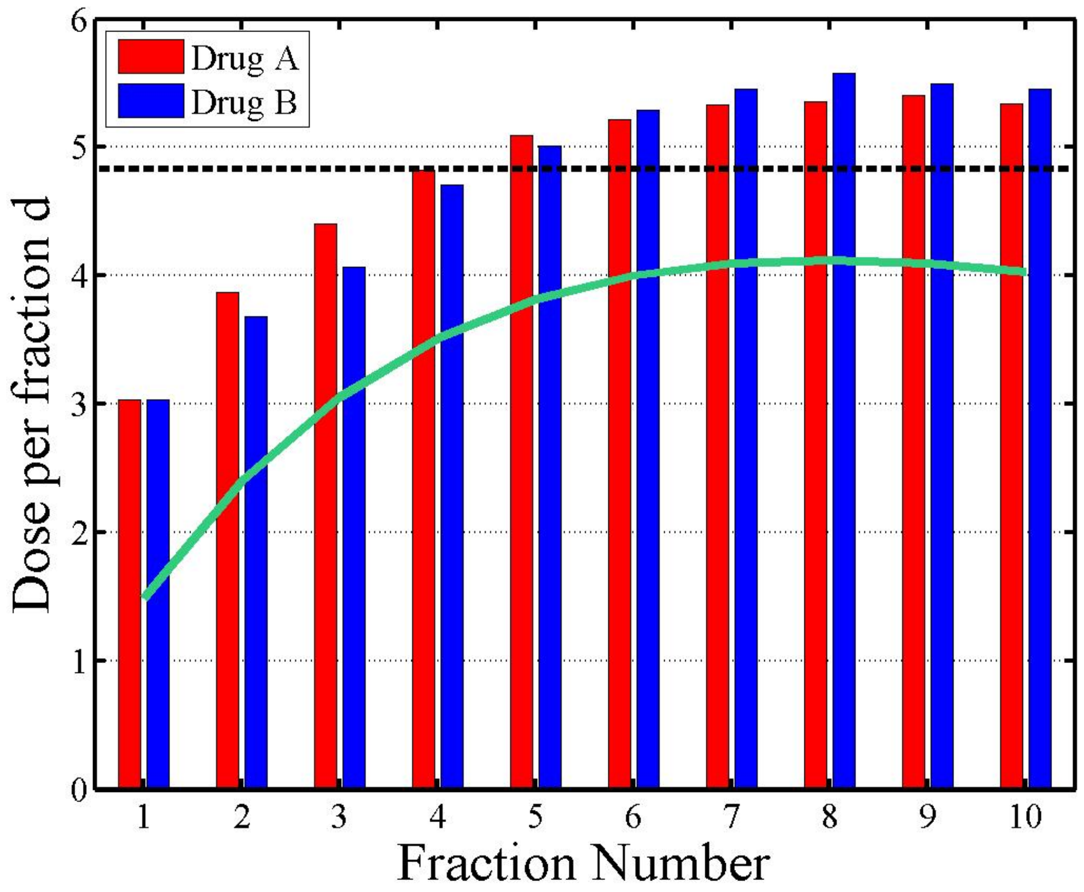
Scenario 1: How much better is the optimal schedule? $\Delta\alpha$ = +20%



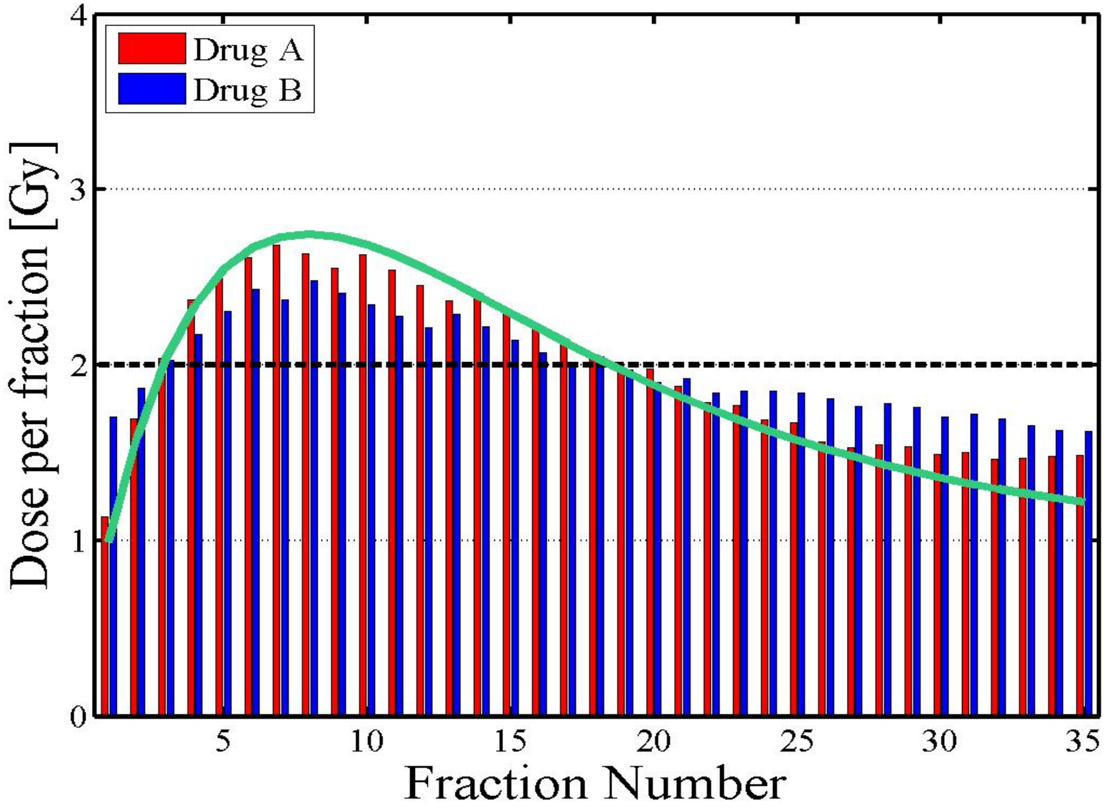
Scenario 1: How much better is the optimal schedule? $\Delta\alpha$ = +100%



Scenario 2: Optimal Schedules



Scenario 2: Optimal Schedules



Summary

- Emphasize method rather than model.
- Dynamic programming is a versatile optimization tool ideally suited for deterministic and stochastic multistage decision problems.
- In the “equal-dose-per-fraction regime” the dose per fraction is proportional to the radiobiological parameters α and β.
- Need effective radiobiological assays, e.g. γ-H2AX staining, to determine sensitivity to radiation.

Lessons Learned

- Practitioners know a lot of details and the modelling process of leaving details out to get to the essentials MUST include them not only to tap this knowledge but also to improve buy in.
- Best to talk to people at the “right” level in a company (even better if this is supported by senior leaders)
- Despite years of hiring quants, “Business” organizations are still typically less technical than “Technology” organizations and the relationship must be managed accordingly
- Best to have a single person who “owns” the problem
- Need to “pay dues”
- Need to expand definition of academic project success: (Publication can sometimes be a challenge, placing students is not)