Optimizing Subphases for LCT-based Anti-Cancer drug response model

C&SBIO185 - Bplate

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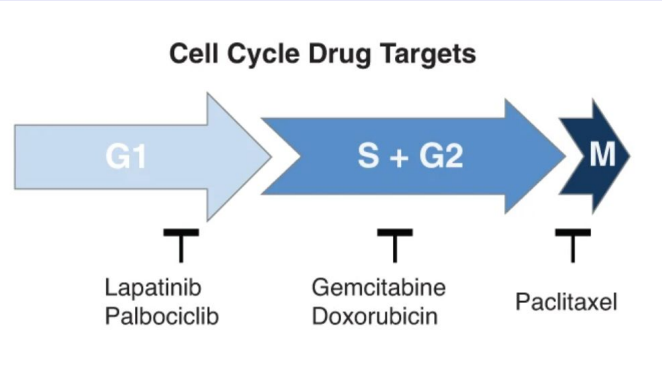
Brief Background

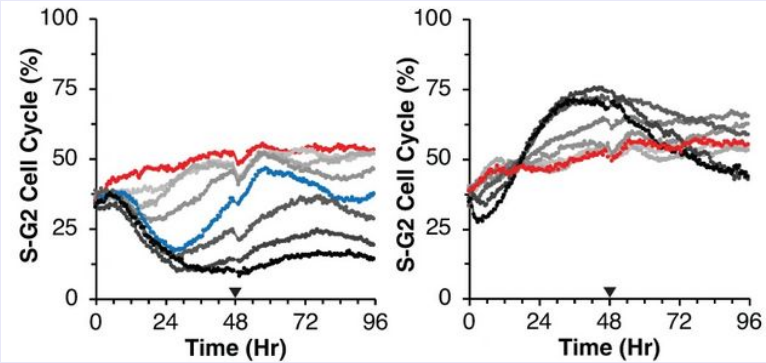
Introduction

- analyzes engineered breast cell cancer that express cell cycle reporter
- analyzes how different drugs impact cell cycle phases of cancer



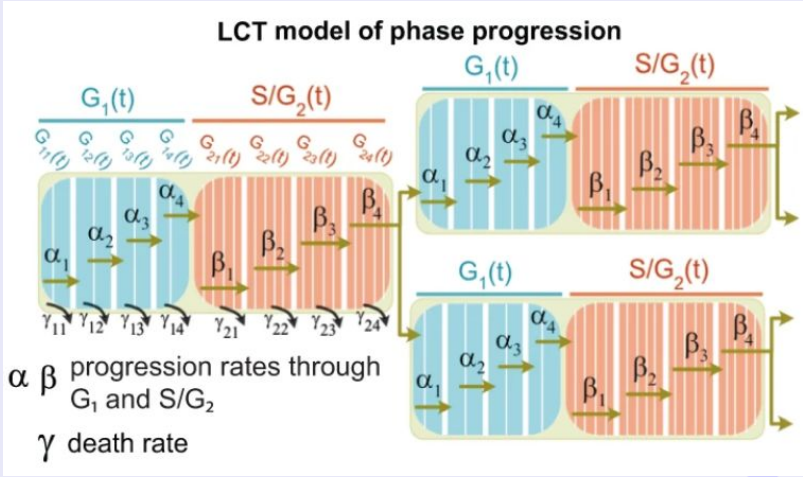
Background Cont.

- Engineered breast cells treated with 5 drugs
  - Change in cells depend on quantity of dosage



Background Cont.

- Computational Method: Linear Chain Trick (LCT)
  - mean-field system of ordinary differential equations (ODEs)
  - capture oscillatory cell cycle behavior and drug effects on specific phases
    - parameter: number of cell cycle subphases



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Problem Statement

Question

What are the optimal G1 and S/G2 sub-phases that should be used to lower the model's error rate?

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Goals & Methods

Goals

- Recreate the LCT model
- Find optimal number of G1 and S/G2 sub-phases that should be used to lower the model's error rate
    - Change small parts of code and combine them to make sure they still work
    - Could we find a more optimal number?

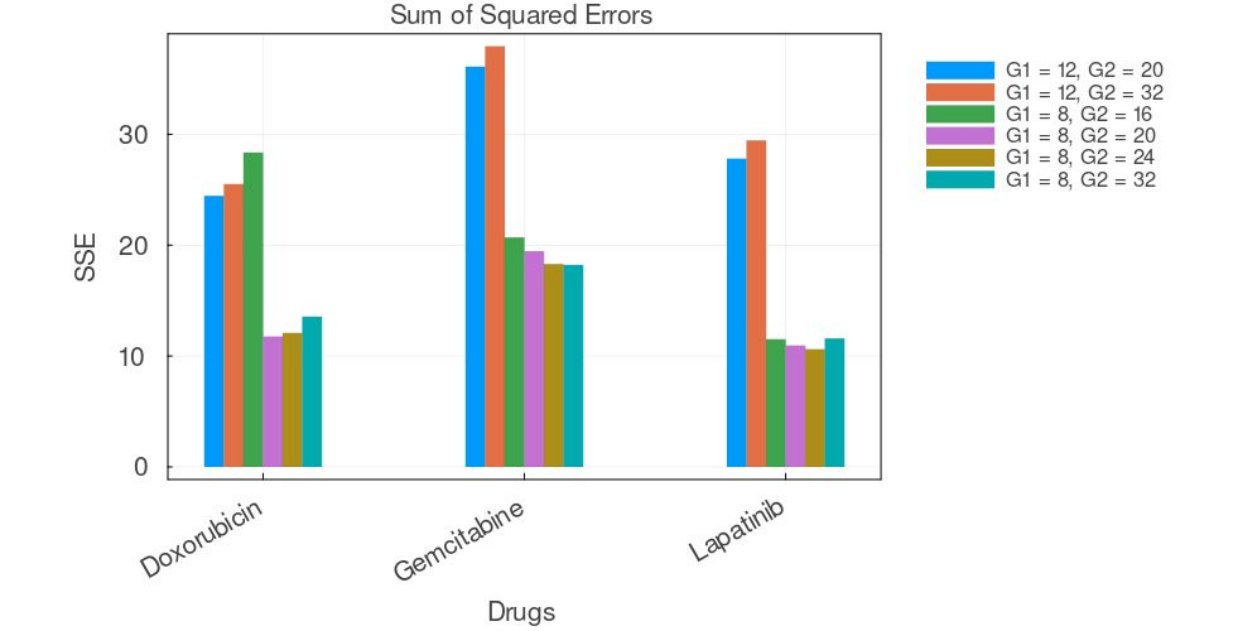
Methods

- An ODE model was used to predict the number of cells in the G1 and G2 phases of the cell cycle
- Tested five different combinations of subphases: (12, 20), (12, 32), (8, 16), (8,24), and (8, 32)
- Also tested across three different conditions of drugs: doxorubicin, gemcitabine, and lapatinib
- To compare findings, we plotted the number of G1 cells and S/G2 cells over times and also compared the sum of squared errors of the model to original data

04

Results

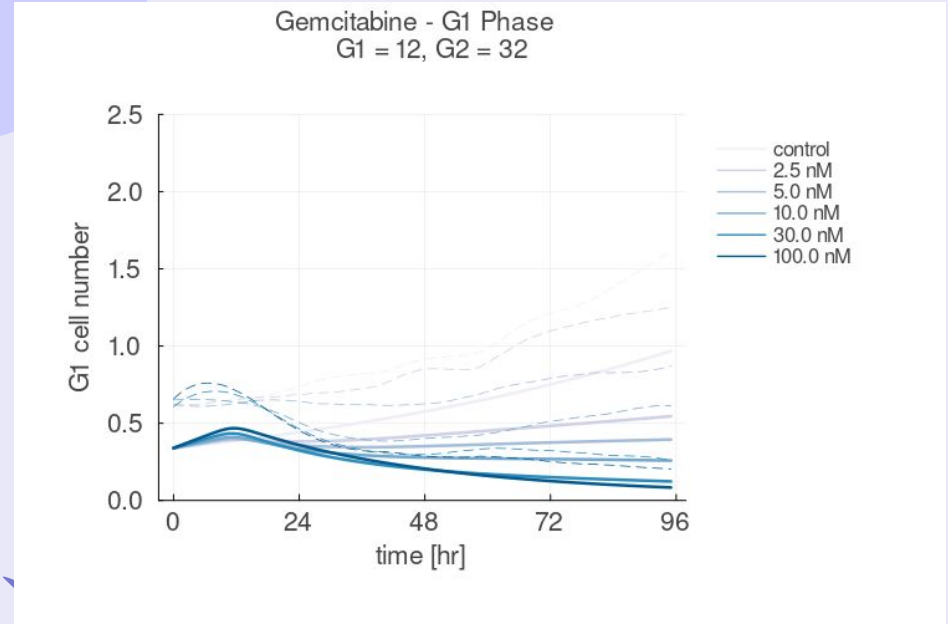
Results

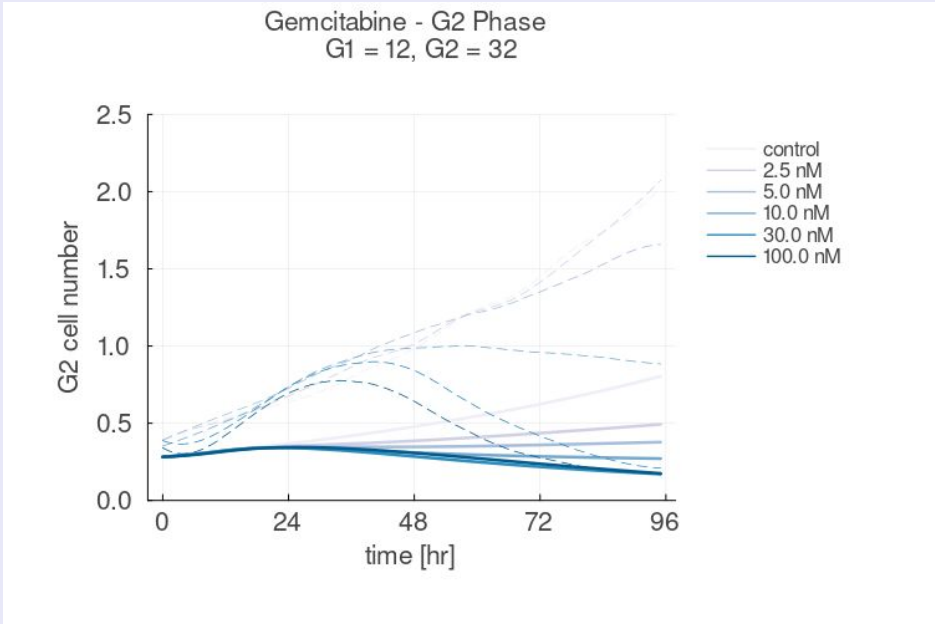


- Highest errors for G1 = 12
- Lowest errors for G1 = 8

Results

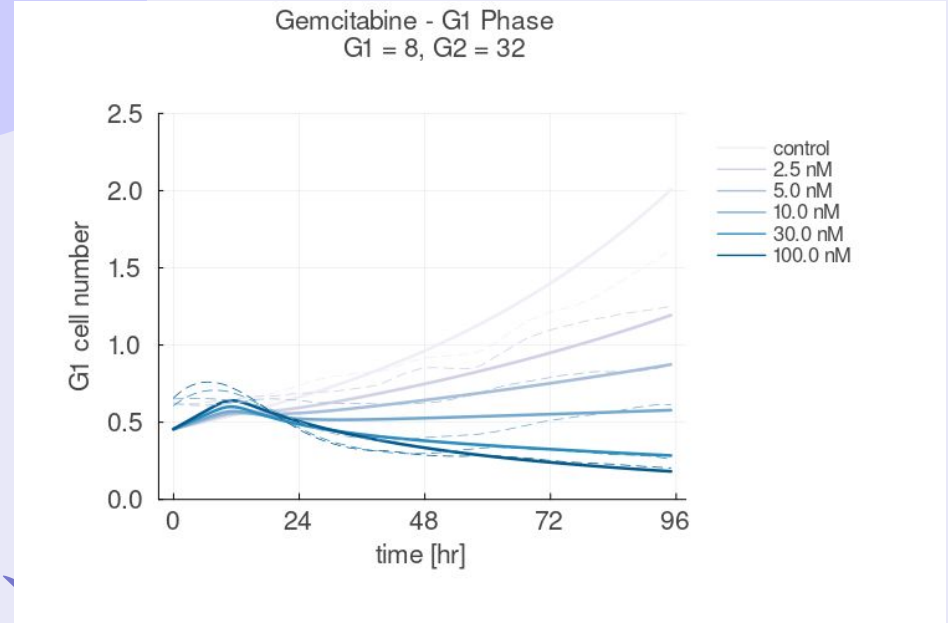
Highest Error for Gemcitabine: (G1, G2) = (12, 32)

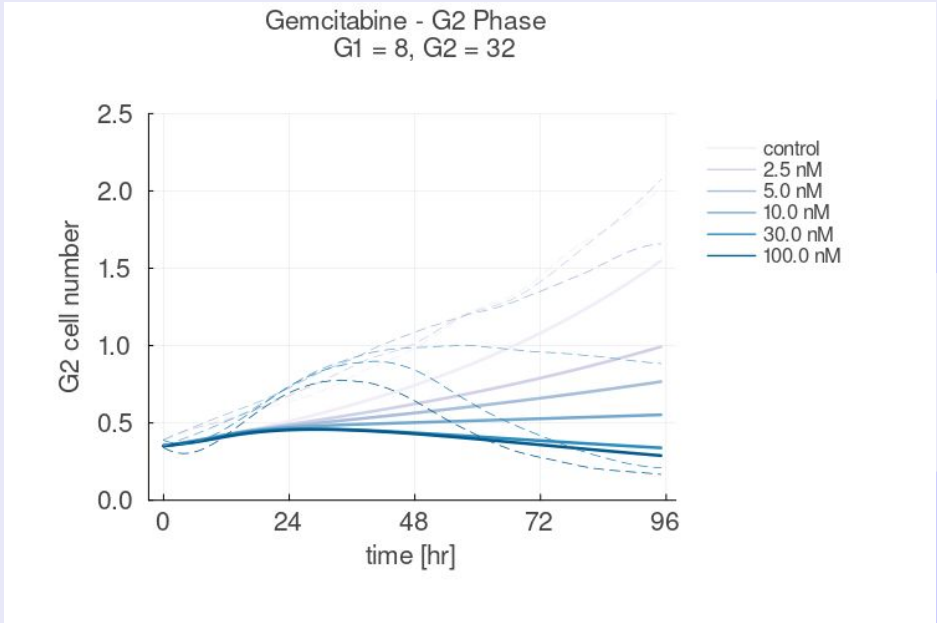




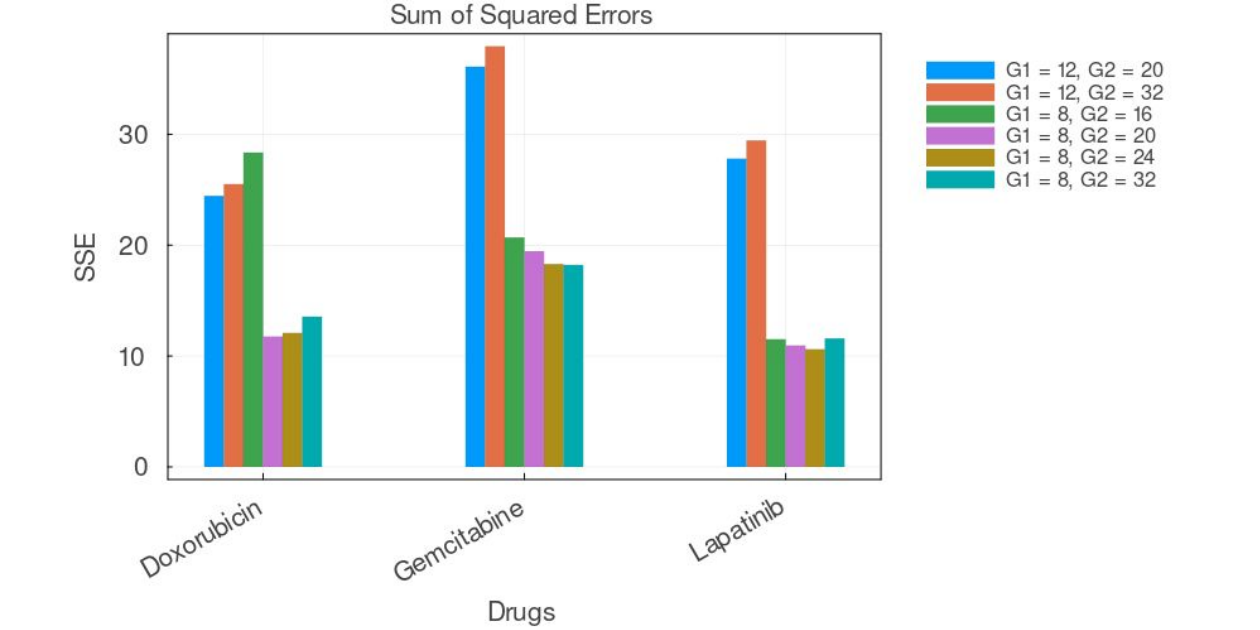
Results

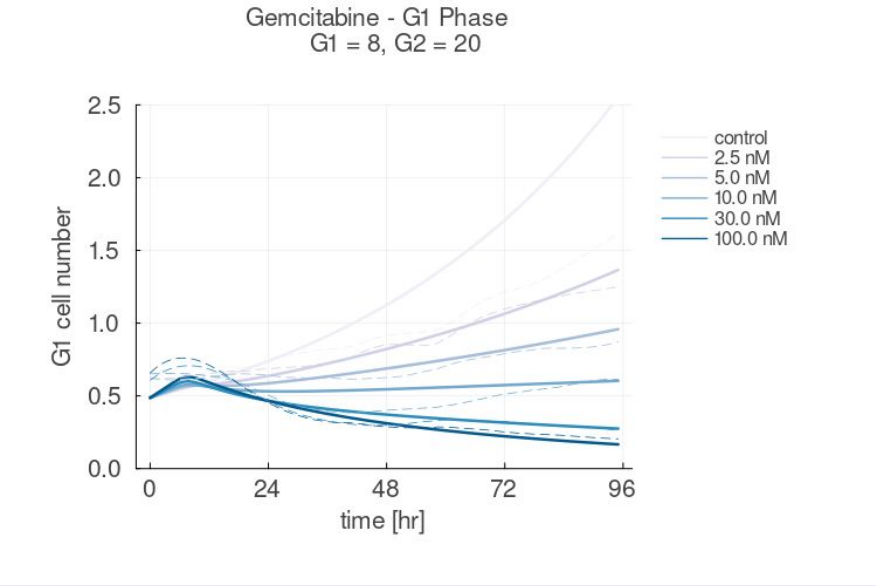
Lowest Error for Gemcitabine: (G1, G2) = (8, 32)

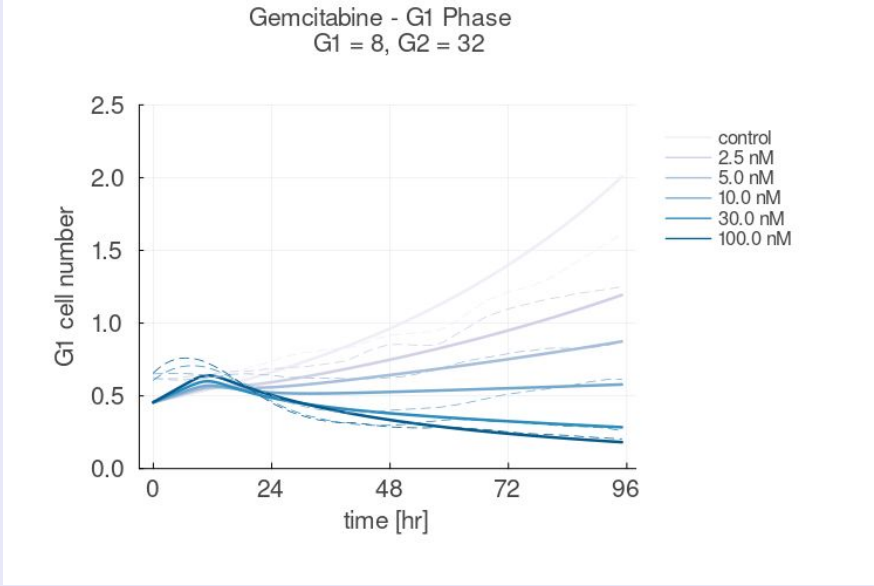




- Combination with lowest error varies across the different drugs







- Minor differences between the two as they keep relatively the same shape
- Final numbers for G2 = 32 are more accurate

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Limitations

Limitations

Base Design

Errors from fundamental design will carry over

Clinically Unproven

Drug combinations and/or sequences outputted by model are still yet to be tested on real patients

Time Constraints

Unable to implement all possible methods to find optimal subphases

06 Broader Implications

Optimized Drug Combinations & Sequencing

Drug Combinations

The LCT model can be used to predict the impact of different drug combinations of cell cycle behavior and find cell numbers associated. Analyzing how drug combinations target cell cycle phases, can gain insight on whether combining specific drugs have synergistic or antagonistic effects.

Drug Sequencing

The findings from this research can inform the development of rational and effective drug sequencing strategies for cancer treatment by considering the cell cycle effects of individual drugs, predicting drug responses to sequential treatments, and validating the efficacy of personal treatment plans for patients through experimental studies.

Thanks

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