PHYSIOMICS

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Cancer Modeling and Drug Schedule Optimization

EPIC

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Introduction to Physiomics plc

- **Business**
  - Founded 2001, Oxford (UK) based, listed on the LSE (AIM) 2004
  - We use computer modelling to understand and predict optimal cancer therapy
- **Focus**
  - Simulation of cell populations (SystemCell® Technology)
  - Combination therapy and scheduling
- **Collaborations**
  - Eli Lilly, Bayer Technology Services
  - Cyclacel Pharmaceuticals, ValiRx, Sareum
  - ILS Swansea University (HPC), ICR, CRT
  - TEMPO (FP6 – EU LifeSciHealth project)

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Applications of Physiomics' modelling

- **Decision-making tools** to address specific key questions during the drug development process:
  - Drug target validation
  - Lead compound selection
  - Demonstrate the mechanism of action (MOA)[1,2]
  - Effects of different genotypes
  - Biomarker validation
  - Drug scheduling and combinations

[1]*Schneider et al, Nature Review Drug Discovery (2008) 7:893-899*
[2]*Chassagnole et al, BioSystems (2006) 83:91-97*

Timing matters

Schedules

Combinations

Chronotherapy

Physiomics has the potential to predict the optimal dosing schedules for a wide class of anti-cancer drugs – alone or in combination – to enhance efficacy and lower side effects

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Schedules and combinations

- Effectiveness of schedule variation in combination therapy has been demonstrated in numerous pre-clinical and some clinical studies

- **Phase II**: Taxol-> Cisplatin sequence[1]
  - **Cisplatin given just after Taxol:** 45% to 60% overall response rate
  - **12 hours delay:** 80% overall response rate and lower toxicity

[1]*Shah A. & Schwartz G., Clinical Cancer Research (2001) 7:2168-2181*

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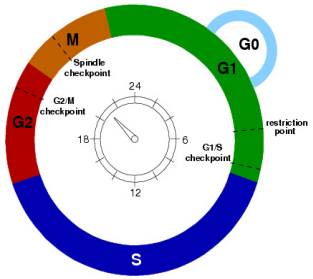
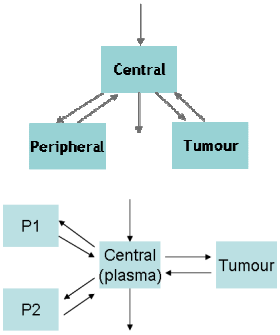
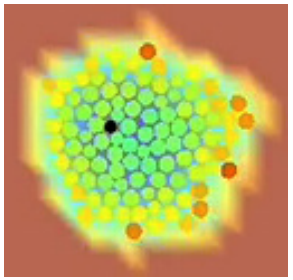
Virtual Tumour simulation platform

PD Model

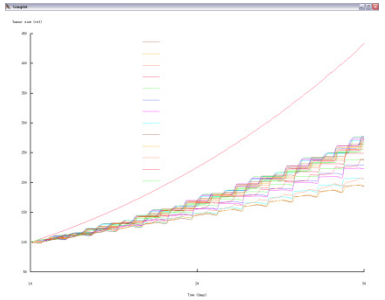


PK Models





SystemCell® Virtual Tumour



Tumour growth predictions

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Case study: Combination and schedule predictions in active oncology program

- We had to predict **two combination schedules** using 2 different cell-cycle targeting drugs
- To calibrate the model we had access to 3 **single drug xenograft timecourses**
- **Blind test:** the results of the combination were revealed after we sent our predictions

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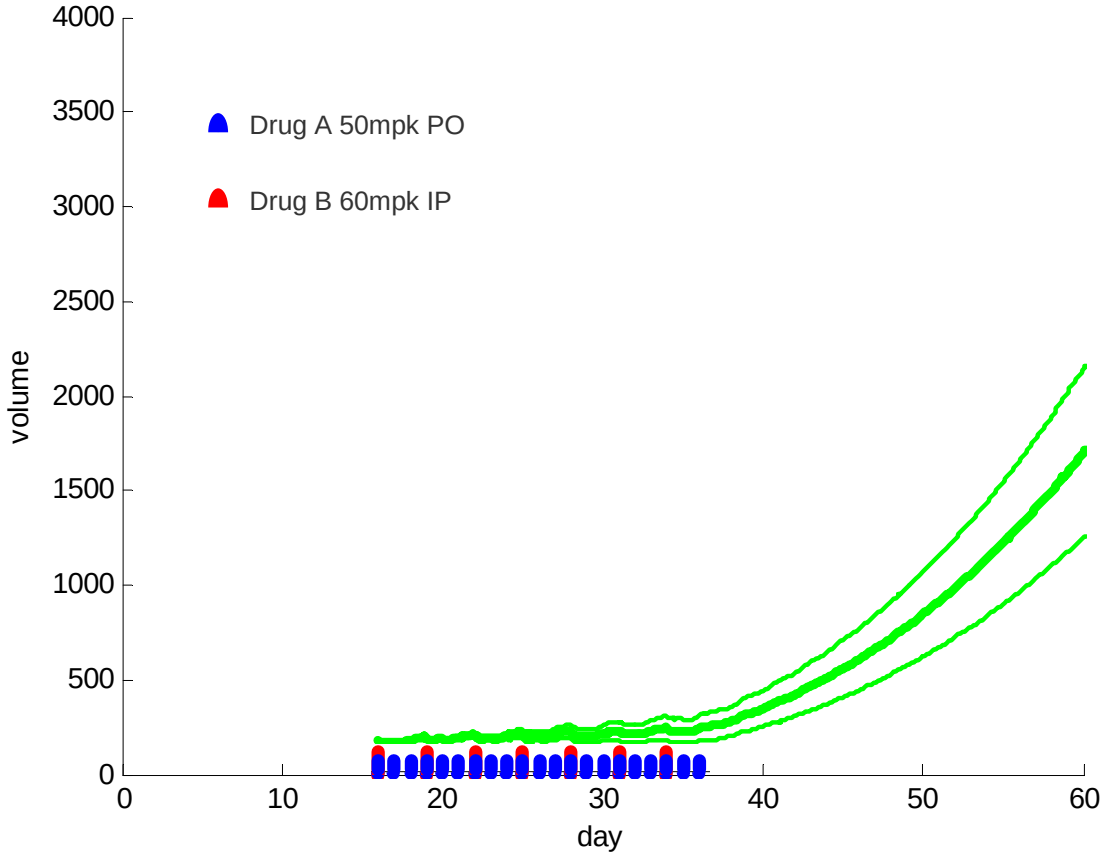
Prediction 1:
Drug A qdx21 + Drug B q3dx7



Green lines: median, upper and lower bounds of predicted tumour growth
Upper and lower bounds give 95% confidence interval

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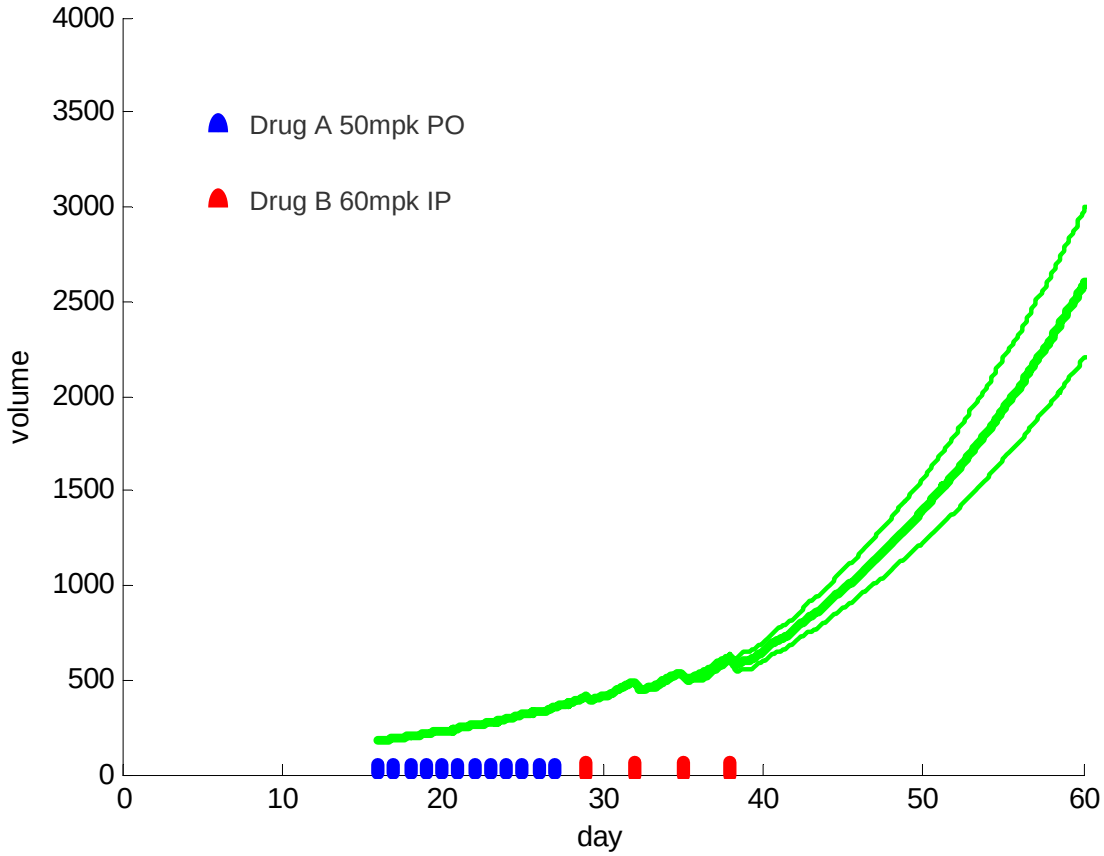
Prediction 2:
Drug A qdx12 → Drug B q3dx4



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Upper and lower bounds give 95% confidence interval

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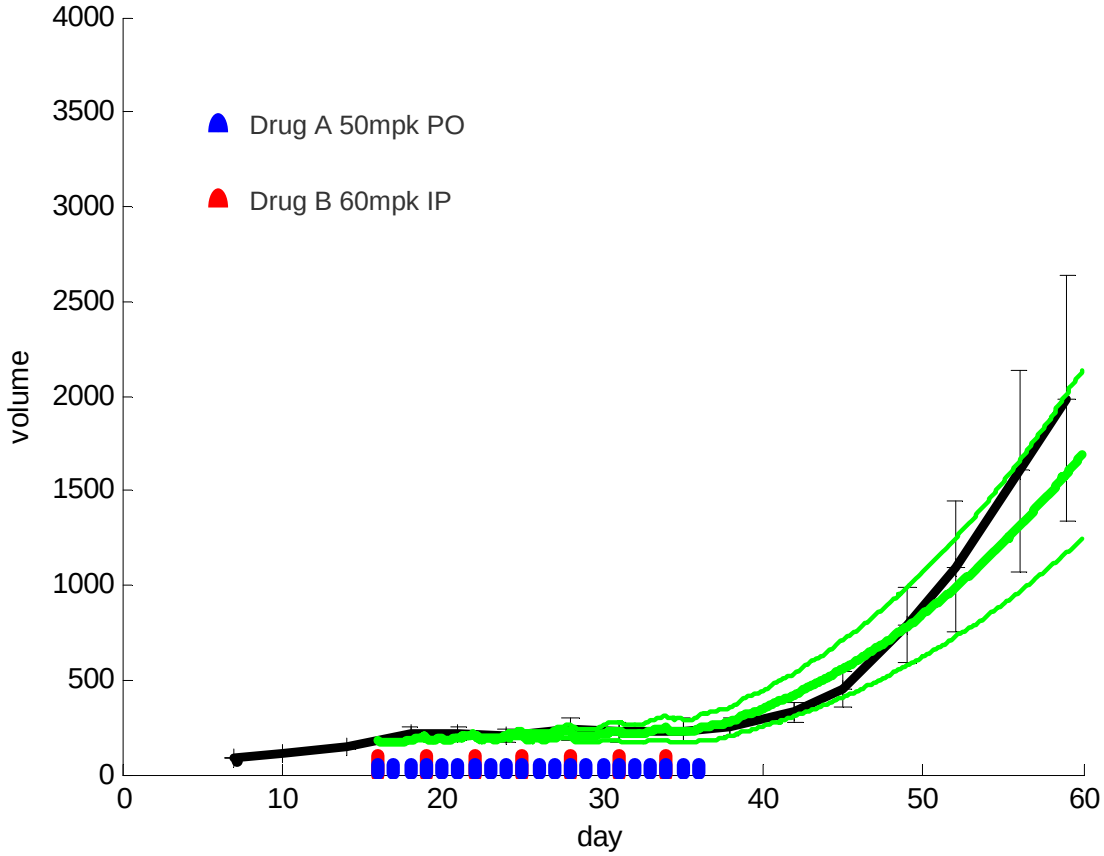
Prediction 1 overlay with experimental results



Green lines: median, upper and lower bounds of predicted tumour growth
Upper and lower bounds give 95% confidence interval
Black line: Experimental measurement – error bars represent 95% confidence interval

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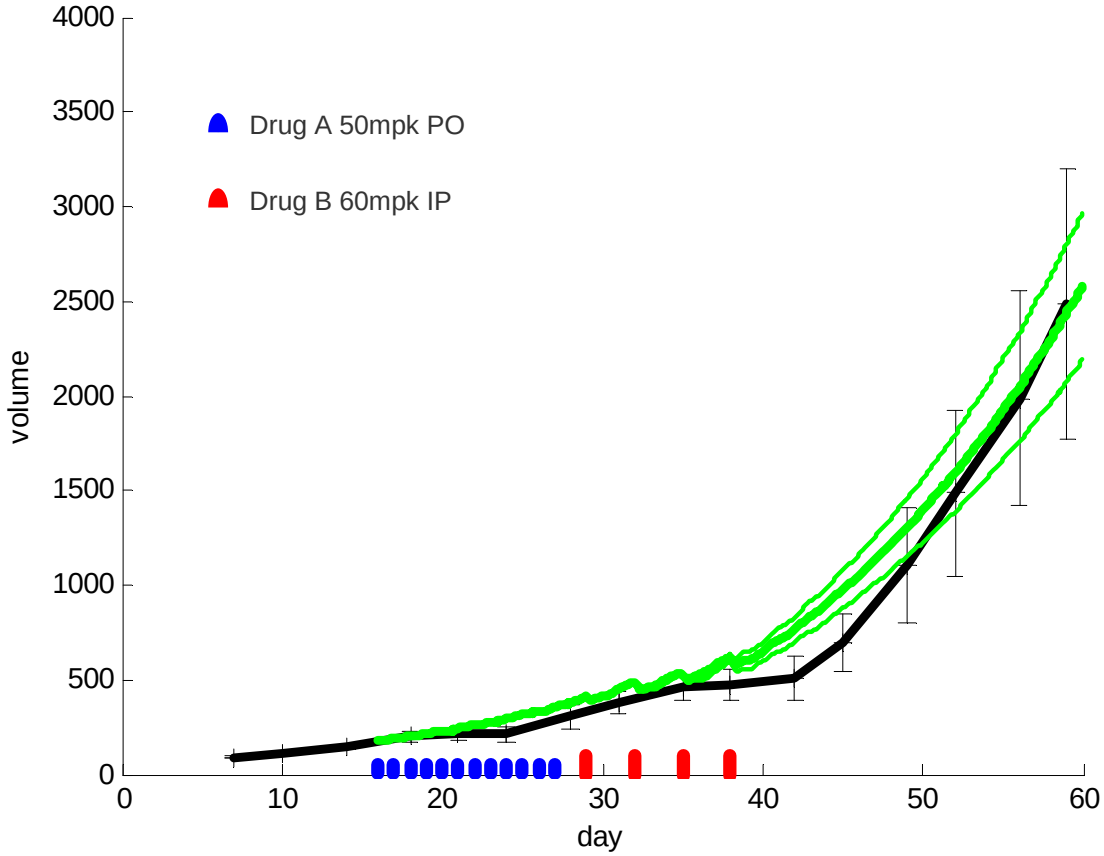
Prediction 2 overlay with experimental results



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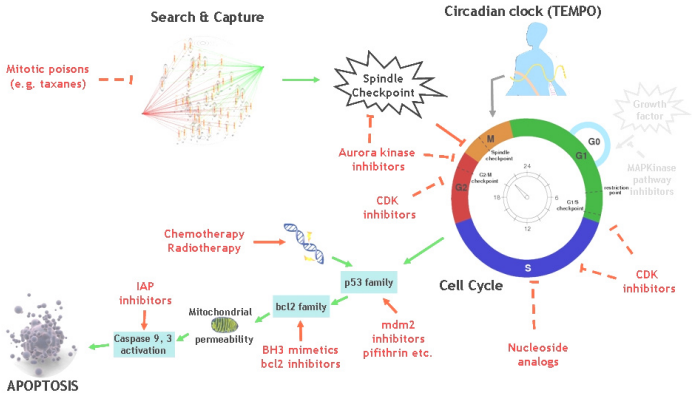
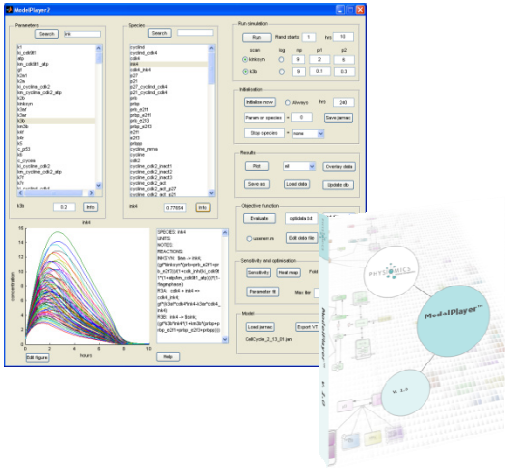
Services and Products

- **Fee-for-service**
  - FTE payment
  - Milestones
- **Shared risk / Success based**
  - Co-development and shared risk
- **Out-Licensing**
  - ModelPlayer™
  - Model database





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