Evolving Treatment Paradigms – A New Mathematical Biomarker

Kit Gallagher[1,2], Maximilian Strobl[3], Robert Gatenby[2], Philip Maini[1], Alexander Anderson[2]

[1] Mathematical Institute, University of Oxford, UK
[2] Integrated Mathematical Oncology, Moffitt Cancer Center, Florida
[3] Theory Division, Cleveland Clinic, Ohio

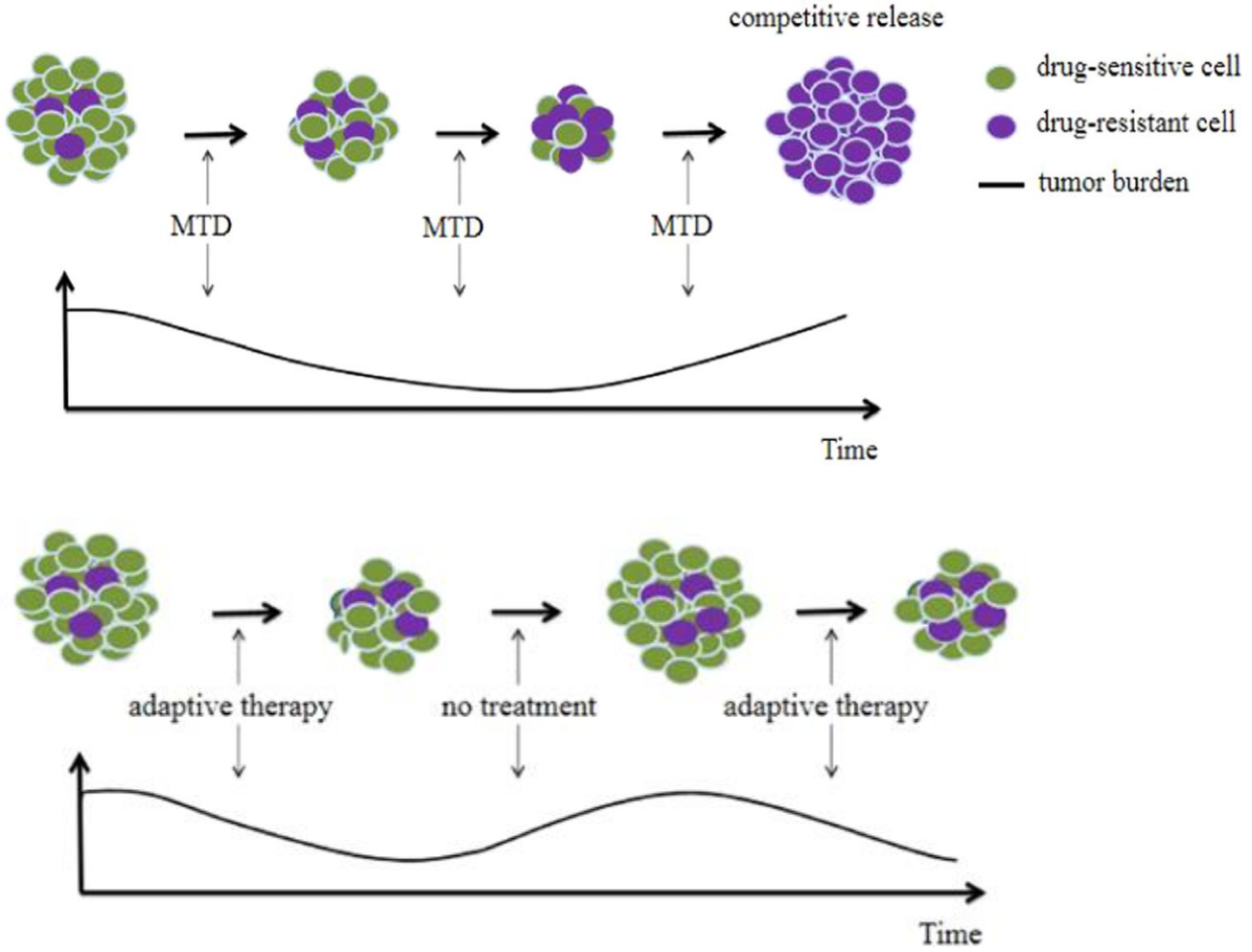
Oxford Mathematics

UNIVERSITY OF OXFORD
Mathematical Institute

Introduction

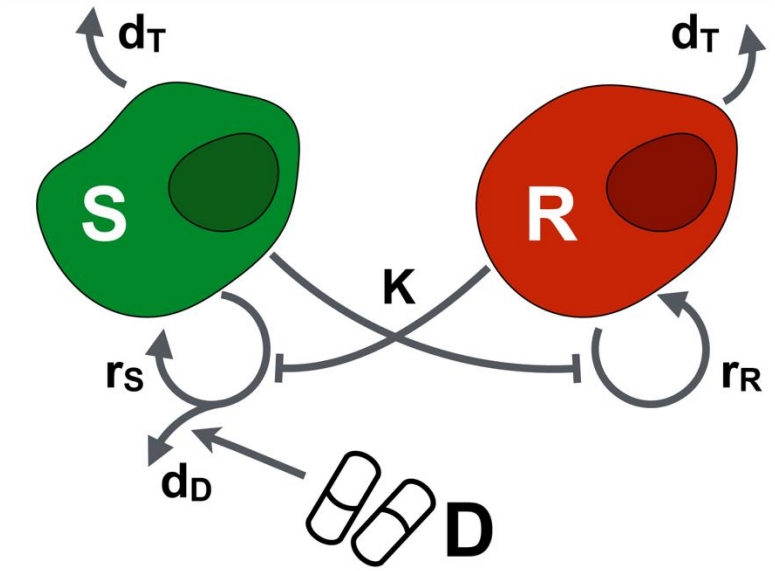
- **Introduction - Adaptive Therapy**
  - Comparison of treatment paradigms
  - Introduction of deep learning model
- Personalized Adaptive Thresholds
  - DRL performance & interpretable strategies
  - Translation to the clinic
- Predicting Patient Outcomes
  - TTP prediction with a probing cycle
  - Varying the treatment interval

Introduction to Adaptive Therapy



Zhang, Lei, Jianli Ma, Lei Liu, Guozheng Li, Hui Li, Yi Hao, Xin Zhang et al. "Adaptive therapy: a tumor therapy strategy based on Darwinian evolution theory." Critical Reviews in Oncology/Hematology 192 (2023): 104192.

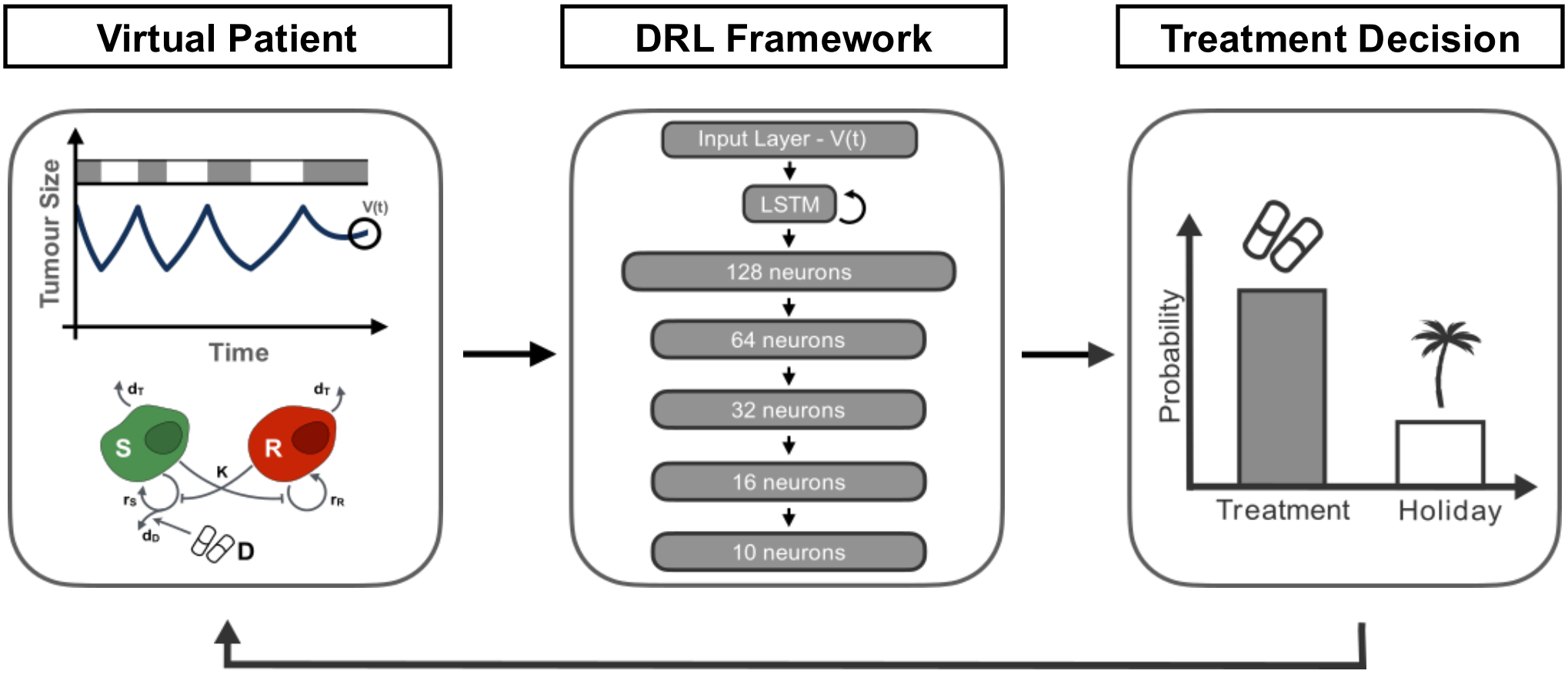
Lotka-Volterra Tumour Model



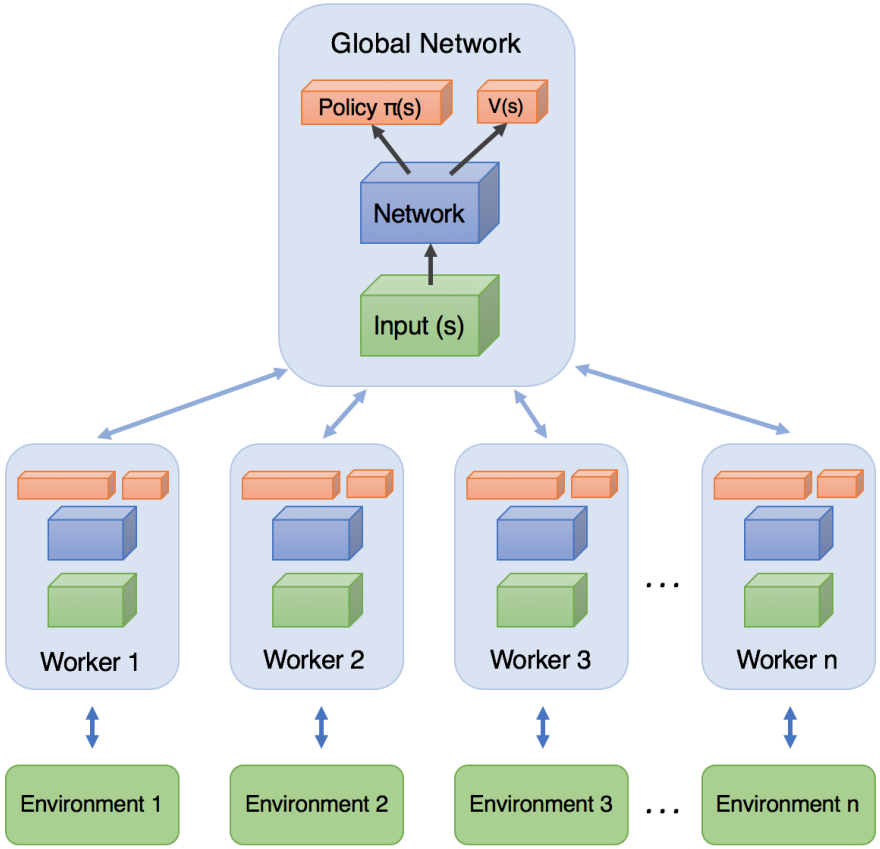
$$\frac{dS}{dt} = r_S S\left(1 - \frac{S+R}{K}\right) \times (1 - d_D D) - d_S S$$

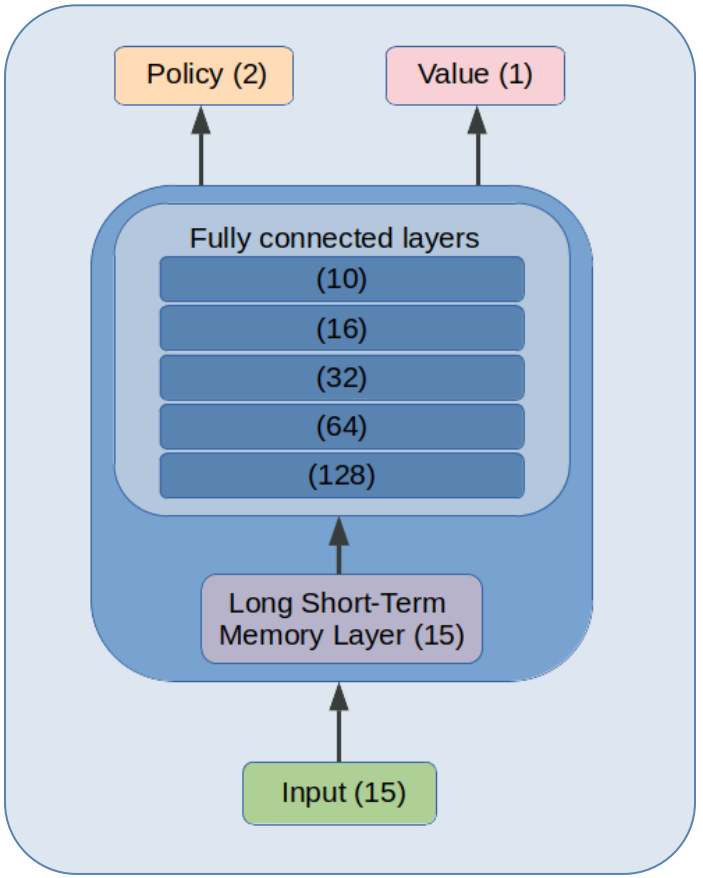
$$\frac{dR}{dt} = r_R R\left(1 - \frac{S+R}{K}\right) - d_R R$$

Improving AT with Deep Learning

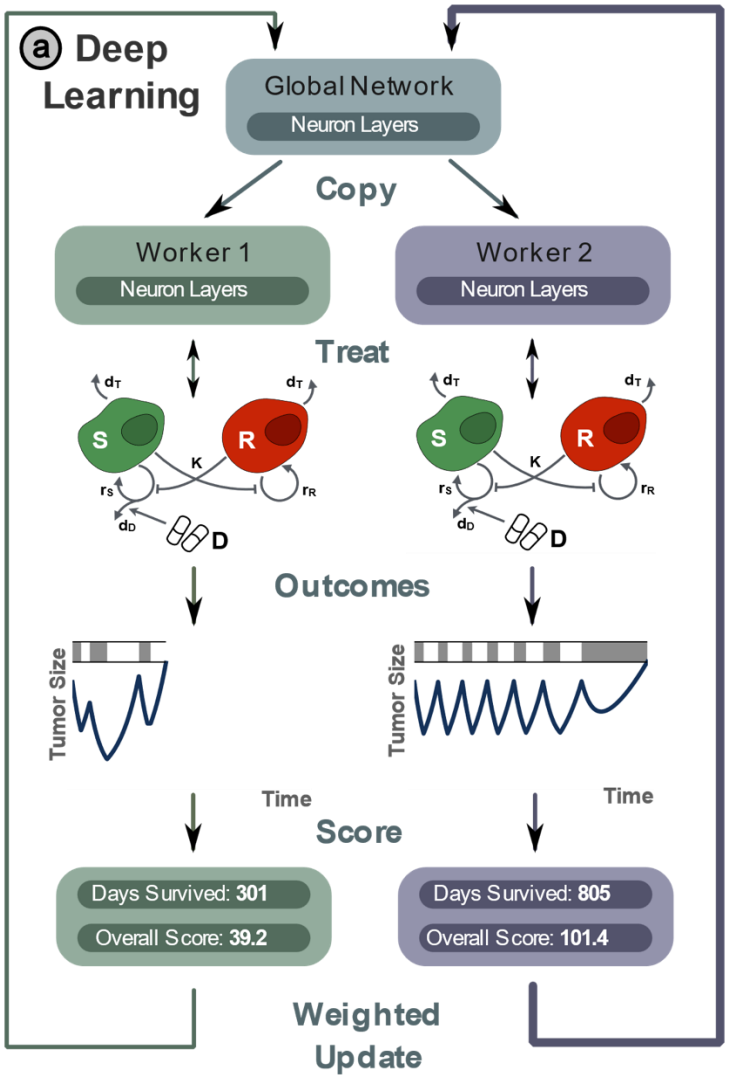


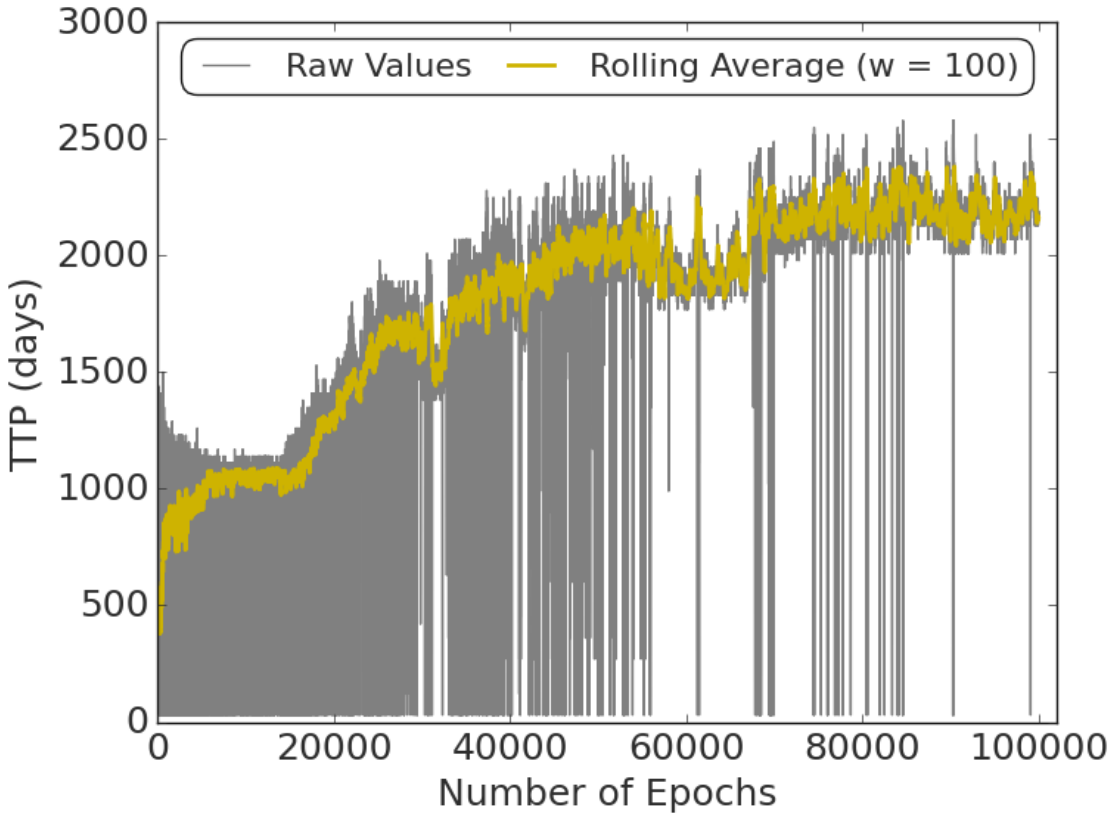
Deep Learning Framework





DRL Methodology





Personalized Adaptive Thresholds

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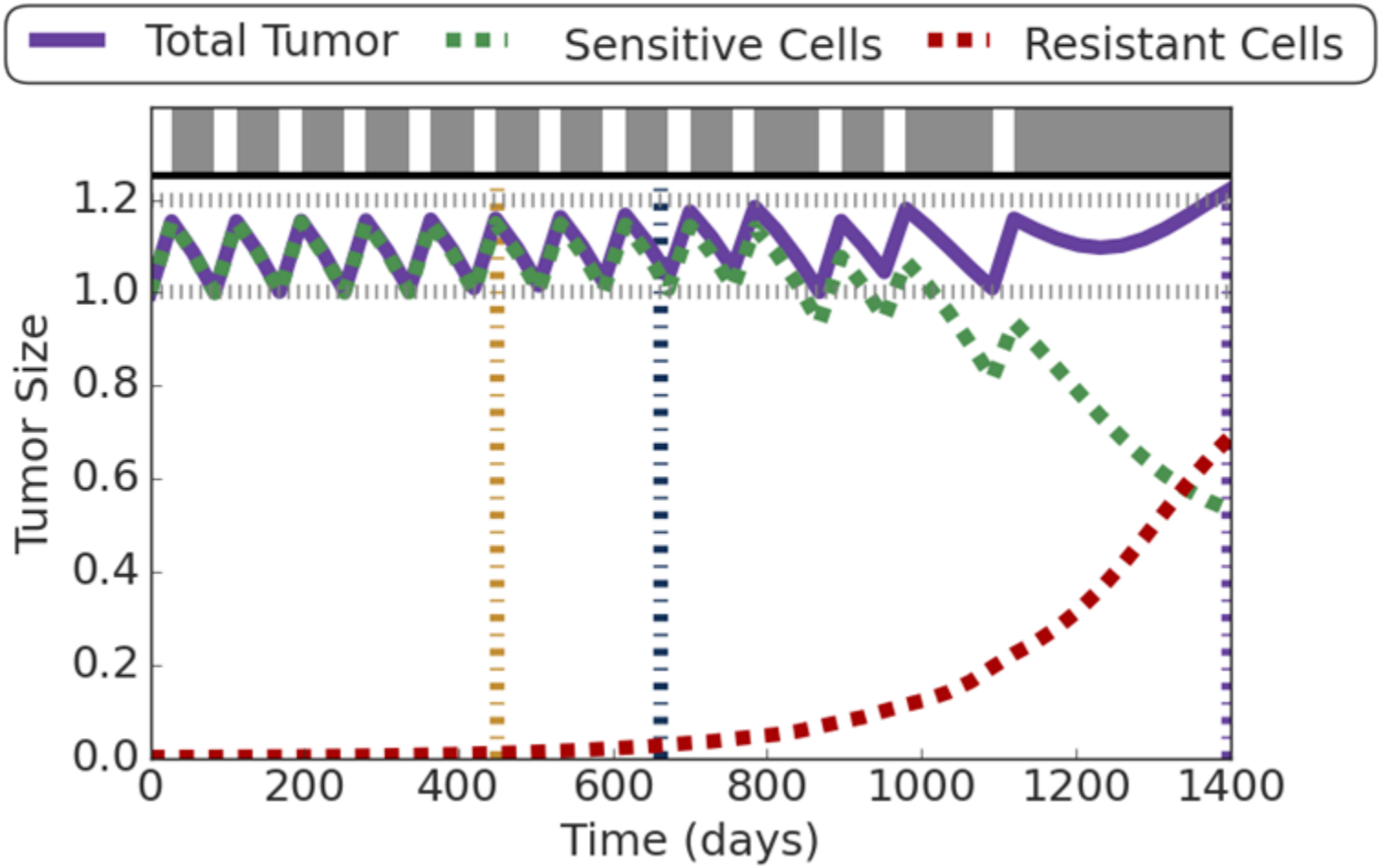
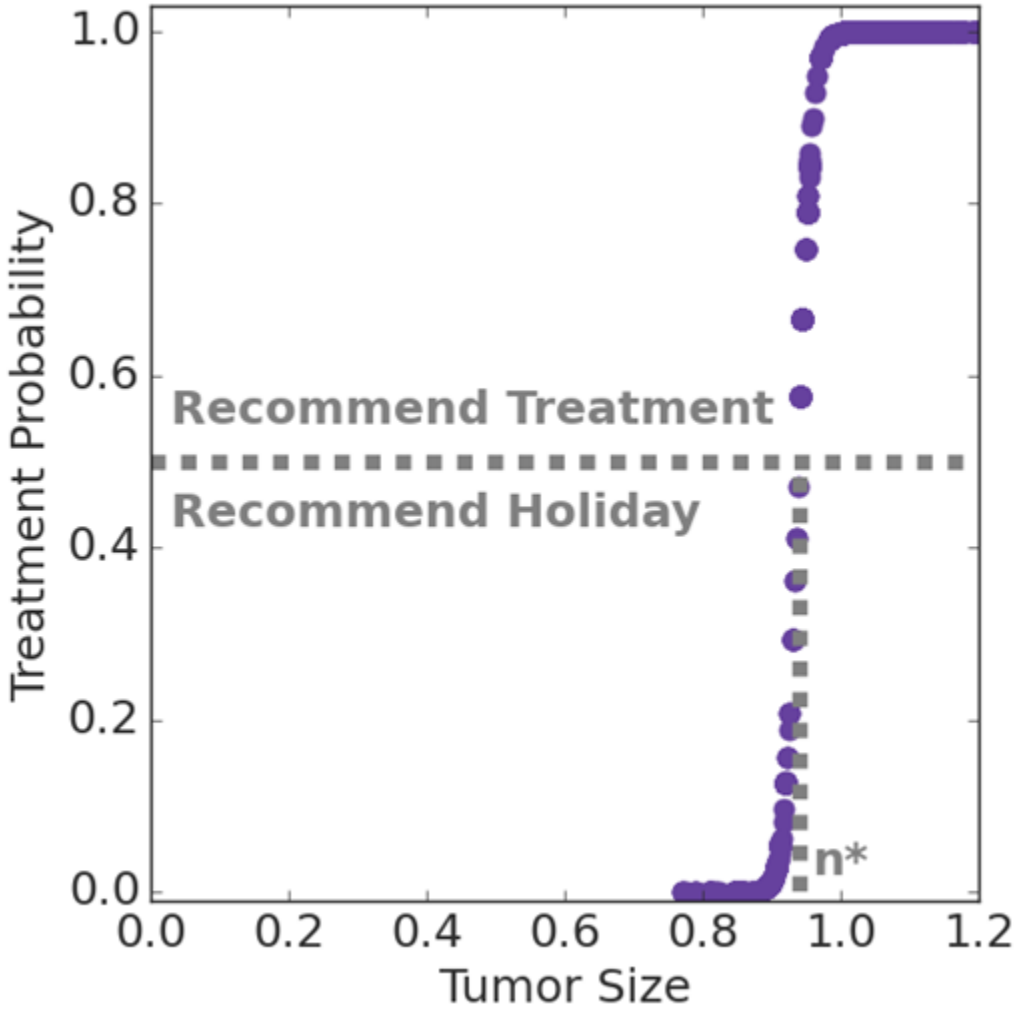
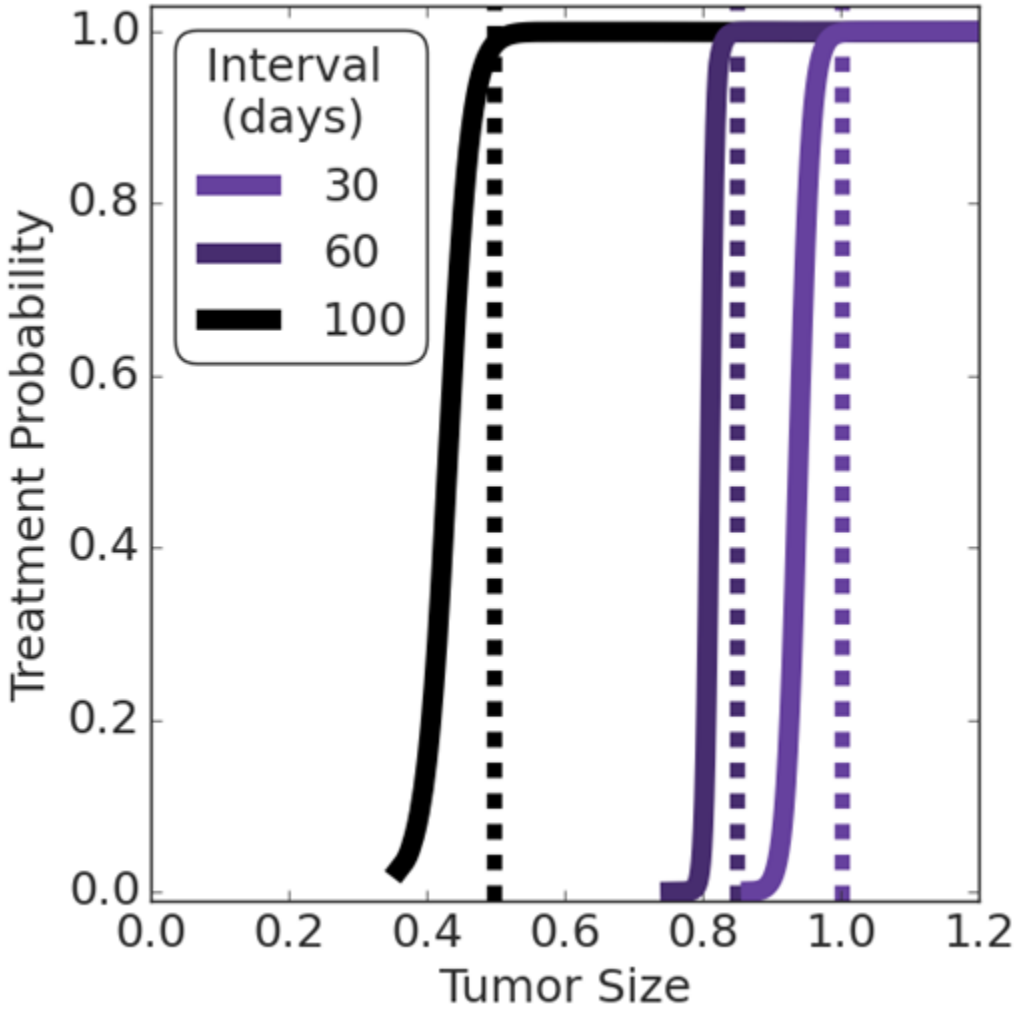
DRL Strategies Outperforms Standard of Care

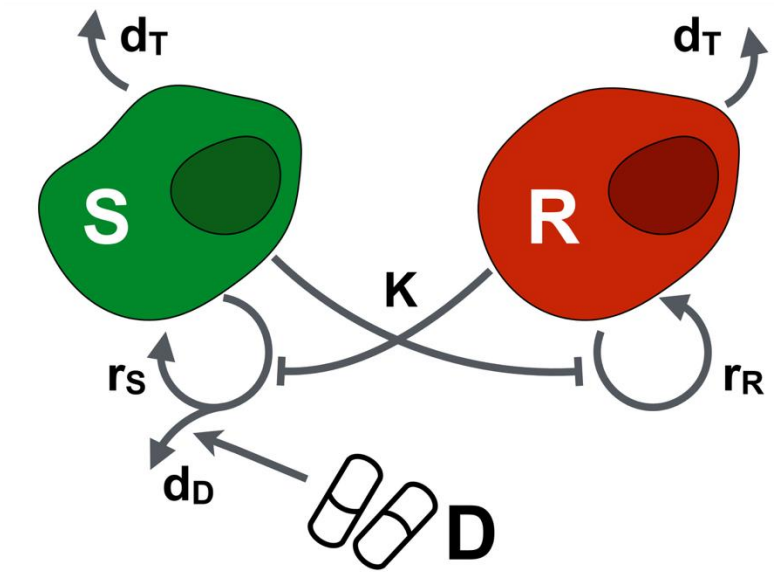


Interpreting the ‘Black Box’ of DRL…



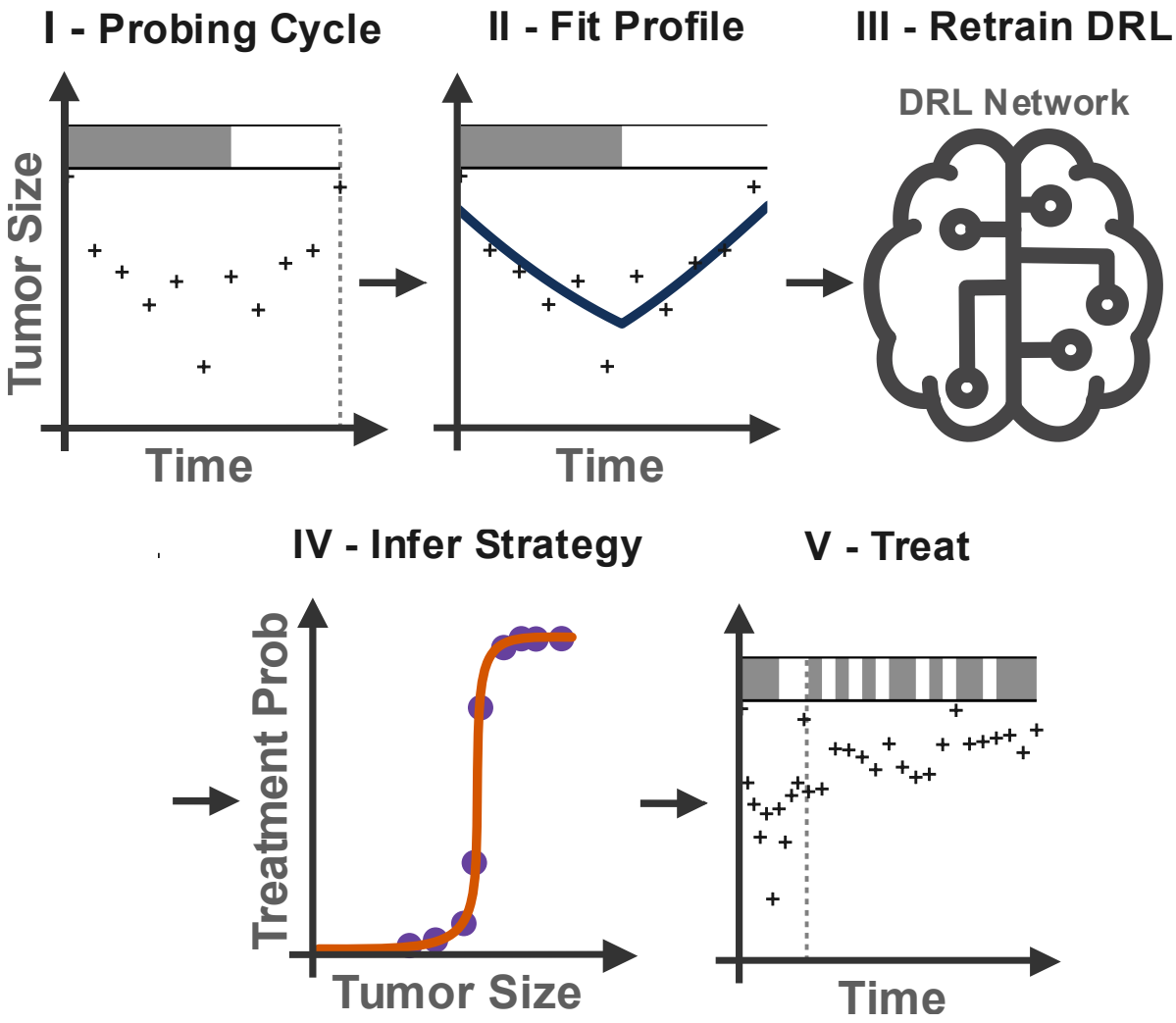
… to find the Optimal Treatment Schedule



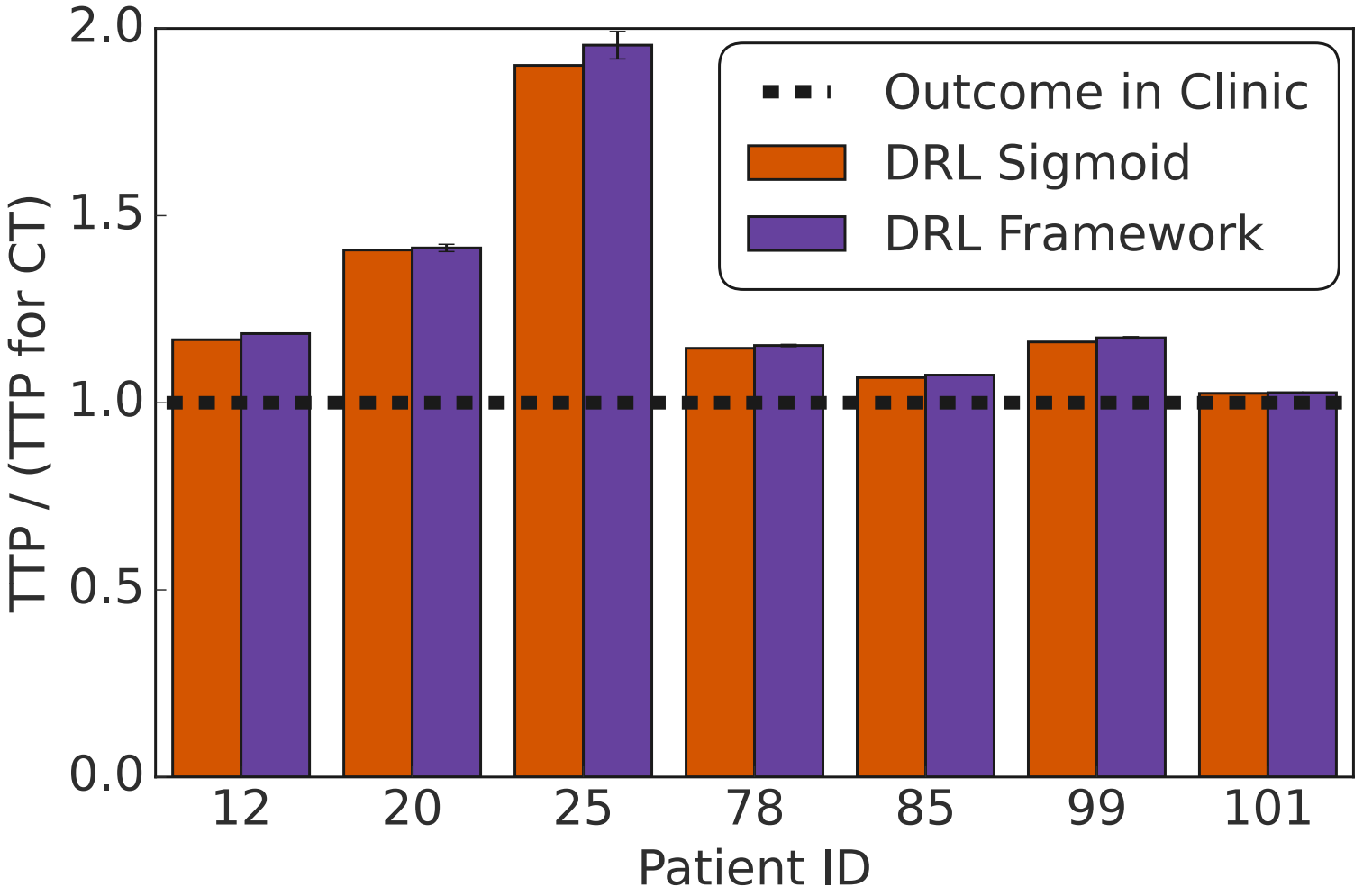


$$n^* = \frac{K(d_S - r_S)}{\left(\frac{K(d_S - r_S)}{1.2n_0} + r\right)e^{(r_S - d_S)\tau} - r_S}$$

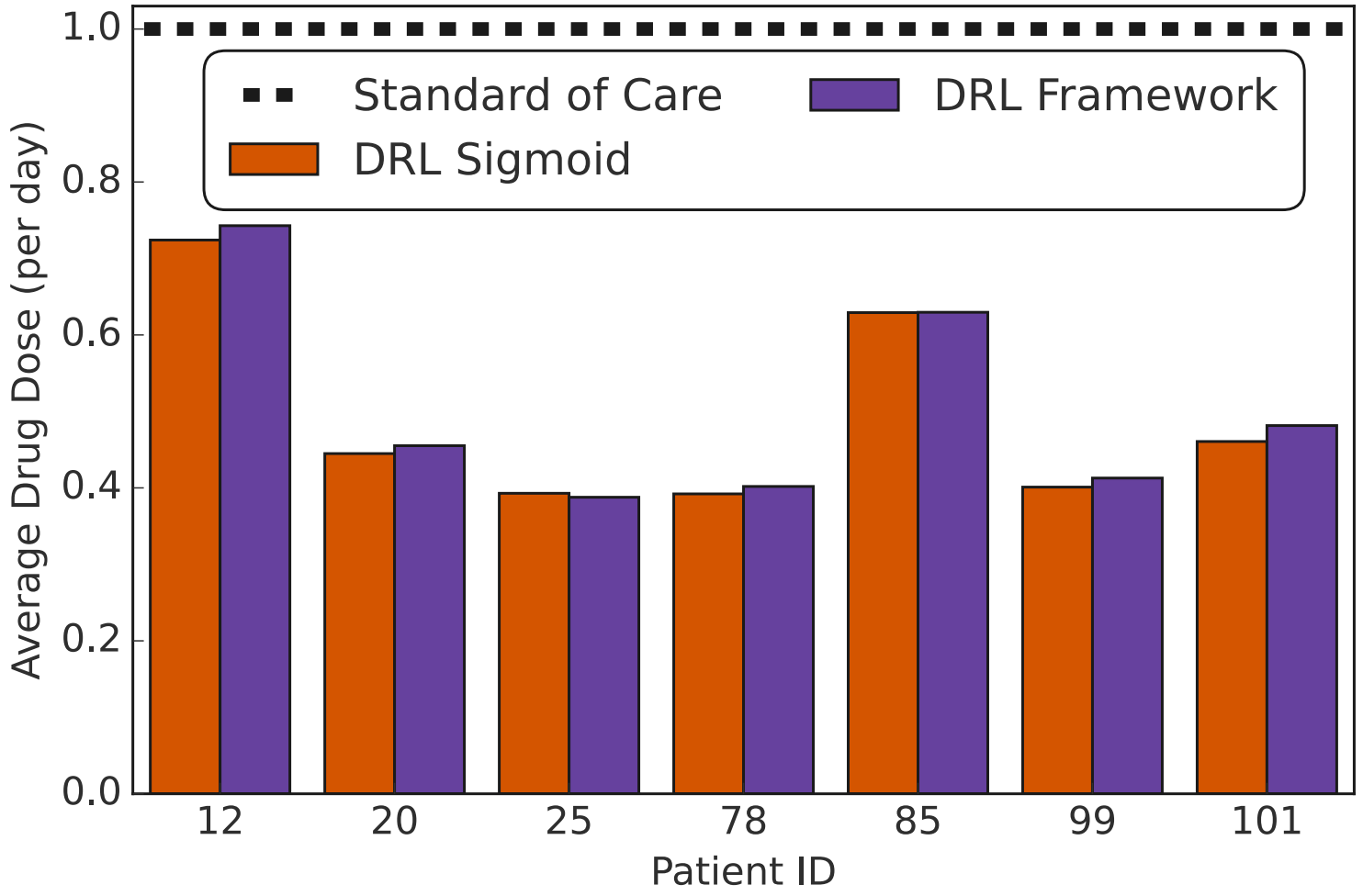
Tailoring Treatment to the Individual Patient



Personalised Treatment Schedules Outperform Clinical Standards



Personalised Treatment Schedules Reduce Cumulative Drug Burden



Summary – Part I

The DRL framework outperforms clinical standards across a range of patients

We can extract interpretable strategies from the DRL framework

These can personalise treatment schedules for individual patients.

Personalized Adaptive Thresholds

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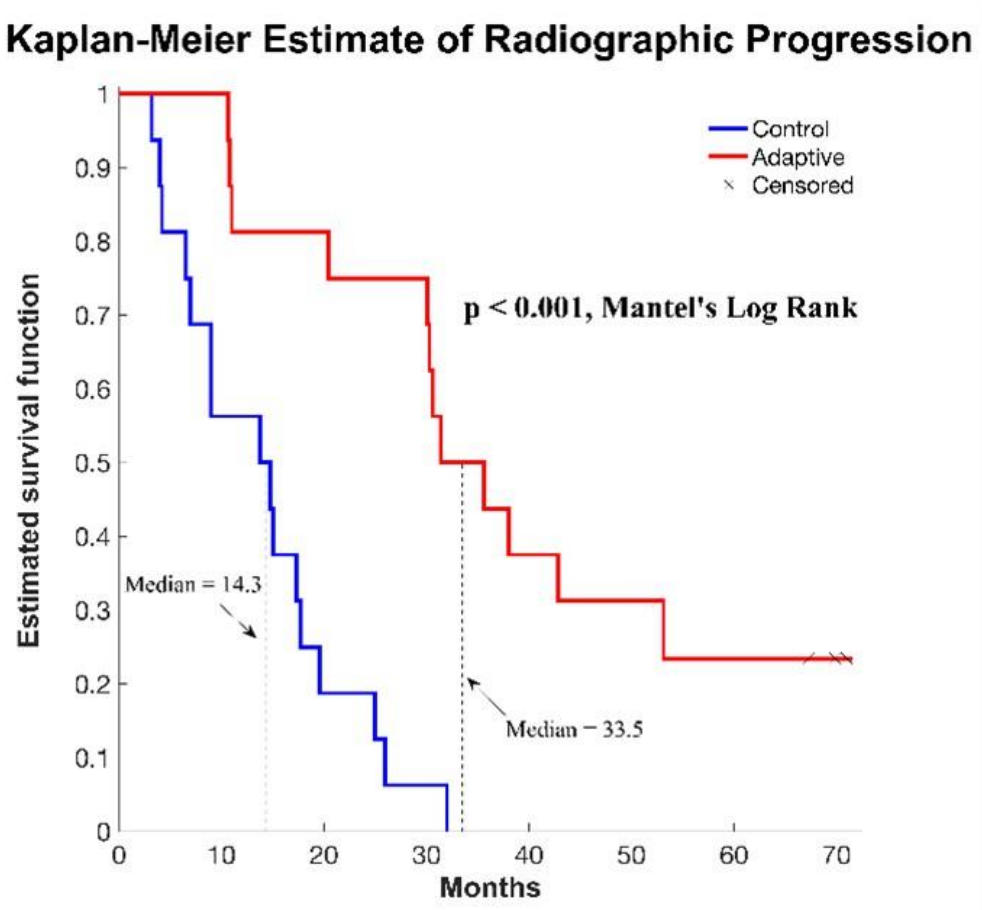
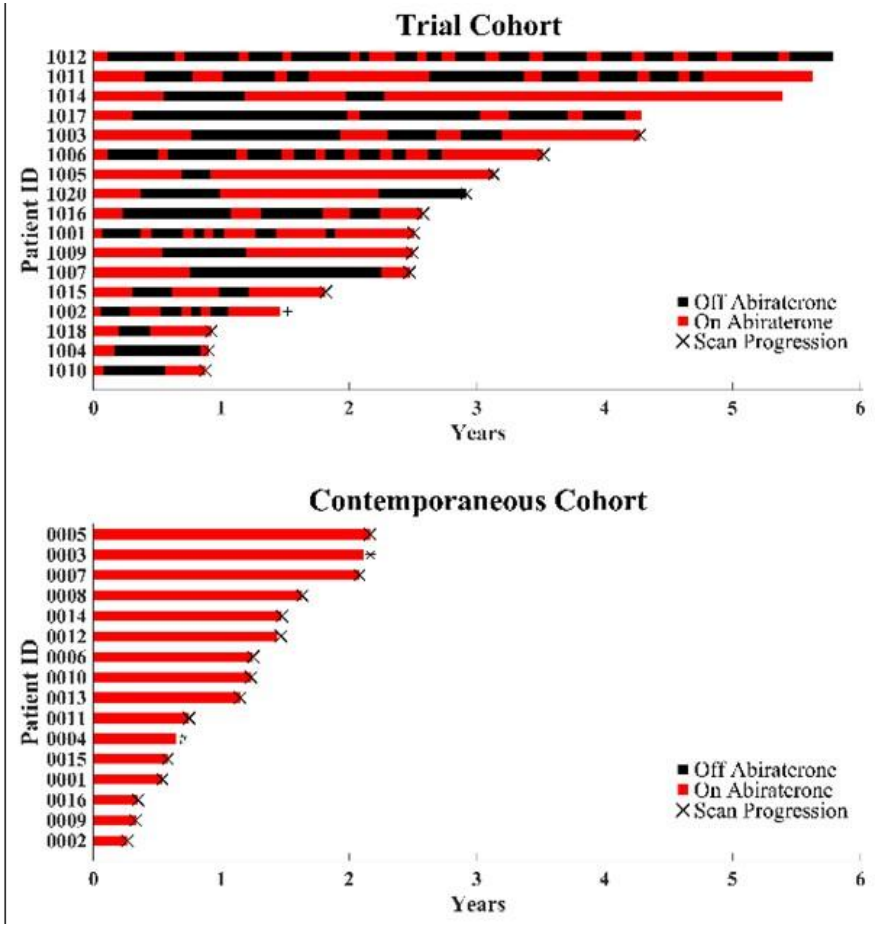
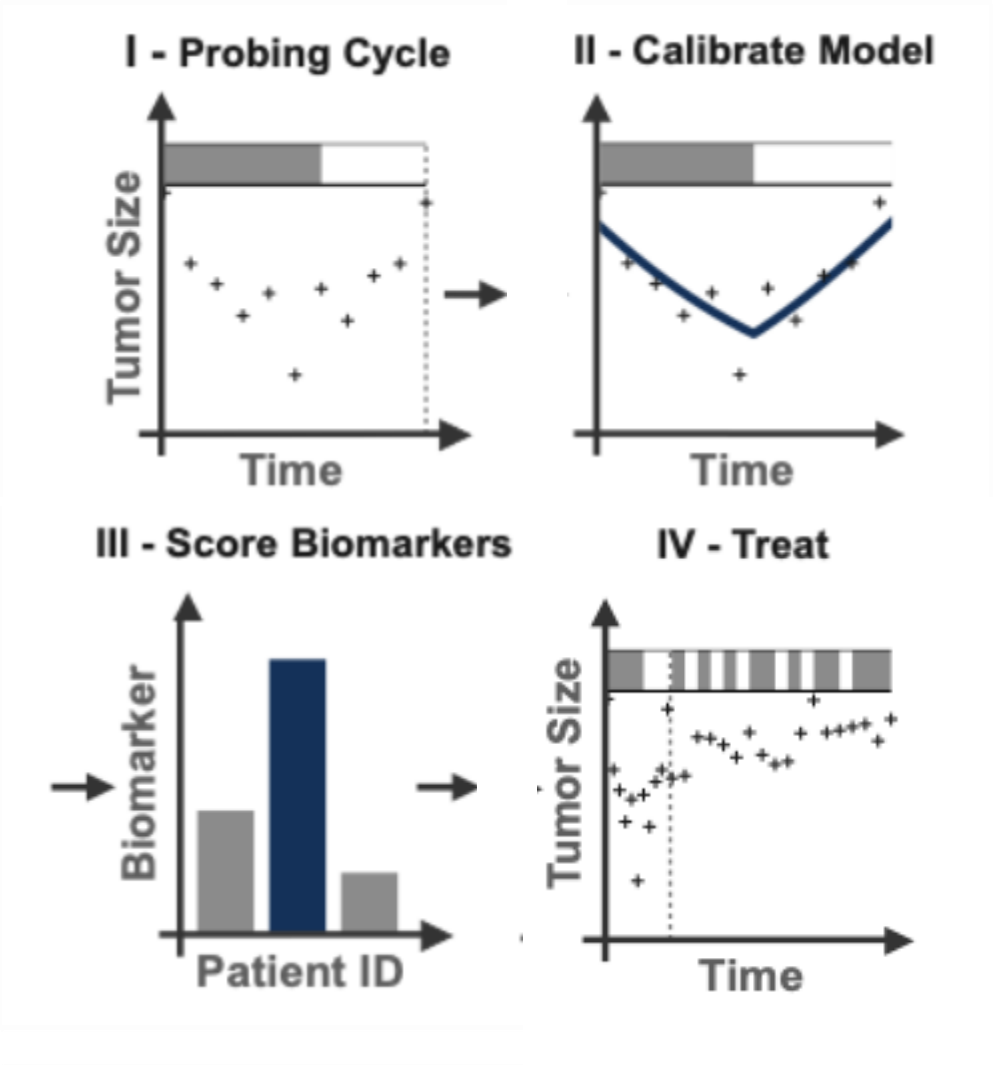
Heterogeneity in Clinical AT Responses



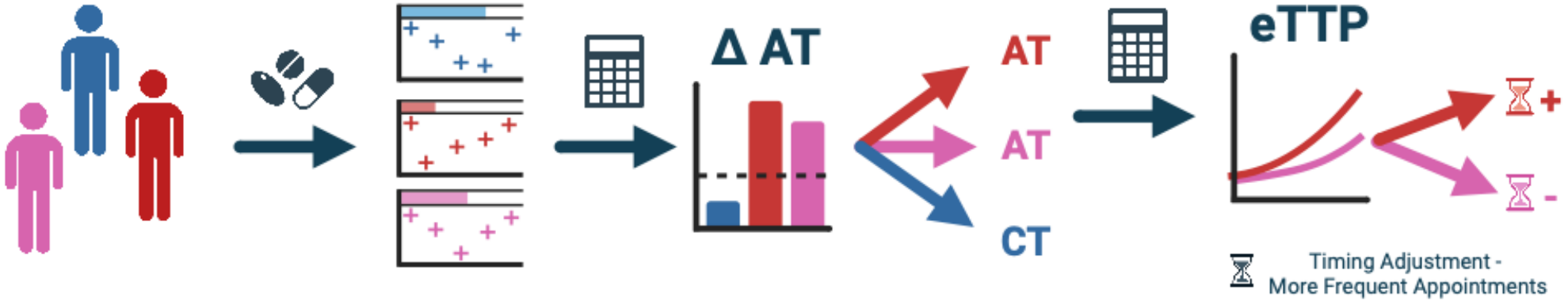


Jingsong Zhang, Jessica Cunningham, Joel Brown, Robert Gatenby (2022) Evolution-based mathematical models significantly prolong response to abiraterone in metastatic castrate-resistant prostate cancer and identify strategies to further improve outcomes. eLife 11:e76284.

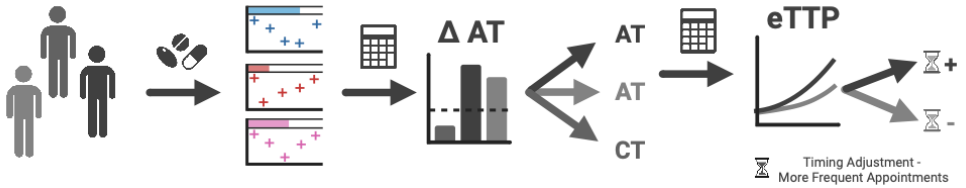
Estimating Patient Dynamics from 1st Cycle

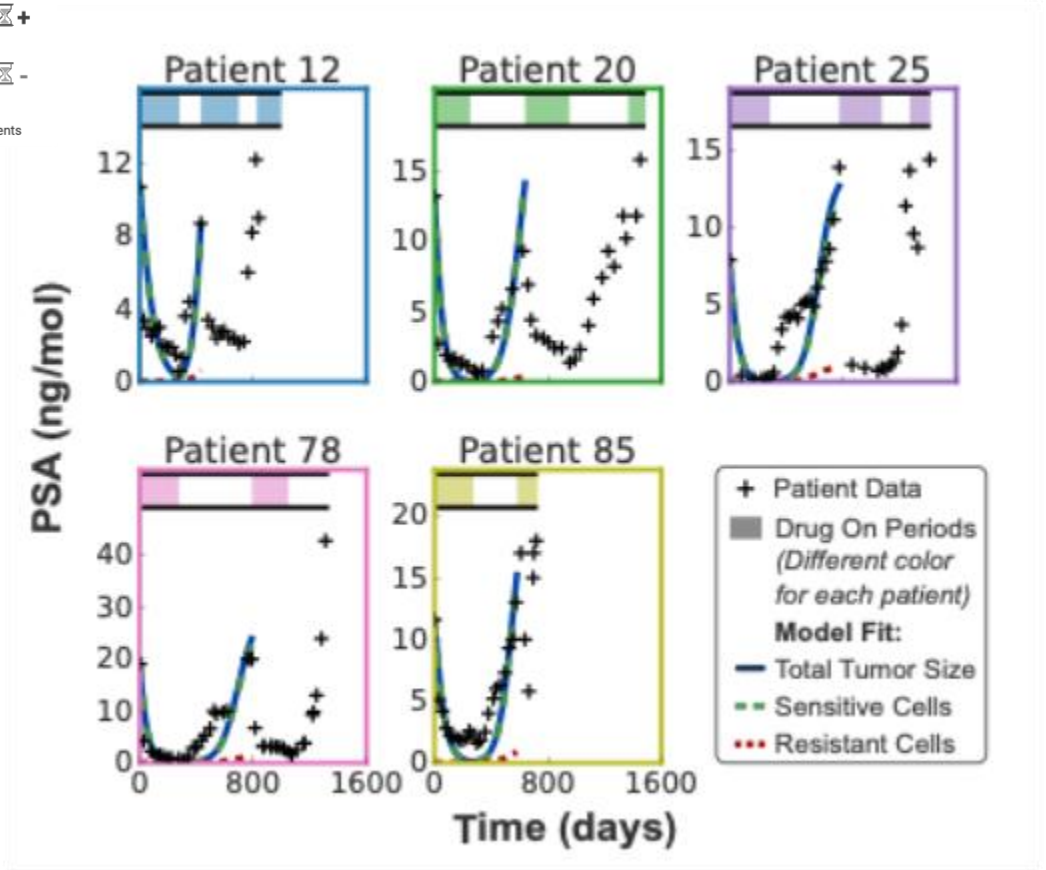


Clinical Implementation of the Mathematical Biomarkers



Stratifying Patient Treatments





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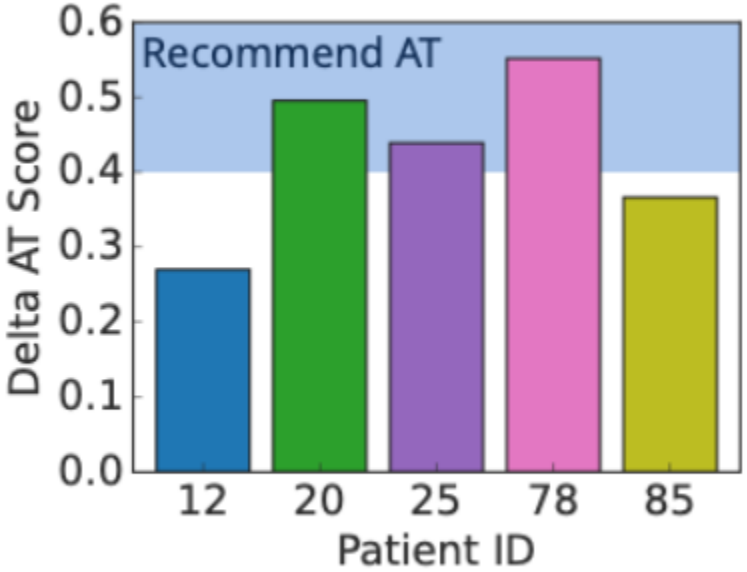

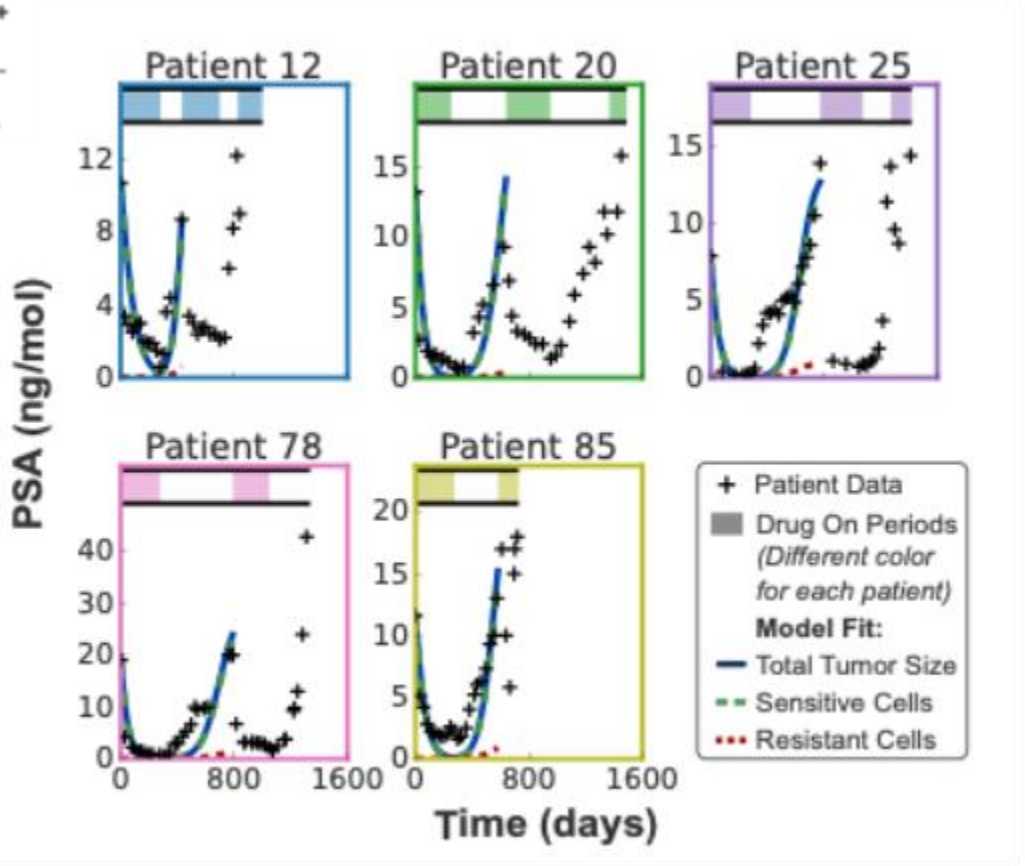

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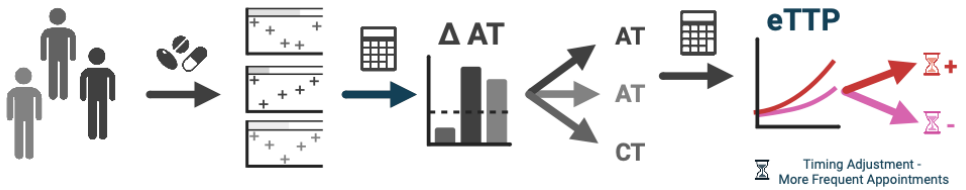
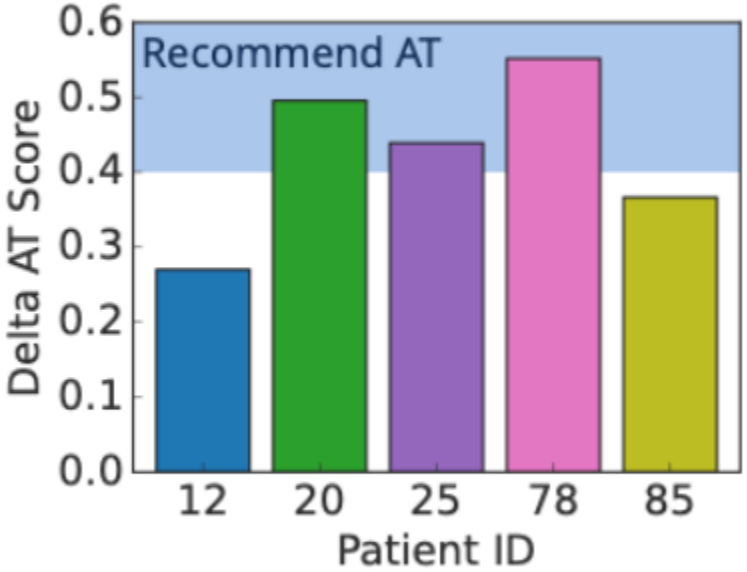
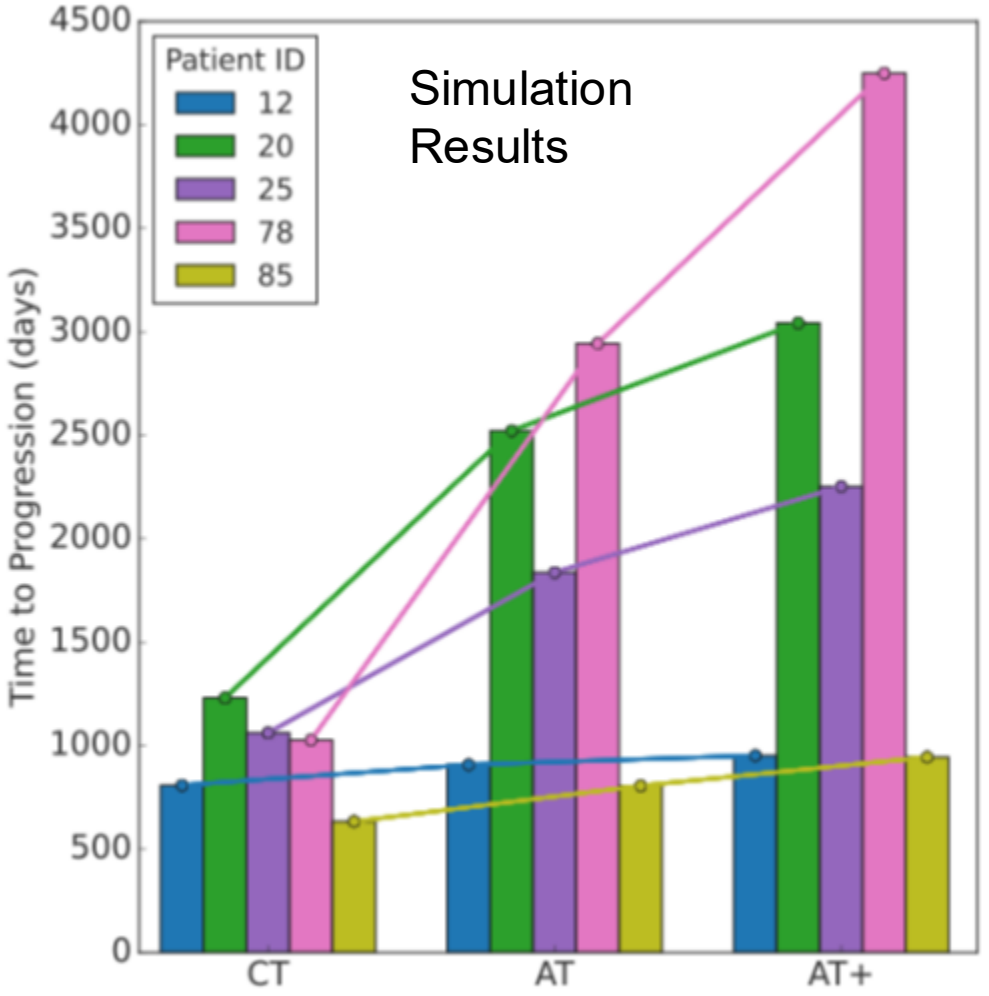






Recommend **AT+** for **Patient 78** based on eTTP score

Summary – Part II

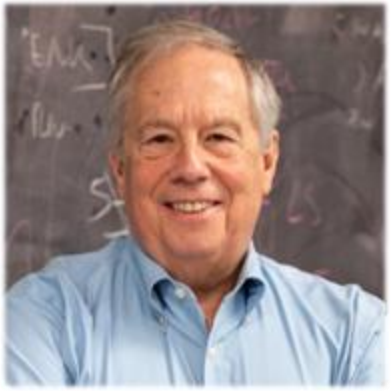
An initial probing cycle can quantify an individual's broad tumor dynamics

We can predict the benefit of adaptive strategies from key patient parameters

Clinically feasible strategies should be tailored to individual patients

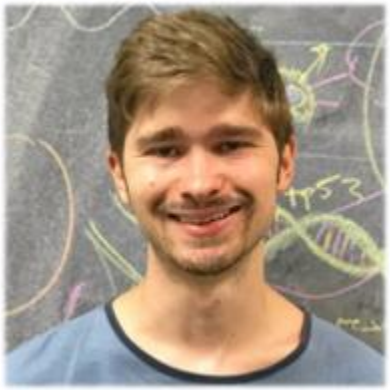
Acknowledgements

Dr Alexander Anderson
Moffitt Cancer Center, Tampa



Dr Robert Gatenby
Moffitt Cancer Center, Tampa

Paper on DRL work



Dr Maximillian Strobl
Cleveland Clinic, Ohio

Prof. Philip Maini
Mathematical Institute, Oxford

Preprint on Math Biomarkers

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