Poster Number - 5088

Using Computer Vision To Resolve Proliferative Dynamics Within Therapeutic Responses in Large-Scale Screens of Patient-Derived Models

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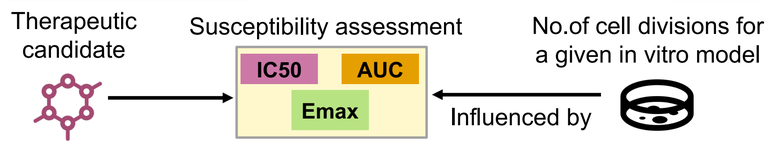
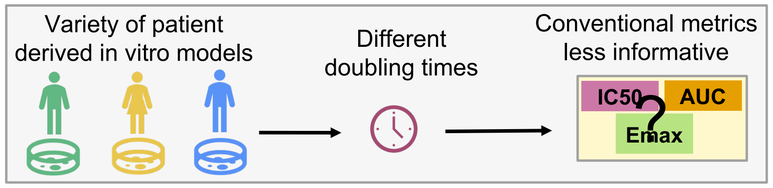
INTRODUCTION





Assay measuring cellular biomass → X → Cytostatic vs cytotoxic mechanism differences overlooked

Endpoint viability → X → Tedious temporal optimization, Difficult cross-therapeutic and cross-model comparisons

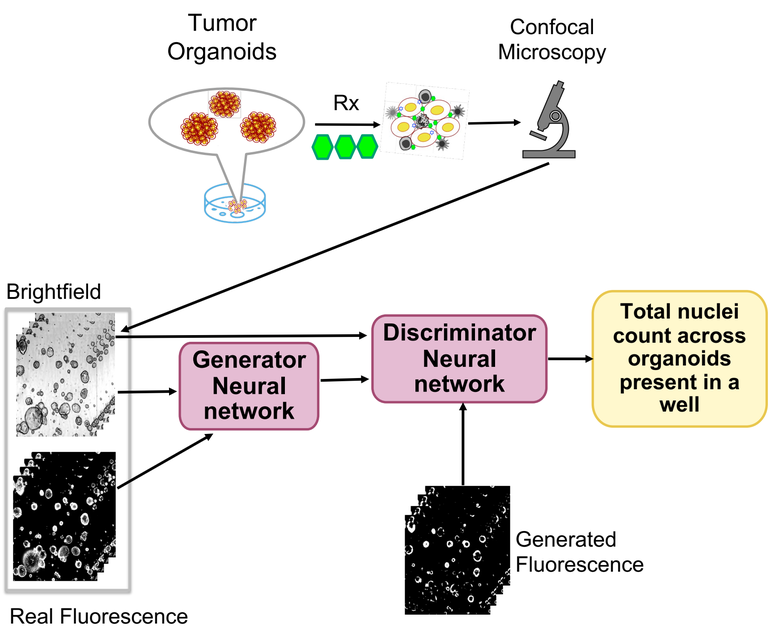
Assay combining above features → ✓ → Accurate measurements of drug effects and growth-adjusted IC50 values

METHODS

Goal: To develop a computer vision model that dynamically tracks proliferation dynamics via label-free longitudinal light microscopy

Outcome:

- To report the total number of nuclei, present within a given experimental well
- Monitoring of cell division and any cytostatic effects.



SUMMARY

This tool will enable cross-comparison of different therapeutic mode of actions as well as enable cross-cancer type/indication comparison for a therapeutic candidate in development to inform early development clinical strategy

RESULTS

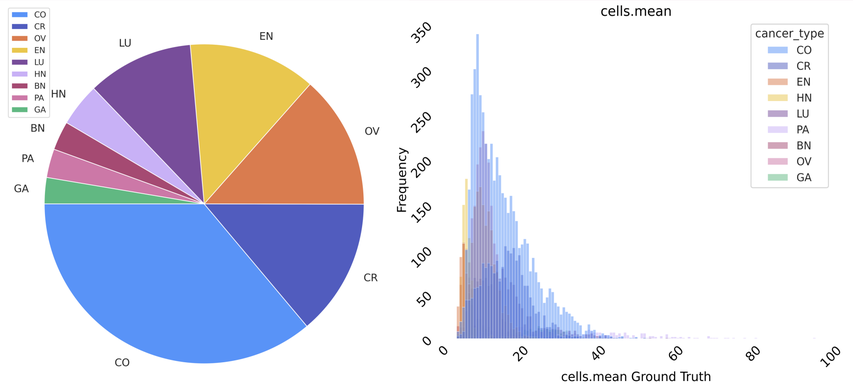


Figure 1 - Distribution of training cohort by cancer type and ground truth total nuclei count

Expt	Description	Pearson R Correlation
allchannel	all 3 stains of the vital dye channel as an input	0.797
blue16bit	Hoescht channel larger tonality, other 2 channels 0	0.809
gray16bit	Hoescht channel larger tonality, other 2 channels same as Hoescht	0.802
blue8bit	Hoescht channel smaller tonality, other 2 channels 0	0.761
gray8bit	Hoescht channel smallertonality, other 2 channels same as Hoescht	0.771

Table 1 - Pearson R correlation scores across 9240 wells for each experimental condition

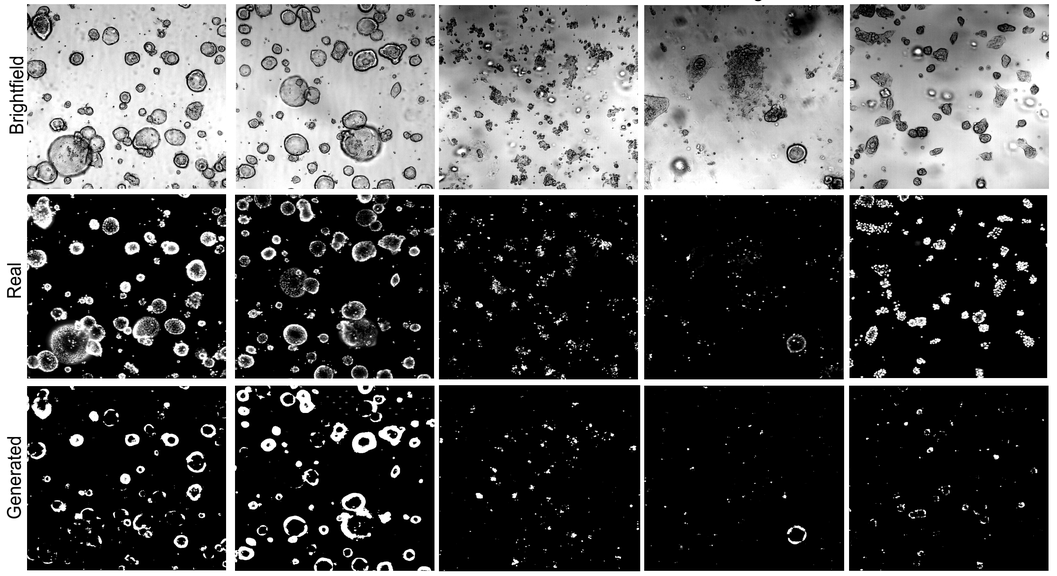


Figure 2 - Visual comparison across differing cancer types for the best experimental condition

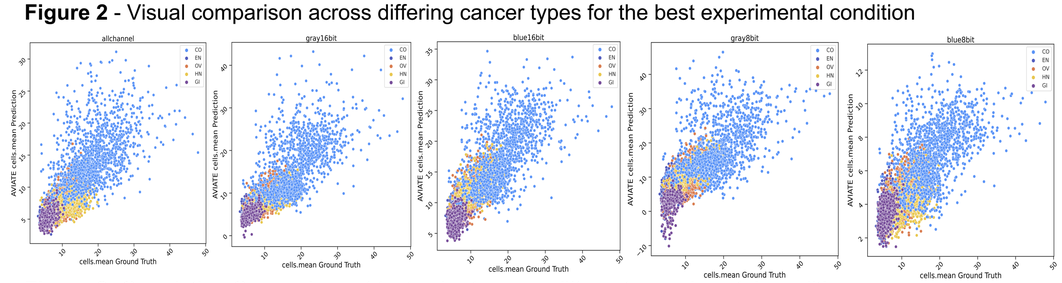


Figure 3- Correlation Comparison of test cohort across different experimental conditions

- Five experiments were conducted during training to test for bit depth and tonality effects of the raw brightfield images acquired from the confocal.
- Inference on 9240 images showed a Pearson R score of 0.8 on the best-performing model
- Overall, the 16bit experiments outperform the 8bit experiments indicating that a potential loss of information deteriorates model performance.
- There was no significant effect between gray and blue channel experiments.
- Our model shows higher variability in predicted total nuclei counts for wells that have a higher recorded number of mean live cells, potentially due to the imbalance in training distribution.
- This model can be applied to simple light microscopy to robustly measure dynamic proliferation phenotypes during drug treatment

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