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Abstract

TODO

1. Introduction

Predicting tumor growth rate is a first step in determining treatment options for cancer patients. Fast growing tumors necessarily require more aggressive treatment. It would be beneficial if patients could avoid aggressive treatments when possible.

Alexandra Sockell of the Fordyce and Curtis labs in the Genetics department of Stanford University has developed a microfluidic device to isolate single cells of a tumor and allow them to grow into organoids within the microwell. Organoids are three dimensional stem cell-like cultures that organize into a "mini-organ" [4], and can be used to study cancer in a more natural environment than traditional cell lines [1]. The objective of her research is to study the mechanisms of tumor growth by studying individual cells across a wide range of treatments and conditions. She has taken 14 days of imaging over approximately 40 conditions. For each day, there are approximate 200,000 wells image, most of the wells do not have any cell, 25% have one cell and smaller portion have more than 1. We believe that this should be a sufficient amount of data and information content to apply deep convolution neural network approach.

Previous approaches for high-throughput analysis of organoid imaging data did not look at single-cell microwell level data. Instead they typically relied upon a large number of cells to quantify cell proliferation or death [3], used cell counting assays to calculate growth [5], or used single cell tracking to calculate cell motility [2]. To our knowledge, no deep learning approaches have been proposed to analyse organoid imaging data, despite the large success in deep learning to analysing imaging data across a broad spectrum of applications.

Data

To achieve the goal of predicting tumor growth, we took the objective as predicting the final size of the tumor after 13 days of growth. The final size is calculated by image segmentation of the interior of the microwell (Fig3). We normalized the sizes to have variance equal to one. However, we did not mean center the data because we believe a final size equal to zero has meaning. A final size equal to zero corresponds to either empty wells or cells that died.

For input we took the day 1 images. We determined that the day 0 images are not suffcient to predict All images are black and white, so we converted them to greyscale and normalized the pixels to have zero mean and unit variance. Our resulting images are 193×193 with a single channel. An example input image is show in figure 3.

Model

To show the feasibility of a deep convolutional approach, we constructed a preliminary deep learning model consist-

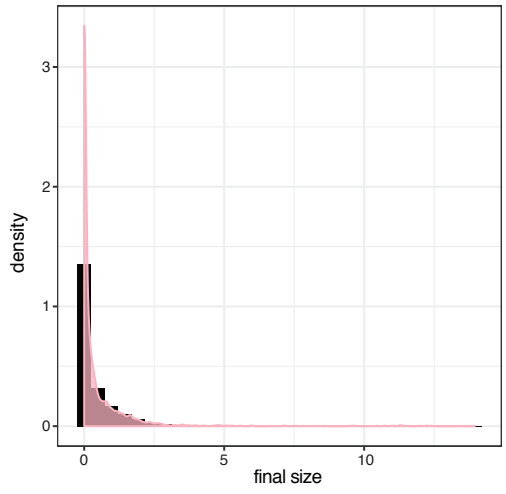

Figure 1. Distribution of normalized final sizes. There is a large peak at zero corresponding to empty wells or cells that died.

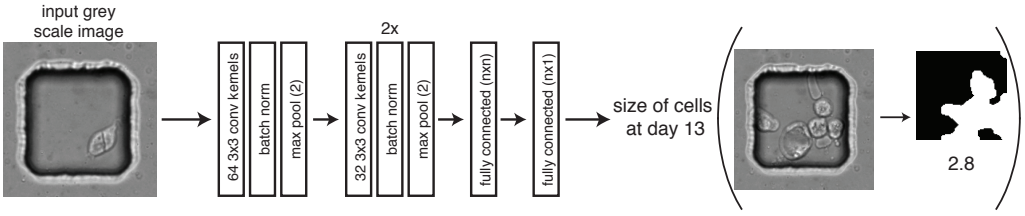

Figure 2. Example workflow of our algorithm. The input is a 193×193 greyscale image of the cell at day one. We pass this through a convolutional neural network to predict the final size, normalized to have variance equal to 1.

ing of three convolutional layers, applying batch normalization and max pooling to each layer, followed by two fully connected layers. As an initial test we use two hundred randomly selected images as a training set and one hundred randomly selected images as a training set.

More details here.

1.1. Miscellaneous

References

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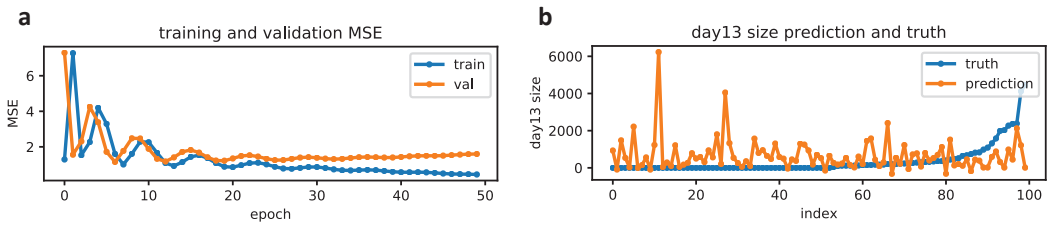

Figure 3. **a** The training error (blue) and validation error (orange) as a function of training epoch. **b** Predicted final size and observed final size, with the index ordered by observed final size.