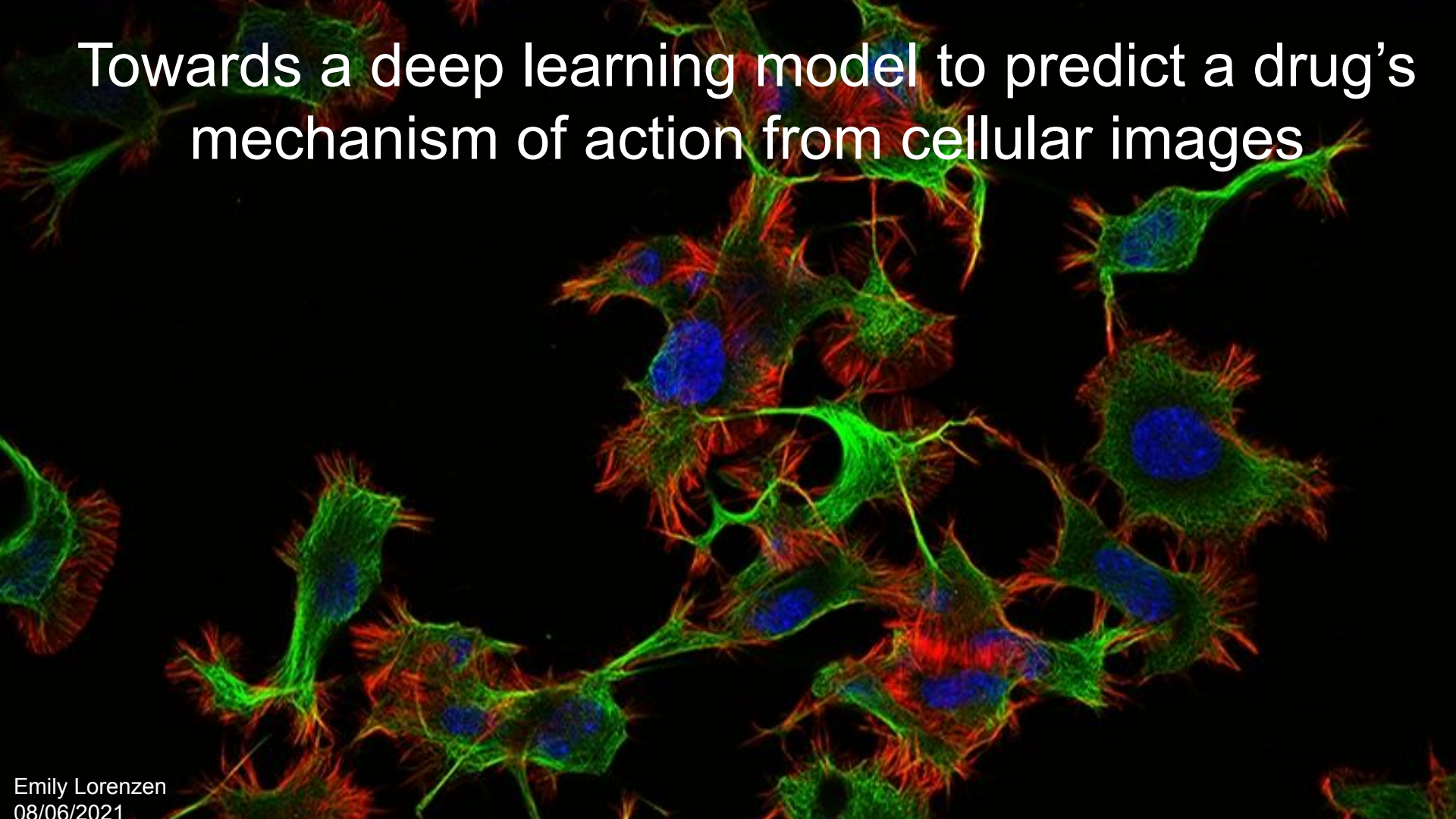
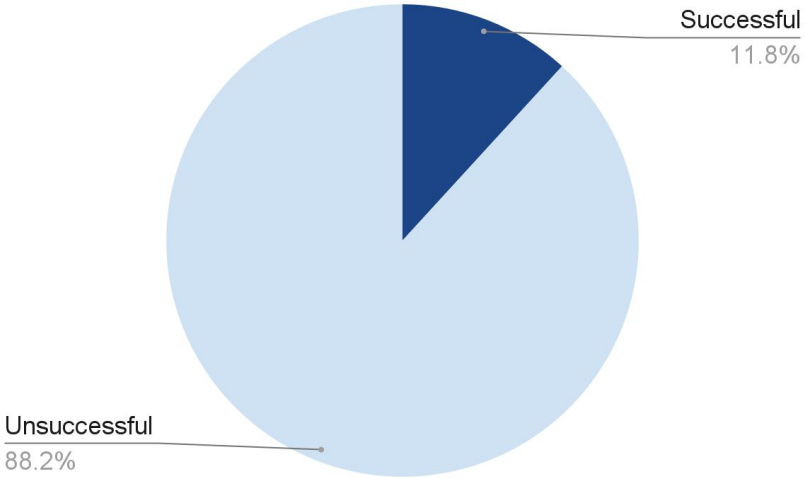
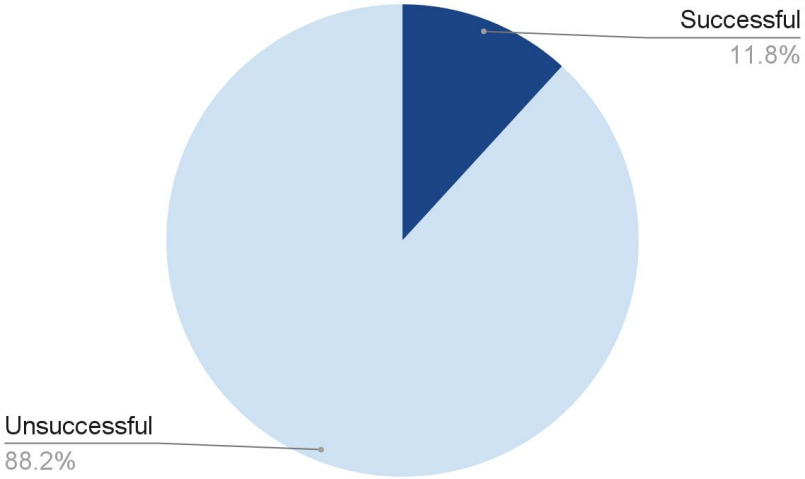
Towards a deep learning model to predict a drug's mechanism of action from cellular images



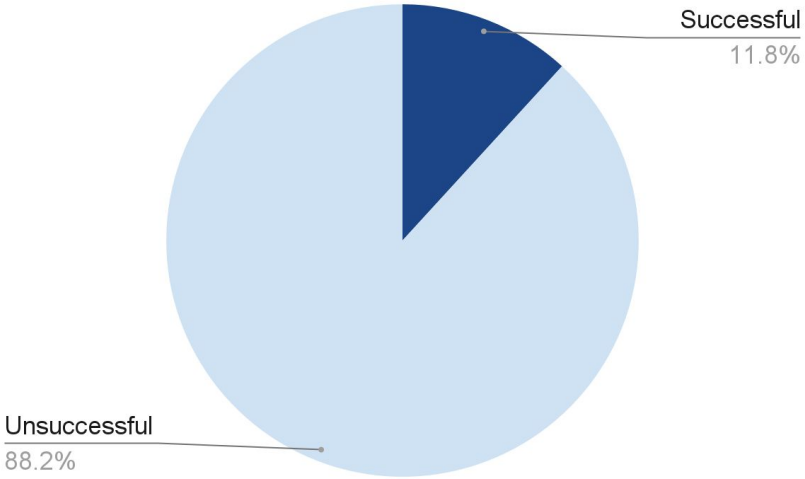
Emily Lorenzen
08/06/2021


Successful
11.8%
Unsuccessful
88.2%



Cost of a failed clinical trial:

~ $800 million



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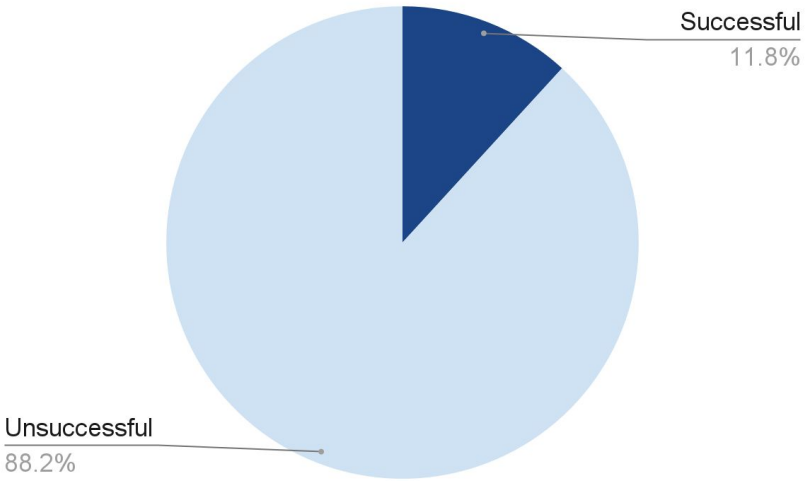

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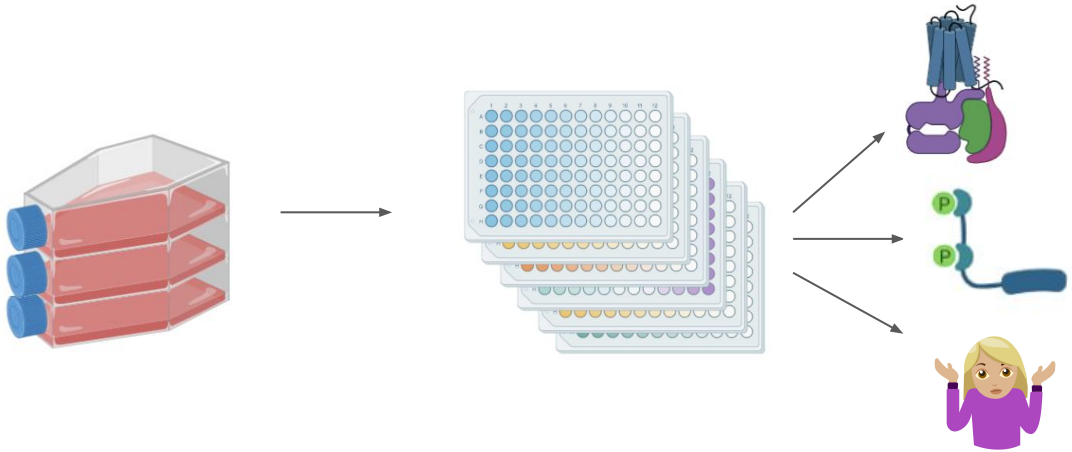
Mechanism of action (MoA) experiments

<u>Current paradigm:</u>

Culture stacks of cells

Perform many assays

Determine MoA if correct assay was chosen



Mechanism of action (MoA) experiments

Current paradigm:

Culture stacks of cells

Perform many assays

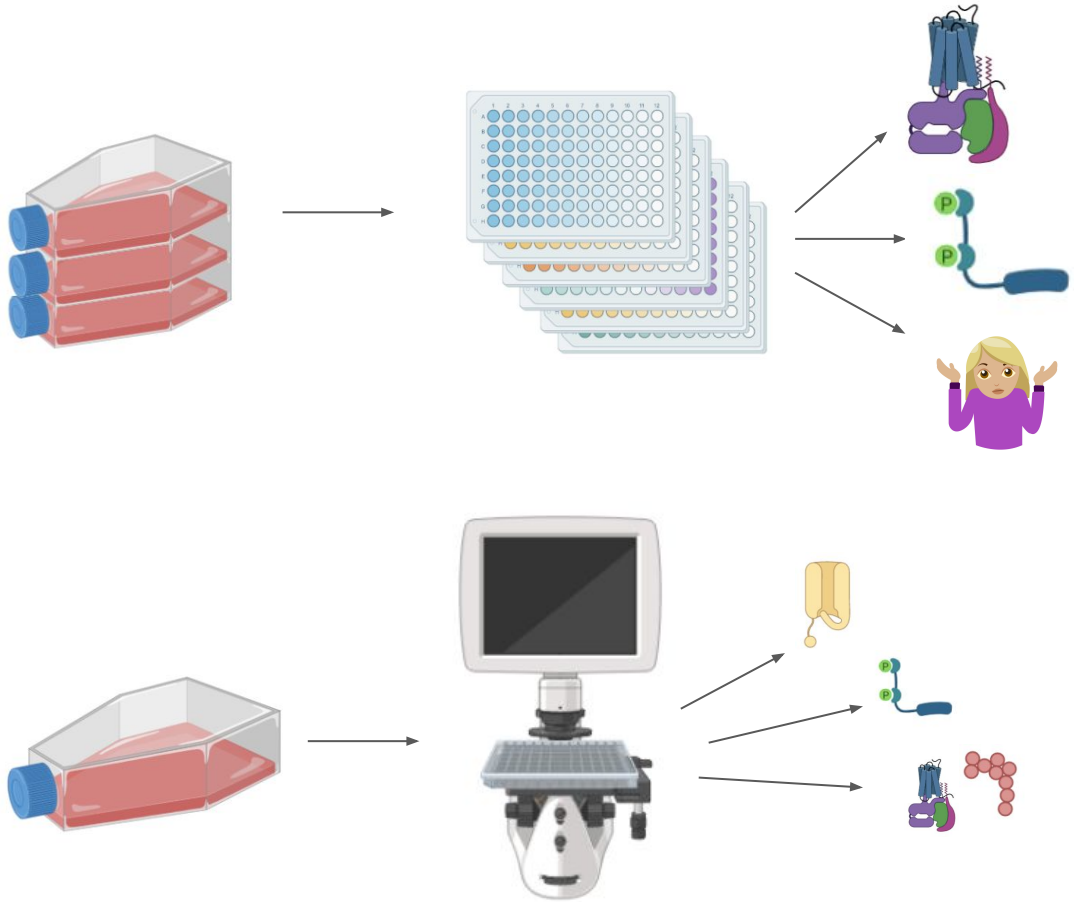
Determine MoA if correct assay was chosen

Future paradigm:

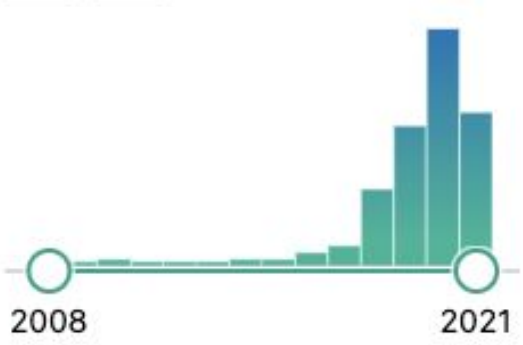
Culture fewer cells

Perform one imaging experiment

Determine MoA based on deep learning models



Application of deep learning to cell imaging



Number of publications in 2020:

256

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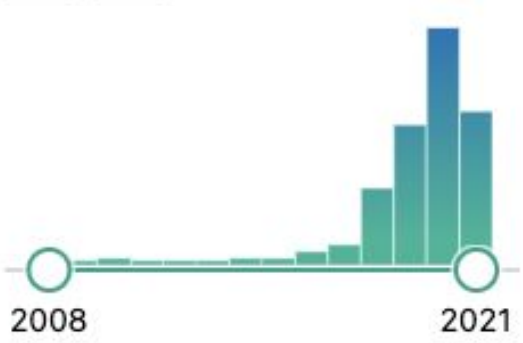

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Article | Open Access | Published: 06 August 2020

Tales of 1,008 small molecules: phenomic profiling through live-cell imaging in a panel of reporter cell lines

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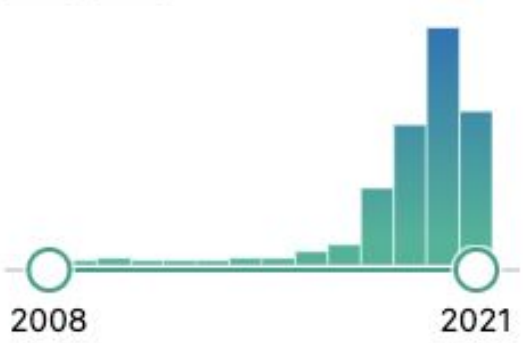

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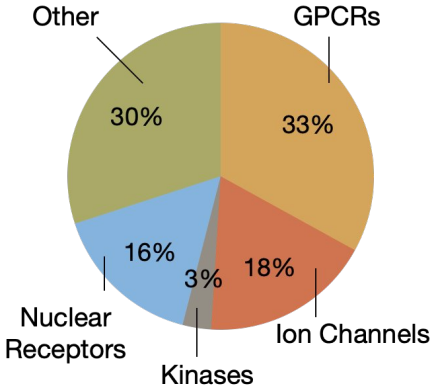
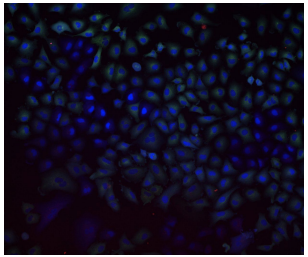
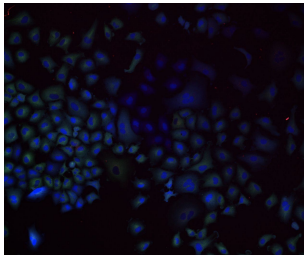
Simplification:

Focus on MoAs involving a GPCR



~33% of FDA-approved drugs target GPCRs





Transform to array

Pre-trained convolution model - MobileNetV2

Flatten

Dense

Dropout

Dense

Final Model

Approach

Manually annotate MoA

Gather and process images

Convolutions

Neural network

Output predictions

Experiments performed

- Add convolutional layer
- Add dense layer
- Change activation function to leaky relu
- Transfer learning
  - **MobileNetV2**
  - ResNet50

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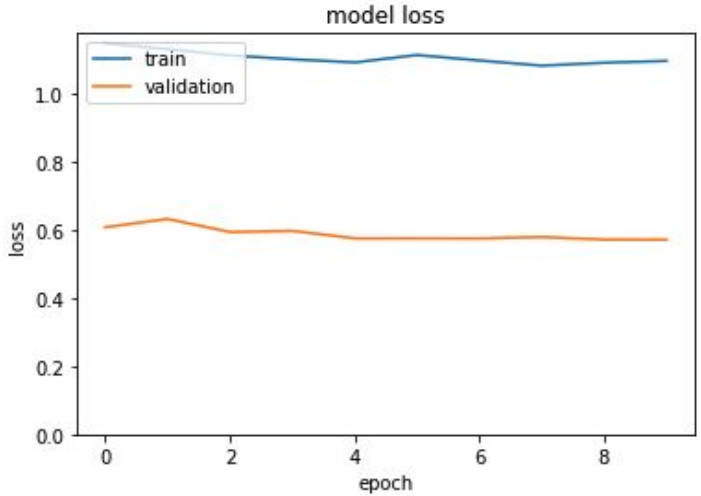

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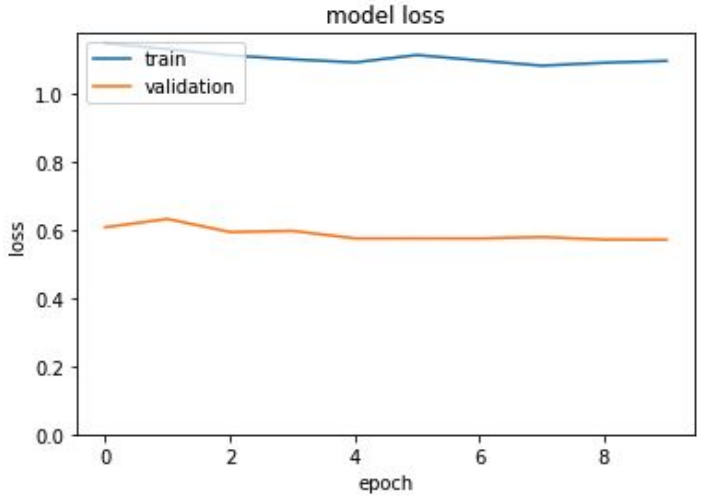

Test data loss

0.6283

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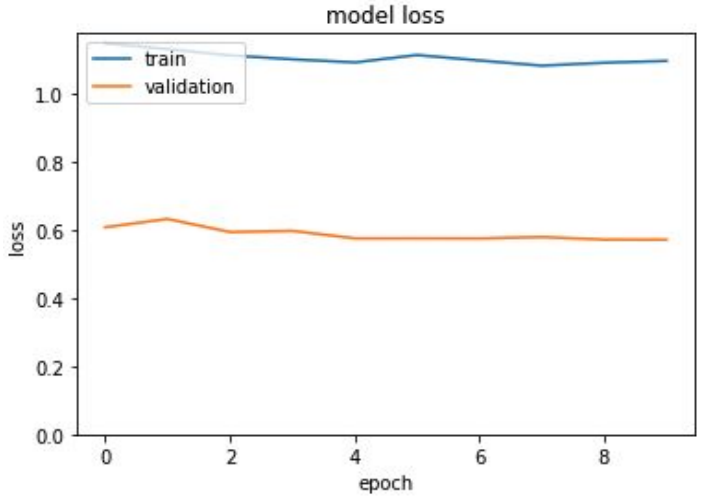

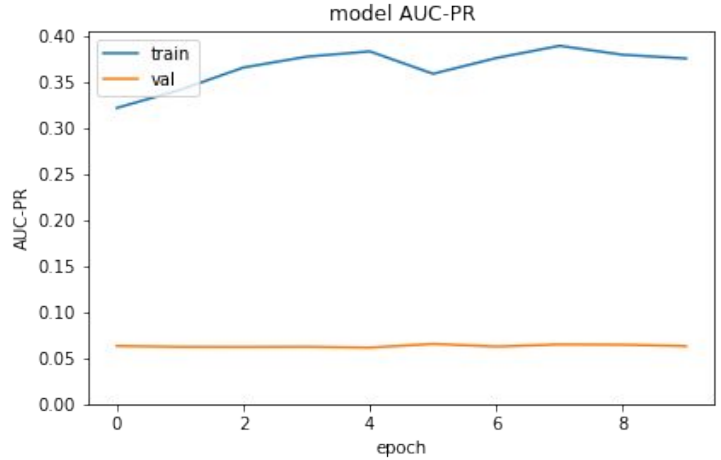

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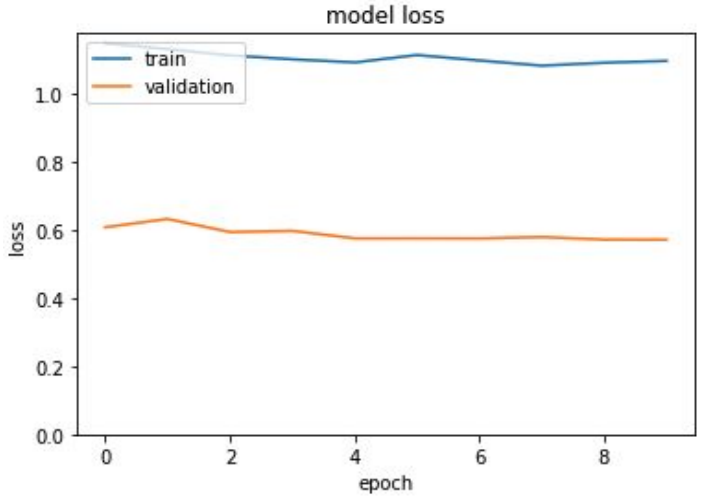

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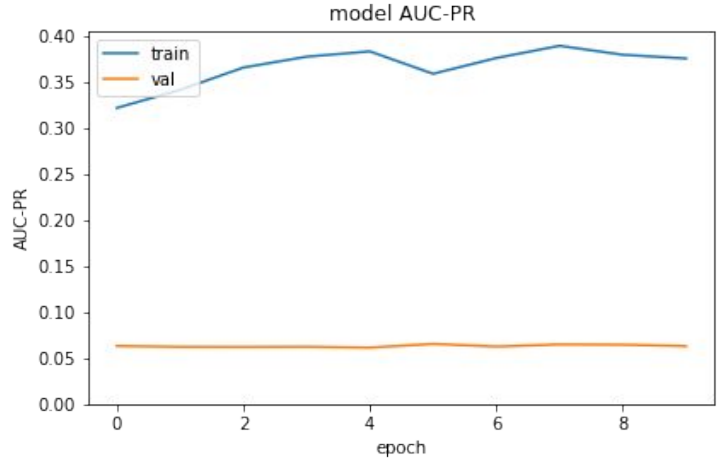
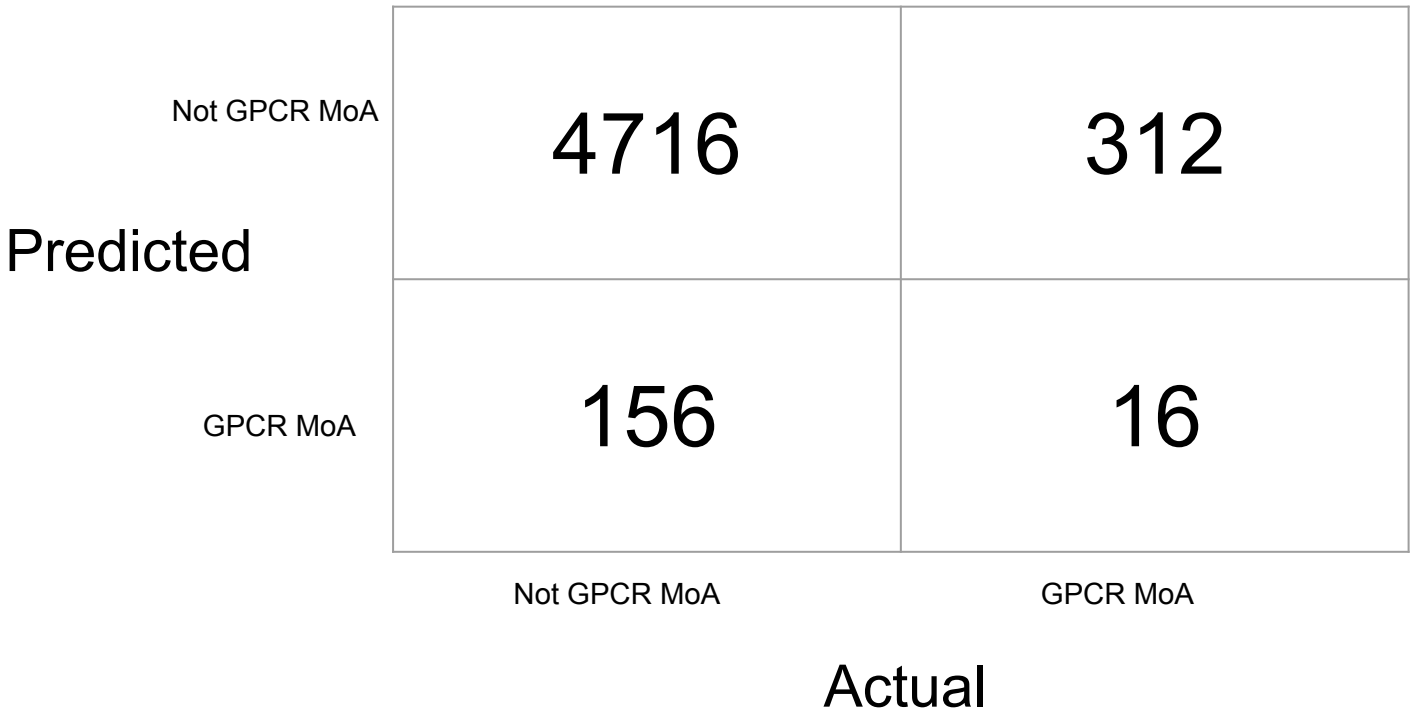


Test data AUC precision-recall

0.0733

Confusion Matrix



Insights for future development

Computationally slow
~350 sec/epoch

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Use GPU instead of CPU

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→ Add regularization methods