Connect the Dots: Quantitative Isothermal Amplification Machine Learning

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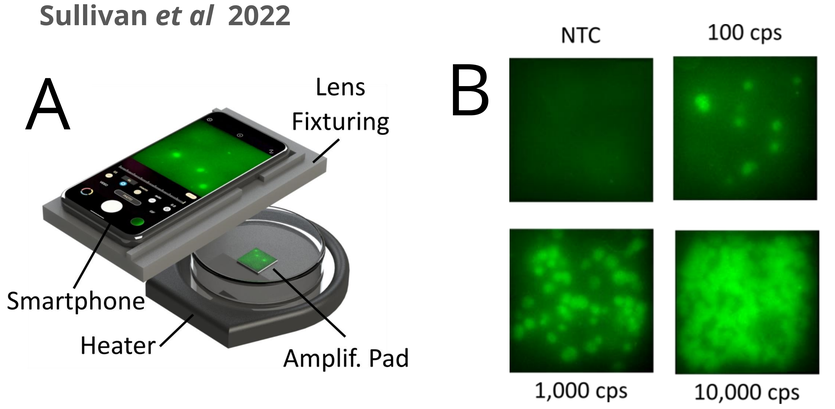
Introduction

- Quantitative nucleic acid amplification tests are critical in clinical diagnosis of infection of pathogens like SARS-CoV-2 and HIV.
- Quantitative PCR is the gold standard in diagnosis but slow time to result, high cost, and fragile substrates limit the distribution of these tests.
- Qualitative binary pregnancy style tests while faster, lower cost, and robust don't inform on disease or infectivity progression.
- Recent publication in the Posner Lab Group has demonstrated successful transformation of a previous qualitative PCR like assay can be quantitative through a site nucleation to initial copy correlation

Background

- Quantitative isothermal amplification on paper membranes using amplification nucleation site analysis.

Sullivan *et al* 2022

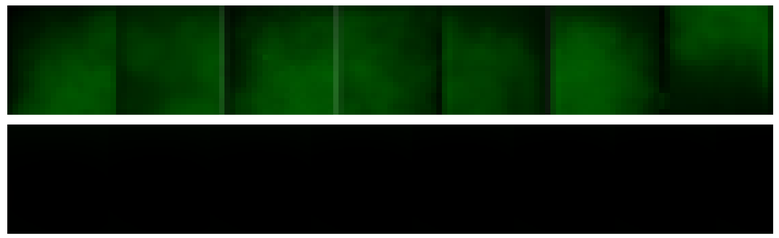


(A) Image acquisition setup. (B) Images a varying DNA input, notice site overlapping. (C) Strong linear correlation with input DNA and number of sites. Blue line is microscope data, Yellow is phone data, Orange is RNA data.

Evaluated technologies

Autoencoder

- Dimensionality Reduction for Pseudo Images
- Failed for Cut Images with Continuous Model but may benefit from Tiff Format
- Boundary Ambiguity & Small Training Size



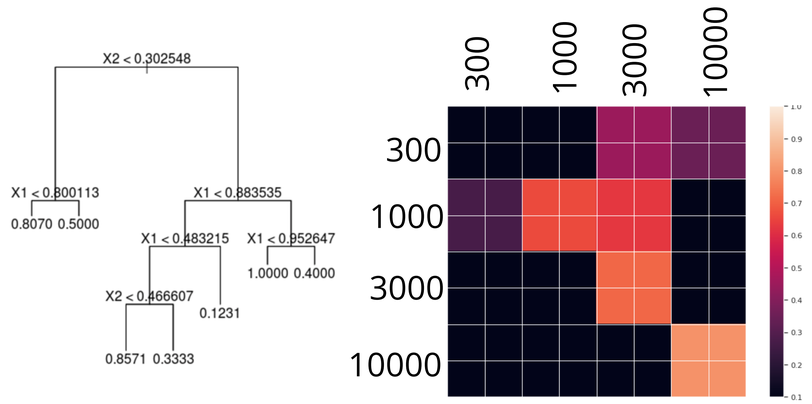
Convolutional Neural Network

- Images split into three categories
- Low, Medium, High input
- Low accuracy hindered by low image count (14)

Fewshot and adaptive learning

- models did not increase accuracy.

Decision Tree model

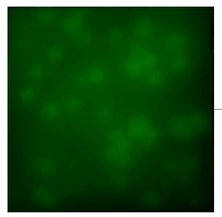


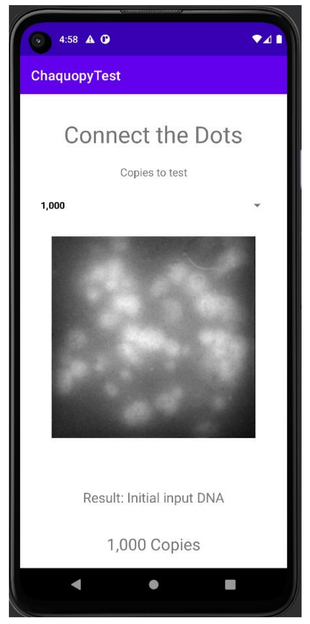
Decision tree learning is a modelling approach that takes in image statistic features to make a prediction. It uses a decision tree (like a 20 questions game) to go from observations about an item to conclusions. The number of branches is how many questions the model asks to make a prediction. We use a variable number of branches (subsequently multiple models) to find the best classification.

Interacting with the model

Streamlit web app

User-interface website enable user to uploaded the selected figure and acquired the prediction result from model.





Android App

- When combined with image acquisition system, allows for edge computing acquisition, preprocessing, and analysis
- Proof of concept of edge computing use case
- Image acquisition and site counting on phone demonstrated by Sullivan *et al*

Conclusion

- Machine learning algorithms can be applied to extend the linear range of previous publication.
- Decision tree model further extends the linear detection range of phone based quantitative site analysis by two orders of magnitude.
- Additional image sets are needed for further validation
- Framework is extendable to future datasets.

Acknowledgements

Quantitative Isothermal Amplification on Paper Membranes using Amplification Nucleation Site Analysis
Benjamin P. Sullivan, Yu-Shan Chou, Andrew T. Bender, Coleman D. Martin, Zoe G. Kaputa, Hugh March, Minyung Song, Jonathan D. Posner
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