

Machine learning supported image analysis of microfluidic droplets

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Microfluidic droplets

- Collaboration with Bio-Pilot Plant at Leibniz-HKI and Fraunhofer IOF
- Encapsulation of single cells in droplets
- Droplets are generated in the range of 100–1000 Hz
- Monitor microbial growth
- Demonstration of encoding of experimental conditions using color beads [1]
- Application of machine learning testing of eight different antibiotics validated by MicroSpotplate (MTP) experiments
- Using Deep Learning to determine growth stages in droplets
- Angle-resolved scattering spectroscopy to determine single cell division events

E. Coli growth calibration curves

Droplet encoding

Droplet content determination

Bead classification

Droplet decoding

- Each droplet has a true code (K_T) and the RF gives a detected code (K_D)
- $K_T = \{k_1, k_2, \dots, k_m\}$
- We are looking for the most likely code given:
 - Bayes theorem: $p(K_D|K_T) = p(K_T|K_D)p(K_T)$
 - The misclassification rate of the RF: $\pi_{K_D} = [k_1, k_2] = [2, 1]$
 - N_C : Number of detected colors
 - A multinomial distribution with equal probability for each color: $p(K_T) = P_{K_T}(p_{K_T}) = \frac{\sum_{i=1}^m n_i}{\prod_{i=1}^m (k_i)} \left(\frac{1}{N_C}\right)^{N_C}$
 - Most probable code: $p(K_D) = p(k_1|g) \cdot p(k_2|g) \cdot p_{K_D}(k_1) \cdot p_{K_D}(k_2) = 7.9 \cdot 10^{-15}$
 - Number of detected colors: $N_C = 2$
 - Antibiotic susceptibility testing: $p(K_D) = p(k_1|g) \cdot p(k_2|g) \cdot p_{K_D}(k_1) \cdot p_{K_D}(k_2) = 1.82 \cdot 10^{-16}$
 - No microbial growth: $p(K_D) = p(k_1|g) \cdot p(k_2|g) \cdot p_{K_D}(k_1) \cdot p_{K_D}(k_2) = 1.39 \cdot 10^{-16}$
 - 18 were wrongly decoded (<0.5%)

Github
github.com/applied-systems-biology/droplet_segmentation

Growth

 3000 droplets: Acc = 0.925, Rec = 0.788 and Pre = 0.992

Future developments

Deep learning

- Use Convolutional Neural Networks to learn growth at different time points
- Tuned version of the EfficientNet-B4 was used [3]
- Trained and evaluated on *E. coli* calibration curves

Angle resolved spectra

References

- [1] Svensson et al. 2019. Small 15(4):e902384
- [2] Svensson et al. 2019. J Immunol Res. 2019:573965
- [3] Liu and Lin. 2018. ArXiv 1805.04842
- [4] Svensson et al. 2021. Appl Opt 60(24):C04-C01

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