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Efficient Large-Scale Microfluidic Design-Space Exploration: From Data to Model to Data

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1 INTRODUCTION

Droplet microfluidics is well poised to improve the gold standard in many fields such as synthetic biology [2]. However, the lack of available design automation tools that can create a microfluidic droplet generator based on a desired performance, forces the design process to be iterative, inefficient, and costly, thus, hampering the wide-spread adoption of droplet microfluidics in the life sciences. Machine learning and design automation tools have advanced many fields with new capabilities, such as genetic circuit design, cell pattern synthesis, and multi-cellular mass formation design [1, 8, 9]. The recent introduction of low-cost rapid microfabrication techniques enables generation of large-scale experimental datasets which was previously not viable in a realistic cost and time-frame [7]. We previously developed an open-source machine learning based design automation tool, DAFD (dafdcad.org) [5], which can utilize the available data to provide both performance prediction and design automation. However, to achieve accurate performance prediction and design automation a full-factorial search in flow conditions (25) and an orthogonal design of experiments for geometry search (25 devices) were used resulting in a total 625 experiments. By analyzing the the contribution of each device to the exploration of the design-space, we identify a more efficient method to map approximately the same design-space with just 5 chips. Therefore, by utilizing a low-cost fabrication method droplet generation design-space was explored, analyzed, and understood, which in turn enables design automation of high-performance and high-end droplet generators in a viable and realistic cost-frame.

2 CONFIDENCE ELLIPSES

The observed performance of a microfluidic droplet generator can be summed up in two parameters: droplet diameter and generation rate. Since, all the 25 microfluidic devices were tested at the same 25 flow conditions, the devices that show a larger variation in the observed performance induced by changing the flow condition, is more efficient in exploring the design-space. A confidence ellipse can be drawn by using the variance of the 25 observed data per device in both directions (droplet diameter and generation rate) as given in Eq. (1):

$$\left(\frac{x}{\sigma_F}\right)^2 + \left(\frac{y}{\sigma_D}\right)^2 = s \tag{1}$$

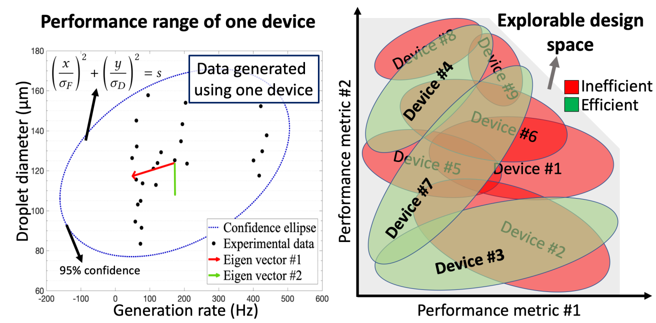

Figure 1: The performance range of a given microfluidic droplet generator design can be estimated by confidence ellipses. Using a dataset generated through a low-cost rapid prototyping method and a low-cost fluid combination, performance range of each design and the amount of performance overlap are approximated. This analysis reduces the necessary number of designs that should be fabricated and tested for extending design automation tools to cover new high-end fluid combinations and fabrication techniques.

where σ_F is the variance in generation rate, σ_D is the variance in droplet diameter, and s defines the size of the ellipse (confidence value). Since droplet diameter and generation rate are independent and by assuming a Gaussian distribution, Eq. (1) becomes a Chi-Square distribution [4], therefore, for a 95% confidence, $s = 5.991$. Using the covariance matrix of the data of each device, the eigenvectors are calculated to determine the angle that the ellipse takes.

3 EFFICIENT DESIGN-SPACE EXPLORATION

The workflow consists of three phases. **Phase 1** starts with cost and time-efficient exploration of the entire design-space using low-cost desktop micromilling to generate the initial large-scale dataset as we previously reported [6]. In **phase 2**, machine learning models are fitted to the data and using metrics such as coefficient of determination the accuracy of the predictive models and the sufficiency and diversity of the dataset are verified. Afterwards, iso-contours of the Gaussian distribution (confidence ellipses) [3] for the data points generated with a single device are used to determine the contribution of each device in exploring the design-space. The devices with a confidence ellipse that shows a lot of overlap with other confidence ellipses signifies an inefficient exploration. On the other hand, the devices with a confidence

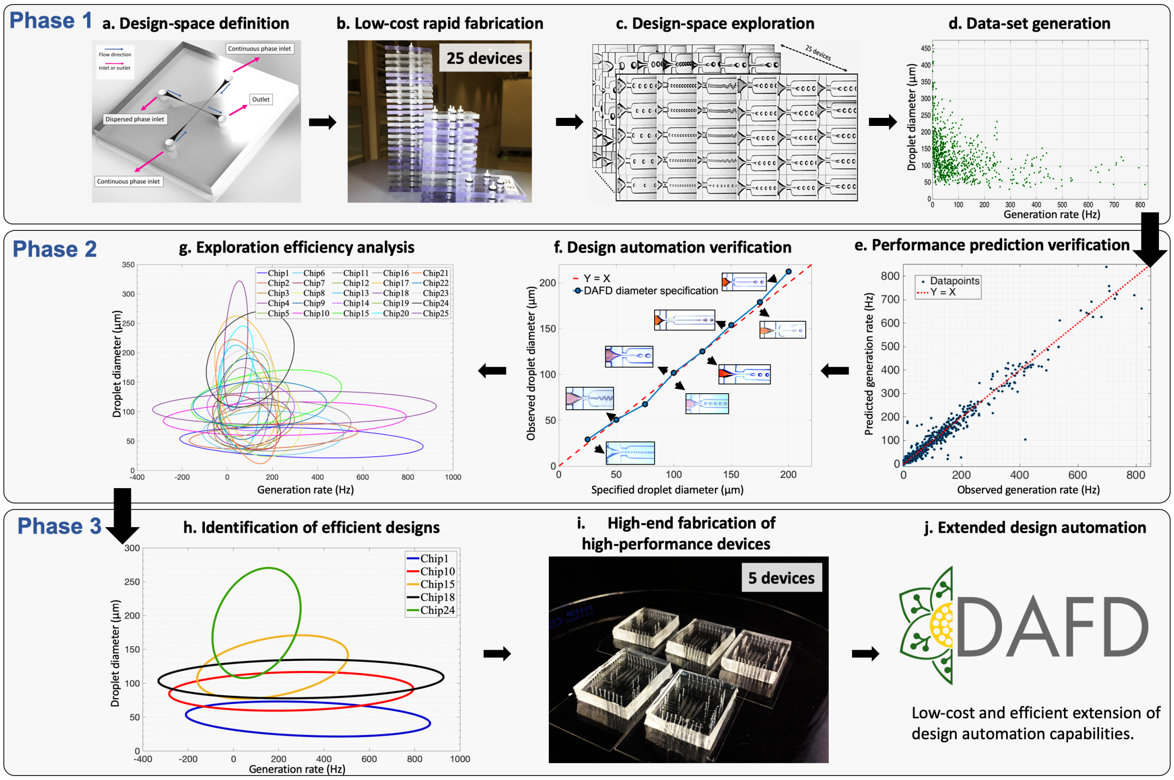

Figure 2: Phase 1: Low-cost rapid prototyping and design of experiments methods are used to generate a large-scale dataset. Phase 2: Machine learning based performance prediction and design automation accuracy and data sufficiency are verified. The dataset is analyzed to find a reduced number of devices that cover a similar design-space. Phase 3: The identified designs can be used for extending the capabilities of design automation tools to support high-end fluids and fabrication methods.

ellipse that has a minimum overlap and encompasses a larger design-space demonstrates a more efficient search. Therefore, in **phase 3**, we can remove the inefficient devices and determine the minimum number of devices that can be used to explore the design-space. Consequently, by significantly reducing the number of microfluidic devices necessary to explore a design-space, high-end fabrication methods and fluid combinations could be used to extend the design automation tool to support high-performance microfluidics in a time- and cost-efficient manner.

4 CONCLUSION AND FUTURE WORK

Machine learning algorithms enable accurate microfluidic design automation. However, generating large-scale datasets required for training these algorithms are resource intensive. Therefore, efficient frameworks are required for extending design automation tools. In here, we used information inferred from a dataset generated using low-cost material to efficient create a dataset for high-end material.

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