Microelectronics Journal 78 (2018) 73–80

Contents lists available at ScienceDirect

Microelectronics Journal

journal homepage: www.elsevier.com/locate/mejo

An adaptive neural-fuzzy approach for microfluidic droplet size prediction

Ali Lashkaripour [a], Masoud Goharimanesh [b], Ali Abouei Mehrizi [c], Douglas Densmore [d,*]

[a] Boston University, Biomedical Engineering Department, 44 Cummington Mall, Boston, USA
[b] Mechanical Engineering Department, Ferdowsi University of Mashhad, Mashhad, Iran
[c] Department of Life Sciences Engineering, Faculty of New Sciences and Technologies, University of Tehran, Tehran, Iran
[d] Boston University, Department of Electrical and Computer Engineering, 8 Saint Mary's Street, Boston, USA

ARTICLE INFO

Keywords:
Microfluidics
Multiphase flow
Droplet size
Neural networks
Fuzzy systems
ANFIS

ABSTRACT

Droplet-based microfluidics is capable of being a superior platform for biological and biomedical applications due to their higher accuracy, throughput and sensitivity, low reagent consumption and fast reaction time. However, the complex and nonlinear behavior of multiphase microfluidic devices and several parameters affecting droplet size simultaneously necessitates costly design iterations to generate droplets with the radius of interest for a certain application. To address this, we exploit soft computing methods to bridge fuzzy systems and neural networks in order to build an adaptive neural-fuzzy inference system (ANFIS) that predicts the droplet size generated in a flow-focusing microfluidic device based on six major parameters, that includes geometry, flow, and fluid properties. This model shows a significant accuracy with a coefficient of determination of 0.96 when compared to the observed data points. Once the ANFIS model is built and verified, we use it to study the effect of each input parameter on droplet size which is challenging and/or expensive to determine experimentally.

1. Introduction

Microfluidics has provided new opportunities and accelerated the progress in several fields including chemistry, medicine, pharmaceutical and biomedical engineering [1–4]. Micrometer-scale feature size, high surface to volume ratio and predictable laminar flow inherent to microfluidic devices provide a unique environment for researchers in the field of life sciences to explore the novel physics that governs the field [5,6]. Droplet-based microfluidic devices offer numerous advantages over continuous-flow microfluidics, such as accurate volume and concentration control, high throughput, high sensitivity, low sample and reagent consumption and low thermal mass, which lead to faster, cheaper and more accurate results [7,8]. However, microfluidic devices are still not widely used in life science laboratories, as the community would have expected a decade ago [5,9]. High barrier of entry to the fabrication process, the complexity of the governing physics and costly and time-consuming device iterations to reach a desired performance, have kept the field of microfluidics from being extensively deployed by most of the research groups in the field of life sciences. Some studies have addressed the fabrication cost issues by proposing cost-efficient substitutes to photo-lithography [10,11]. Nonetheless, designing a droplet generator is heavily reliant on several design iterations and experience of the designer to perform as required for a certain application. This is due to the fact that there are several parameters acting simultaneously which determine the droplet size [12]. To clarify the complex governing physics of droplet generation, some studies explained droplet generation with dimensionless numbers through a number of simplifying assumptions [13]. Scaling laws were also suggested for T-junction droplet generation [14], however, weak control over droplet size and undefined droplet break-up point led researchers to adopt flow-focusing droplet generators as the standard method of microfluidic droplet production [15]. However, the complexity of the governing physics in flow-focusing devices has prevented accurate prediction of droplet size through scaling laws [16]. Therefore, predictive models which explain the role of each parameter on the performance of the device and approximate the droplet size based on given inputs can be extremely useful. These models are capable of clarifying the effects of the parameters that are hard to determine experimentally. Moreover, they can play a significant role in reducing the development time of droplet-based microfluidic devices.

Soft computing methods such as fuzzy logic and neural networks can be used to make predictions of systems behavior and performance [17]. Fuzzy systems are capable of converting logical statements to math-

---

* Corresponding author.
E-mail address: dougd@bu.edu (D. Densmore).

https://doi.org/10.1016/j.mejo.2018.05.018
Received 15 December 2017; Received in revised form 9 May 2018; Accepted 29 May 2018

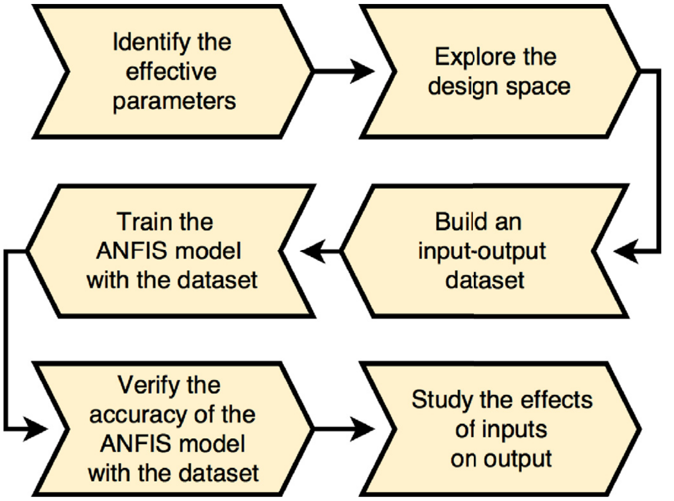

Fig. 1. The overall flow of building an ANFIS predictive model. In this study, we identified six effective parameters in determining droplet size in microfluidic flow-focusing droplet generation. We built a dataset of input-output relations using an experimentally verified numerical model. Using this dataset we trained and verified our proposed ANFIS model. Through the ANFIS model we studied the effects of each parameter on droplet size which is difficult and/or expensive to carry out experimentally.

ematical equations, thus, serving as a tool for simplifying the representation and modeling of complex systems [18]. More importantly, fuzzy logic is capable of grouping and clustering data to several categories. However, fuzzy systems are unable to learn from data and evolve to become more accurate overtime [19]. On the contrary, artificial neural networks are able to learn from data to accurately capture input-output relations. The ability of neural networks in discovering the nonlinear relations between inputs and output and establishing a complex dynamic model of these data is significant [20,21]. However, when dealing with a system that behaves differently depending on the state of the system, neural networks will lose their accuracy, unless, multiple neural networks are proposed for each state of the system. To avoid this, and exploit the clustering power of fuzzy systems and learning capabilities of neural networks, adaptive neural-fuzzy inference systems (ANFIS) were introduced [22]. ANFIS models enable researchers to match any given input-output relation regardless of its complexity or nonlinearity, even if the system has multiple modes.

In this paper, we present an accurate predictive ANFIS model that converts six major inputs of a microfluidic droplet generator to an output droplet radius. Once we verify the accuracy of the ANFIS model with an observed dataset, we investigate how changes in input parameters affect the droplet size to further clarify the governing physics of microfluidic flow-focusing droplet generation, as shown in Fig. 1. Also, this model can be further utilized to reduce the number of costly design iterations required for developing microfluidic droplet-based devices. The remainder of this study is as follows. In Section 2 and 3, we introduce microfluidic flow-focusing droplet generation and its design space that we used to build an input-output dataset. In Section 4, we build and train the proposed ANFIS model, also, we introduce the underlying fuzzy membership functions for each input parameter. The accuracy of the ANFIS model is verified in Section 5, by comparing the data predicted by ANFIS to the dataset derived from the numerical model. Finally, we use this verified model to study the effects of each parameter on droplet radius.

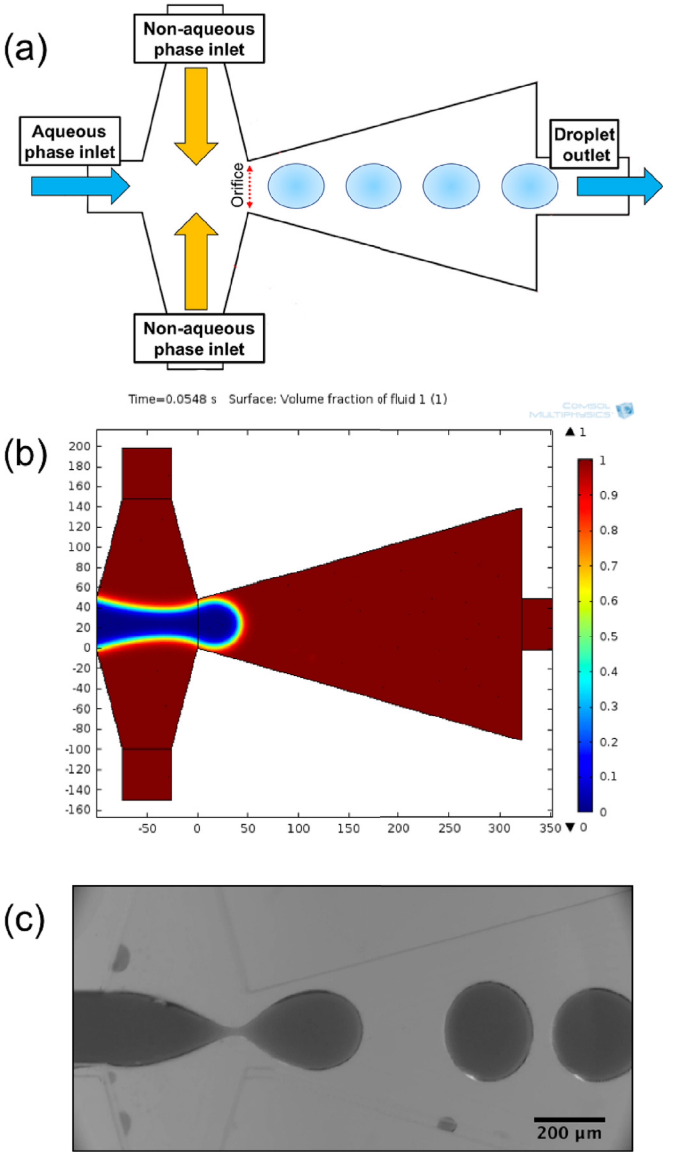

Fig. 2. Microfluidic droplet generation can be achieved by flowing an aqueous and a non-aqueous phase through a narrow channel called orifice. (a) The schematic and the flow direction of water and oil in a flow-focusing geometry. (b) A numerical model of microfluidic droplet generation in COMSOL Multiphysics environment (c) An experimental snapshot of microfluidic droplet generation, using Mineral oil as the non-aqueous phase and DI water as the aqueous phase.

2. Microfluidic droplet generation

Microfluidic flow-focusing droplet generation can be achieved by flowing an aqueous phase and a non-aqueous fluid through a narrow channel called orifice as shown in Fig. 2. The geometry of the microfluidic flow-focusing device is adopted from Ref. [15]. Due to the presence of a nozzle, which creates a unique velocity field, this geometry produces monodispersed droplets with a superior control over droplet size and its breaking point. Normally, to characterize how variations in droplet generation parameters affect the droplet size, one would have to build numerous different devices, testing each device at different flow conditions and fluid properties. This process can be very expensive and time-consuming. Moreover, although some parameters such as geometry, oil, and water flow rate can be varied and studied experimentally, the effects of other parameters such as surface tension, oil viscosity, and density are hard to study experimentally due to the limited number of available water and oil combinations. Therefore, to clarify the impact of these parameters on droplet size, a numerical model of microfluidic droplet generation was developed and veri-