Microelectronics Journal 46 (2015) 1152–1161

Contents lists available at ScienceDirect

Microelectronics Journal

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

Heat and mass transfer reduced order modeling approach of droplet microreactor based Lab-on-a-Chip devices

Márton Németh *, Ferenc Ender, András Poppe

Budapest University of Technology and Economics, Department of Electron Devices, Magyar tudósok körútja 2, Building Q, section B, 3rd floor, Budapest H-1117, Hungary

ARTICLE INFO

Article history:
Received 10 June 2015
Received in revised form
11 September 2015
Accepted 15 September 2015
Available online 19 October 2015

Keywords:
Reduced order modeling
Heat and mass transfer
Segmented slug flow
Lab-on-a-Chip
Calorimetry

ABSTRACT

The paper presents a novel reduced order model, which enables the heat and mass transfer analysis of microchannels consisting of continuously moving microdroplets with enzymatic reactions inside. Due to the low Reynolds number, which is typical in microfluidic applications, the hydrodynamics can be described as Taylor-flow. The reduced order model contains the main features of Taylor-flow such as microcirculation and back flow. These are needed to achieve an accurate model of the convective heat and mass transfer. The model has been validated by a standard CFD simulation for two cases: firstly, for a purely thermal problem with constant heat flux through the wall; secondly, for an enzymatic reaction with multi-component diffusion. The results show that in the first case the model yields results with around 5% error. In the second case the error is less than 10%. The accuracy was tested for a wide range of Reynolds numbers. With this novel approach the temperature profile on the channel wall can be calculated in a few hours compared to conventional numerical techniques which would require weeks.

1. Introduction

A significant number of **Lab-on-Chip** (LoC) platforms use the so-called droplet microreactors. The growing interest and growing complexity in LoC platforms require fast and accurate models to describe the thermal and chemical behavior of the droplet microreactors realized in microchannels. This means a gas–liquid, or liquid–liquid two-phase flow in the microchannel, where the phases are situated separately along the tube. This enables the usage of the droplets as separated individual microreactors, with different chemical processes.

The bio-chemical microreactors are typical applications of microfludics for medical diagnostic purposes. The motivation to design and manufacture microreactors is to reduce the sample volume and achieve high throughput. Chemical microreactors are often completed with microcalorimetry, which is a non-labeled sensing method for almost every chemical reaction. Microcalorimetry is based on the heat generation of the reaction. During a bio-chemical reaction the heat generation density is low due to the low concentrations of the reagents. As a consequence of the low heat generation density and the small volume, the microcalorimetric method in bio-chemistry requires measurement of a very small amount of heat [1]. On one hand this means that accurate and very sensitive thermometers need to be integrated into the microreactors with a signal processing circuitry. On the other hand, the microcalorimetric design process becomes more complex, therefore simulations during the design process require fast and accurate reduced order model of the microreactors.

The typical method to simulate a microfluidic environment is to build a **detailed CFD** (Computational Fluid Dynamics) model and perform multi-physics simulation (as it can be Fig. 1), which handles both the hydrodynamics and the thermodynamics in the flow. Such a simulation can be completed with the calculation of heat generation caused by the (bio)chemical reactions. The detailed CFD simulation yields precise results, but the simulation of a complex microfluidic system is very slow [2].

To design a complex device the modeling process has to be fast and accurate. This requirement inspired the development of the thermal **compact model** of microchannels described by Ender et al. [3,4]. Their model was based on a detailed CFD simulation and the authors proposed generating an electric circuit model of the thermal problem. Such a compact model perfectly fits the design process because of the electrical representation. Although it is a very useful tool, but it yields valid and accurate results only in a relatively narrow range of the relevant system variables.

This paper presents a novel **Reduced Order Modeling** (ROM) method to reduce the time needed to build a compact model from a detailed CFD model. As shown in Fig. 1 the CFD-based compact modeling is bypassed in the design flow by our reduced order modeling approach by achieving still accurate thermal and chemical

* Corresponding author. Tel.: +36 1 463 3073; fax: +36 1 463 2973.
E-mail addresses: nemeth@eet.bme.hu (M. Németh), ender@eet.bme.hu (F. Ender), poppe@eet.bme.hu (A. Poppe).

http://dx.doi.org/10.1016/j.mejo.2015.09.008
0026-2692/

Nomenclature

A_{Bubble}	cross-sectional area of the bubble (m^2)
A_{Chan}	cross-sectional area of the channel (m^2)
Ac	enzyme activity (mol/dm^3 s)
c	concentration (mol/dm^3)
C_V	volumetric specific heat capacity (J/m^3 K)
Ca	capillary number
Co	Courant number
$\dot{c}'$	concentration generation (mol/s dm^3)
D	diffusion coefficient (m^2/s)
δ_F	fluid film thickness (m)
δ	Kronecker delta
ΔT_{Avg}	average temperature rise on the wall (K)
H_r	reaction enthalpy (J/mol)
k_1, k_2, k_3	enzyme reaction rates
λ	thermal conductivity (W/m K)
$\underline{\underline{L_1 L_2}}$	first and second part of the cylindrical Laplace matrix
μ	dynamic viscosity (Pa s)
N	number of axial nodes in ROM
$\dot{q}'$	heat generation rate (W/m^3)
$\dot{q}''$	heat flux (W/m^2)
$\underline{r}$	vector of position (m)
R	radius (m)
R_{chan}	radius of the channel (m)
R_{bub}	radius of the bubble (m)
r	radial coordinate (m)
Re	Reynolds number
res	resolution of the model (m)
ρ	density (kg/m^3)
T	temperature (K)
t	time (s)
v	average velocity (m/s)
V	volume (m^3)
$[S], [E], [ES], [P]$	concentration of substrate, enzyme, enzyme–substrate complex, product (mol/dm^3)

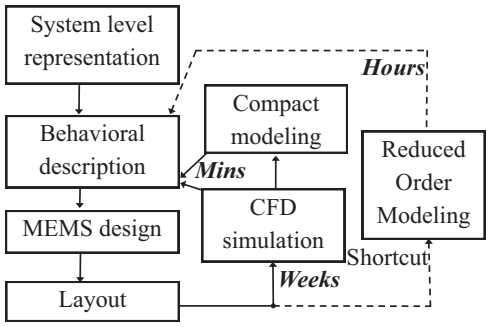

Fig. 1. Simplified IC-MEMS co-design flow.

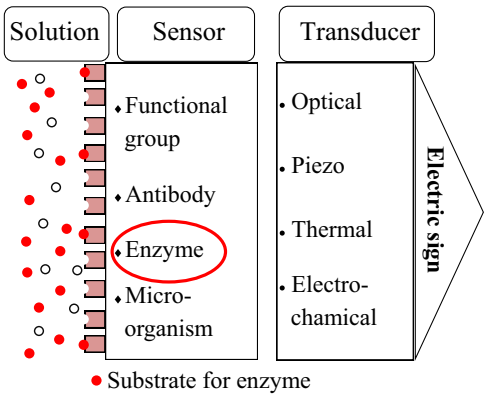

Fig. 2. Substrate sensing method.

results. The model is based on discretization of the microchannel in space and time. The heat and mass transfer equations are solved like in a detailed CFD simulation, but the hydrodynamical behavior is taken into account in a pre-defined transport route way to describe its main features only.

1.1. State of the art

The droplet-flow is a moving series of slugs of two phases which could be gas and liquid or two immiscible liquids. This type of flow – often referred to as Taylor-flow – is special in hydrodynamics due to the separated fluid segments and microcirculation, which assure outstanding heat and mass transfer rates. Taylor-flow is widely used in chemical and bio-chemical analysis. A couple of "classical" papers describes the most important results in **droplet-microfluidics**. Chan et al. described high-temperature synthesis of CdSe **nanocrystals** in liquid–liquid droplet microfluidical environment [5]. Liu et al. used liquid–liquid droplet flow for **Polymerase Chain Reaction** (PCR) [6] and Guo et al. presented results regarding a high throughput **screening method** [7]. **Drug discovery** possibilities have been reviewed in the paper by Dittrich et al. [8]. These examples illustrate the impact and variegation of the droplet flow.

The main structure of a microfluidical chemical analyzer is shown in Fig. 2. The sample contains a solution of the molecule to be found. The main goal of the device is to recognize the presence or determine the concentration of this molecule. In this paper we deal with the latter type of devices. The sensing methods can be different in different device constructions, but the sensor reacts with the molecule and finally the transducer provides an electric signal proportional to the concentration. In our present study we focus on an enzymatic reaction model for calorimetric measurements.

Calorimetry means direct measurement of the generated heat, so enthalpy changes can be determined, which appear in all cases of *antibody–antigen*, *protein–ligand* or *enzyme–substrate* interactions at any biomedically relevant case, such as diagnostics of cancer, metabolic diseases, and communicable diseases. Calorimetry is traditionally a low throughput method, but with micro-scale realization higher reaction rates and parallel measurements can be achieved since in a microfluidical environment the throughput can be higher [9]. Continuous flow [10,11] and droplet microcalorimetry platforms were already reported [12,13] and demonstrated in various biological applications such as biomolecular and bacteria characterization [14,15]. **Thermal design** is the key factor in creating a calorimetric measurement setup. In case of developing a biochemical sensor the low level of heat generation – which can fall in the nano-Joule range – further necessitates accurate thermal design [1].

2. Modeling

2.1. Governing equations

The modeling approach applied in our work is based on the differential equations describing diffusion and thermal conduction:

$$\frac{\partial c}{\partial t} - D\Delta c = \dot{c}'(\underline{r}, t) \tag{1}$$