Accurate *and* Efficient Simulation of Microfluidic Networks

Gerold Fink*, Philipp Ebner*, Medina Hamidović†, Werner Haselmayr†, and Robert Wille*‡
*Johannes Kepler University - Institute for Integrated Circuits, Linz, Austria
†Johannes Kepler University - Institute for Communications Engineering and RF-Systems, Linz, Austria
‡Software Competence Center Hagenberg GmbH (SCCH), Hagenberg, Austria
{gerold.fink,philipp.ebner,medina.hamidovic,werner.haselmayr,robert.wille}@jku.at

ABSTRACT

Microfluidics is a prospective field which provides technological advances to the life sciences. However, the design process for microfluidic devices is still in its infancy and frequently results in a "trial-and-error" scheme. In order to overcome this problem, simulation methods provide a powerful solution—allowing for deriving a design, validating its functionality, or exploring alternatives without the need of an actual fabricated and costly prototype. To this end, several physical models are available such as *Computational Fluid Dynamics* (CFD) or the *1-dimensional analysis model*. However, while CFD-simulations have high accuracy, they also have high costs with respect to setup and simulation time. On the other hand, the 1D-analysis model is very efficient but lacks in accuracy when it comes to certain phenomena. In this work, we present ideas to combine these two models and, thus, to provide an accurate *and* efficient simulation approach for microfluidic networks. A case study confirms the general suitability of the proposed approach.

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1 INTRODUCTION

Microfluidics is a prospective field which provides technological advances to the life sciences [1] and finds a broad application in chemistry, pharmacology, biology, healthcare, etc. and is an enabling technology when it comes to, e.g., biological cell studies, high throughput drug development, and diagnostic screenings [2]. Devices realizing such experiments are called *Lab-on-Chip* (LoC, [3, 4]), which minimize, integrate, and automate typical lab operations such as mixing, heating, incubation, etc. on a single chip.

Droplet-based microfluidics [2, 5, 6] provides a particular form of LoCs in which small droplets of one fluid (called dispersed phase) flow inside closed micro-channels and are transported by a second immiscible fluid (called continuous phase), which acts as a carrier fluid for the droplets. Typically, these droplets confine certain biochemical samples in order to conduct specific experiments or operations such as triggering a reaction when they get mixed.

However, designing such microfluidic devices which implement a desired functionality is a very complex task, since a huge number of physical parameters need to be considered (e.g., the dimensions of the channels, the used fluids, etc.)—all depending and affecting each other [7]. Thus far, designers often rely on their expertise and derive the design based on manual calculations, simplifications, as well as assumptions. In fact, the current design process results in a "trial-and-error" scheme, i.e., a first prototype gets fabricated as well as tested and, if it does not show the intended behavior (which frequently is the case, particularly in first iterations), the designer has to revise the design, repeat the fabrication process, and test its functionality again. Even for simple microfluidic devices, this can lead to multiple iteration loops—yielding a time-consuming and rather costly design as well as production process.

Simulation methods can substantially improve this design flow. To this end, even rather sophisticated models such as *Computational Fluid Dynamics* (CFD, [8]) or the *1-dimensional (1D) analysis model* [9] are available which can serve as basis for corresponding tools. These tools allow to derive a design, validate its functionality, as well as explore alternative designs, even before the first prototype gets fabricated. But unfortunately, those methods are heavily limited in their applications. More precisely, CFD requires substantial setup efforts and cause high computational costs—making it applicable for rather small designs only. Vice versa, simulations employing the 1D-analysis model are easy to set up and fast in computation time, but lacking in accuracy which is needed in many evaluations. Because of that, methods for simulation of microfluidic devices hardly got established amongst designers thus far.

In this work, we aim to address this unsatisfactory situation by proving ideas towards an alternative simulation approach which combines the advantages of existing solutions while, at the same time, mitigating the respective drawbacks. The main idea is to rest the overall simulation on the more abstract 1D-analysis model—providing an *efficient* basis for simulation. For components, however, for which a dedicated physical behavior is of interest, CFD-simulations are employed—providing an *accurate* basis for simulation. More precisely, such components are pre-simulated with CFD-tools and, afterwards, the obtained information is captured inside a 1D-representation of the component. Since those pre-simulations (at CFD-level) need to be conducted only for single components (and can be re-used for all instances of this component), efforts and simulation time are kept small. Combined with the 1D-simulation, this shows a path towards an accurate *and* efficient simulation scheme.

The remainder of this work is structured as follows: The following section briefly reviews CFD- and 1D-simulations and discusses the respective pros and cons. Based on that, the general idea of combining both simulation approaches is illustrated in Section 3. Afterwards, Section 4 describes in detail the implementation of the proposed idea—in particular the respectively needed abstraction process. The suitability of the resulting simulator has been confirmed using the design of a microfluidic device for drug screening which serves as practically relevant example. The results of this case study are summarized in Section 5, before the paper is concluded in Section 6.

2 BACKGROUND & CONSIDERED PROBLEM

In order to develop corresponding design automation tools and simulation methods, physical models which describe the behavior of microfluidics are needed. Here, several proposals from the microfluidic domain can be utilized for this purpose—most prominently models for CFD and the 1D-analysis model. In the following, we briefly review the capabilities and drawbacks of the corresponding simulation approaches. Afterwards, we compare both models and, motivated by that, describe the resulting problem considered in this work.

2.1 CFD-Simulations

In CFD-simulations, the Navier–Stokes equations [10], which describe the fluid flow inside microfluidic devices, are solved in a numerical way. Hence, CFD-simulation tools like COMSOL Multiphysics [11], Ansys [12], and OpenFOAM [13] allow to describe the behavior of fluids in a very detailed and accurate way. Due to this high precision, it is possible to simulate complex phenomena, such as droplet splitting, merging, deformation, etc. However, this high level of physical detail comes with a high price: It requires a complex simulation setup (e.g., a proper mesh generation) and also causes high computational costs. As a result, CFD-simulations are especially useful for small designs or single components, but are inappropriate to quickly simulate the behavior of large-scale microfluidic networks. Reviews of corresponding simulation tools are provided in [8, 14, 15].

2.2 1D-Simulations

The 1D-analysis model is applicable at low Reynolds numbers when the flow is laminar, viscous, and incompressible [9], which is typically the case in microfluidics. The model abstracts the exact geometric design of microfluidic networks by describing its channels only by their hydrodynamic resistances, i.e., it reduces the network (inherently a 3D object) to an 1D-hydraulic circuit. Moreover, it also considers the influence of droplets on the hydrodynamic resistance of channels [16, 17]. Due to this high abstraction, corresponding simulations are very efficient and, thus, it is possible to simulate even large-scale microfluidic networks in negligible run-time. Furthermore, the complete simulation setup usually needs fewer requirements and is substantially less complex compared to a corresponding CFD-setup. However, the model does not allow designers to predict complex phenomena like droplet mixing, deformation, or splitting [16, 18]. As a result, the 1D-analysis model is typically used early in the design process for deriving the specification of a design where certain physical details are of no interest yet (see, e.g., [19]).

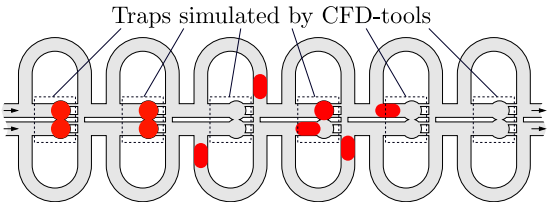


Figure 1: Microfluidic network with droplet traps

2.3 Comparison and Resulting Problem

The brief review from above already sketches the respective strengths and weaknesses of both simulation approaches. For a more explicit one-to-one comparison, Tab. 1 additionally summarizes the differences with respect to accuracy, simulation time, setup efforts, required hardware, and needed experience.

Overall, this obviously leads to the following conclusions: In situations in which large networks need to be considered and, at the same time, complex physical phenomena are of interest, neither of these approaches is suitable. This frequently forces designers to choose between two bad choices: Either opting for CFD but, then, only focusing on a small portion of the network; or opting for the 1D-approach but not being able to simulate certain effects. To date, no satisfying solution for this dilemma has been proposed yet. In this work, we aim to address this problem.

3 GENERAL IDEA OF PROPOSED SOLUTION

In this work, we aim to combine the advantages of the existing solutions while, at the same time, mitigating the respective drawbacks. That is, being able to simulate complex physical phenomena in case of CFD-simulations and being rather efficient (even for large networks) in case of 1D-based simulations. The basic idea is to use a more precise simulation (i.e., a CFD-simulation) for components where dedicated physical behavior is of higher interest such as a complex geometry, traps, etc. On the other hand, a less precise simulation (i.e., a 1D-based simulation) is used for the remaining components of the network, e.g., channels, where the designer is mostly interested in the position/velocity of a droplet, but does not care much about the actual deformation of the droplet. Such a separation scheme eventually allows to precisely simulate certain components with the desired accuracy, while all other parts of the network can be covered by the much more efficient method.

Example 1. *In order to illustrate the proposed idea, we are considering the microfluidic network as originally proposed in [20] and depicted in Fig. 1. This network includes droplet traps and is able to trap, merge, and mix droplets from two different droplet streams—allowing to screen drug compounds that inhibit the tau-peptide aggregation. Simulating this network completely with CFD-tools is infeasible, because of the high effort for the setup and (more importantly) the huge simulation run-time. Vice versa, simulating this network solely using the 1D-based approach would require many simplifications or assumptions due to the complexity of the droplet traps—resulting in a behavior which might not be accurate enough. However, a combination of both approaches could accurately simulate the trap components using CFD-tools (as highlighted in Fig. 1), while the rest of the network can efficiently be simulated by the 1D-model.*

Table 1: Comparison between CFD- and 1D-simulations

	CFD	1D
Accuracy	High precision, when it comes to complex phenomena.	Due to the high abstraction, many phenomena cannot be simulated.
Simulation Time	High, due to expensive numeric operations.	Negligible, due to the high abstraction.
Setup Effort	High, since many subjects have to be considered, e.g., geometry generation, meshing, boundary conditions, etc.	Low, since only basic information (such as pump pressure, network structure, size/length of channels, etc.) needs to be provided.
Hardware Requirements	To cope the high simulation time, expensive hardware is needed.	Since only little computational power is needed, even regular desktop PCs can be used.
Experience	CFD-tools are complex programs and, thus, need experienced users which can handle them.	The simple setup of the 1D-simulation allows lesser experienced users to interact with it.

However, combining both simulation approaches is a non-trivial task and additionally requires a proper *interface* between both representations. In the following, we propose to accomplish that by *pre-simulating* the precise behavior of components, where a higher precision is needed, using the existing CFD-tools reviewed above. Then, the resulting behavioral information is stored in a particular representation which, afterwards, can be accessed by the 1D-simulator. More precisely, we utilize the 1D-model as the basic backbone of our simulation and use the results of the pre-simulations in order to establish a model inside the 1D-realm, which emulates the same behavior as the corresponding component. This finally allows to conduct a simulation which (1) is capable to simulate even large-scale networks, (2) is fast (in fact, often negligible) in run-time, and (3) provides the respectively needed accuracy.

Obviously, the representation of the new model(s) inside the 1D-realm (basically constituting the interface between both simulation approaches) is most crucial for the success of the proposed idea. Hence, in the remainder of this work, we propose a process which determines such an abstraction for a particular component. This abstraction process employs the following steps: (1) Define the component and the whole setup under which it is used, (2) pre-simulate the component and observe its behavior, (3) transform the observed behavior into a corresponding model inside the 1D-realm, and (4) validate the behavior and refine the model if necessary.

In order to illustrate these steps, we apply each of them on the following component which will act as a running example throughout the remainder of this work.[1]

Example 2. *Consider again the microfluidic network from above—including the droplet traps which need to be simulated with higher precision and are illustrated in more detail in Fig. 2. Those components work as follows: A droplet which flows into one of the round chambers gets stuck in it and, afterwards, blocks the two gaps connected to the outlet. When the same happens in the other chamber, the two droplets merge and the fluids of the two droplets get mixed—usually triggering some kind of reaction. Due to the complex geometry of the trap, a directly established model inside the 1D-realm (which does not rely on pre-simulations as proposed in this work) would require many simplifications/assumptions—resulting in a behavior which might not be accurate enough. Hence, a reliable 1D-model should be obtained by pre-simulating the trap with CFD-tools.*

[1]The proposed process can accordingly be employed for other components of microfluidic networks as well.

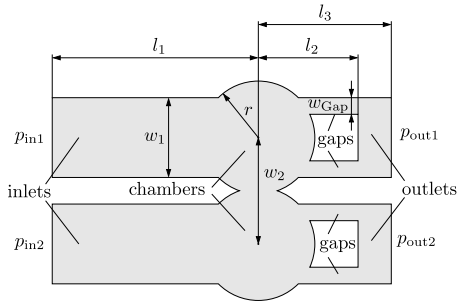


Figure 2: Detailed sketch of a droplet trap

4 ABSTRACTION PROCESS

In this section, we describe the abstraction process proposed above and illustrate each step using the example of the trap as introduced in Example 2. To provide the necessarily required basis for that, we provide a more thorough review of the 1D-analysis model and its corresponding equations first. Afterwards, the four steps introduced above (definition of component and setup, pre-simulation, transformation, as well as validation) are described in detail.

4.1 1D-Analysis Model

The 1D-analysis model assumes that pumps produce a fully developed, laminar, and incompressible flow (usually at low Reynolds numbers), which is typically satisfied in microfluidic devices. Then, the flow inside a channel can be described by Hagen-Poiseuille's law [21] as

$$\Delta p = Q \cdot R\,, \tag{1}$$

where Q is the volumetric flow rate, Δp the pressure drop along the channel, and R the hydrodynamic resistance of the channel. This hydrodynamic resistance depends on the channel's geometry (i.e., its length l, width w, and height h) as well as the dynamic viscosity of the continuous phase μ_c. More precisely, for rectangular channels with a section ratio $h/w < 1$, the hydrodynamic resistance can be determined by [22]

$$R\,(l, w, h, \mu_c) = 12\left[1 - \frac{192h}{\pi^5 w}\tanh\left(\frac{\pi w}{2h}\right)\right]^{-1}\frac{\mu_c l}{wh^3}\,. \tag{2}$$

Moreover, droplets also increase the resistance of a channel. As proposed in [23], a droplet with the length l_D increases the resistance of the segment it occupies inside the channel by $2-5$ times. As a rule of thumb, we will use the factor 3 in this work

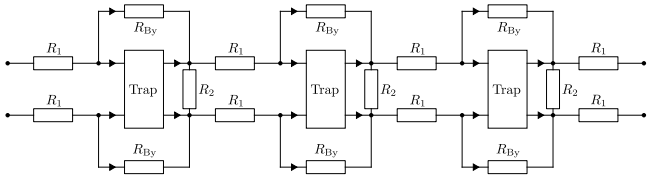


Figure 3: Equivalent electrical network

(however, this value can always be adjusted to the users needs and setup) leading to

$$R_D = 3\ R\left(l_D, w, h, \mu_c\right)\ . \tag{3}$$

This 1D-analysis model can now be used to describe the behavior of a microfluidic network. In order to realize this, the channels of such networks are represented by their hydrodynamic resistances, which leads to the so-called *equivalent electrical network* [9]. This equivalent electrical network is then used to compute the volumetric flow rates inside the channels—using Kirchhoff's laws. Once the flow rates are obtained, the droplet velocities and droplet paths can be determined.

Example 3. *Consider again the microfluidic network as discussed before in Fig. 1. Converting this network into the 1D-realm results in the equivalent electrical network illustrated in Fig. 3. Note that, in this example, no 1D-description of the traps is available yet. Instead, traps are supported following the ideas presented in Section 3 and described in detail next.*

4.2 Definition of Component and Setup

In the first step of the abstraction process, the component to be supported and the whole setup under which it is applied are defined—providing the initial parameters for the CFD-tool to be used for pre-simulation. This includes parameters such as the used fluids, the geometry, and exact dimensions of the component, the considered droplet volumes, etc. This is required, because variations in these parameters also change the behavior of the component and, thus, the whole transformation into the 1D-realm would not work as expected. This process is basically identical to the setup efforts needed for CFD-simulations in general. However, rather than doing it for an entire network, we only require it for the respectively considered component.

Example 4. *Let's consider the trap introduced earlier. The geometry and corresponding exact dimensions are provided in Fig. 2 and in Tab. 2a, respectively. Next, the used fluids for the continuous and dispersed phase (i.e., dynamic viscosity μ and density ρ) as well as the inter-facial tension σ between them are defined in Tab. 2b (these values are directly taken from [20], where the initial design was proposed). The definition of the volume of a single droplet is important, since different droplet sizes may have different effects on the actual behavior of the trap. For obvious reasons, we define the volume V_D for a single droplet in such a way that it matches the volume of a single chamber, i.e., $V_D = r^2\pi h = 1.36 \times 10^6\ \mu m^3$. Finally, we define that the pressure difference between the two inlets and the pressure difference between the two outlets is 0, i.e., $p_{in1} = p_{in2} = p_{in}$ and $p_{out1} = p_{out2} = p_{out}$, respectively. This is to stay consistent with the physical realization of the whole network as described in [20] and, at the same time, this reduces the amount of simulation parameters which have to be considered.*

4.3 Pre-Simulation

Having the component itself as well as its setup described in detail, simulations can be conducted using a CFD-tool. This is utilized to do the proposed pre-simulations, i.e., to obtain all information on the behavior of the component that is later needed for the actual 1D-simulation process considering the entire network. More precisely, the component is simulated using a CFD-tool (as reviewed in Section 2.1) under various conditions such as different pressure values, different droplet positions, etc. The amount of conditions to be considered (i.e., the amount of pre-simulation runs) depends on the respective use cases of the final simulation, which gets conducted later on the entire network within the 1D-realm (if it turns out later that not all the required behavior has been captured, further pre-simulation runs can be conducted to close possible gaps). By this, eventually an understanding of the working principles of the component is gained which, in the next step, is used to transform it into a corresponding model for the 1D-realm.

Table 2: Setup of the trap [20]

(a) Dimensions of the trap in μm

w_1	w_2	w_{Gap}	h	r	l_1	l_2	l_3
120	80	25	60	85	310	150	200

(b) Fluid Properties

	μ in Pa s	ρ in kg m^{-3}	σ in N m^{-1}
Continuous Phase	0.005	913	0.042
Dispersed Phase	0.001	1000	0.042

Example 5. *Again, let's consider the trap and the setup defined in Example 4. After realizing the whole setup in a CFD-tool (in our case, OpenFOAM [13] was used), the trap was simulated under various conditions such as different pressure gradients $\Delta p = p_{in} - p_{out}$ along the trap as well as different droplet positions. All these necessary pre-simulations took about 10 hours. However, they only have to be conducted once for a single component. This eventually resulted in the following main scenarios describing the behavior of the trap:*

No droplet is present inside the chambers: *Since no droplet is present, the gaps connected to the outlet are not blocked and, thus, the continuous phase can freely flow through the trap. As a result, the trap behaves like a normal channel (although with a complex geometry) and realizes a certain hydrodynamic resistance (which, in the 1D-analysis model, can be employed using Eq. 1).*

One droplet is present inside a single chamber:[2] *Because a droplet is inside a chamber, the gaps, which are connected to the respective outlet, are blocked. Hence, the flow rate through the corresponding chamber relaxes to 0, while the continuous phase can freely flow through the gaps of the other chamber. However, this condition only holds as long as the pressure Δp is below a certain threshold. Once Δp exceeds this threshold, the droplet gets squeezed through the gaps and the continuous phase can again freely flow through the trap.*

Two droplets are present inside the chambers: *In this scenario, both droplets block all gaps to the outlets and, thus, the volumetric flow rate through the trap completely stops. Again, this condition only holds as long as the pressure Δp is below a certain threshold. If Δp is higher than this threshold, the droplets get squeezed through the gaps and the continuous phase can again freely flow through the traps.*

4.4 Transformation

Having information on the behavior of the trap, a corresponding model for the 1D-realm can be defined, i.e., the behavior captured

[2] Please note that, due to the symmetry of the trap, this scenario holds for both chambers.

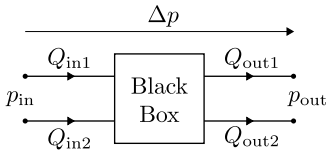


Figure 4: Approach to model a trap inside the 1D-realm

by the pre-simulations at the CFD level is *transformed* to corresponding 1D-model formulations[3]. Of course, the resulting model depends on the particular component whose behavior should be transformed and, thus, it is hard to propose a generic approach for this step. However, a good way is to establish the model as a *black box* that reacts on certain events/conditions that occur at its boundaries, e.g., when certain pressure values are reached. Once such an event occurs, the black box performs a specific action that correspond to the behavior of the pre-simulated component. In the following, the example illustrates these approaches.

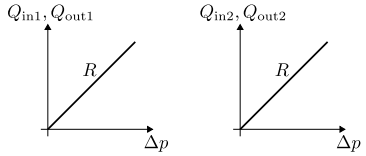
Example 6. *Let's consider the observed behavior of the trap from Example 5. In order to establish a corresponding model in the 1D-realm, we will use the black box shown in Fig. 4. Accordingly to the geometry of the trap, the black box has two inlets and two outlets, where each inlet and outlet has its own volumetric flow rate. Based on the setup discussed in Example 4, the pressure levels at the two inlets have the same value p_{in} and the pressure levels at the two outlets also share the same value p_{out}; resulting in the pressure drop $\Delta p = p_{in} - p_{out}$. Then, the black box is able to employ a certain function between the pressure Δp and each volumetric flow rate of the in- and outlets. Of course, this kind of mapping is done for each of the three scenarios and the black box switches accordingly between them, when the corresponding scenario occurs (e.g., a droplet flows into one chamber). More precisely:*

No droplet is present inside the chambers: *As described before, when no droplet is present inside any chamber, the trap acts like a normal channel and realizes a certain hydrodynamic resistance (cf. Eq. 1). Hence, all dependencies of the flow rates are linear with respect to Δp and, thus, the behavior of the black box can be described by the two diagrams shown in Fig. 5a. We simulated the trap with different pressure values in order to gain the value of the hydrodynamic resistance (i.e., the slope of the linear function), which was then defined by $R = 5.321 \times 10^{12}\,\mathrm{Pa\,s\,m^{-3}}$.*

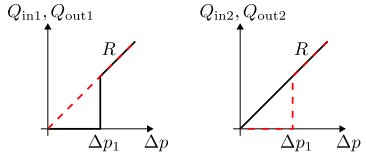
One droplet is present inside a single chamber: *This scenario can be modeled by the two diagrams shown in Fig. 5b (the black and red dotted line indicates that a droplet is present in the first and second chamber, respectively). More precisely, as long as the pressure Δp is below the threshold Δp_1, the flow rate through the corresponding chamber is zero, since the droplet blocks the gaps to the outlet. On the other hand, the flow rate through the non-occupied chamber behaves like in the previous scenario, i.e., the flow rate is linear with respect to Δp. Once Δp exceeds the threshold Δp_1, the droplet gets squeezed through the gaps and the continuous phase can again freely flow through the whole trap. The CFD-simulations showed that the value of this threshold is at $\Delta p_1 = 2500\,\mathrm{Pa}$. However, since the purpose of the trap is to capture the droplets, the case where a droplet gets squeezed through the gaps is actually not desired. Hence, in this case we define that the 1D-simulation should raise an error and warn the designer, which allows to adapt the design accordingly.*

Two droplets are present inside the chambers: *In this scenario, both droplets block the gaps to the outlets and, thus, the volumetric flow rate through the trap completely stops, which allows to model the behavior as shown in the two diagrams in Fig. 5c. However, once Δp is higher than the threshold Δp_2, both droplets get squeezed through the gaps and the trap behaves again like in the first scenario, i.e., the flow rates are linear with respect to Δp. In this case, we gained the value $\Delta p_2 = 2525\,\mathrm{Pa}$ from the CFD-simulations. Again, the 1D-simulation should raise an error, when the droplets get squeezed through the trap.*

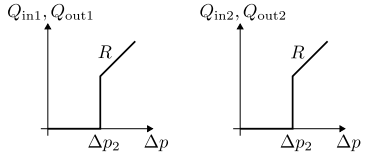
[3]Please note, that the 1D-formulation does not have to capture the entire behavior of the component, but should be sufficient enough for the corresponding application.



(a) No droplet is present inside the trap

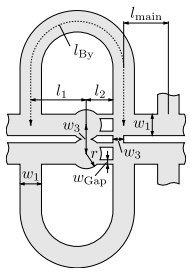


(b) One droplet is present inside the first chamber (black line) or inside the second chamber (red dotted line)

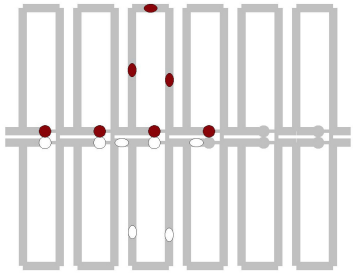


(c) Two droplets are present inside the trap

Figure 5: Dependencies of the flow rates with respect to Δp



(a) Structure



(b) Simulation screenshot

Figure 6: Simulated network

4.5 Validation

Finally, it is validated whether the transformed 1D-formulation properly describes the behavior as captured during pre-simulation. Moreover, this step also serves as opportunity to fine-tune the parameters of the 1D-model in order to make the representation of the component as accurate as possible. However, if the 1D-model does not show the intended behavior and even fine-tuning of the model parameters does not solve this, then more parameters have to be considered (or strategies to increase the robustness [24] need to be explored). That is, more pre-simulations have to be conducted and additional parameters must be incorporated into an adapted 1D-model, which finally allows to describe the behavior properly.

5 APPLICATION

The methods proposed and described above have been implemented using OpenFOAM [13] as engine for the pre-simulations and the 1D-based simulator proposed in [25] for the simulation of the overall network. In this section, we now demonstrate the applicability of the resulting solution. To this end, we consider a large-scale

instantiation of the microfluidic network proposed in [20] which is used for drug screening and was already reviewed in Example 1. The network itself consists of multiple structures such as shown in Fig. 6a, which are all connected in series as illustrated in Fig. 1 (for demonstration purposes we use 6 structures). Moreover, a single trap inside such a structure was pre-simulated with OpenFOAM (which took about 10 hours) and, afterwards, transformed into a corresponding 1D-representation, as discussed in Section 4. Then the entire network could be efficiently simulated with proper accuracy. In the following, the final setup of the resulting simulation environment and the obtained results are summarized.

5.1 Simulation Setup

While most parameters such as the fluid properties presented in Tab. 2b, the droplet volumes $V_D = 1.36 \times 10^6\,\mu\text{m}^3$, and the dimension of a trap (cf. Tab. 2a) stay the same as before, we have to consider additional parameters in order to simulate the whole network. That is, the pressure drop $\Delta p_{\text{pump}} = 4000\,\text{Pa}$ along the whole network, the remaining channel dimensions in order to completely define a single structure in Fig. 6a ($w_3 = 60\,\mu\text{m}$, $l_{\text{Main}} = 250\,\mu\text{m}$, and $l_{\text{By}} = 4000\,\mu\text{m}$), as well as the injection interval $\Delta t = 100\,\text{ms}$ of the droplets (i.e., in which time interval the droplets enter the network). Moreover, the parameters which were obtained in the previous section and define the 1D-model of our trap are given by $R = 5.321 \times 10^{12}\,\text{Pa s m}^{-3}$, $\Delta p_1 = 2500\,\text{Pa}$ and $\Delta p_2 = 2525\,\text{Pa}$. Once all these parameters are passed to the 1D-simulator, the simulation can be finally conducted, which was done on a regular laptop with an Intel Core i5-8250U @ 1.60/1.80GHz and 8GB RAM running Windows 10.

5.2 Simulation Results

While a video of the simulation was uploaded to YouTube with the link https://www.youtube.com/watch?v=PixtJPILrYQ, a simulation screenshot is also depicted in Fig. 6b (note that the simulation output is shown in an abstracted fashion, but it still provides all the relevant information). As it can be observed from the results, the traps work as expected and hold the droplets inside the chambers. Furthermore, when we increase the pressure of the pumps higher than $\Delta p_{\text{pump}} = 6960\,\text{Pa}$ and start the simulation again, the simulator raises an error in the moment a droplet flows inside a trap, because the pressure drop along the trap is too high and the droplet gets squeezed through the gaps.

While these scenarios confirm the accuracy of the simulation, the fact that (even for this large network) each simulation run took only about 5 s shows the huge capabilities of the proposed approach. Hence, not only allows this approach to simulate a complex behavior in an accurate fashion, but it can do this in negligible run-time.

6 CONCLUSION

In this work, we presented ideas to combine CFD- with 1D-simulations. This is motivated by the fact that simulations with CFD-tools are accurate, but have high costs with respect to setup and computation time. On the other hand, simulations utilizing the 1D-analysis model are very efficient, but often lack in accuracy when it comes to certain phenomena. Therefore, we proposed an approach which combines these two abstraction levels by only simulating the components/regions inside a microfluidic device which require high precision with CFD-tools, while the remaining overall network is covered by the 1D-analysis model. Eventually, this shows a path towards efficiently simulating microfluidic networks, while maintaining a proper accuracy.

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REFERENCES

[1] G. M. Whitesides, "The origins and the future of microfluidics," *Nature*, vol. 442, no. 7101, pp. 368–373, 2006.
[2] S.-Y. Teh, R. Lin, L.-H. Hung, and A. P. Lee, "Droplet microfluidics," *Lab on a Chip*, vol. 8, pp. 198–220, 2008.
[3] D. Mark, S. Haeberle, G. Roth, F. von Stetten, and R. Zengerle, "Microfluidic Lab-on-a-Chip platforms: requirements, characteristics and applications," *Chemical Society Reviews*, vol. 39, no. 3, pp. 1153–1182, 2010.
[4] P. S. Dittrich and A. Manz, "Lab-on-a-chip: microfluidics in drug discovery," *Nature Reviews Drug Discovery*, vol. 5, no. 3, p. 210, 2006.
[5] H. Gu, M. H. Duits, and F. Mugele, "Droplets formation and merging in two-phase flow microfluidics," *International Journal of Molecular Sciences*, vol. 12, no. 4, pp. 2572–2597, 2011.
[6] M. Hamidović, W. Haselmayr, A. Grimmer, R. Wille, and A. Springer, "Passive droplet control in microfluidic networks: A survey and new perspectives on their practical realization," *Nano Communication Networks*, vol. 19, pp. 33–46, 2019.
[7] A. Grimmer, W. Haselmayr, and R. Wille, "Automated dimensioning of Networked Labs-on-Chip," *Trans. on Computer-Aided Design of Integrated Circuits and Systems*, 2019.
[8] T. Glatzel, C. Litterst, C. Cupelli, T. Lindemann, C. Moosmann, R. Niekrawietz, W. Streule, R. Zengerle, and P. Koltay, "Computational fluid dynamics (CFD) software tools for microfluidic applications–a case study," *Computers & Fluids*, vol. 37, no. 3, pp. 218–235, 2008.
[9] K. W. Oh, K. Lee, B. Ahn, and E. P. Furlani, "Design of pressure-driven microfluidic networks using electric circuit analogy," *Lab on a Chip*, vol. 12, no. 3, pp. 515–545, 2012.
[10] R. Temam, *Navier-Stokes equations: theory and numerical analysis*. American Mathematical Soc., 2001, vol. 343.
[11] C. Multiphysics, "Comsol multiphysics user guide (version 4.3 a)," *COMSOL, AB*, pp. 39–40, 2012.
[12] I. Ansys, "Ansys fluent theory guide," *Canonsburg, PA*, p. 794, 2011.
[13] C. J. Greenshields, "Openfoam user guide," *OpenFOAM Foundation Ltd, version*, vol. 3, no. 1, 2015.
[14] J. Liu and N.-T. Nguyen, "Numerical simulation of droplet-based microfluidics-a review," *Micro and Nanosystems*, vol. 2, no. 3, pp. 193–201, 2010.
[15] M. Wörner, "Numerical modeling of multiphase flows in microfluidics and micro process engineering: a review of methods and applications," *Microfluidics and Nanofluidics*, vol. 12, no. 6, pp. 841–886, 2012.
[16] M. Schindler and A. Ajdari, "Droplet traffic in microfluidic networks: A simple model for understanding and designing," *Physical Review Letters*, vol. 100, no. 4, p. 044501, 2008.
[17] A. Grimmer, W. Haselmayr, and R. Wille, "Automatic droplet sequence generation for microfluidic networks with passive droplet routing," *Trans. on Computer-Aided Design of Integrated Circuits and Systems*, 2020.
[18] A. Biral, D. Zordan, and A. Zanella, "Modeling, simulation and experimentation of droplet-based microfluidic networks," *Trans. on Molecular, Biological, and Multi-scale Communications*, vol. 1, no. 2, pp. 122–134, 2015.
[19] A. Grimmer, X. Chen, M. Hamidović, W. Haselmayr, C. L. Ren, and R. Wille, "Simulation before fabrication: a case study on the utilization of simulators for the design of droplet microfluidic networks," *RSC Advances*, vol. 8, pp. 34 733–34 742, 2018. [Online]. Available: http://dx.doi.org/10.1039/C8RA05531A
[20] X. Chen and C. L. Ren, "A microfluidic chip integrated with droplet generation, pairing, trapping, merging, mixing and releasing," *RSC Advances*, vol. 7, no. 27, pp. 16 738–16 750, 2017.
[21] H. Bruus, *Theoretical microfluidics*. Oxford university press Oxford, 2008, vol. 18.
[22] M. J. Fuerstman, A. Lai, M. E. Thurlow, S. S. Shevkoplyas, H. A. Stone, and G. M. Whitesides, "The pressure drop along rectangular microchannels containing bubbles," *Lab on a Chip*, vol. 7, no. 11, pp. 1479–1489, 2007.
[23] T. Glawdel and C. L. Ren, "Global network design for robust operation of microfluidic droplet generators with pressure-driven flow," *Microfluidics and Nanofluidics*, vol. 13, no. 3, pp. 469–480, 2012.
[24] G. Fink, A. Grimmer, M. Hamidović, W. Haselmayr, and R. Wille, "Robustness analysis for droplet-based microfluidic networks," *Trans. on Computer-Aided Design of Integrated Circuits and Systems*, 2019.
[25] A. Grimmer, M. Hamidović, W. Haselmayr, and R. Wille, "Advanced simulation of droplet microfluidics," *Journal on Emerging Technologies in Computing Systems*, 2019.