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Novel microsystems for concentration gradient generation through computer optimization with validation using optical instrumentation

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Abstract

Novel microfluidic resistive network designs have been evaluated theoretically and experimentally. Such networks are an important component of microreactor technology and are used in analytical and biomedical applications for precisely controlled and evenly stepped dilution.

A detailed model and a simplification algorithm have been devised for these networks. Their combination produces novel simplified network designs that exhibit less hierarchical branching over existing network designs. Rapid prediction and optimization of a layout that meets an arbitrary outlet profile is also possible.

High levels of linearity were achieved on three microdevice fluidic networks. Good agreement of the experimental results from tested devices with the model was obtained. In addition, CFD simulation of one of the designs gave good agreement with results from the model presented, a good linear outlet profile being obtained.

Keywords: Microfluidics; Microfabrication; Concentration gradient; Microreactor technology

1. Introduction

Microreactors for dilution gradient generation are of great value where precise control of concentration and flow rate is required. For example, gradient generators have found wide use in biological processing [1,2].

The idea for an x-inlet y-outlet concentration gradient generator was first presented in 2000 [3]. While various models have been described [4,5], they do not fully address all possible parameters of such a network. A recent report [6] focused on reducing the number of network levels required in such a device. However, the concentration steps produced by the resulting device are not those desirable in most practical applications.

The scope of this work is to produce a fully characterized, less complex fluid network for gradient production using an adaptable model that results in a gradient of wide practical use and is valid for any combination of x inlets and y outlets.

2. Modelling and simulation

The networks presented sequentially mix and divide fluids in a branching arrangement of channels to produce a concentration gradient profile. Fig. 1a shows a conventional $(2,6)$ network design (i.e. 2 equal-flow inlets and 6 equal-flow outlets) that produces a linear concentration gradient from 0 to 100% with 20% increments.

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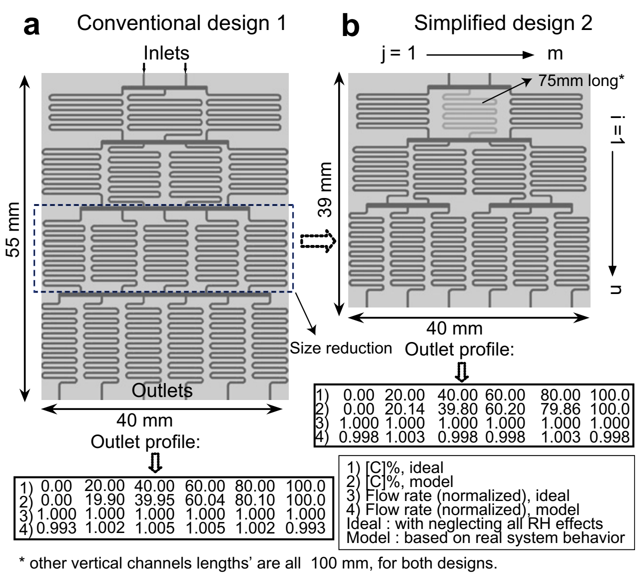

Fig. 1. Optimization and simplification of: (a) conventional (2–6) design to (b) a new design, along with modelled outlet profiles, together with ideal results. Channels are labelled using (i,j) notation, where i-indicates the level and j-indicates the channel position from left (e.g. $m = 6$ and $n = 4$ for design 2).

Assuming a negligible flow resistance (R_H) for the horizontal channels [3,7], together with equal resistances (R_V) for the vertical channels, makes predicting both flow rate and concentration distribution in the network relatively easy. However, this approach is not valid when the design layout is modified or scaled non-uniformly; the new model overcomes this limitation.

The model assumes perfect mixing, and hence that the networks can be characterized by: steady state material balance at branching points and pressure drop balance around 'fluidic' loops (analogous to Kirchhoff's current and voltage laws [8]); and concentration balance at branching points [6]. CFD modeling was used to determine the domain in which the results of the new model would be valid.

There are three major applications of the model, summarized as follows:

a. Simplifying network structure

The simplified structure is shown in Fig. 1b. Compared to the conventional network (Fig. 1a), it is one network level less complex though it maintains the same outlet flow rates, concentration profile and is symmetrical. This simplification was achieved by reducing the channel (2, 2) to 75% of the original (i.e. 75 mm, as highlighted in Fig. 1).

The new length of channel (2, 2) was easily predicted analytically. For computation of the necessary channel lengths for devices requiring more levels, such as the (2–11) design for production of a 10% interval gradient shown in Fig. 2b, an algorithm (Fig. 2a) was developed, and then implemented in GAMS (v. 20.0), which is valid for any combination of x inlets and y outlets.

The conventional approach would require eight levels to produce an equal-flow rate (2–11) gradient: the new algorithm gives a four level network. This reduction produces a more practical design with an improved pressure drop across the network. The algorithm also enables the network footprint to be specified (in this particular case $40 \times 55\ mm^2$) and maintains a symmetrical layout. The new design is given in Fig. 2b along with the CFD-ACE+ (ESI Group) simulated concentration distribution (at 0.1 μl/s inlet flows of water and amaranth solution – amaranth diffusion coefficient $= 6.9 \times 10^{-6}\ cm^2/s$ – with central mixing converging, 2nd order limiter solver and gridding of 407210 cells and 1047 blocks). Comparison of the outlet concentration gradients calculated by CFD and using the algorithm indicated a high level of agreement (Fig. 2c).

a. Network geometry selection

Changing the channel geometry has a considerable effect on device performance; it is therefore essential that geometrical parameters are incorporated into the model. For the (2–6) designs vertical channels of 400 μm width, 400 μm depth and 100 mm length, and horizontal channels of 800 μm width, 400 μm depth and 3.4 mm length were specified. Calculation gave differences from the ideal case of <1% and <0.5% in concentrations and flow rate respectively, as shown in Fig. 1. Higher deviations are expected with lower R_V/R_H.

a. Designs with different output performance

The algorithm given in Fig. 2a, can be used to determine both the closest approach to an arbitrary outlet profile (flow rates and concentration) achievable for given manufacturing constraints and the corresponding channel geometry. This will be of particular benefit in biomedical applications [9].

3. Microsystems fabrication

Both (2–6) microdevices were micromachined (CNC milling) directly into PMMA sheets (as described by the authors [10]). The fabricated chips were sealed using polyester adhesive laminate. Fluid inlets/outlets were formed from $1\ mm^2$ uninsulated bootlace ferrules (RS, Corby, UK).

4. Experimental

4.1. Procedures and instrumentation setup

Two syringe pumps (VersaPump 6 Model 54022, Kloehn Europe, Bondaduz, Switzerland) operated in parallel using a LabVIEW (v 8.0.1, National Instruments, TX, USA) program written in-house were used to deliver 1×10^{-3} M of amaranth solution (100%) and deionized

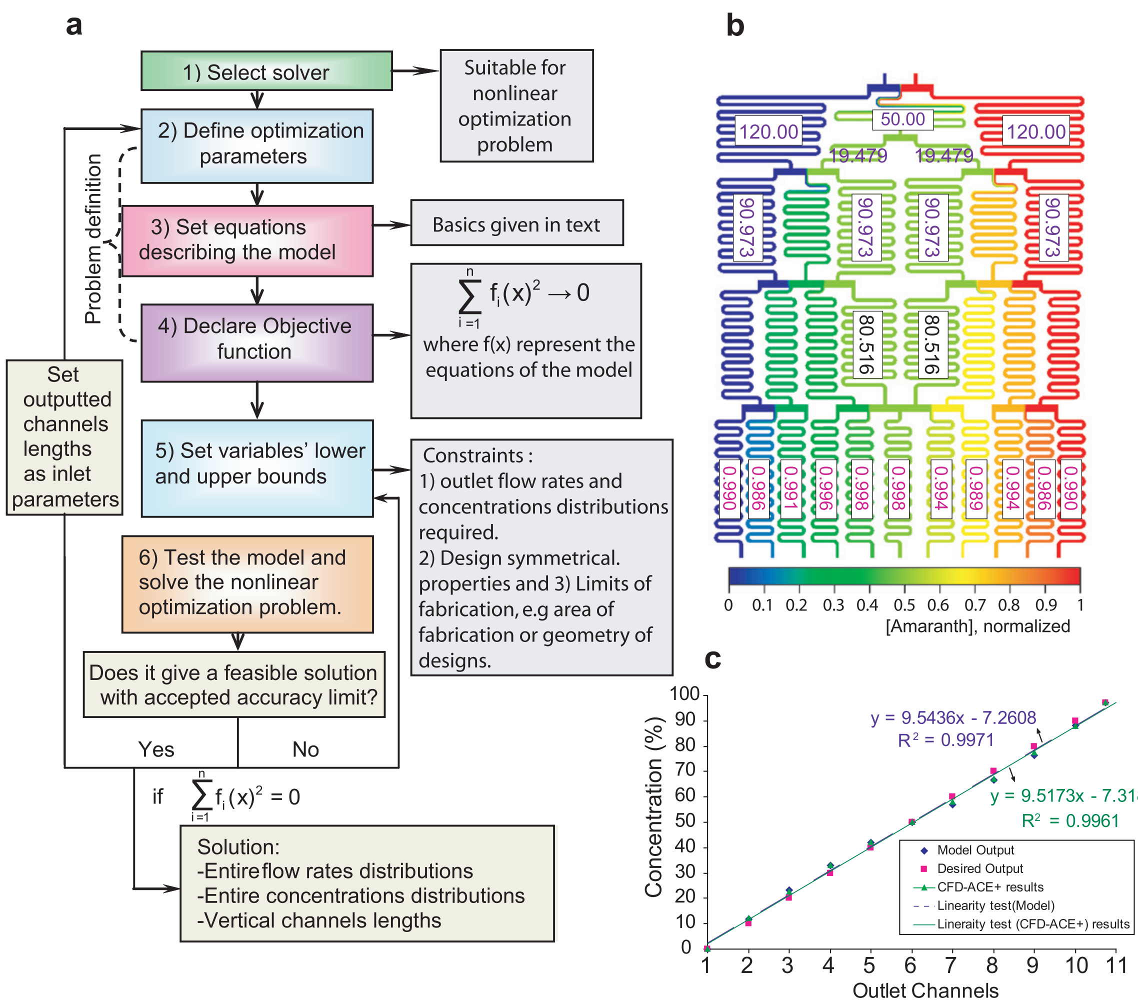

Fig. 2. (a) An algorithm for the generation and optimization of simplified *x*-inlet- *y*-outlet networks. (b) Performance of the optimized (2–11) design: flow rates (given on the last level network in relative units) and channels length (in mm) calculated using the optimization algorithm are superimposed on the concentration distribution found by CFD simulation (CFD-ACE+) (for simplicity only vertical channel lengths and outlet profiles are shown). All unlabelled vertical channels were 60 mm, with similar channel widths and depths to (2–6) designs). (c) Comparison of CFD and model output for the outlet concentration distribution of amaranth.

water (0%) at 0.1 μl/s to the microfluidic reactor. Solutions were in-line filtered (0.45 μm filter units (Millipore, Co. Cork, Ireland).

4.2. Optical detection system

All images were taken using a 1.3 Megapixel camera (Lu 125M, Lumenera Co., Ontario, Canada), with a 25 mm fixed focal length lens (A54789, Edmund Optics, UK). The illumination source was a light box fitted with an optical filter. The average pixel intensity at all positions of interest was evaluated using image J (v 1.37) and all data was background-corrected and corrected for the relative intensity changes between images.

4.3. Experiment validation

Fig. 3 presents the results for the conventional and simplified designs. The experimental results show minor artifacts, in that negative and >100% concentration values were produced. This was mainly due to the non-uniformity of the illumination used (future work will use a more even light source). However, as shown in Fig. 3d, good linearity of the outlet profile was achieved with both designs, thus validating the new model.

Furthermore, the simplified network had additional practical benefits over the conventional design: any bubbles formed were more easily removed and the device withstood higher inlet pressures.

5. Conclusion and further work

A computer-based optimization procedure for generation of simple, novel, designs of microfluidic diluters that produce equivalent performance to conventional designs has been developed, giving output flow rates and concentrations very close to those specified. Calculations using the procedure show high agreement with the results of

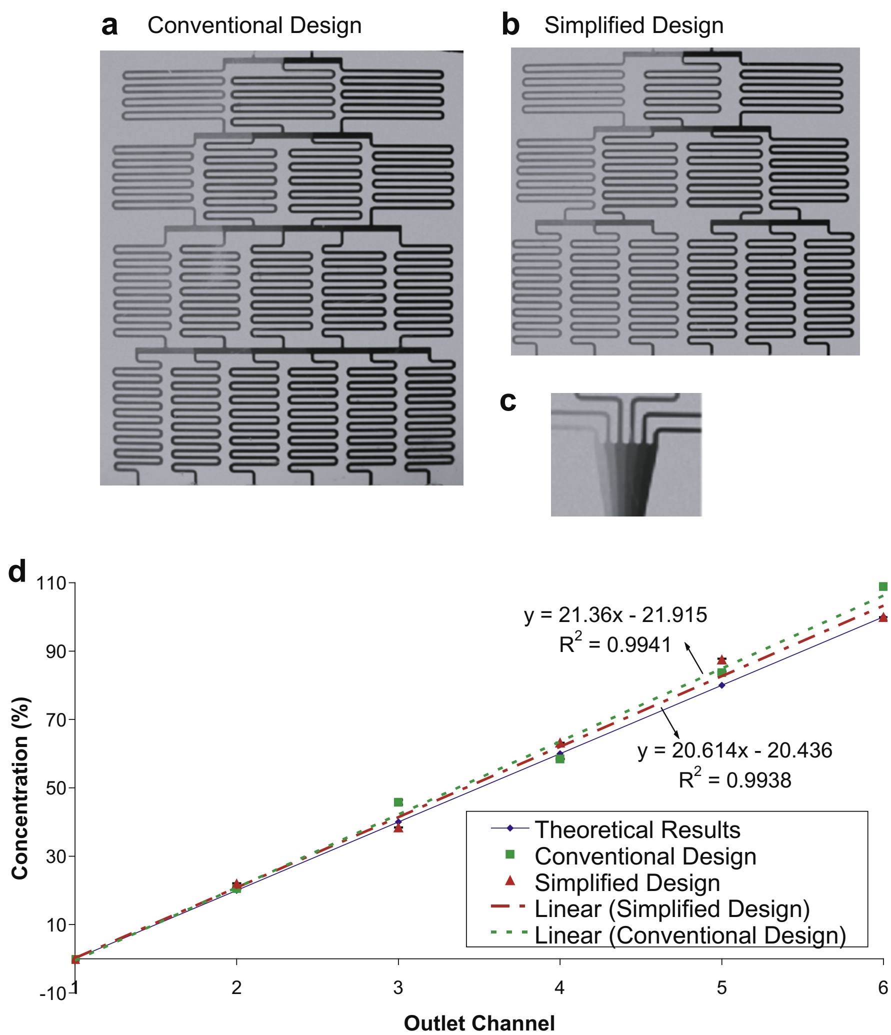

Fig. 3. (a) and (b) Images of concentration gradient generated by the (2–6) designs. (c) A close-up of the combined outlet of the conventional (2–6) design network. (d) Comparison of the outlet concentration profile of both designs showing good linearity (relative standard deviation for both designs is <1.54%).

experiments and CFD simulations, thus validating the method.

Further work will consider improving the instrumentation, modifying the designs for higher throughput applications, and will study the effect of inlet variables on diluter systems.

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