A Hybrid Micromixer with Planar Mixing Units

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Herein is a detailed description of aforementioned concepts and methods. The file includes:

- History of design of experiments (DOE)
- Detailed description of Taguchi method as a statistical approach
- Mixing Experiments
- Grid Study of the Numerical Simulations
- Numerical Results of DOE table
- Exact dimension of the fabricated microchip
- Comparison of numerical and experimental results of design number of 7, and 21
- Tesla units in the “hybrid” micromixer
History of design of experiments (DOE)

The history of the design of experiment (DOE) method comprises four different eras. Its initial principles were primarily developed by R. A. Fisher in the agricultural field between the 1920s and 1940s. His works primarily depended on the factorial design and analysis of variance (ANOVA) [1]. The second era, coined as the first industrial era saw the response surface method employed by Box and Wilson in the chemical industry from 1951 to the end of the 1970s [2]. The second industrial era, or the quality revolution, started from the late 1970s until 1990. After the Second World War, during the degradation of the quality of the company’s products, scientists began to use two techniques, total quality management (TQM) and continuous quality improvement (CQI). A Japanese engineer, Genichi Taguchi [3], presented a developed technique to find the optimal design parameters by introducing orthogonal arrays. His method could be applied to both categorical and numerical factors, and his major achievement was variance reduction, in which the total number of experiments were significantly reduced [4, 5]. The optimal values of the parameters could be chosen by the concept of signal to noise ratio (S/N ratio). The last era, the “modern era,” started in 1990 and saw companies utilize previously developed statistical and management techniques to improve the quality of their products and minimize cost. It is of vital importance to mention that the corresponding DOE methods render the experiments of researchers more accurate and convenient and are particularly relevant to microfluidic projects. Therefore, numerous research groups have utilized DOE in the microfluidic field, especially in clinical trials, in order to reduce the developing time of new products, improve performance and reliability of their available products, optimize their current product, and develop a new product [6, 7]. Even though numerous DOE studies have been proposed in microfluidics, an extensive workflow with a methodized procedure is sadly lacking, especially for the combination of several mixing units together.
**Detailed description of Taguchi method as a statistical approach**

Sir Fisher was the pioneer of selecting certain experiments in which many factors exist, and the approach name was set as the factorial design of experiments. The full factorial design considers all possible combinations of factors. In light of the fact that in real industrial projects so many factors play a specific role, investigating of all their combinations cannot carefully be managed, let alone with repetition. Therefore, scientists came to realize that a selection of experiments have to be performed while all features of the factors are tested [8].

Dr. Genichi Taguchi, a Japanese scientist at the telecommunications company NTT during the 1950s and 1960s, attempted to use statistical techniques to both reduce total number of experiments and gain the optimum results in a low-cost manner. After careful evaluations, he comprehended that for a design process, three stages have to be analyzed with significant attention. These are design of system, parameters, and tolerance. System design accounts for identification of the major elements of a system, considering both creativity and innovation. Parameter design, otherwise known as robustification, is about providing the proper amount of parameters for the design element. Tolerance design is centered around controlling and minimizing the effect of sensitive design parameters on the quality of the system’s output [9].

The most important fact in the Taguchi method is that the factors have to be independent of each other. For instance, pressure and velocity are related in a laminar flow within a microchannel; therefore, these two parameters are dependent and cannot be assumed in the Taguchi method at the same time. In the Taguchi method, a specific combination of parameters is used and named as an orthogonal array. By using these values, details of all parameters which affect final results are identified. Although many standard orthogonal arrays are available, each of them is specific to a particular set of design variables and their parameters. For instance, in this study, the effects of six variables (which are locations of mixing units) and five levels (which are mixing units) are to be analyzed; therefore, an
orthogonal array of L25 is chosen. The arrays take into consideration the interactions between units to ensure each variable assessed is independent. This fact can be observed in this study where mixing units are independent, and the performance of one units does not impact others. The layout of $L_{25}(5^6)$ is shown in Table S1 [3].

In Table S1, it is obvious that the parameters in the leftmost columns change at a slower rate than the rightmost columns. Considering the L25 orthogonal array, the selected features present are listed as follows:

- **Balancing property**: all levels of each variable have to be repeated equally in the vertical column. For instance, in mixing unit 6, all levels appear quintuple.
- All levels of mixing units are present in Table 1.
- In the end, to satisfy Taguchi orthogonal array, the level sequence should not be changed for performing the simulations. In other words, in experiments 1, the level for variable 1 has to be 1.

The minimum number of experiments can be calculated by equation (1)

$$N = 1 + N_V(L - 1)$$

where $N_V$ is total number of experiments and $L$ in number of levels. Where factors with different levels are available, summation of those levels are used instead.

In this study, $N_V = 6$ and $L = 5$, therefore: $N=25$. 

Table S1 Table of Taguchi for six variables, each of which has five levels

| Experiments | Unit 1 | Unit 2 | Unit 3 | Unit 4 | Unit 5 | Unit 6 |
|-------------|--------|--------|--------|--------|--------|--------|
| 1           | 1      | 1      | 1      | 1      | 1      | 1      |
| 2           | 1      | 2      | 2      | 2      | 2      | 2      |
| 3           | 1      | 3      | 3      | 3      | 3      | 3      |
| 4           | 1      | 4      | 4      | 4      | 4      | 4      |
| 5           | 1      | 5      | 5      | 5      | 5      | 5      |
| 6           | 2      | 1      | 2      | 3      | 4      | 5      |
| 7           | 2      | 2      | 3      | 4      | 5      | 1      |
| 8           | 2      | 3      | 4      | 5      | 1      | 2      |
| 9           | 2      | 4      | 5      | 1      | 2      | 3      |
| 10          | 2      | 5      | 1      | 2      | 3      | 4      |
| 11          | 3      | 1      | 3      | 5      | 2      | 4      |
| 12          | 3      | 2      | 4      | 1      | 3      | 5      |
| 13          | 3      | 3      | 5      | 2      | 4      | 1      |
| 14          | 3      | 4      | 1      | 3      | 5      | 2      |
| 15          | 3      | 5      | 2      | 4      | 1      | 3      |
| 16          | 4      | 1      | 4      | 2      | 5      | 3      |
| 17          | 4      | 2      | 5      | 3      | 1      | 4      |
| 18          | 4      | 3      | 1      | 4      | 2      | 5      |
| 19          | 4      | 4      | 2      | 5      | 3      | 1      |
| 20          | 4      | 5      | 3      | 1      | 4      | 2      |
| 21          | 5      | 1      | 5      | 4      | 3      | 2      |
| 22          | 5      | 2      | 1      | 5      | 4      | 3      |
| 23          | 5      | 3      | 2      | 1      | 5      | 4      |
| 24          | 5      | 4      | 3      | 2      | 1      | 5      |
| 25          | 5      | 5      | 4      | 3      | 2      | 1      |

The common orthogonal arrays are listed as follows:

- 2-level: $L_4$, $L_8$, $L_{12}$, $L_{16}$, $L_{32}$
- 3-level: $L_9$, $L_{18}$, $L_{27}$
- 4-level: $L_{16}$, $L_{32}$

**Mixing Experiments**

As it is illustrated in Fig. S1a, two samples were simultaneously injected from inlets by a syringe pump (Harvard Co., USA) at the same Re number. Afterwards, snapshots and the related video files were taken along the length of the micromixers to evaluate the mixing quality of the devices by comparing them with the numerical ones. The fabricated microchannels were filled with red dye for better detail as depicted in Fig. S1b.
Grid Study of the Numerical Simulations

In order to complete the Taguchi table, a total of 25 simulations were done. Accuracy and the number of elements were mutually exclusive. On the one hand, a few elements led to increased computational speed, but could not bear high accuracy. But on the other hand, a myriad of elements can give a guarantee that the accuracy of simulations is high, even though it is time-consuming and requires advanced computer configurations. Thus, to find out the optimal grid numbers, six distinct mesh elements were applied with a total number of grids varying from 89145 to 2379097. Fig. S1c shows the mixing index of the 11\textsuperscript{th} design number in the DOE table for different mesh element as one example of grid study in this paper and Fig. S1d illustrates the corresponding error when meshes are refined.

As the number of elements increases so does the variance, as a result of which, the mixing index will be decreased. Beyond the element number of 1367415, the effect of increasing the number of elements on the accuracy of the result is not significant. Therefore, this number of meshes was selected for further investigation on the micromixer. The type, size, refinement, and type of mesh distribution were essential for the accuracy and speed of the results. In this regard, Fig. S1e shows the mesh quality of the nominated grid. The picture reveals that the elements are refined at the corners and edges of the geometry. By using the statistical method and in accordance with FEM theory, it is proven that the average mesh quality is as high as 0.65 which is enough to solve the micromixer models. For all other micromixer designs, the procedure for mesh study is same as what was already mentioned.

Numerical Result of DOE table

Concentration, velocity, and pressure distribution of design No.7 in the DOE table is illustrated in Fig. S2. Other designs have the same trend as Fig. S2.
**Exact dimensions of the fabricated microchip**

In this study, in order to measure the exact dimension of the microchip, the profilometer is used. The profilometer of design numbers 12, 16, 25, and the nominated design are illustrated in Fig. S3. The outputs of this figure will be inputs for calculating the hydraulic diameter. By doing so, the velocity corresponding to the desired Re number will be accurate while the noise in results will be minimized.

**Comparison of numerical and experimental results of design number of 7, and 21**

Fig. S4 accounts for the comparison between numerical and experimental results for certain micromixers. The experimental results are identified by a loosely dash-dotted rectangle. In addition, over the length of the micromixer, the numerical results are consistent with the experimental results, confirming their accuracy. This can be observed in the selected sections visible in Fig. S4. As the comparison reveals, the CFD code well-matched with the experimental results.

**Tesla units in the “hybrid” micromixer**

In the “hybrid” micromixer, it is noteworthy to take heed of units 5 and 6, which are Tesla units. Tesla unit exhibits the “Coanda effect,” which induces additional chaotic advection for better mixing which was introduced by Chien-Chong Hong et al. [10]. The Coanda effect can be defined as the tendency of the fluid which is in contact with a curved surface, to follow the surface curvature rather than the straight line. Fig. S5 describes this phenomenon for the diffusion- and advection-based mixing processes. In Fig. S5a, fluids are guided through two different routes and then joined together. Since they join at opposite directions, the diffusion path decreases, and helps to increase the mixing efficiency. As the velocity increases, a low-pressure vortex is created which leads to additional advection at the transverse section. At the
outlet of the units, for a Re number of 0.5, fluids pass the microchannel, and the molecules on one side do not have any chance to diffuse with the molecules on another side. On the other hand, for the Re number of 25, due to the low-pressure vortices, there is additional possibility for fluids to be mixed together. For better illustration, arrow lines are drawn on Fig. S5.
List of Figures:
**Fig. S1** a) Micromixers are mounted on the microscopes and connected to the syringe pump and b) the selected microchips were filled with red dye for a better view of the microchip details c) grid study of the eleventh simulation from Taguchi table at Re=5 d) a table for the number of elements and the corresponding mixing index and e) the mesh quality of nominated grid with 1367415 elements
Fig. S2 a) Concentration, b) velocity, and c) pressure distribution along the length of combined micromixer with mixing unit for the seventh micromixer in DOE table
Fig. S3 Profilometer for design numbers of a) 12 b) 16 c) 25 and d) the nominated micromixer with MURO
**Fig. S4** Comparison of numerical and experimental results of the design number of a) 7, and b) 21
Fig. S5 “Coanda effect” as well as effects of low-pressure vortices in mixing procedure of units 5 and 6.
Supporting Movie- experimental results certain micromixers

The video provided in this study is a comparison between experimental and numerical results to find out how are the quality of the simulated micromixers. For this aim, design numbers of 7, 12, 16, 21, 25, and the “hybrid” micromixer are tested. The “hybrid” micromixer is also tested in a wide range of Re numbers. The flow behavior of the experimental and simulation results show that there is not any discrepancy between the results, and the parameter settings for numerical simulations are adjusted well.

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