CASE STUDY

Bartels mikrotechnik

with passion for microfluidics

Passive, semi-active and active fluid mixing in microfluidics for bioprocesses in life sciences

December 2022

Author:
Florian Siemenroth

Microfluidic fluid mixing

Diagnostics, biosensing, DNA analysis & sequencing

Fluid mixing is the principle of merging two immiscible fluids to a homogenous ratio. As microfluidics is an enabling technology for bioprocesses in life sciences, mixing plays a very big role in applications such as biotechnological diagnostics, biosensing, DNA analysis and sequencing, but also in flow chemistry and micro reaction applications.

In microfluidics, turbulent flow leads to cross-flows which fasten mixing. Adding active mixing principles like agitation completes the efficient mixing processes. In microfluidics laminar flow commonly is the governing flow type. The lack of cross-flows leads to the fact diffusion is the governing mixing principle. Diffusion is a very slow process and this would need very long flow channels which would lead the characteristics of microfluidics ad absurdum. So, scientists have developed many principles for introducing cross-flows artificially. Even active mixing is possible at microfluidic footprint.

The objective of this case study is to give a quick overview of the general mixing behavior in microfluidics and to demonstrate three different mixing principles.

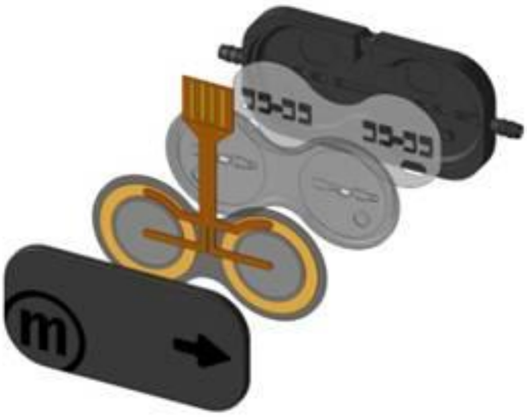
What is microfluidics?

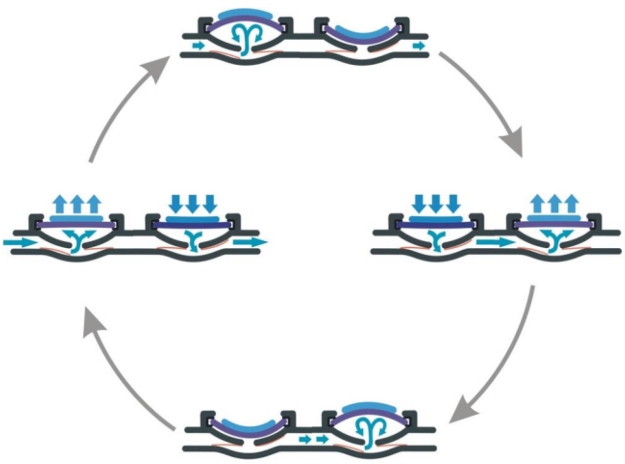
Microfluidics is the fine art of creation and manipulation of small portions of fluids, often realized by flow within small, sub-millimeter-scale channels. These small dimensions allow the fluid flow to be controlled with exquisite precision (Seifert, Thiele; 2020).

About the mp6 micropump

The available, industrialized and commercialized example is the mp6 micropump by Bartels Mikrotechnik GmbH. This micro pump is a positive displacement membrane pump utilizing piezo buzzers. The alternating displacement of the piezo acutators lead to the following typical fluidic values of the pump:

- Liquids (eta = 1 mPas): q = 5 - 8000 µl/min in free flow and p > 600 mbar
- Gas: q > 25 ml/min in free flow and p > 150 mbar





Flow Types

There exist two different flow types in fluid dynamics: Laminar flow and turbulent flow.

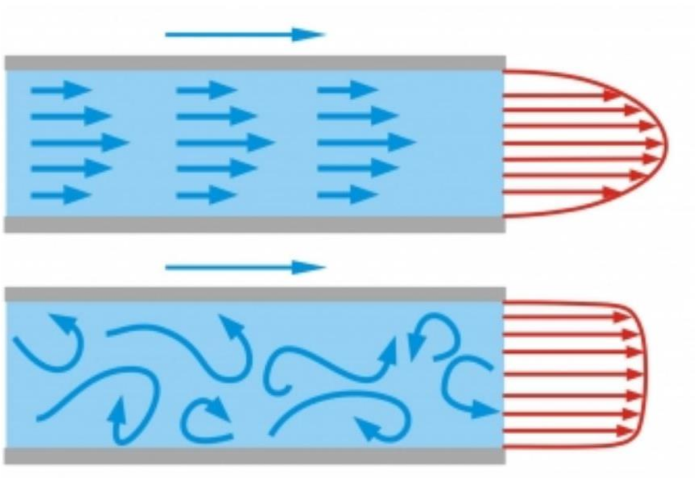


Figure 1 Laminar flow (top), Turbulent flow (bottom), Source: https://www.gunt.de/de/produkte/rohrreibung-bei-laminarer-turbulenter-stroemung/070.15001/hm150-01/glct-1:pa-119:pr-548

These flow types are described by the nondimensional Reynolds number:

$$Re = \frac{\rho v d}{\eta}$$

Whereas ρ is the density, v the flow speed, d a characteristic dimension (commonly diameter) and η the viscosity. For Re > 2300 there is turbulent flow, for Re < 2300 there is laminar flow. It is objective that variables v and d are governing if one compares micro- and macrofluidics. In microfluidics there are only very small dimensions and very slow speeds. So laminar flow is usually the governing flow type.

Diffusion

Diffusion is the principle of two regimes distributing heterogeneously. It is defined by Fick's law:

$$J = -D\frac{\partial n}{\partial x}$$

Whereas J is the particle current density, D is the diffusion coefficient, n is the concentration and x is the path. Diffusion is dependent on temperature and a very slow process. Whether a regime is governed by diffusion or advection can be estimated utilizing the Peclet number:

$$Pe = \frac{L * v}{a}$$

Whereas L is the path, v is the flow speed and a the thermal conductivity. For Pe > 1 there is advection and for Pe < 1 there is diffusion.

In microfluidics there is mainly diffusion. Mixing at high ratios would need very long channels which would not make sense from the microfluidic perspective. Therefore, cross-flows for advection need to be introduced. Scientists have researched and developed microfluidic structures that evoke the necessary advections.

Passive Micro Mixers

Many passive micro mixers have been developed. In this case study, we point out three different types.

The **meander and pearl-chain mixer** have an increased flow path which leads to an increased diffusion driven mixture since the contact time is increased. Plus, the pearl-chains evoke cross-flows, so advection takes place also. In the figure below one can see an example of a pearl-chain mixer by microfluidic ChipShop. Two differently colored water samples are induced by two micropumps. The setup has got a very small, well-plate format. One can see that at the beginning there is only diffusion, so nearly no mixing process as the colored water samples are separated from each other. As soon as the two regimes reach the meander, pear-chain structure a more efficient mixture process starts.

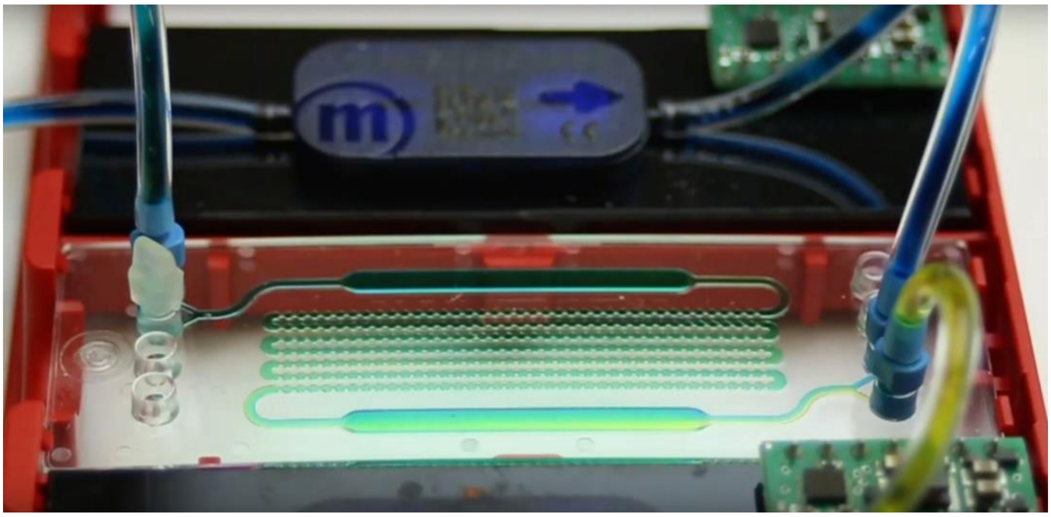


Figure 2 Pearl-Chain mixer setup driven by micropumps on a well-plate format

Another option of mixing in microfluidics is the **herringbone mixer**. It evokes an asymmetric flow behavior and therefore cross-flows for advection. The speed of the mixing process is increased.

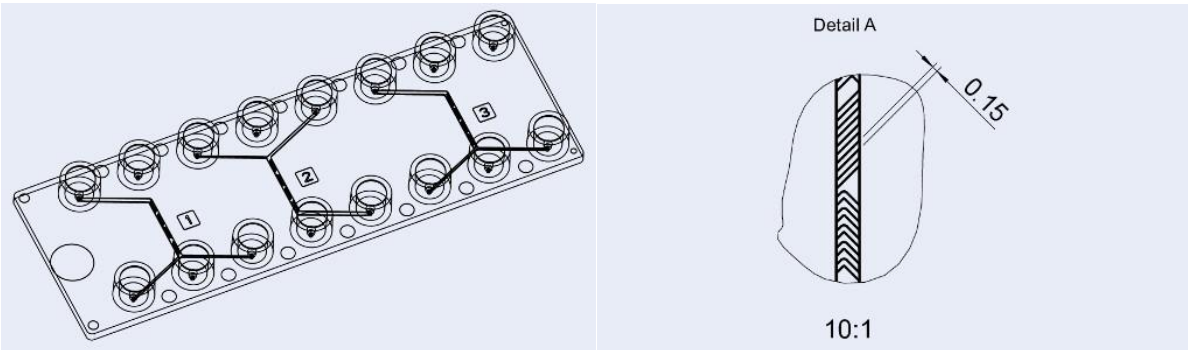


Figure 3 Example of a Herringbone mixer by microfluidic ChipShop Source: https://www.microfluidic-chipshop.com/catalogue/microfluidic-chips/polymer-chips/micro-mixer/micro-mixer-fluidic-187/

A third alternative for mixing is a 3D structured microfluidic chip, the **3D serpentine chip**. It forces the flow into different directions. Again, cross-flows for advection is increased and the efficiency of mixing is boosted.

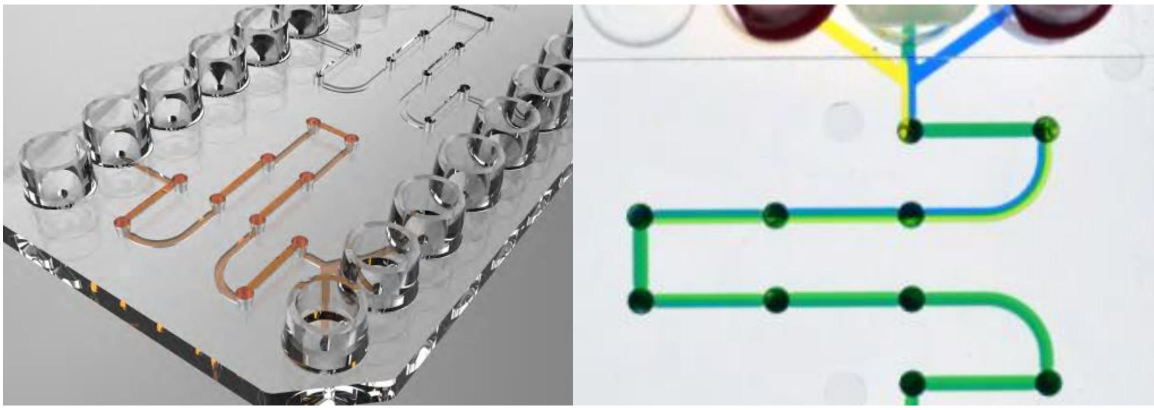


Figure 4 3D Serpentine mixer by microfludic ChipShop; Source: https://www.microfluidic-chipshop.com/wp-content/uploads/2021/01/ApNoteFluidic1079_ApJA1079V1.pdf

The benefit of these passive processes is
- mixing within an in-line flow is possible and
- one does not need an active unit which saves space, costs and power.

On the other hand, the mixture results can be poorer than the results from the active mixing processes.

Semi-active mixing

The semi-active principle is an extension of the passive mixing principle. It is based on passive structures, but it also utilizes active microfluidic units moving a mixture back and forth. That leads to a high contact time within in the mixing region and evokes more advection and a higher mixing ratio compared to the passive mixing principles. Here, an example is displayed in which one-directional micropumps have been combined with a logic arrangement of valves realizing a bi-direction flow for pumping liquid column within the pearl-chain mixer realizing a much higher mixture ratio.

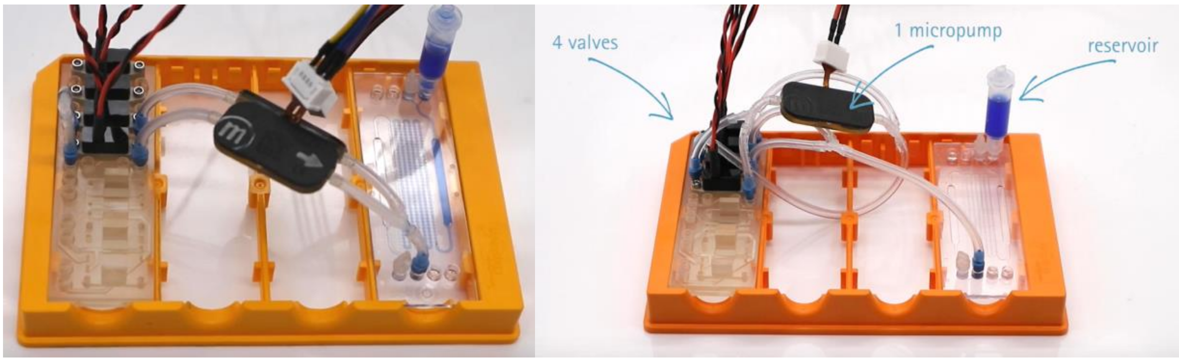


Figure 5 Semi-Active Fluid mixing utilizing unidirectional micropumps and logic valve arrangements

Two concepts for semi-active fluid mixing are possible. On the one hand, utilizing two 2/2- way valves and two micropumps for a separately controllable back and forth way (below on the left). On the other hand, there is the option of utilizing four 2/2-way valves or two 2/3-way valves and one micropump decreasing the amount of micropump parameters (below on the right).

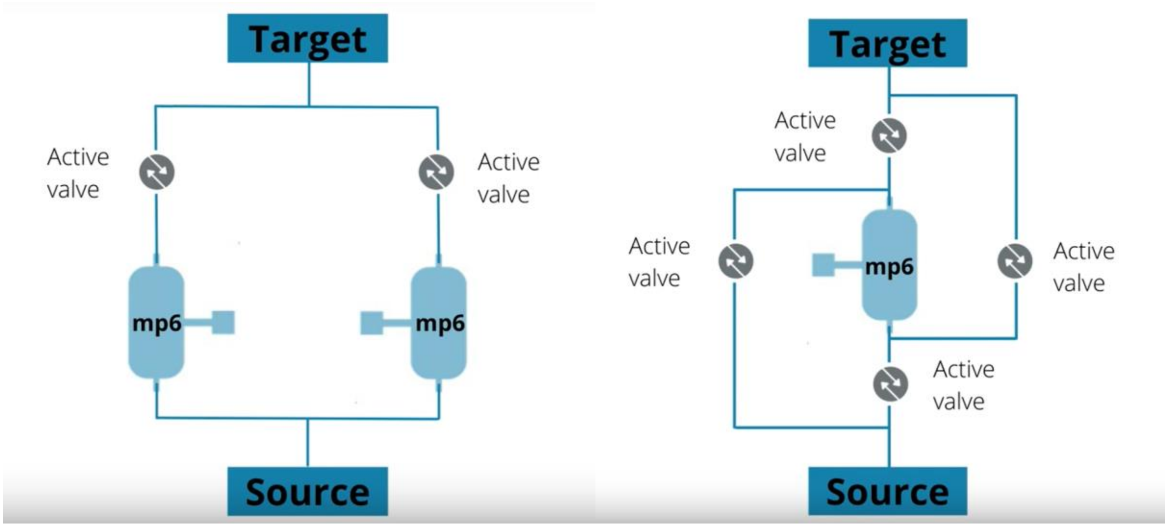


Figure 6 Two valve concepts for bi-directional flow utilizing one-directional micropumps

The advantage is that one is able to achieve high mixing ratios, but the issue is that these processes are appropriate for in-line processes as it always has a percentage of an iterative process.

Active Mixing

A third option of mixing is the full active mixing principles known from macrofluidics, i.e. stirring for instance. There are industrialized microfluidic structures or chips that offer the possibility of stir bar activated mixing processes that evoke advection offering an intense ration of mixtures.

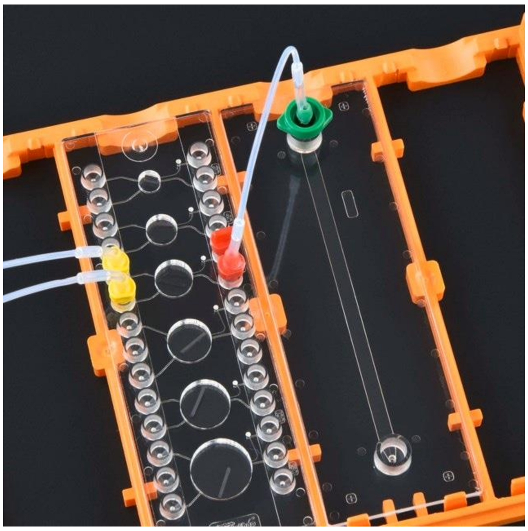


Figure 7 Stir bar activated chip by microfluidic ChipShop; Source: https://www.sigmaaldrich.com/DE/de/product/aldrich/926272

In these cases, it is hardly possible to realize a dynamic in-line mixing procedure and it has the need of a complex equipment of the microfluidic structures such as adding stir bars. But of course, as stated before, the mixing result is highly heterogeneous.

Conclusion

As one can see microfluidics is not as trivial as macrofluidics at certain points. Due to its fluid dynamic characteristics, mixing in microfluidics bares some issues that are uncommon in macrofluidics. Only relying on diffusion would require very long channels and therefore it would not fit to the idea of microfluidics. Scientists and engineers have developed a bunch of reasonable passive and active mixing principles that go with many different applications.

Components used

- mp-Multiboard2 incl. mp6 micropump drivers and valve drivers by Bartels Mikrotechnik
- mp6 micropumps by Bartels Mikrotechnik
- microfluidic mixer chips by microfluidic Chipshop: Fluidic 286, Fluidic 1079, Fluidic 658 & Fluidic 187
- NC-valve series09 by memetis

Acknowledgement:

Our partners *microfluidic ChipShop* from Jena and *memetis* from Karlsruhe were instrumental in defining our research path, whereby we were able to develop great solutions for fluid mixing. For that, we are extremely grateful and we are looking forward to our close collaboration. In case you are interested in the above-described microfluidic components or if you are interested in getting in touch with either one of us, *microfluidic ChipShop*, *Memetis* or *Bartels Mikrotechnik*, please feel free to contact us. You can find the contact details below.

Bartels mikrotechnik

Bartels Mikrotechnik is a globally active manufacturer and development service provider in the field of microfluidics. In the microEngineering division, the company supports industrial customers in the modification, adaptation and new development of high-performance and market-oriented product solutions through the innovative means of microsystems technology. The second division, microComponents, produces and distributes microfluidic products and systems, especially for miniaturized and portable applications. Our key products are micropumps that convey smallest quantities of gases or liquids and are used in a variety of ways in biotechnology, pharmaceuticals, medical technology and numerous other applications.

Bartels Mikrotechnik with passion for microfluidics!

Contact us:

Bartels Mikrotechnik GmbH
Konrad-Adenauer-Allee 11
44263 Dortmund Germany

www.bartels-mikrotechnik.de
info@bartels-mikrotechnik.de
Tel: +49-231-47730-500

Follow Bartels: