Micro annular gear pumps generate controlled two-phase flow for Lab-on-a-Chip applications

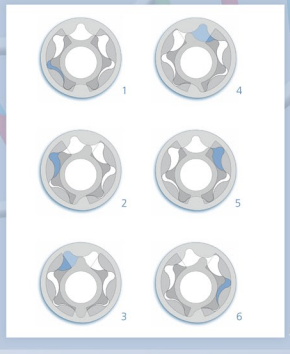
Dorothee M. Runge[1], Ronny Borchert[2], Thomas Heinze[1]

[1]HNP Mikrosysteme GmbH, Parchim
[2]Department of Computer Science, Fachhochschule Stralsund

Introduction • Micro annular gear pumps are implemented in volume controlled generation of two-phase flows in micro channels (diameter: 300 x 260 µm, length: 3,4 m). The optimized system can be used for automated continuous analysis and synthesis in chemical or fermentation processes. One application using two-phase flows is continuous Polymerase Chain Reaction (PCR), where the increase of DNA during the production of vaccines helps to monitor the fermentation process over time and allows optimization of production and product quality.
To generate a stable two-phase flow the extremely precise dosing of carrier fluid and sample fluid is essential. Such demanding metering tasks of few micro liter per minute or hour can be achieved by micro annular gear pumps in combination with volume flow controllers. These pumps are characterized by high performance and precision as well as low pulsation and continuous flow.
By integration of micro annular gear pumps into functional modules a compact design is warranted for Lab-on-a-Chip applications.

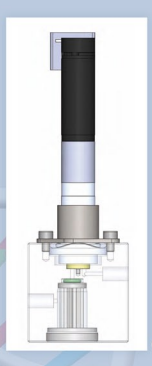
Functional module of filter, pump and volume flow meter

Fig. 1 Micro annular gear pumps are positive displacement pumps with an internal rotor and an external rotor turning around slightly eccentric axes. Both rotors are interlocked at any time and form a system of several chambers **(A)**. As the rotors turn around their offset axes, the chambers increase on the induction side and simultaneously decrease on the delivery side of the pump. A homogeneous flow is generated between the kidney-like inlet and outlet.
Part C of the figure shows the CAD-model of a modular micro annular gear pump mzr-2521 in a manifold with integrated filter (filter mesh 7 µm). Two of these compact units combined with a check valve and a volume flow meter **(B)** can be used to generate two-phase flows.
Depending on the fluids used, either pumps mzr-2521/mzr-2921 of the low pressure series (materials in contact with fluid: stainless steel/ tungsten carbide) or of the modular series mzr-2542/mzr-2942 (materials in contact with fluid: ceramics, Alloy C22, PEEK, tungsten carbide) can be used.



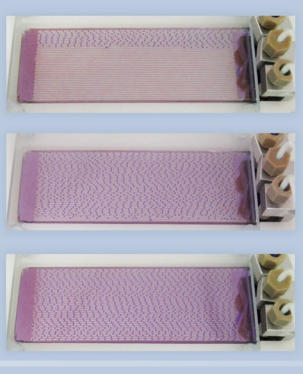
A


B

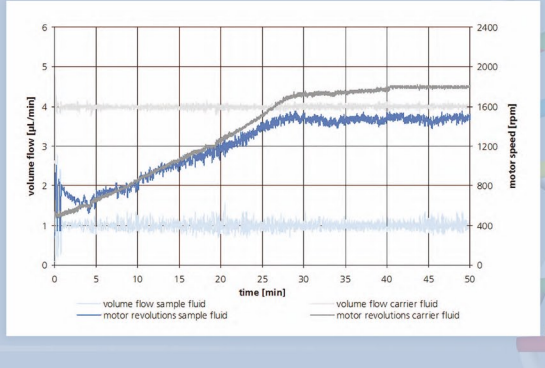

C

Volume flow controlled two-phase flow

Fig. 2 **Part A** of the figure shows how the PCR-Chip is filled with carrier and sample fluid in a two-phase flow, starting with the chip filled with carrier fluid only, volume flow at 4 µL/min. Sample fluid is introduced at 1 µL/min.
The graph in **part B** displays the volume flows of the two fluids over time as they are controlled by the volume flow meters and the increase in motor revolutions with the increase of fill level of the PCR-Chip.



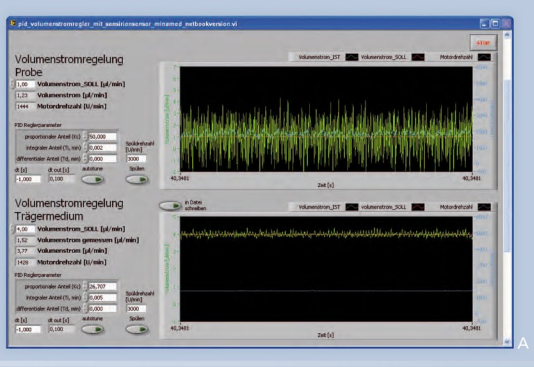
A



B

Volume flow regulation using LabView

Fig. 3 Volume flow of the carrier fluid is controlled at 4 µL/min, sample fluid at 1 µL/ min **(A)**.
This results in a volume flow on the PCR-Chip of 5,7 µL/min **(B)**. Distance between the drops of sample fluid is considered constant. Control of volume flow is realized using LabView.

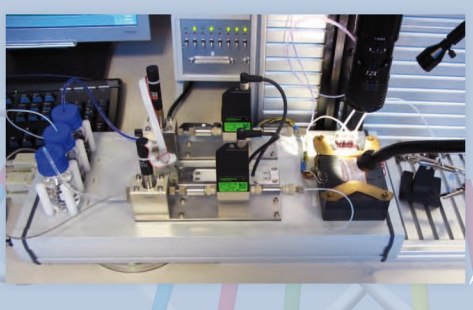


A

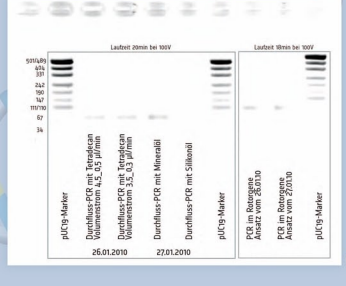

B

Continuous PCR in two-phase flow on Chip

Fig. 4 **Part A** of the figure shows the setup used for continuous PCR on a chip. A Peltier heating element is placed under the chip, controlled by a heating system. Three temperature zones are created, the sample flow over those temperature zones is volume flow controlled.
Part B shows the view through the camera positioned above the PCR-Chip. Sample drops are of equal size, spaces generated by carrier fluid do vary a little.
Part C shows the image of an agarose gel of PCR products generated by continuous PCR on a chip. On the left side samples of different volume flows in line 2 and 3 and of different carrier fluids in line 4 and 5 were separated, on the right side reference samples amplified in a regular PCR-apparatus are shown as positive controls of the PCR-process.


A


B



C

Summary and conclusions • A stable two-phase flow is generated in micro channels by two micro annular gear pumps combined with volume flow meters that control the volume flow via a program generated in LabView. This system can be used for continuous DNA-amplification by PCR, a method used to monitor fermentation processes over time. Small sample size as well as short processing time allows a closer monitoring of complex and expensive production of biological and pharmaceutical products.
By combining sample collecting devices with close contact to bioreactors with suitable offline sample processing devices and analytical instruments, even complex analytical problems can be solved.

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