proceedings

MDPI

Proceedings

High Throughput Roll-to-Roll Production of Microfluidic Chips †

Martin Smolka [1,*], Stephan Ruttloff [1], Dieter Nees [1], Christine Prietl [1], Valentin Satzinger [1], Bernhard Lamprecht [1], Philipp Hütter [1], Jan Hesse [1], Georgios Kokkinis [2], Günther Kriechhammer [2], Daniel Scheidl [2] and Bianca Wilfing [2]

[1] MATERIALS Institute, JOANNEUM RESEARCH Forschungsg. mbH, Weiz 8160, Austria; stephan.ruttloff@joanneum.at (S.R.); dieter.nees@joanneum.at (D.N.); christine.prietl@joanneum.at (C.P.); valentin.satzing@joanneum.at (V.S.); bernhard.lamprecht@joanneum.at (B.L.); philipp.huetter@joanneum.at (P.H.); jan.hesse@joanneum.at (J.H.)

[2] Pessl Instruments GmbH, 8160 Weiz, Austria; georgios.kokkinis@metos.at (G.K.); Guenther.kriechhammer@metos.at (G.K.); daniel.scheidl@metos.at (D.S.); Bianca.wilfing@metos.at (B.W.)

* Correspondence: martin.smolka@joanneum.at; Tel.: +43-316-876-3419

† Presented at the Eurosensors 2018 Conference, Graz, Austria, 9–12 September 2018.

Published: 4 December 2018

Abstract: A high throughput manufacturing process of microfluidic chips based on Roll-to-Roll imprinting is presented. With this procedure, microfluidic patterns can be produced on large area polymer substrates. The subsequent steps of inlet drilling, bonding and electrode printing are set-up on large area processes, too. Overall, this strategy allows highly parallelized processing of large numbers of chips—all costly steps of individual chip handling are avoided. The chips were used for the characterization of inorganic ions for soil nutrient analysis.

Keywords: Capillary Electrophoresis Microfluidic Chip; high throughput production; Roll-to-Roll production; Lab-on-a-Chip; Capacitively Coupled Contactless Conductivity Detection (C4D), soil nutrient analysis; plant macronutrient sensor

1. Introduction

Microfluidic systems promise revolutionary new approaches for measurement devices—compact, portable and with low sample consumption. Anyhow, the concept often bases on exchangeable single use chips. Hence, a breakthrough of the technology is only expectable if the chips can be produced at low prices. In this context, several researchers investigated the implementation of Roll-to-Roll (R2R) based processes, which allow continuous high throughput production of microfluidic chips. With this technology, microfluidic channels are produced by imprinting processes on polymer foil or paper based substrates. So far, this was realised by R2R hot embossing (see e.g., [1]) and PDMS imprinting [2]. Replication of channels with depths of up to 50 µm with hot embossing or 100 µm with PDMS imprinting was achieved. Whenever the needed microfluidic channels do not exceed these depths, R2R imprinting offers an attractive alternative to injection moulding. In addition, the major advantage of R2R technologies is given in the following post processing steps. Printing of sensor molecules or detection electrodes as well as bonding of a cover foil can be done in large area processes for many chips at the same time. This high degree of process parallelization without the need for complex single chip handling offers an essential potential for unit price reduction.

This contribution demonstrates the production of microfluidic patterns in an imprint process on large area polymer films by Roll-to-Roll Ultraviolet-Light-Assisted Nanoimprint Lithography

(R2R UV NIL) [3]. For the first time, this technique is demonstrated together with a full process flow, including laser inlet cutting, bonding, as well as large area printing of detection electrodes. The produced chips were equipped for measurements of ion concentrations in liquid samples.

2. Materials and Methods

2.1. Chip Production

Chip design: The chips have a size of 25 mm × 35 mm and consist of a separation channel (300 µm width × 50 µm depth). The sample is introduced through an injection channel (20 µm width × 50 µm depth), which crosses the separation channel in a T-junction. Towards the end of the separation channel, a pair of detectors is placed for ion detection based on Capacitively Coupled Contactless Conductivity Detection (C^4D, for details please refer to [4,5] and papers cited therein). The length of the separation channel between injection junction and detector is 81 mm.

Imprint stamp mastering for Roll-to-Roll production: A polymer based master was produced by photolithography with a glass-chromium mask containing the fluidic channel design of 8 chips (7 inch mask). A 125 µm thick PET Foil (Melinex ST506) with the size of 630 mm × 150 mm was used as substrate and the dry film resist Ordyl FP 450 was laminated with an office laminator at 100 °C. Due to its big area, the substrate was UV exposed with the same mask in 4 turns so that the design of the 8 chips was replicated 4 times. The resist was developed in 1% Na_2CO_3 and flushed with deionized water. For the following imprinting process, this lithography master was metalized by magnetron sputtering with 100 nm Cr. This metal surface was treated with an anti-adhesive coating. The imprint stamp mounted on a cylinder roll is shown in

Imprinting of microfluidic channels: Microfluidic channels were produced by R2R UV NIL. In this process, a liquid UV curable resin is uniformly deposited on a polymer based substrate foil (PET, Kemafoil HSPL80). A cylindrical imprint stamp is then continuously pressed into this liquid layer. During stamp contact the resin is exposed by UV through the transparent PET substrate foil. This initiates the curing reaction and the resin replicates the inverted pattern of the master. During detaching from the imprint stamp, microfluidic channels are produced in a continuous way. This imprint process is illustrated in Figure 1a). In this case, the cylindrical imprint stamp consisted of an imprint roller around which the flexible polymer imprint master with 4 × 8 chips was wrapped (see Figure 2a). An acrylate based UV curable resin (NILcure) was used for imprinting and the machine was operated with a web speed of 0.5 m/min (a foil of imprinted chips is shown in Figure 2b). With this speed, the UV initiated acrylate radical polymerization was not fully terminated. In this way, form stability of the imprinted material is reached but reactive acrylate groups remain, which can be used for further cross linking in the following bonding process.

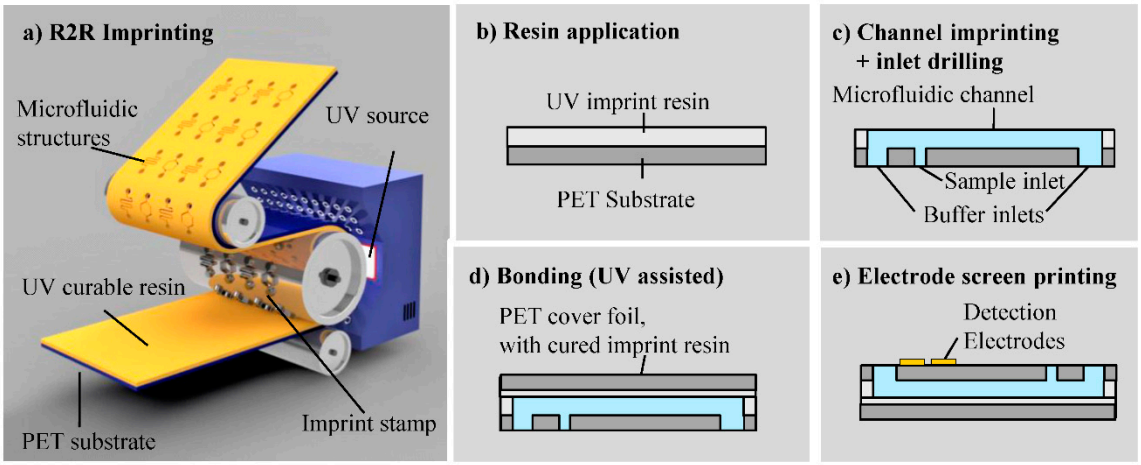

Figure 1. (**a**) Schematics of the R2R UV NIL process. (**b**–**e**) Process flow of capillary electrophoresis chip manufacturing.

Inlet cutting: Inlet holes at the two ends of the separation channel as well as at the end of the injection channel were produced by laser drilling with a femtosecond pulse laser.

Bonding: UV initiated bonding was performed by the combination of two surfaces of an only partly polymerized acrylate resin. Thus, the cover layer was also produced with the same material as the imprinted microfluidic patterns. In this case, a uniform layer of the acrylate resin was produced on PET (Kemafoil HSPL80). This layer was laminated to the imprinted microfluidic channels at room temperature. Cross linking of the remaining acrylate groups in both layers was initiated with UV exposure so that a chemical bond of the two layers was achieved.

Electrode printing: The detection electrodes for ion concentration measurements were produced by screen printing with silver ink. The full process flow is demonstrated in Figure 1, a fully assembled chip with electrodes is shown in Figure 2c)

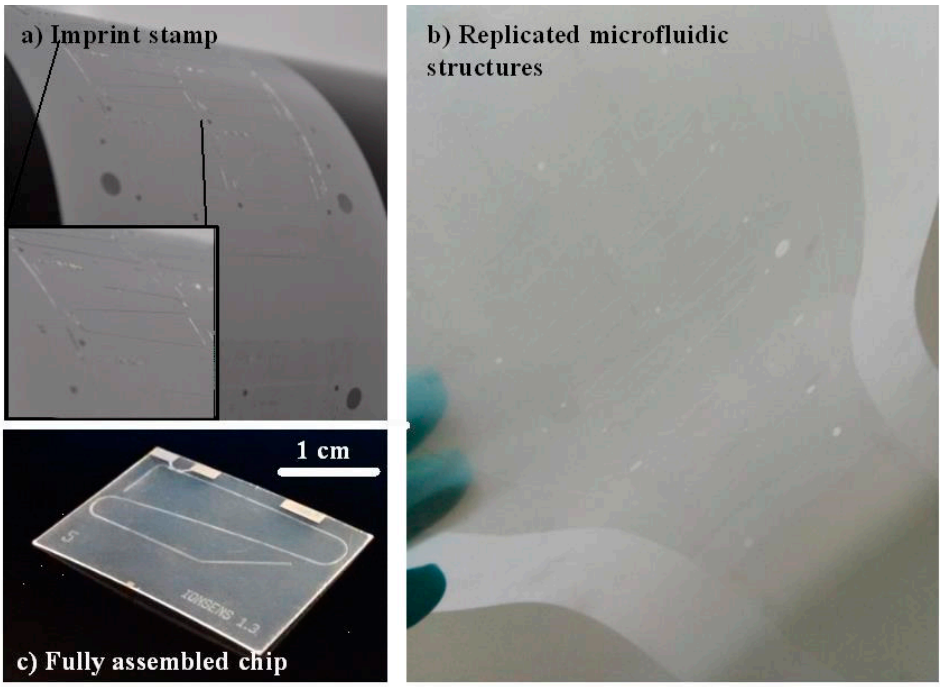

Figure 2. (**a**) The flexible metalized polymer imprint stamp wrapped around an imprint cylinder. (**b**) microfluidic structures replicated in UV NIL Roll-to-Roll process. (**c**) A fully assembled microfluidic CE chip.

2.2. Capillary Electrophoresis Measurements

CE measurements were performed with a device from Pessl Instruments GmbH (Austria) which was described in detail by Kokkinis et al. [4]. Once a chip is inserted, the device flushes the microfluidic channels with a buffer solution. The sample is injected from a bottom less container which is pressed on the chip. Injection and separation are activated with a high voltage supply. The complete device is compact and portable—a prerequisite for on-site field measurements. For all detailed measurement conditions please refer to [4].

3. Results and Discussion

A sample containing Cl^-, Br^-, NO_3^- and SO_4^{2-} ions was analysed. Br^- was added to the sample as internal standard [4]. All ions were fully separated and measured within 3 min, which can be seen in the electropherogram in Figure 3. The peak areas were evaluated with a peak recognition algorithm [4]. The peak area of each analyte peak as well as of the internal standard peak was calculated.

By applying an internal standard as reference to the before named ions, variations in chip manufacturing as well in each sample injection could be normalized. This allows the stable

implementation of the measurement technique with the presented high volume manufacturing process.

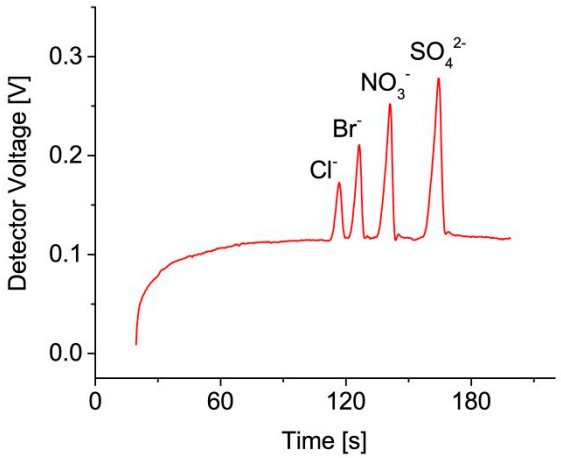

Figure 3. An electropherogram with baseline separation of a sample containing the ions Cl^-, Br^-, NO_3^- and SO_4^{2-}.

4. Conclusions

A full process flow for the production of microfluidic CE chips based on R2R imprinted microfluidic channels is presented. As all following steps are also suitable for large area, high throughput production, the technology opens the way to future high volume production of analytic chips.

Author Contributions: M.S. wrote the paper, D.N. and S.R. performed R2R imprinting, C.P. was responsible for the photolithography process development, P.H. developed chip electrode printing, B.L. and V.S. were in charge of Laser cutting. J.H. supervised the project. G.Kr. and B.W. were responsible for CE measurements, G.Ko. and D.S. were responsible for the CE device design.

Acknowledgments: This work was funded by the Austrian Research Funding Agency FFG under the project number 853407. The authors want to thank Harald Parizek for the Cr coating of the imprint stamps and acknowledge Coveme spa (Italy) for providing the PET substrate foils with brand name Kemafoil HSPL80.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Wang, X.; Liedert, C.; Liedert, R.; Papautsky, I. A disposable, roll-to-roll hot-embossed inertial microfluidic device for size-based sorting of microbeads and cells. *Lab Chip* **2016**, *16*, 1821–1830, doi:10.1039/C6LC00215C.
2. Hiltunen, J.; Liedert, C.; Hiltunen, M.; Huttunen, O.-H.; Hiitola-Keinänen, J.; Aikio, S.; Harjanne, M.; Kurkinen, M.; Hakalahti, L.; Lee, L.P. Roll-to-roll fabrication of integrated PDMS–paper microfluidics for nucleic acid amplification. *Lab Chip* **2018**, *18*, 1552–1559, doi:10.1039/C8LC00269J.
3. Leitgeb, M.; Nees, D.; Ruttloff, S.; Palfinger, U.; Götz, J.; Liska, R.; Belegratis, M.R.; Stadlober, B. Multilength Scale Patterning of Functional Layers by Roll-to-Roll Ultraviolet-Light-Assisted Nanoimprint Lithography. *ACS Nano* **2016**, *10*, 4926–4941, doi:10.1021/acsnano.5b07411.
4. Kokkinis, G.; Kriechhammer, G.; Scheidl, D.; Smolka, M. Lab-on-a-chip device for soil nutrient measurements. *Proc. HAICTA* **2017**, *2017*, 220–223. Available online: http://ceur-ws.org/Vol-2030/HAICTA_2017_paper24.pdf (accessed on 24 April 2018).

5. Smolka, M.; Puchberger-Enengl, D.; Bipoun, M.; Klasa, A.; Kiczkajlo, M.; Śmiechowski, W.; Sowiński, P.; Krutzler, C.; Keplinger, F.; Vellekoop, M.J. A mobile lab-on-a-chip device for on-site soil nutrient analysis. *Precis. Agric.* **2016**, *18*, 152–168. doi:10.1007/s11119-016-9452-y.