# Design of Experiment Evaluation of a 2.5D Printing Process for Implantable PDMS-based Neural Interfaces

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Abstract-Current laser fabrication processes for PDMSbased neural interfaces are associated with excessive costs, due to time-consuming manual handling and expensive machinery. The products of this process, specifically embedded metallic electrical tracks, are prone to breakage under mechanical loading, as well as delamination from their surrounding PDMS substrates. In this work, we develop an alternative 2.5D printing process, using electrically conductive PDMS material for the tracks. The entire electrode was fabricated in a custom-made printing setup, which features the possibility of rapid prototyping. The printing performance of the selected materials was evaluated with the aid of statistical methods for experimental design. We found optimal printing parameters for conductive and non-conductive PDMS which allows the fabrication of flexible and stretchable neural interfaces, while simultaneously minimizing the track resistivity.

*Clinical Relevance*— 2.5D printing processes pave the way for individualized neural interfaces to suit the specific needs of every single patient.

# I. INTRODUCTION

Neural interfaces provide the link between the nervous system and electronic medical devices. The state-of-the-art photolithography-based fabrication methods for these interfaces offer the advantages of micron-scale integration density but lack the practicality, cost-effectiveness, and speed needed to support their rapid customization to suit the needs of patients. This has motivated the development of alternative technologies, such as laser direct writing or rapid prototyping.

For this work, we considered the state-of-the-art PDMSbased neural interfaces as a reference, which consist of metallic conductive elements (tracks, electrode/assembly sites) embedded in a bulk silicone matrix. Among the essential design requirements for these interfaces is their flexibility, to allow their structural integration with the host environment. However, the use of metal foil as an electrically conductive material in the PDMS bulk limits the design choices of the electrodes, as well as their mechanical flexibility and robustness. Therefore, the need for customized implants to suit different patients remains yet unfulfilled [1]. Furthermore, the time-consuming fabrication steps, as well as high machinery costs, are indeed striking. This process requires the use of a ps-laser patterning system, as well as a considerable amount of manual handling of the metal foil while positioning and laminating it, and later when removing the excess material [2]. The goal of this work was to develop an electrode with improved flexibility, as well as reduced

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material waste and machinery costs. These had to be coupled with the preservation of the metal sites for cable assembly and electrode contacts, for the assembly of connecting cables (e.g., soldering), and biological interfacing purposes, respectively. Therefore, the developed concept involved the replacement of only the metal tracks by a flexible, electrically conductive PDMS material. The conductive network between



Figure 1 Sketch of layered approach for printing flexible neural interfaces showing the base layer with openings for contact sites, the track layer connecting the metal contacts, the fill layer to level the surface around the track, and finally the cover layer to encapsulate the track completely.

the metal contacts would be completely embedded in the PDMS matrix, with openings for contact and assembly sites. A layered approach was selected for this, as depicted in Figure 1. The technology chosen for fabrication was 2.5D-printing, which allowed the combination of all process steps into one machine, thereby significantly reducing production and material costs. The factors expected to influence the printing process were defined, and a factorial experimentation strategy was implemented to characterize the process. This strategy had the advantage that factors were varied together – instead of one at a time – thereby also considering the interaction between them. Additionally, this strategy made the most efficient use of the experimental data, thereby saving considerable time and material expenses.

## II. MATERIALS AND METHODS

# A. Material selection

The selection of materials for the printing process was based on their usability and their electrical, mechanical, and curing properties. For printing the bulk of the electrodes, the medical-grade silicone MED-1000 (NuSil Technology LLC, Carpinteria, CA) was used. This polymer had been proven effective in the manufacture of PDMS-based electrodes [3]. For the conductive tracks, EC-6601 (Dow Corporate, Midland, MI) was used due to its superior properties compared to other similar conductive silicones. EC-6601 PDMS is a one-part, moisture-curing PDMS with silver filler and a volume resistivity of 0.0027  $\Omega$ cm. Its applications

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include printed circuit board (PCB) grounding, electrical connections, and adhesive/sealant gaskets designed for electromagnetic compatibility solutions [4]. Further, no cure inhibition was observed in contact with MED1000.

An alloy of platinum and iridium (PtIr10) was used for the electrode sites, due to its long history and excellent properties in various types of medical implants [5] and its use in the standard process for the whole conductive network.



Figure 2. Schematics of the printing system setup, showing the vacuum chuck, where the substrate is fixed, and which is movable in the y-axis direction. The syringe is also depicted at a z-distance from the substrate (gap height, in mm), connected to the pressurized air inlet and movable in the x- and z-axis directions. This setup shows the combination of the three main factors, namely pressure (bar), gap height (mm) and speed (mm/min).

#### B. Equipment

A computer numerical control (CNC) machine (isy CAM 3.6, isel Germany AG, Eichenzell, Germany) with an original function of milling was used since it already comprised the most important building blocks required of a printer. It consisted of a motorized maneuverable tool and platform, controlled by machine instructions in G-code.

The machine was adapted to change its milling function into printing: The three-axis system was used as in the milling function, only the z-axis was kept constant while printing, and the gap height was set for each layer. An adjustable compressed air outlet was adapted to control the extrusion of PDMS from a syringe by pushing the plunger. For the alignment of printing tips between the layers, a vacuum chuck with alignment bolts for substrate alignment was added to the platform, and a syringe holder with fixed positioning for different syringe tips was integrated with the tool (Figure 2).

## C. Factorial Experimentation Strategy

In most problems of science and engineering, the relationship between factors and responses of a system requires observation and experimentation to be understood. Careful planning of experiments is important because the manner of collecting data largely determines which conclusions are drawn about the process and its variables.

The right approach, in this case, was the factorial experiment, which allowed factors to be varied together, thereby considering interactions between them. In this work, the factorial experimentation strategy (Design of Experiment) was used for designing the printing process.

When starting an experiment, its objectives must be set. The system model is visualized as a combination of variables – called *factors* – that cause input to change into an output. This output has one or more measurable *responses*. The system model shows how to obtain the desired response value through varying the main factor values. Some of the factors can be controlled by the experimenter, while others are uncontrollable (noise). One of the outcomes of learning how the system works is knowing how to minimize the influence of the uncontrollable factors on the responses, by finding the right set points of the controllable influential factors [6].

The input factors that elicited a response from the system were defined and rated by order of relevance to the process. The factors can be either categorical or continuous variables. The type of substrate (adhesive tape or MED-1000) was a categorical variable, for which both categories were tested. The continuous factors that were determined to affect the response were: the pressured air level (in bar), the distance between the tip and the substrate (in  $\mu$ m), and the speed of printing (in mm/min), seen in TABLE I below.

TABLE I THE FACTOR LEVELS SELECTED FOR PRINTING THE TEST STRUCTURES FOR THE CHARACTERIZATION OF THE PRINTING PROCESS. IN A FACTORIAL EXPERIMENT, COMBINATIONS OF THE DIFFERENT FACTOR

LEVELS ALLOW THE TESTING OF ALL FACTORS AT THE SAME TIME, AS WELL

AS THE INTERACTION BETWEEN THE FACTORS										
Factors	Levels									
Pressure, bar	0.6	0.8		1.0	1	.2	1.5	č.	1.7	1.9
Z-offset, mm	0.15	0.2	0.25		0	0.3		5	0.4	0.45
Speed, mm/min	2	200			4(	00			800	
Substrate type	Adhesive tape					MED-1000				

In the printing process, the goal was to print continuous contours and to fill areas homogeneously. To study the system model, the approach was to print lines or tracks of a defined length and to fill defined areas, then observe them qualitatively and quantitatively. The heights and widths of the tracks were the continuous measurable responses, which varied according to changes in the input factors. For the electrically conductive PDMS, the resistance of the tracks was an additional continuous measurable response.



Figure 3. Movement strategies for printing a filled square. From left to right: contour parallel from inside, from outside, and parallel lines. The % path spacing was the parameter determining how tightly packed the lines were, relative to the diameter of the printing head.

For the filled areas of MED-1000, the homogeneity of the filling was observed, and the height of the printed layer was measured at several locations. The percentage path spacing (overlap) and the printing strategy (contour-parallel from inside/outside or around islands, or parallel lines) also determined the homogeneity of filled areas. The printing

strategies, shown in Figure 3, were used by the CAD/CAM software to generate the routes. The requirement was to reduce the overlap between the lines, enough to create a homogeneous filled area but not to dispense more PDMS than needed. For this, test areas were filled using the different strategies and levels of overlap.

To model the system using its input factors, a range of values was defined for each one. Within each range, additional value points were added to study the interactions between the factors at their different levels. The designs used for examining the responses were arrays of seven straight 2 cm lines. The lines were printed on adhesive tape and a spin-coated layer of MED-1000 at z-height increments of 0.05 mm, starting from 0.15 mm. A total of 15 arrays were printed for seven pressure levels and three printing speed levels (TABLE I). The pressure range was defined from the minimum value to extrude PDMS (0.6 bar) and up to 1.3 bar above that value. The speed levels were kept within the common operating range of the milling machine. The z-height range was selected between the smallest distance that allowed extrusion and the furthest distance, beyond which the printed tracks no longer were continuous.

The data collection of the responses was carried out for the factor combinations indicated by the design model. In this experiment, a custom design and a response surface methodology were used to optimize the factor levels to produce the desired responses. The experiment was performed for MED-1000 twice, once on a substrate with a layer of adhesive tape and once on a spin-coated PDMS layer, to study its behavior when it is the first (base) layer and when it is the fill or cover layer. For EC-6601, the experiment was performed once on a layer of MED-1000. For MED-1000, the used syringe tip was a standard I- $\emptyset$  = 0.25mm, gauge 25, and for EC-6601 a tapered I- $\emptyset$  = 0.41mm, gauge 22 was used.

The responses of the indicated factor combinations were measured. For both materials, the height and width of the tracks were measured using a micrometer dial indicator (Digitale Messuhr ID-C 543-394B, Mitutoyo AG, Switzerland) and a microscope (Leica DFC, Leica Microsystems Ltd, Heerbrugg, Switzerland), respectively, at three points along each track and the mean value was calculated. As for the electrically conductive tracks, an additional measured response was the end-to-end resistance of each track, using a multimeter.

#### III. RESULTS

#### A. Factor Study

The recorded responses were used to build the statistical model, which showed the impact of each factor alone and in combination with the other factors. For EC6601 tracks, a summary of the results is depicted in a plot for the model's predictions in Figure 4. The model was set to favor factor settings that minimized the resistance values of the tracks.

The optimized settings are shown in red, with speed at 448.7 mm/min, the pressure at 0.98 bar, and the gap height at 0.28 mm for a resistance optimized at  $0.01 \pm 0.8 \Omega$ . Data were collected from a total of 32 measurements. As for MED-1000, the optimized settings for printing on both substrates (adhesive tape and spin-coated PDMS) were 400 mm/min, 0.8 bar, and 0.25 mm, in addition to a diameter setting of 0.3 mm, path spacing of 100 %, and a parallel lines strategy.



Figure 4. The prediction profiler for factors influencing track resistance of EC-6601 tracks on a spin coated PDMS substrate, namely speed, pressure, and gap height. The optimized factor settings were 448.7 mm/min, 0.98 bar, and 0.28 mm, respectively.

An exemplary sample of printed conductive tracks is depicted in Figure 5 (left). It could be observed that the tracks became wider when pressure levels were increased for the same speed and an increase in gap height caused them to become narrower.



Figure 5 Samples from the factor study, showing EC 6601 tracks (left) printed at pressure values 0.6, 0.8, 1.0, and 1.2 bar for the same speed (200 mm/min) and for each set, seven tracks printed at 0.05 mm increments of gap height, starting from 0.15 mm. The track width increased with increasing pressure. MED 1000 tracks (right) are shown from a single set, printed at a speed of 800 mm/min and a pressure of 0.8 bar. The discontinuous tracks at the higher increments in gap height showed the effect of the combination of high speed, low pressure, and a large gap height on the printing quality.

A single set of printed MED-1000 tracks are depicted in Figure 5 (right), which were printed at a speed of 800 mm/min, and a pressure of 0.8 bar.

TABLE II. MEASUREMENTS OF THE HEIGHTS OF PRINTED MED-1000 SQUARES WITH A SPEED OF 400 MM/MIN, A GAP HEIGHT OF 0.2 MM, A DIAMETER SETTING OF 0.3 MM, AND A PRINTING STRATEGY OF "CONTOUR PARALLEL FROM OUTSIDE".

	Path	Pressure, bar	Measured height, µm					
	Spacing, %		Edges $(n = 4)$	Center $(n = 1)$	Diagonals (n = 4)			
	70	0.6	$131.75\pm0.4$	83	$113\pm8.8$			
	70	0.8	$210.75\pm5.2$	115	$154.5 \pm 6.3$			
ĺ	100	0.8	91.5 ± 2.3	95	$119.5 \pm 11.0$			

The tracks were all narrow, and an increase in gap height beyond 0.35 mm led to discontinuities in them (two top tracks), as the speed of printing (movement of the printing head) exceeded that of extrusion (controlled by pressure) for those heights. The selected printing strategy for filling MED-1000 areas was parallel lines, due to height irregularities seen in the contour parallel strategy, as seen in . The increase in pressure from 0.6 to 0.8 bar for 70 % path spacing only increased the overall height but did not improve the unevenness throughout the filled area. In the case of 100 % path spacing, the center and edges became more homogeneous, but the diagonals were nonetheless lower in height and therefore uneven.

# IV. DISCUSSION

The structured approach to developing a process through the study of its influencing factors required a clear set of priorities. For printing conductive PDMS, the desirable outcome was the minimization of the track resistance and only of secondary importance the dimensions of the tracks. Had the aim been the minimization of the printed prototypes or the optimization of printed track density per area, the optimal factor settings would have turned out differently. The purpose of this work was to show the feasibility of the concept and to establish an initial set of factor values that enable the printing of homogenous conductive tracks, regarding their width or height only as far as the resistance is concerned. As for the bulk PDMS, the optimization of its filled areas involved more factors. The movement strategy and path spacing were imperative in the achievement of homogeneously filled areas,



Figure 6 An electrode array, fabricated using the developed printing process and assembled with cables at one end.

with enough overlap and no unwanted gaps.

During the factor study, for both MED 1000 and EC 6601, the range selected for each of the factors was adjusted to omit levels that produced undesirable results, such as very wide tracks in the case of pressure values above 1.2 bar. The tracks produced by those pressure values (1.5, 1.7, and 1.9 bar) were therefore not inserted in the model, to reduce the time required in measuring the dimensions and resistances of the tracks. Furthermore, when the tracks were discontinuous, it was not possible to measure their dimensions or resistances. This occurred when a combination of low pressure, large gap height, and high speed were used (e.g., 0.6 bar, 0.45 mm gap, and 800 mm/min). As a result, the pressure values included in the study were only 0.6, 0.8, 1.0, and 1.2 bar. The gap height and speed ranges were kept the same and only the cases where a combination of factors made the tracks discontinuous were omitted.

Furthermore, two factors that might influence the curing speed, as well as flow properties of uncured PDMS materials, are temperature and humidity. Since the printed tracks for the factor study were printed on the same day, these factors were considered negligible. They nonetheless should be considered if they are prone to variations.

Summing up, the model for EC 6601 was set to minimize the resistance, which led to the optimal factors being the speed at 448.65 mm/min, the pressure at 0.928 bar (set to 1.0 bar on valve knob), and gap height at 0.28 mm. As for MED 1000, the set of factors used were 400 mm/min, 0.8 bar, and 0.25 mm, in addition to a diameter setting of 0.3 mm, path spacing of 100 %, and a parallel lines strategy. A sample printed with these process settings is shown in Figure 6.

This application paves the way for a fully automated electrode manufacturing process. Compared to the state-ofthe-art process, not only are the manufacturing costs of the electrodes diminished, since fewer manual steps are required, but also the material waste can be significantly reduced. In addition, the printed electrodes were, in contrast to the stateof-the-art electrodes, highly flexible and stretchable, which promises to increase robustness and longevity.

## V. CONCLUSION

This work was a proof of concept and a feasibility study for the printing of PDMS-based electrodes for interfacing the nervous system. Materials were selected based on their usability and their electrical, mechanical, and curing properties. The printing system was set up by adapting an already available milling machine, thus avoiding the need for designated machinery for this proof-of-concept stage.

Moreover, the printing process factor settings for desirable responses were successfully obtained with the aid of experimental design methodology. This allowed a better understanding of the main influencing parameters and their interactions, as well as provided a starting point to produce the first electrode prototypes. Finally, various tests are planned for the mechanical, electrochemical, and biological evaluation of the prototypes, as well as their aging behavior.

#### REFERENCES

- J. Stieghorst, A. Bondarenkova, N. Burblies, P. Behrens, and T. Doll, "3D silicone rubber interfaces for individually tailored implants," *Biomed Microdevices*, vol. 17, no. 3, p. 9960, 2015, doi: 10.1007/s10544-015-9960-y.
- [2] F. Kohler, M. Schuettler, and T. Stieglitz, "Parylene-coated metal tracks for neural electrode arrays - fabrication approaches and improvements utilizing different laser systems," *Annu Int Conf IEEE Eng Med Biol Soc*, vol. 2012, pp. 5130–5133, 2012, doi: 10.1109/EMBC.2012.6347148.
- [3] Avantor, "NuSil MED-1000: Silicone adhesive," Rev. B.
   [Online]. Available: https://www.avantorsciences.com/nusil/en/product/MED-1000/rtv-silicone-adhesive, accessed: 03.05.2021
- The Dow Chemical Company, "DOWSIL™ EC-6601 Electrically Conductive Adhesive," Form No. 11-4002-01, 2019.
   [Online]. Available: https://www.dow.com/en-us/pdp.dowsil-ec-6601-electrically-conductive-adhesive.488708z.html, accessed: 03.05.2021
- [5] A. Cowley and B. Woodward\*, "A Healthy Future: Platinum in Medical Applications," Platin Met Rev, vol. 55, no. 2, pp. 98– 107, 2011, doi: 10.1595/147106711X566816.
- [6] D. C. Montgomery, *Design and analysis of experiments*. Hoboken NJ: John Wiley & Sons Inc, 2013.