Electronic Supplementary Material (ESI) for Lab on a Chip.

Supporting Information

Microphysiological Pancreas-on-Chip Platform with Integrated Sensors to Model Endocrine Function and Metabolism

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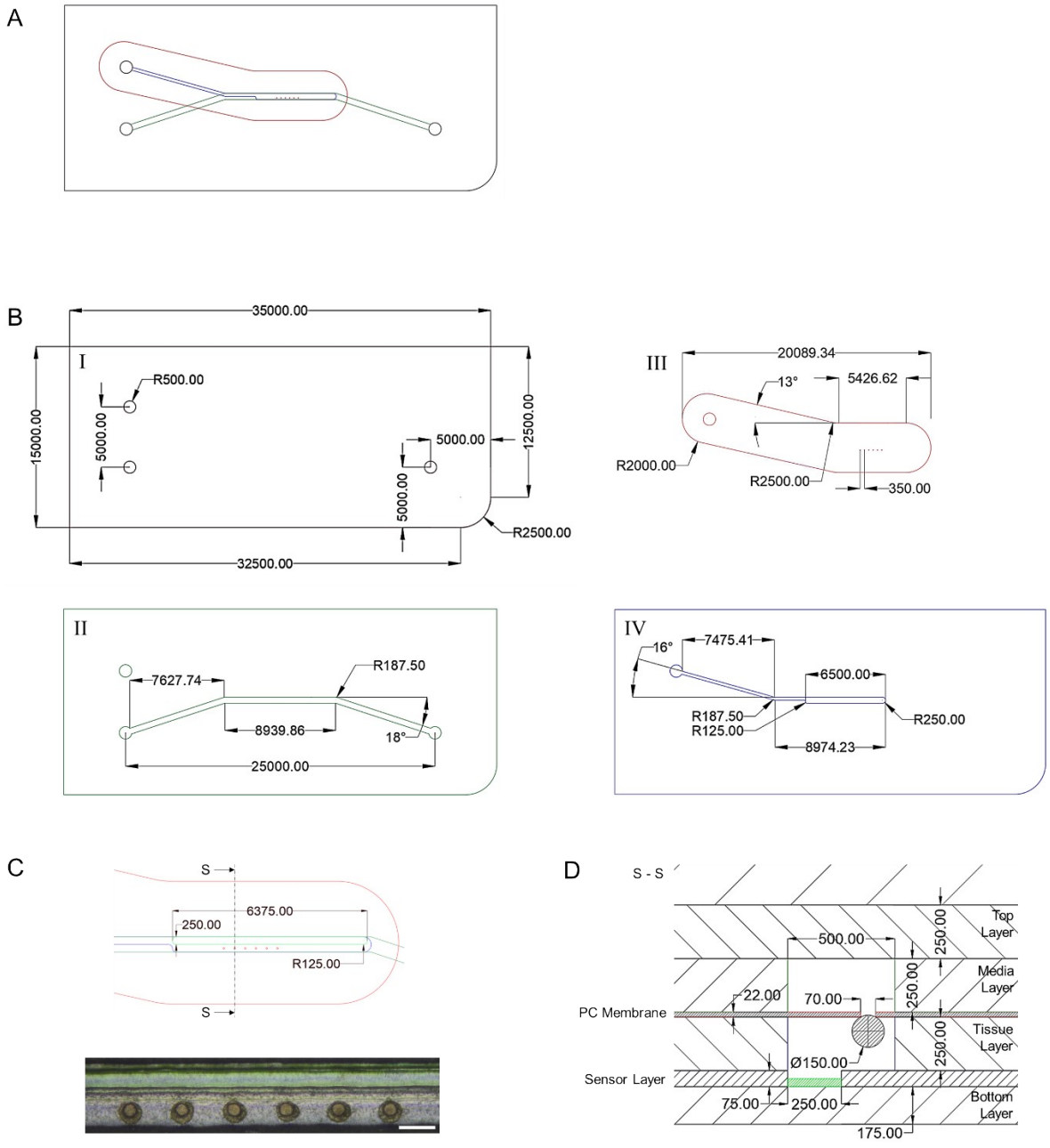

Figure S1: Microfluidic chip set-up and design. (A) Top view of all chip layer drawings showing the alignment of tissue and media channel. (B) Dimensioned drawings of all chip layers (in µm; top layer (I), media layer (II), membrane (III) and tissue layer (IV)). The PDMS connection layer has the same dimensions

as shown for the top layer (I) with inlet and outlets according to Table S1. The PMMA bottom layer of the chip system has the same dimensions as the top layer (I) without the inlet and outlets. Fillet radius is only indicated once per layer and consistent for the rest of the structures. (C) Optional integration of the sensor line layer indicated in the dimensioned drawing as neon green (top). Microscopy image of a loaded chip system showing the spatial extent and location of the fluorescent sensor relative to the pseudo-islets and both channels (bottom). (D) Vertical cross section through the chip system including the optional sensor line layer containing the recess area to host the oxygen sensitive spotted line (indicated in neon green). Spheroid located at the trapping hole.

Table S1: **Materials and dimensions of the microfluidic pancreas-on-chip**

Compart-ment		**Height (mm)**	**Width (mm)**	**Area (mm^2)**	**Volume (µL)**	**Layer material**
Tissue	Inlet+loading channel	250	250	2.6	0.65	PMMA
	Tissue chamber*	250	500	3.8	0.975	
Media		250	500	13.6	3.4	PMMA
In-/Outlets Connection Layer	Tissue channel	3	Ø 0.75	0.44	1.33	PDMS
	Media channel	3	Ø 0.75 or 0.35	0.44 or 0.096	1.33 or 0.28	
		Heigth (mm)	**Radius (mm)**	**Pore/Trap Density**		**Material**
Membrane	Pores	0.022	0.003	$1.6*10^6$ cm^{-2}		PC
	Trapping structures	0.022	0.07 ± 0.01	6 per membrane		

**overlapping region with media channel*

Table S2: Oxygen plasma process parameters for different chip fabrication steps.

Material	**Treatment for**	**Power (W)**	**Volume O_2 (sccm)**	**Time (min)**
PMMA	APTES	75	10	0.7
PDMS	APTES	75	10	0.5
PDMS	PDMS-PDMS Bonding	75	10	0.5
Chip	Surface Activation	75	10	5.0

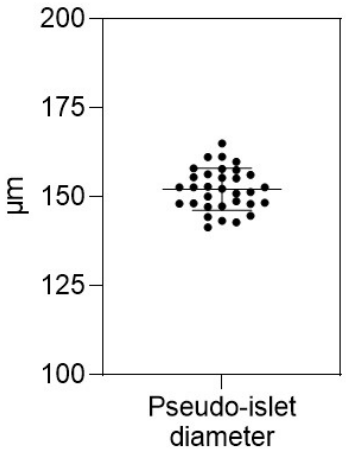

Figure S2: Pseudo-islet size evaluation (152.2 ± 5.8 µm, n=32 pseudo-islets), analyzed on Day 3 after seeding 500 INS-1E cells/well to ULA 96-wellplate. Diameter measured using open source software Fiji (ImageJ version 1.53t).

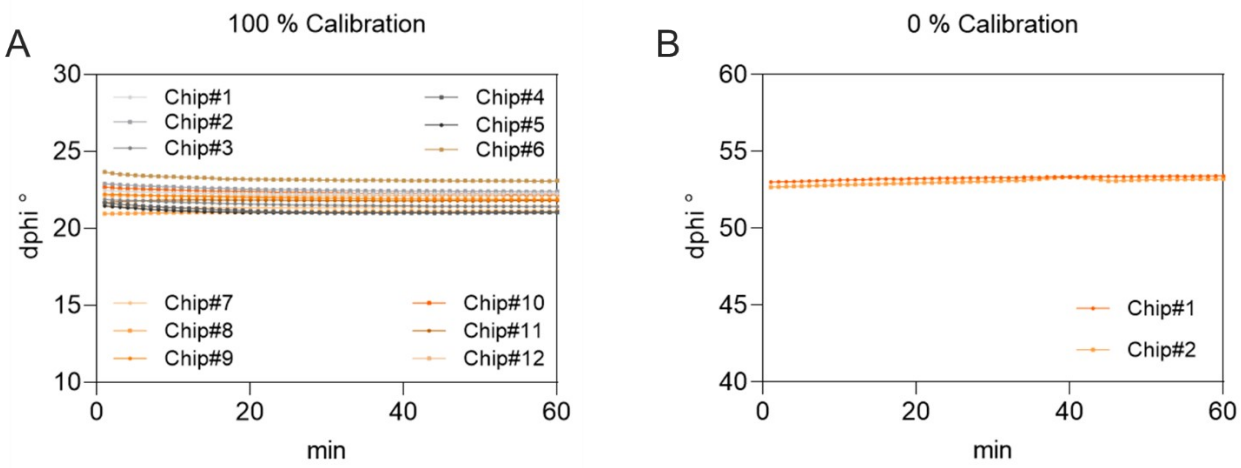

Figure S3: Two-point calibration of the oxygen sensors by determining the corresponding phase shift (dphi). Calibrations were performed in the final experimental set-up. (A) Representative example of 100 % calibration of individual sensors of one experiment. Chips were perfused with air-saturated PBS- until stable dphi value was reached. (B) 0 % calibration was determined by flushing the media channel with a strong reductant sodium sulfite (100 g/L) in DI-water to create anoxic conditions. The mean dphi value after equilibration for 60 min of the calibration chips was used for all following experiments.

Video S1: Loading of pseudo-islets to chip system. Pseudo-islets are trapped one after the other at the designated trapping locations on the membrane until all traps are occupied. Video acquired with a Zeiss Observer 7 microscope. Loaded traps are annotated with a circle.

Video S2: Loading of collagen-I-based hydrogel by hydrostatic-pressure driven flow to the tissue chamber surrounding the pseudo-islets. Hydrogel visualized by addition of FluoSpheres™ Carboxylate-Modified Microspheres (Invitrogen™). Video acquired with a Zeiss Observer 7 fluorescence microscope.