Supplementary Information (SI) for Lab on a Chip.


# SUPPLEMENTAL DATA

## TABLE S1

Dimensions of the microfluidic chip indicating values for tubing before the chip entry port (blue), the chip itself (red) and after the exit port (green) to the fraction collector.

| | Device | Length (mm) | ID (mm) | Width | Height |
|---|---|---|---|---|---|
| Before the chip | Distributor | 18 | 0.5 | | |
| | High resistance tubing 1 | 202 | 0.178 | | |
| | High resistance tubing 2 | 89 | 0.254 | | |
| | Flow sensor | 73 | 0.43 | | |
| | Negligeable resistance tubing 1 | 122 | 0.254 | | |
| | Connector | 0 | 0.794 | | |
| | Ground tubing | 30 | 0.5 | | |
| | Connector | 19 | 0.794 | | |
| | Negligeable resistance tubing 2 | 45 | 0.508 | | |
| Microfluidic chip | Inlet channel | 4 | | 0.55 | 0.3 |
| | Microfluidic chip | 4 | | 2.5 | 7 |
| | Outlet channel | 4 | | 0.55 | 0.3 |
| After the chip | Negligeable resistance tubing 1 | 57 | 0.254 | | |
| | Connector | 22 | 0.397 | | |
| | Ground tubing | 30 | 0.5 | | |
| | Connector | 25 | 0.397 | | |
| | Negligeable resistance tubing 2 | 600 | 0.508 | | |
| | Collector | | Average every minute | | |

**FIG S1**

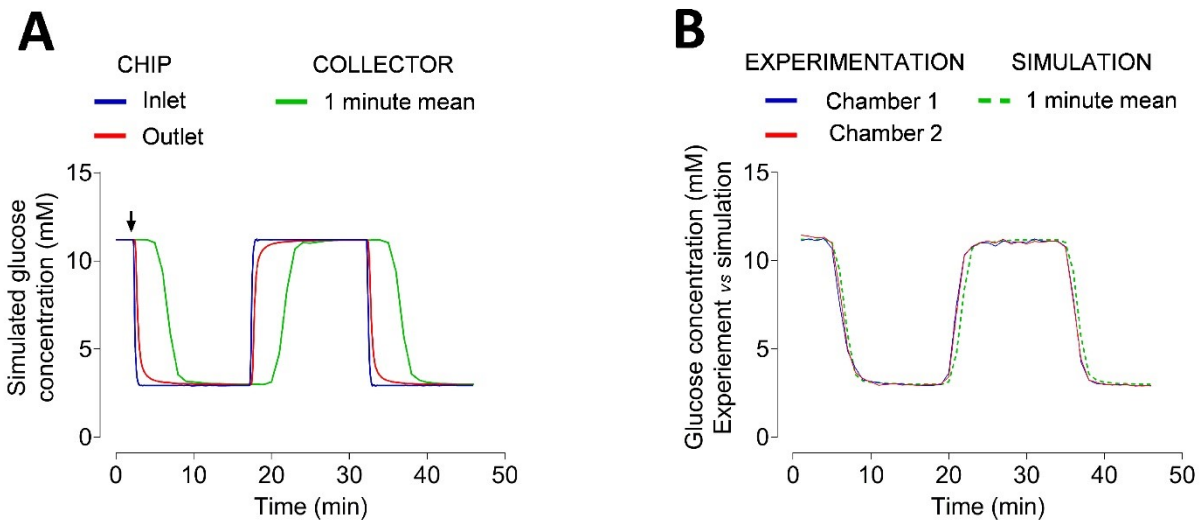


Fig S1. Model validation in COMSOL for characterisation of microfluidic flow. (A) Simulated glucose concentrations for the two chambers at the inlet and the outlet of the chip (red and blue lines) and collection of flow media in 96 well plates (fraction collector, green line; 600 mm from chip outlet). (B) Experimental determination of glucose concentrations (red and blue lines) and comparison to simulation (dashed green line), both at 50 µl/min. For chip dimensions, see Table S1.

**Fig. S2**

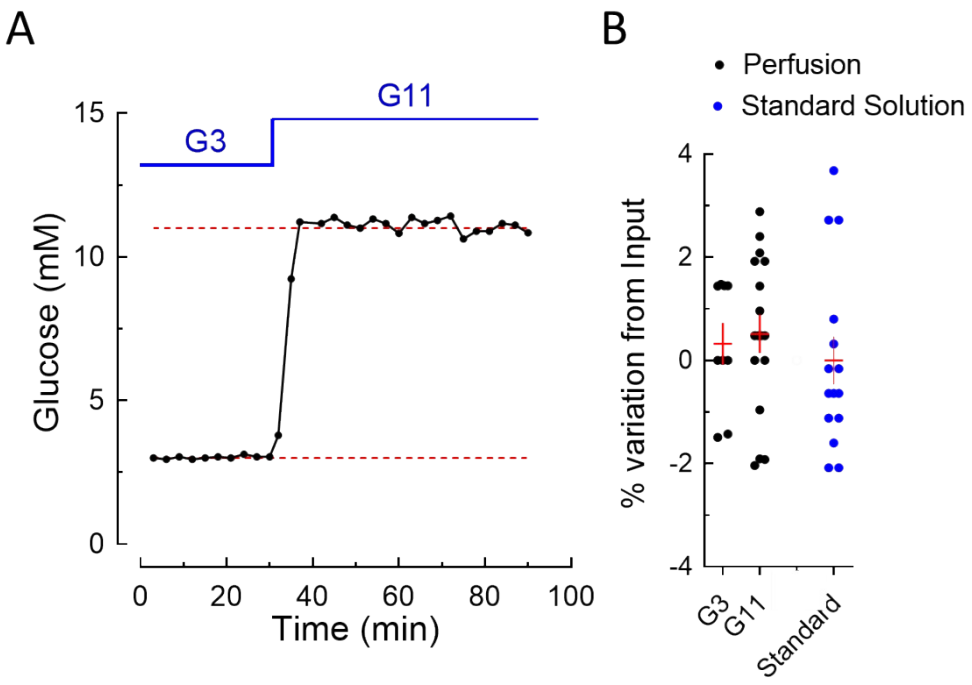


Fig. S2. Glucose concentrations at the outlet of the microfluidic chamber in the presence of islets. **A**. 40 islets were seeded in the chamber and perfused 4 days later at 50 µl/min at indicated glucose concentrations. Glucose concentrations after passage through the chamber were measured. B: Variations in % of input concentrations for all values at G3 (3 to 30 min) and G11 (38 to 90 min) and variations of measurements of the G11 solution (Standard) before passage through the microfluidic device.

**FIG S3**

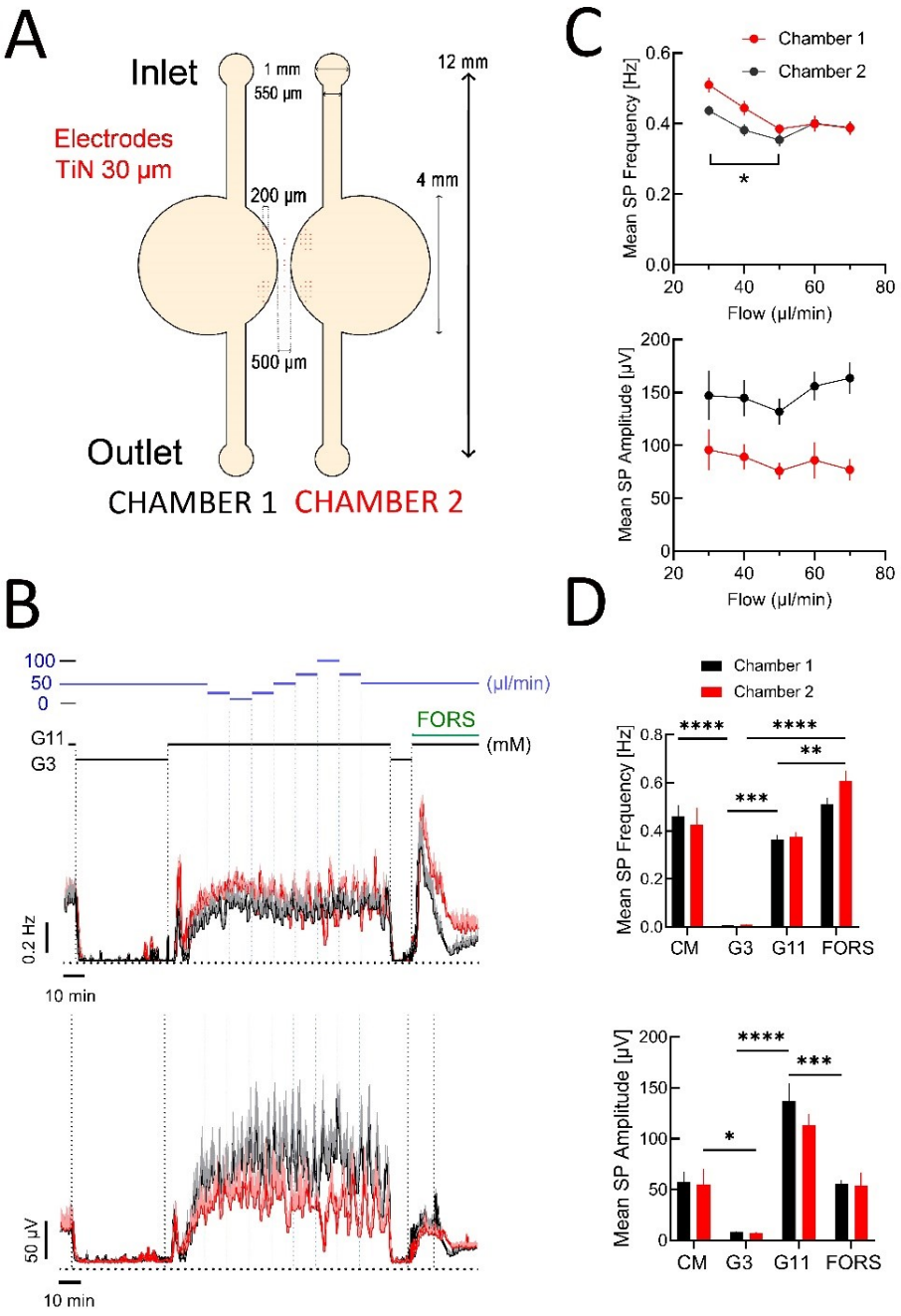


Fig S3. Characterisation of islet β-cell activity on the initially designed microfluidic chip. (A) Scheme and dimensions of the initially designed chip. Electrodes (TiN, Ø30 µm) were spaced 200 µm apart. (B) Recording of slow potentials in complete medium (CM), 3 mM glucose (G3) and at 11 mM (G11) glucose under different flow rates for chamber 1 (black) or chamber 2 (red). Given are SP frequencies and amplitudes (mean ± SEM), n=8. SEMs are given in grey or light red. (C) mean SP frequencies and amplitudes for both chambers at different flow rates, n=8. (D) effect of complete medium (CM), 3 or 11 mM glucose (G3, G11) or the adenylyl cyclase activator forskolin (FORS, 10 µM) on mean SP frequency and amplitude (mean ± SEM), n = 8; *, *** $2p<0.05$ or 0.001 (ANOVA/Tukey).

**Fig. S4**

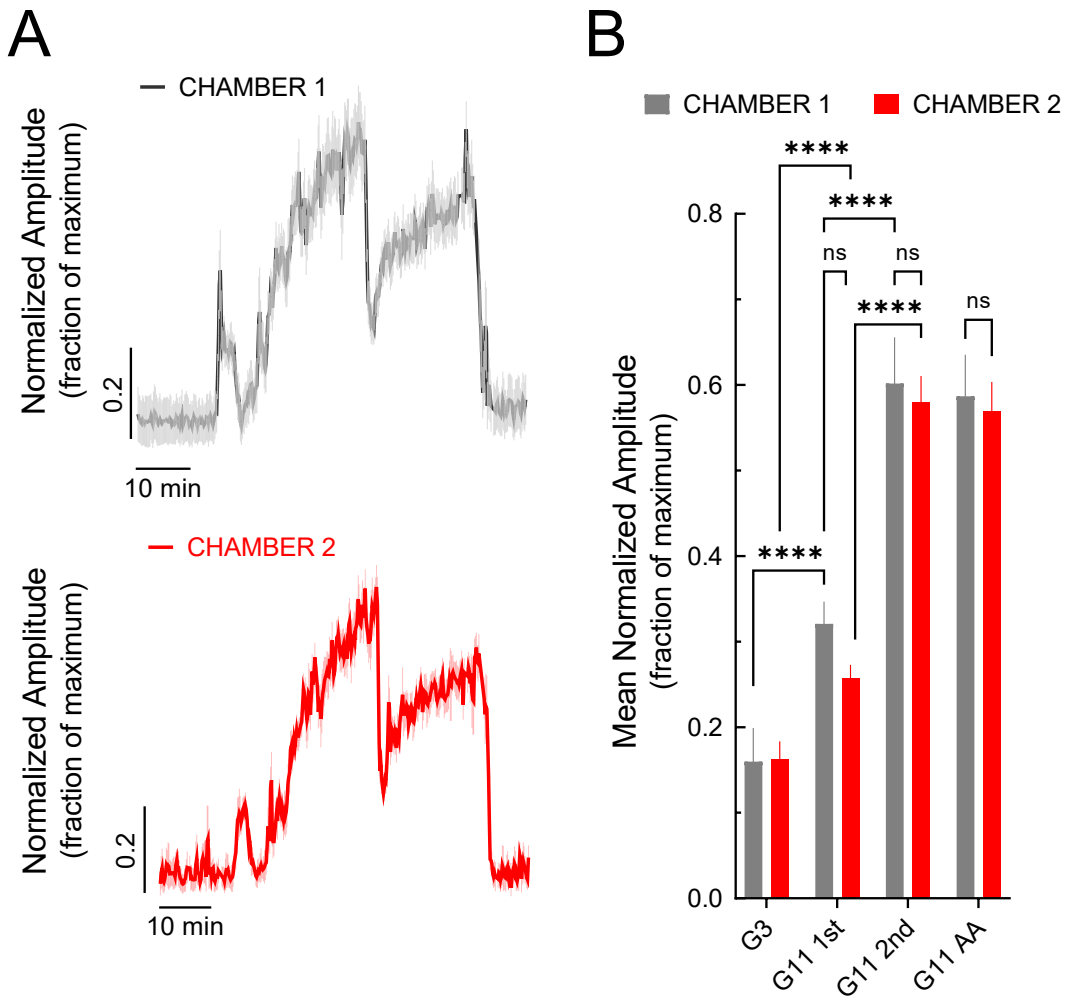


Fig S4. Normalisation of amplitude values. (A) Values of amplitudes of each chamber as given in Fig 5A (lower left panel) were normalized for each electrode over the 40 s period of its maximal value. (B) Statistics of means of normalized amplitudes. n = 22; *, **** 2p< 0.0001 (ANOVA/Tukey).

**Fig. S5**

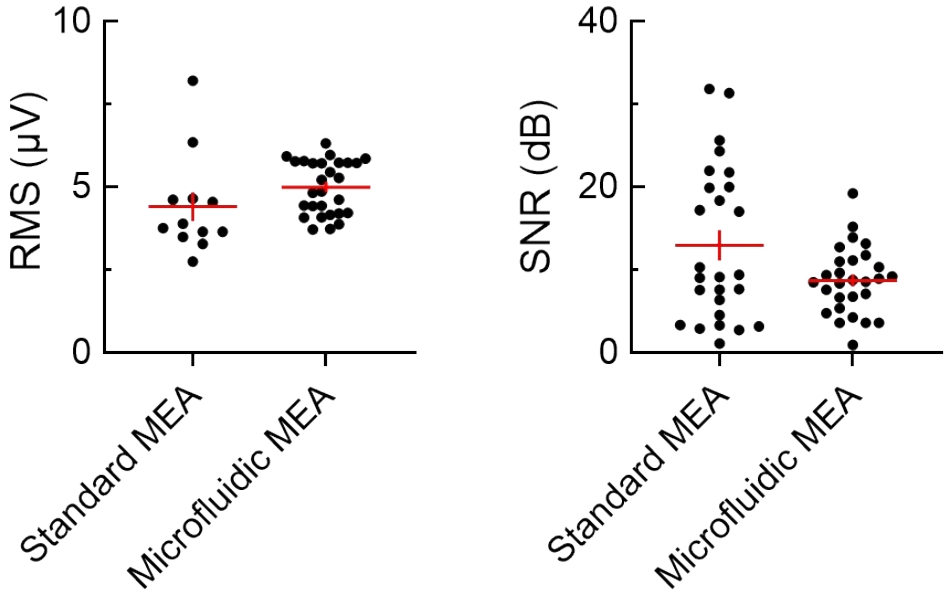


**Fig. S5: Comparison of root mean square (RMS) noise levels and signal-to-noise ratios (SNR) between standard and microfluidic MEAs.** The standard MEAs were the 60MEA200/30iR-Ti-gr MEAs perfused with a conventional peristaltic macrofluidic system [7] and the microfluidic MEAs are those characterized in the current manuscript. **A,** RMS noise levels were measured as described on unfiltered recordings (N=3-4, n=12-28, *p<0.05 Mann-Whitney test). **B,** SNR were determined from the ratio of RMS noise levels measured on electrodes with and without islets upon glucose stimulation (N=3-4, n=26-28, not significant).

**Fig. S6**

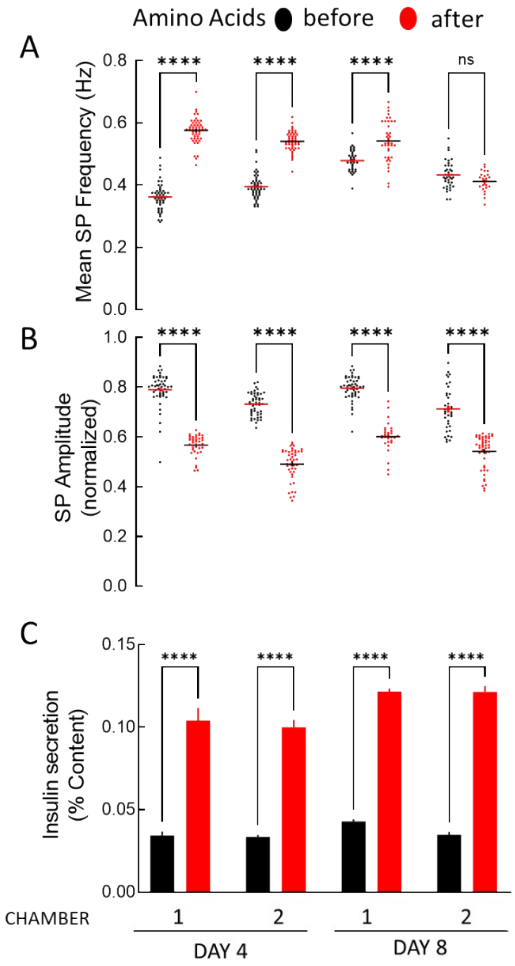


**Fig. S6: Comparison of slow potential frequency, amplitudes and insulin secretion before and after addition of amino acids.** Data presented in Fig 5 were used for this analysis. (A) Slow potential frequencies during the 6 minutes before (black symbols) and 6 minutes after (red symbols) the addition of amino acids to 11 mM glucose. (B), as A for normalized slow potential amplitudes. Note that same statistical significances were observed for non-normalized values. (C) Insulin secretion before and after the addition of amino acids. Chambers and days are indicated. ns, non-significant; ***, $p<0.001$; ****, $p<0.0001$; ANOVA and Dunn post-hoc test.