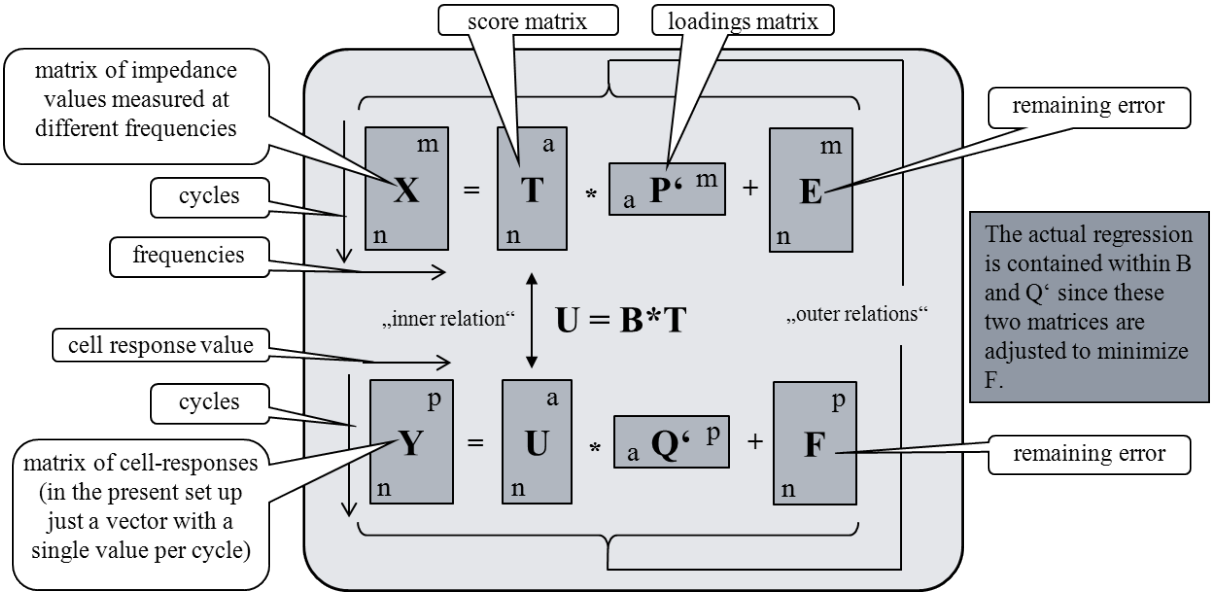
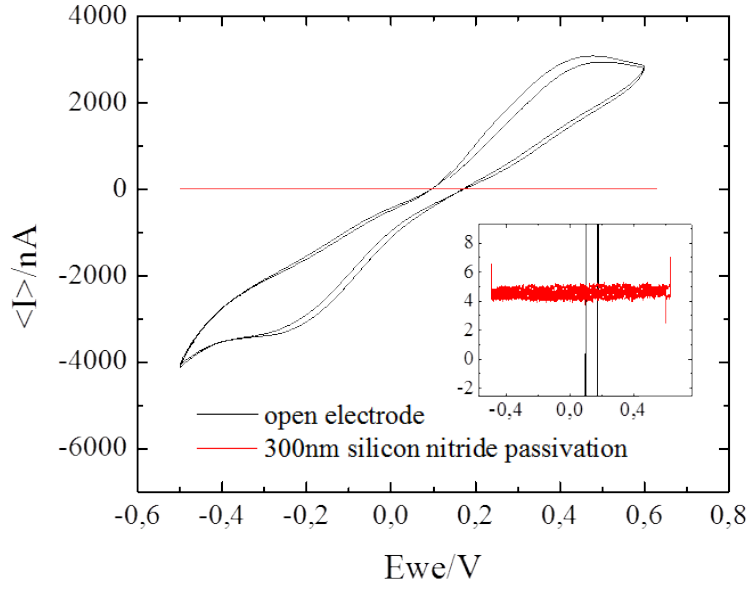
Electronic Supplementary Material (ESI) for Analyst.

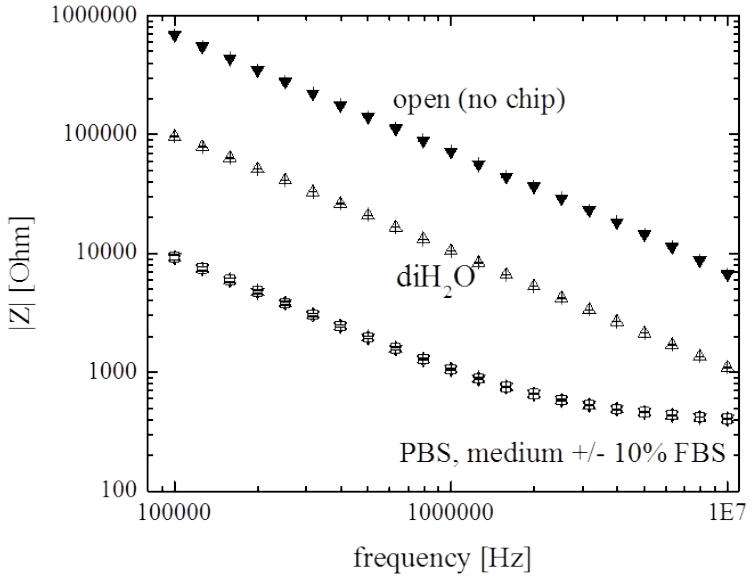


Suppl. Fig. 1: Concept of partial least squares (PLS) regression on impedance spectral data. Matrix **X** contains the independent data (impedance values measured at **m** frequencies over **n** cycles) while matrix **Y** contains the dependent data (single cell response value (**p** = 1) at each of the **n** cycles). Principal components (**a** is the number of principal components, which needs to be defined *a priori*) are calculated for both **X** and **Y** resulting in score matrices (**T** and **U**), which represent location of the original data in the new coordinate system, and loading matrices (**P'** and **Q'**), which describe the orientation of the principal components relative to the original coordinate system. Error matrices **E** and **F** contain the information of how closely the principal component matrices represent the original data. The two decompositions of **X** and **Y** into principal components plus error matrices are called *outer relations*. The regression model is then set up between the score matrices **T** and **U** (not the original data), where the *inner relation* **U=B*T** describes the correlation between **X** and **Y**. The PLS algorithm aims at minimizing the error (norm of **F**) while keeping the correlation between **X** and **Y**. In that sense, the elements of **B** are merely the regression coefficients.

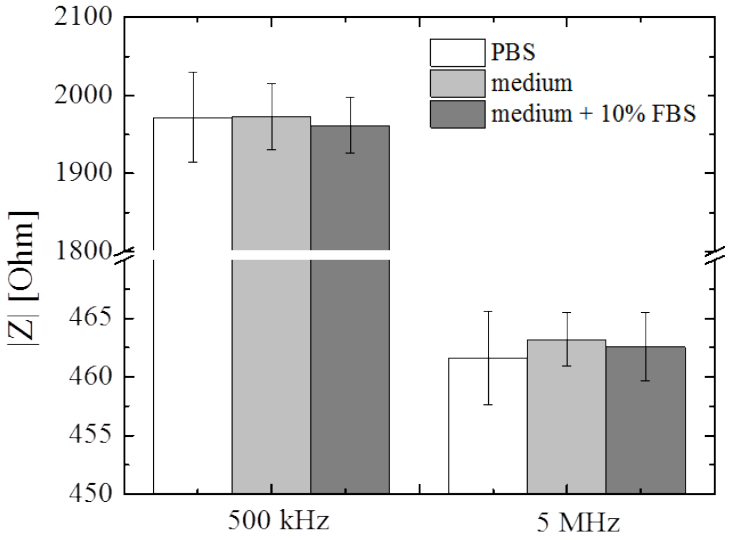
A)


4000
2000
0
-2000
-4000
-6000
<I>/nA
-0,6
-0,4
-0,2
0,0
0,2
0,4
0,6
0,8
Ewe/V
open electrode
300nm silicon nitride passivation
8
6
4
2
0
-2
-0,4
0,0
0,4

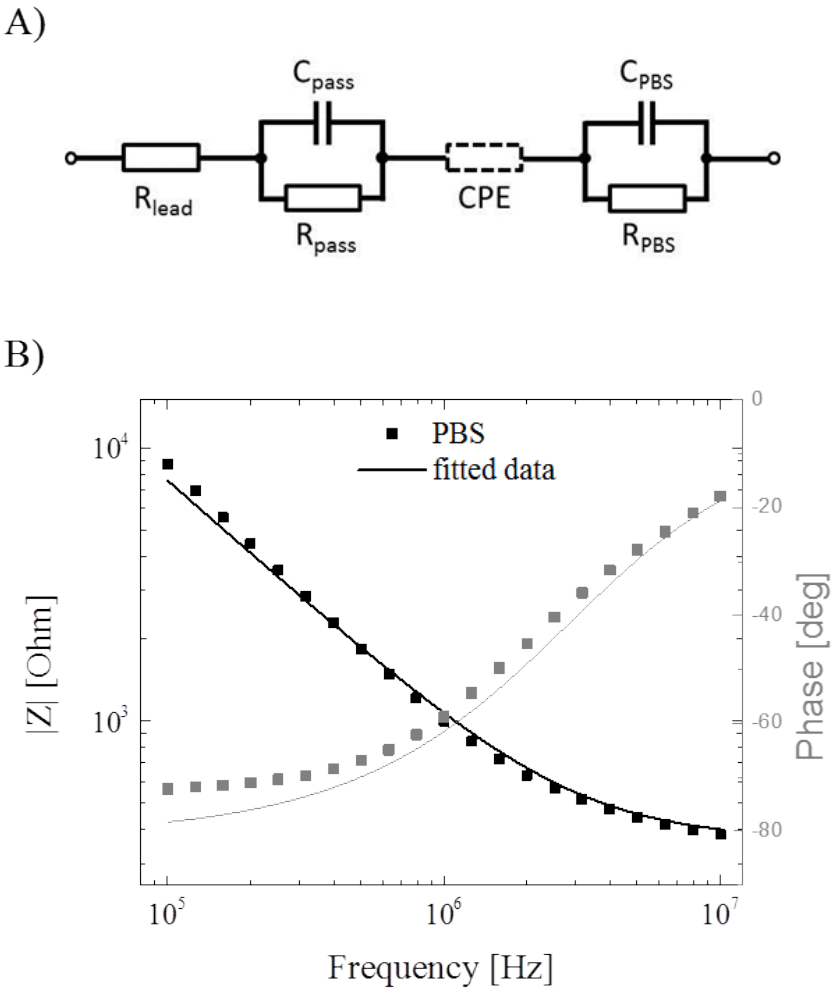
B)


1000000
100000
10000
1000
100
|Z| [Ohm]
open (no chip)
diH2O
PBS, medium +/- 10% FBS
100000
1000000
1E7
frequency [Hz]

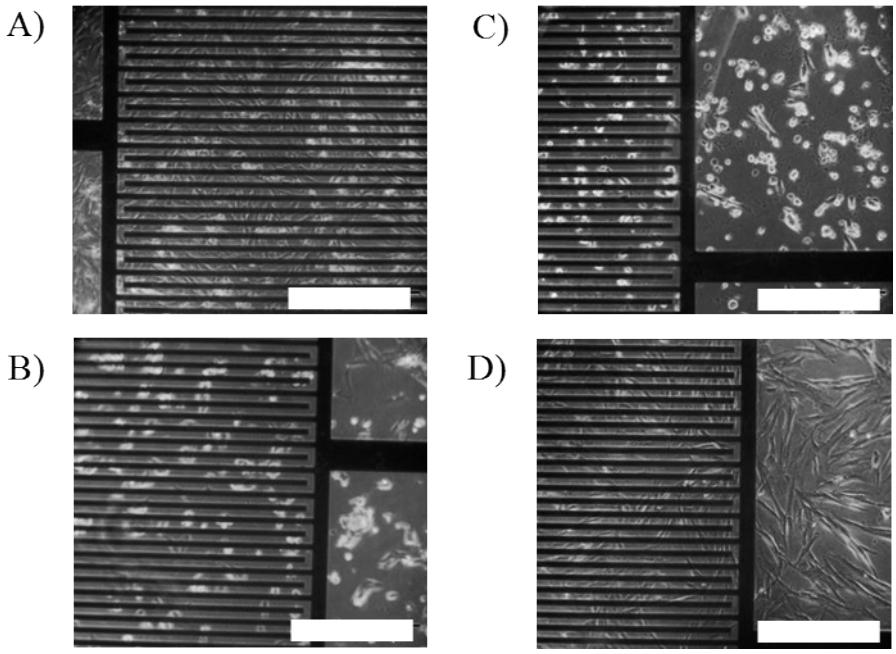
C)


2100
2000
1900
1800
465
460
455
450
|Z| [Ohm]
PBS
medium
medium + 10% FBS
500 kHz
5 MHz

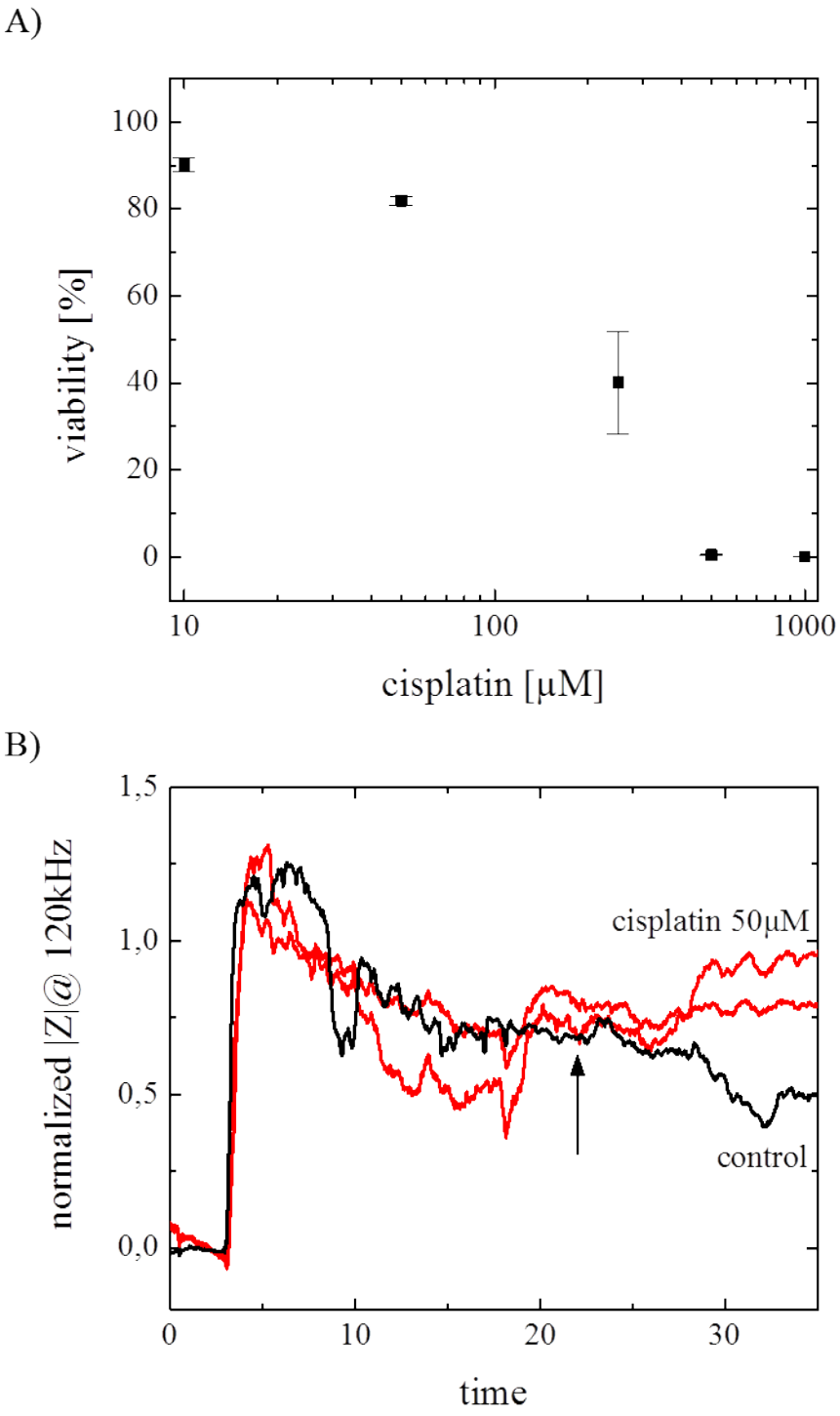
Suppl. Fig. 2: A) Cyclo voltammetric (CV) quality control of the passivation layer. The graph shows faradaic current and redox reactions for an open gold electrode compared to an electrode fully passivated with 300 nm thick silicon nitride (magnified in the inset). CV solution was 10 mM ferro and ferri-cyanide in 1x PBS. The measurement was performed at room temperature against a silver wire working electrode. B) Impedance frequency scans of an open circuit (no chip mounted) and different analytes (deionized water, PBS, cellulture medium with and without 10% serum) on a 20 µm IDES. Data averaged from $n \geq 5$ individual runs at 37°C. C) Highlights the impedance readings of 3 isotonic analytes (PBS, cell culture medium with and without 10% serum) at 500 kHz and 5 MHz.



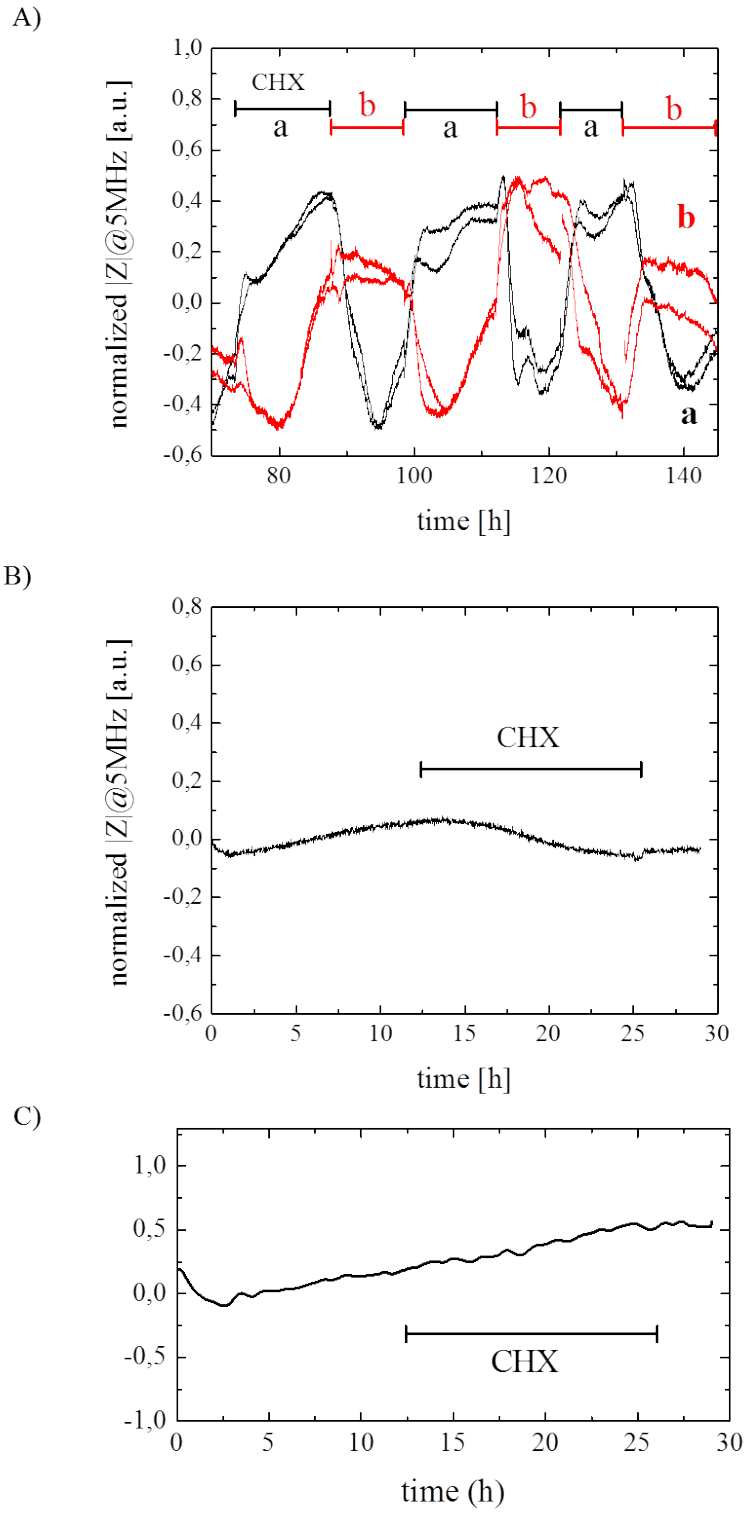
Suppl. Fig. 3: Electrical equivalent circuit model and parameter fitting. A) The model represents relevant electrical elements in the measured frequency range. Only phenomena which are occurring in the studied frequency range (10^5-10^7 Hz) are included in the model while e.g. the double-layer was not accounted. The serial resistance R_{lead} represents the gold leads while the passivation layer is modeled as a capacitance C_{pass} and parallel resistance R_{pass}. The constant phase element (CPE) represents a steady phase shift possibly caused due to surface phenomena. The characteristic of the electrolyte solution is represented as R_{PBS} and C_{PBS}. B) Absolute impedance spectra with corresponding phase trend. Solid line represents fitted data with following values: R_{lead}=60 Ω, C_{pass}=10 nF, R_{pass}=9.88E14 Ω, $CPE_{amplitude}$=8.45E-10 $S(rad/s)^{-1}$, CPE=0.898, R_{PBS}=300.76 Ω, C_{PBS}=1.79 pF.



Suppl. Fig. 4: RGDS inhibition of cell adhesion. Phase contrast images of RGDS-treated NHDF cells cultivated on IDES (black structures) in microfluidic chambers (4 µL/min). Microscopic pictures show cell morphology and sensor coverage 10h after seeding: 100% confluent control cells (A), cells in the presence of 100 µM (B) and 200 µM (C) RGDS and 100 µM RGDS for 84 min followed by recovery in control medium (D). Scale bars represent 400 µm.

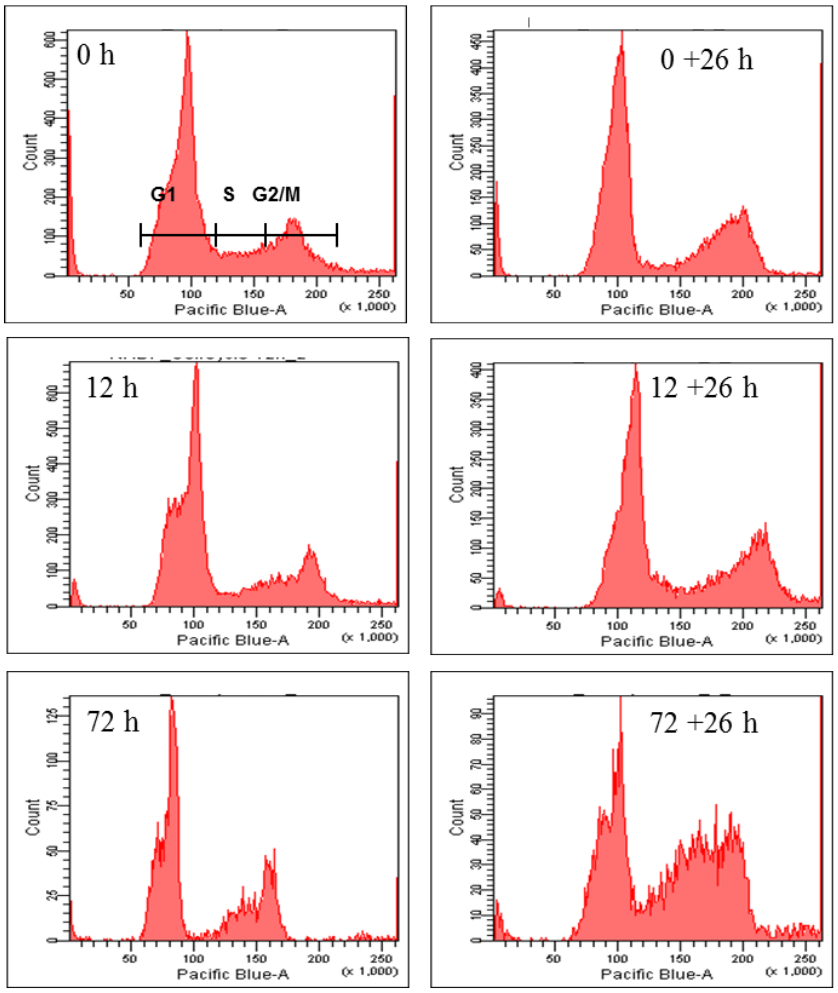


Suppl. Figure 5: A) Flow cytometric quantification of NHDF viability. A confluent cell layer was exposed to 0, 10, 50, 250, 500 and 1000 µM cisplatin for 24 h. Cells were stained by LIVE/DEAD® viability/cytotoxicity kit for mammalian cells. B) shows impedance time traces of formation of confluent NHDF cultures and exposure to 50 µM cisplatin (arrow) as well as control cells at 120 kHz. Curves are normalized to impedance values before cisplatin exposure (20 h).

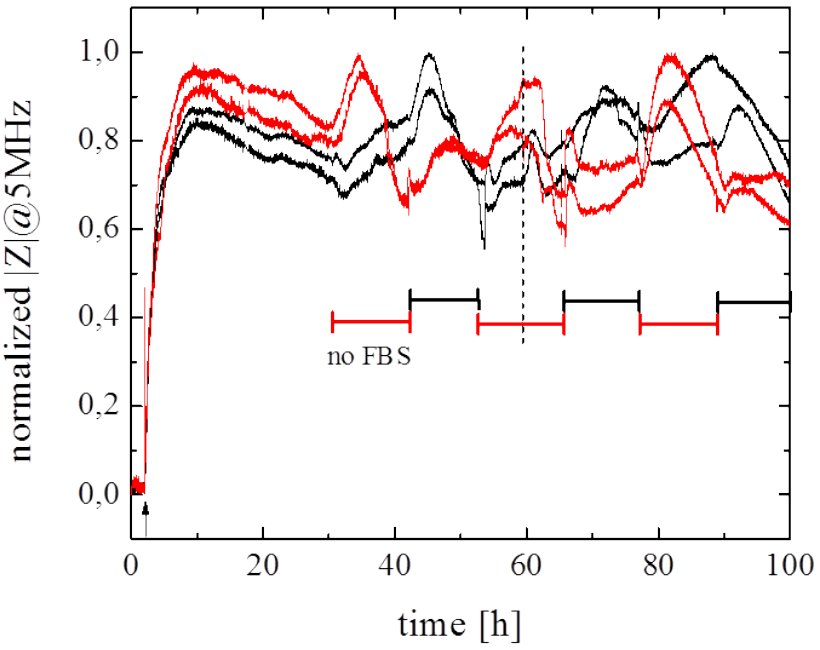


Suppl. Fig. 6: A) Impedance-time traces of an NHDF cell layer repeated exposed to 1µM cycloheximide (CHX) for 12h time periods. Data of 2 pairs (a – black; b – red) of individual sensors, that were alternatingly perfused with CHX containing and normal cultivation medium. B) impedance data and C) PLS data of a control measurement of CHX perfusion in a cell-free system.

A)


0 h
G1
S
G2/M
0 +26 h
12 h
12 +26 h
72 h
72 +26 h
Count
Pacific Blue-A
(x 1,000)

B)


normalized |Z|@5MHz
1,0
0,8
0,6
0,4
0,2
0,0
no FBS
0
20
40
60
80
100
time [h]

Suppl. Fig. 7: A) Flow Cytometry analysis of NHDF cell cycle distribution in response to varying periods of serum starvation (0, 12 and 72 h) with and without additional 26 h recovery time (application of cultivation medim with 10% serum). B) Impedance-time traces of NHDF adhesion and susequent repeated exposure to serum free culture medium (no FBS) for 12 h time periods. The bars indicate the alternating serum removal in the two pairs of microchambers.