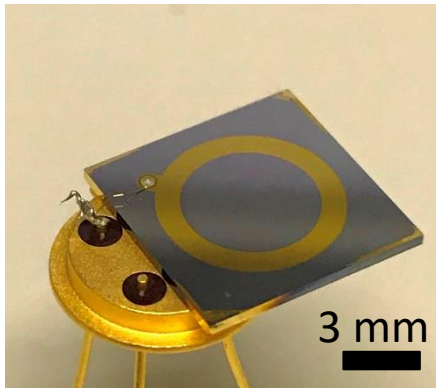


Impedance BioCHiPs for dilution free cell counting

Ziel des Vortrags:

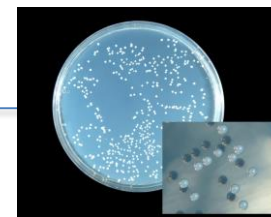


- Industrie-Partner für Evaluierung der Qualität des Zellzählens mittels Impedanz-Messungen im OD-Bereich (OD=0.1-16.0) gesucht
- Kooperationspartner gesucht:
 - Optische Dichte-Messungen
 - Zellzählen in der Mikrotiterplatte
 - Zellzählen in der Mikrofluidik

I. Skorupa, S. Krüger, L. Rebohle, A. Damm, D. Blaschke, H. Schmidt

Methods for cell count

- ✓ Cell count is needed in biomanufacturing, medical diagnosis and advanced therapy [ISO 20391-2:2019]
- ✓ Cell count describes cells in suspension (general cell concentration) and cells adherent to a substrate (generally area density of cells) [ISO 20391-1:2018]
- ✓ Direct counting by plating and optical microscopy
→ time consuming, needs dilution, poor statistics
- ✓ Indirect counting by optical density (OD) measurements
→ needs elaborated calibration
- ✓ Indirect counting with novel impedance Biochips:
<10 min, dilution free, good statistics, novel calibration approach

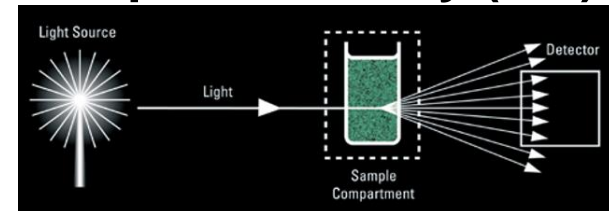


Plating



ibidi.com, bacteriainphotos.com

Optical density (OD)



B. Matlock et al., Analyzing Differences in Bacterial Optical Density Measurements between Spectrophotometers, 2011

Impedance BioCHIPS
3 mm

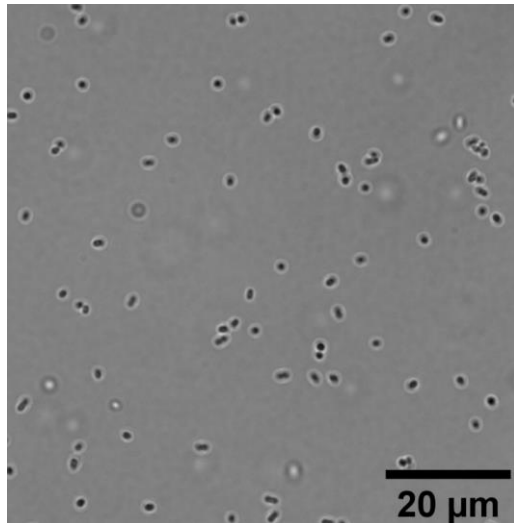


[Link to Homepage](#)

Cell count with Impedance BioCHiPs (results in detail)

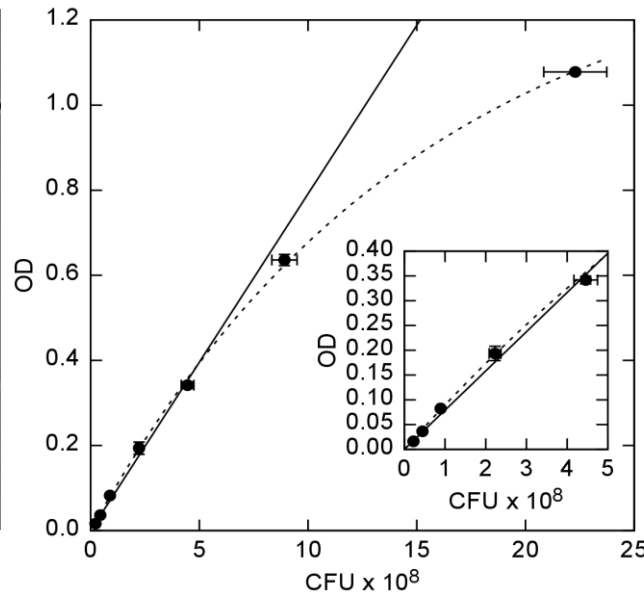
E.coli (0.02..1.26 10^9 cells/ml)

Colony forming units (CFU) from direct counting using **plating**



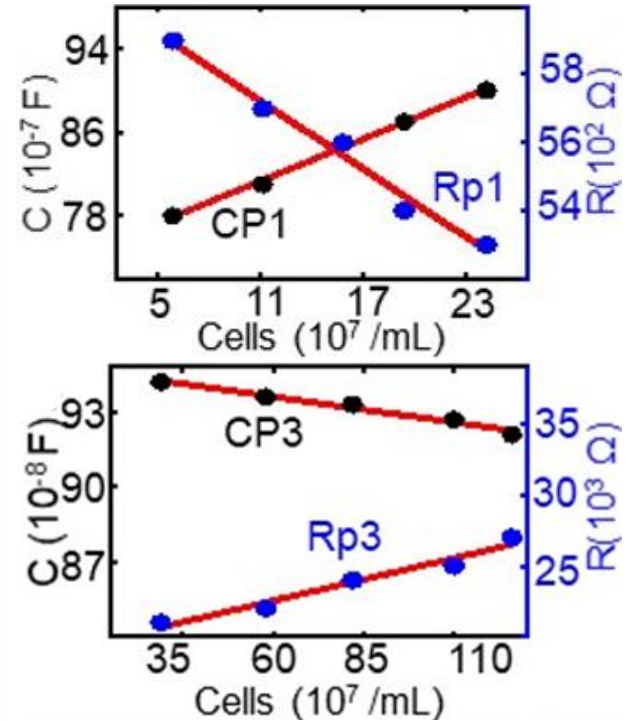
Time consuming, needs dilution, poor statistics

Cell density from indirect counting using **optical density (OD)**



Needs elaborated calibration

Cell density from modelled impedance parameters (CP1, Rp1, CP3, Rp3) of **Impedance BioCHiP**



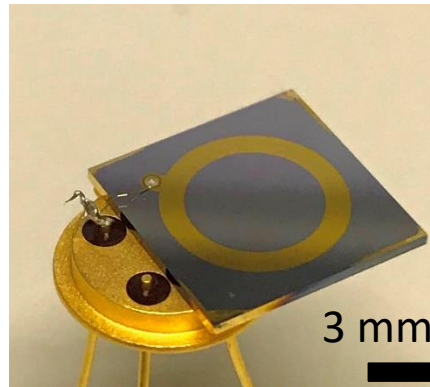
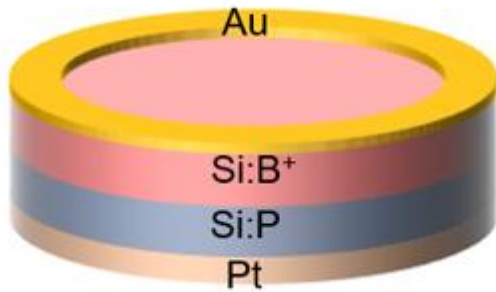
Looking for cooperation to evaluate quality of cell counting

Cell count with Impedance BioCHIPs

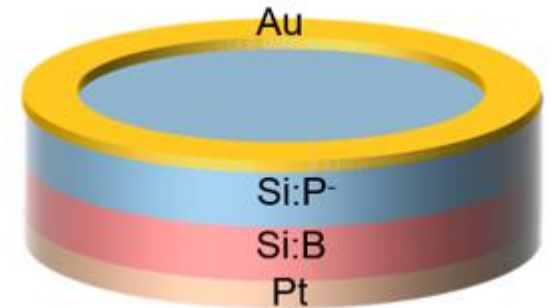
➤ Structure of impedance BioCHIP

- BS: Si wafer with p+n junction, PS: Si wafer with n+p junction
- Area of Au ring electrode (wirebonded): 2.4 mm², Inside area: 2.6 mm²
- Bottom electrode: unstructured Pt (wirebonded)

BS impedance BioCHIP



PS impedance BioCHIP



➤ Analytes

- 10...50 µl liquid without or with cells (OD=0.1...16.0)

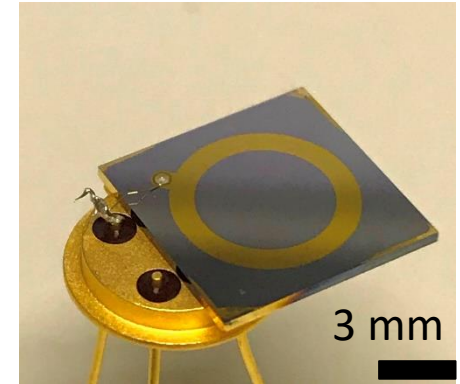
➤ Impedance measurements

- Impedance analyzer, e.g. Agilent 4294A or LCR meter
- $f_{ac} = 40 \text{ Hz} \dots 2 \text{ MHz}$, $U_{ac} = 10 \text{ mV}$, $U_{dc} = 0 \text{ V}$

(<http://hzdr-innovation.de/leistungen/polcarr/>)

Cell count with Impedance BioCHIPs (results in overview)

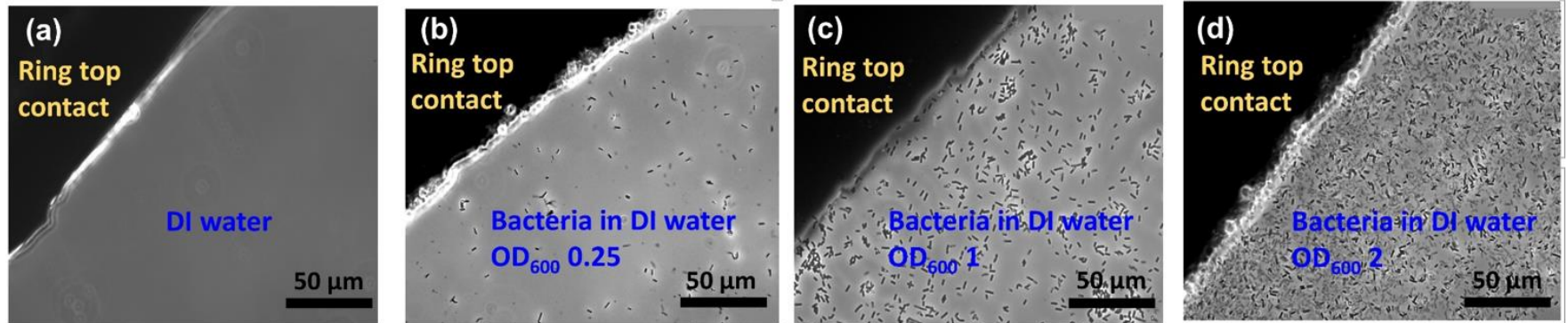
Impedance BioCHIP US10088443B2



- ✓ Cell count (OD=0.1..16.0) with impedance BioCHIPs
 - ✓ Counting **E.coli** ($\varnothing=1.1-1.5 \mu\text{m}$, length: 2-6 μm)
 - ✓ Counting **Lysinibacillus sphaericus** ($\varnothing=2-3 \mu\text{m}$)
 - ✓ Counting **Yeast/Saccharomyces cerevisiae** ($\varnothing= 5-10 \mu\text{m}$)

Counting of *Lysinibacillus sphaericus* ($1.2 \cdot 10^9$ cells/ml)

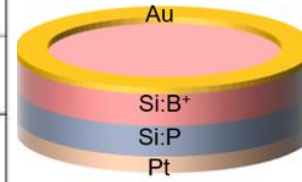
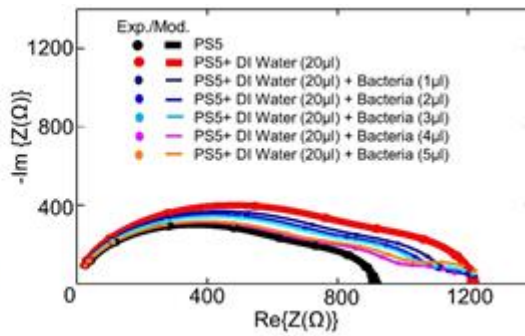
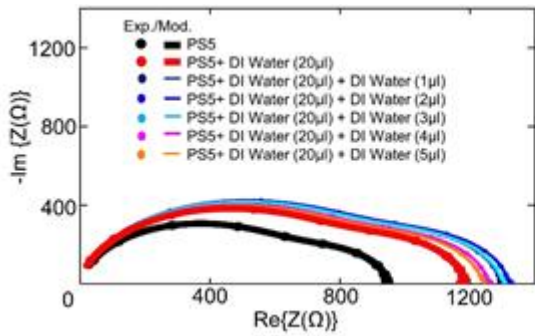
- Solid bacterium in Uranium mining waste pile
- Potential industrial application in metal remediation by recycling
- Diameter ($\varnothing=2-3 \mu\text{m}$)



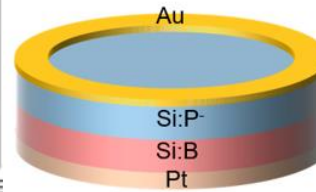
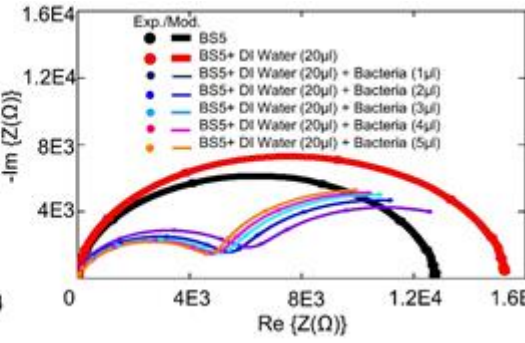
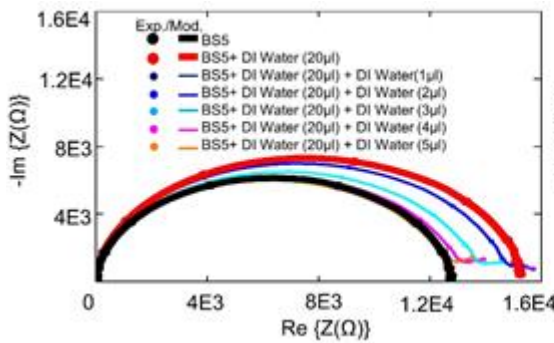
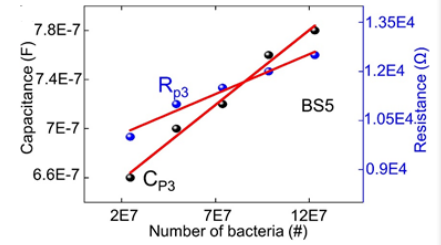
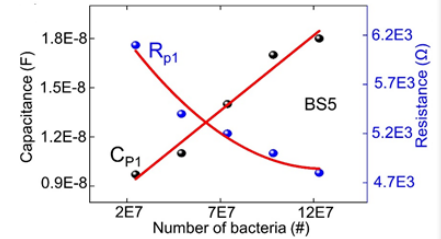
Counting of *Lysinibacillus sphaericus* ($1.2..6.2 \cdot 10^9$ cells/ml)

Impedance measurement with impedance BioCHIP

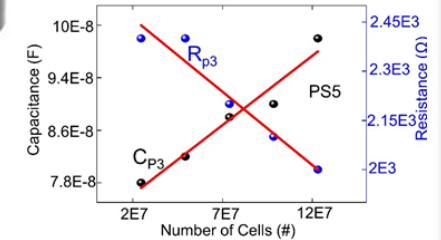
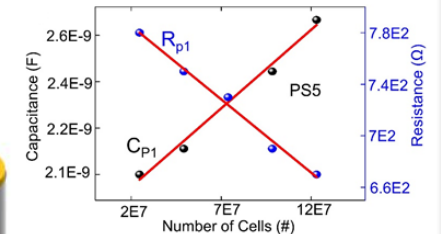
Multiparameter analysis



BioCHIP BS



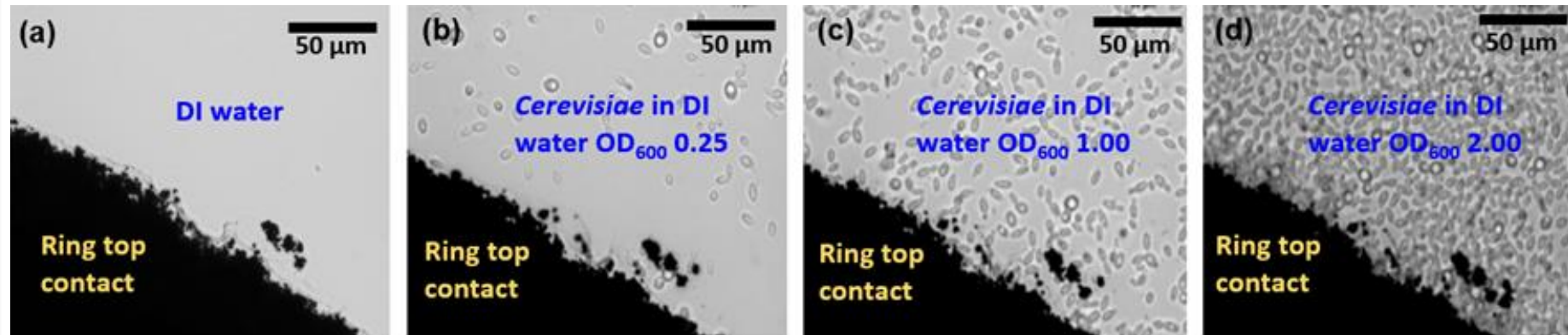
BioCHIP PS



M. Kiani, N. Du, M. Vogel et al., Biosensors 2019, 9, 120

Counting of yeast/*Saccharomyces cerevisiae* ($0.3..1.7 \cdot 10^8$ cells/ml)

- Converts sugar into ethanol and CO_2
- Fabricates recombinant protein (interferon and insulin)
- Diameter ($\varnothing=5-10 \mu\text{m}$)

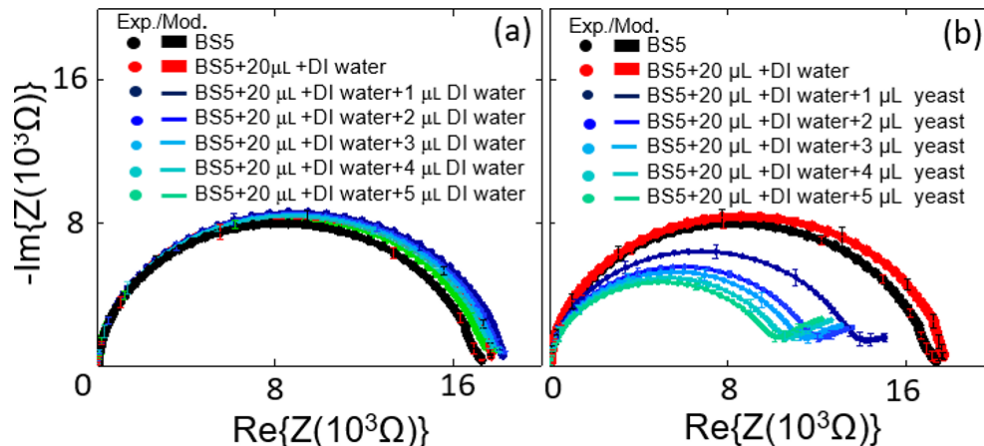
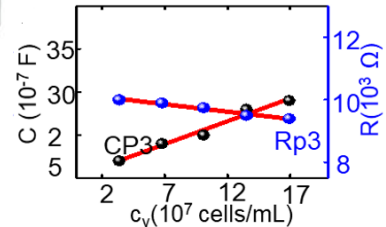
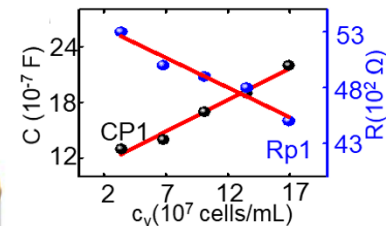
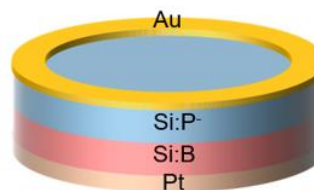
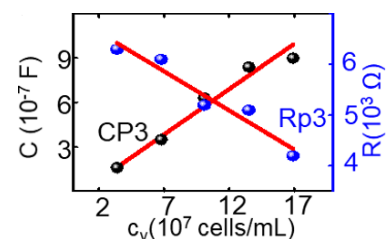
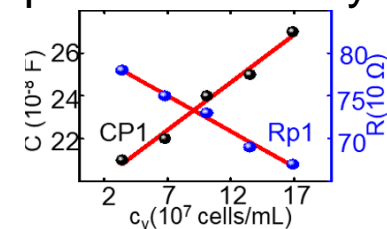
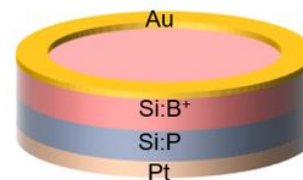
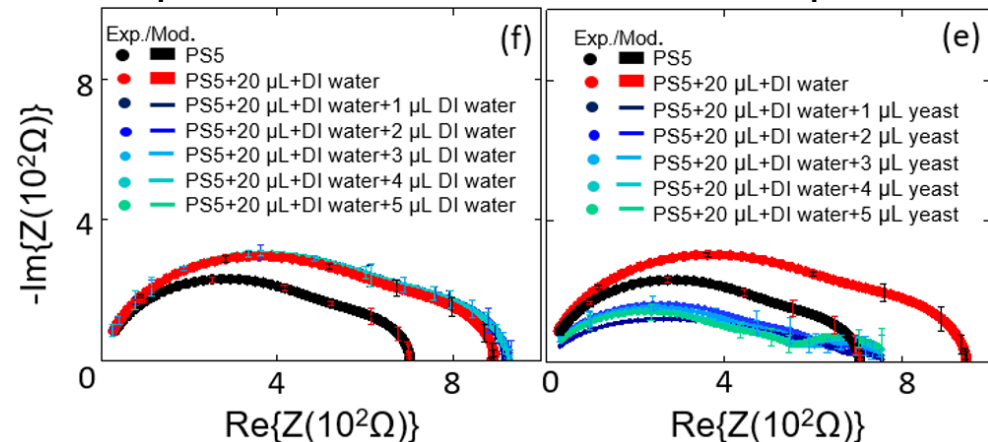


M. Kiani, N. Du, M. Vogel et al., Biosensors 2020, 10, 7

Counting of yeast/Saccharomyces cerevisiae (0.3..1.7 10⁸ cells/ml)

Impedance measurement with impedance BioCHIP

Multiparameter analysis



M. Kiani, N. Du, M. Vogel et al., Biosensors 2020, 10, 7

- **Industrie-Partner für Evaluierung der Qualität des Zellzählens gesucht**
- **Kooperationspartner gesucht:**
 - Optische Dichte-Messungen
 - Zellzählen in der Mikrotiterplatte
 - Zellzählen in der Mikrofluidik

Weitere Information und Bestellungen unter: <http://hzdr-innovation.de/leistungen/polcarr/>

Contact: s.krueger@hzdri.de