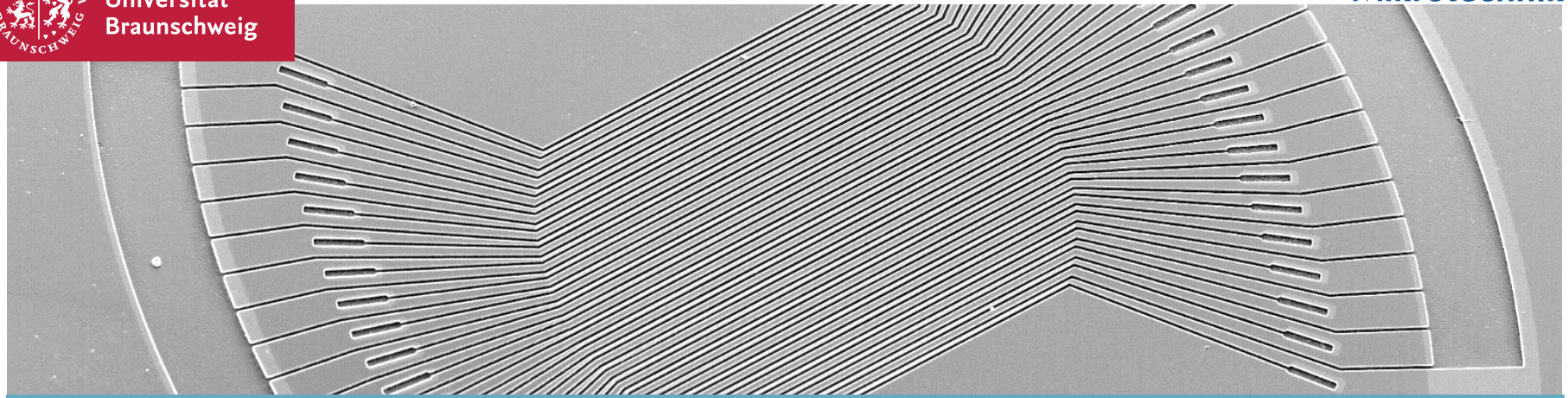
Technische Universität Braunschweig

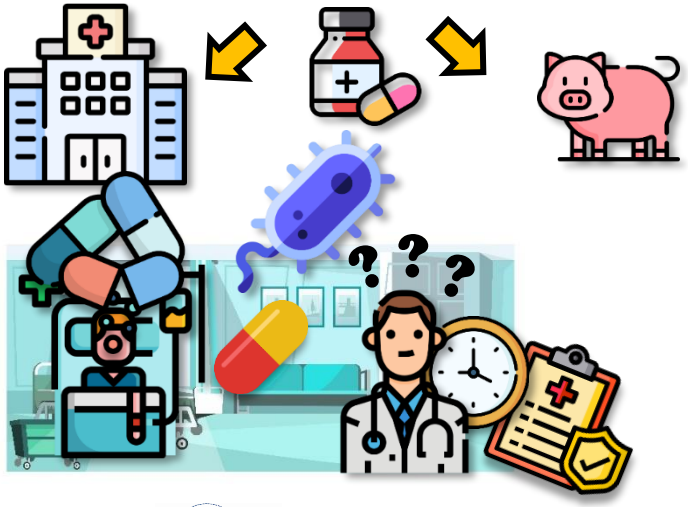
Institut für Mikrotechnik



# Antibiotic Susceptibility-Testing based on nanofluidic cell immobilization and growth detection in an optofluidic system

Ann-Kathrin Klein
Institute of Microtechnology, Technische Universität Braunschweig

# Motivation




- Drug resistance on the rise
- Misuse of antibotics

- Broadband antibiotics
- Only for emergencies

- Fast and PoC diagnosis



Bilder: Flaticon.com

# State of the Art

VITEK2®

BD Phoenix®

MicroScan WalkAway®

Phenotypic testing

Sample preparation

External cultivation

Turbidity measurments

Detection time[1] >30 h

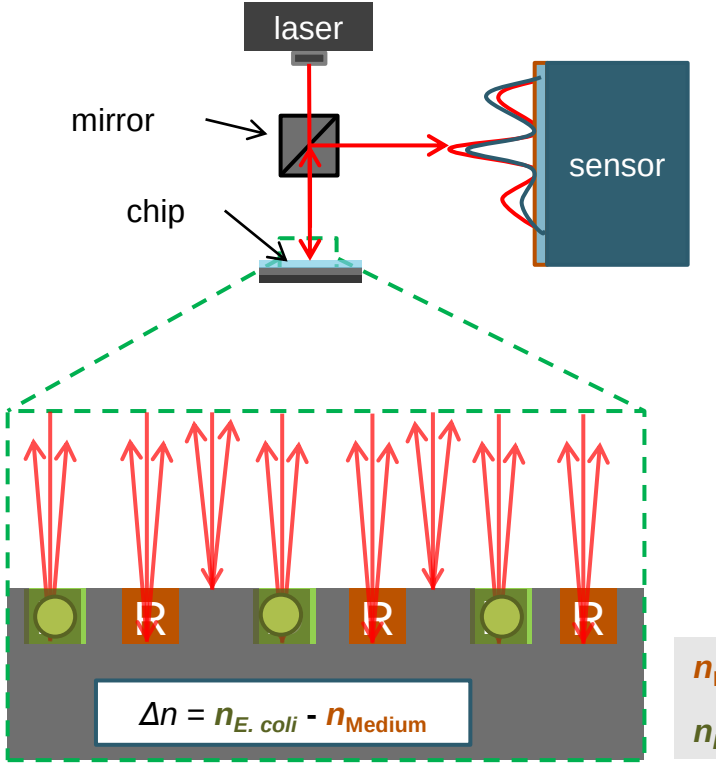
Not fast enough

[1]van Belkum et al. (2020) *Nature reviews*



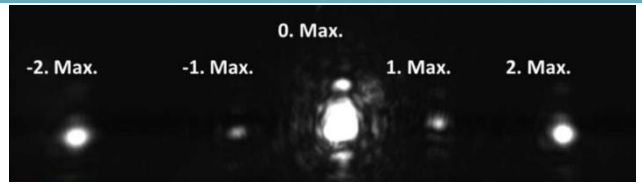
https://www.biomerieuxusa.com/
https://www.bd.com, https://media.beckmancoulter.com

# Measuring principle




$n_{Medium} = 1{,}34$

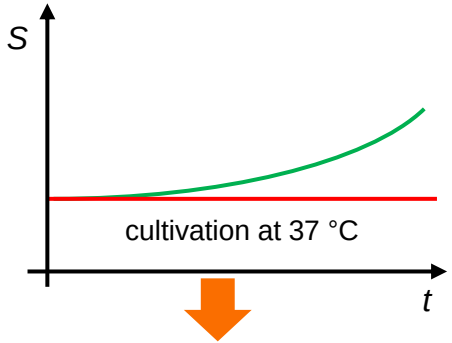
$n_{E.\ coli} = 1{,}37$




Purr, F. et al. (2017) Lab on a Chip

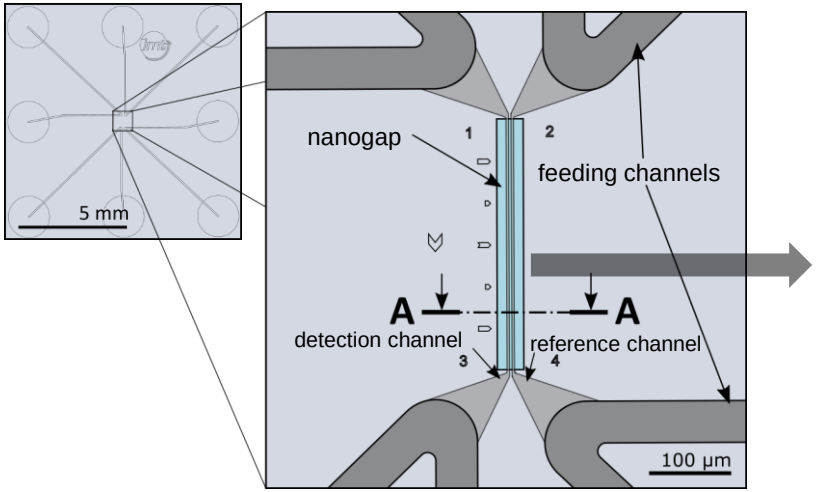
$$I_m \neq I_{-m} \qquad S_m = \frac{I_m - I_{-m}}{I_m + I_{-m}}$$

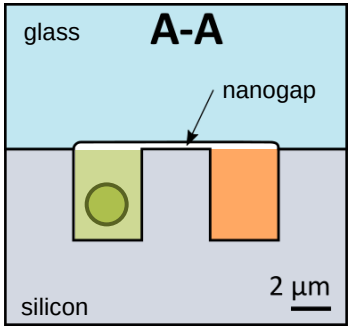
refractive index change




**growth → resistance**: yes/no

# Immobilization principle




**reference- and detection channel:** 3 µm × 4 µm

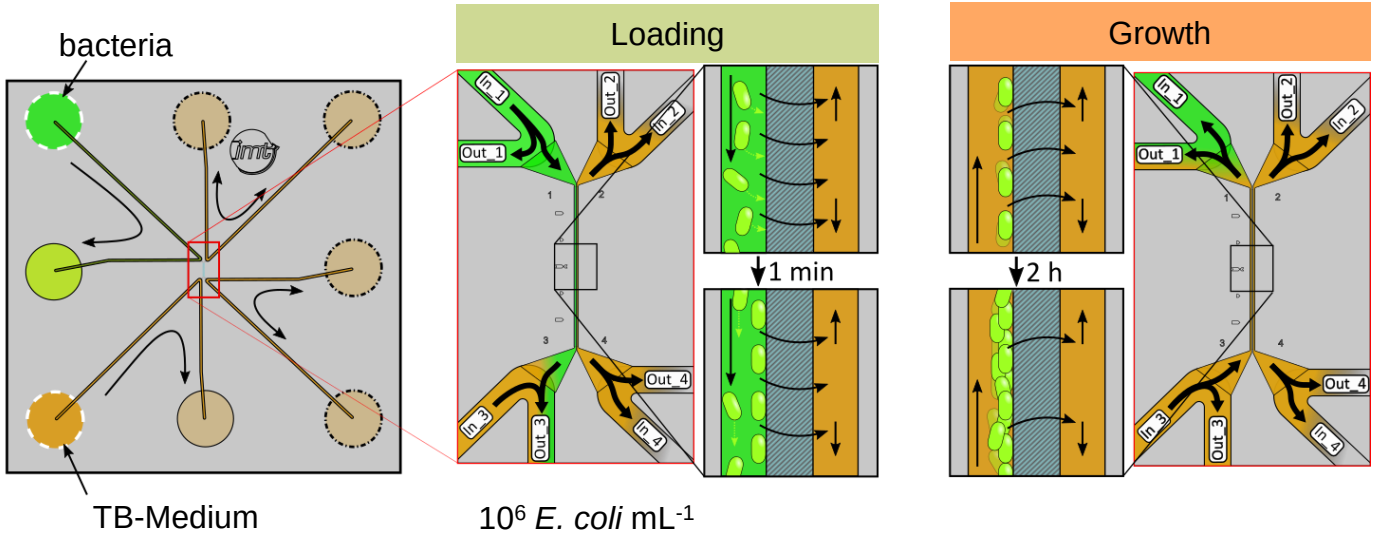
**distance:** 3 µm

**length:** 296 µm

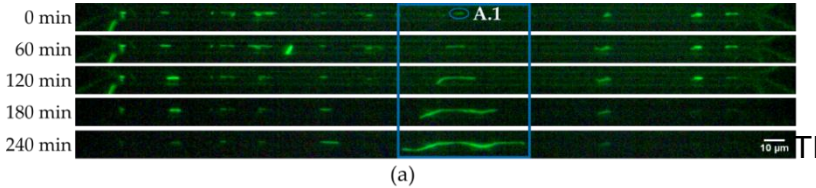
**nanogap:** 590 nm

**feeding channels:** 50 µm × 50 µm

# Experimental procedure

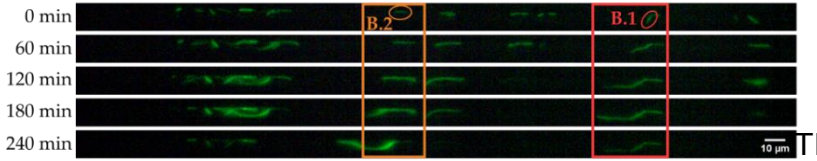


# GFP-measuring



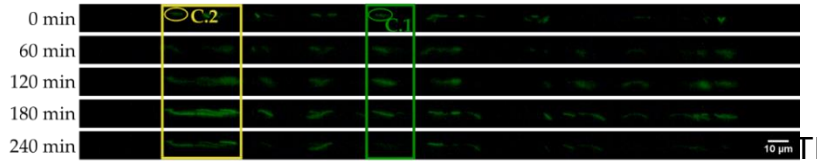

TB-Medium

(a)




TB-Medium

(b)

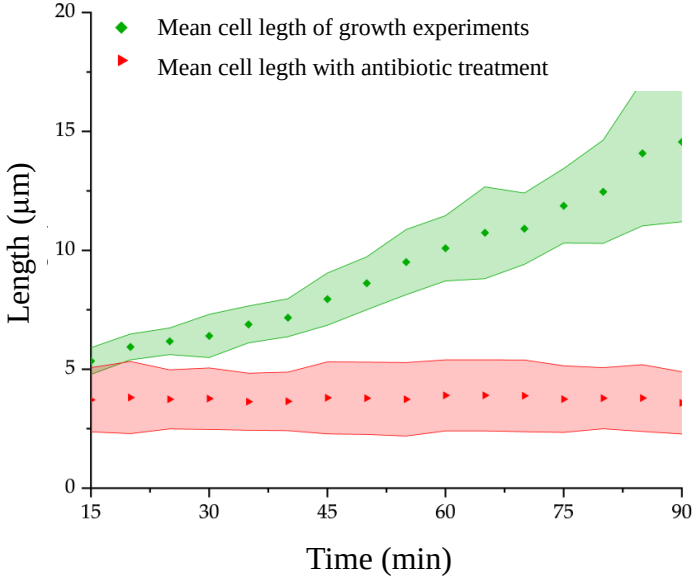


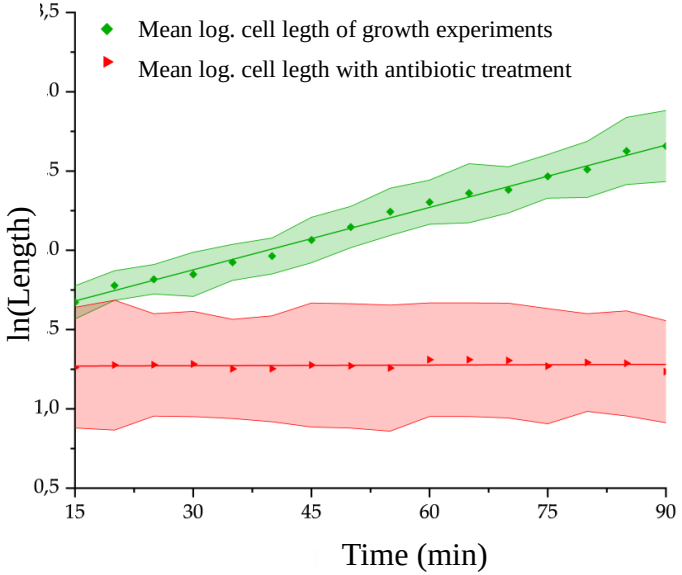

TB-Medium

(c)

doubling time: 53 min

# Results





micromachines

Article

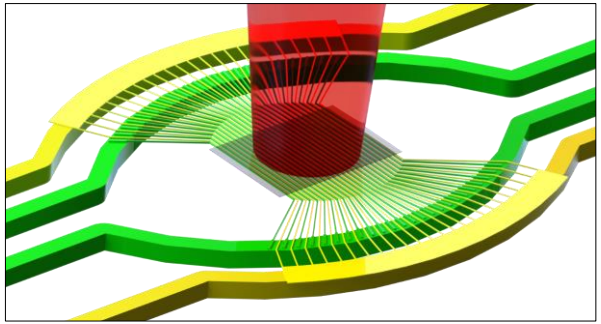
Cross-Flow Filtration of *Escherichia coli* at a Nanofluidic Gap for Fast Immobilization and Antibiotic Susceptibility Testing

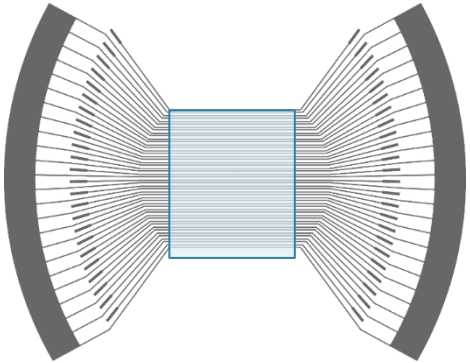
Micromachines 2019, 10, 691; doi:10.3390/mi10100691

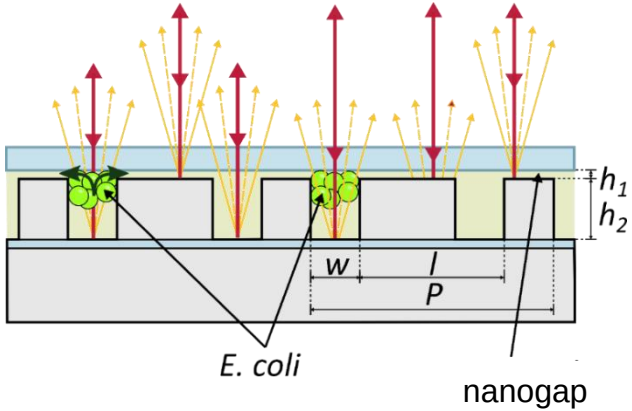
- ✓ growth of immobilized E. coli possible
- ✓ antibiotic effect detectable

→ Optofluidic grating

# Optofluidic grating principle

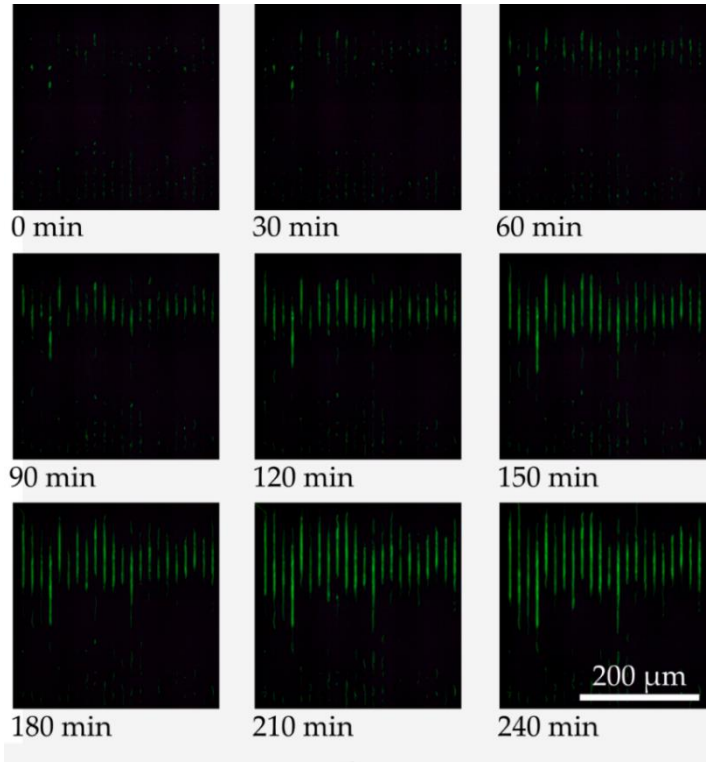




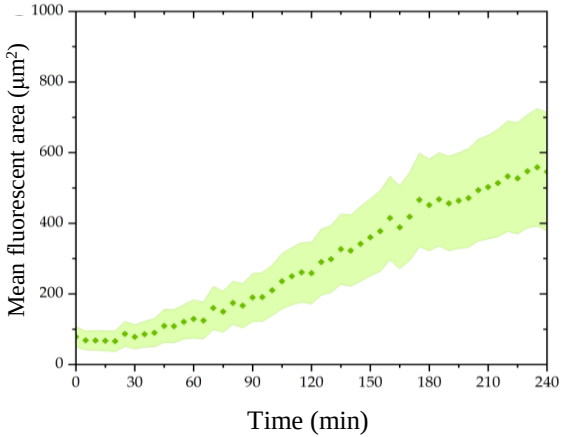



**24 detection channel** 3 µm × 4 µm
**24 reference channel** 3 µm × 4 µm
**nanogap** 590 nm × 296 µm
**feeding channel** 50 × 50 µm

# GFP-measuring

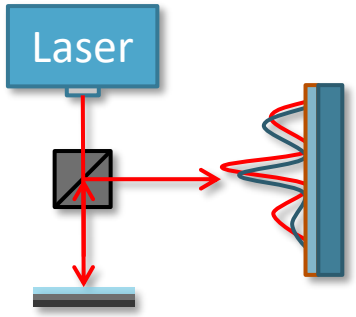


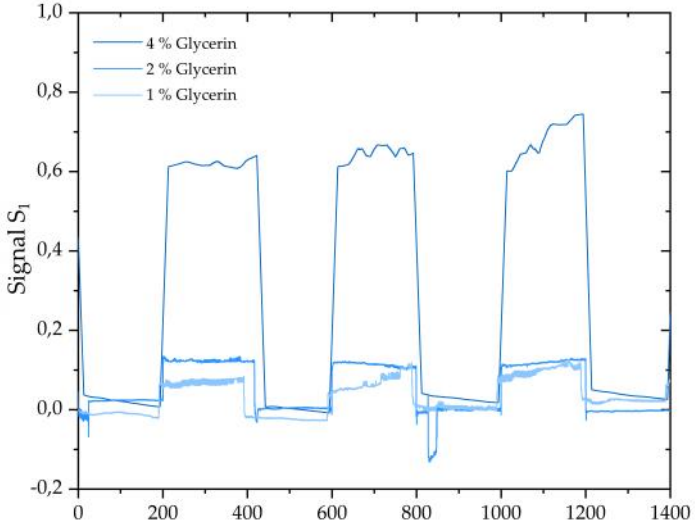

- ✓ doubling time 61 min
- ✓ immobilization successfull
- ✓ growth in desired area

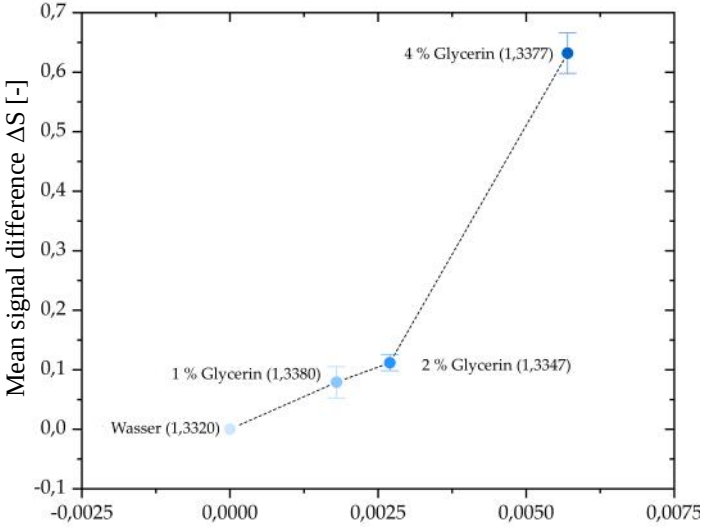



✓ GFP-measuring of growth of immobilized E. coli possible

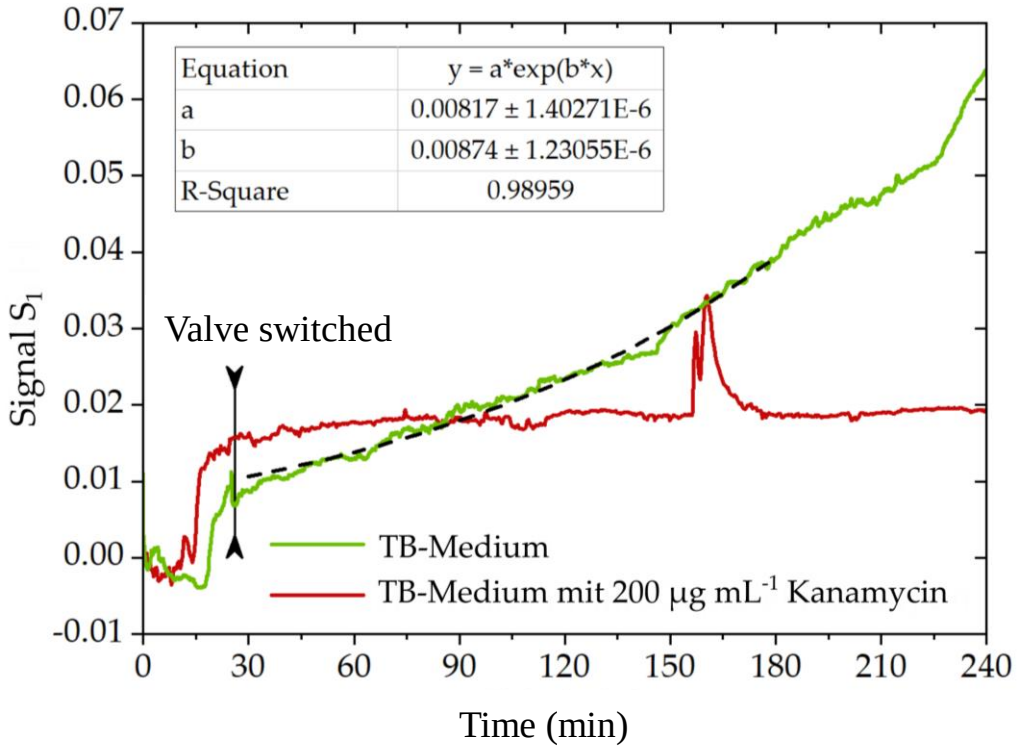
# Refractive index measurement



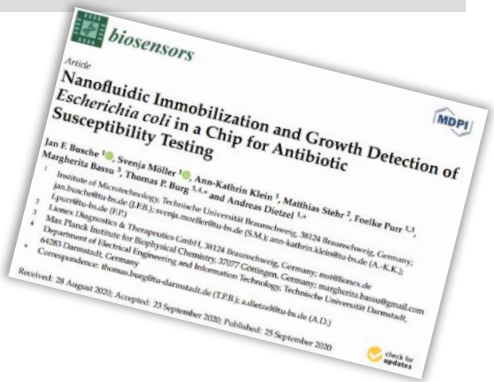



# Susceptibility Test




Detection of the growth of *E.coli*

- ✓ under 4 h
- ✓ doubling time 79 min
- ✓ sample volume 187 µl


biosensors

Article

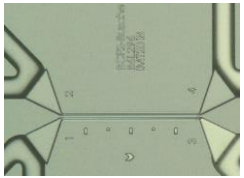
Nanofluidic Immobilization and Growth Detection of *Escherichia coli* in a Chip for Antibiotic Susceptibility Testing

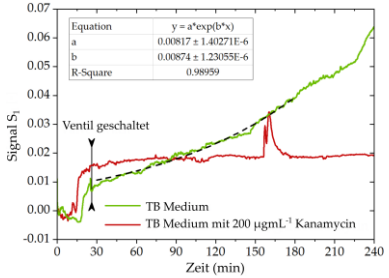
Jan F. Busche [1], Svenja Möller [1], Ann-Kathrin Klein [1], Matthias Stehr [2], Foelke Purr [1,3], Margherita Bassu [3], Thomas F. Burg [3,4,*] and Andreas Dietzel [1,*]

Received: 28 August 2020; Accepted: 23 September 2020; Published: 25 September 2020

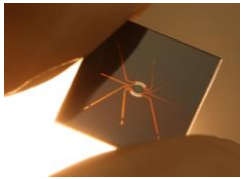
# Summary

Nanogap



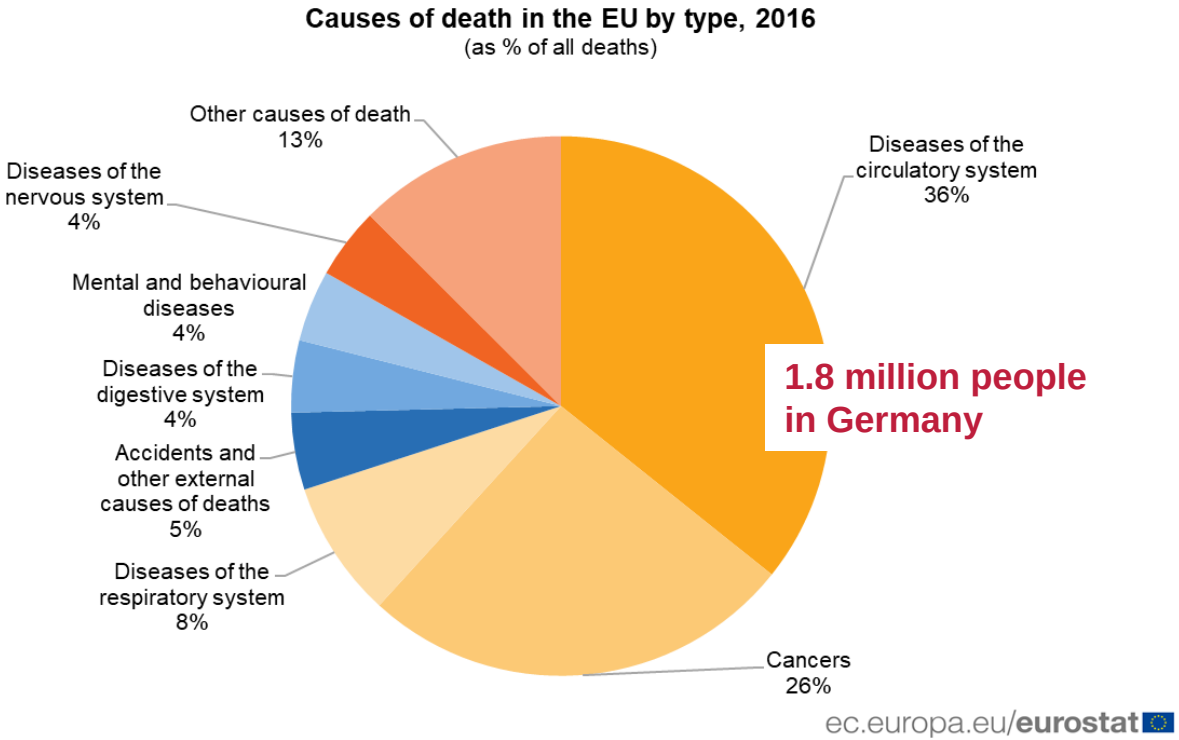



Optofluidic grating

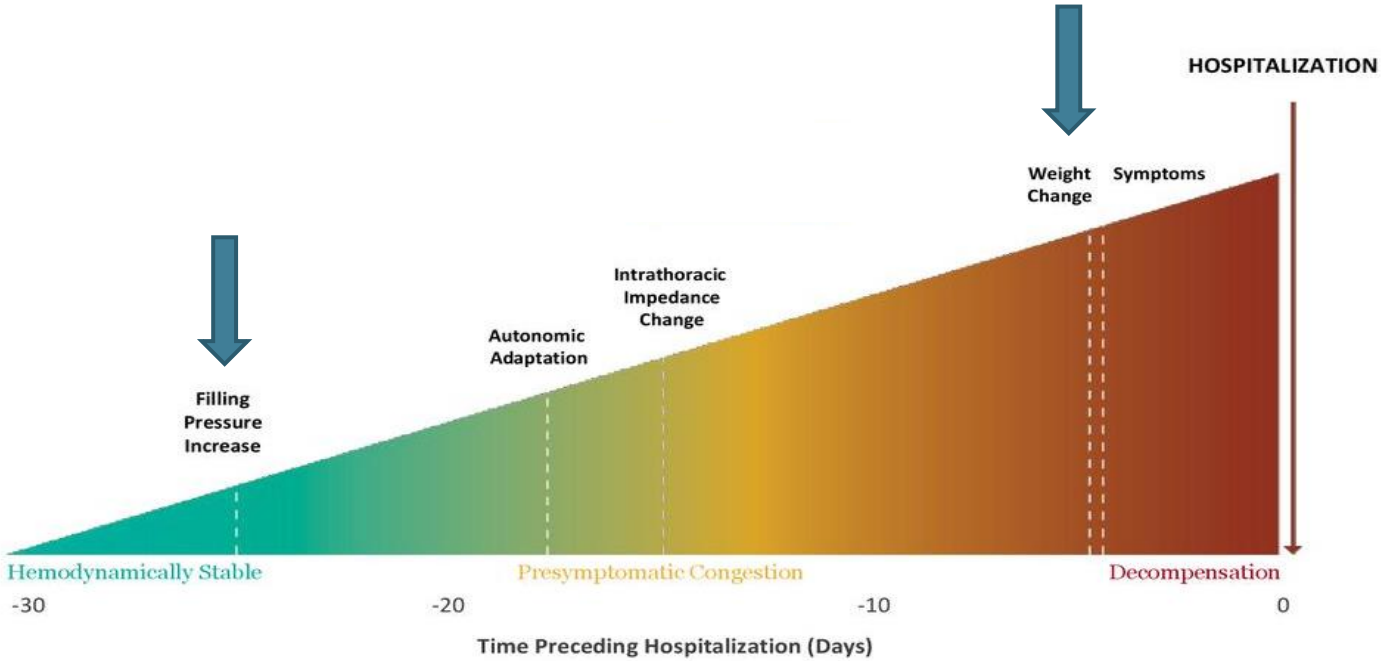


**Phenotypic growth detection**

# Motivation


Causes of death in the EU by type, 2016
(as % of all deaths)
Other causes of death 13%
Diseases of the nervous system 4%
Mental and behavioural diseases 4%
Diseases of the digestive system 4%
Accidents and other external causes of deaths 5%
Diseases of the respiratory system 8%
Cancers 26%
Diseases of the circulatory system 36%
1.8 million people in Germany
ec.europa.eu/eurostat

# Motivation

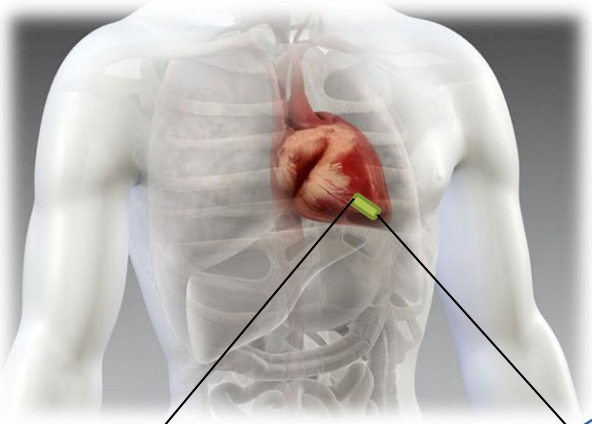


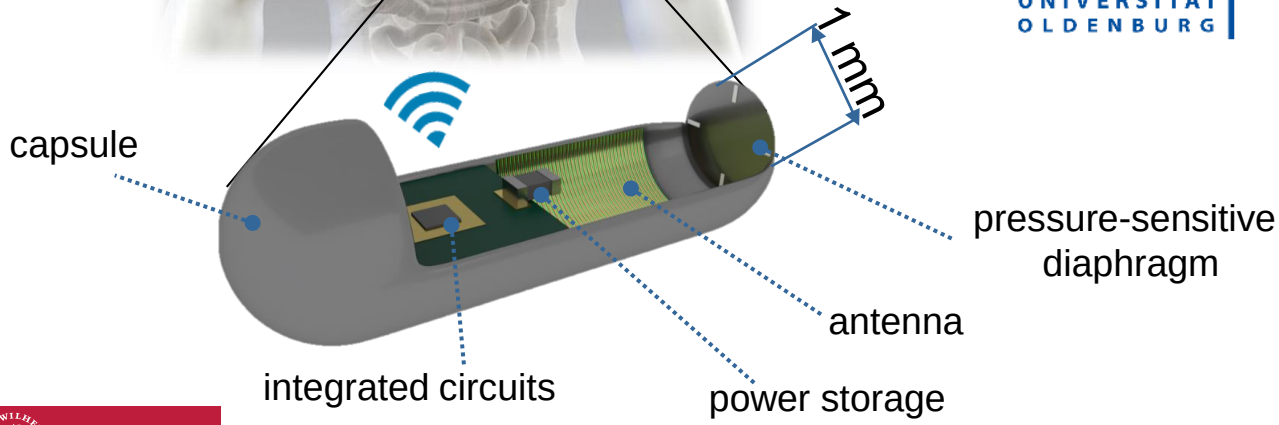



Graph adapted from Adampson PB, et al. Curr Heart Fail Reports, 2009.

# ForMat-CARDIO - Long-term cardiovascular implant

**Duration:** 4 years (March 2020 – March 2024)






nanoScale systems gmbh

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HDZ NRW

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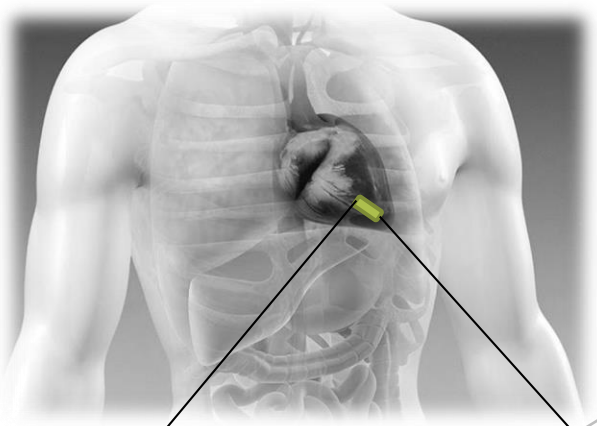
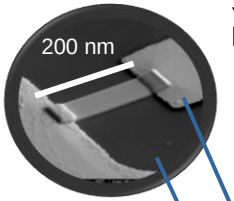
Gefördert vom

Bundesministerium für Bildung und Forschung

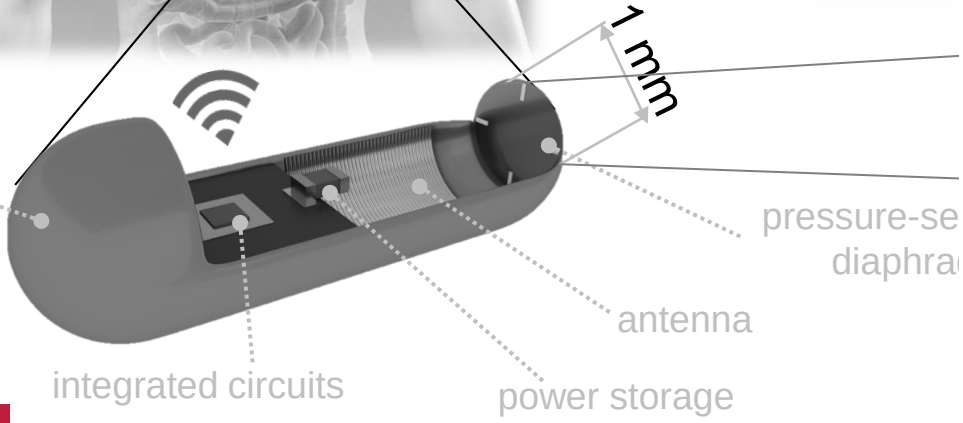
# ForMat-CARDIO - Long-term cardiovascular implant

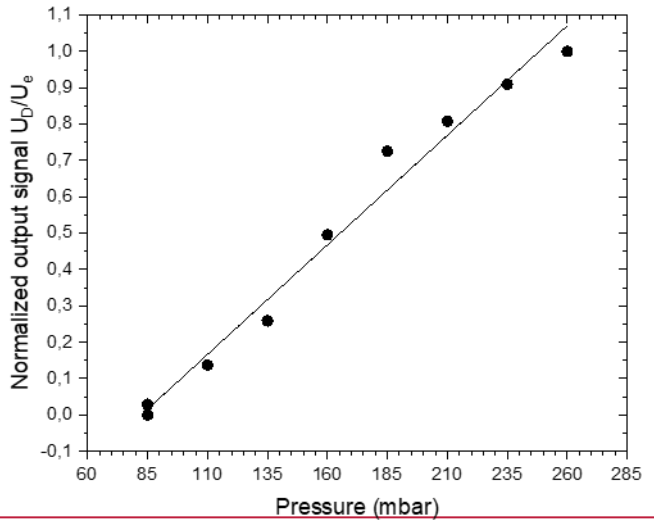





Strain sensitive
Nanosensor

Blood Pressure



# Thank you for your attention!

The results of the BmBF-funded KeimOut-project were achieved by the Institute of Microtechnology of the Technische Universität Braunschweig  research group Andreas Dietzel (project collaborator: Jan Busche) in cooperation with the research group Thomas Burg "Integrated Micro-Nano-Systems" of the Technische Universität Darmstadt.

The results of the BmBF-funded ForMat-CARDIO-project were achieved in cooperation with the company NanoScale systems GmbH and Claus Burkhardt of the NMI Natural and Medical Sciences Institute at the University of Tübingen.