Willkommen
Welcome
Bienvenue

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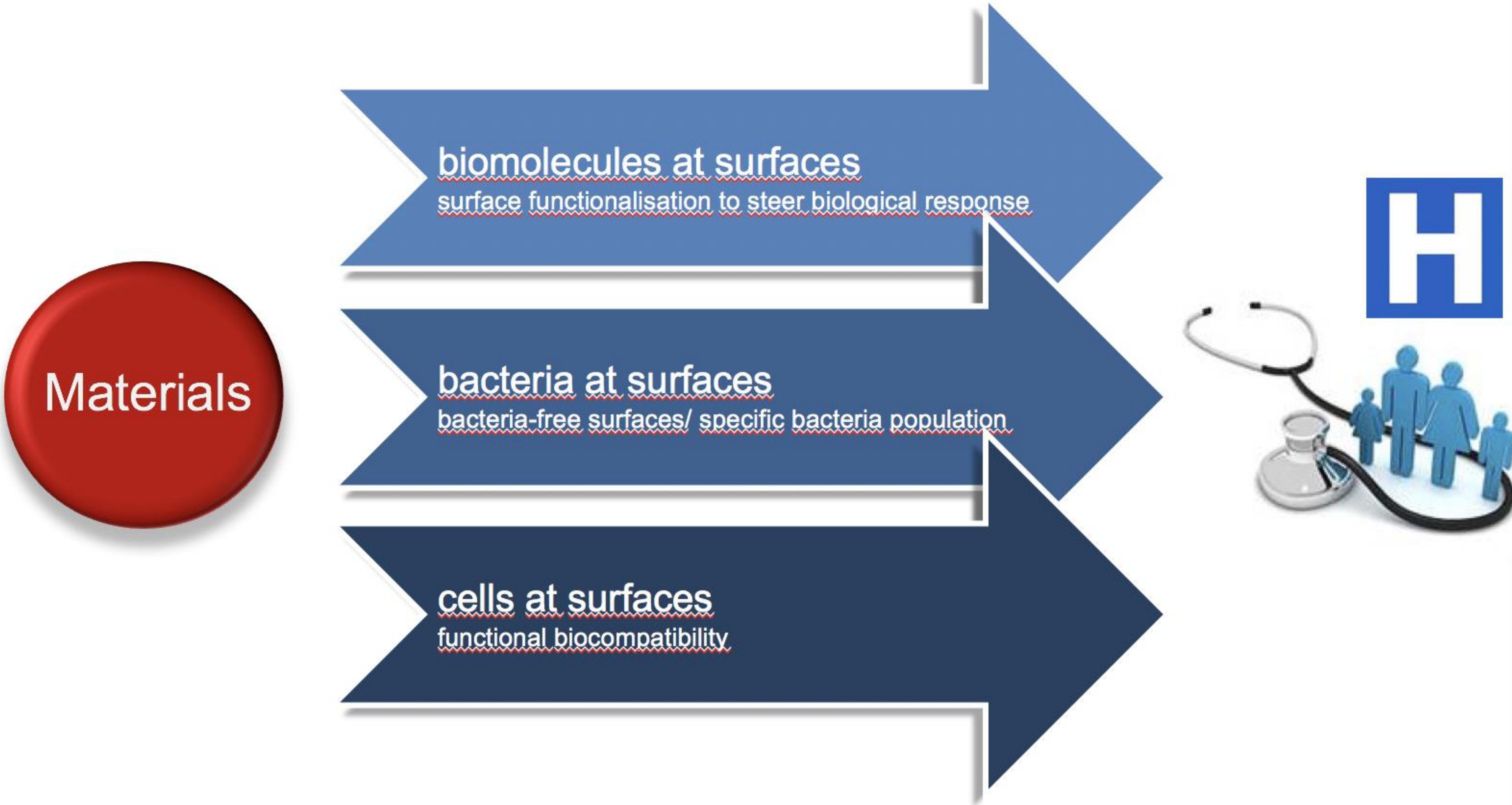
In vitro studies for antibacterial concepts in the field of bone implant materials

Katharina Maniura, Biointerfaces, Empa

Bone Innovation Summit 2019
Feb 12-14, 2019

Biointerfaces

MATERIALS MEET LIFE



Biomaterials solve & *generate* problems

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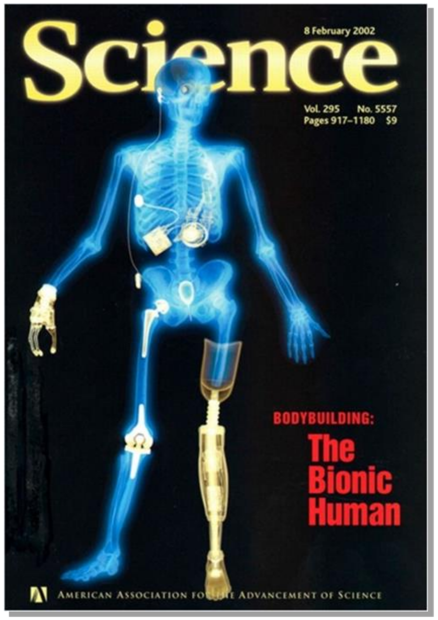
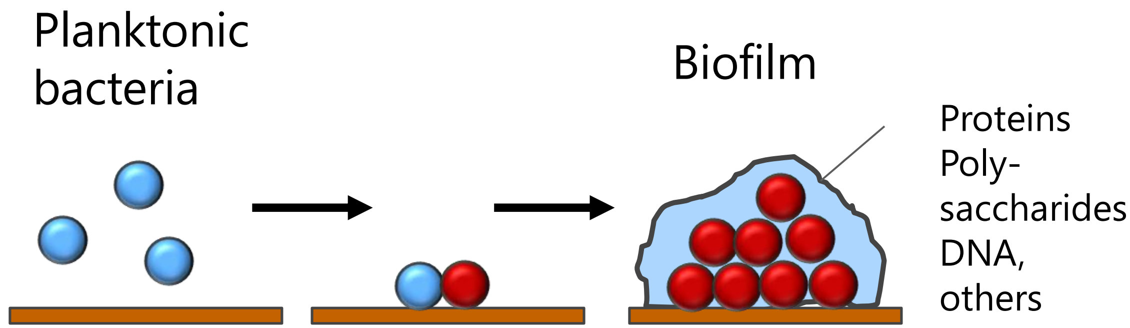




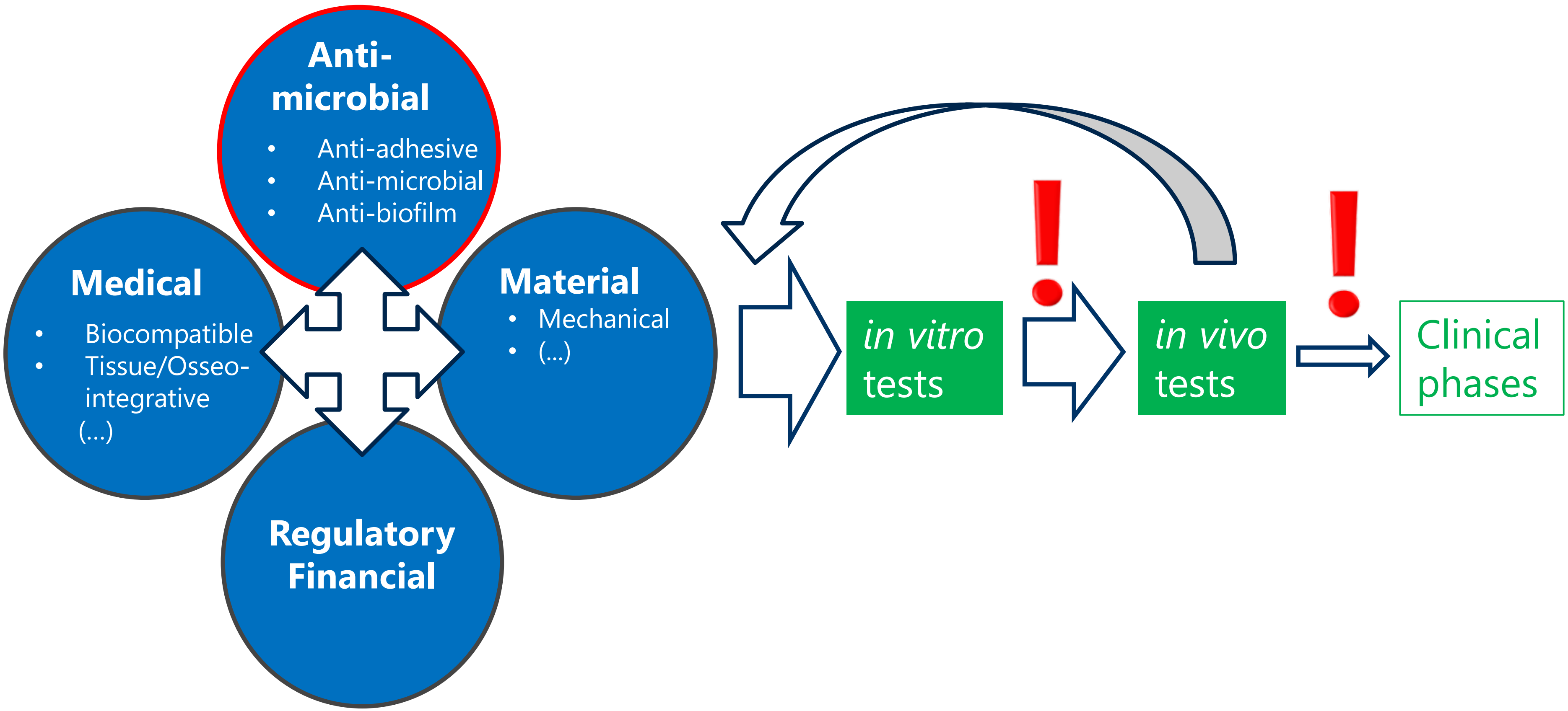
Biofilms: Communities of microorganisms embedded in a matrix of extracellular polymeric substances

Bacteria in biofilms tolerate the ~1000-fold antibiotics concentration, compared to planktonic populations

➔ Antimicrobial materials with anti-biofilm properties are highly demanded

Steward and Costerton, The Lancet, 2001
Nature Reviews Drug Discovery 12(10):791-808

Many promising antimicrobial biomaterials show decent *in vitro* activity but only poor *in vivo* efficacy



Requirements

➔ Partially due to the lack of predictive laboratory biofilm *in vitro* models

Buhmann *et al*, Trends in Biotechnology 2016

The site of action defines the antimicrobial strategy – and the *in vitro* bioassay

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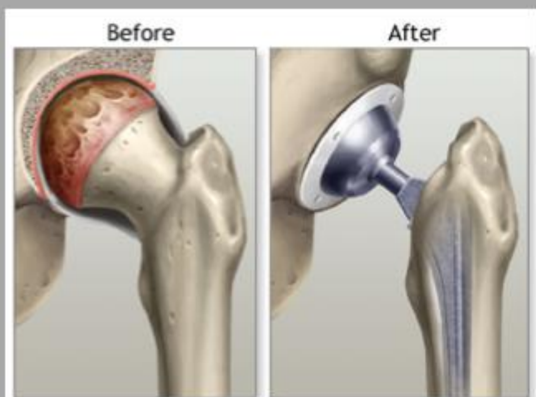
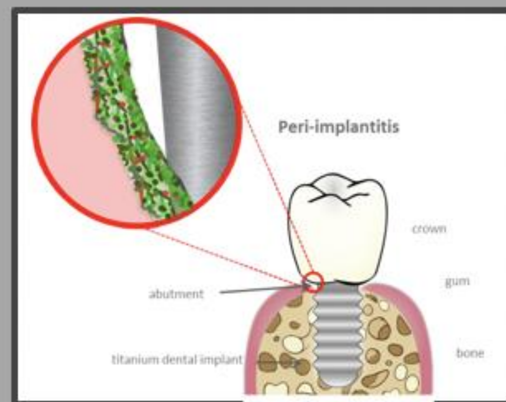
Hip joint implants



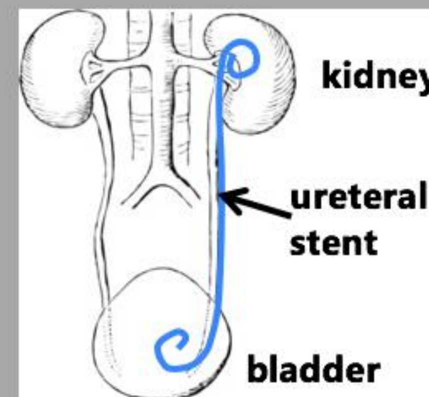
Low bacterial load
(infection during surgery
or late infections)

Dental implants



High bacterial load
multiple species involved

Medical devices: Ureteral stents



Low to high
bacterial load ?

https://medlineplus.gov/ency/presentations/100006_5.htm
http://coronationdentalspecialty.ca/
Olek Remesz; https://commons.wikimedia.org/wiki/
File:Foley_catheter_inflated_and_deflated_EN.svg

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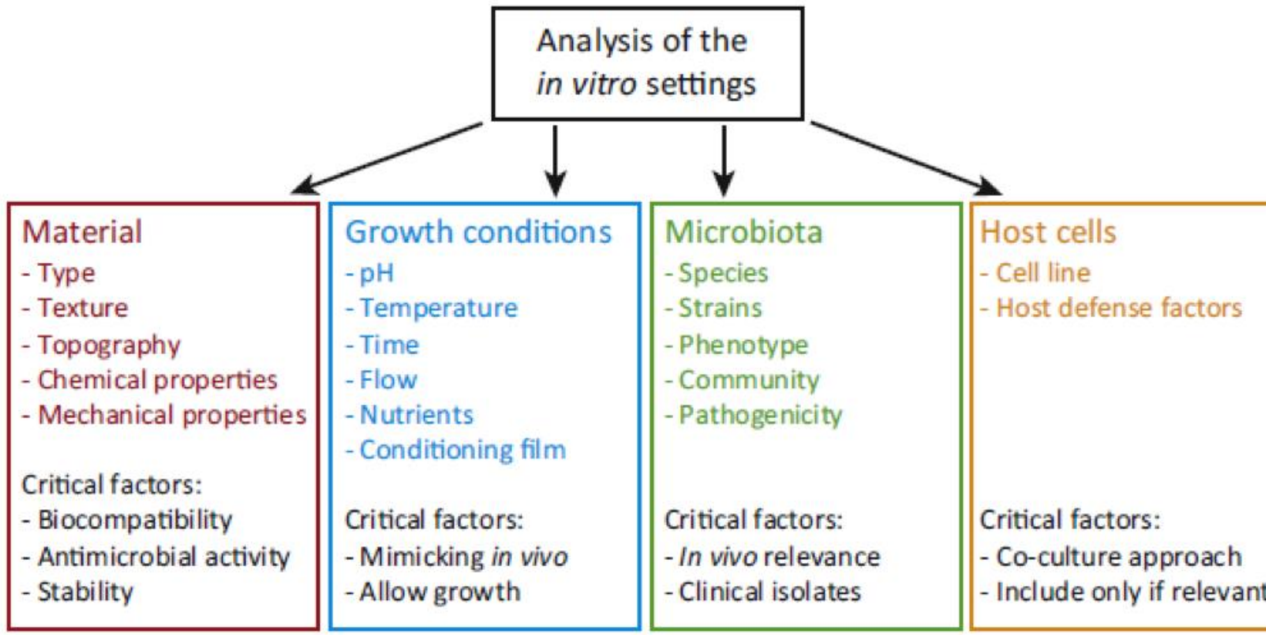
Important factors for *in vitro* biofilm assessment

in vitro *in vivo*

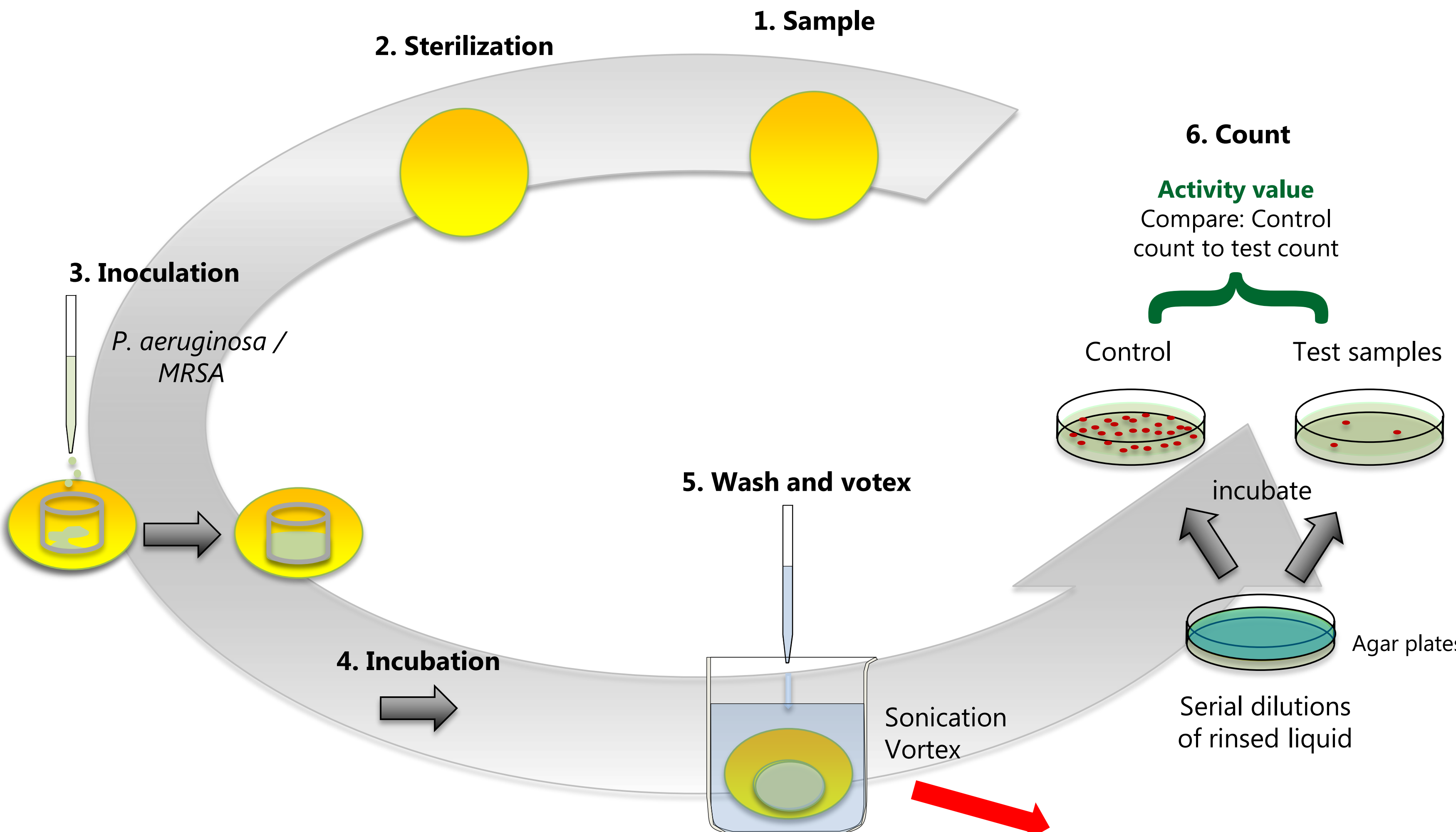


Objective:
Better, predictive biofilm *in vitro* models for antimicrobial materials testing

Buhmann et al., "*In Vitro* Biofilm Models for Device-Related Infections"
Trends in Biotechnology 2016

How are materials tested?

Example: standard antibacterial assays



Surfaces are often not analyzed

Stainless steel implants: one example

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External fixation

High rate of pin track infection

Inefficient treatment

Origin of Pin-Tract Infection

Bacterium	%
Staphylococcus aureus	**47.1**
Staphylococcus epidermidis	11.8
Escherichia coli	9.4
Pseudomonas aeruginosa	9.4
Streptococcus spp.	3.5
Enterococcus faecalis	2.4
Serratia marcescens	2.4
Vibrio vulnificus	2.4
Mixed flora	3.5
Other	8.1

Antoci at al. Am J Orthop. 2008;37(9):E150-E154

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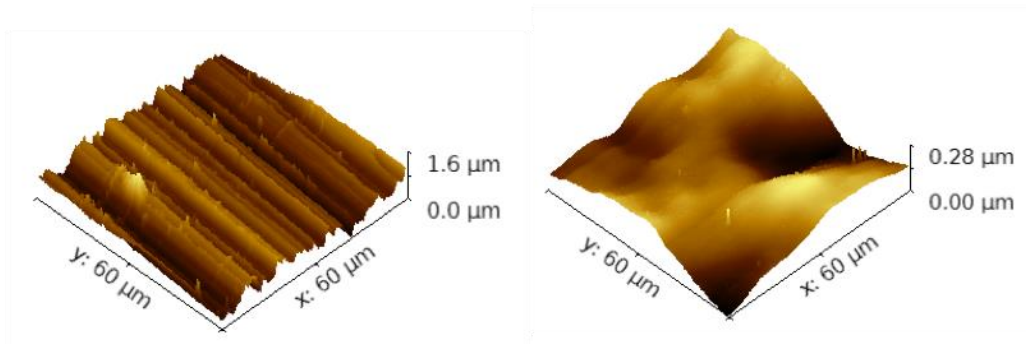
Characterization of surface properties of stainless steels



	Roughness (nm) R_a, R_q	Contact angle (°) $\theta_{w\parallel}$, $\theta_{w\perp}$	Contact angle (°) $\theta_{mi\parallel}$, $\theta_{mi\perp}$	Zeta potential (mV)
Untreated	172.5 217.9	77.1 101.7	42.3 85.8	– 40.0
P240s	45.2 56.6	80.4 78.8	47.4 47.4	– 46.8

Wu, et al, ACS Omega 2018, 3, 6456−6464

Influence of surface roughness on bacterial adhesion

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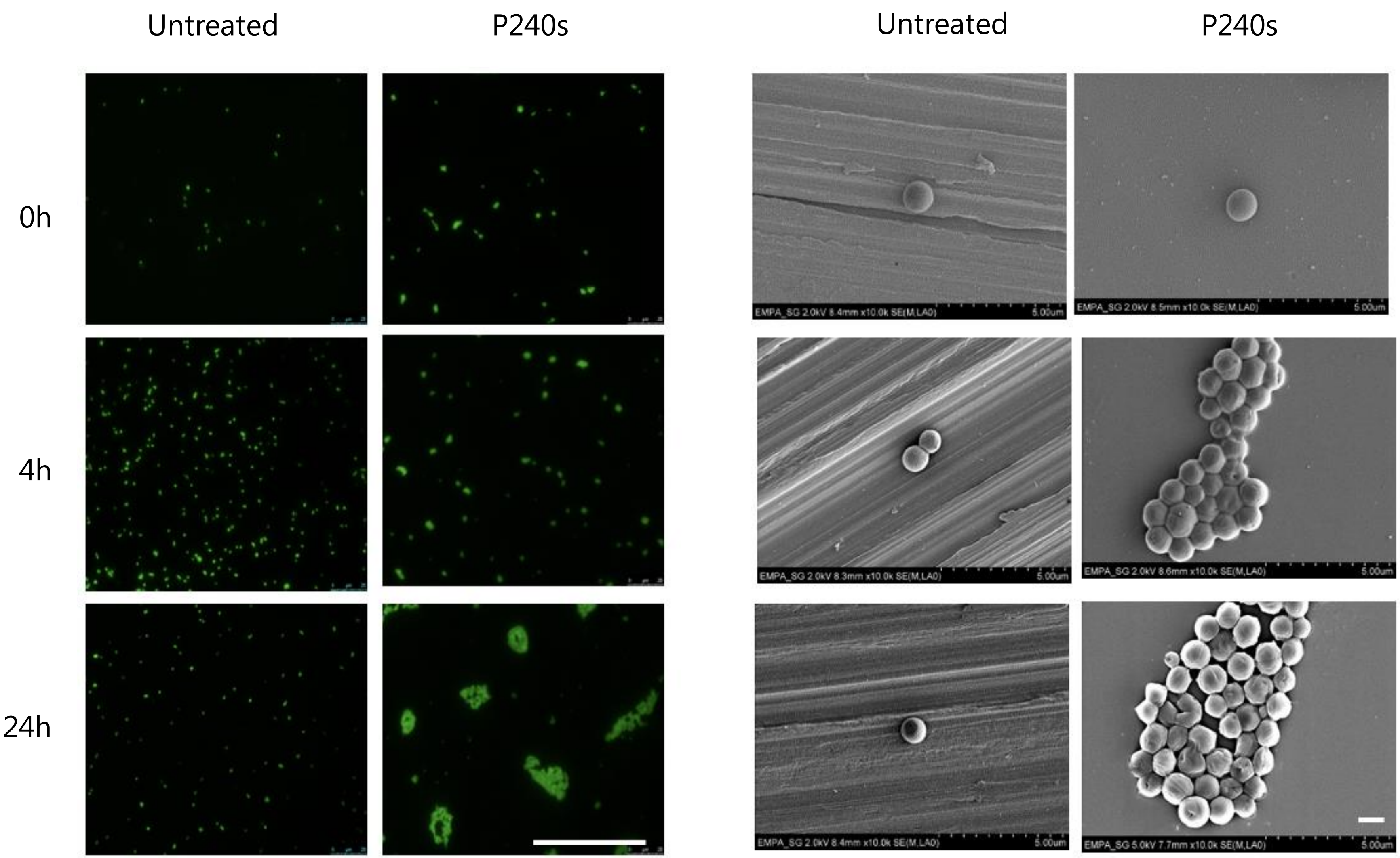

Surface topography influences greatly bacterial colonization

Wu, et al, ACS Omega 2018, 3, 6456−6464

Bacterial adhesion on stainless steels

	Roughness (nm) R_a, R_q		Contact angle (°) $\theta_{w\parallel}$, $\theta_{w\perp}$		Contact angle (°) $\theta_{mi\parallel}$, $\theta_{mi\perp}$		Zeta potential (mV)	S.a. Viable cells (CFU/mL)*
Untreated	172.5	217.9	77.1	101.7	42.3	85.8	– 40.0	3.1×10^2
P240s	45.2	56.6	80.4	78.8	47.4	47.4	– 46.8	1.9×10^4

*: adhered viable cells after incubation of 4 h; S.a.: *S. aureus*

Surface topography influences greatly bacterial colonization

Wu, et al, ACS Omega 2018, 3, 6456−6464

Take home messages

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Analysis of the *in vivo* setting

material
- type
- texture
- topography ✓
- chemical properties
- mechanical properties

critical factors:
- biocompatibility
- antimicrobial activity
- stability

growth conditions
- pH
- temperature
- time
- flow
- nutrients
- conditioning film

critical factors:
- mimicking *in vivo*
- allow growth

microbiota
- species
- strains
- phenotype
- community
- pathogenicity

critical factors:
- *in vivo* relevance
- clinical isolates

host cells
- cell line
- host defense factors

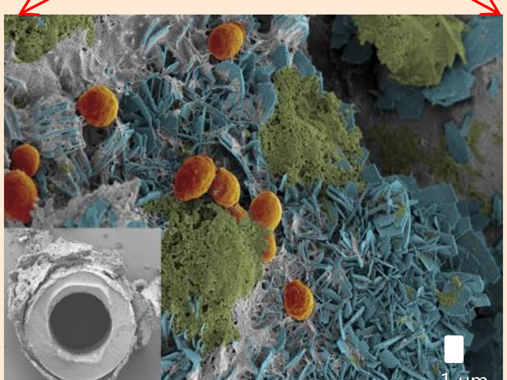
critical factors:
- co-culture approach
- include only if relevant

Examples: model systems

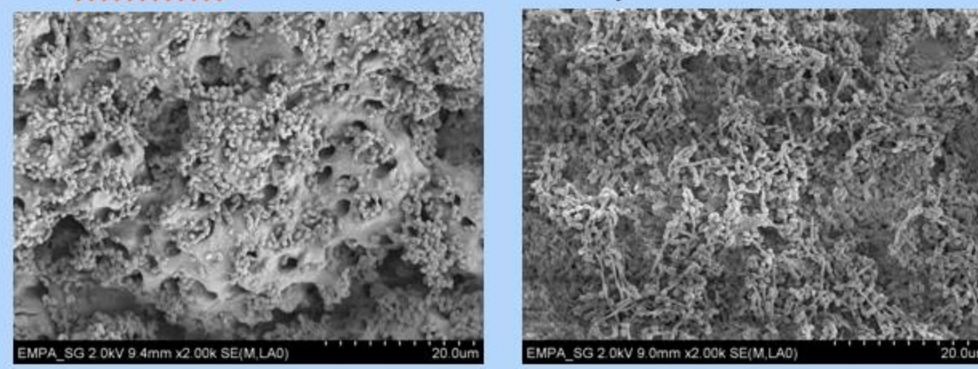
Single- & multi-species biofilm

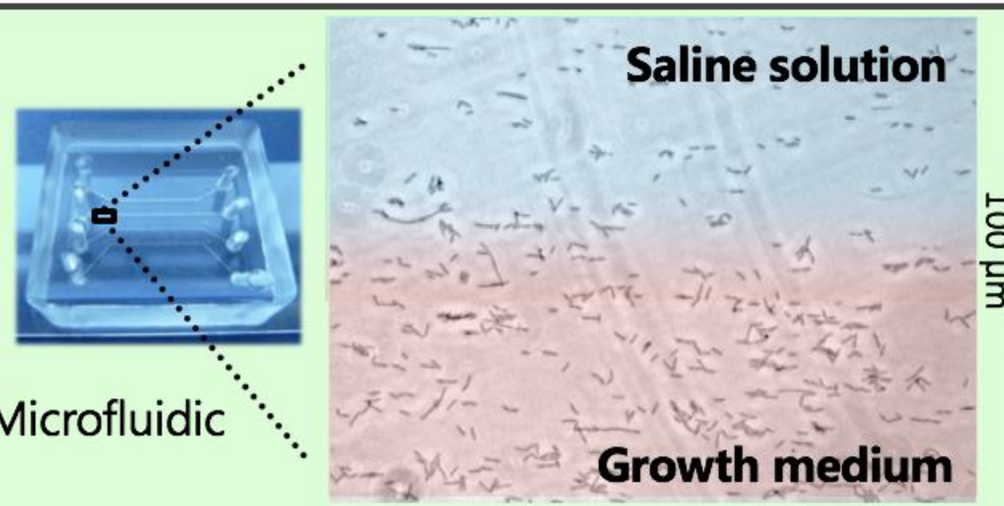
Devices for in situ studies

Biofilm formation and quantification



E. faecalis biofilm | 5-species biofilm





Microfluidic

Different physiological environment

Major need

Understanding the limitations of in vitro studies -> developing predictive assays


Thank you
EMPA_SG 2.0kV 9.9mm x5.00k SE(M,LA0)
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