

- **Faculty of Technology and Metallurgy, University of Belgrade**
- **Biomedical engineering laboratory**
- **Head:** Prof. Dr. Bojana Obradović
- **Participants:** 3 postdoctoral researchers, 3 PhD students
- **Research topics:** biomimetic bioreactors, bioactive composite scaffolds for skeletal tissue engineering, multifunctional wound dressings
- **Research expertise:** bioreactor design and operation, nanocomposite biomaterials, biomaterial evaluation under biomimetic conditions
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## Bioreactor with dynamic compression



## Perfusion bioreactors



hydrodynamic shear stresses

## Bioreactor with hydrostatic pressures



pressure: up to 50 bar  
continuous perfusion

dynamic compression:  
337.5  $\mu\text{m/s}$ , 0.1-1 Hz, 5-10 % strain  
continuous perfusion: 10 – 500  $\mu\text{m/s}$

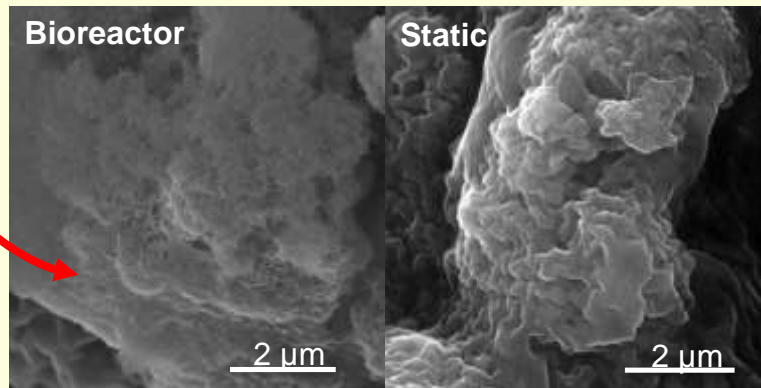
Petrovic, et al., *Chem. Ind. Chem. Eng.*, 2009  
Stojkovska, et al., *J Mater Sci: Mater Med.*, 2010  
Stojkovska et al., *Hem. Ind.*, 2020

- Scaffolds with hydroxyapatite (HAp) precursors:
  - polymer hydrogels (alginate, poly(vinyl alcohol), gellan gum (GG))
  - bioactive nanoparticles ( $\beta$ -tricalcium phosphate ( $\beta$ -TCP) and bioactive-glass (BAG))

## Macroporous scaffolds with open and interconnected pores for bone tissue engineering



GG and BAG



continuous perfusion of simulated body fluid (SBF) significantly enhanced HAp formation in scaffolds

## Biphasic implants for osteochondral tissue engineering

bottom layer: GG and BAG  
upper layer: GG hydrogel

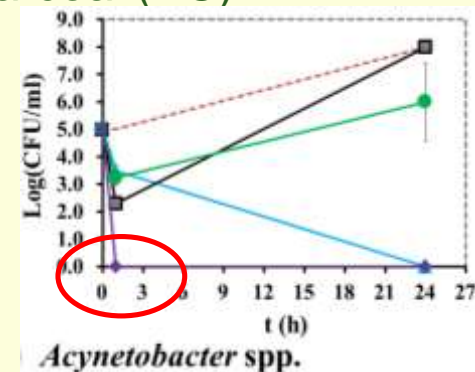
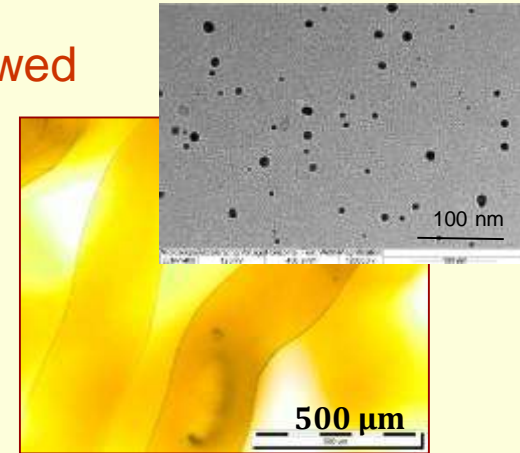


good integration

bioactivity and preserved mechanical stability under dynamic compression and perfusion

Zvicer, et al., Polymer Testing, 2019

- Ca-alginate hydrogels with silver nanoparticles (AgNPs) as antimicrobial agents and honey components
  - Chemical synthesis of AgNPs in honey solutions followed by production of Ag/honey/alginate hydrogels in different forms: disks, microbeads and microfibers
  - Released silver concentration of  $\sim 9 \mu\text{g/ml}$  induced strong antibacterial activities against standard and multiresistant hospital strains (*A. baumannii* and *Pseudomonas aeruginosa*)
- Ca- and Zn-alginate hydrogels with immobilized activated charcoal (AC) particles with adsorbed povidone iodine (PVP-I)
  - Release AC particles without PVP-I desorption
  - Strong bactericidal effects of both composites
  - Stronger antibacterial activity of Zn-composites could be related to the additional release of Zn ions

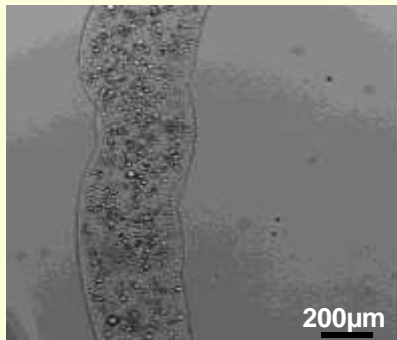


Stojkovska, et al., Appl Microbiol Biotechnol, 2019 Osmokrovic, et al., Carbohydr. Polym., 2018, Osmokrovic, et al., Hem. Ind., 2019

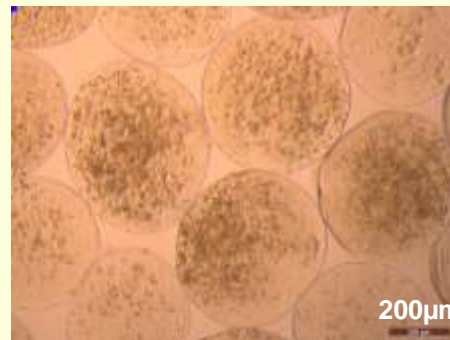
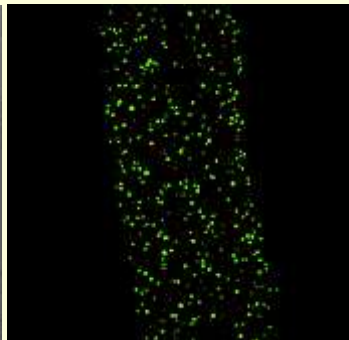


- 3D tumor model system based on alginate hydrogels with immobilized different cancer cells followed by cultivation in perfusion bioreactors

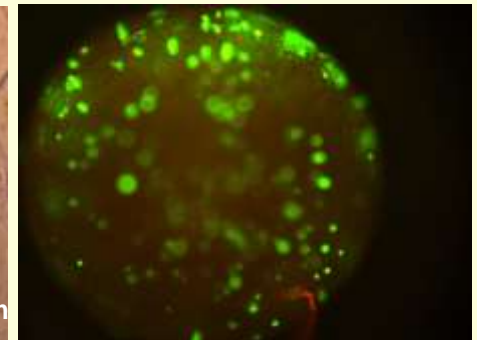
Alginate hydrogels with immobilized cells



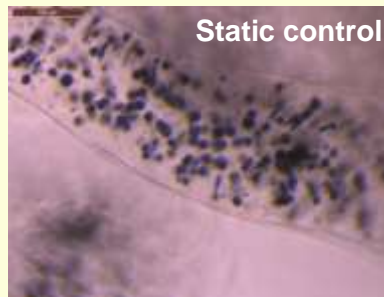
glioblastoma brain tumor (U87 cells)



embryonal carcinoma NT2/D1 cells



- After short term cultivation in perfusion bioreactors under continuous flowrate immobilized cells stayed viable and metabolically active



Stojkovska, et al., *Hem. Ind.*, 2020

- **Laboratory for animal cell cultivation:** biohazard laminar hood, CO<sub>2</sub> incubators, microscopes, biomimetic bioreactors
- Biomimetic bioreactor systems (perfusion, with dynamic compression, with hydrostatic pressures) for biomaterial evaluation under controlled *in vivo*-like conditions (e.g. cytotoxicity studies on animal cells, biodegradation, release kinetics of active substances)

## Expertise

- Design, development and scale-up of novel bioreactors
- Immobilization of active substances and cells in hydrogels and development of controlled release systems
- Consulting on 3D cell and tissue cultures
- Mathematical modeling



- Evaluation of novel biomaterials in cultures of human cells in a biomimetic environment
- Investigation of antibacterial properties of the developed biomaterials against a broad spectrum of standard bacterial strains, as well as multiresistant hospital strains
- Biomaterial market analysis including a detailed study of global and regional markets, competitive analysis, assessment of potentials of new products
- Identification of business partners and business negotiation strategies

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