COMSOL CONFERENCE ROTTERDAM2013

Modeling drug release from materials based on electrospun nanofibers

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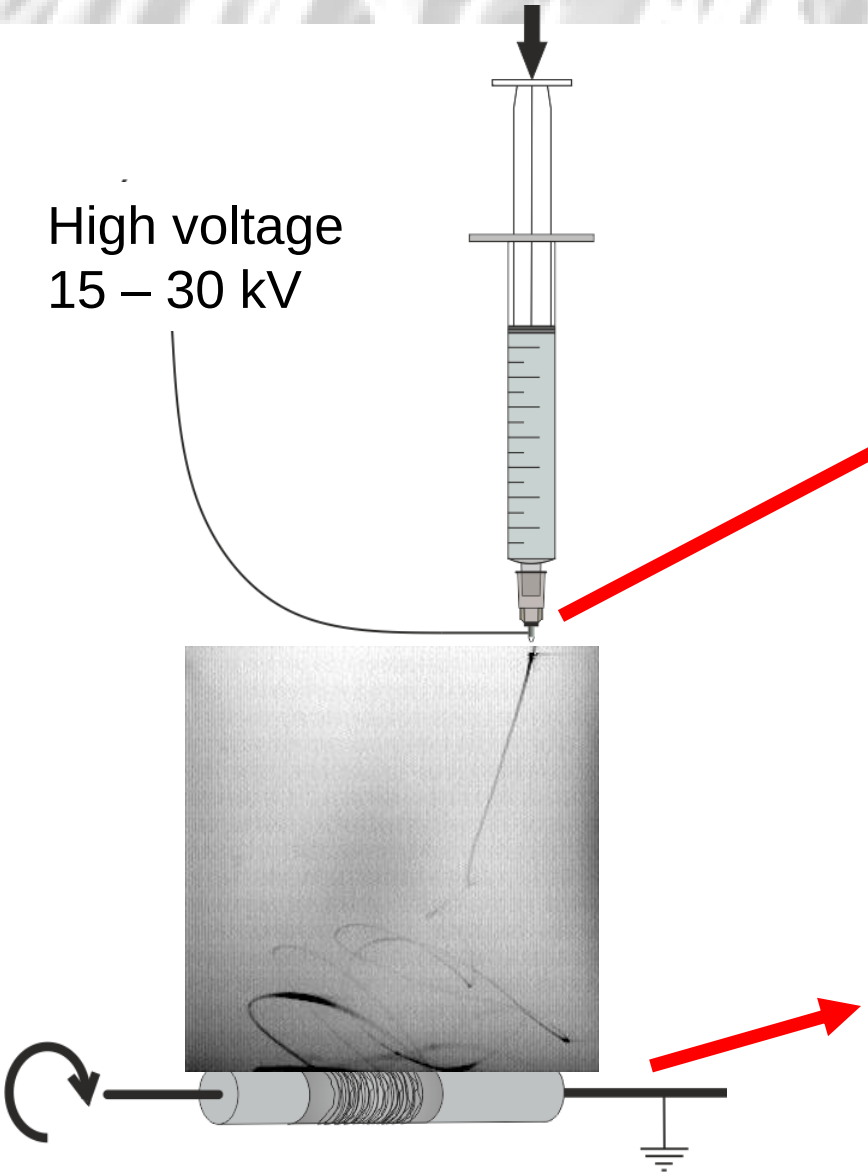
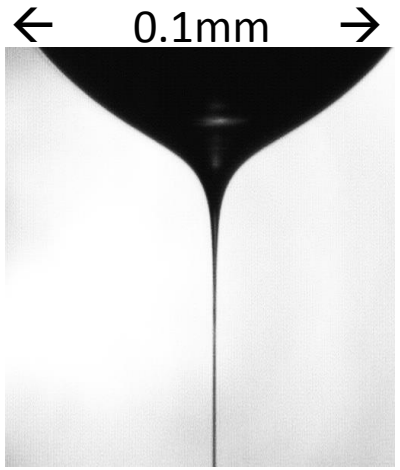
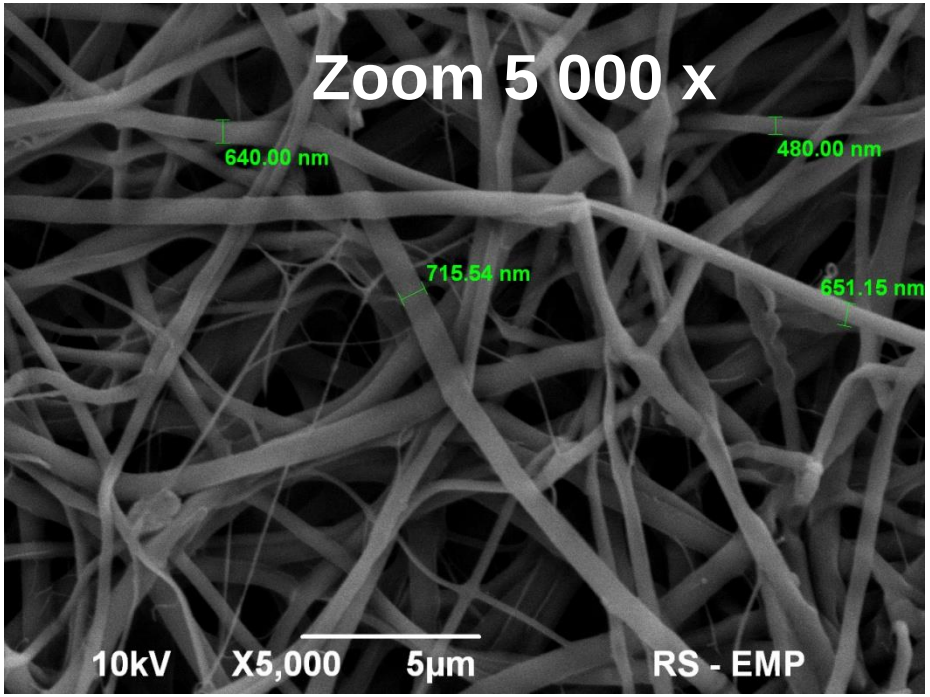
Electrospinning





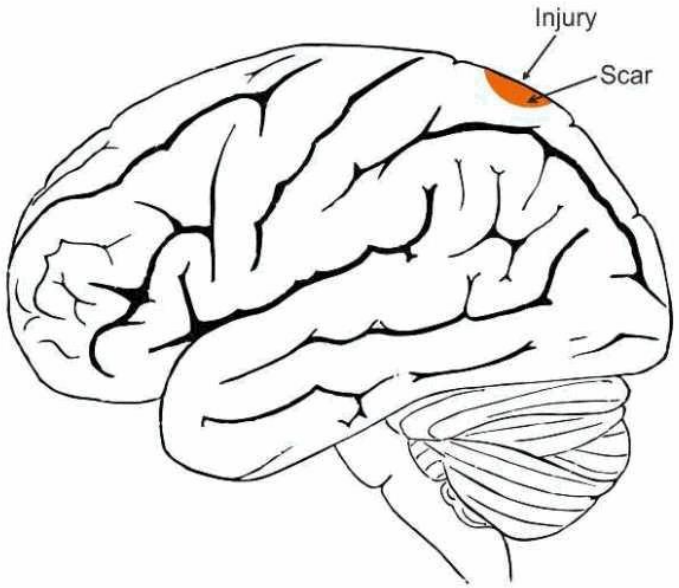


Motivation

The lack of effective neuroprotective products for postoperative treatment of brain injures that lead to scar tissue formation and in the worst case to death of the patient.

Traumatic Brain Injury:

In EU every year 30-40/10 000 people suffer extensive damage from brain injury and only 45% back to normal life.



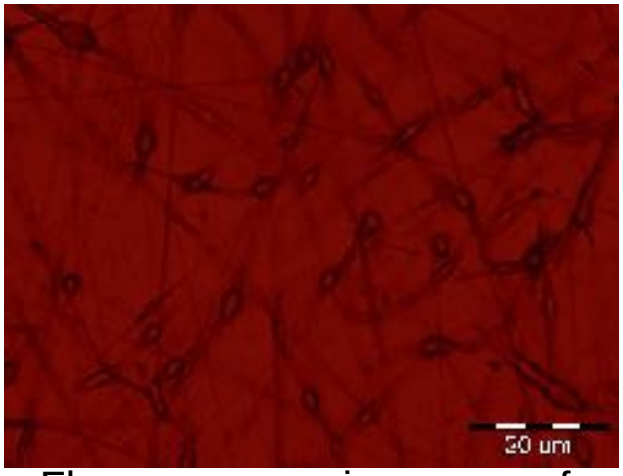
Optimal release profile

Characteristics of the optimal implant:

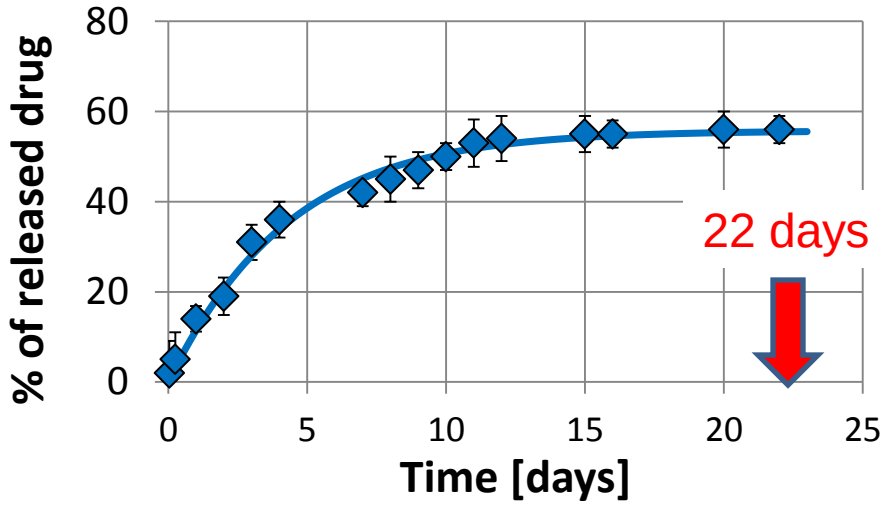
- Maintance of drug levels in the desired therapeutic window
- Time of drug release from the implant - about 14 days

How to obtain optimal release profile:

- Selecting desired drug-polymer configuration
- Selecting optimal material structure (porosity, multilayer)
- Verifying release profiles for „analog system” and targeted one
- Modeling, verifying and validating models

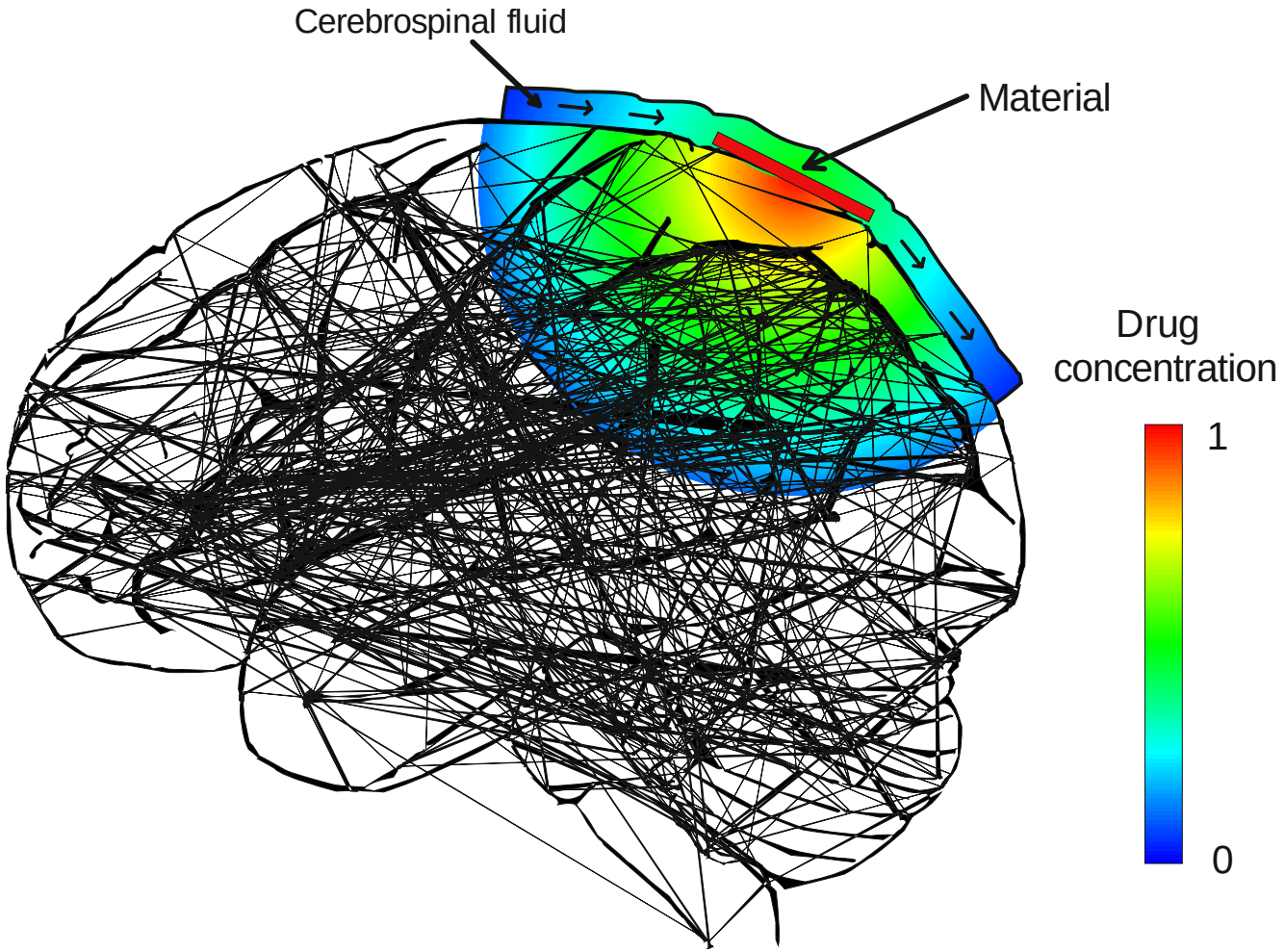


Fluorescence microscopy of encapsulated Rhodamine B



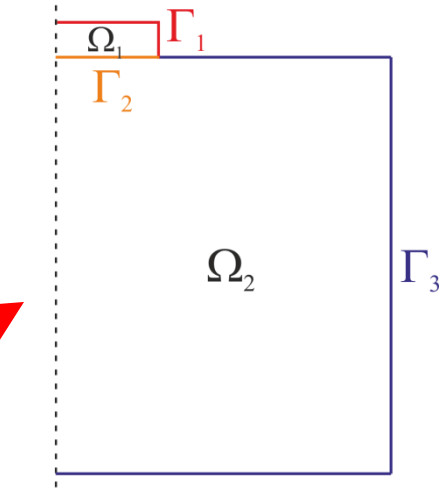
Release profile of α-tocopherol from PLCL fibers

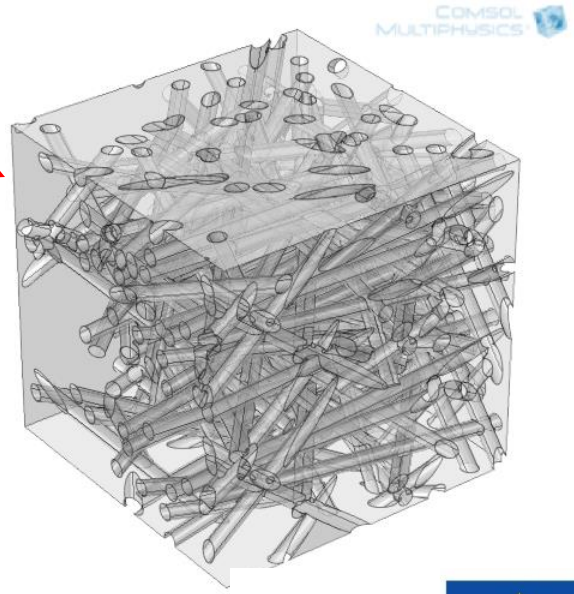
Fluid systems



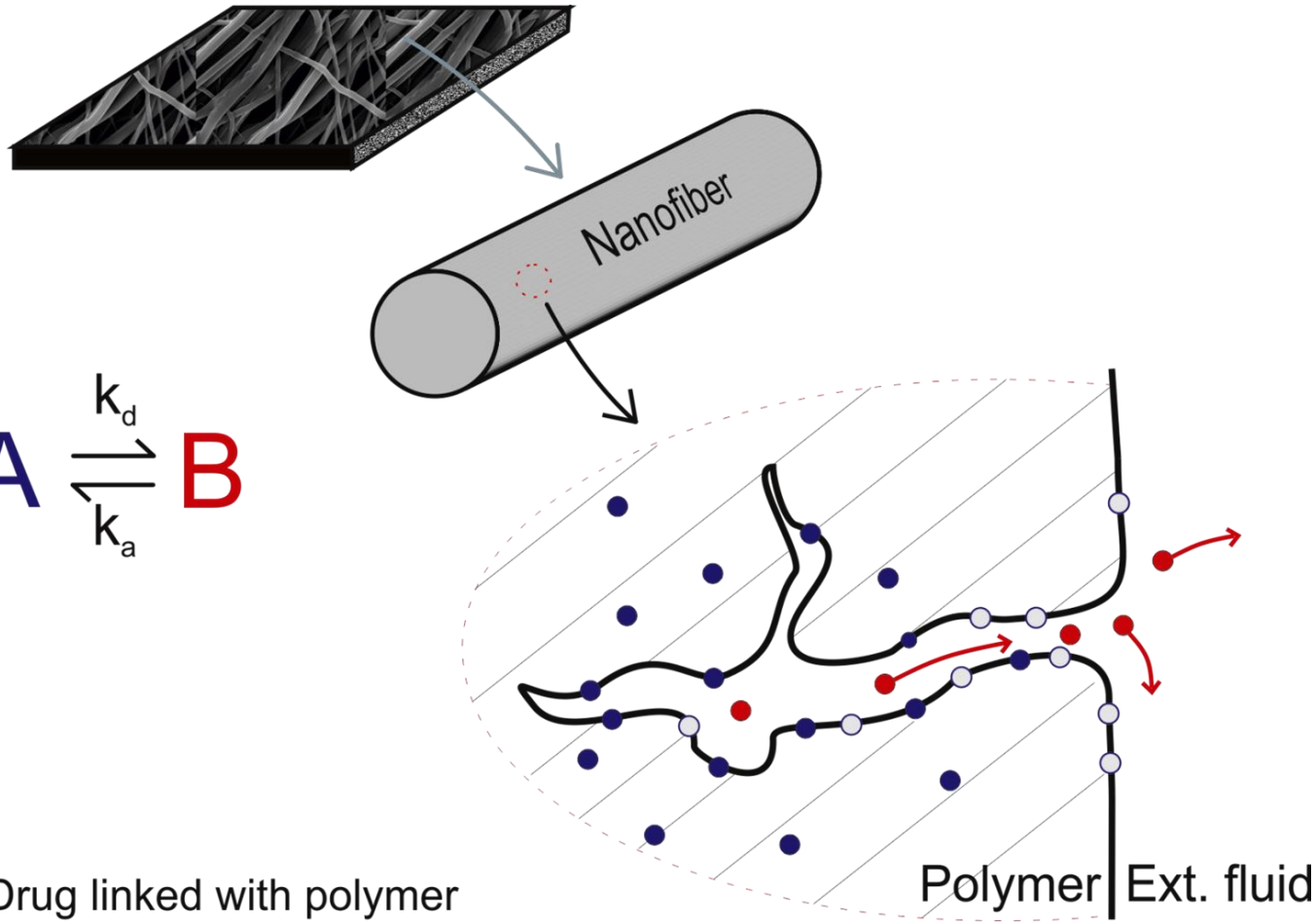
2D – diffusion in the brain
3D - Representative Unit Cell of the material

Target system	Analog system
Brain tissue $D_{tracer} = 1,3 \cdot 10^{-11}$ m²/s $k_{elim} = 0,014$ 1/s	PVA – borax, hydrogel $D_{rodB} = 6,3 \cdot 10^{-11}$ m²/s
Cerebrospinal fluid Volume exchange ≈ 3 * V /day V ≈ 100ml	PBS solution (buffer pH=7,4) Perfect mixing conditions T = 37°C





Desorption – diffusion model in porous material



Desorption – diffusion model in porous material

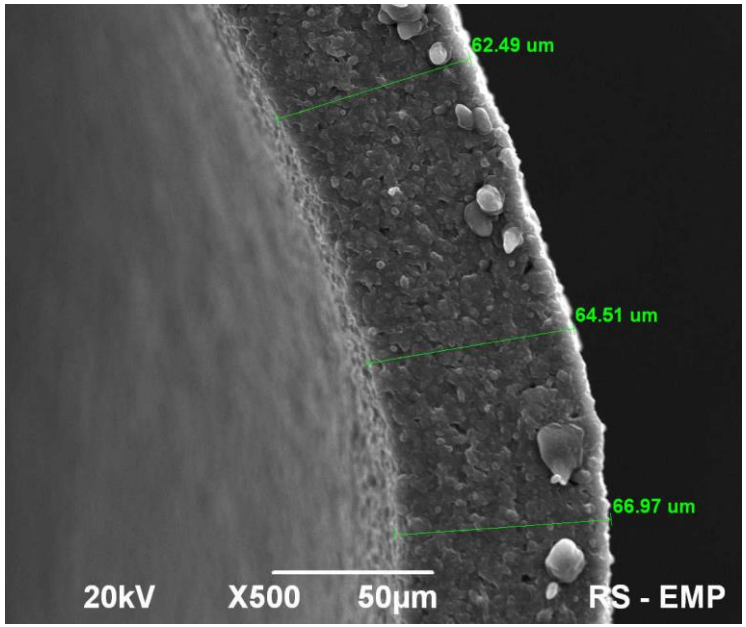
$$\frac{\partial c_A}{\partial t} = k_a \left(c_A^{\max} - c_A\right) c_B - k_d \; c_A$$

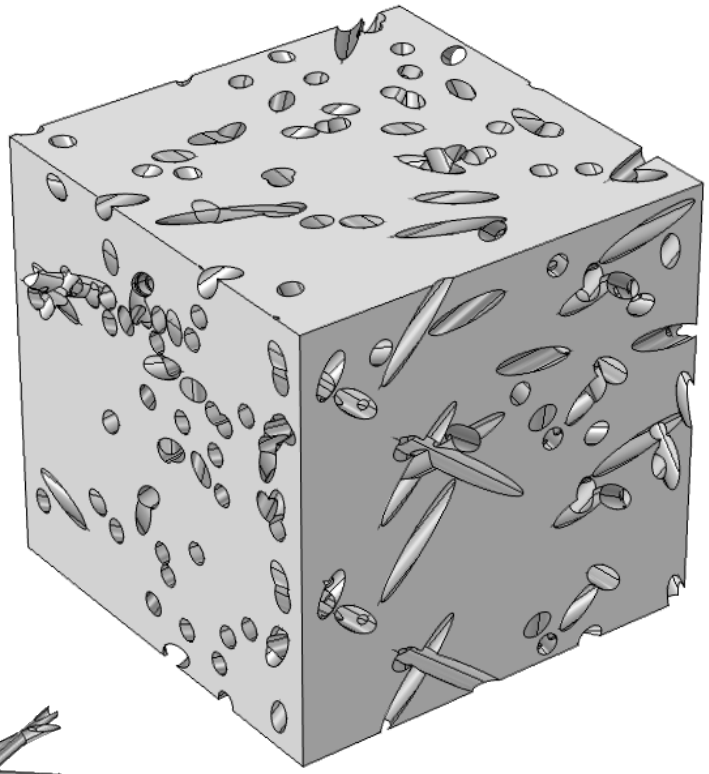
2D $$\varepsilon \frac{\partial c_B}{\partial t} = \varepsilon \nabla \cdot \left(D_{Beff} \nabla c_B\right) - \left(1-\varepsilon\right) \rho_p \frac{\partial c_A}{\partial t}$$

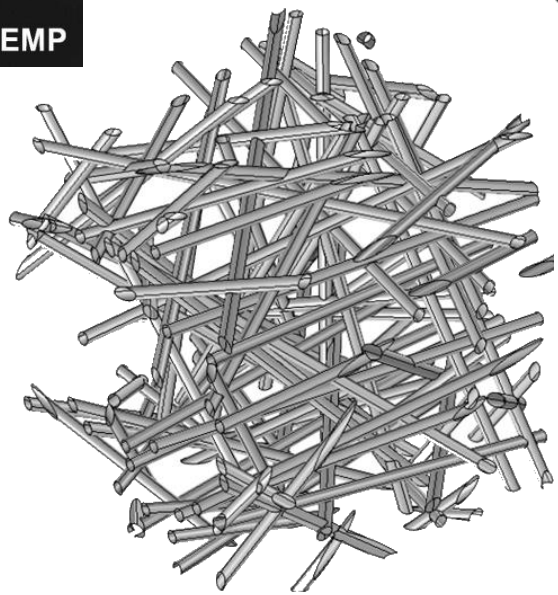
3D $$\frac{\partial c_B}{\partial t} = \nabla \cdot \left(D_B \nabla c_B\right) - \rho_p \frac{\partial c_A}{\partial t}$$

C_A – drug concentration at the nanofiber surface [kg/ kg of the material]
C^{max}_A – maximal drug concentration at the nanofiber surface [kg/ kg materiału]
C_B – drug concentration in the pores of the material[kg/m^3]
ε – porosity of the material[-]
D_B – diffusion coefficient in the fluid [m^2/s]
ρ_p – polymer specific density[kg/m^3]
k_a, k_d – adsorption and desorption constant

Numerical simulations of drug release in RUC

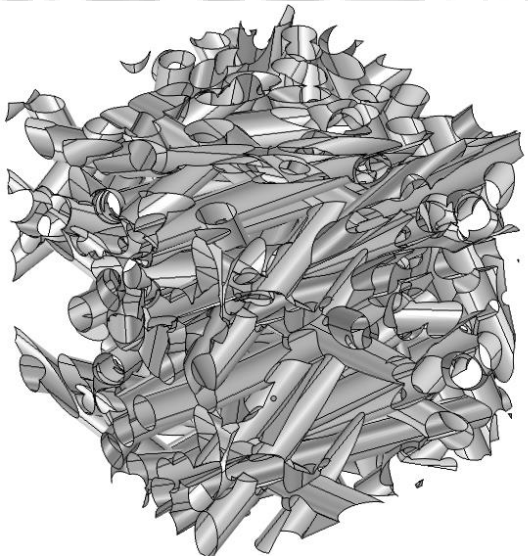


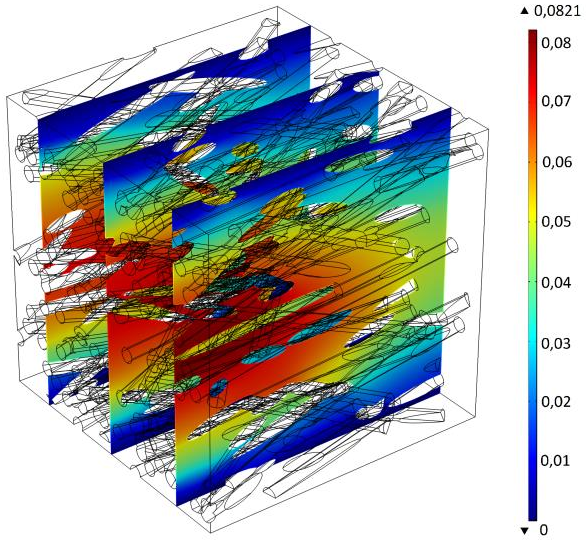




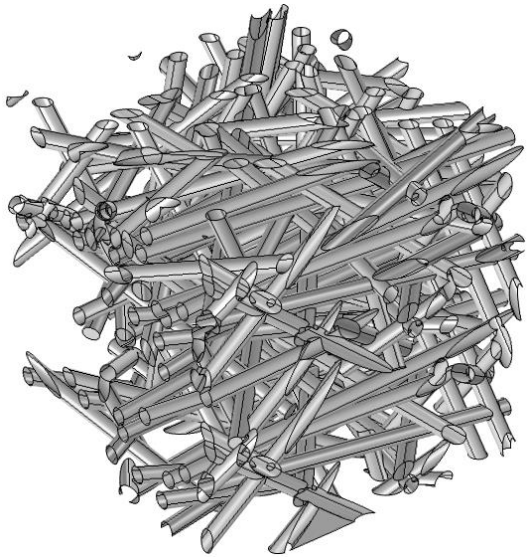
Numerical results for materials with different porosity

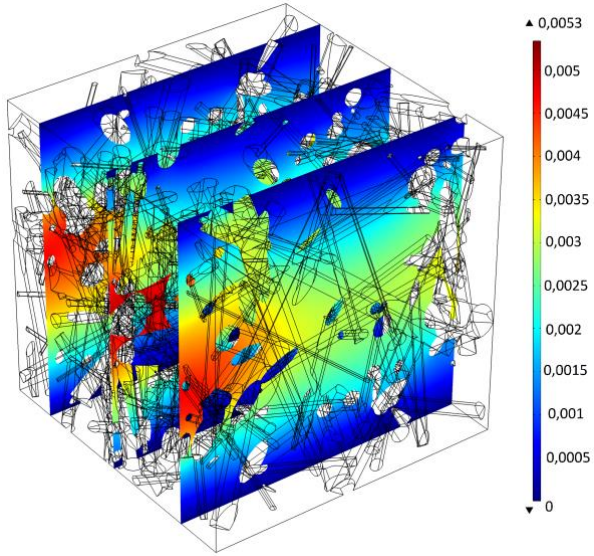
ε = 0.4



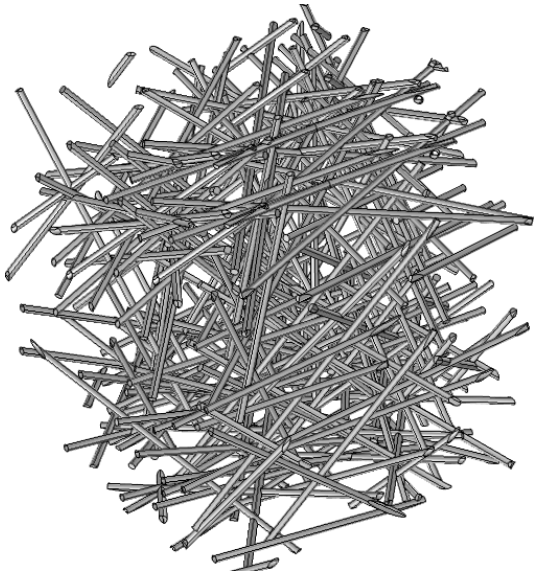


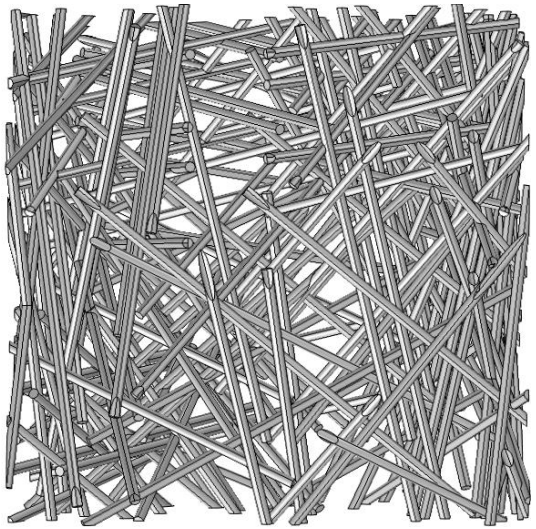
ε = 0.78

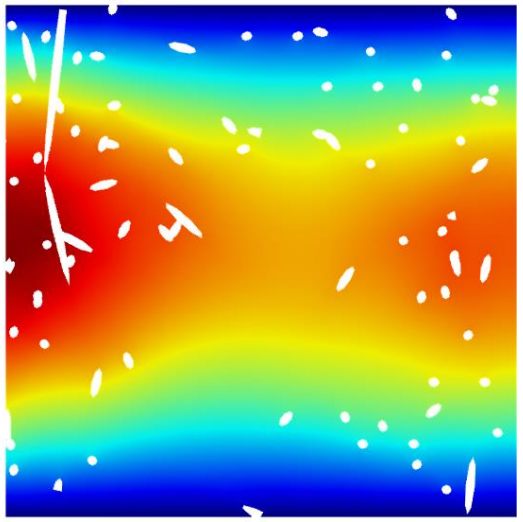


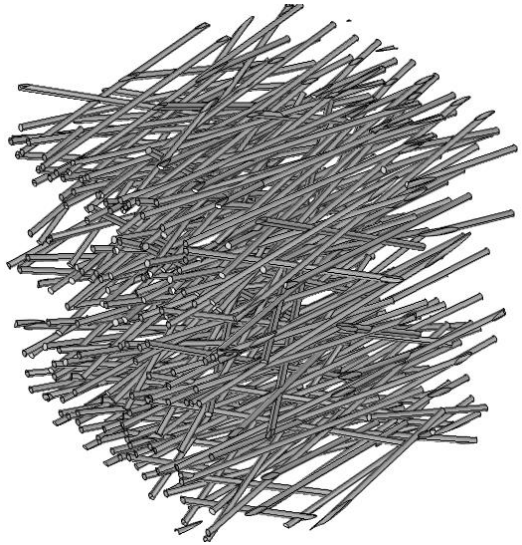


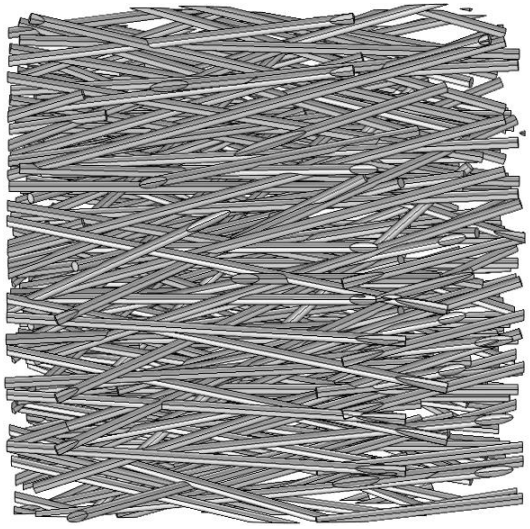
Numerical results for materials with different fibers orientation

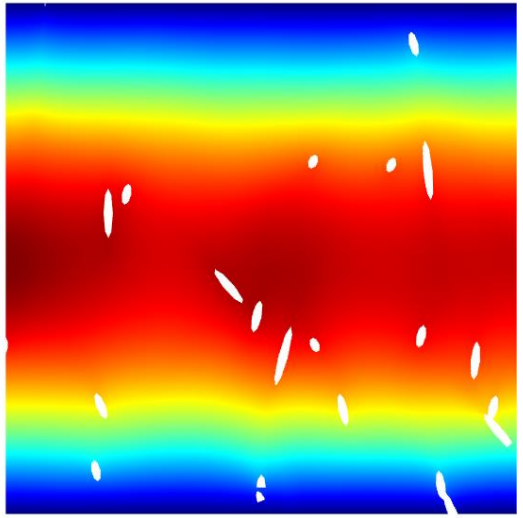




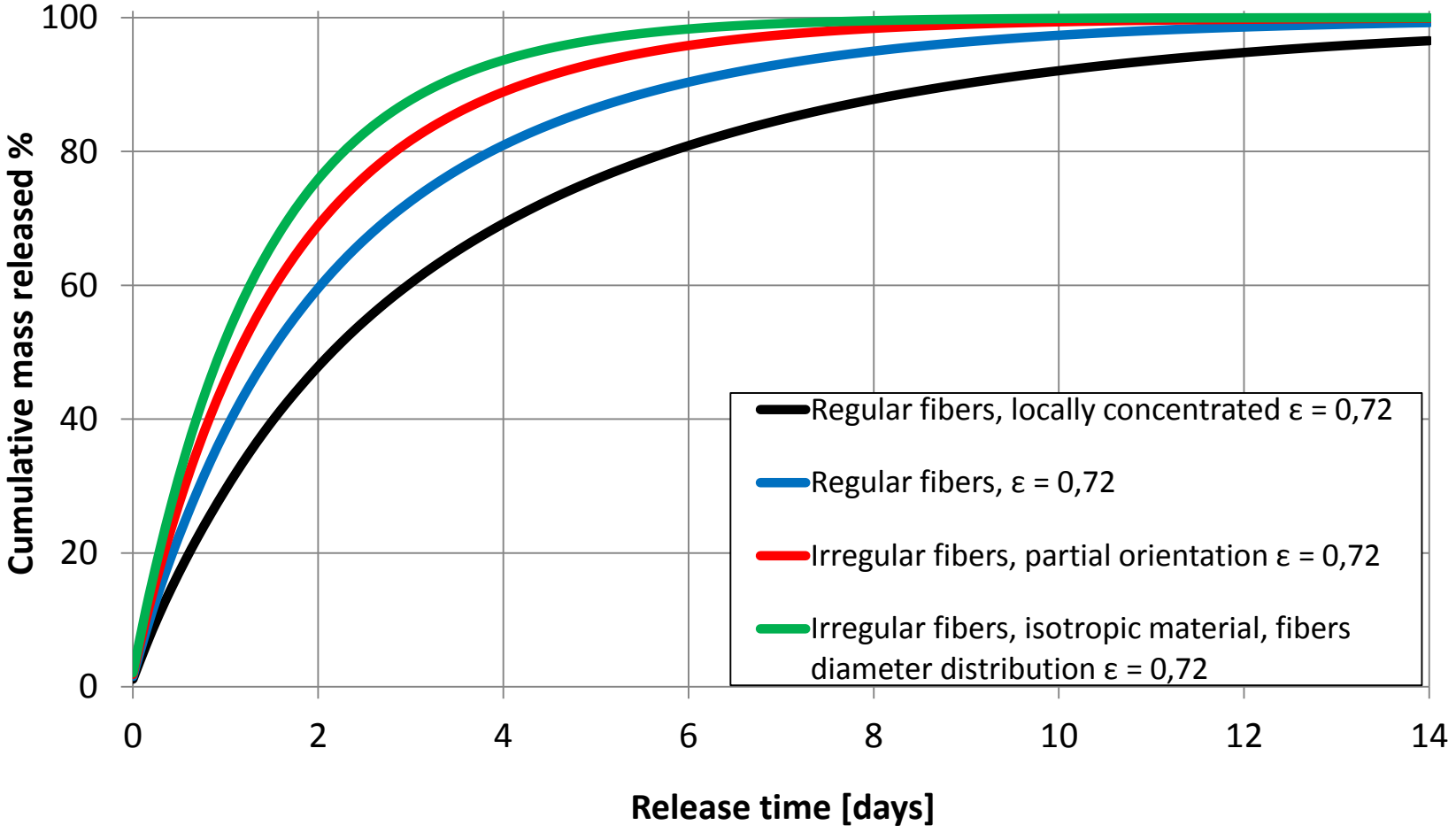




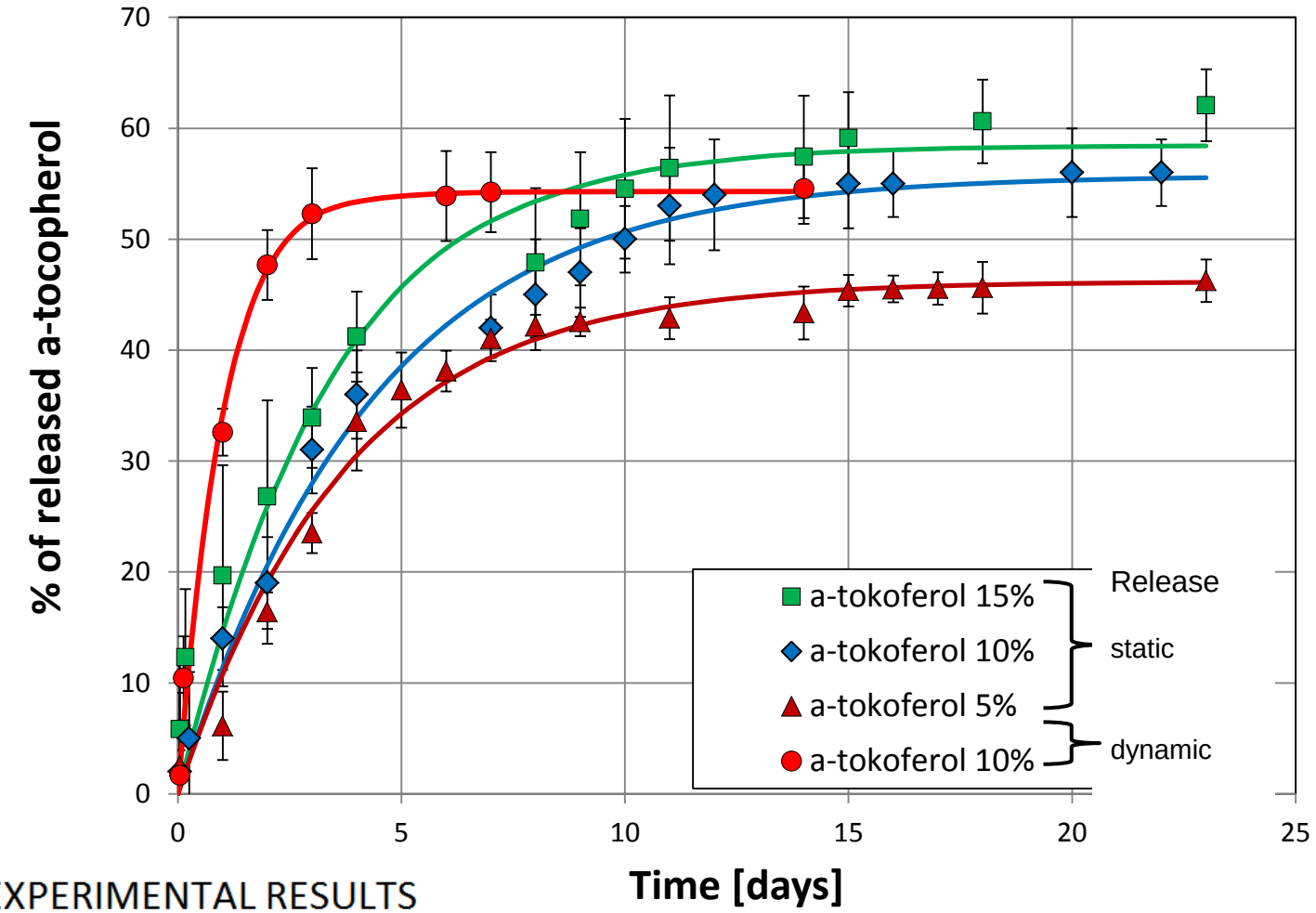




Numerical results for materials with different fibers arrangement



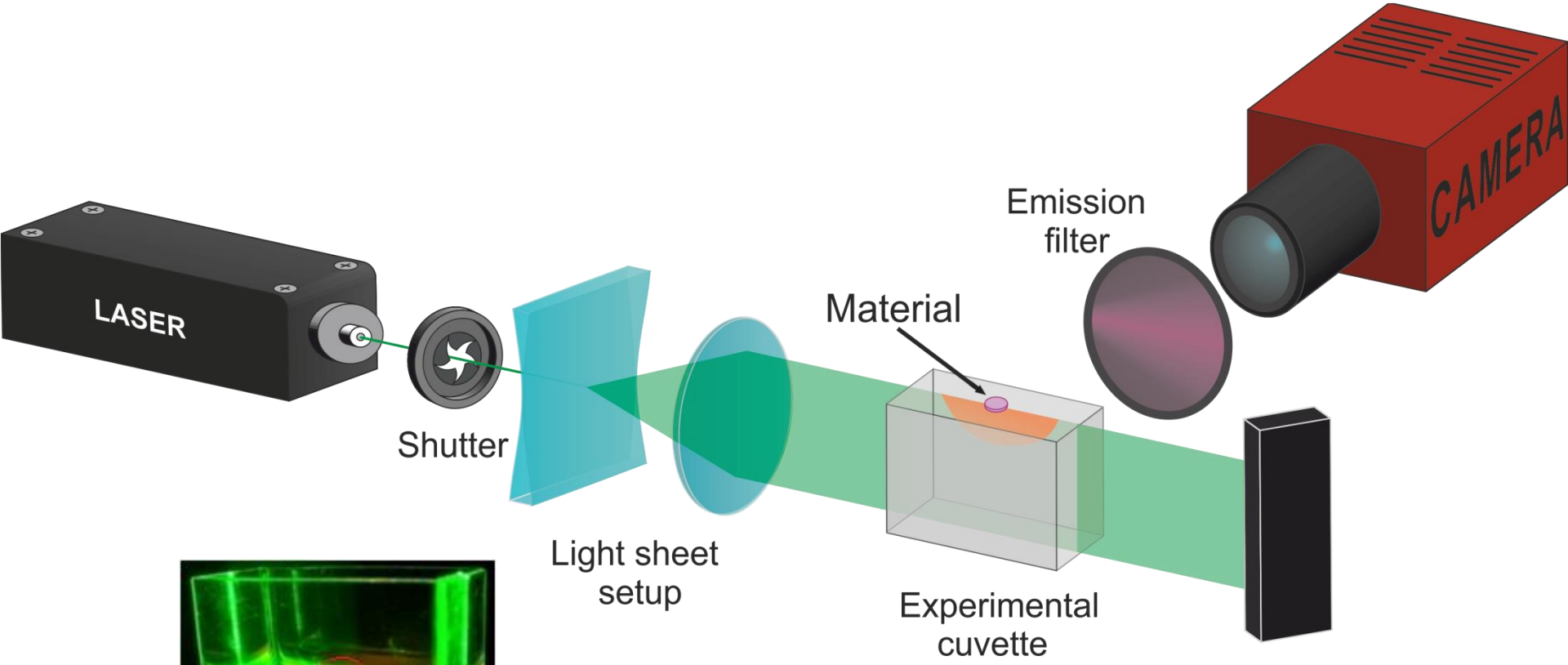
Experimental results of α-tocopherol release

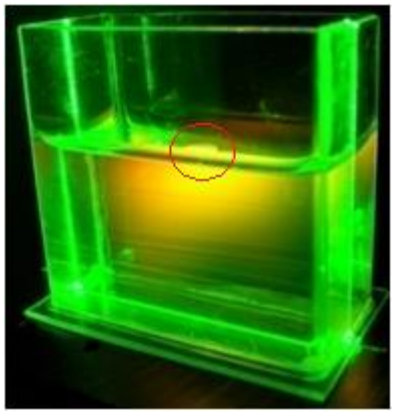


■ EXPERIMENTAL RESULTS

NUMERICAL RESULTS

Experiments with analog drug systems
Rhodamine release from nanofibrous mats



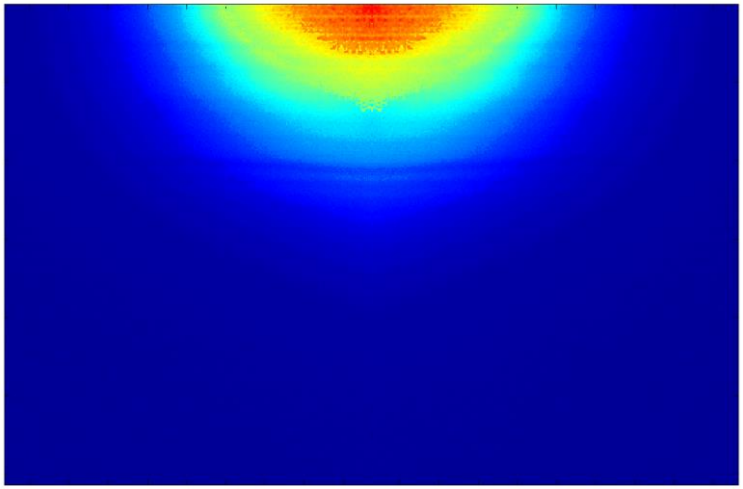


Cuvette with material on the top of the PVA hydrogel

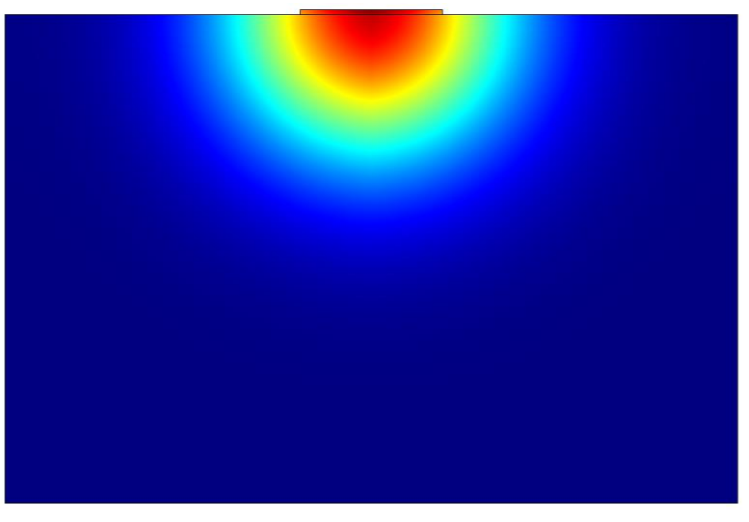
Samples dimension:
Radius = 2,5 mm
Thickness = 150 μm

Experiments with drug analog quantitative study

Optical measurement at the experimental setup



Simulation results from COMSOL Multiphysics



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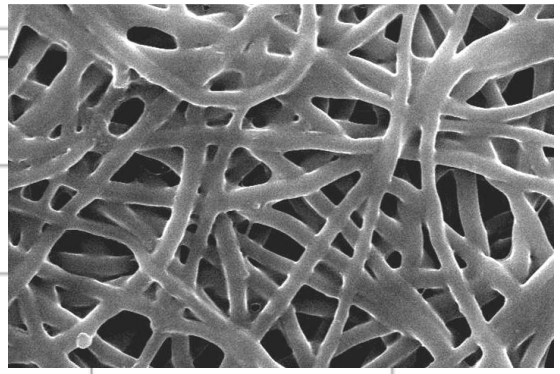
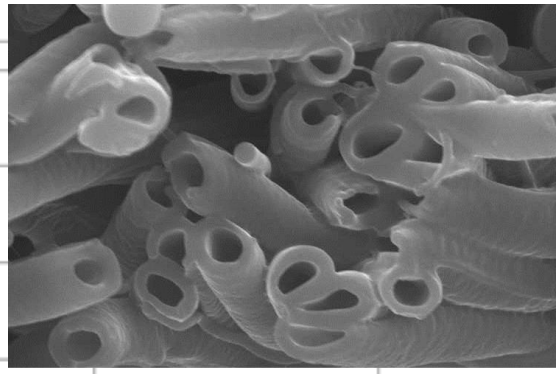
Rhodamine B release results in the hydrogel random nanofibers

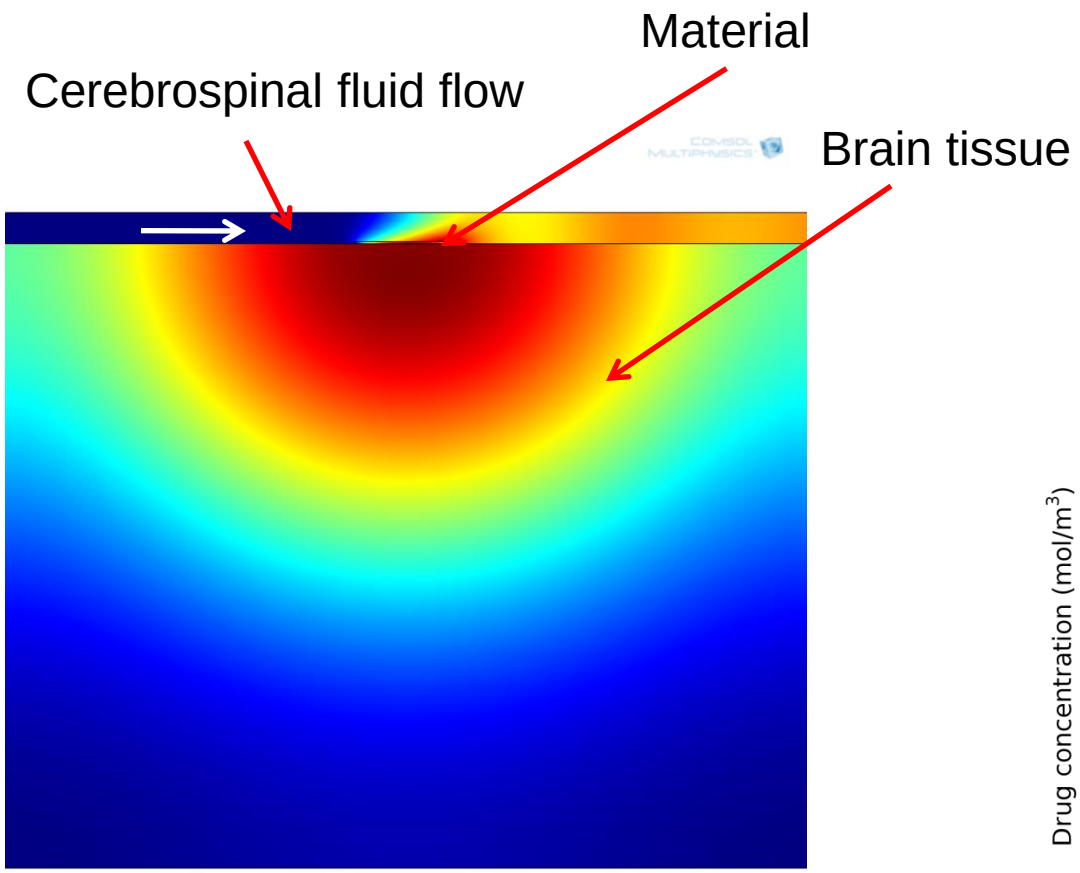


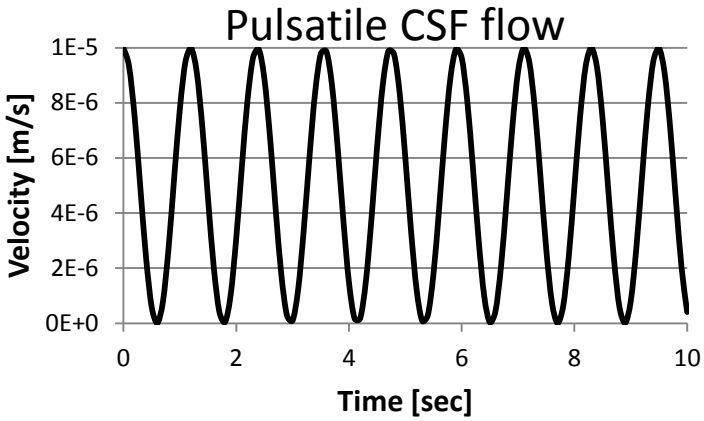
Diffusion coefficient **D** = 6,3 ·10^{-11} m^2/s
Desorption conts. $\mathbf{k_d}$ = 3,4 ·10^{-4} 1/s
Porosity **ε** = 0,69

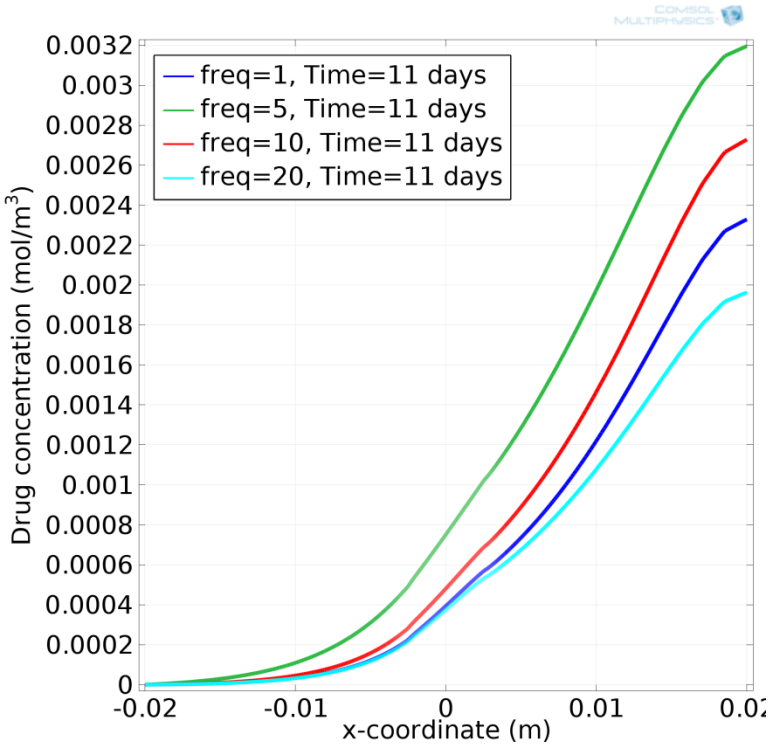
Rhodamine B release results in the hydrogel core-shell nanofibers



Numerical results of the release to CSF and brain tissue







Thank you!

Nanofibers application

Medicine:

- Protective intraoperative dressings
- The reconstruction of blood vessels, ureter and bladder
- Scaffolds for cell culturing
- Drug delivery systems

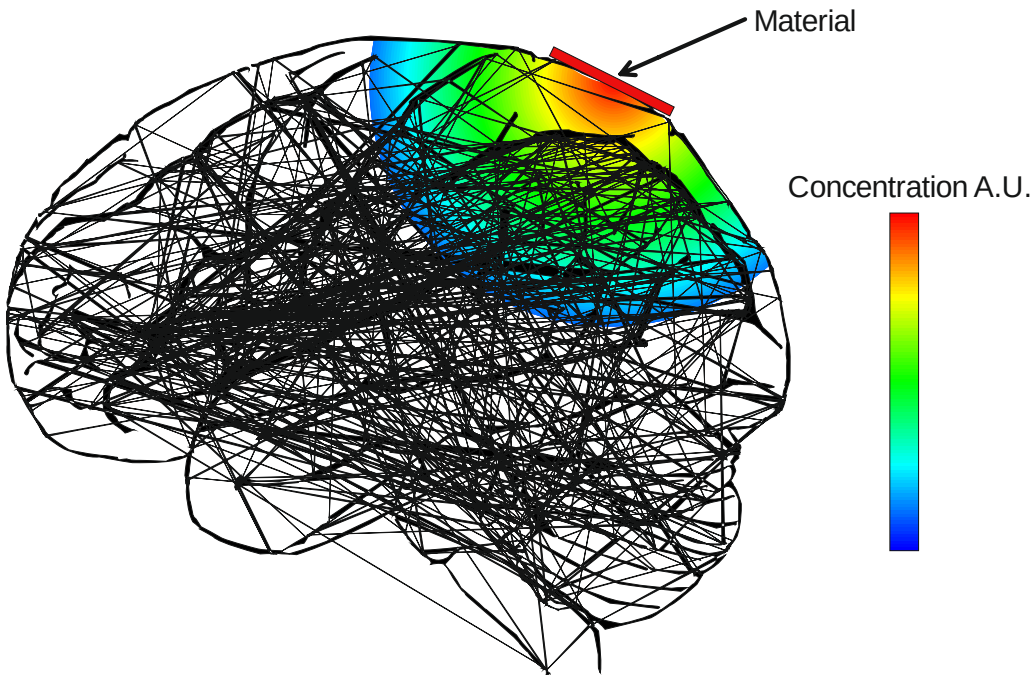
Industry and other:

- Textiles
- Filtration
- Catalyst
- Sensors

http://www.nanofibersolutions.com

Drugs used in nanofibers

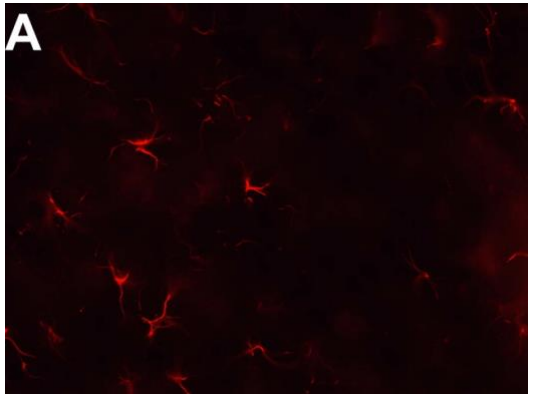
- Vitamin E – antioxidant
- NGF – nerve growth factor
- BDNF – brain derived neurotrophic factor specific for brain tissue



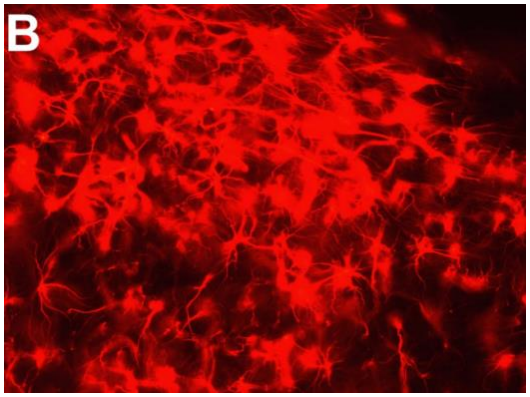
Drug and analog systems

Target system	Analog system
Lipophilic – solid nanofibers, core-shell	
α-tocopherol 430Da, r_H = 0,9nm	Rhodamine B 479Da, r_H = 0,9nm
Hydrophilic – core-shell, emulsion	
Sodium glutamate 169Da, r_H = 0,6nm	Methylene blue 320Da, r_H = 0,8nm
Nerve Growth Factor 13,4kDa, r_H = 2,8nm	Bovine Serum Albumin-FITC 66kDa, r_H = 4,8nm
Brain Derived Neurotrophic Factor 13,6kDa, r_H = 2,8nm	

Neuroprotection after brain injury nanostructure favorable tissue recovery

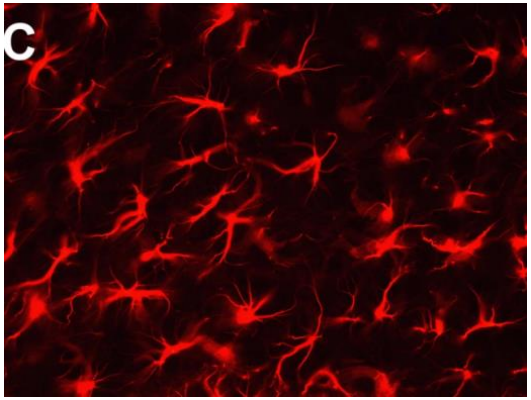


Control group
without injury and dressing

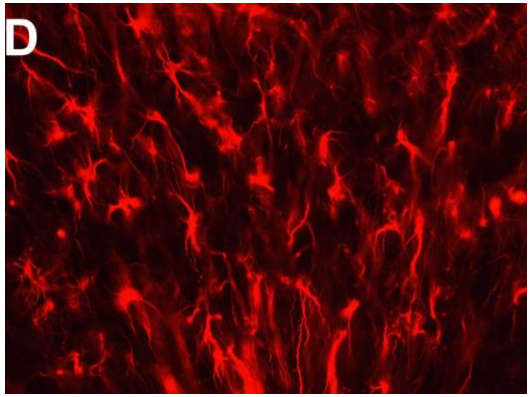


4 days after injury
without dressing

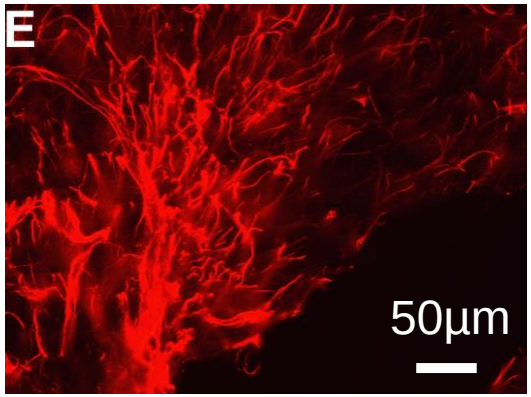
M. Frontczak-Baniewicz,
D. Sulejczak,
J. Andrychowski



4 days after injury
with dressing



14 days after injury
with dressing



30 days after injury
with dressing

Porosity and orientation of the fibers impact on diffusion

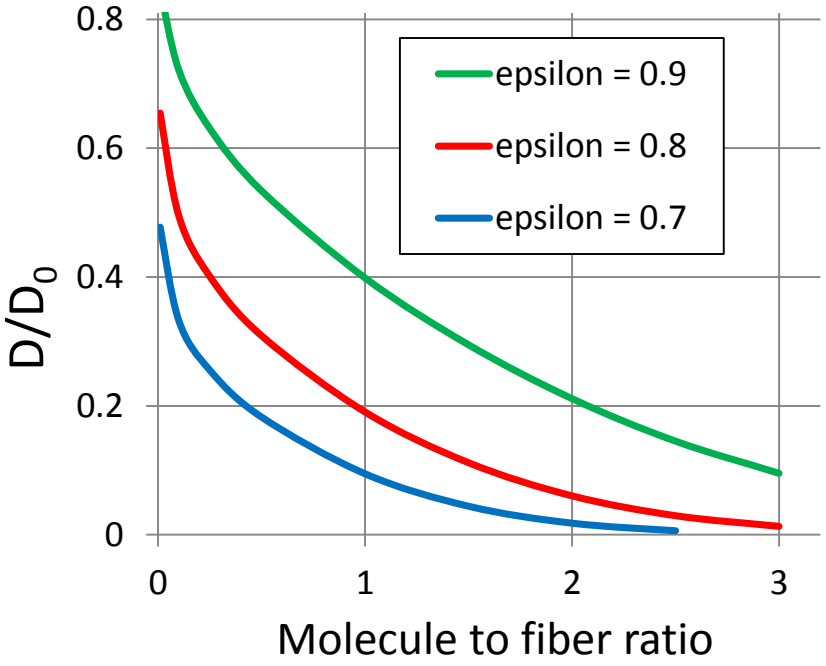
$$\frac{D}{D_0} = F \cdot S = e^{-a\phi^b} \cdot e^{-0{,}84 f^{1{,}09}}$$

$\frac{D}{D_0}$ – diffusion coefficients in porous material / diffusion coefficients in fluid

F – hydrodynamic interactions

S – steric factor

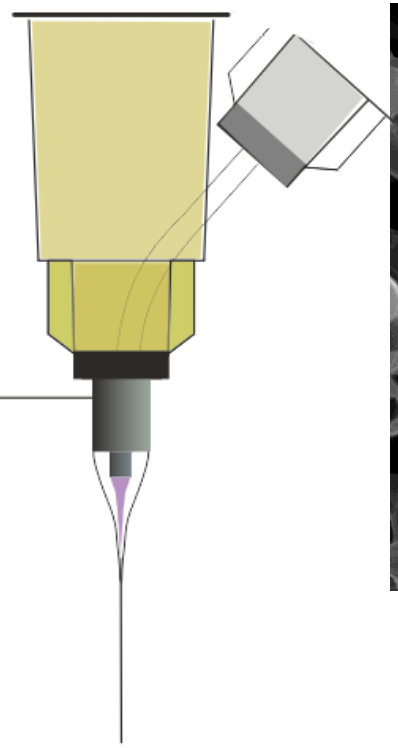
ε – porosity of the materials

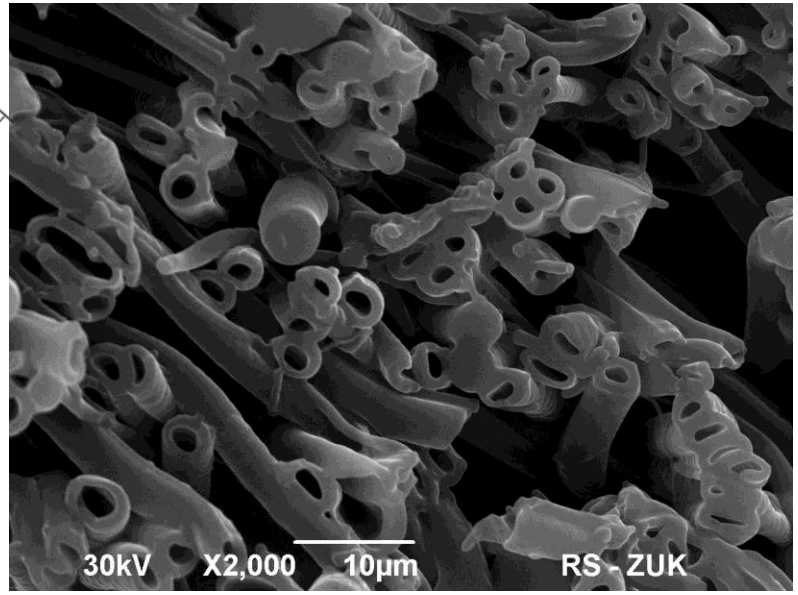


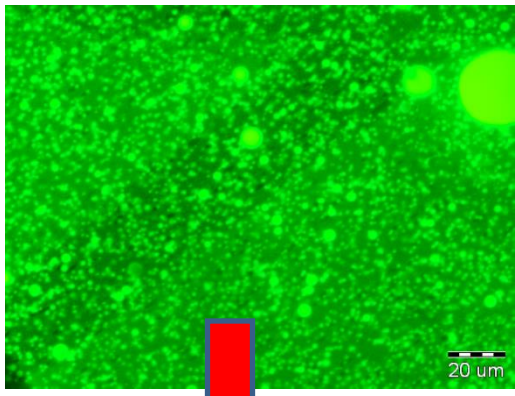
Clague and Phillips, *Phys. Fluids*, 1996

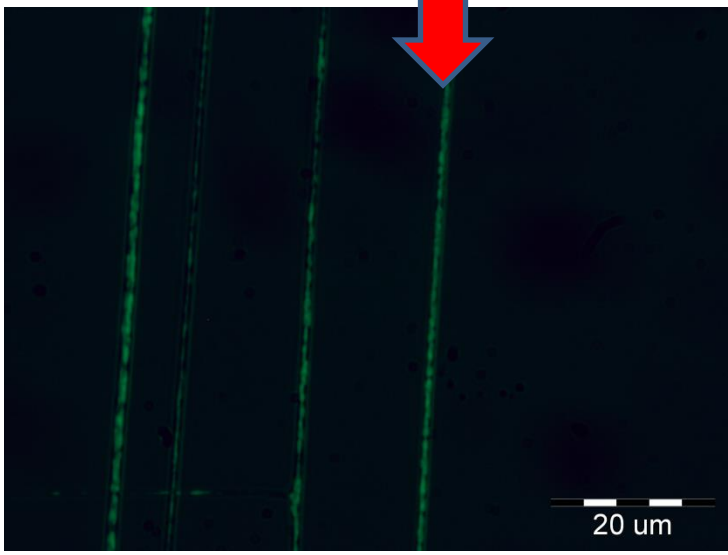
Drug encapsulation methods

- Solid fibers (lipophilic drugs)
- Emulsions (hydrophilic drugs)
- Core-shell (hydrophilic, lipophilic)



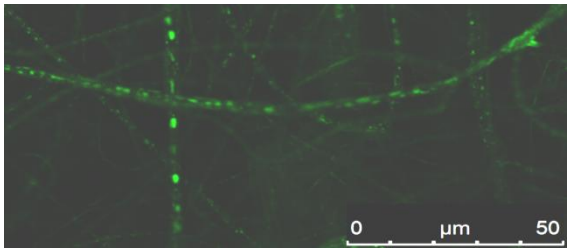




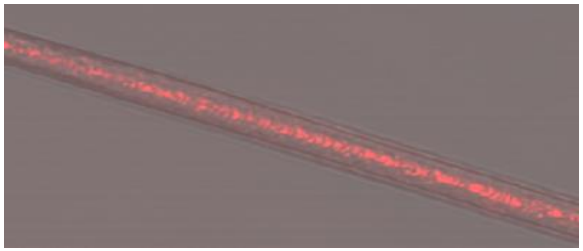


Nanofibers made by emulsion electrospinning

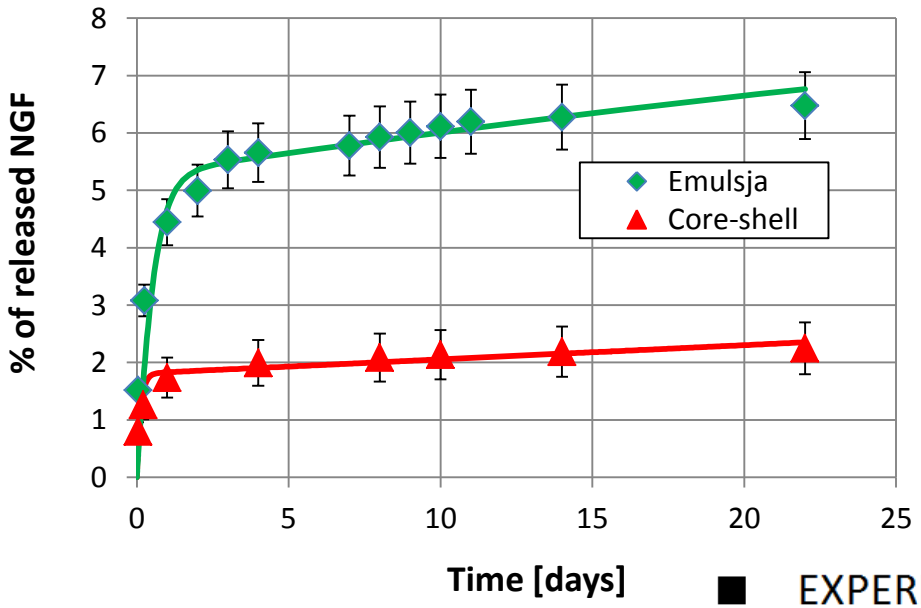
Experimental results of drugs release : NGF and BDNF

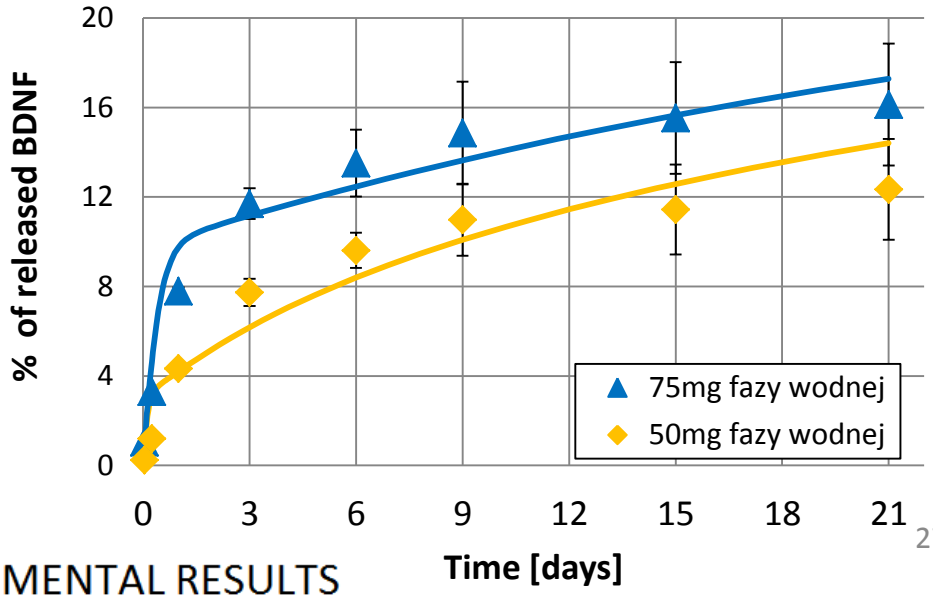


Comparison of NGF release for different type of electrospinning



Comparison of protein release for different amounts of the aqueous phase





■ EXPERIMENTAL RESULTS

NUMERICAL RESULTS