Analyzing Drug Delivery and Osteoblast Growth on a Porous Scaffold in a Perfusion Bioreactor

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UCLA Engineering

VA DESERT PACIFIC
HEALTHCARE NETWORK

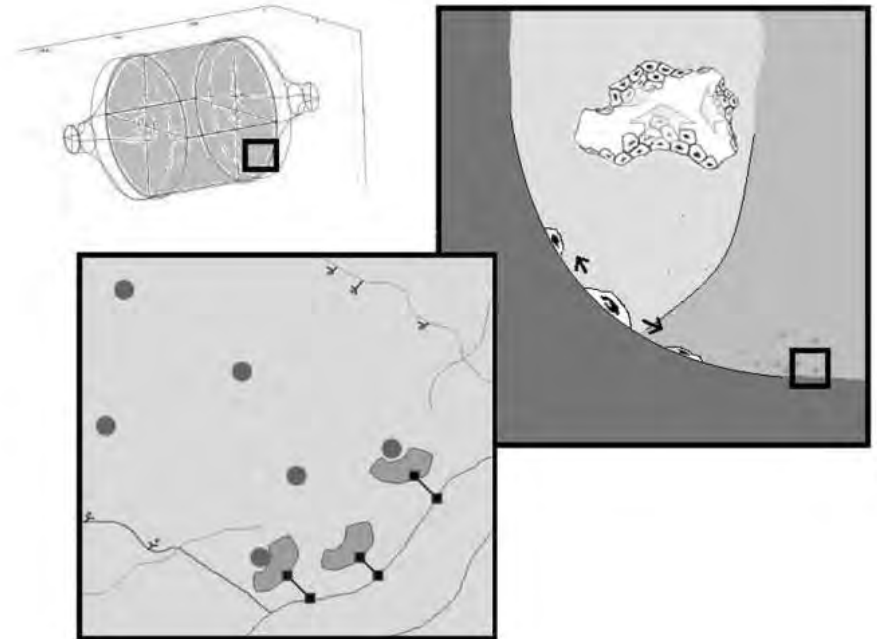Implantable Collagen sponges as Drug Delivery Scaffolds in Spinal Surgery

Balance between bone growth and adverse diffusion effects

Porous sponge as scaffold for Osteoblast growth

Fluid shear mediates biological effects

Model release of scaffold-bound growth factor

Model convection and diffusion

Coupled Governing Equations

$$\nabla \cdot \left[\frac{\eta}{\varepsilon} (\nabla \mathbf{u} + (\nabla \mathbf{u})^T) + p\mathbf{I} \right] = \frac{\eta}{\kappa} \mathbf{u}$$

$$\varepsilon(t) = \varepsilon_o \left(1 - \frac{m e^{\mu t}}{\rho_c V_s} \right) \qquad \frac{\partial c_i}{\partial t} + \nabla \cdot \left(-D_{i,sbd} \nabla c_i + \xi c_i \mathbf{u} \right) = R_i$$
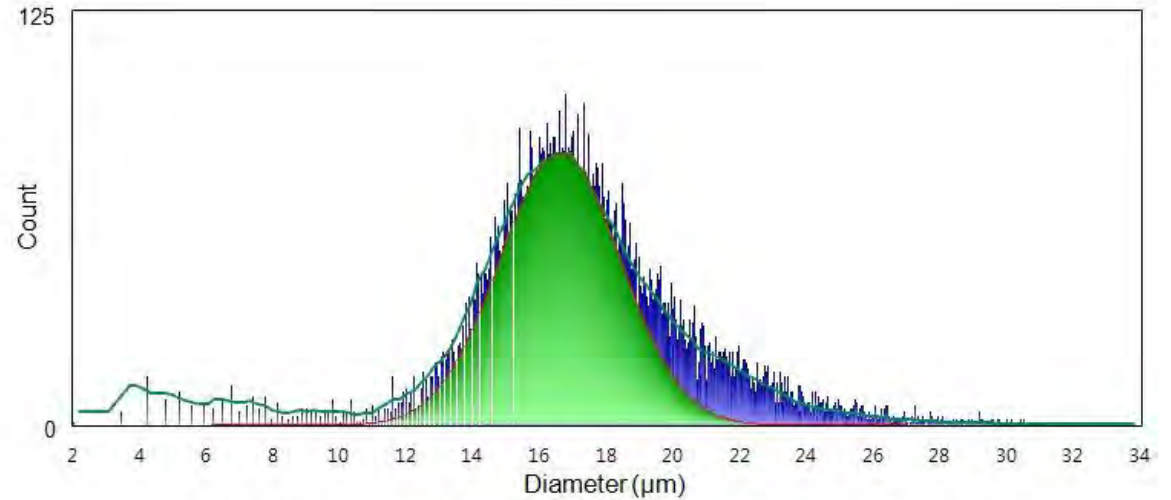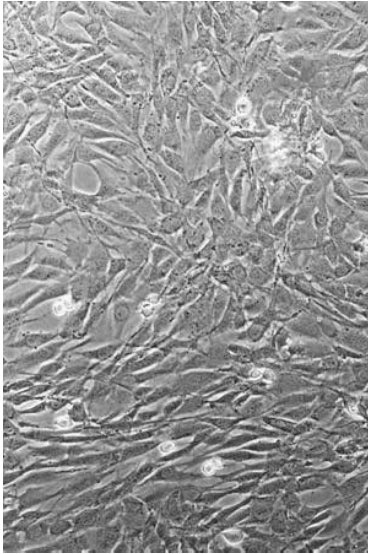
Rate Equations

$$\frac{dC_{BMP-2,free}}{dt} = R_1 = k_d C_{BMP-2,bound} - k_a C_{BMP-2,free} (C_o - C_{BMP-2,bound})$$

$$\frac{dC_{BMP-2,bound}}{dt} = R_2 = k_a C_{BMP-2,free} (C_o - C_{BMP-2,bound}) - k_d C_{BMP-2,bound}$$

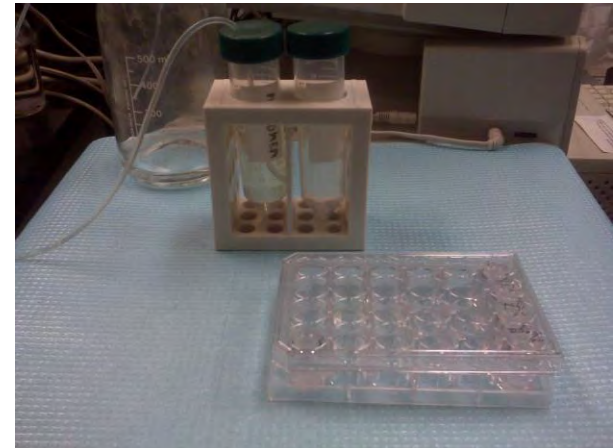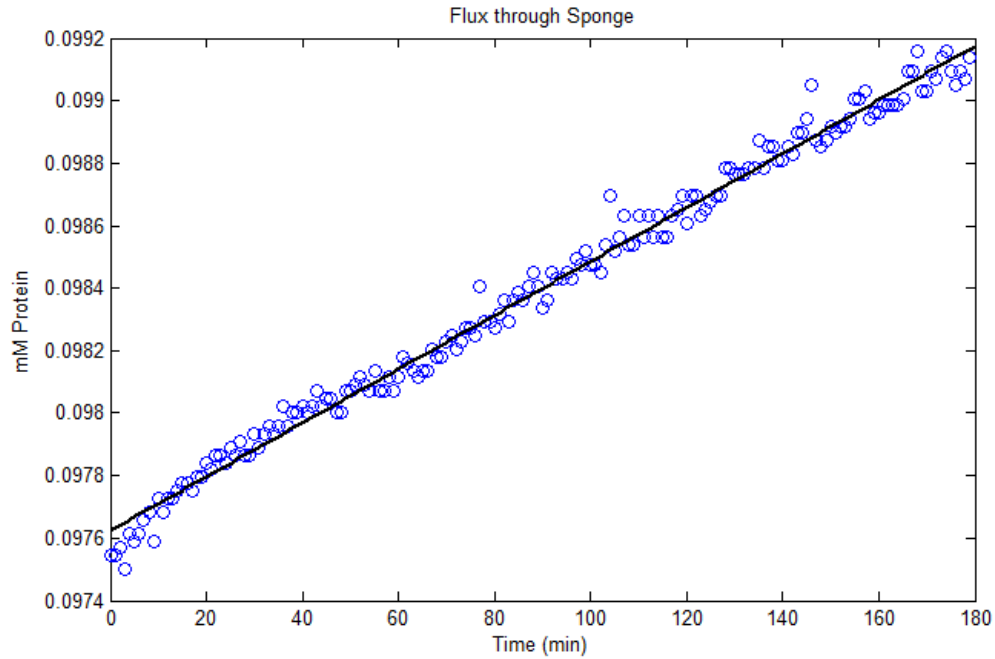| Parameter	Description	Value
η	Viscosity perfusion media	1×10^{-3} Pa·s
a	Inlet Area	1.957 mm^2
u_o	Inlet Velocity	4.364 μm/s
ε_o	Porosity -sponge only	0.9
m	Mass per cell	10.397 ng
μ	Cell Growth Rate	1.070 s^{-1}
ρ_c	Cell Mass Density	1.023 g/cm^3
V_s	Scaffold Volume –quarter	0.07453 cm^3
κ_o	Permeability -sponge only	9.7249 m^2
$D_{1,1}$	Diffusivity of free BMP-2	13×10^{-7} cm^2/s
$D_{1,2}$	Diffusivity of free BMP-2 (Porous Phase)	11×10^{-7} cm^2/s
$D_{2,2}$	Diffusivity of bound BMP-2	0.66×10^{-7} cm^2/s
C_o	Initial Bound BMP-2	7.982 μM

Cellular Parameters

Concentration: 5.04e+005 cells/mL   Mean Cell Diameter: 16.572 µm
Count: 20153   Mean Cell Volume: 2.383 pL

Sudo, H.; Kodama, H. et al, *J Cell Biol, **Volume 96, pp. 191-98***

Diffusion Assay for $D_{1,2}$

Protein	Affinity	Value
bspp24 (full length)	k_d	$2.29 \times 10^{-3}\ s^{-1}$
	k_a	$3.86 \times 10^{5}\ L/mol \cdot s$
spp14.5 (truncated)	k_d	$3.60 \times 10^{-3}\ s^{-1}$
	k_a	$1.53 \times 10^{4}\ L/mol \cdot s$
cBBP (peptide)	k_d	$0.72 \times 10^{-3}\ s^{-1}$
	k_a	$1.35 \times 10^{5}\ L/mol \cdot s$

$$\frac{dC_{BMP-2,free}}{dt} = R_1 = k_d C_{BMP-2,bound} - k_a C_{BMP-2,free}(C_o - C_{BMP-2,bound})$$

$$\frac{dC_{BMP-2,bound}}{dt} = R_2 = k_a C_{BMP-2,free}(C_o - C_{BMP-2,bound}) - k_d C_{BMP-2,bound}$$
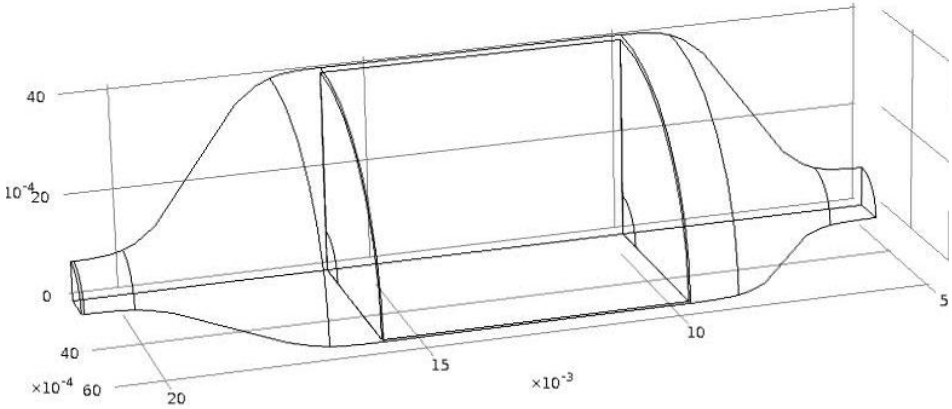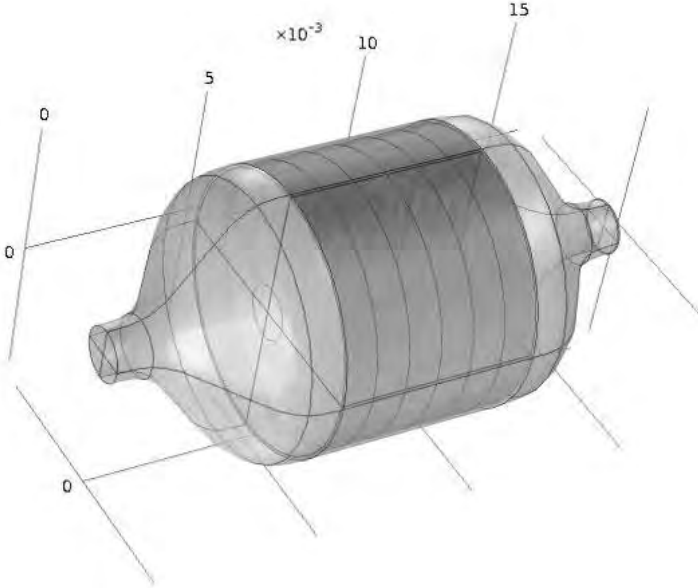
Reactor Design Schematic

Porous Phase
Diam: 8 mm
Length: 6 mm
Vol: 255.4 μL

Total Reactor Vol:
    305.2 μL
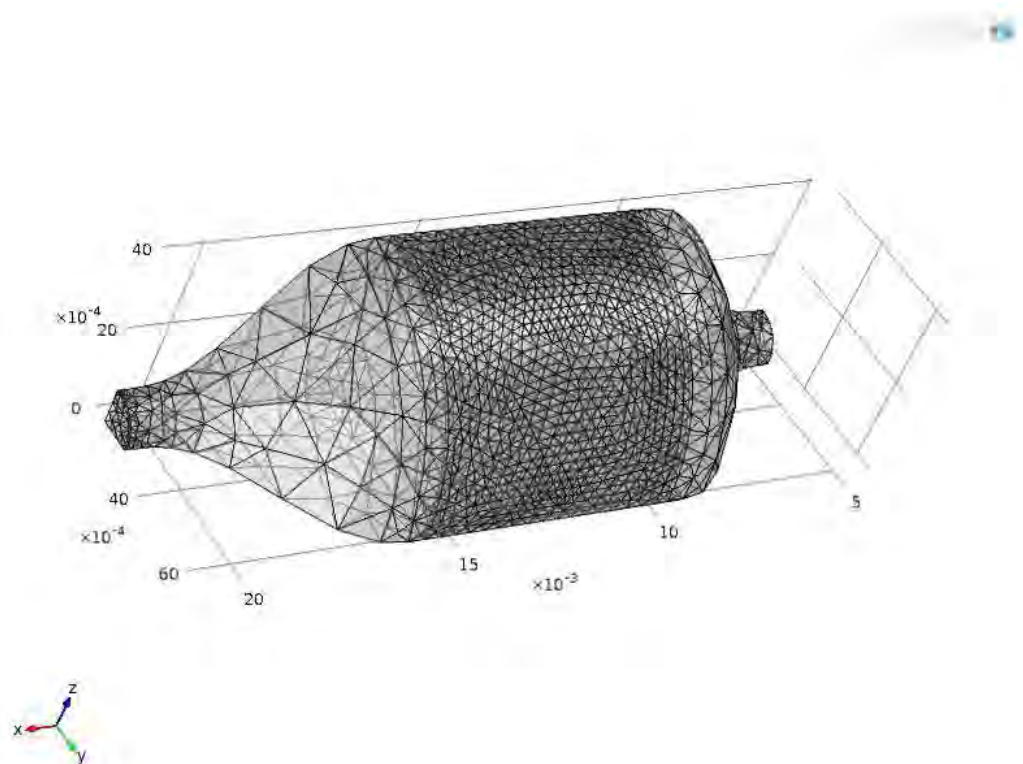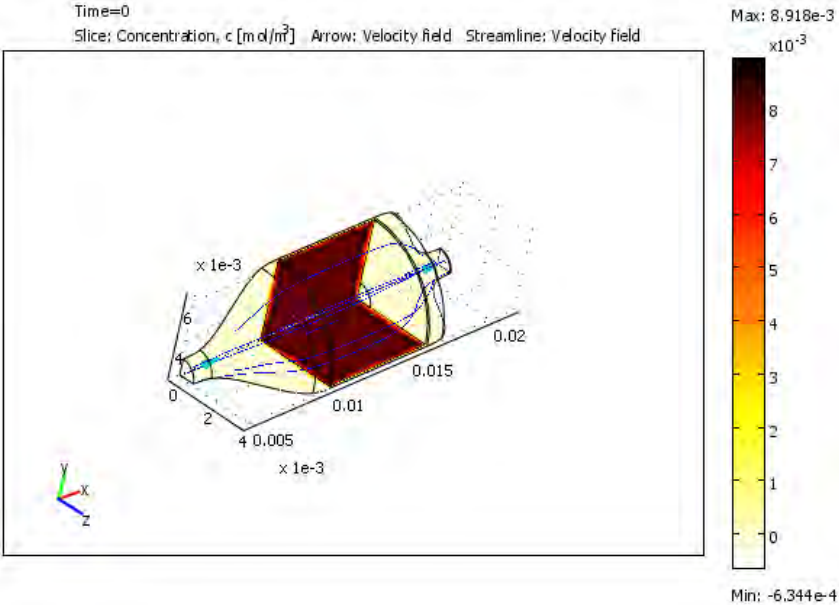
Quartered Geometry
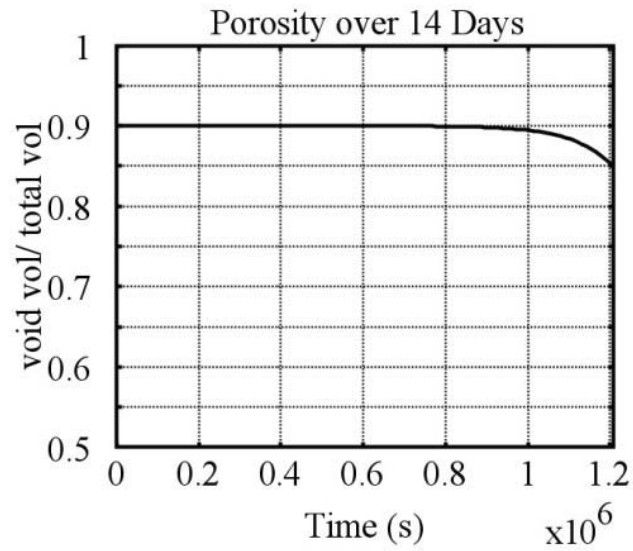
Simulation Parameters

Parameter	Value
Mesh Elements	10,790
Av Solution Time (min)	71
Iterative Solver	Biconjugate Gradient Stability
Preconditioner	Incomplete LU
Simulation Length (hr)	18
Step	30 min

Animation

Simulation Results

Porosity over 14 Days

Permeability over 14 Days

Simulation Results