

Mathematical challenges in controlled drug delivery

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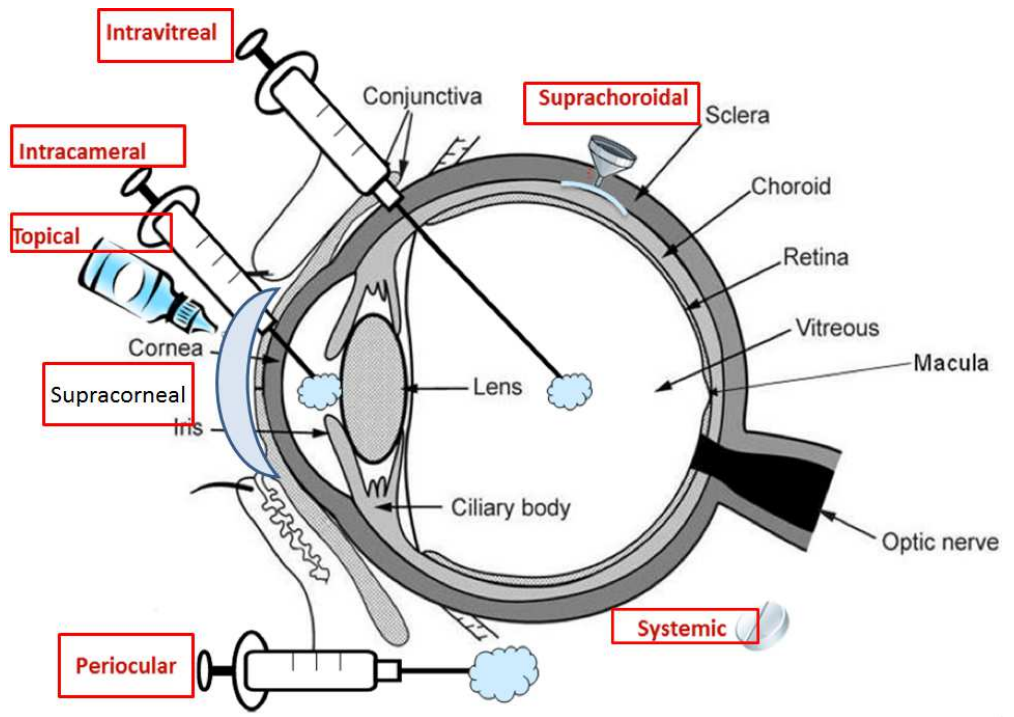
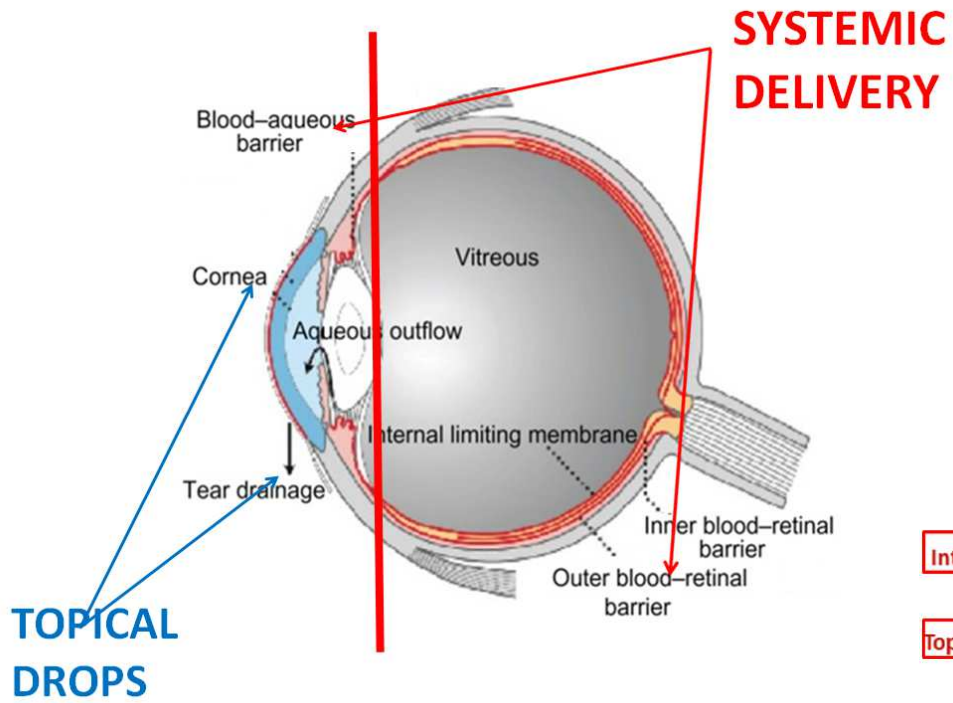
Summary

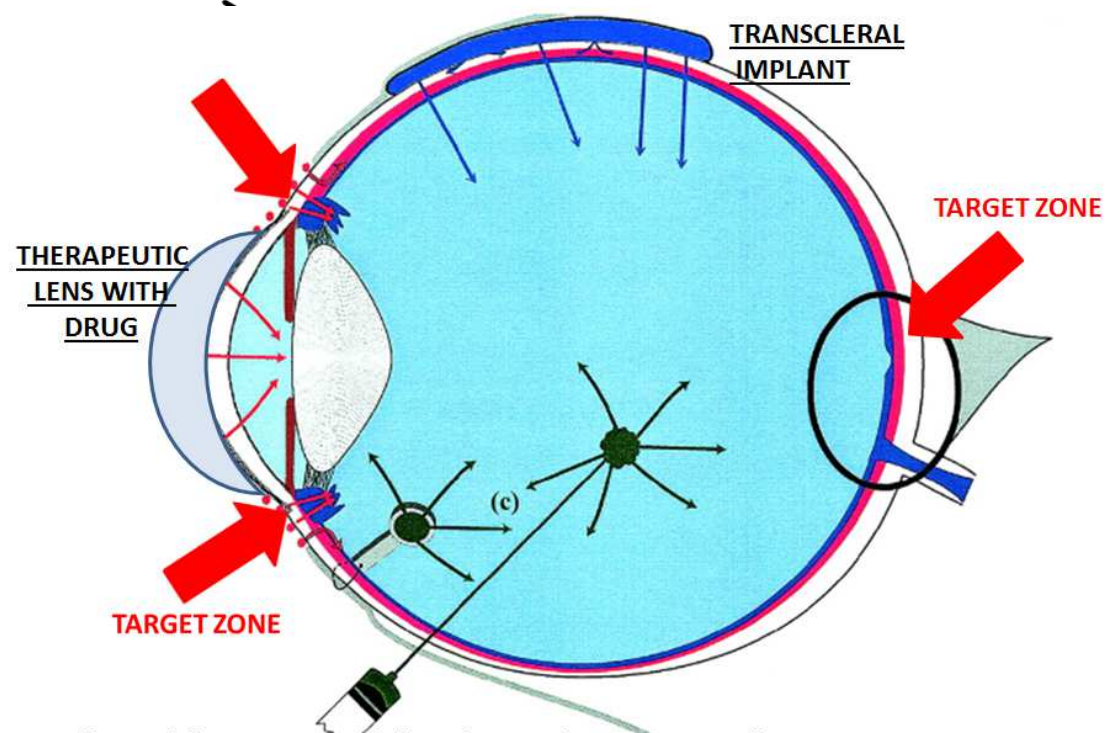
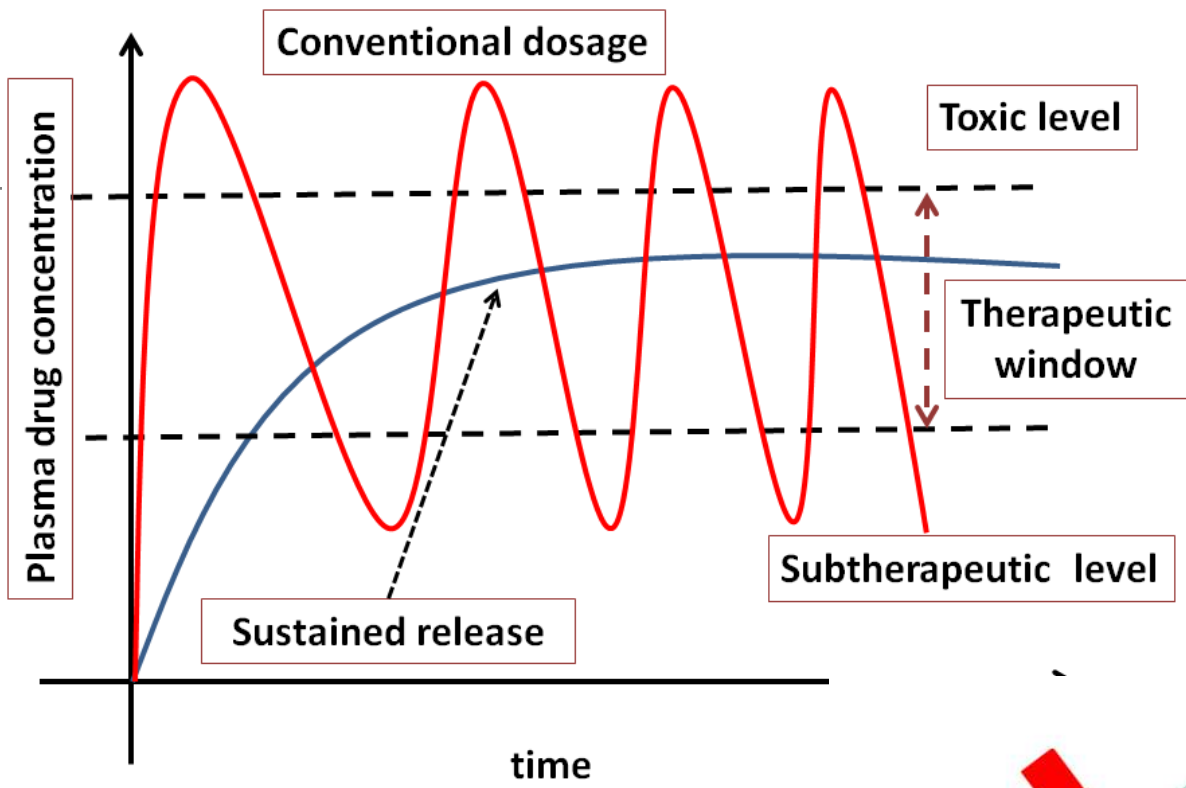
1. **DDS - ophthalmology**
2. **DDS - cardiovascular system**

Joint work with

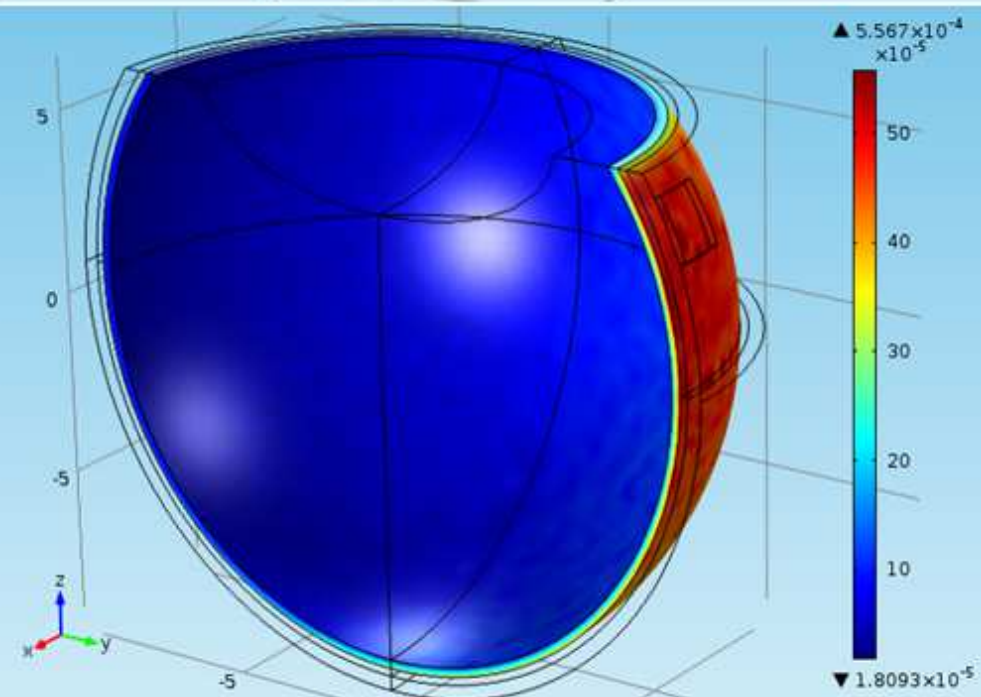
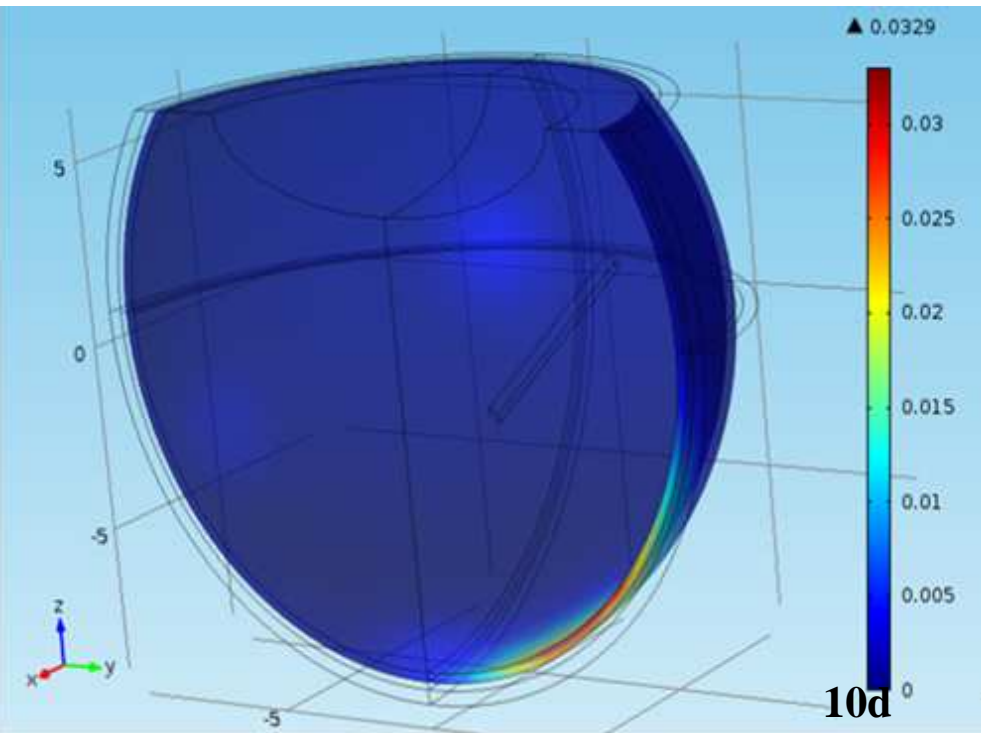
- Paula de Oliveira
CMUC, Department of Mathematics - University of Coimbra
- Pascoal Silva
CMUC, ISEC - Coimbra Institute of Engineering
- Jahed Naghipoor
Department of Mathematics - University of Coimbra
Institute for Structural Mechanics, Bauhaus University of Weimar
Weimar, Germany

DDS in ophthalmology - intravitreal and transcleral implants





Geroski DH, Edelhauser HF. Drug delivery for posterior segment eye disease. Investigative ophthalmology & visual science 2000; 41: 961-964.



Objective: Study the effect of vitreous composition and different retinopathies in drug distribution for intravitreal and transcleral implants

- **Mathematical description of the drug release and drug transport in**
 - implant
 - vitreous humor
 - retina

- **Computational platform to simulate**

- **Different scenarios: vitreous and retina**
- **Different implants**

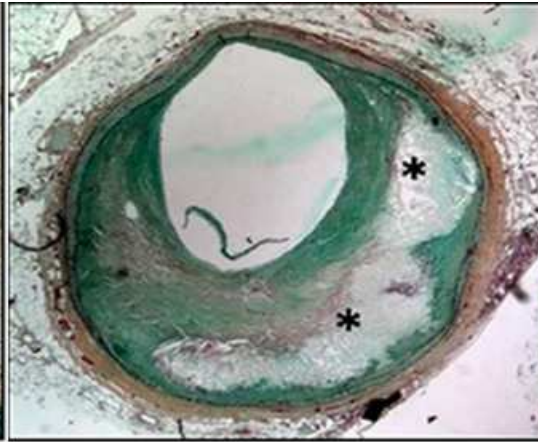
J. Murta, Department of Ophthalmology
Coimbra Hospital Center

R. Silva, Institute for Biomedical Imaging and Life
Science, University of Coimbra

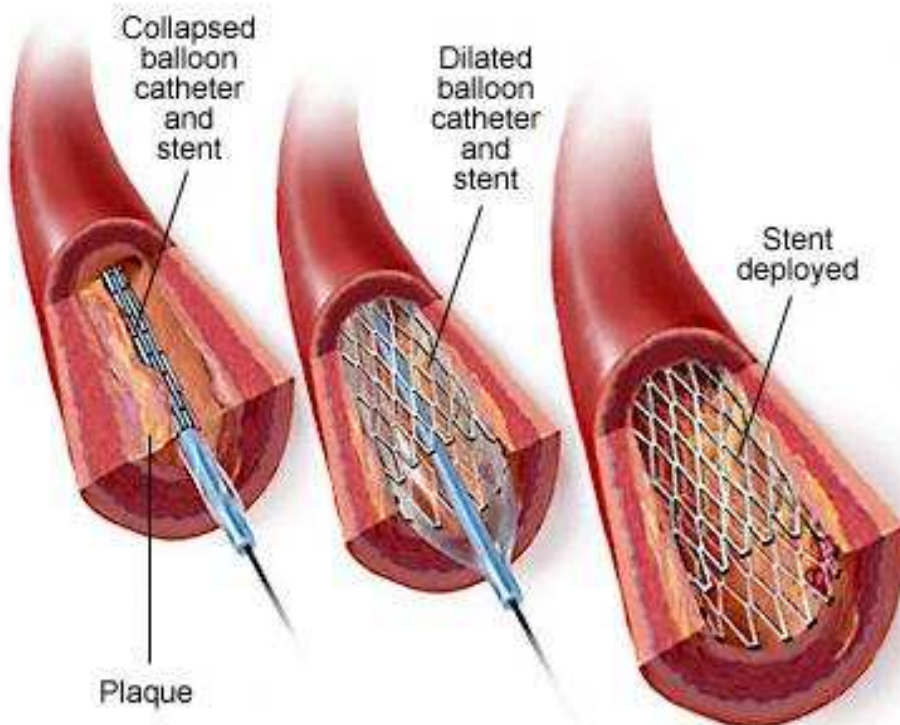
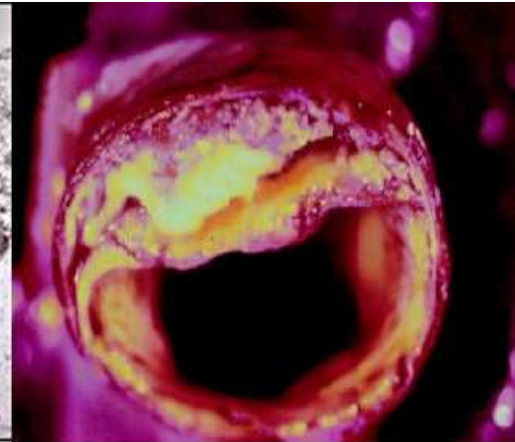
Cardiovascular system: Atherosclerosis



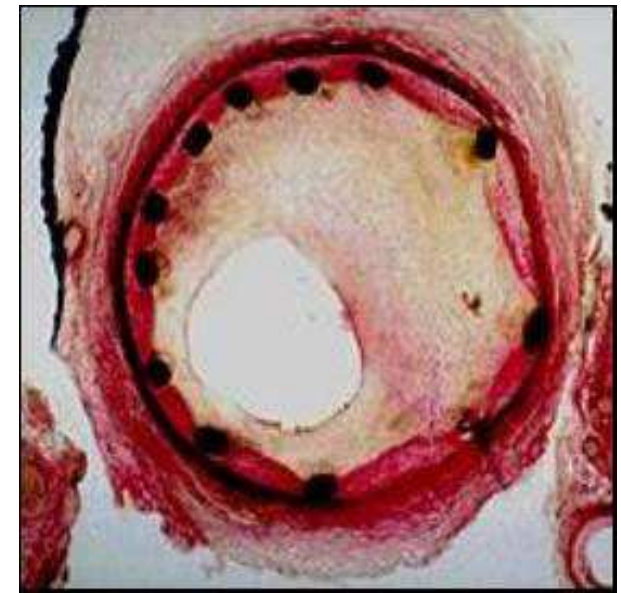
Calcium plaques



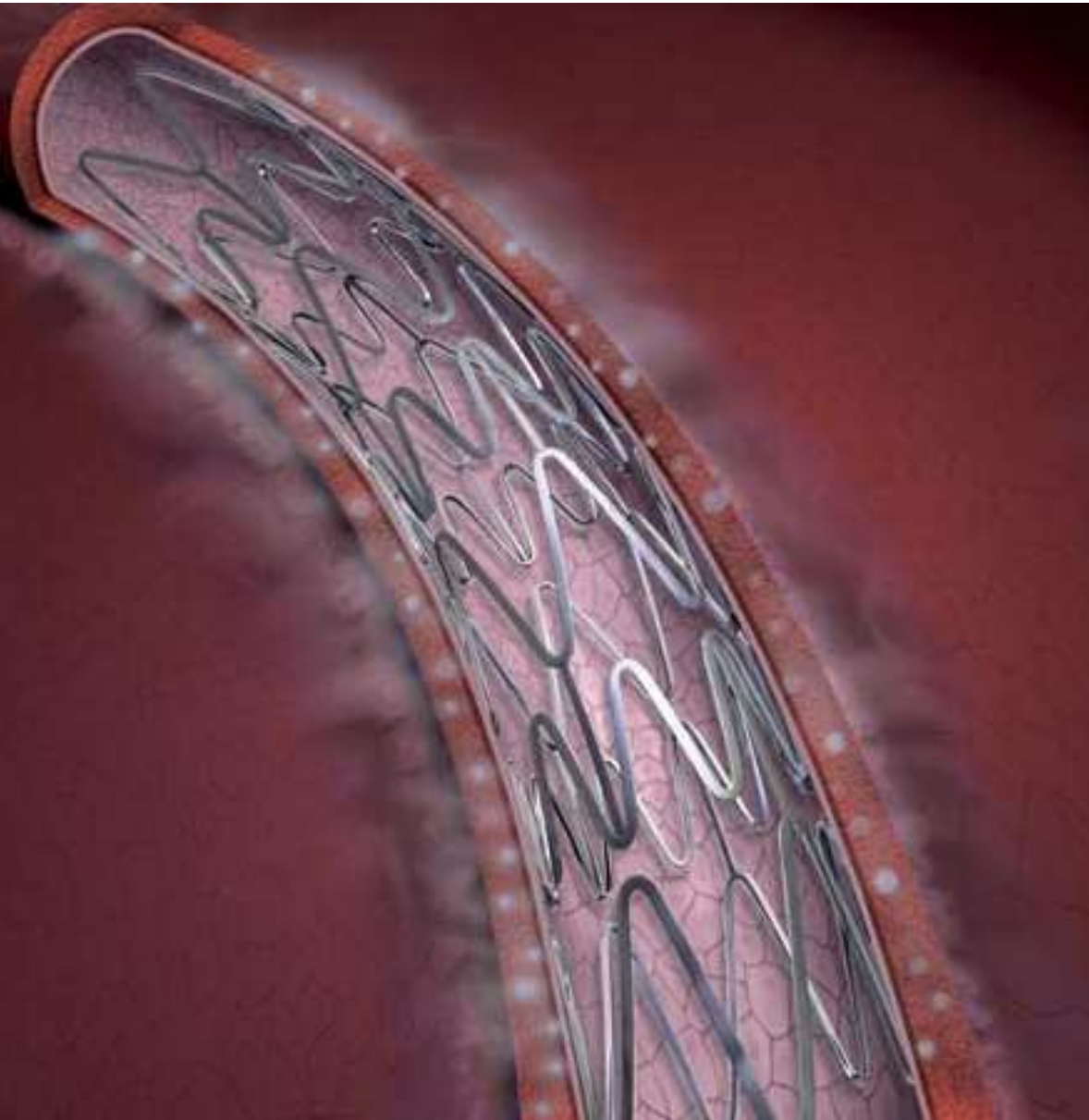
Lipidic plaques



Stenting Procedure



Drug eluting stents



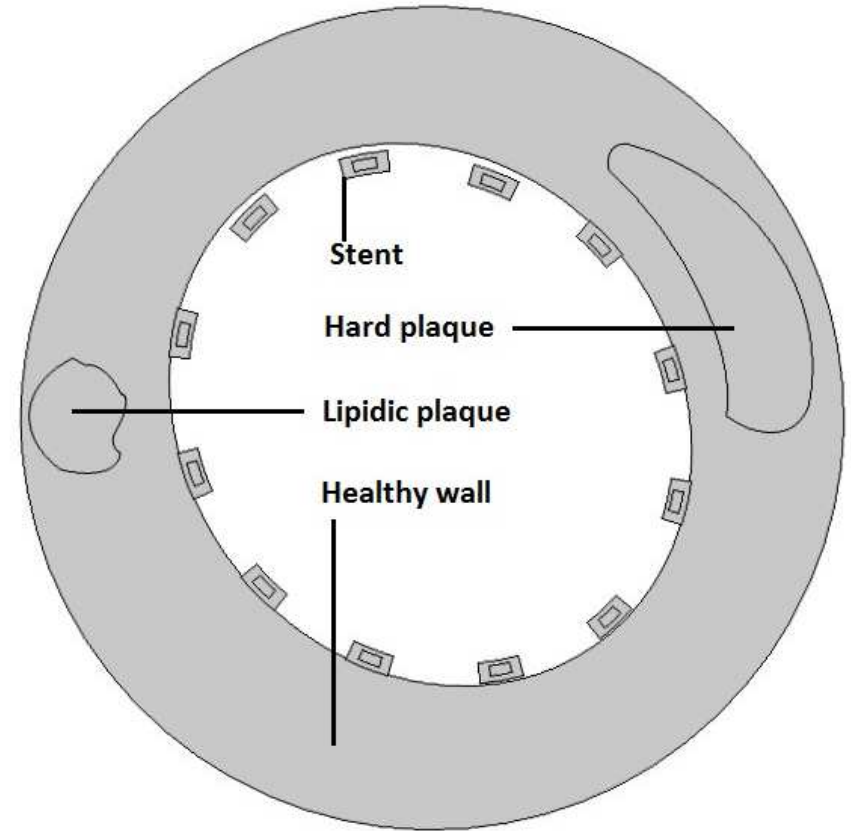
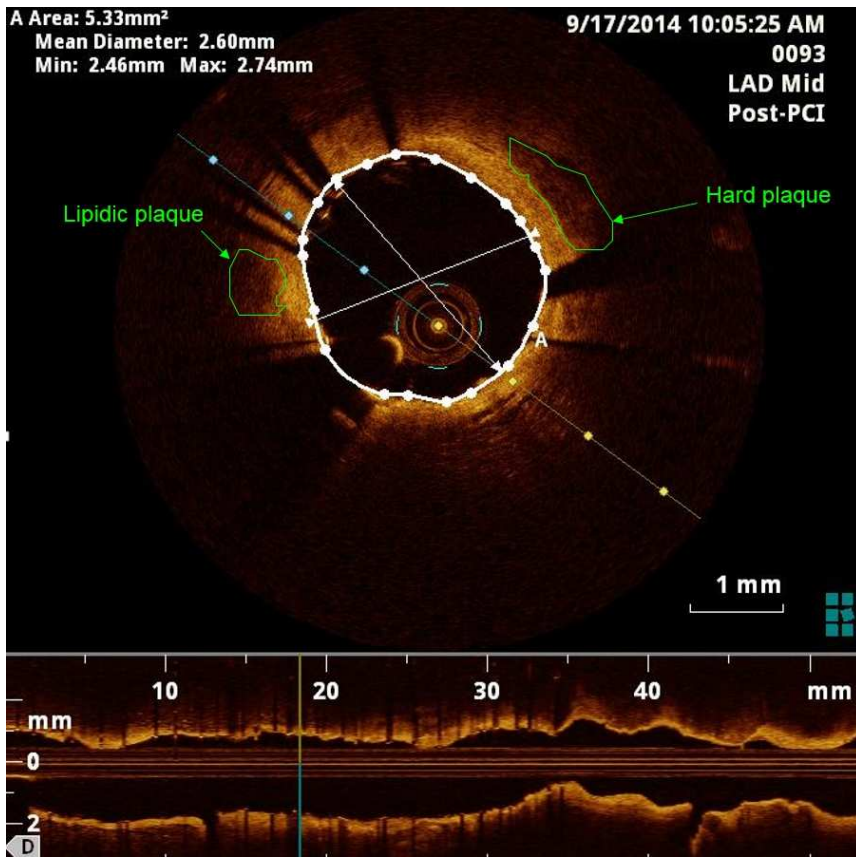
- **Metallic structure coated with a biodegradable polymer (polylactic acid (PLA)) with an entrapped drug**

- **Reduce smooth muscle cell growth that respond to the inflammatory process**

- **Drugs: Sirolimus, Paclitaxel**

Main objective: Effect of the stiffness of atherosclerotic plaques in drug distribution

Geometry



Mathematical description

- **Polymeric matrix:**

 - Degradation of polymeric coating**

 - Drug dissolution**

 - Drug transport (diffusion -porous medium)**

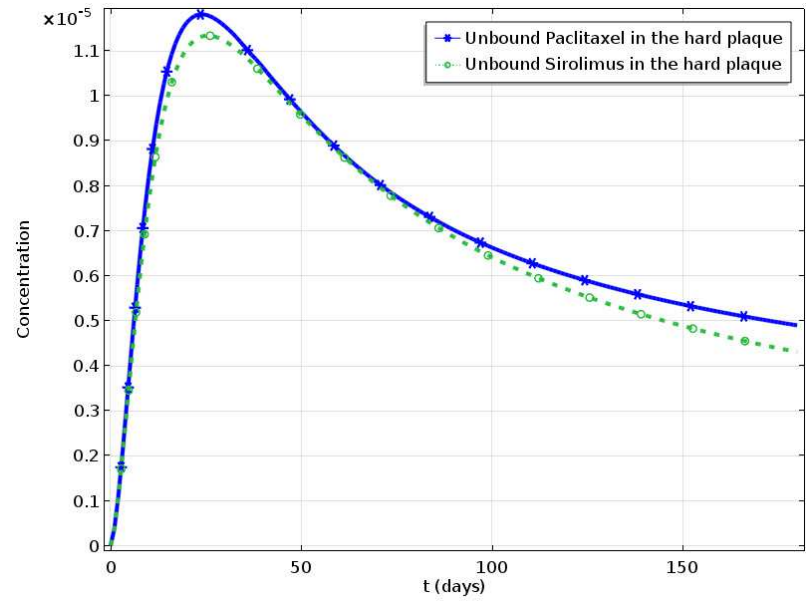
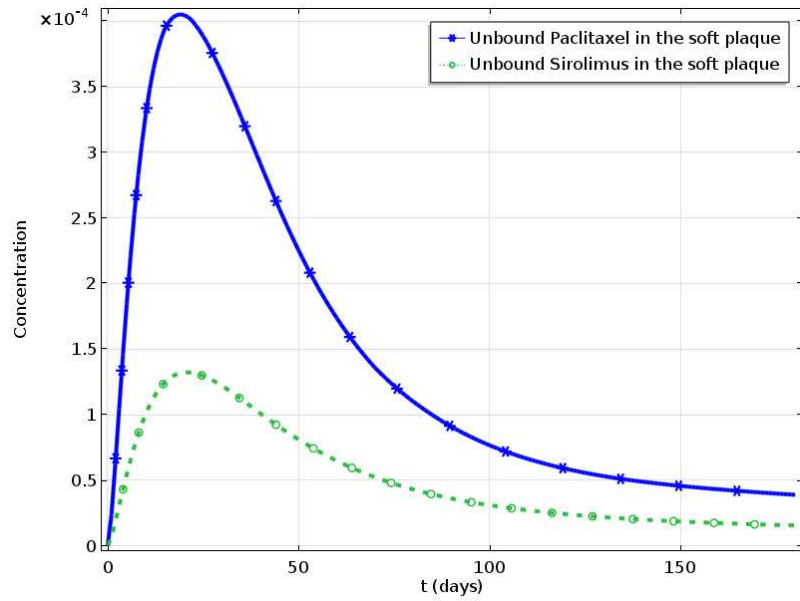
- **Vessel wall (Health tissue, Plaques):**

 - Binding and unbinding**

 - Drug transport(diffusion, convection, viscoelastic effect)**

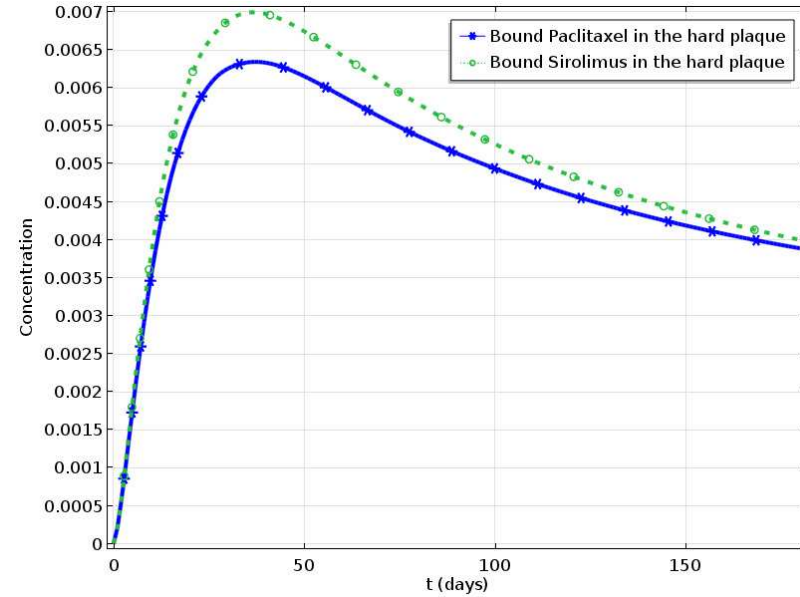
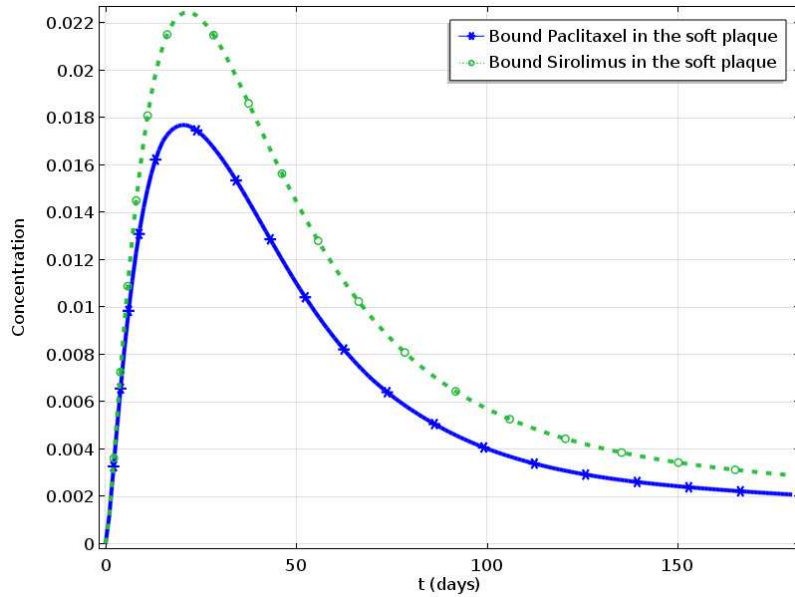
- **Blood flow wash effect**

IBVP: Diffusion-reaction equations (stent) coupled with integro-differential equations (vessel)



Paclitaxel presents higher concentrations of unbound drug

Efficacy (Paclitaxel) \geq Efficacy (Sirolimus)



Sirolimus presents higher concentrations of bound drug (plaques without calcified core)

Residence time (Sirolimus) \geq Residence time (Paclitaxel)

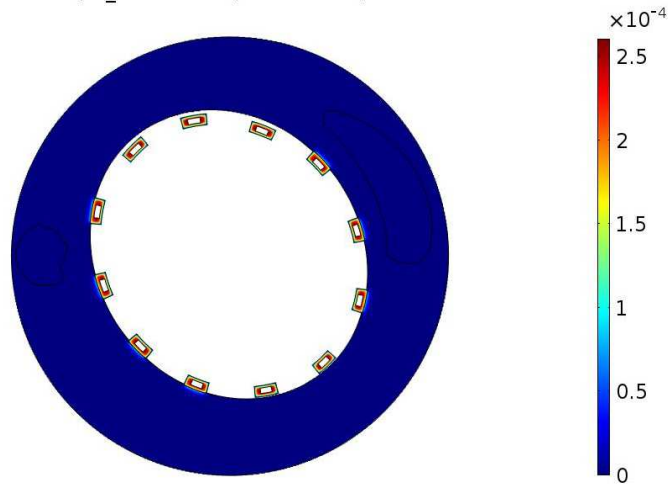


Efficacy (Paclitaxel) \leq Efficacy(Sirolimus)

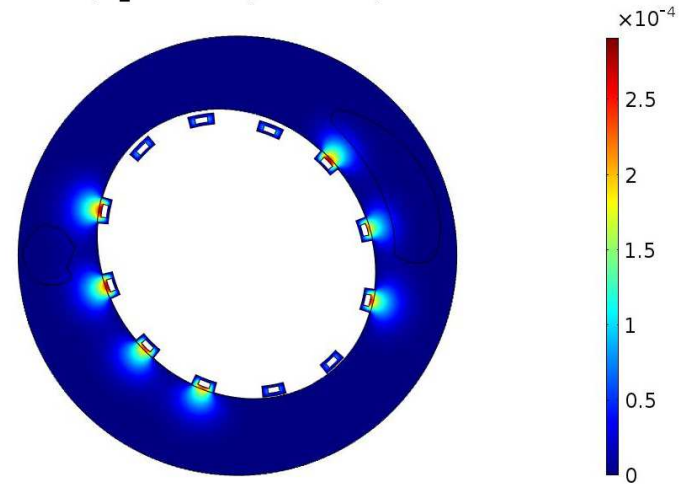
Restenosis (Paclitaxel) \geq Restenosis (Sirolimus)

Drug distribution - Sirolimus

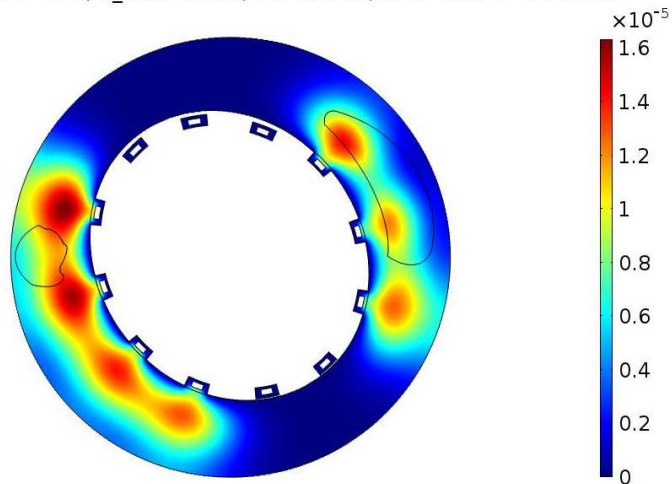
183: Time=1 d, $B_{\max}=0.366$, $K_d=0.0026$, $DD2=7.7E-8$ Sirolimus



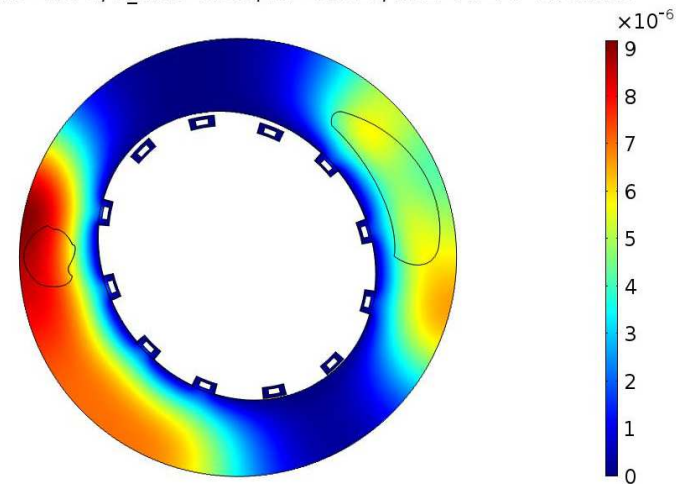
212: Time=30 d, $B_{\max}=0.366$, $K_d=0.0026$, $DD2=7.7E-8$ Sirolimus



272: Time=90 d, $B_{\max}=0.366$, $K_d=0.0026$, $DD2=7.7E-8$ Sirolimus



362: Time=180 d, $B_{\max}=0.366$, $K_d=0.0026$, $DD2=7.7E-8$ Sirolimus



 Occurrence of restenosis is higher in the regions with stiff plaques.

Thank you