

A virtual pharmacokinetic model of human eye

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Motivation

Increasing standard of living:

- **increasing life expectancy**
- **increasing number of posterior eye diseases:**
 - **age related macular degeneration; in USA 2 million**
 - **diabetic retinopathy**
 - **ganglion cell damage due to glaucoma**

Drug therapy of posterior eye very difficult

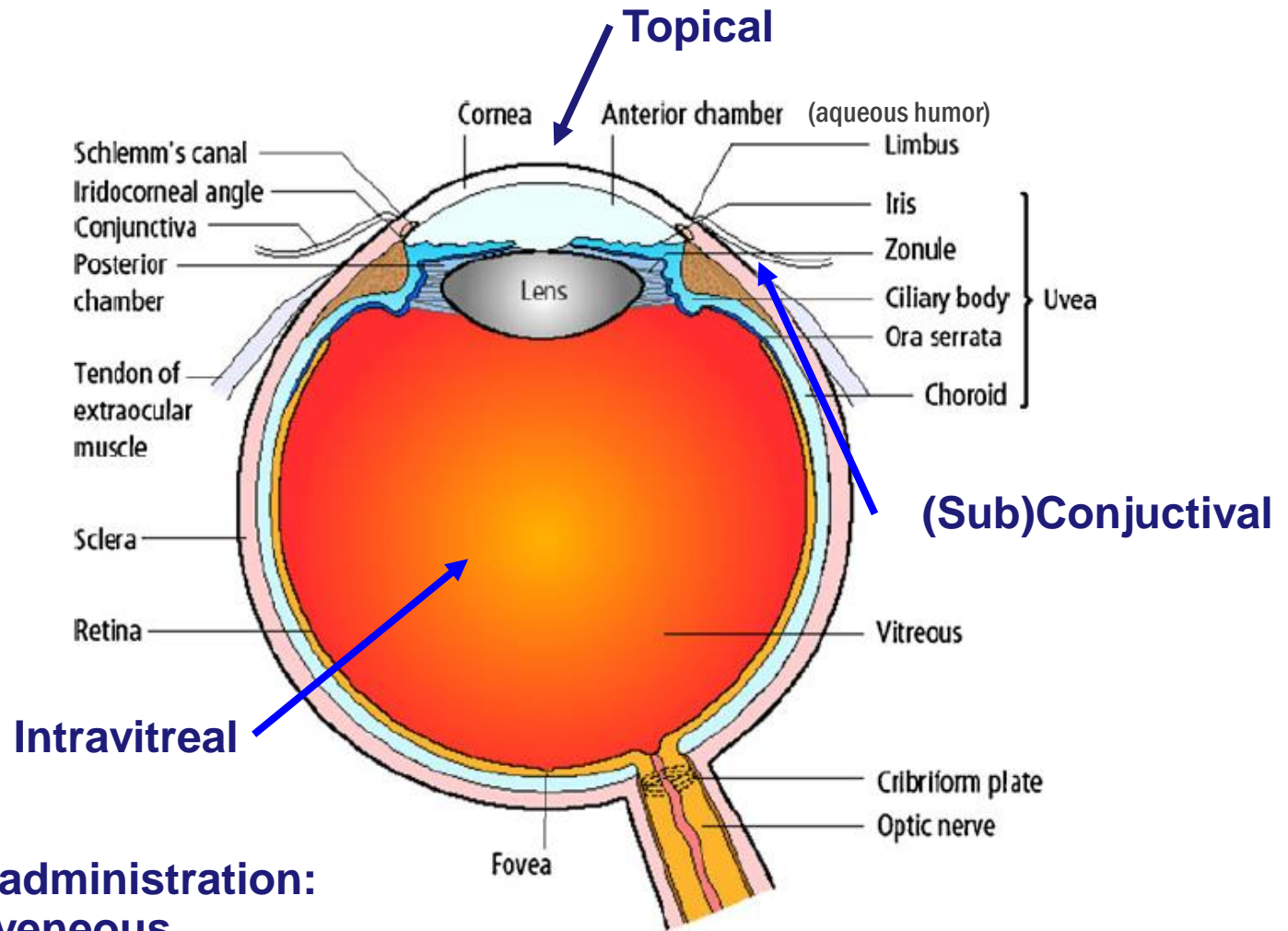
- **direct injections to eye, for example**

Modeling of drug distribution in eye is one way of facilitating the development of eye therapies

A Solution: Finite Element Method (FEM) through Comsol Multiphysics

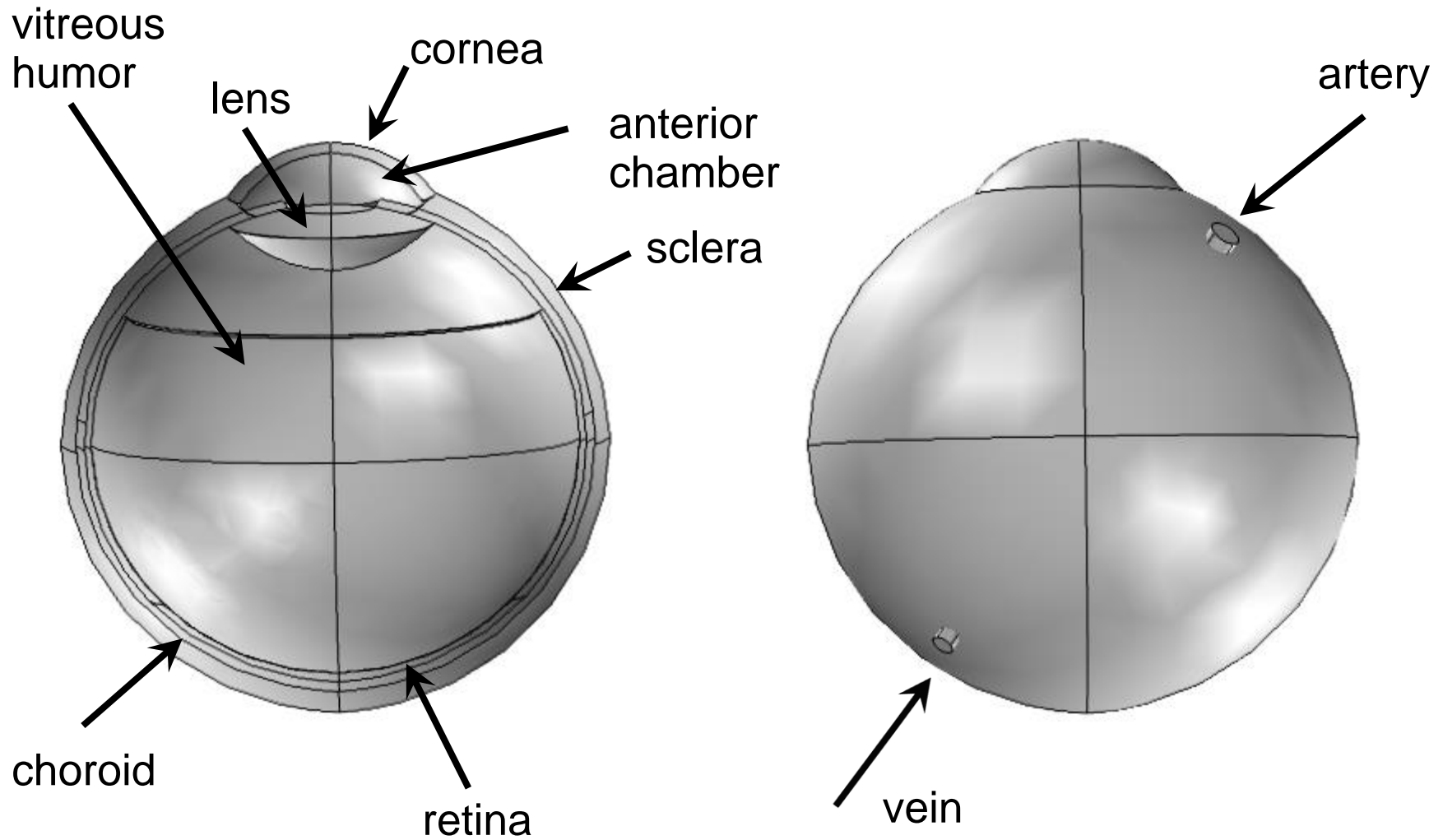
- **based on Matlab scripts**
- **graphical user interface**
- **simultaneous solution of multiple equations**
- **automatic continuity conditions**
- **versatile possibilities to tune the model and solution**
- **automatic script creation**
- **fitting to experimental data**

Cross-section of human eye and administration routes



**Systemic administration:
oral, intravenous**

COMSOL drawing



Equations

- **Incompressible Navier-Stokes, laminar flow at steady-state, in choroid**
- **Transient convective diffusion in choroid**
- **Transient diffusion elsewhere**

Mobility in various tissues:

- **Blood, $\eta \approx 3$ cP, $\rho \approx 1.03$ g/cm³**
- **vitreous humor \approx hydrogel, $\eta \approx 4000$ cP**
- **Calcein labelled Bovine serum albumin and a polypeptide in hydroxyl propyl methyl cellulose**
- **FRAP Experiments, diffusion in vitreous humor is far too high, 4000 folds higher than water**

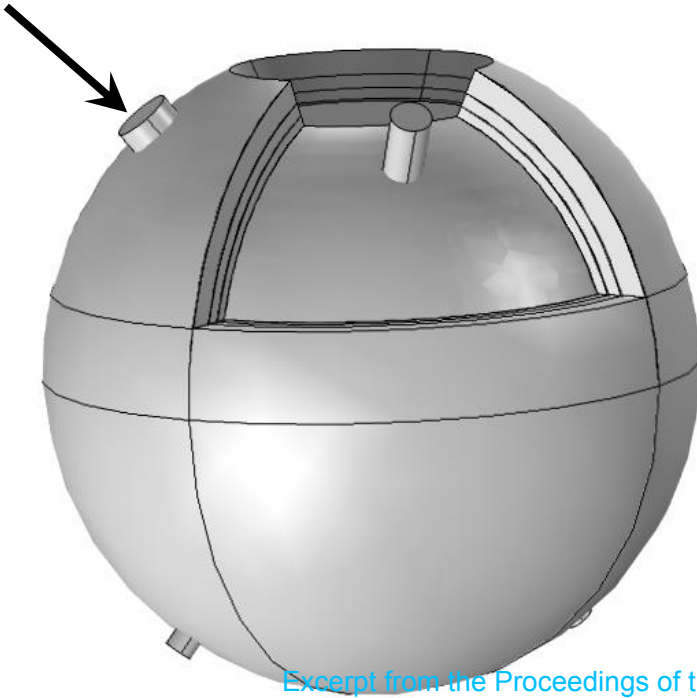
Case study: release from patch in 100,000 seconds

Studied parameters:

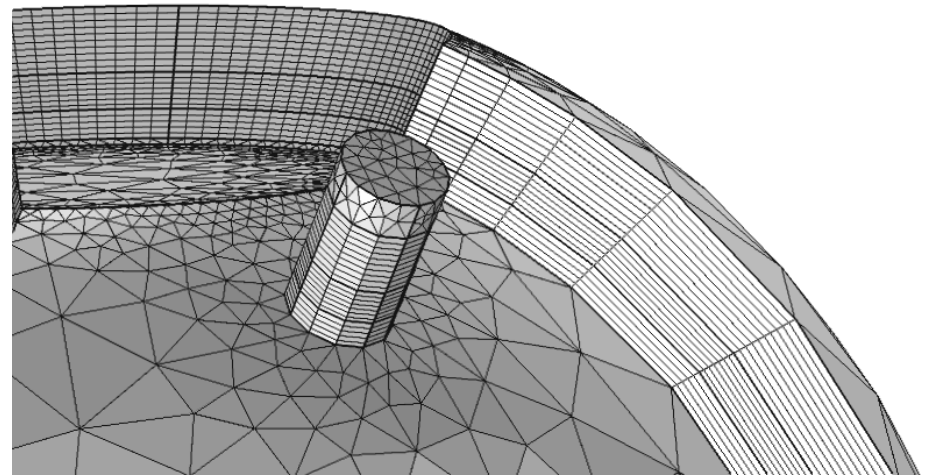
- Diffusion coefficient in sclera, 1, 5, 10 and 50×10^{-7} cm²/s
- Permeability coefficient sclera-choroid 1, 3, 10 and 30×10^{-5} cm/s

cornea, anterior chamber
and lens ignored

patch

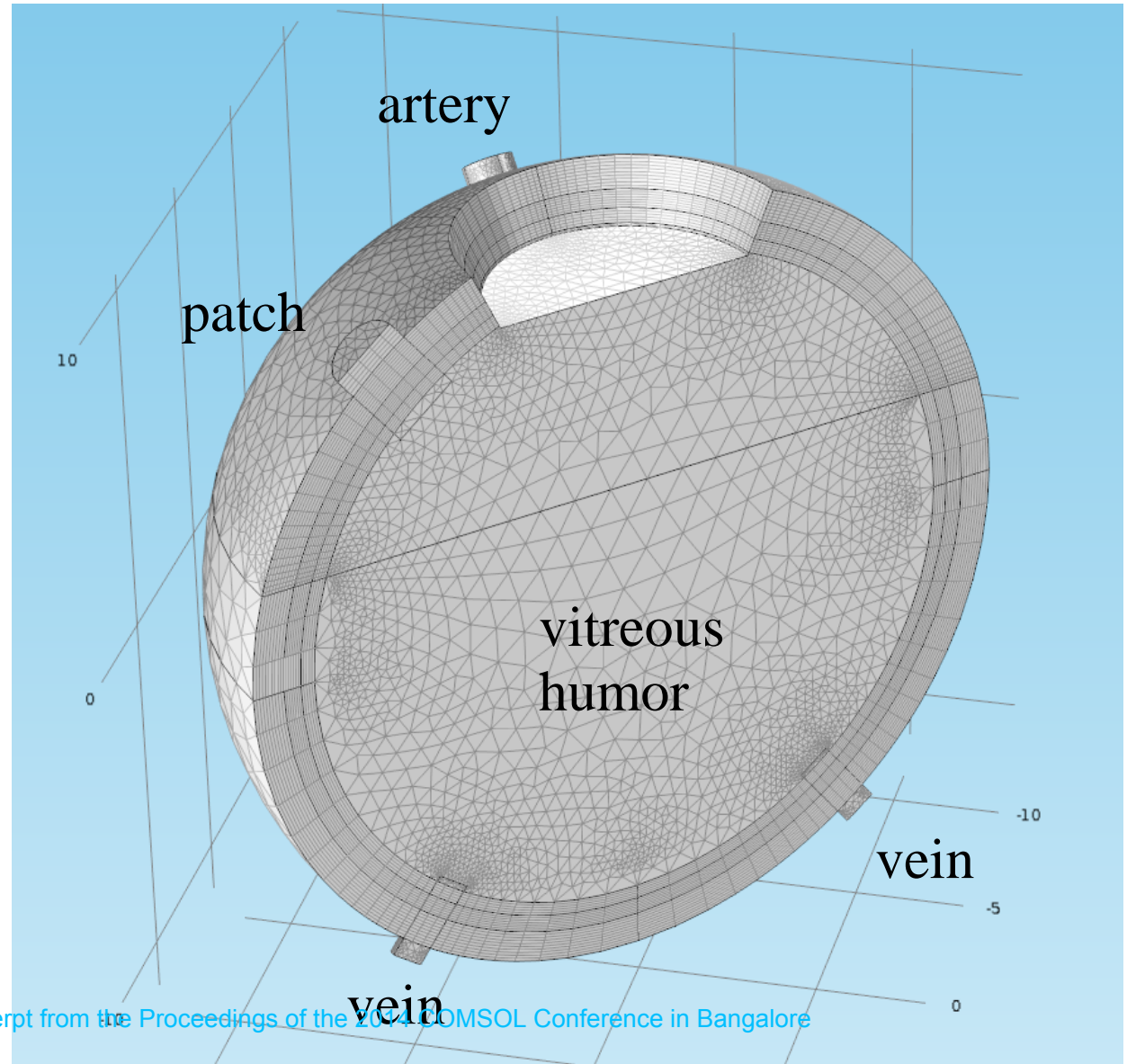


simulation mesh consists of
200,607 elements
simulation time ~10000 s



Cross section of eye by Comsol drawing, with calculation mesh

- Sclera =10 layers in radial direction by swept mesh, 0.9mm
- Choroid=0.7mm, retina=0.5mm

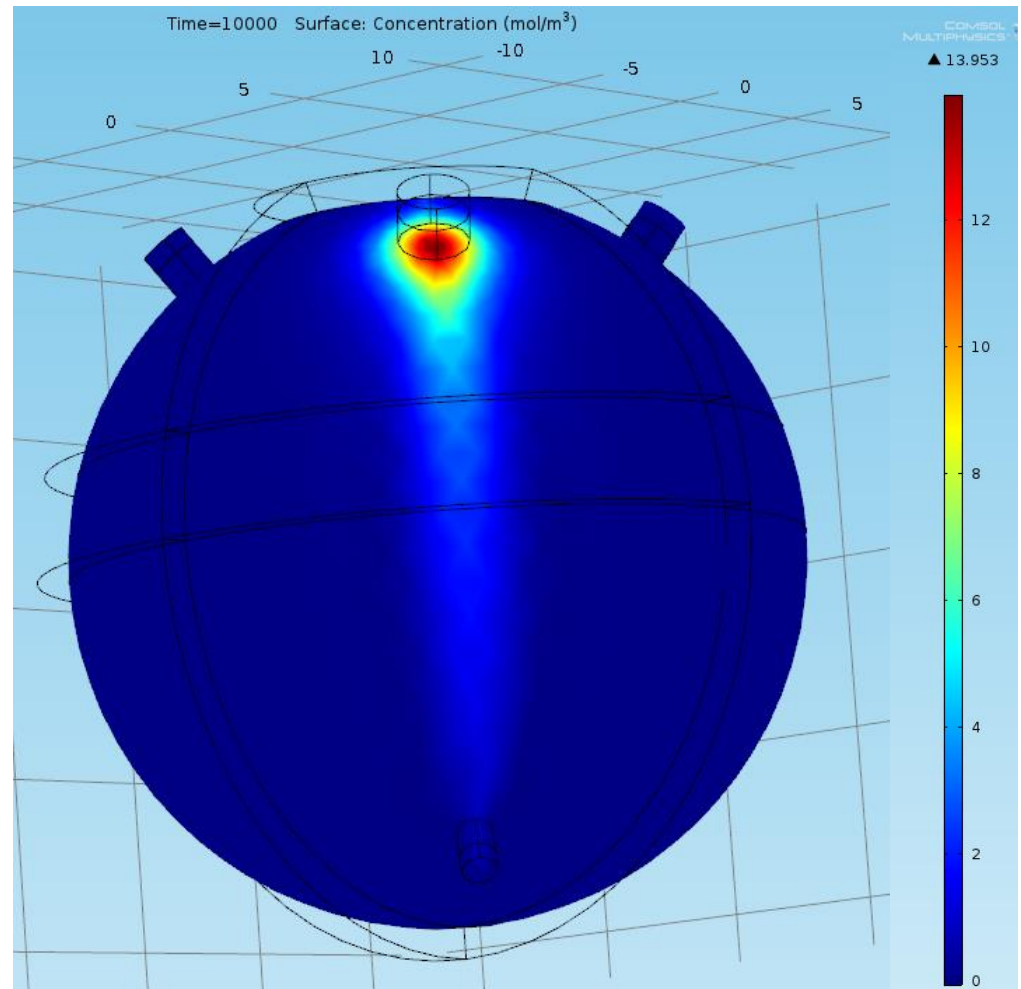


Excerpt from the Proceedings of the 2024 COMSOL Conference in Bangalore

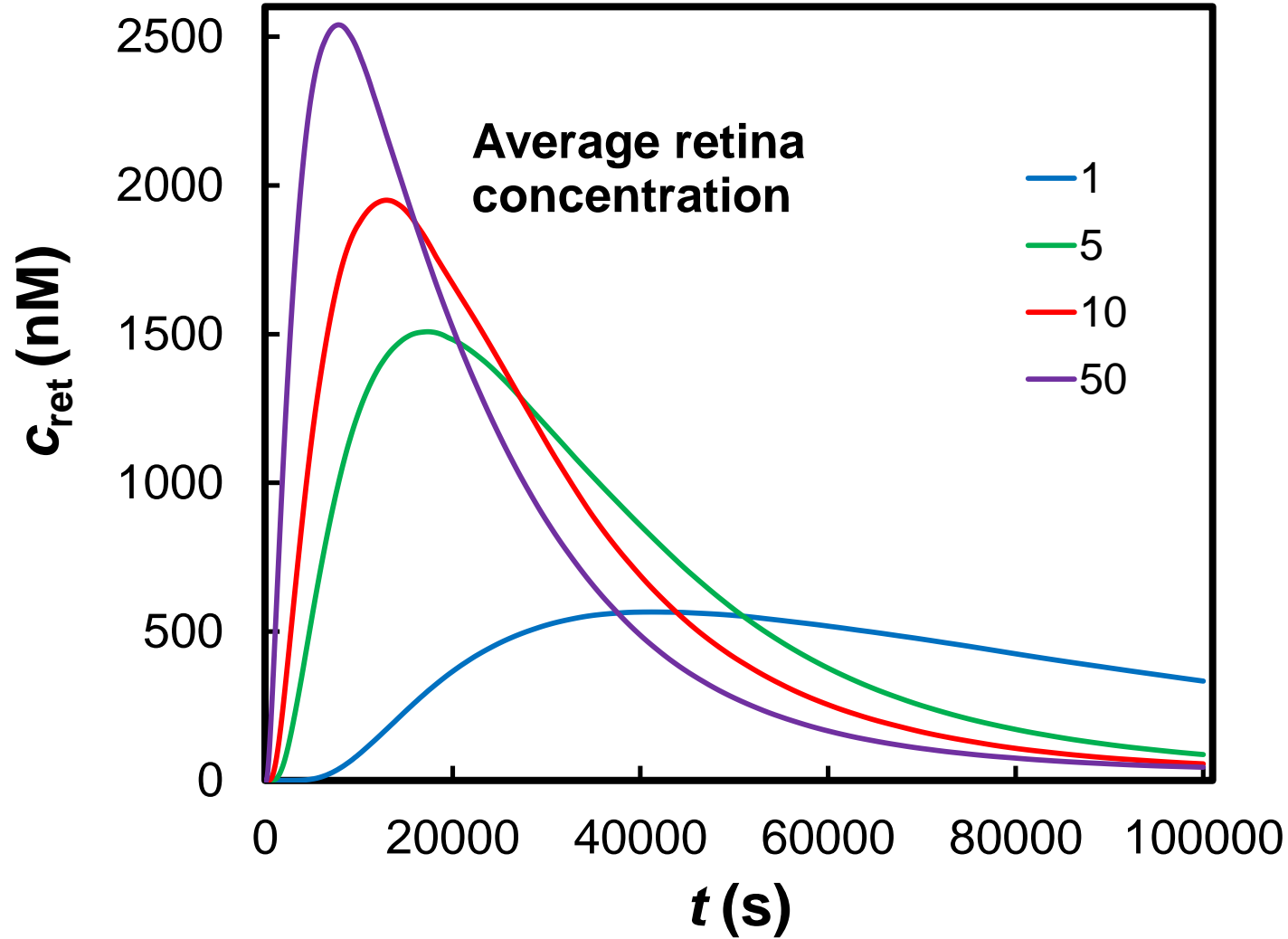
Drug concentration on the choroid surface at t=10000 s

Drug is partitioned in choroid, blood flow washes part of it by veins

-Drug removed from the simulation domain due to blood circulation must be calculated and integrated as a function of time for mass balance



Effect of sclera diff. coeff. ($\times 10^{-7} \text{ cm}^2/\text{s}$), $K_{\text{scl/cho}} = 10^{-4} \text{ cm/s}$



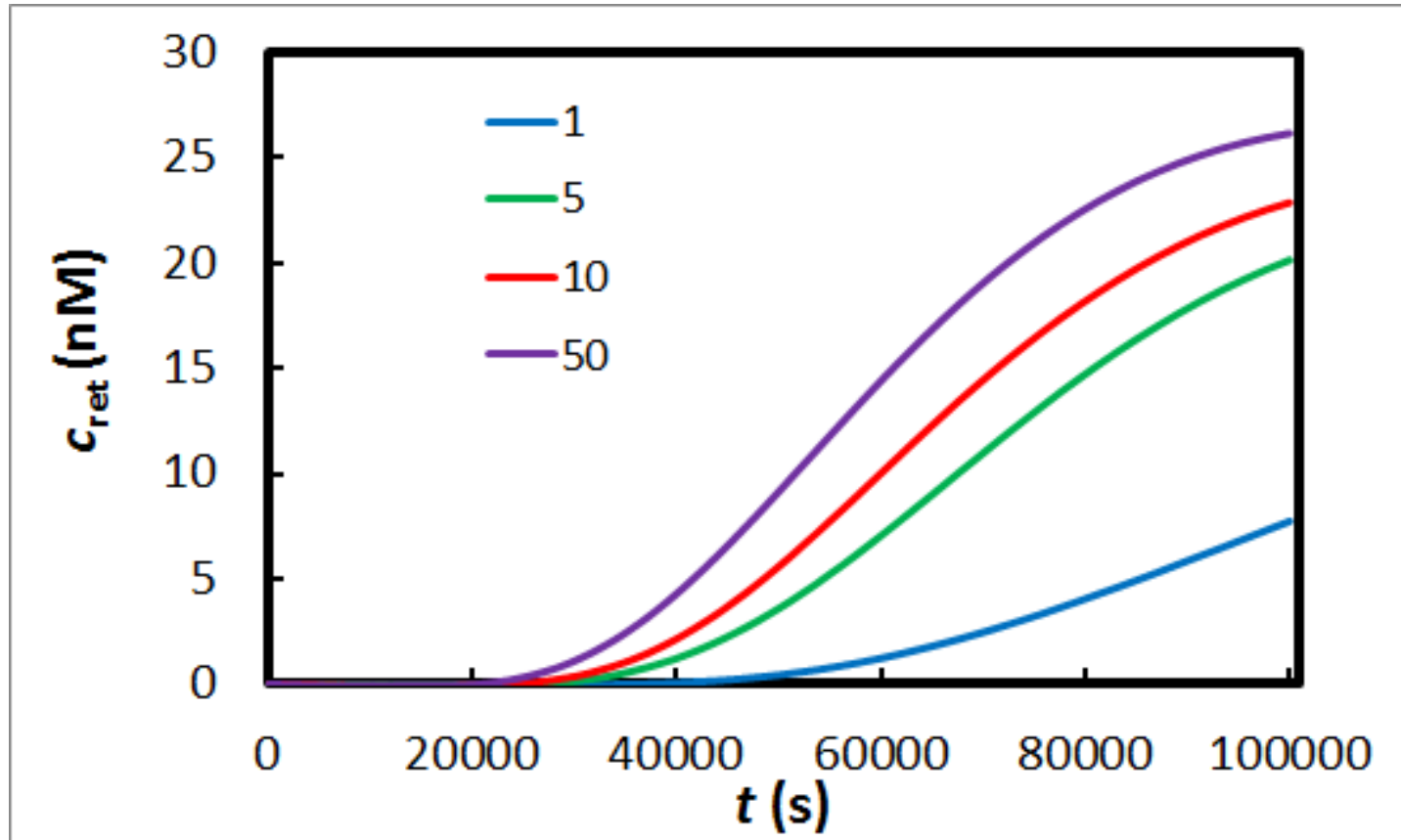
-Sclera is quite hydrophilic, enabling large molecules to pass

Excerpt from the Proceedings of the 2014 COMSOL Conference in Bangalore

www.helsinki.fi/yliopisto

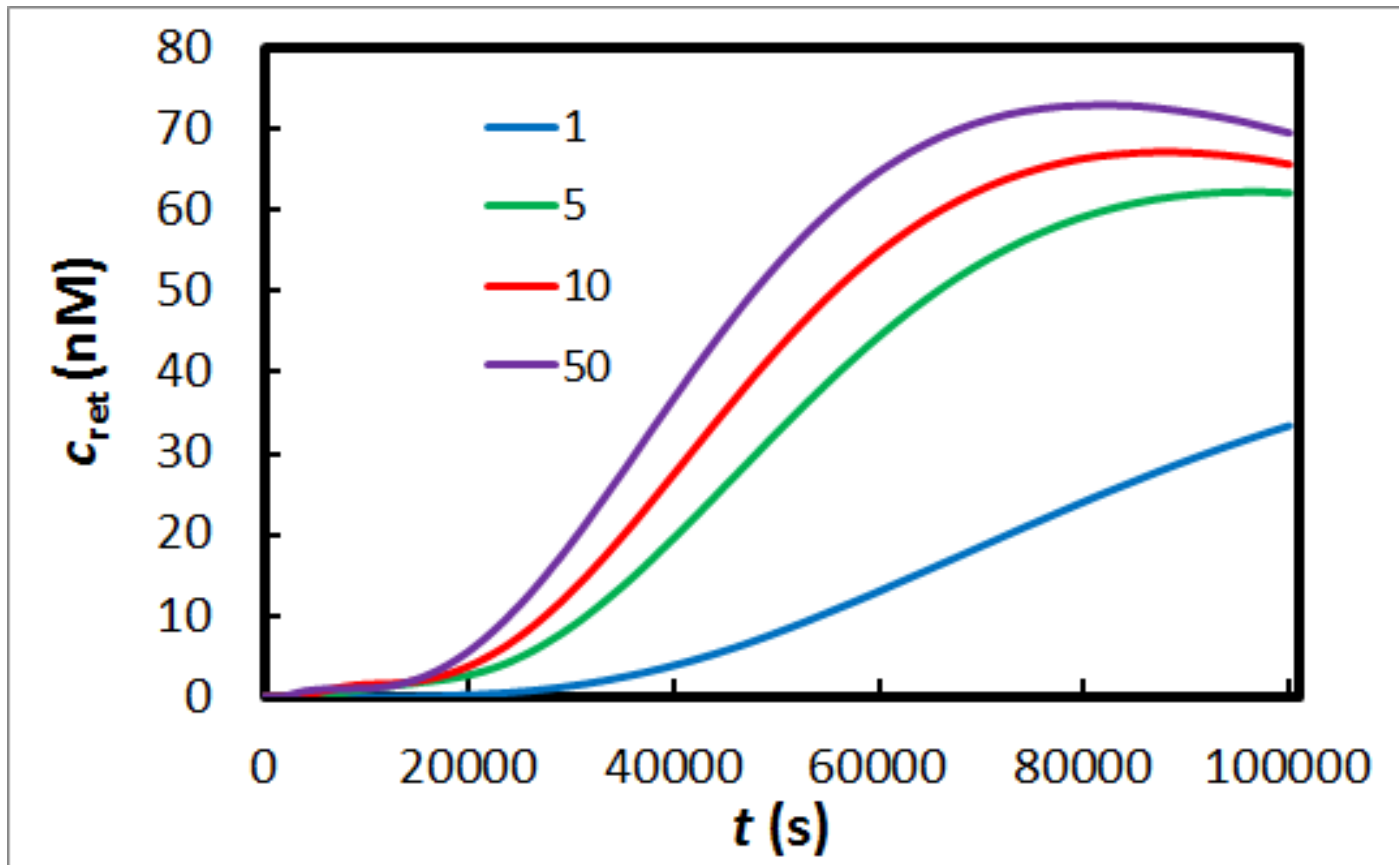
Effect of sclera diff. coeff. ($\times 10^{-7} \text{ cm}^2/\text{s}$), $K_{\text{scl/cho}} = 10^{-4} \text{ cm/s}$

Point evaluation in retina, opposite to patch, on "equator"



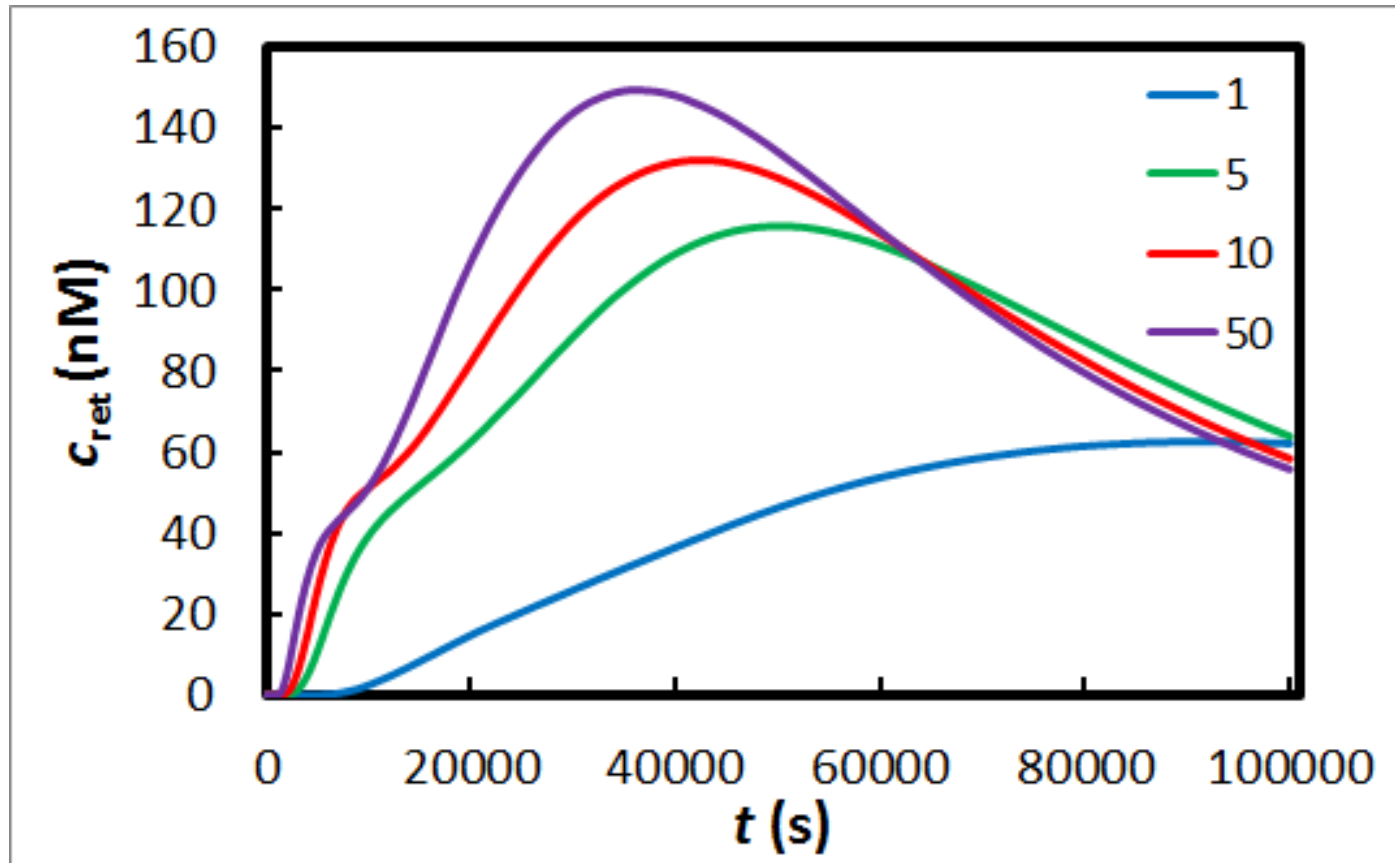
Effect of sclera diff. coeff. ($\times 10^{-7} \text{ cm}^2/\text{s}$), $K_{\text{scl/cho}} = 10^{-4} \text{ cm/s}$

Point evaluation in retina, on the bottom



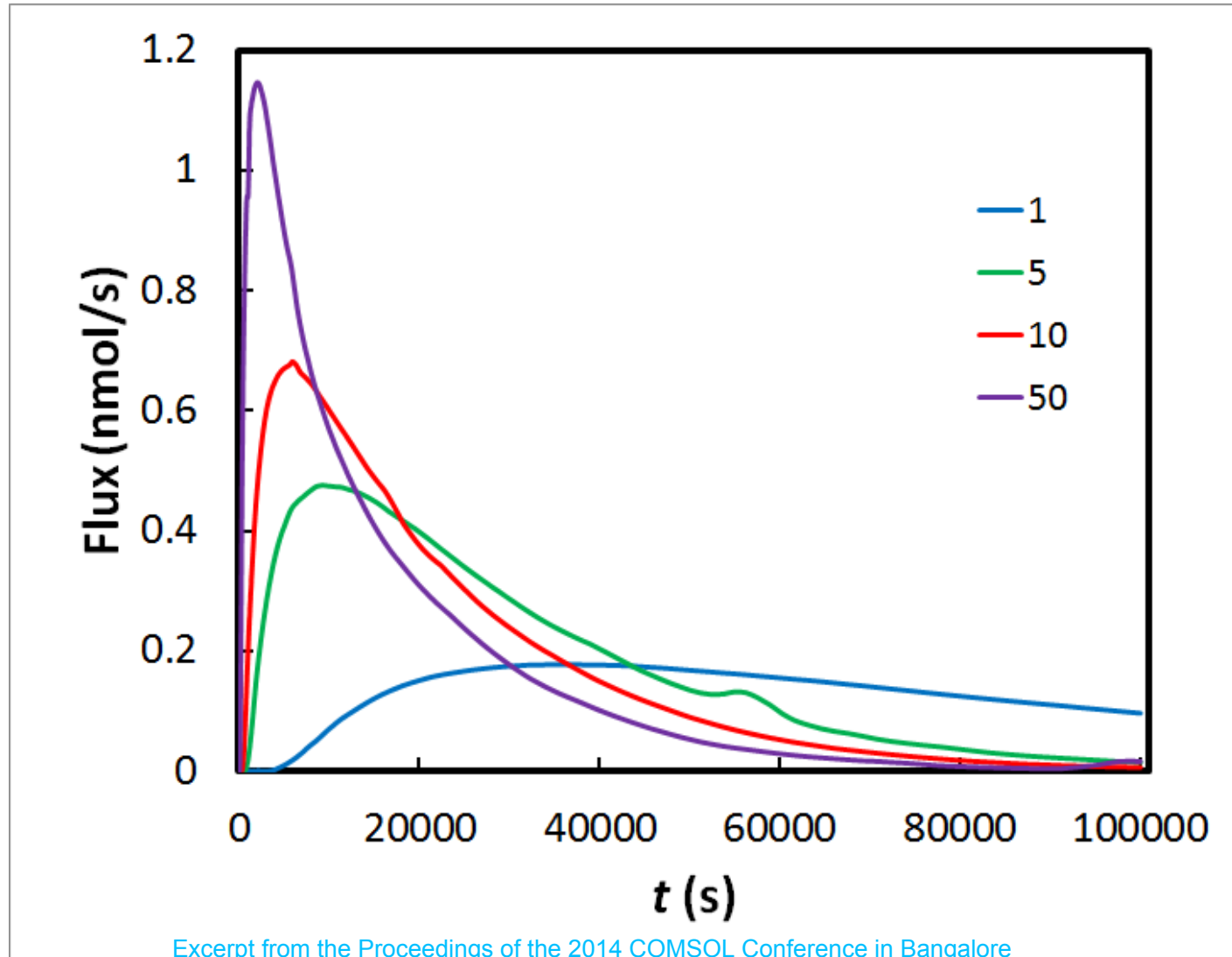
Effect of sclera diff. coeff. ($\times 10^{-7} \text{ cm}^2/\text{s}$), $K_{\text{scl/cho}} = 10^{-4} \text{ cm/s}$

Point evaluation in retina, next to patch, on "equator"



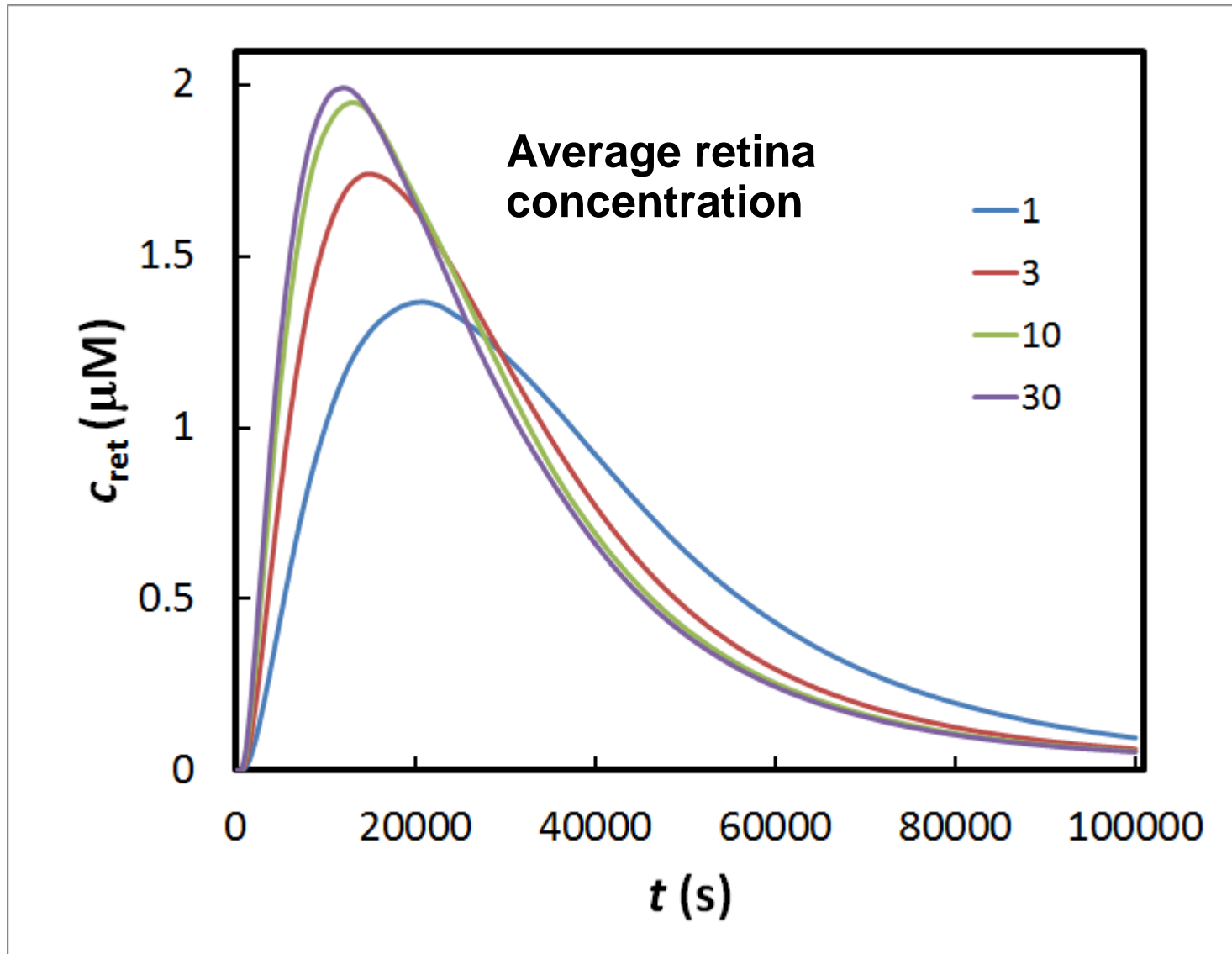
Effect of sclera diff. coeff. ($\times 10^{-7} \text{ cm}^2/\text{s}$), $K_{\text{scl/cho}} = 10^{-4} \text{ cm/s}$

Convective flux out of choroid



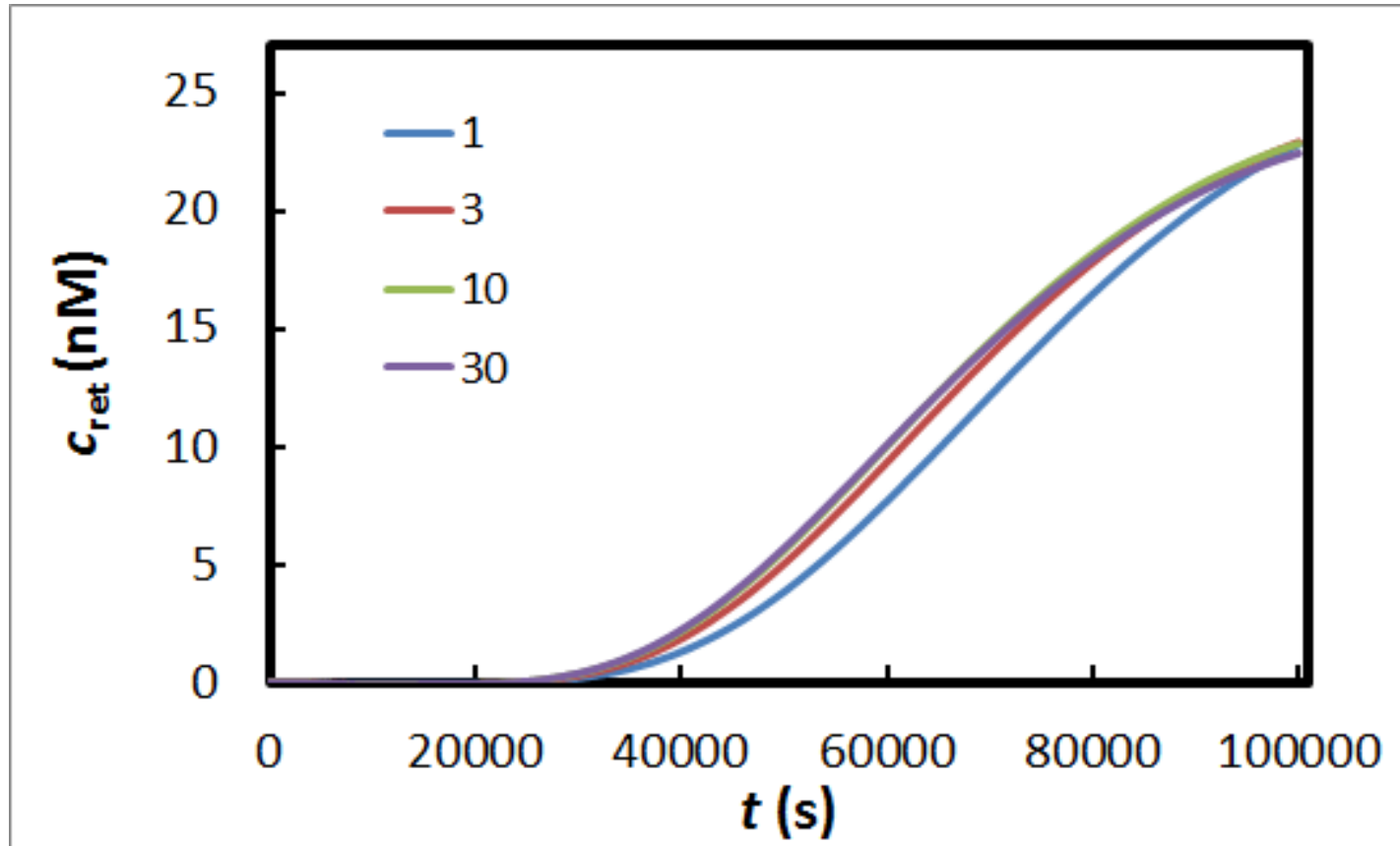
Excerpt from the Proceedings of the 2014 COMSOL Conference in Bangalore

Effect of $K_{scl/cho}$ ($\times 10^{-5}$ cm/s), $D_{scl} = 10^{-6}$ cm²/s



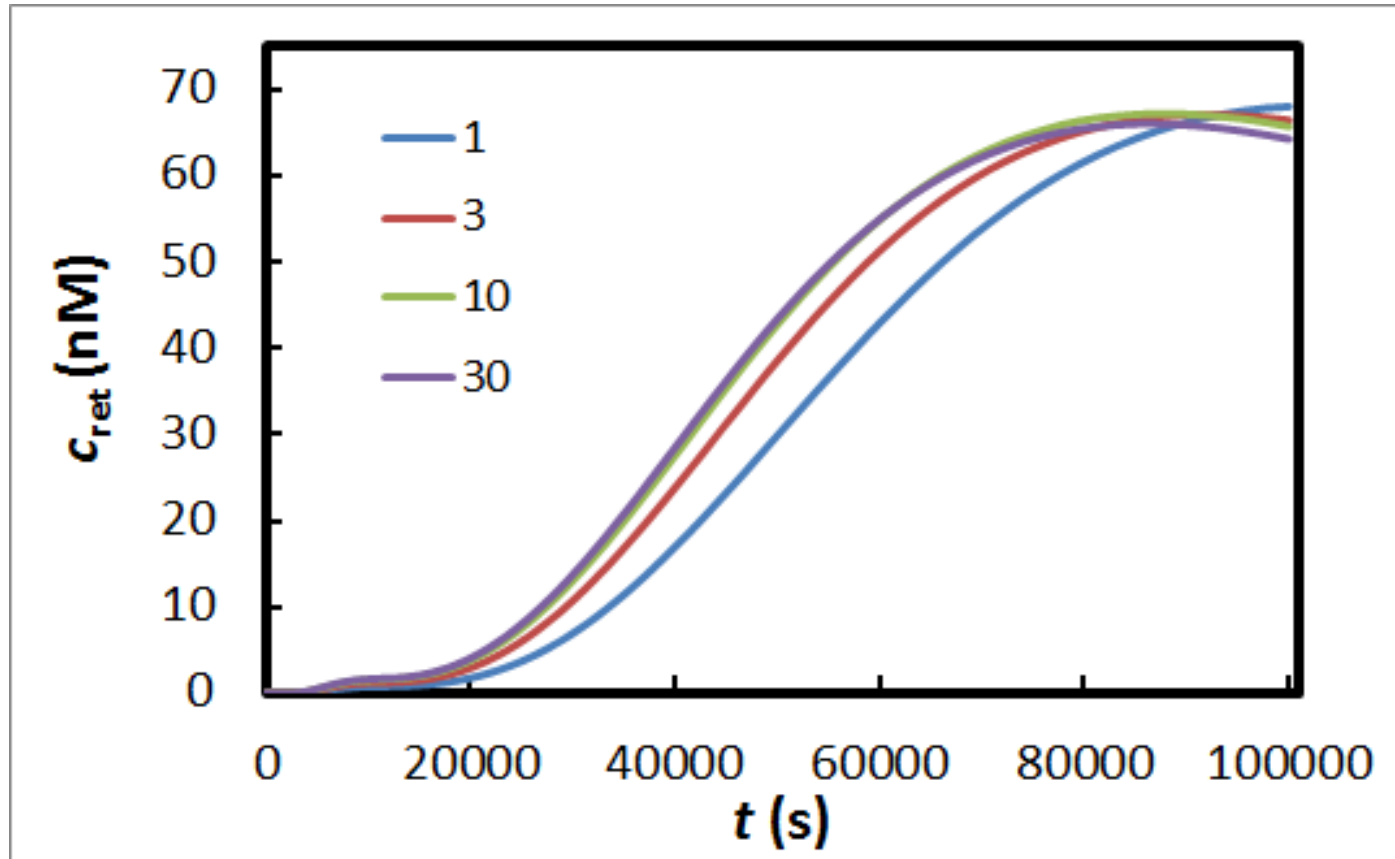
Effect of $K_{\text{scl/cho}}$ ($\times 10^{-5}$ cm/s), $D_{\text{scl}} = 10^{-6}$ cm²/s

Point evaluation in retina, opposite to patch, on "equator"



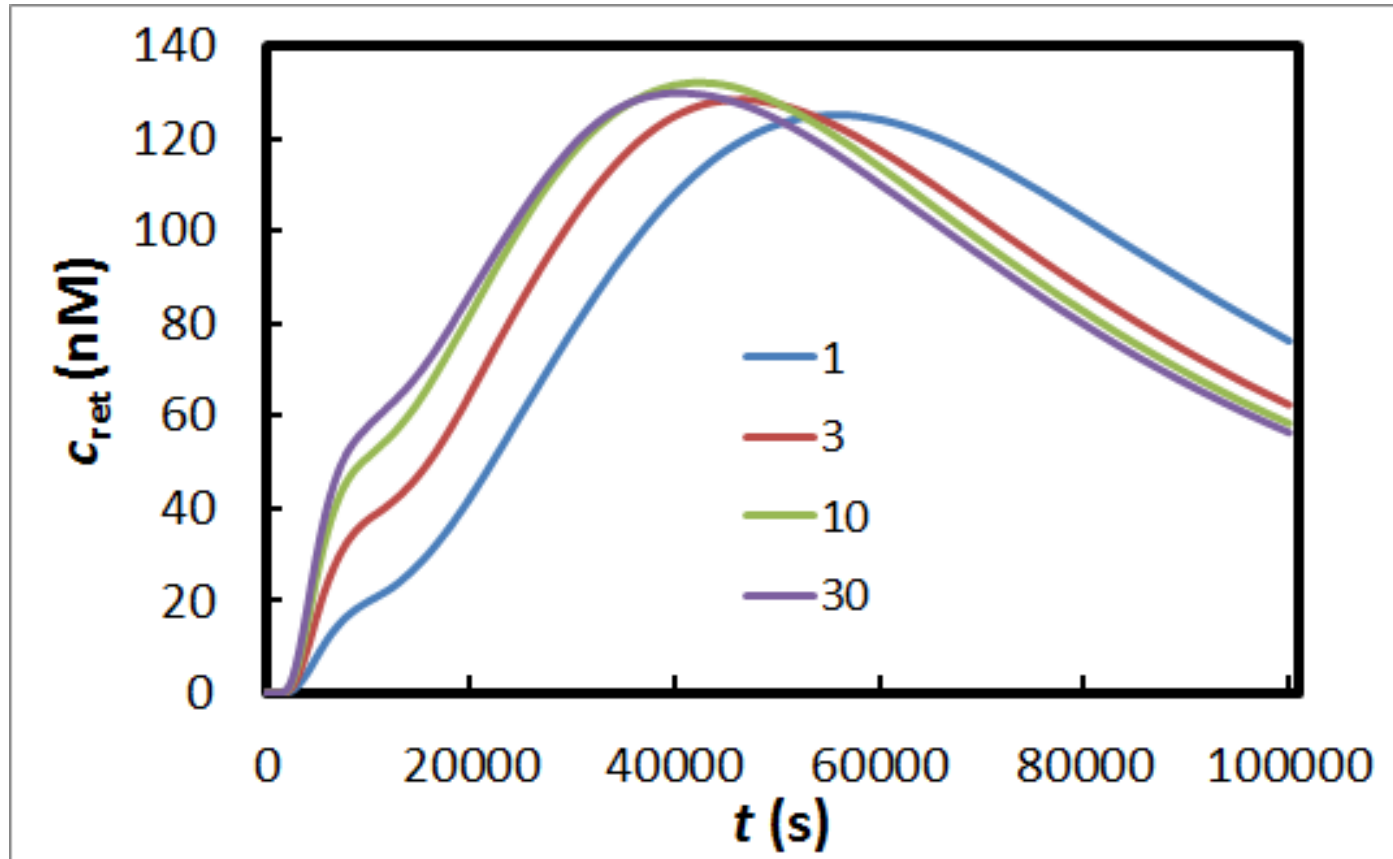
Effect of $K_{\text{scl/cho}}$ ($\times 10^{-5}$ cm/s), $D_{\text{scl}} = 10^{-6}$ cm²/s

Point evaluation in retina, on the bottom



Effect of $K_{scl/cho}$ ($\times 10^{-5}$ cm/s), $D_{scl} = 10^{-6}$ cm²/s

Point evaluation in retina, next to patch, on "equator"



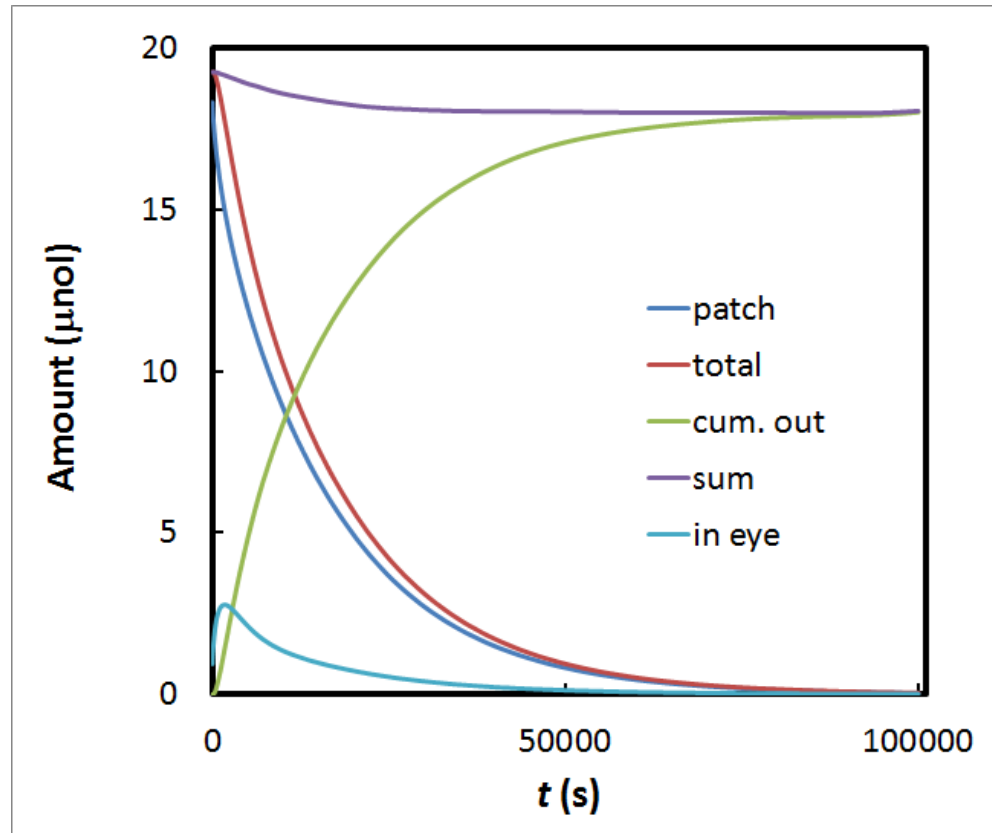
-Transport between vitreous humor and retina boundary

- Higher partition, the more hydrophilic is the drug
- Concentration of the drug is higher near to the patch
- Permeability increases the retina concentration, hence from vitreous to retina
- Partition coefficient decreases concentration in retina

Transport between retina and choroid boundary

Permeability coefficient between conclusion that retina concentration depends on the rate of efflux and influx

CHECK MASS BALANCE!



~OK

Flux of the drug out of the veins is integrated with comsol surface integral feature