UTAustin | Portugal Workshop on Modeling and Simulation of Physiological Systems

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Coagulation and Inflammation - Physiological Process for Numerical Studies

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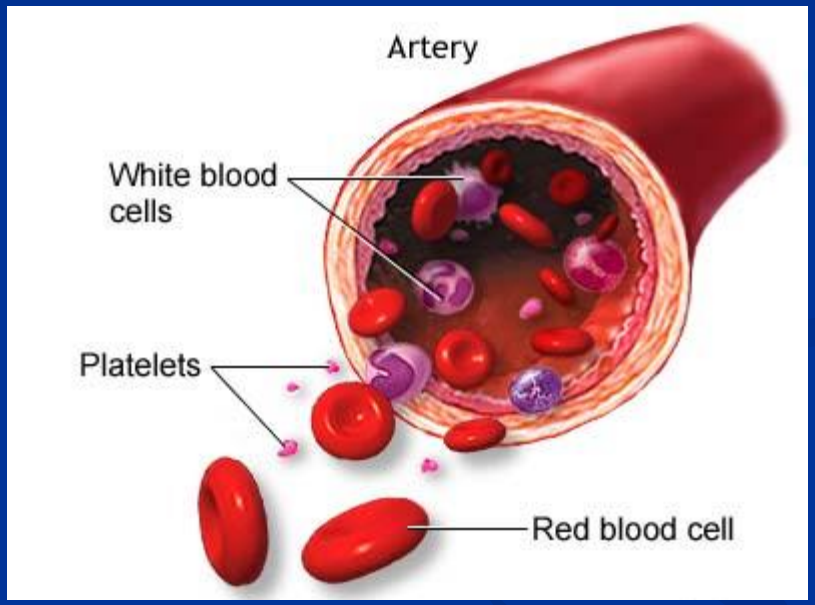
- Inflammatory response
- Experimentally addressing the inflammatory process
- Results from numerical simulations
- Conclusions

Erythrocytes, leukocytes and platelets

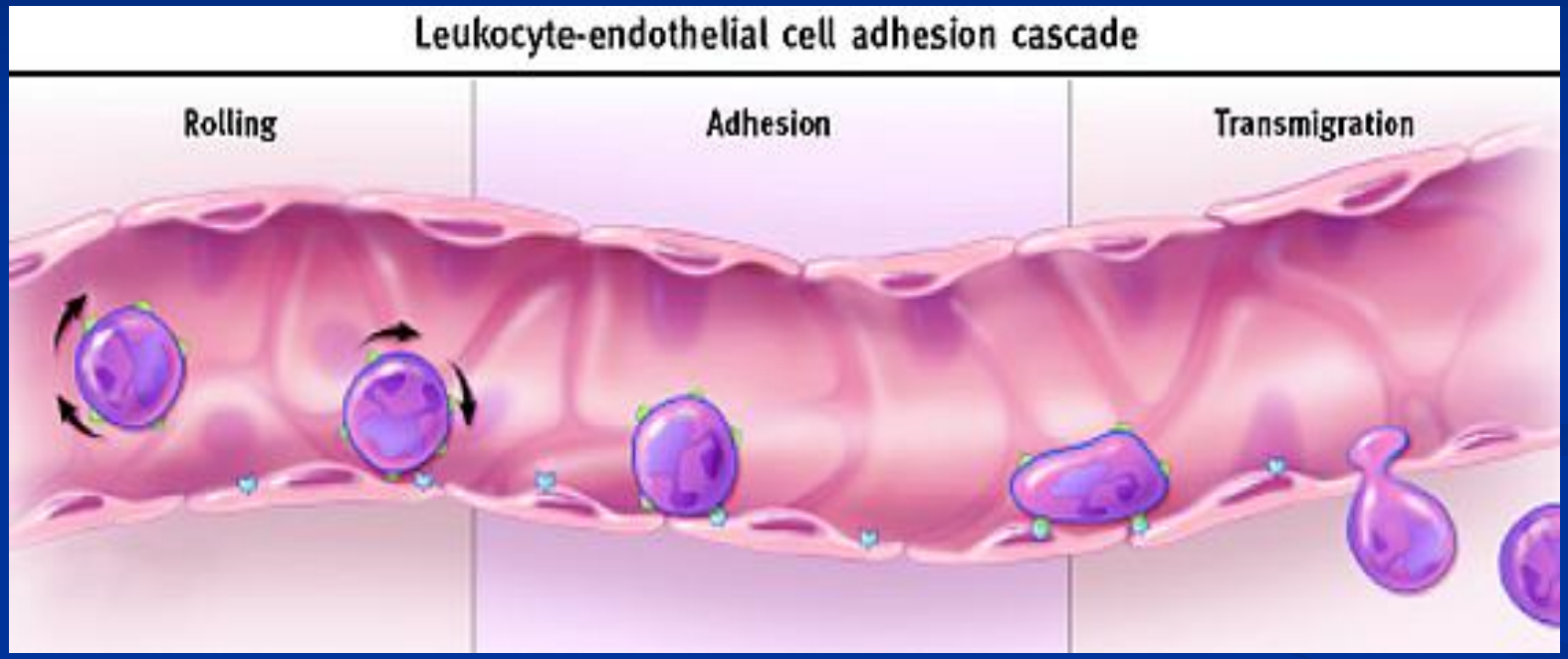
- mechanical properties of blood
- responsible for different physiological phenomena and diseased states



coagulation diseases

inflammatory process

Inflammatory process



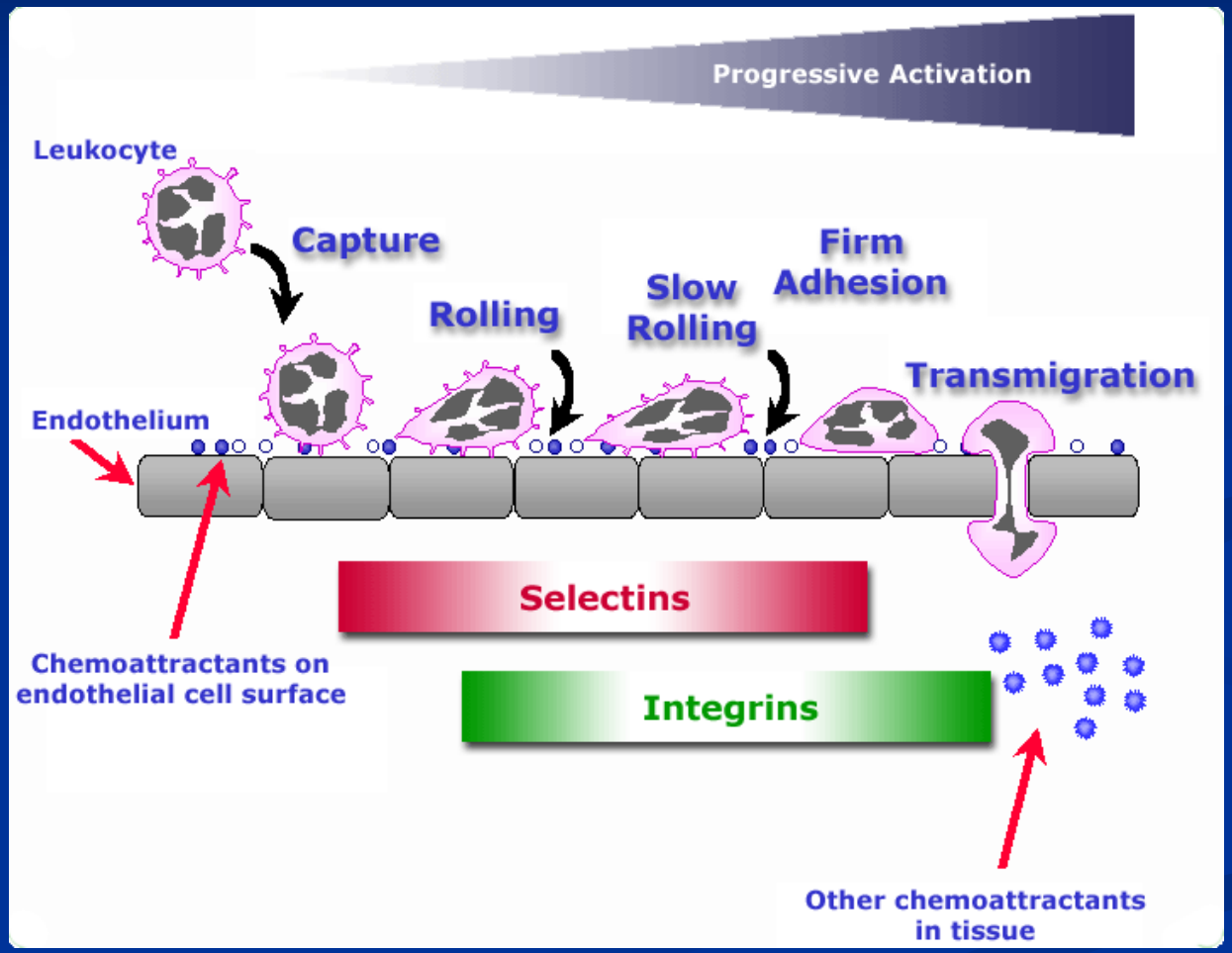
- Leukocyte recruitment (multi-step process)

Inflammatory response
Leukocytes

- activation of vascular endothelium
- attachment of leukocytes to endothelial cells
- an initial attachment is followed by low velocity rolling, then arrest of leukocytes that precedes transmigration
- Selectins are responsable for the initial attachment and for the leukocytes rolling
- Leukocytes adhesion require integrins activation

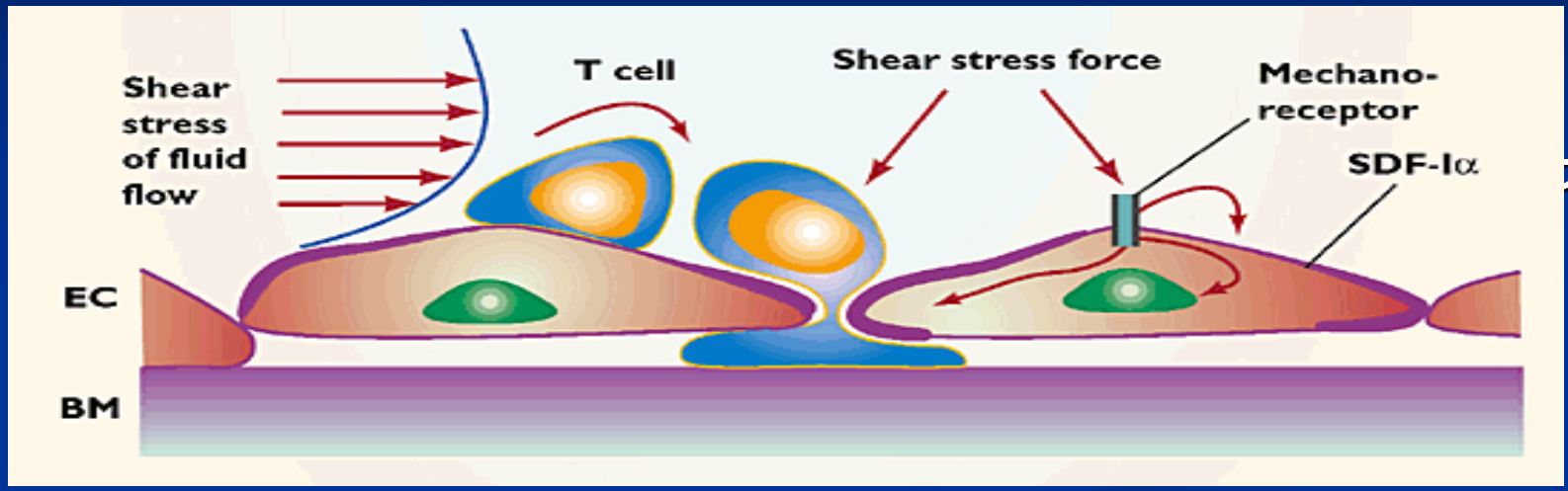
Inflammation

Inflammatory response



Inflammation

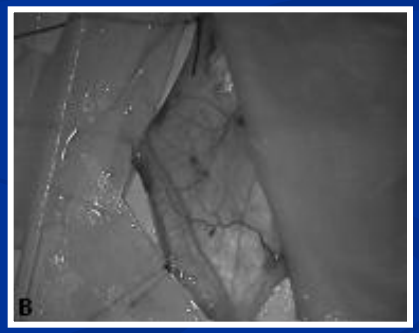
Inflammatory responses



lack the complexity of the *in vivo* situation
(RBCs, platelets and plasma which influence the blood viscosity)

Experimentally…

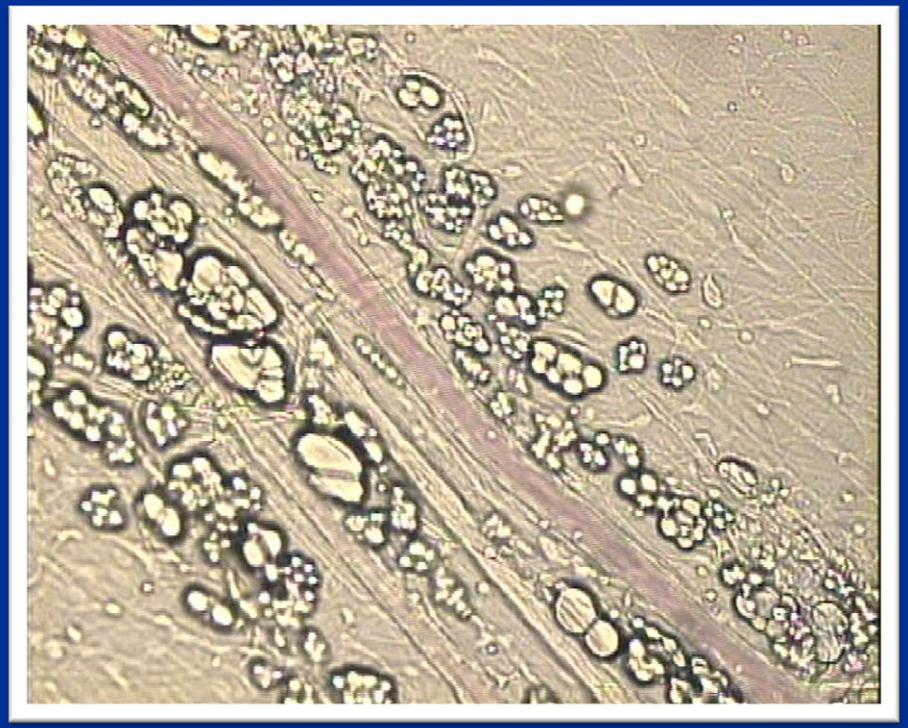
- The recruitment process can be observed in the microcirculation of *post*-cappillary venules by intravital microscopy



- Cremaster muscle preparation for microscopy observation

Experimentally…

- Post-capillary venules observation in an inverted microscope

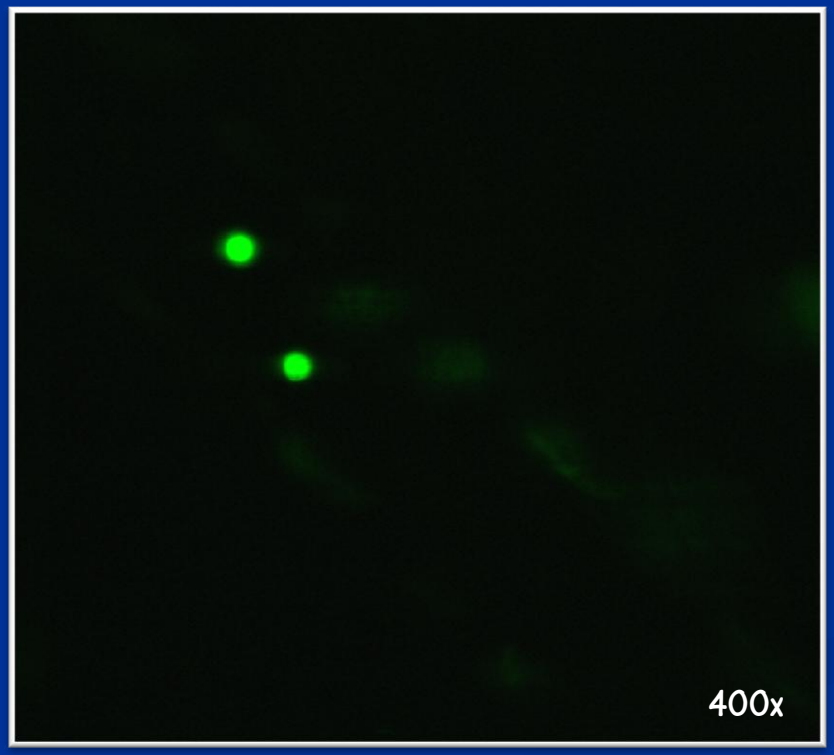


200x

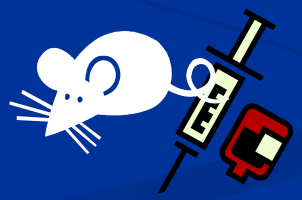
- Venule diameter
- Leukocyte diameter
- Leukocyte flux
- Adherent and rolling leukocytes
- RBC flow velocity

Experimentally…

- Intravital microscopy enables the *in vivo* determination of leukocyte-endothelial cell interactions during an inflammatory response



- *In vitro* determination of hemorheological parameters after blood sample collection



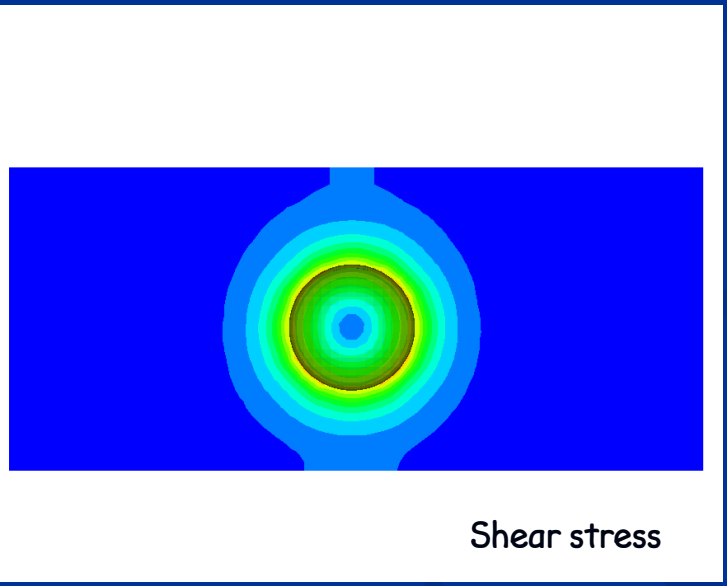
Hematocrit

Blood viscosity

Erythrocyte aggregation and deformability

From experimental results to…. numerical simulations

- using data from an *in vivo* model of inflammation
- blood as non-newtonian fluid

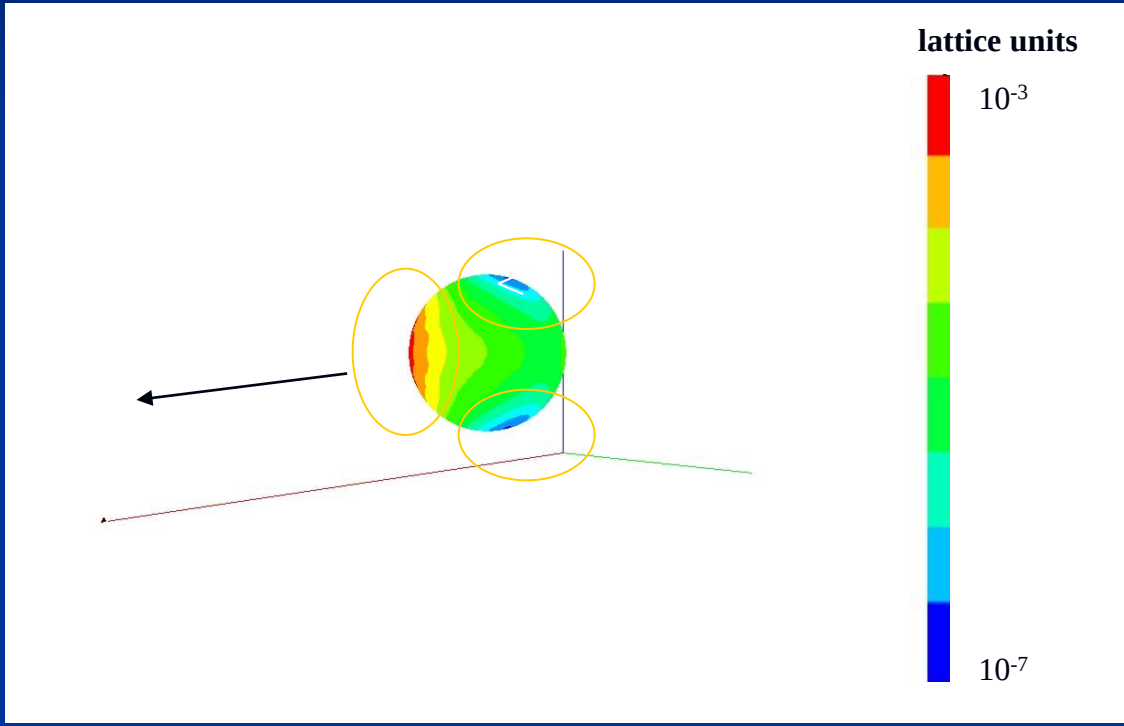


Movement towards the wall disturbes the flow at longer distances

Clin Hemorheol Microcirc 39 (1-4): 375-380 (2008)

Numerical Simulations

Single leukocyte recruitment



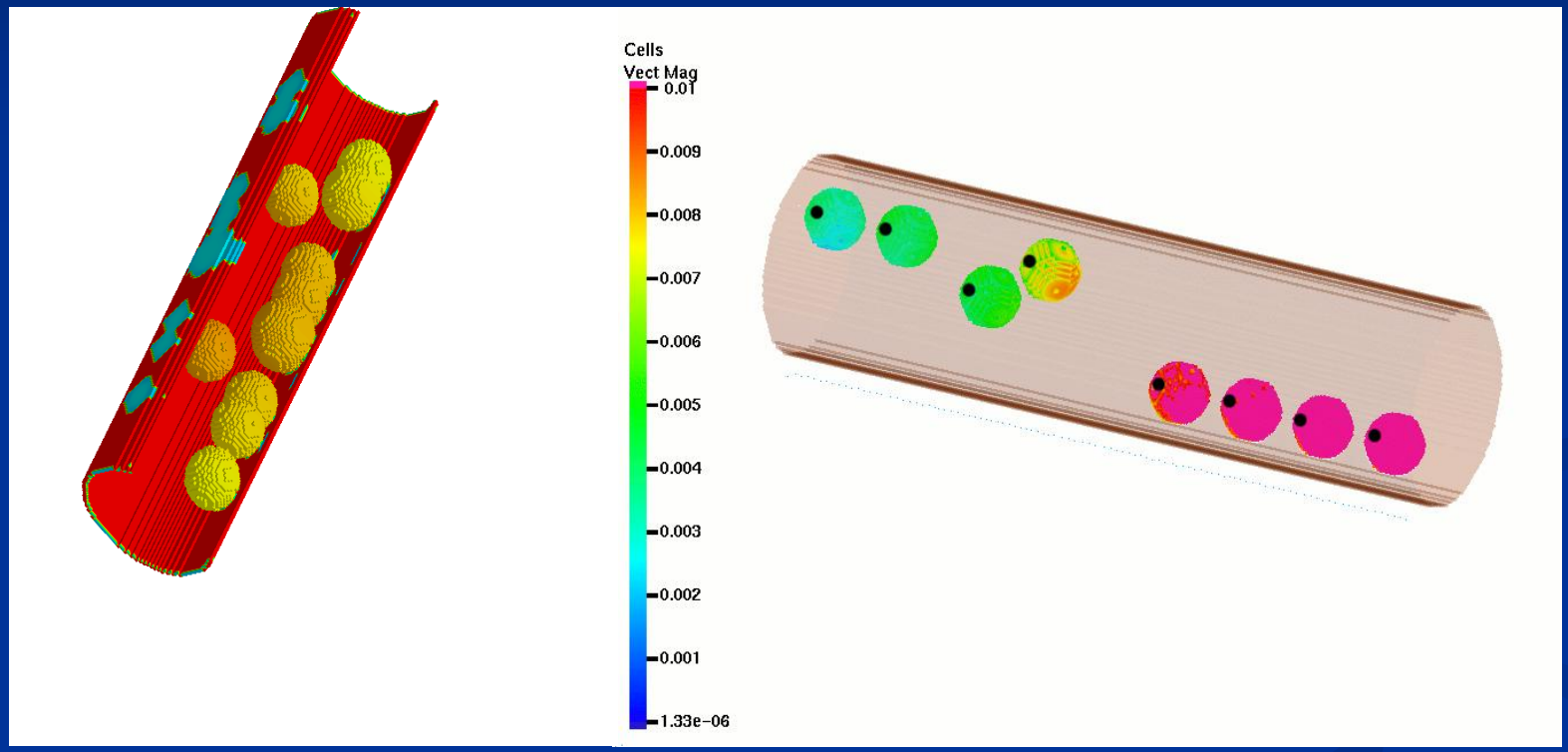
Shear stress on the leukocyte surface

Regions of maximum/minimum shear-stress probably related with maximum/minimum selectins distribution

Rolling is hydrodynamically assisted

Numerical Simulations

Multiple leukocytes kinetics

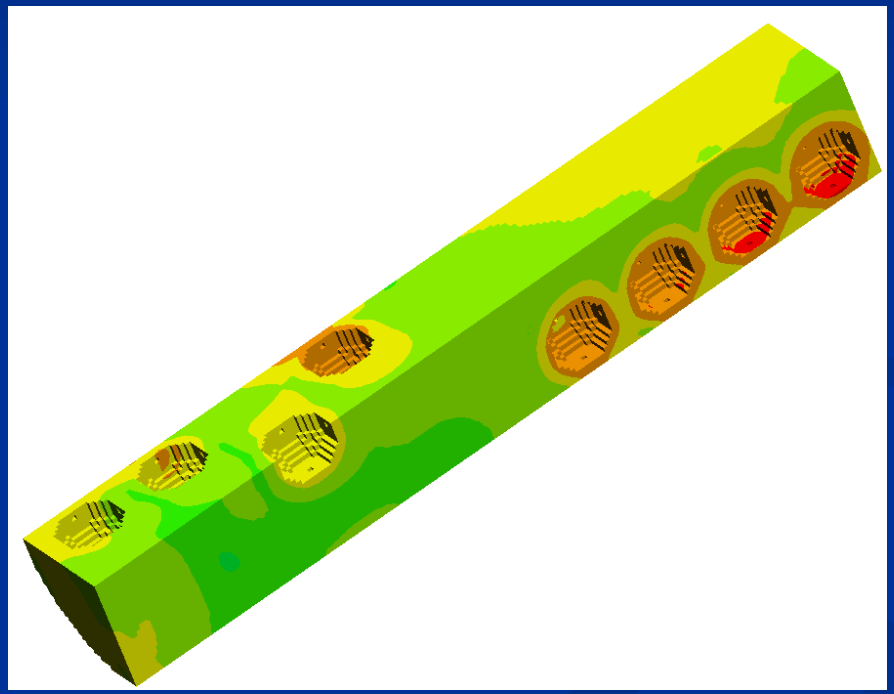


Moving clusters of leukocytes

Numerical Simulations

Multiple leukocytes kinetics

- shear stress at the endothelium gets higher when a cluster of leukocytes moves in the main stream



Initialization of the rolling process

Recruited or rolling leukocytes largely influence the endothelium wall shear stress

Conclusions

from numerical simulations

- Leukocyte accumulation is a recruitment process in which hydrodynamics is a main recruiter
- Each leukocyte influences the endothelial wall shear stress differently and can be susceptible to different mediated interactions

expression of selectins and integrins

Conclusions

- The inflammatory process is a multifactorial process
- Experimentally it is not possible to manipulate/study, at the same time, all the involved parameters

Numerical modeling can be a strong tool because a higher number of parameters can be taken into account

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Professora Doutora Carlota Saldanha
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Thank you!

Professora Doutora Adelia Sequeira

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