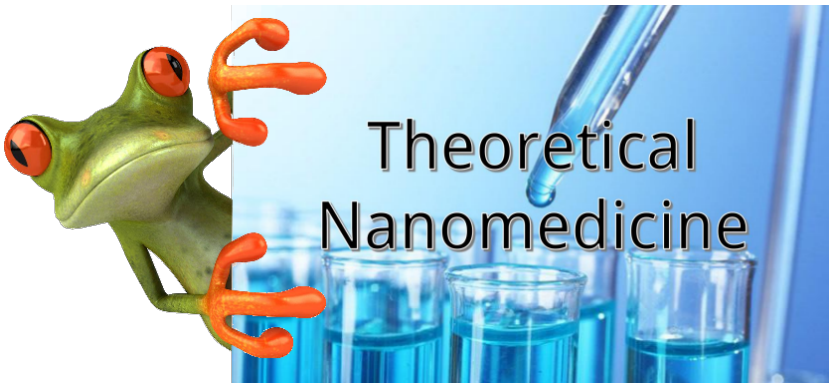
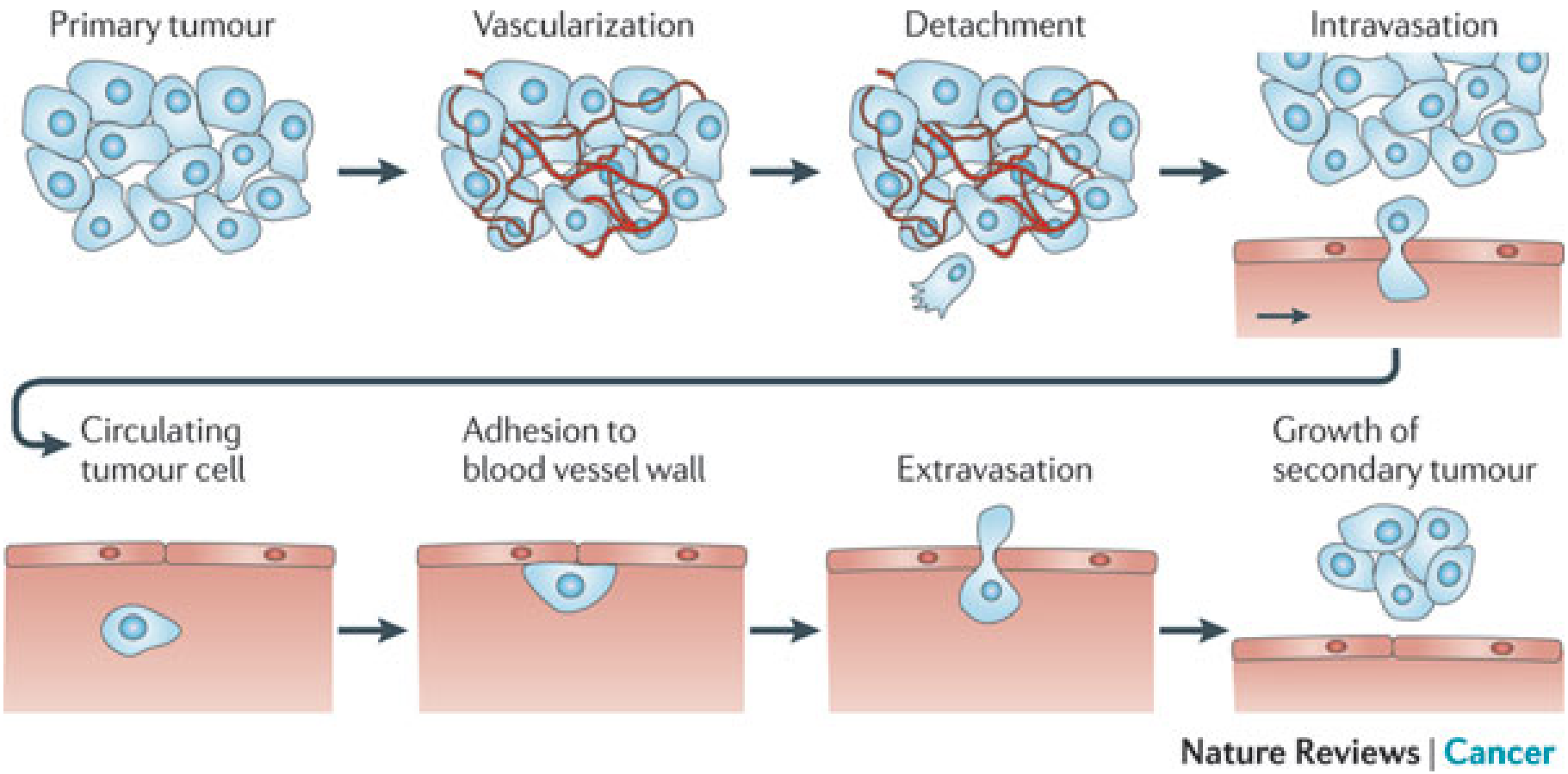
ISTITUTO ITALIANO
DI TECNOLOGIA
NANOTECHNOLOGY
FOR PRECISION MEDICINE

Vascular transport of adhesive particle in capillary flows



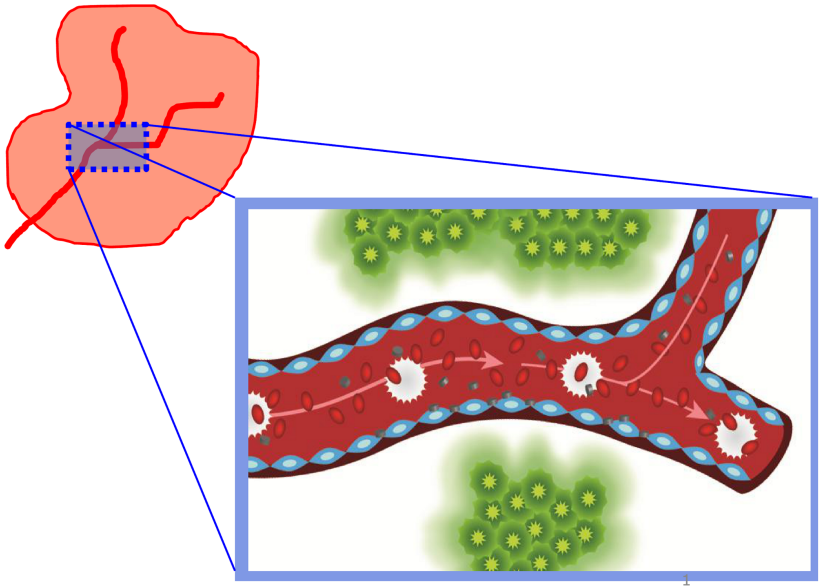
Alessandro Coclite, PhD

May nanomedicine address the challenge?



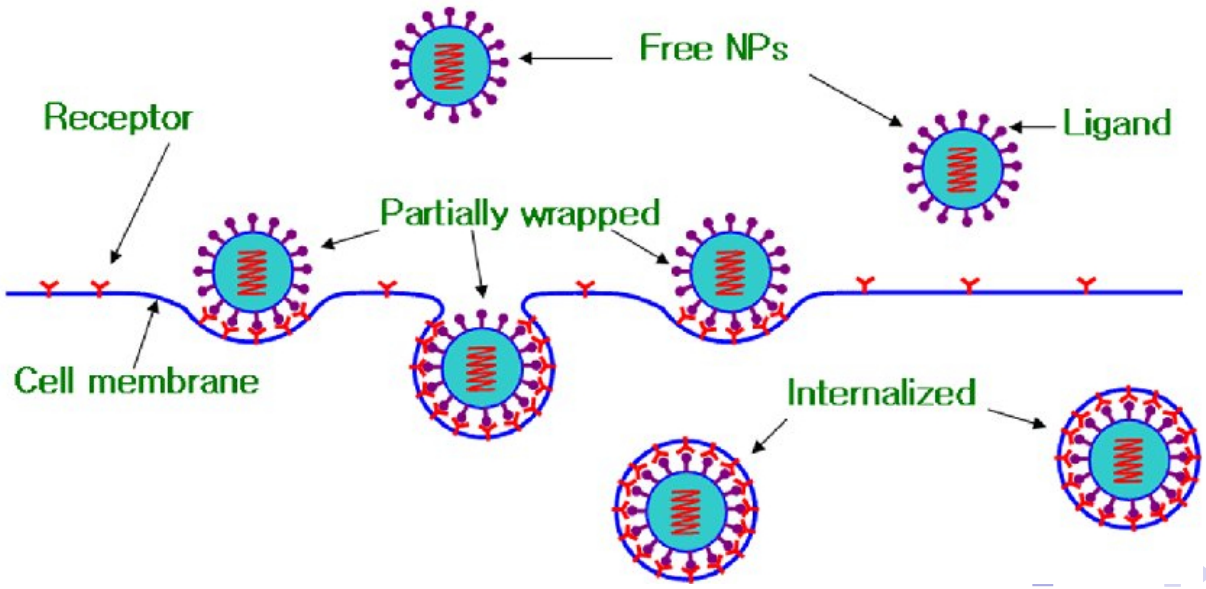
Wirtz, D. et al. "The physics of cancer: the role of physical interactions and mechanical forces in metastasis." Nature Rev. Cancer 11, 512522 (2011)

Vascular journey of a particle: Margination and adhesion.

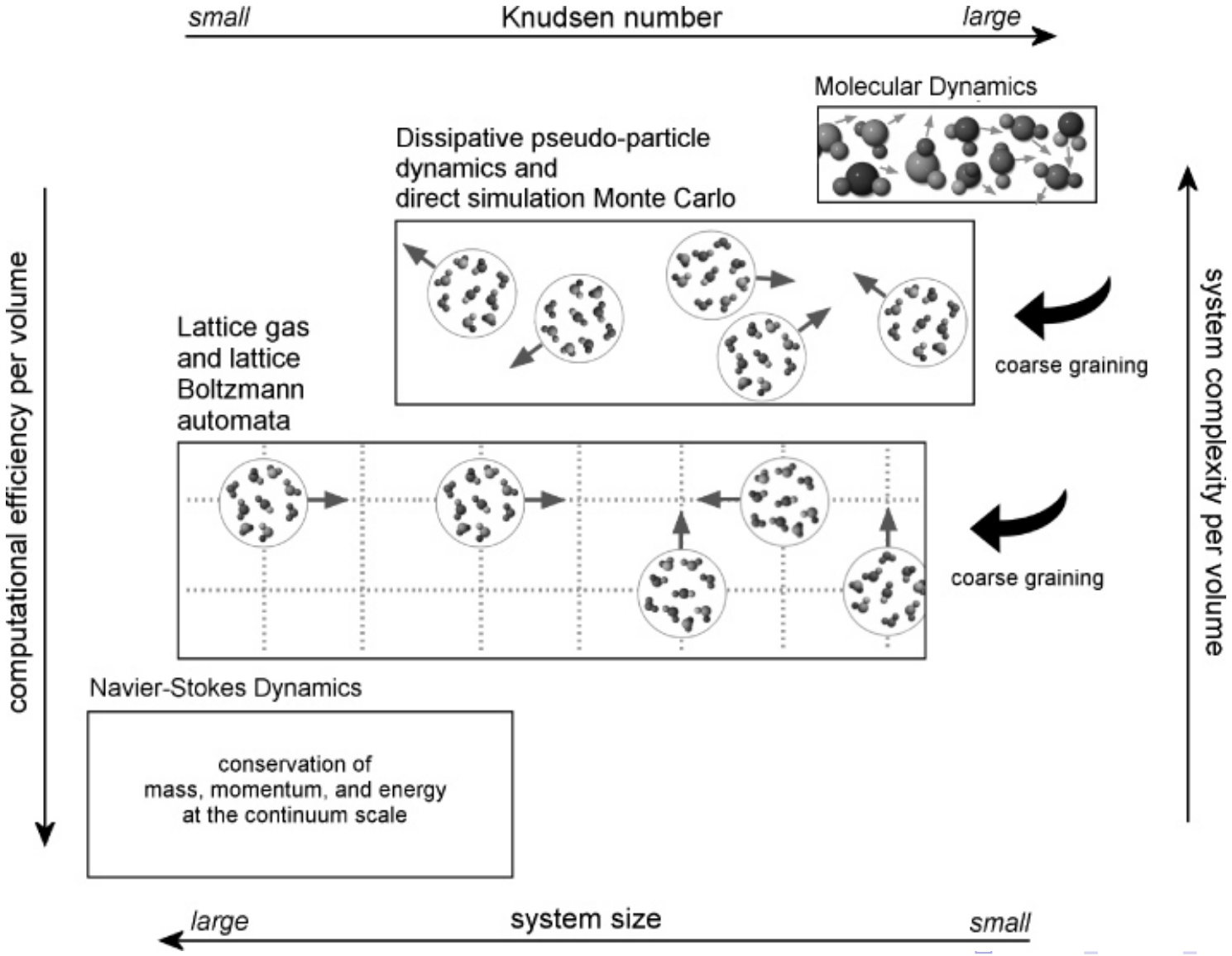


Design parameters:

- Size, Shape, Stiffness, and Surface properties;
- Reynolds number, Shear rate;
- Particle/fluid density ratio.

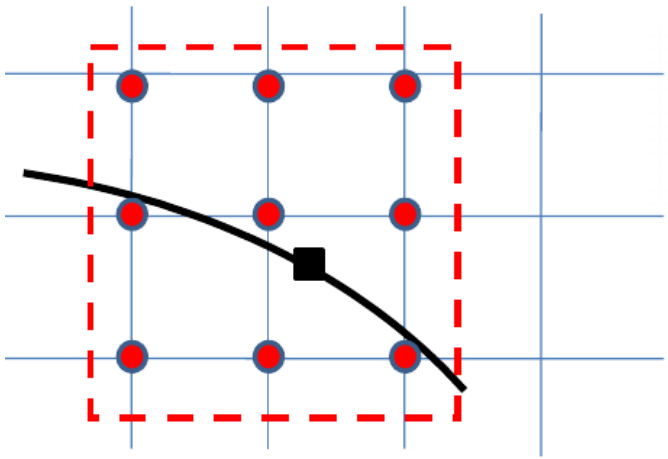


Why do we need to solve Boltzmann's equation?



Lattice-Boltzamnn–Immersed-Boundary Method

- Compute forcing at the Lagrangian markers
- Transfer the forcing at the Eulerian grid points
- The scaling factor, c_l, is such that the total forcing is not altered by the transferring process



$$\hat{\boldsymbol{U}}(\boldsymbol{x}) = \sum_{k=1}^{ne} \phi_k^l(\boldsymbol{x})\, \hat{\boldsymbol{u}}_k$$

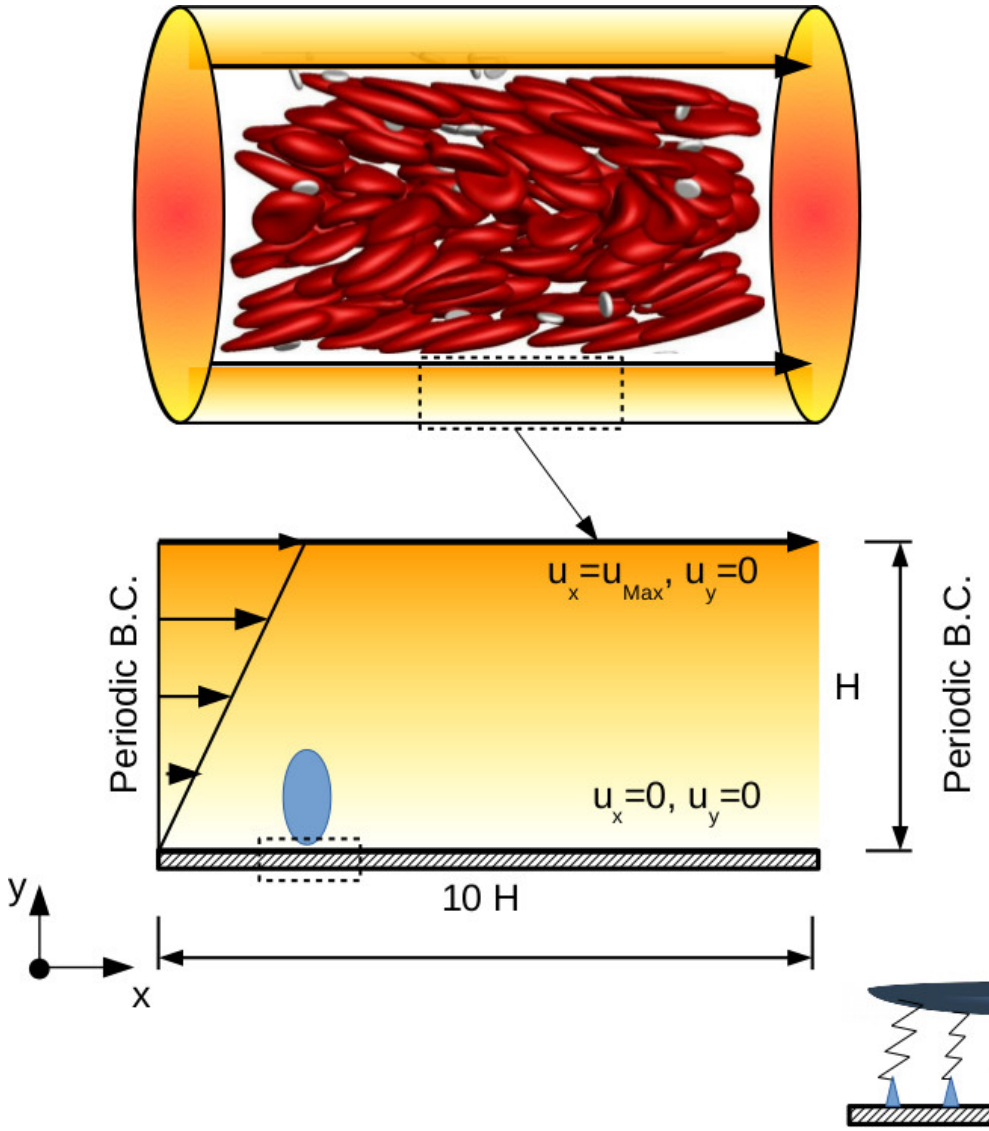
$$\hookrightarrow \quad \boldsymbol{F} = \frac{\boldsymbol{U}_b - \hat{\boldsymbol{U}}}{\Delta t}$$

$$\hookrightarrow \quad \boldsymbol{f}^k = \sum_{l=1}^{nl} c_l\, \phi_k^l \boldsymbol{F}_l$$

$$\mathcal{F}_i = \left(1 - \frac{1}{2\tau}\right)\vec{\omega}_i \left[\frac{\vec{e}_i - \vec{u}}{c_s^2} + \frac{\vec{e}_i \cdot \vec{u}}{c_s^4}\vec{e}_i\right] \cdot \vec{f}\,,$$

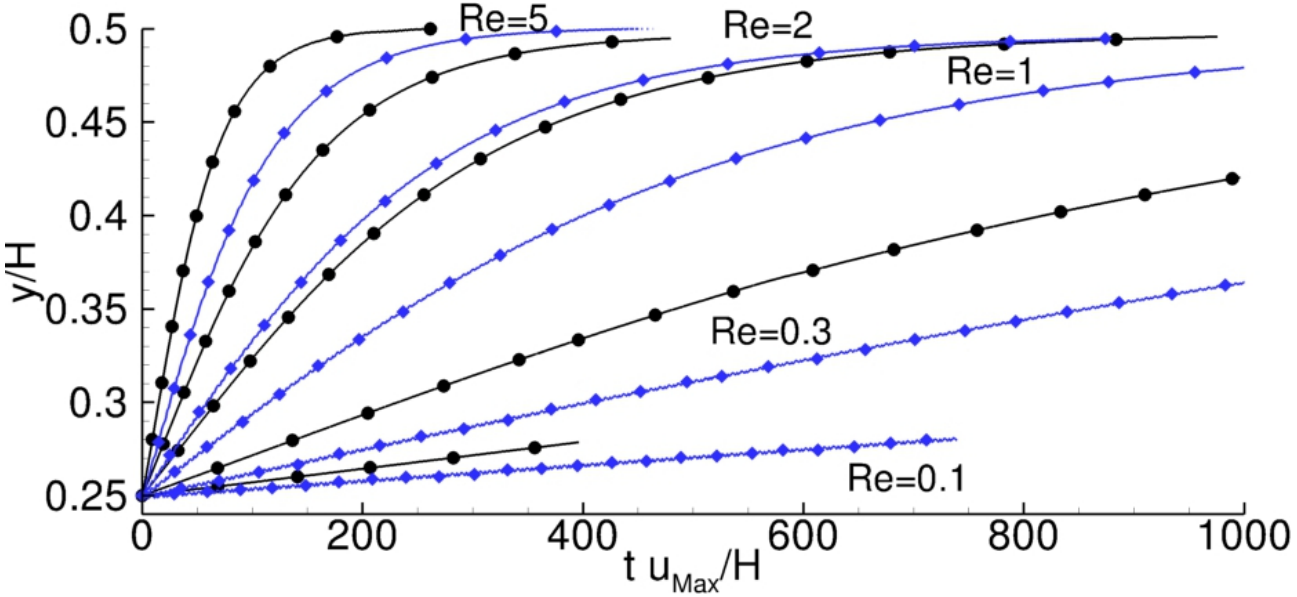
$$f_i(\vec{r} + \vec{e}_i \Delta t, t + \Delta t) - f_i(\vec{r}, t) = -\frac{\Delta t}{\tau}[f_i(\vec{r}, t) - f_i^{eq}(\vec{r}, t)] + \Delta t \mathcal{F}_i\,.$$

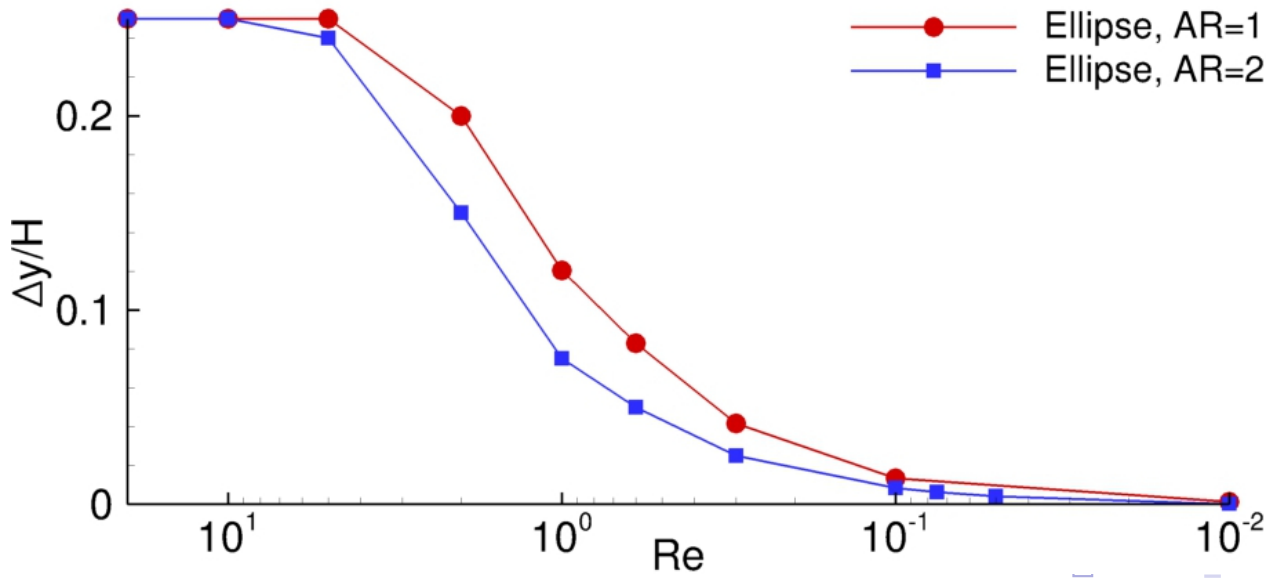
Physical problem



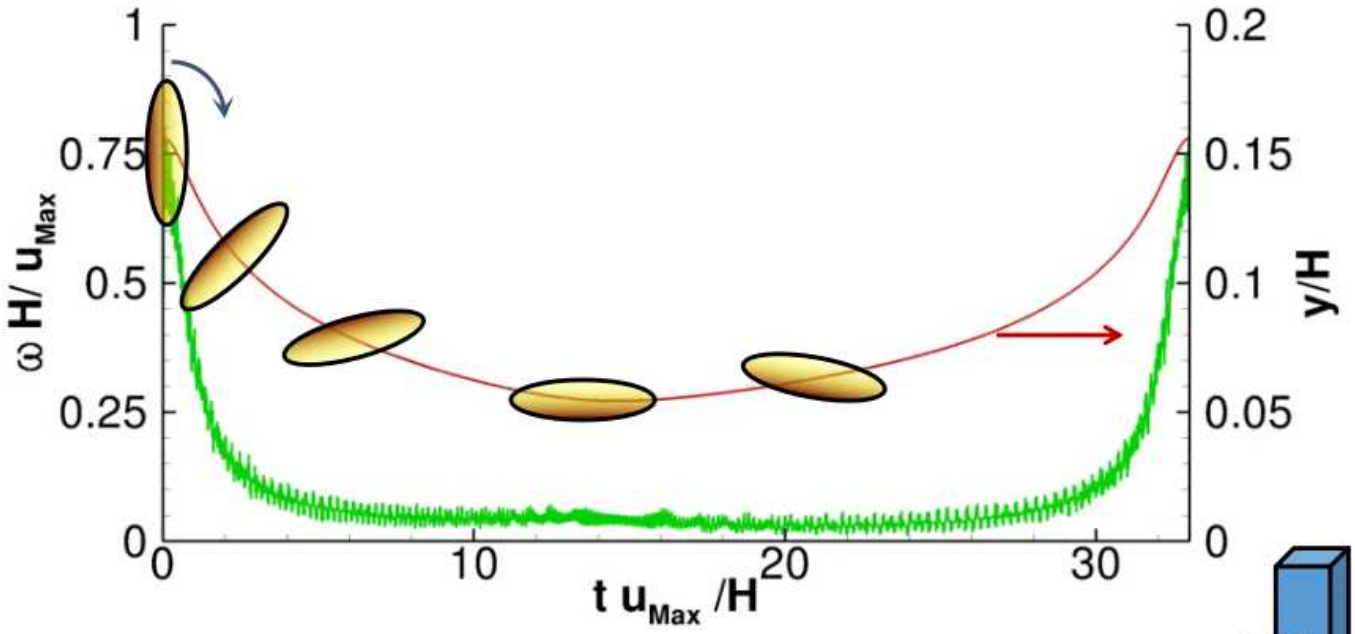
- $\mathrm{Re}=\frac{u_{Max}\,L_{ref}}{\nu}$ =0.1, 0.01
- L_{ref} =H,
- $\rho_l = N_l/A$ =0.3–0.9,
- $\rho_r = 1$,
- $BR = 4$,
- $H_k = 5 \times 10^{-21}$ J,
- $\sigma = 2 \times 10^{-3}$ N/m,
- $AR = 1, 2, 3$.

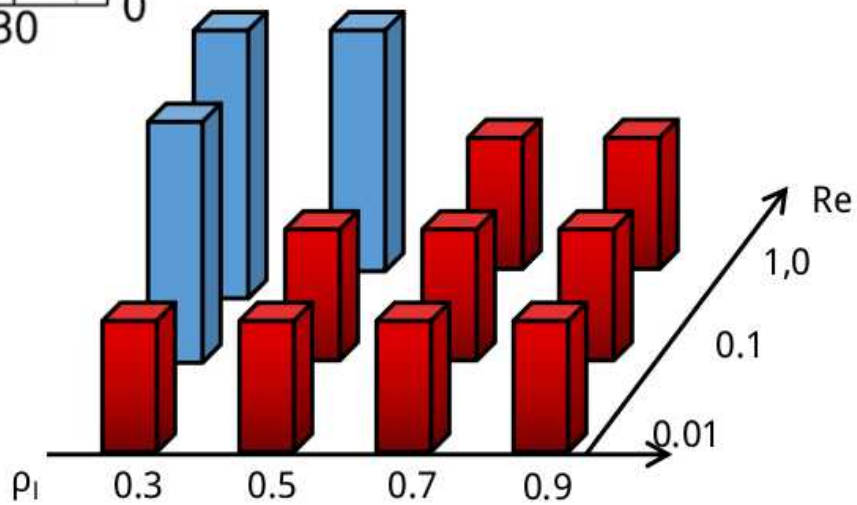
Elliptical Cylinder, AR=1,2 (Re=20, 0.1) transport



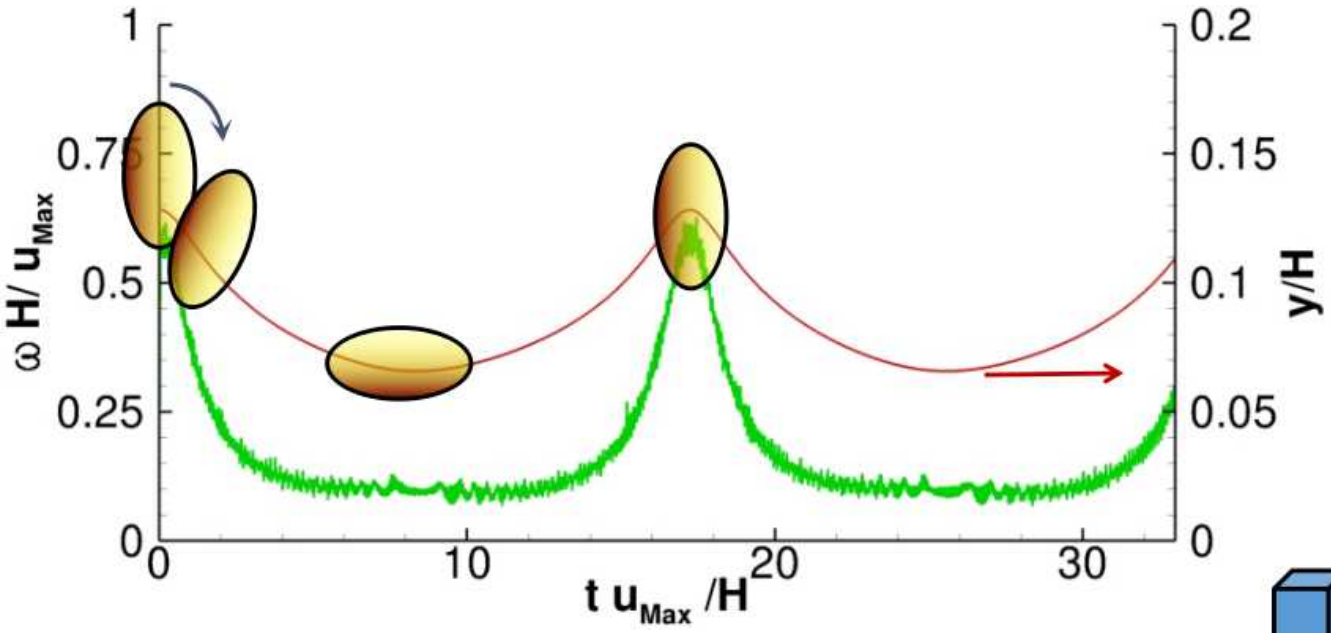


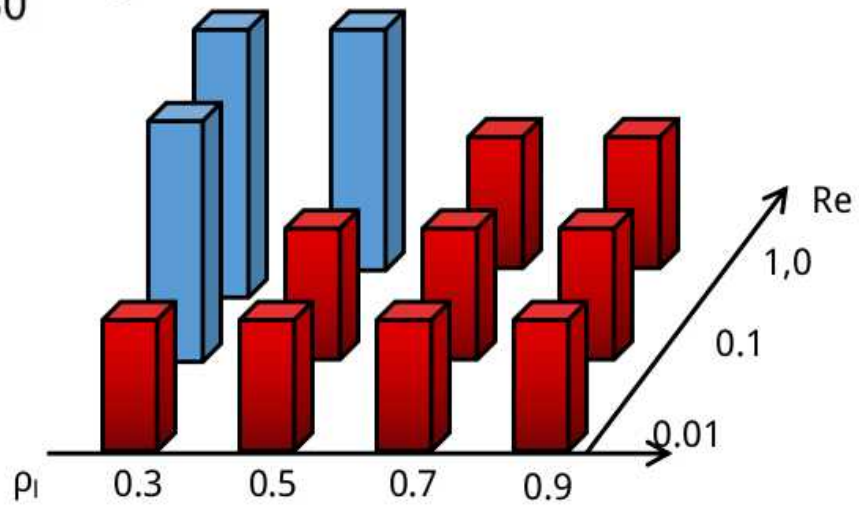
Elliptical Cylinder, AR=3 (Re=0.1) near wall motion





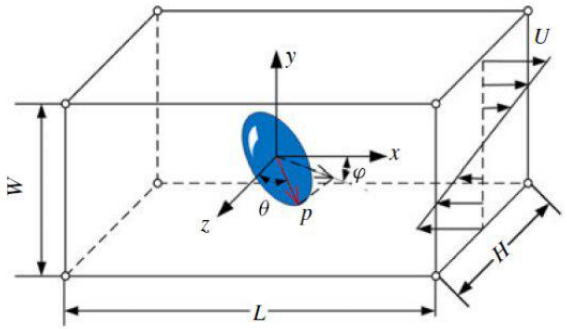
Elliptical Cylinder, AR=2 (Re=0.1) near wall motion

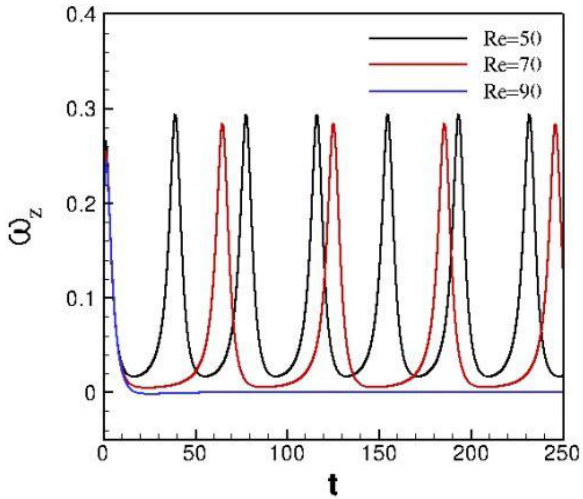


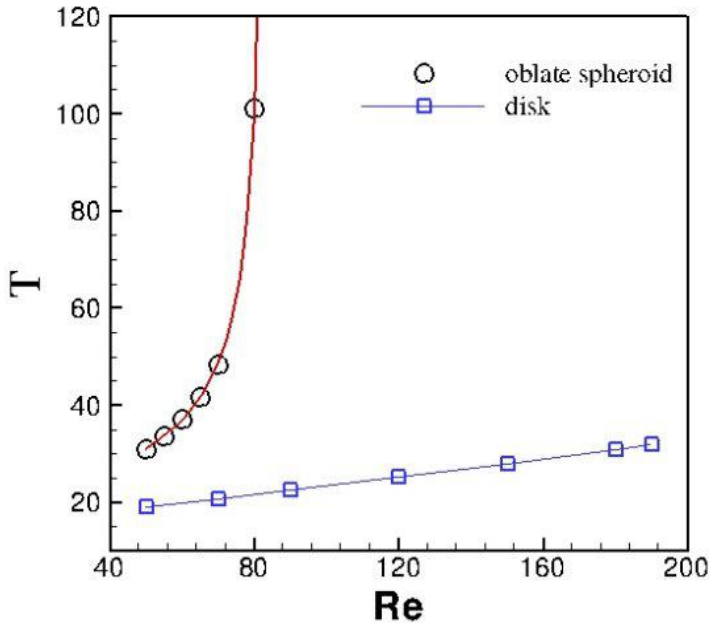


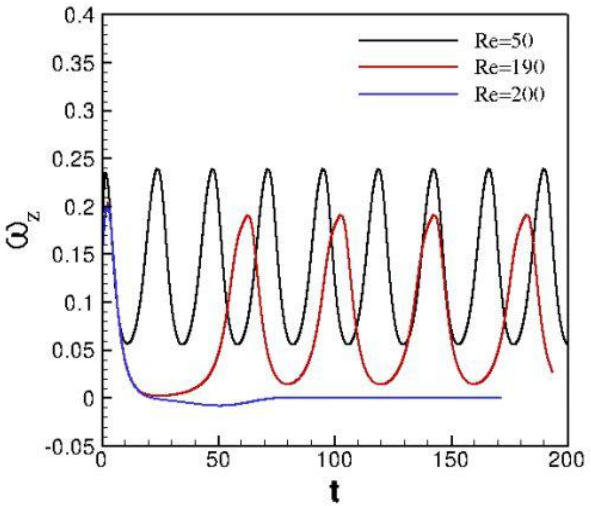
3D-particle in shear flow. (by Dr. Ing. S. Ranaldo)

- *Domain: 4 a x 4 a x 4 a*
- *Re = $8Ua^2/(W\nu) = 0.5$*

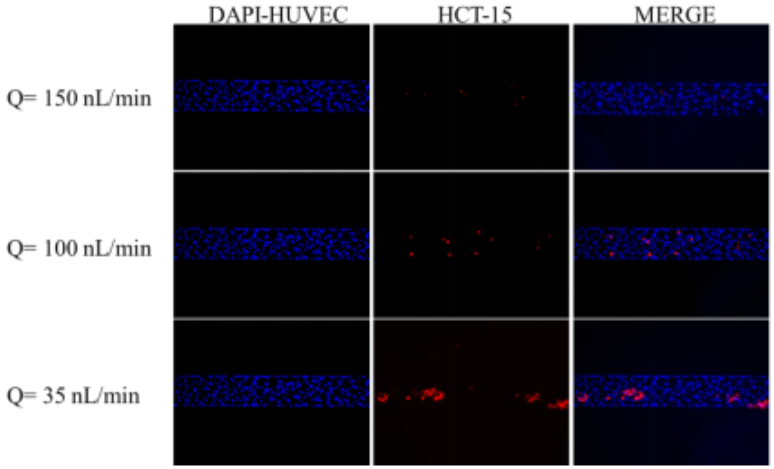


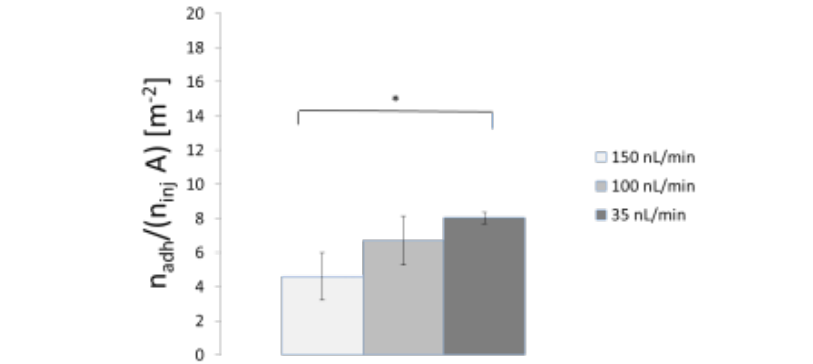




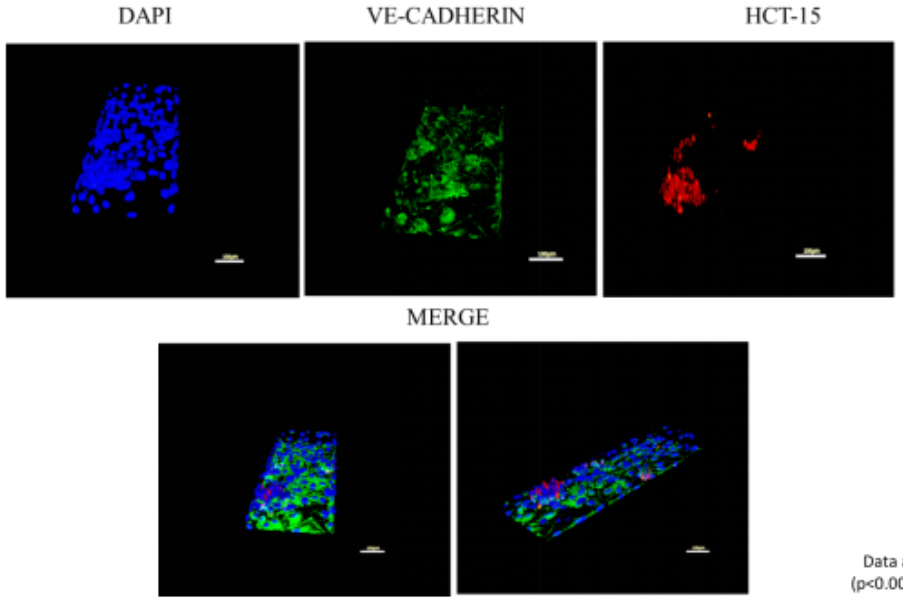


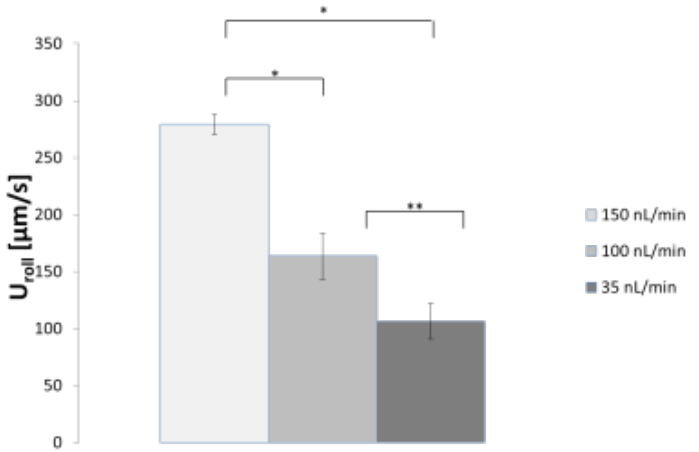
Cells adhesion mechanics. (by Dr. H. Mollica)





The number of firmly adhering cells is normalized by the total number of injected cells (10^6) and the area of the region of interest ($A=1,22*10^{-6}$ [m^2]). Data are plotted as mean ± SD. N=3. Statistical analysis ANOVA. The star symbol denotes significant difference ($p<0,05$) as compared to 35 nL/min





Rolling velocity of HCT-15 cells on Huvec monolayer at 150, 100 and 35 nL/min
Data are plotted as mean ± SD. N=3. Statistical analysis Anova. ** symbol denotes significant difference ($p<0.001$) as compared to CTR 100 nL/min. * symbol denotes significant difference ($p<0.001$) compared to CTR 150 nL/min

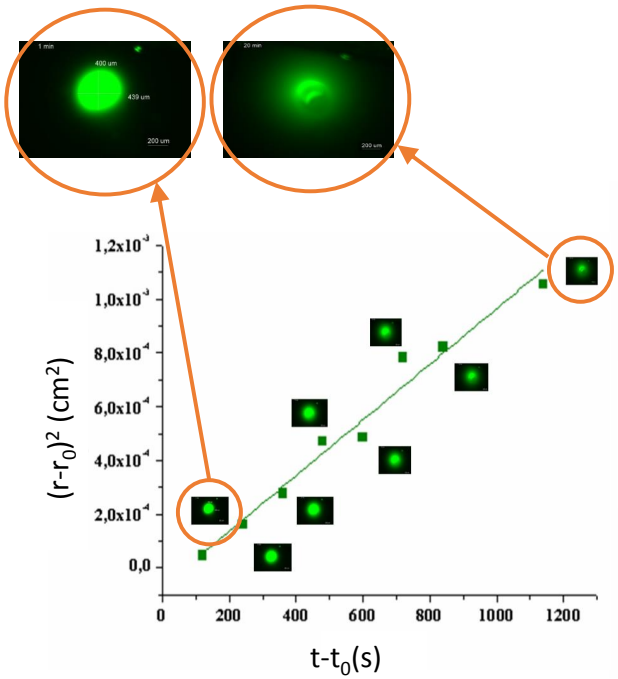
Free-drugs VS Nanoparticulate-drugs. (by Dr. V. Lusi)

Diffusion study of **3 drug models** In **Tumoral Extracellular Matrix model made by Collagen type I**.

$$D^*_{xx} = \frac{<MSD_x>}{2t} \qquad < MSD_x > = \frac{1}{n}\sum_{i=1}^{n}\left(x_i(t) - x_i(0)\right)^2$$

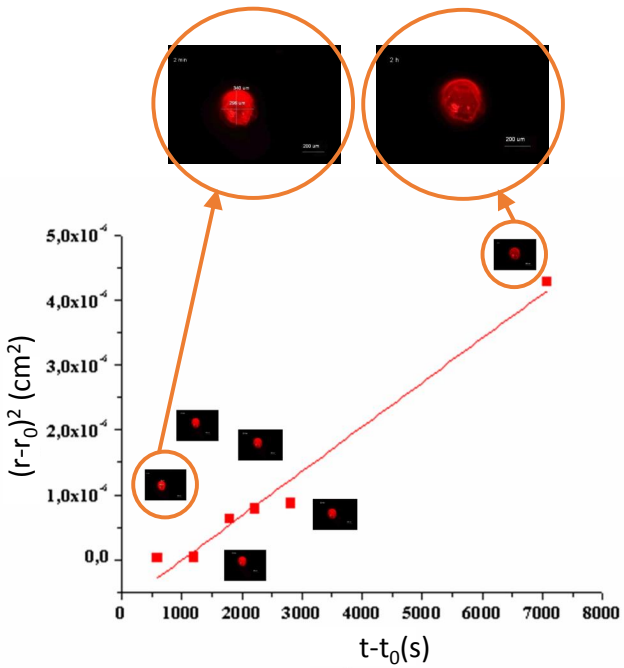
Free drug model

D=2,5x10^{-7}± 1,73x10^{-7} cm^2/s



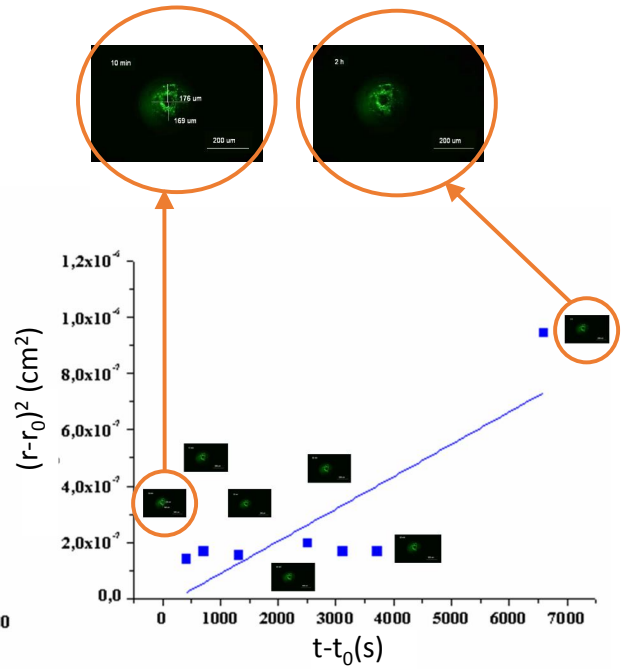
Nanoparticulate drug model (200 nm beads)

D=1,99x10^{-10}± 1,24x10^{-10} cm^2/s



Nanoparticulate model (750 nm beads)

D=8,30x10^{-11}± 6,28x10^{-11} cm^2/s



Decuzzi Lab

Antonio Cervadoro, Ph.D. - BioEng.
Alessandro Coclite, PhD - Comp. Mech.
Daniele Di Mascolo, PhD - BioEng.
Miguel Ferreira, PhD - Chemistry
Francesca Macchi, PhD- Neuro Biol.
Chiara Manneschi, PhD - BioPhyhsics
AnnaLisa Palange, PhD - Biotechn.
Roberto Palomba, Ph.D. - Cancer Biol.
Rui Perreira, PhD - Tissue Eng.
Marianna Colasuonno, PhD Student
Martina Di Francesco, PhD - Pharma
Valeria Lusi, PhD student
Hilaria Mollica, PhD student
Rosita Primavera, PhD Biotech
Ilaria Francesca Rizzuti, PhD Student
Marco Miali, PhD student

Financial Supports

CPRIT Cancer Prevention & Research Institute of Texas
National Cancer Institute
DARPA
Alliance for NanoHealth
TATRC
AIRC Associazione Italiana per la Ricerca sul Cancro
erc European Research Council Established by the European Commission
iit nPMed Istituto Italiano di Tecnologia Nanotechnology for Precision Medicine

(FP7/2007-2013) ERC Grant Agreement n° 616695