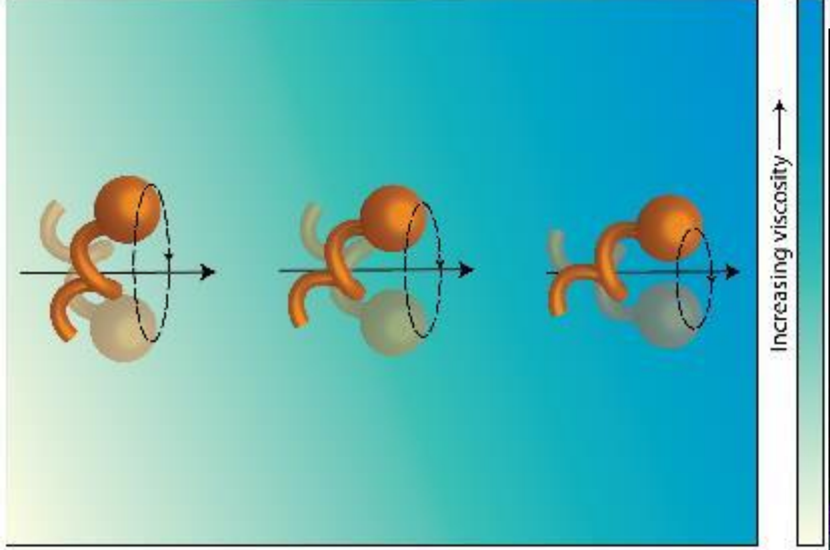
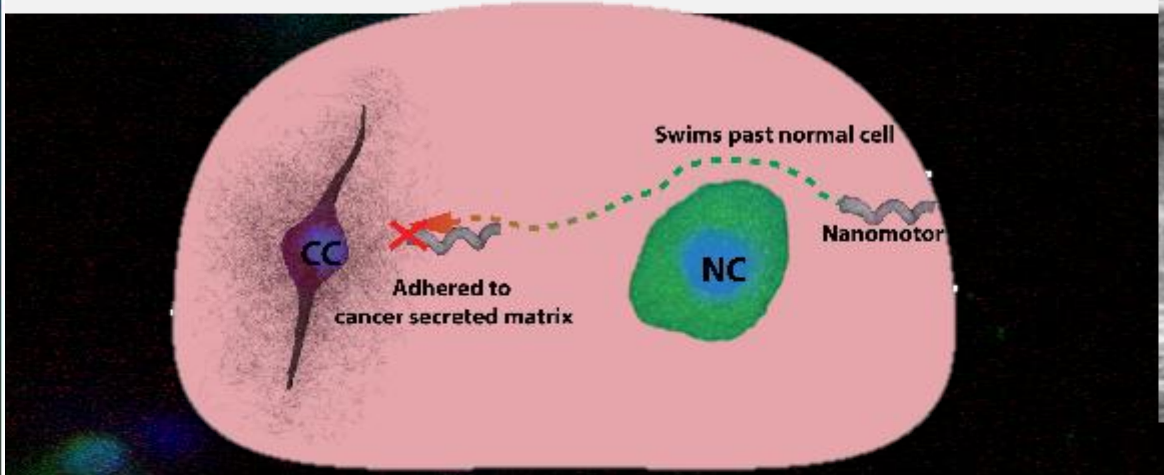
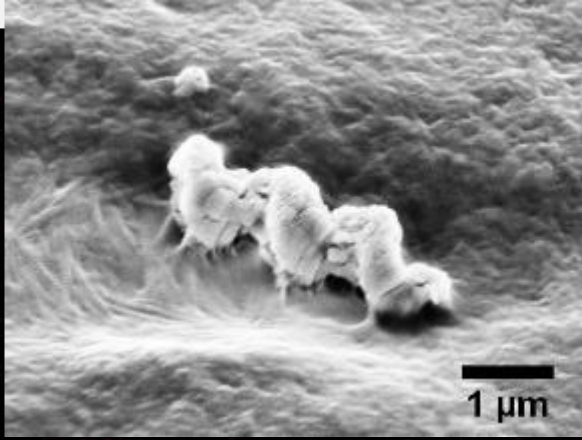
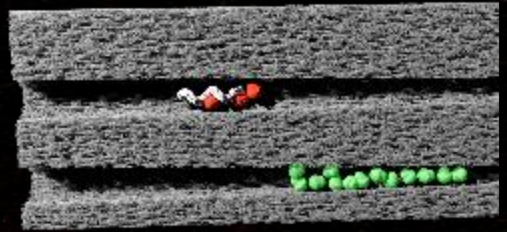








APPLICATIONS OF MAGNETIC HELICAL NANOMOTORS

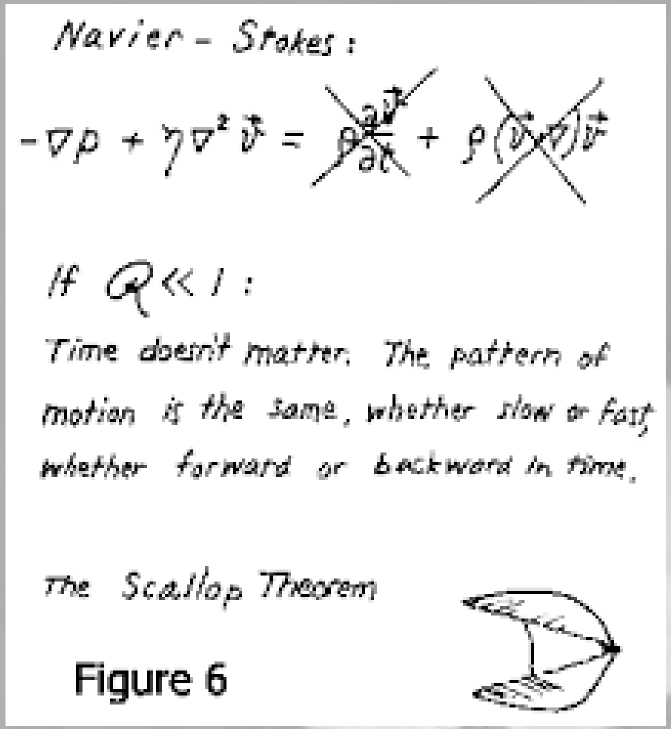
Debayan Dasgupta

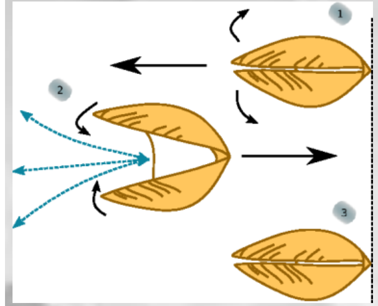
Outline

- Micro-rheology using nanomotors
- Probing the cancer microenvironment
- Nanomotors in real world

Helical Swimmers

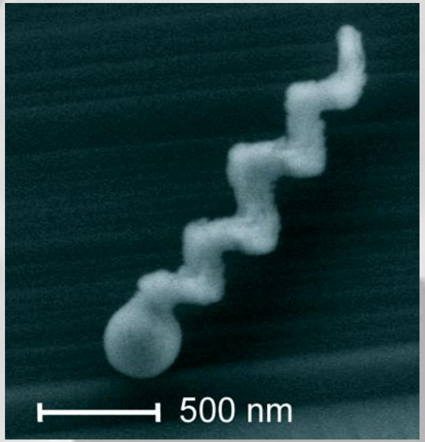
Helix satisfies the non-reciprocal condition needed to swim at low Reynolds number





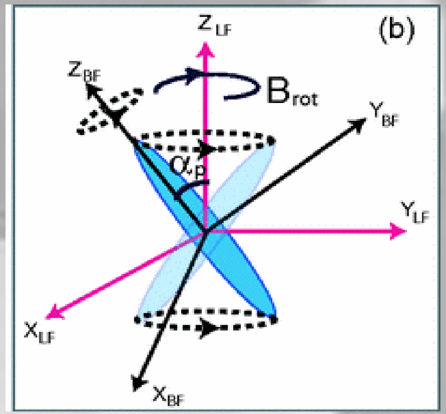
American Journal of Physics 45, 3 (1977)

Glancing Angle Deposition to fabricate helix



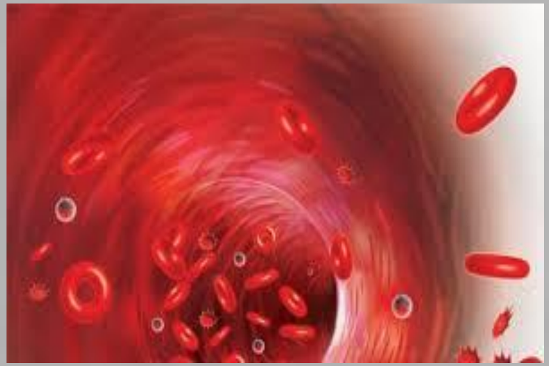
Nano Lett. 2009, 9, 6, 2243–2245

Dynamics of nanomotors

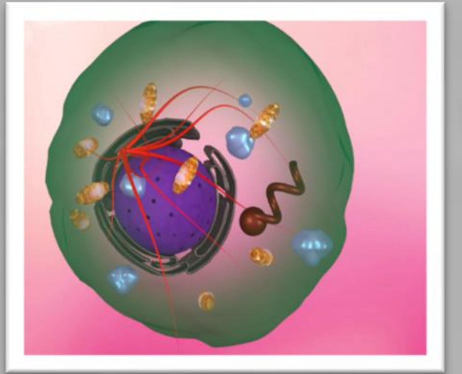


Phys. Chem. Chem. Phys., 2013, **15**, 10817-10823

Applications in Biology

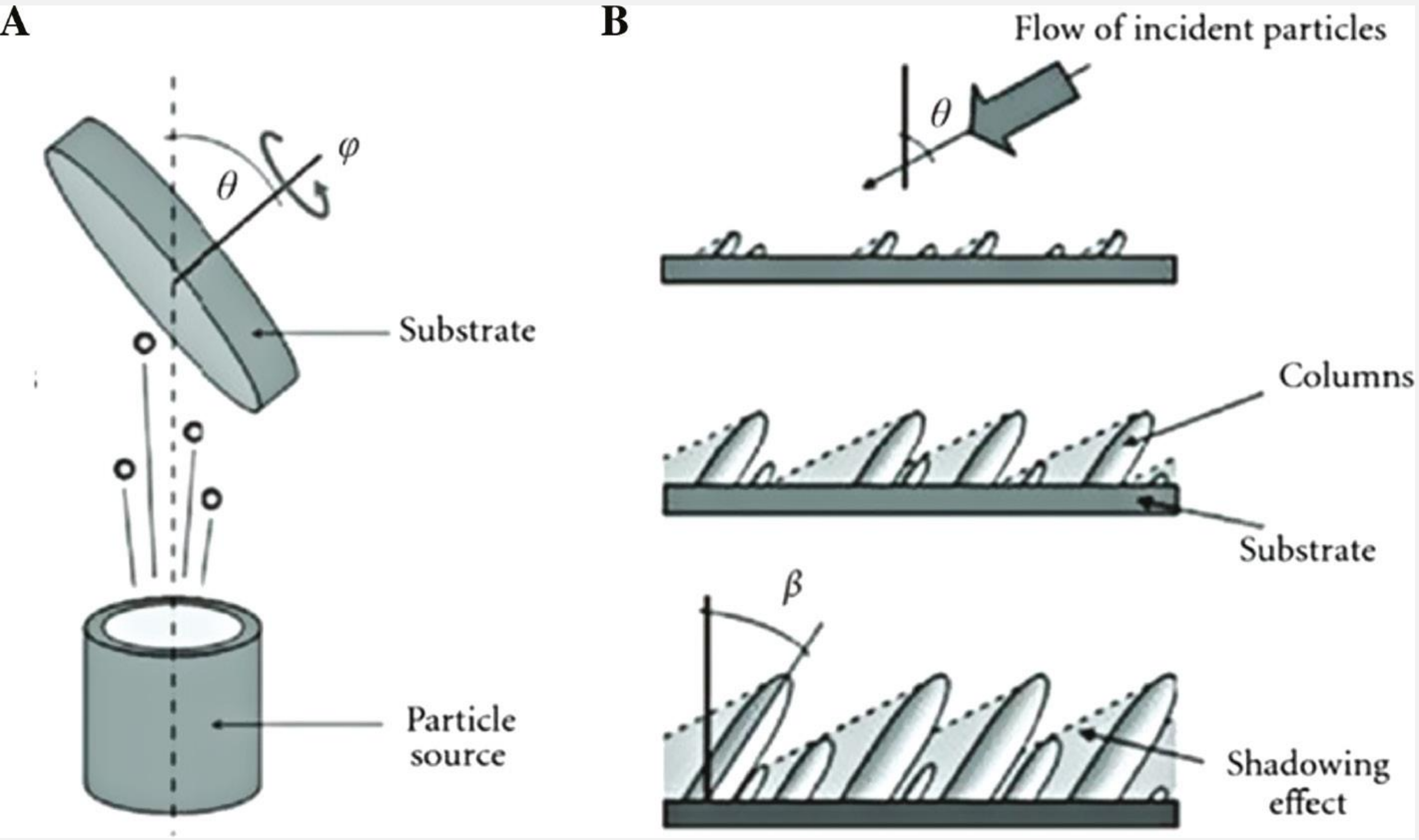


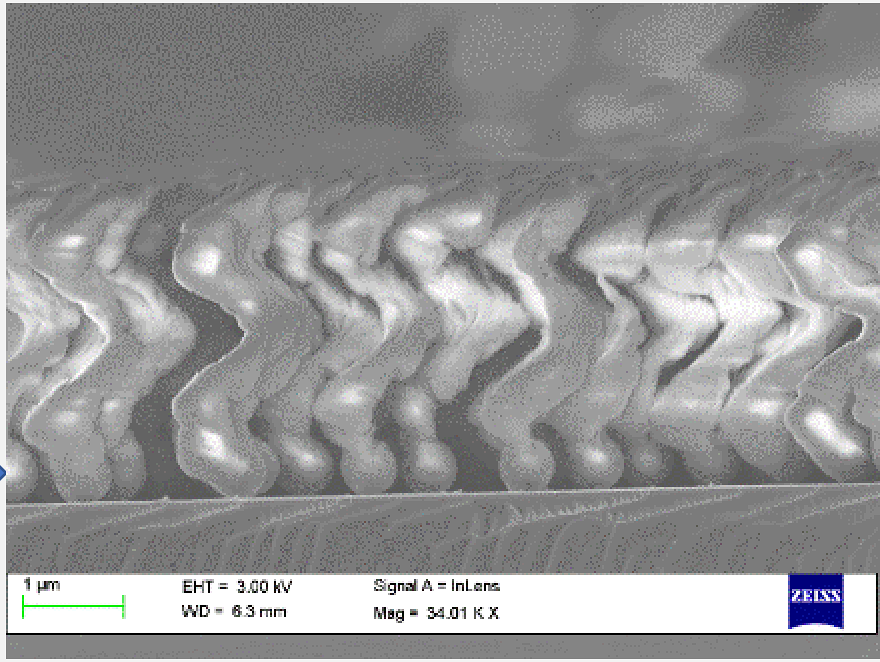
Nano Lett. 2014, 14, 4, 1968–1975

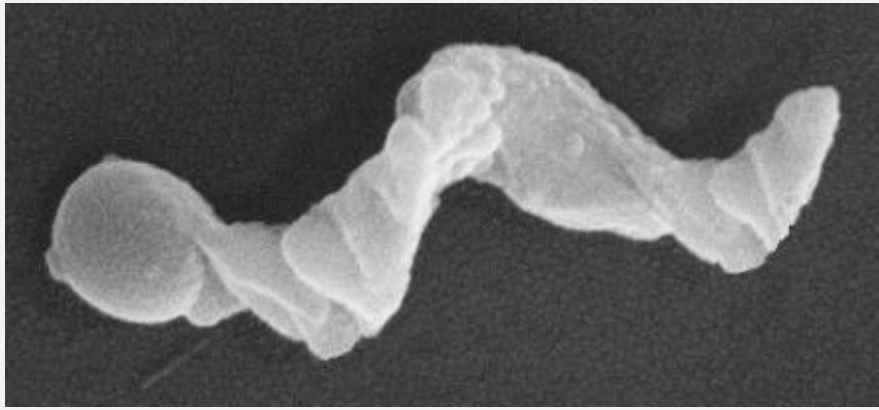


Adv. Mater. 2018, 30, 1800429

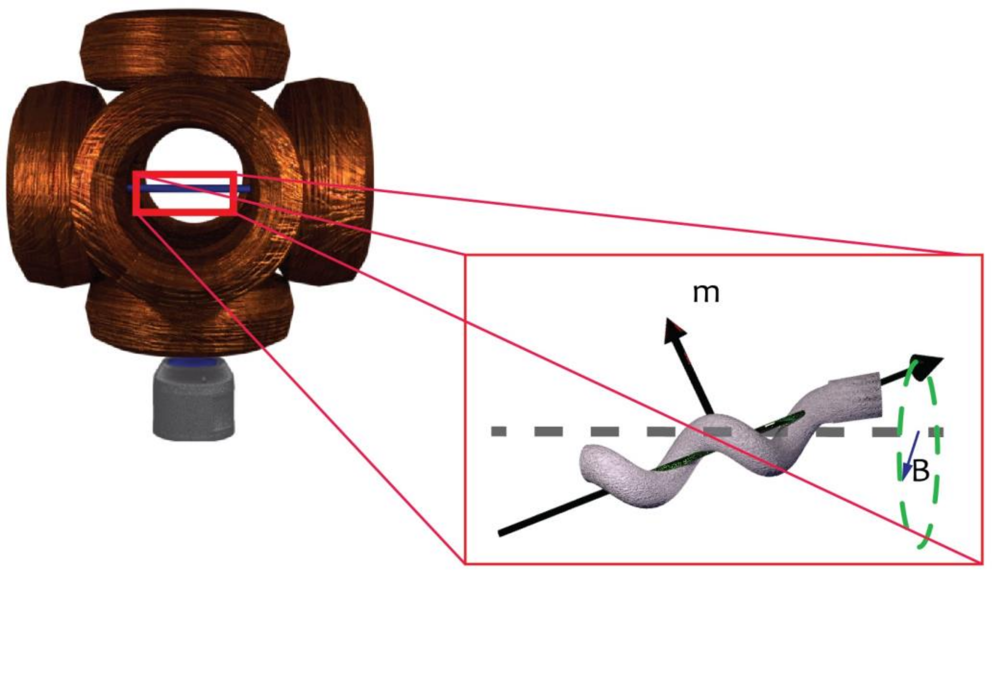
Fabrication of nanomotors: GLancing Angle Deposition (GLAD)

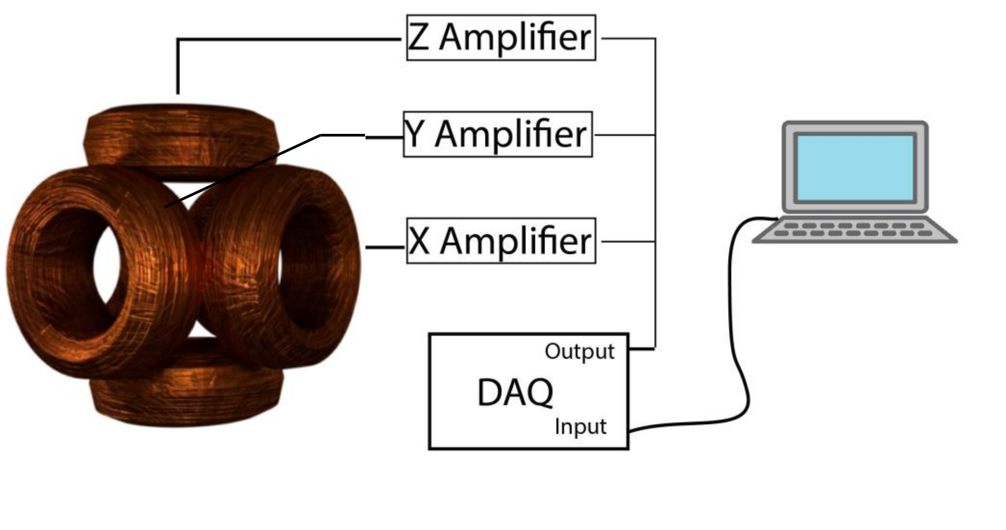


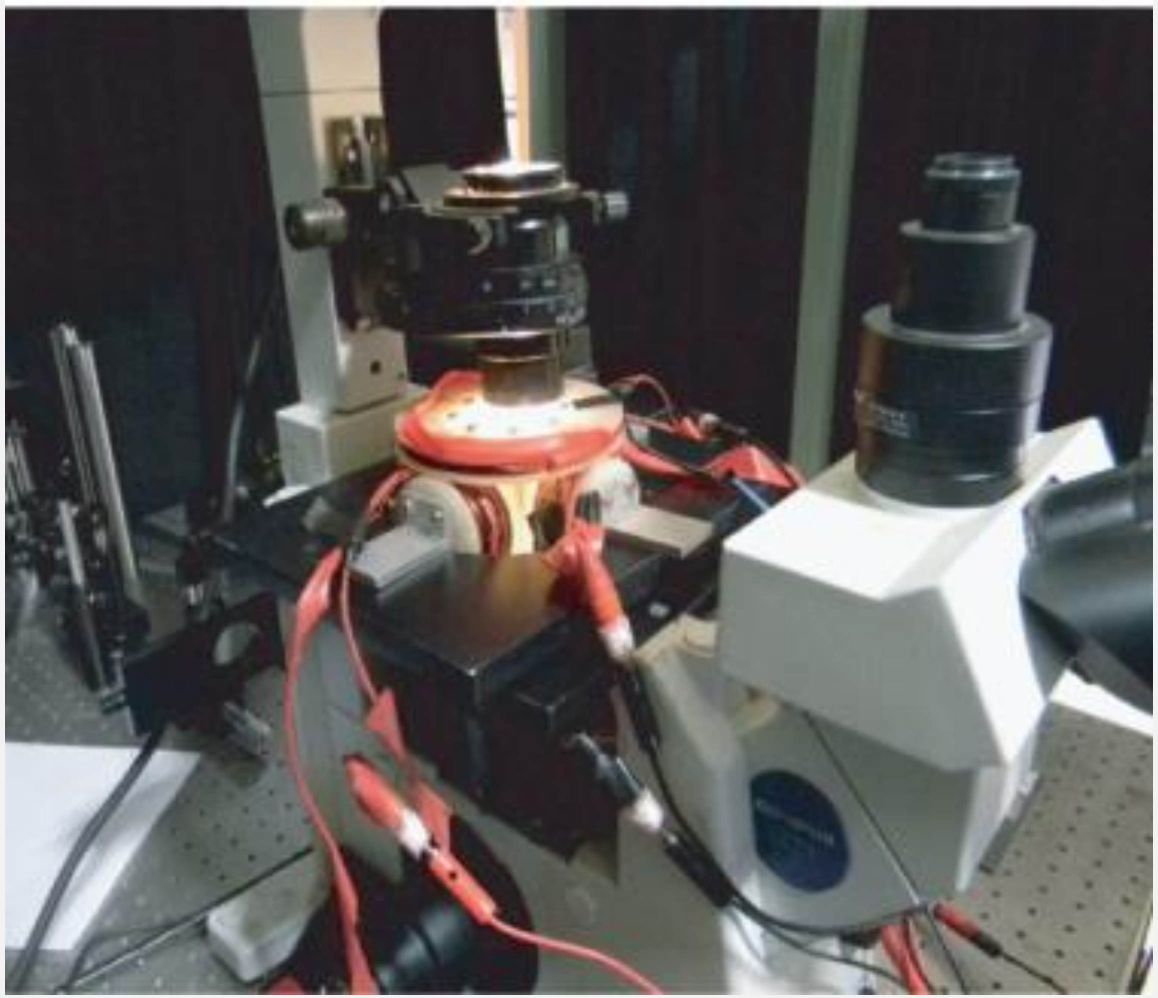




The setup







Micro-rheology using nanomotors

- Localized viscosity measurement using nanomotors
- Viscosity measurement in Newtonian and non-Newtonian fluids
- Viscosity measurement in fluids whose property changes in real-time
- Viscosity measurement in miscible fluids

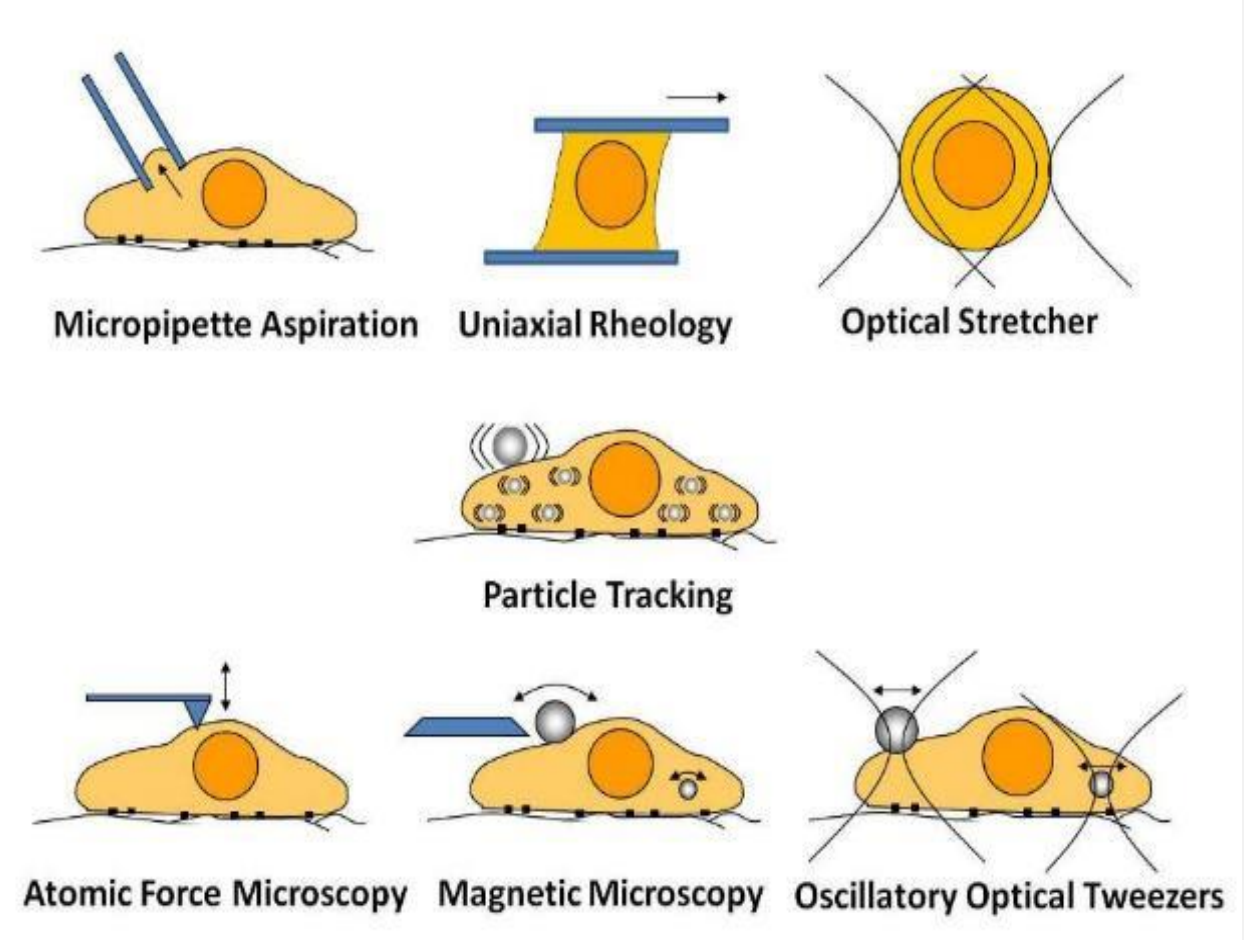
Probing the cancer microenvironment

Nanomotors in real world

Microrheology using nanomotors: Advantages

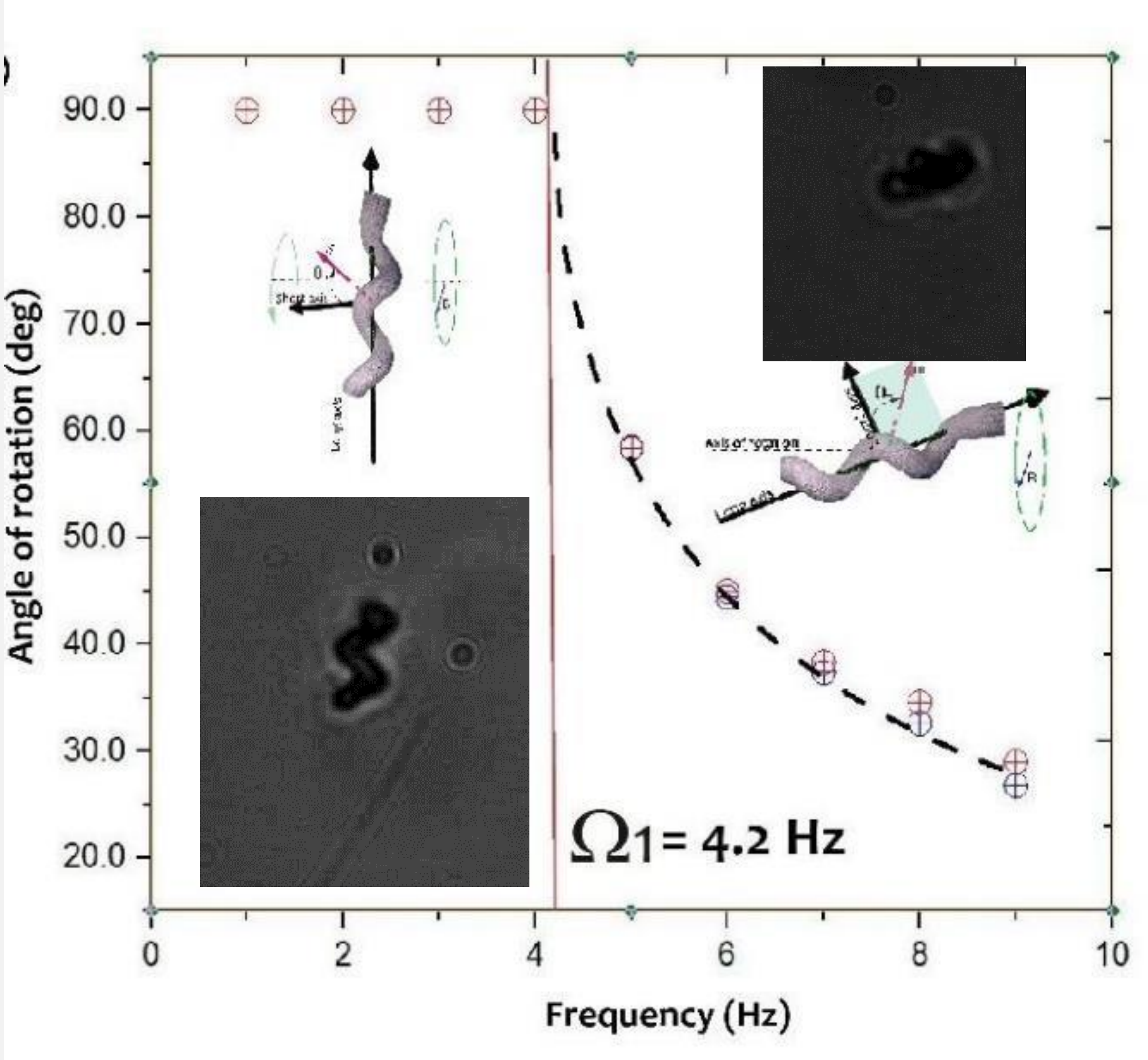
Compared to present microrheology techniques:

- Faster
- Measure local heterogeneity
- Higher spatio-temporal resolution
- Ease of creating a spatio-temporal map of viscosity in 3D

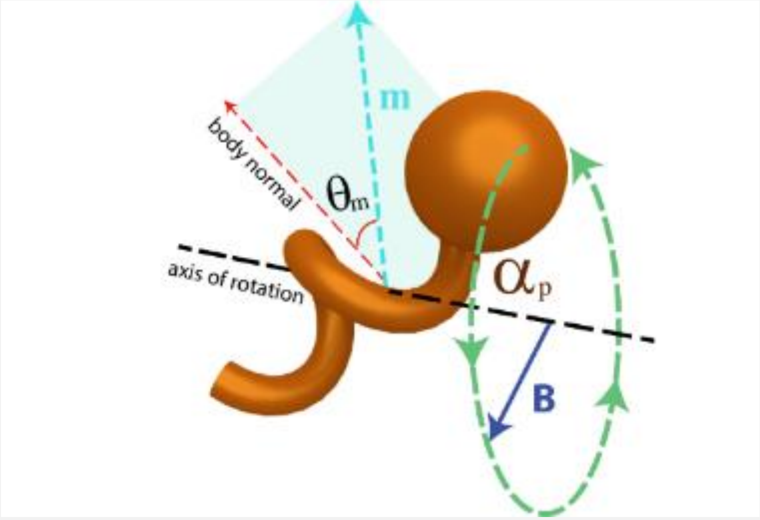


Wei, Ming-Tzo, "Microrheology of soft matter and living cells in equilibrium and non-equilibrium systems" (2014).Theses and Dissertations.Paper 1666

Microrheology using nanomotors: Technique

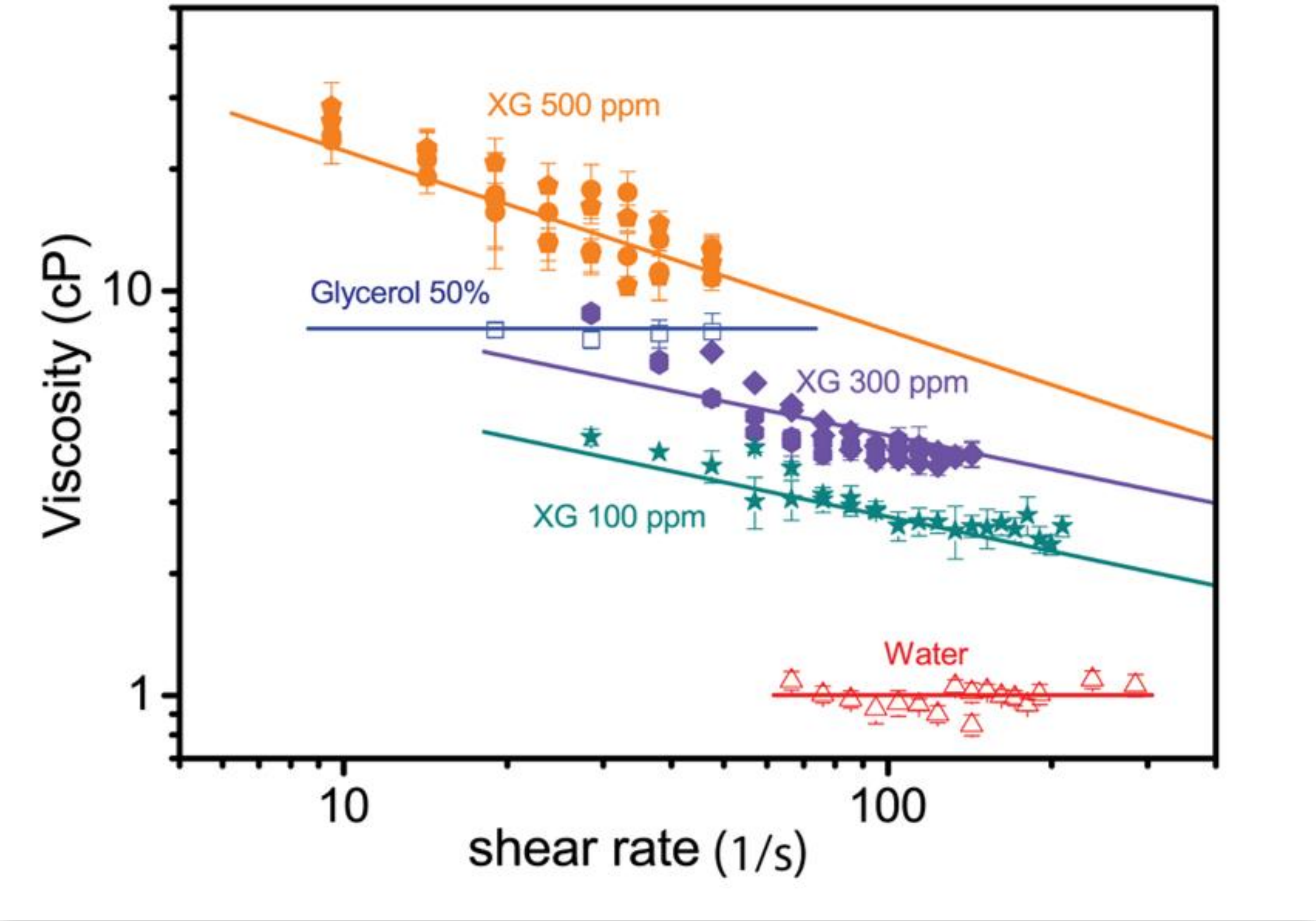


How is viscosity measured



$$\alpha_p = sin^{-1}\left(\frac{m\ B\ \sin(\theta_m)}{2\pi\eta f_s\Omega_B}\right)$$

$$\eta = \frac{m\ B\ \sin(\theta_m)}{2\pi\ f_s\ \Omega_B\ \sin(\alpha_P)}$$

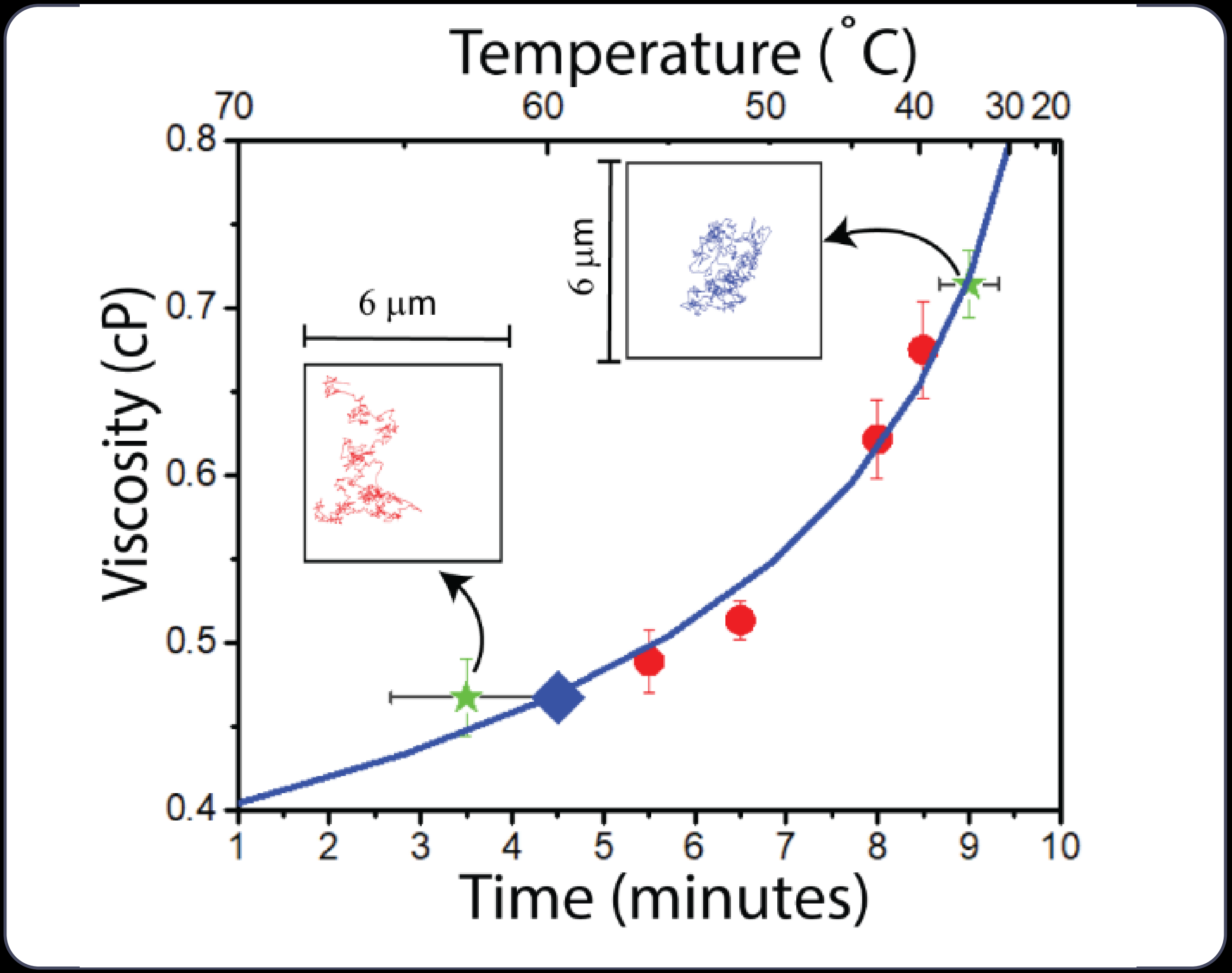


Newtonian and non-Newtonian fluids

Change in viscosity with time

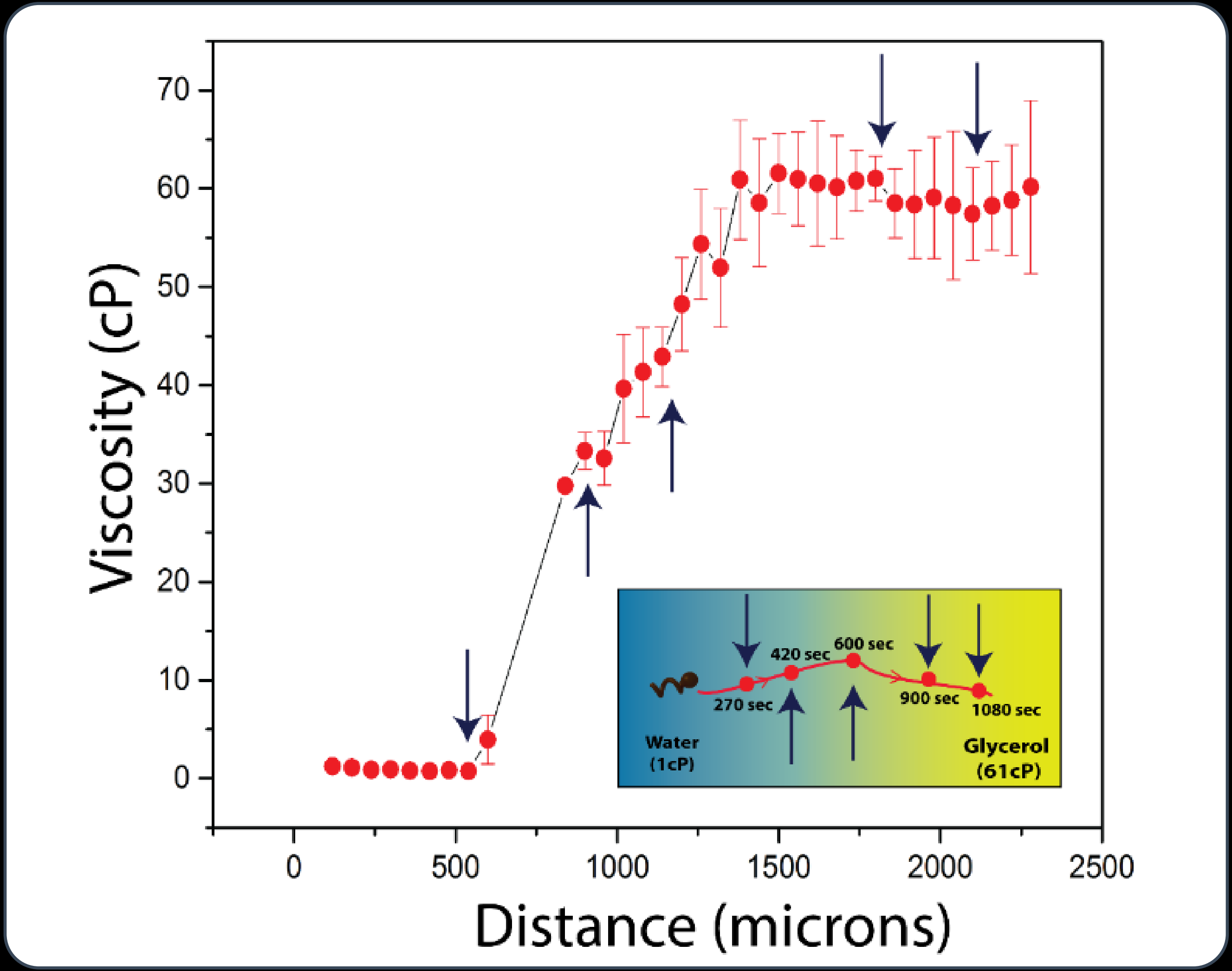
- Heated water was allowed to cool down

- Temperature measured with IR thermometer – correlated with Brownian motion of beads.

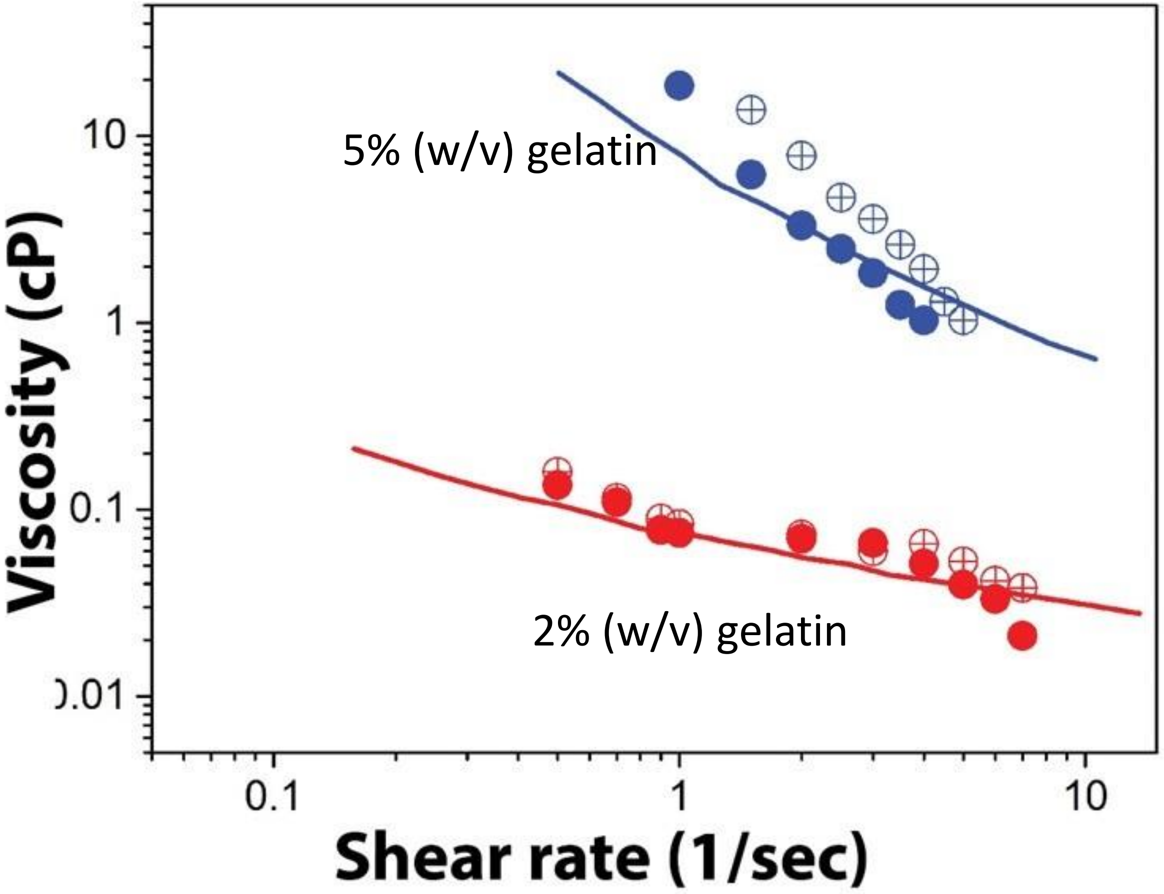


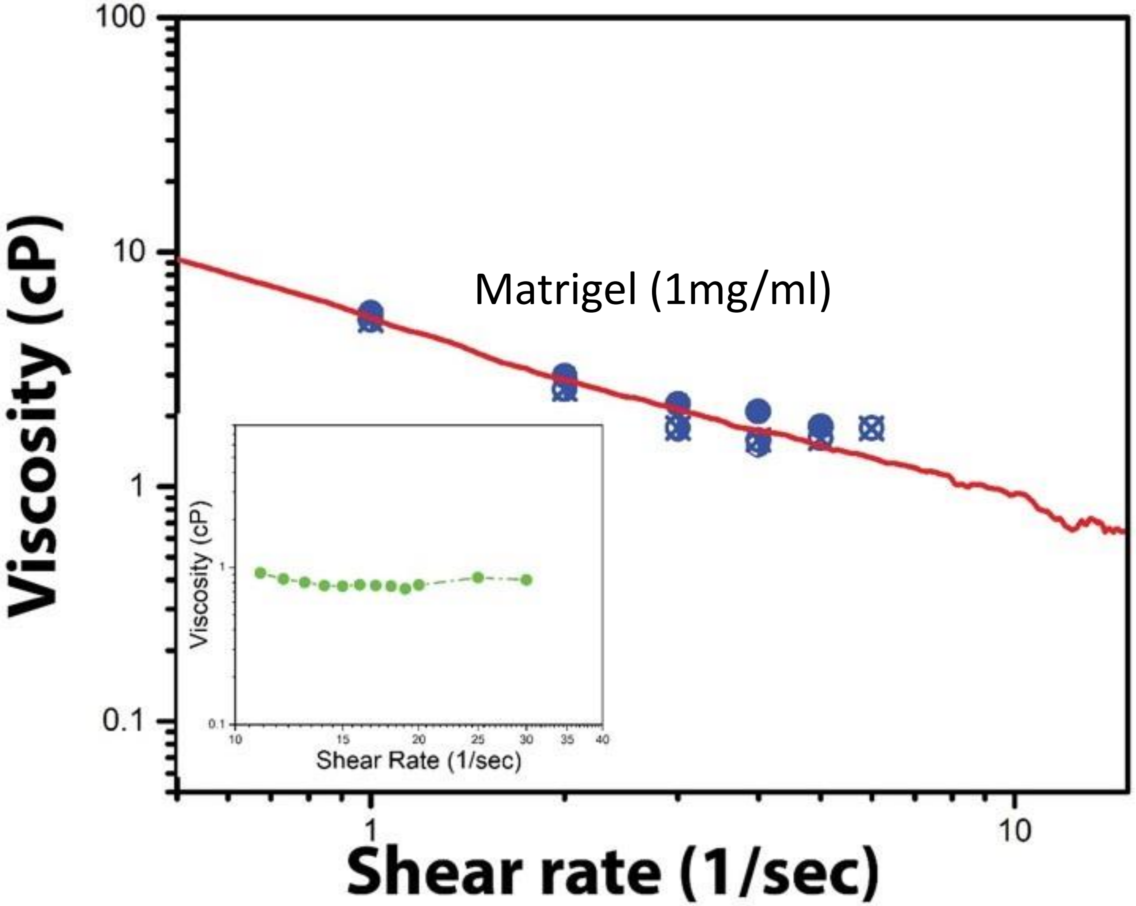
Spatial change in viscosity

- Nanomotor was driven from DI water towards glycerol.
- Nanomotor was faster than the mixing time of 60 cP glycerol and water.



Rheology in Biofluids





Microrheology using nanomotors

Measure viscosity in Newtonian and non-Newtonian fluids with high spatio-temporal accuracy.

↓

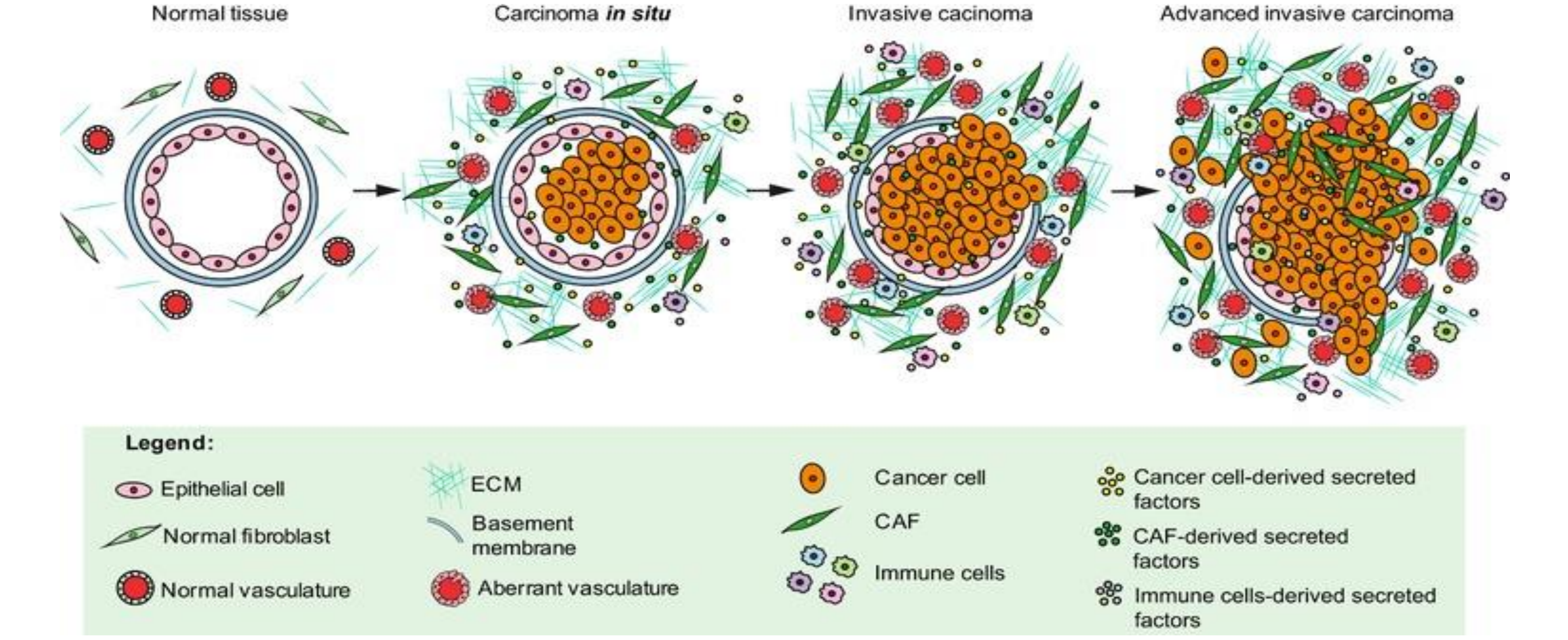
Viscosity map of dynamic fluids

Micro-rheology using nanomotors

Probing the cancer microenvironment

- Maneuverability in tumor model
- Targeting cancer cells using changes in cancer microenvironment
- Discovery of new physico-chemical properties of cancer secreted matrix

Nanomotors in real world

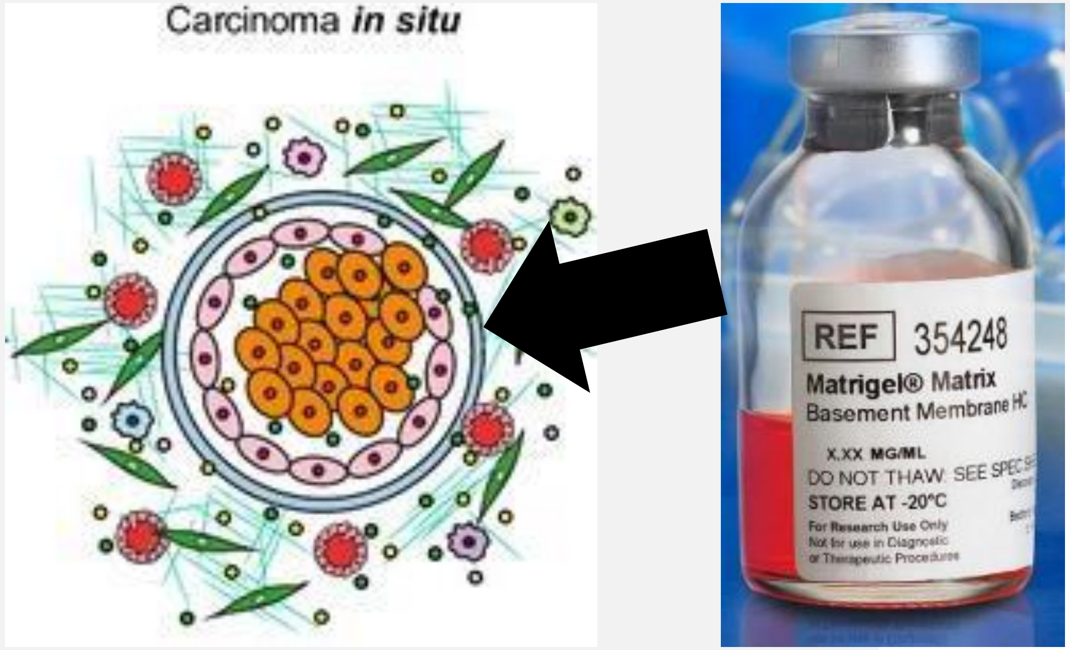


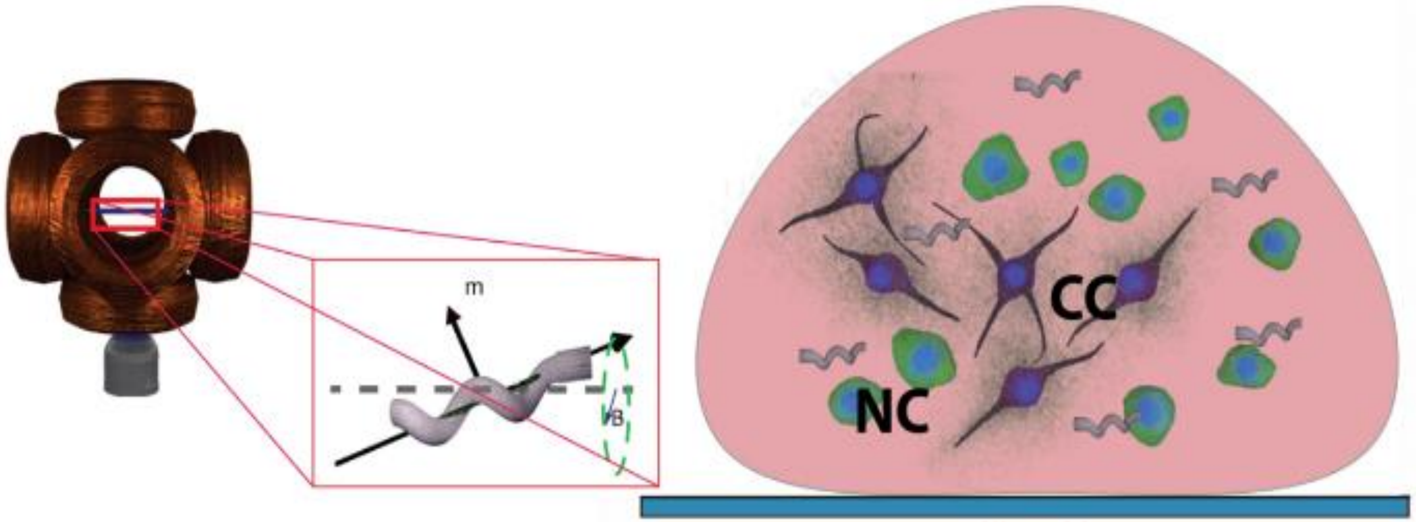
https://onlinelibrary.wiley.com/doi/full/10.1002/pmic.201700167

Cancer Microenvironment : The ECM

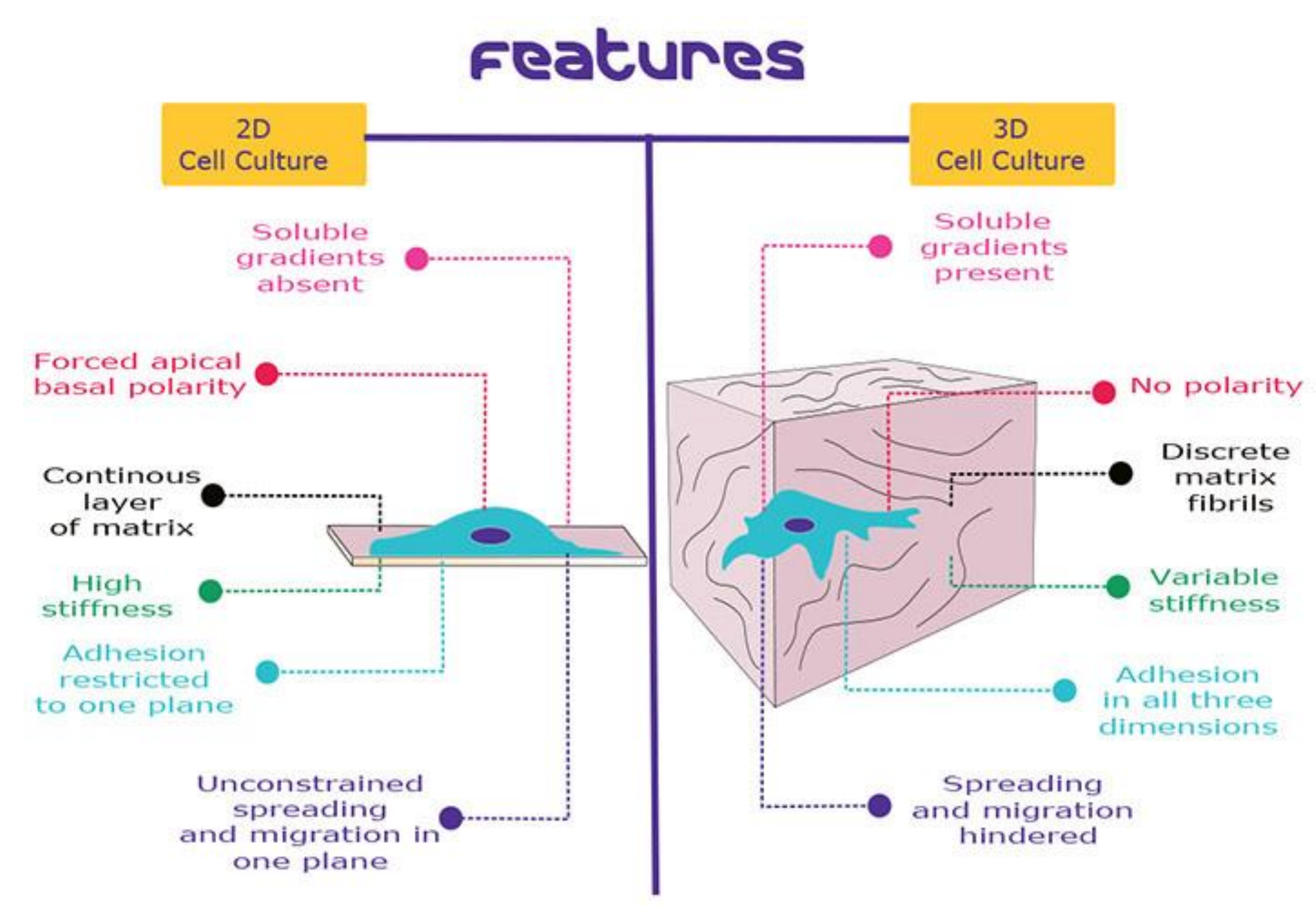
- The extracellular matrix (ECM): non-cellular component of tissue
- ECM is composed of and interlocking mesh of water, minerals, proteoglycans, and fibrous proteins secreted by resident cells.
- ECM is responsible for cell–cell communication, cell adhesion, and cell proliferation.

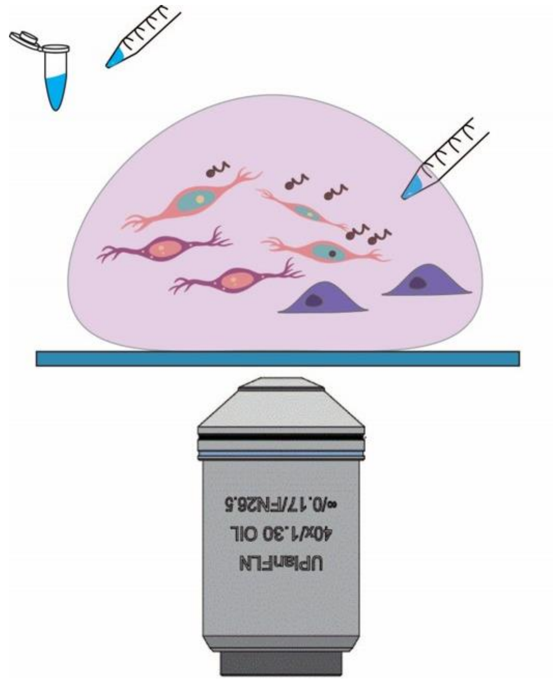
Probing Cancer Microenvironment: The setup





Nanomotors are injected and driven through a tumor model made by incubating cells in Matrigel droplets https://www.sigmaaldrich.com/technical-documents/articles/biology/3d-hydrogels.html



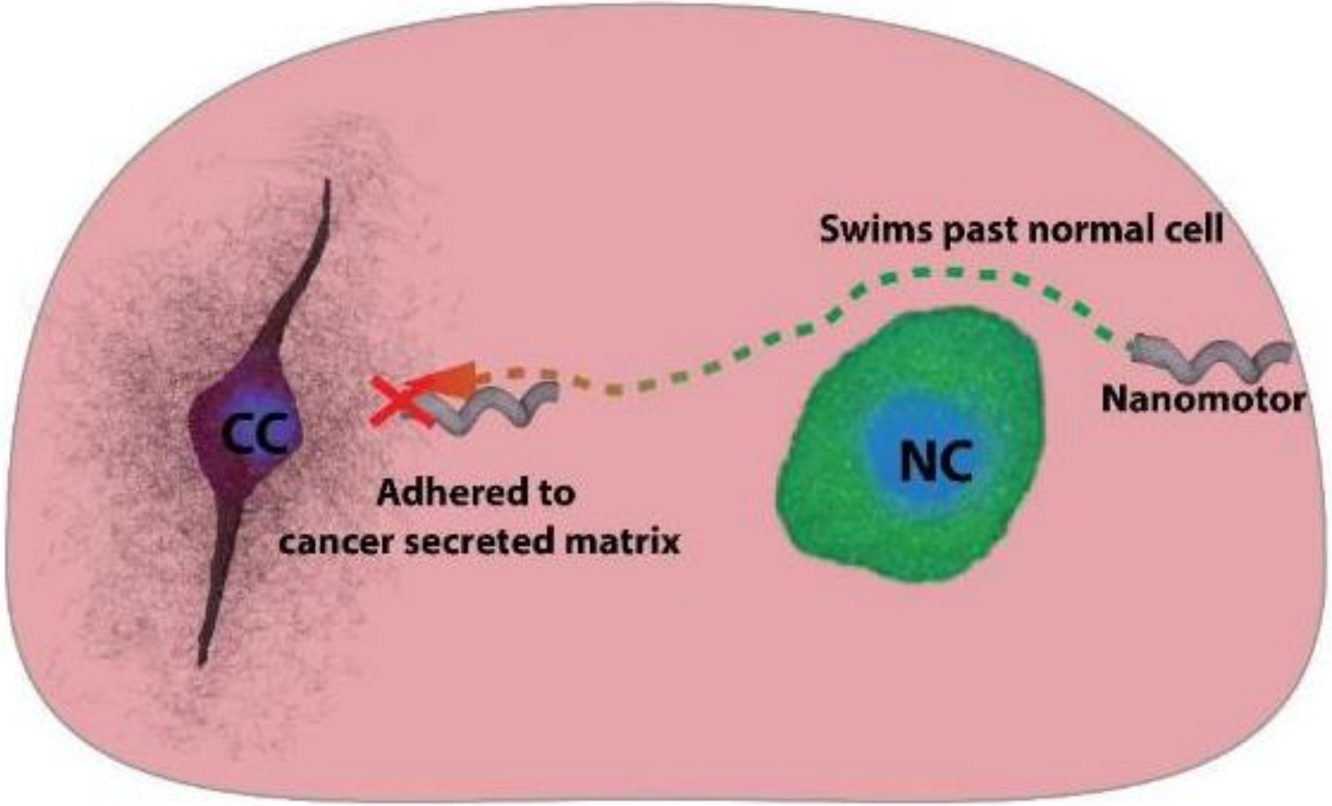


Why 3D?

Nanomotors adhere near cancer cells

No adhesion to normal cell – proximal ECM

May eventually adhere to the cell surface



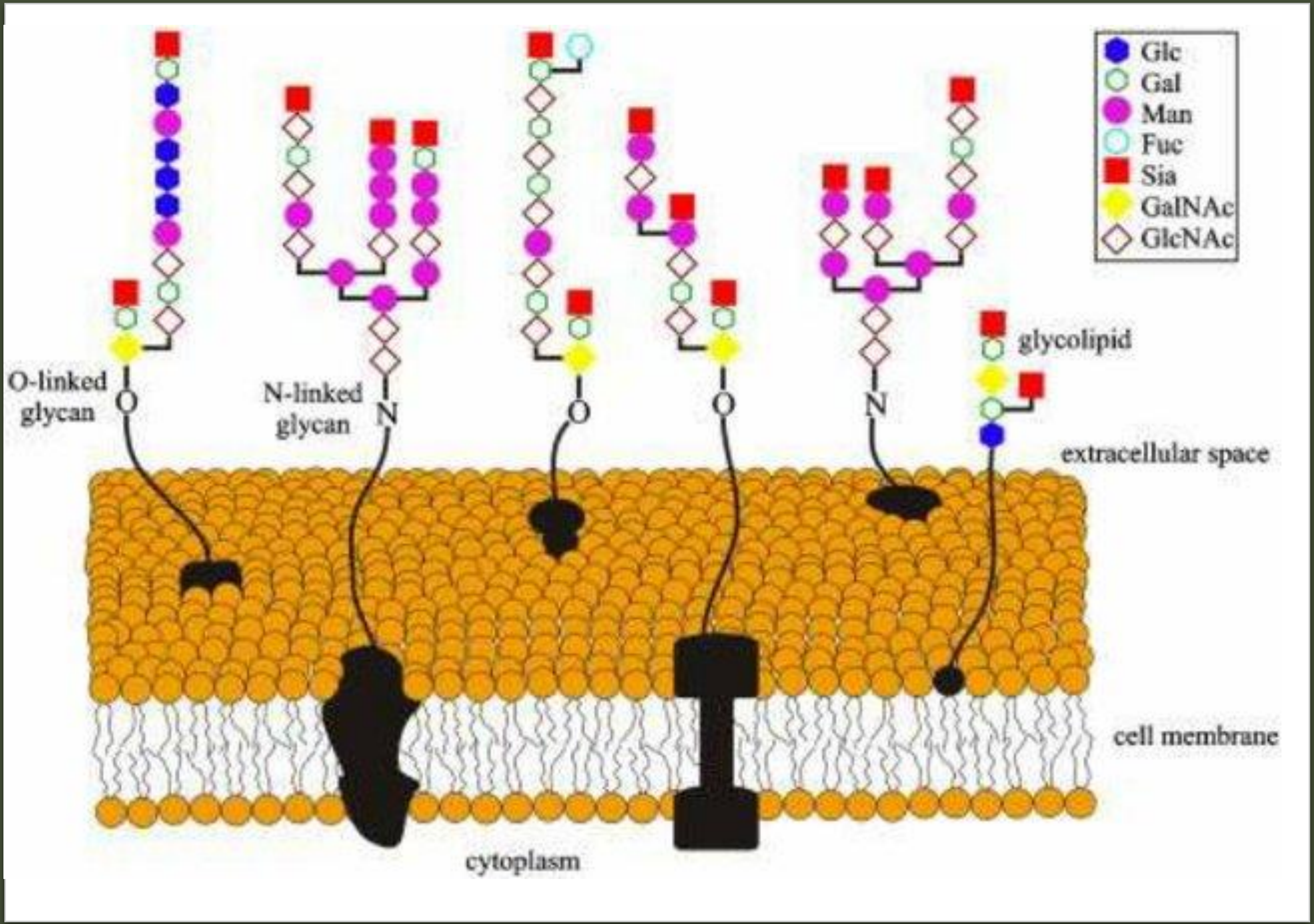
- Nanomotor adhere to the ECM around cancer cells.
- Adhesion is observed upto ~40µm from cell surface

Probing Cancer Microenvironment: Results

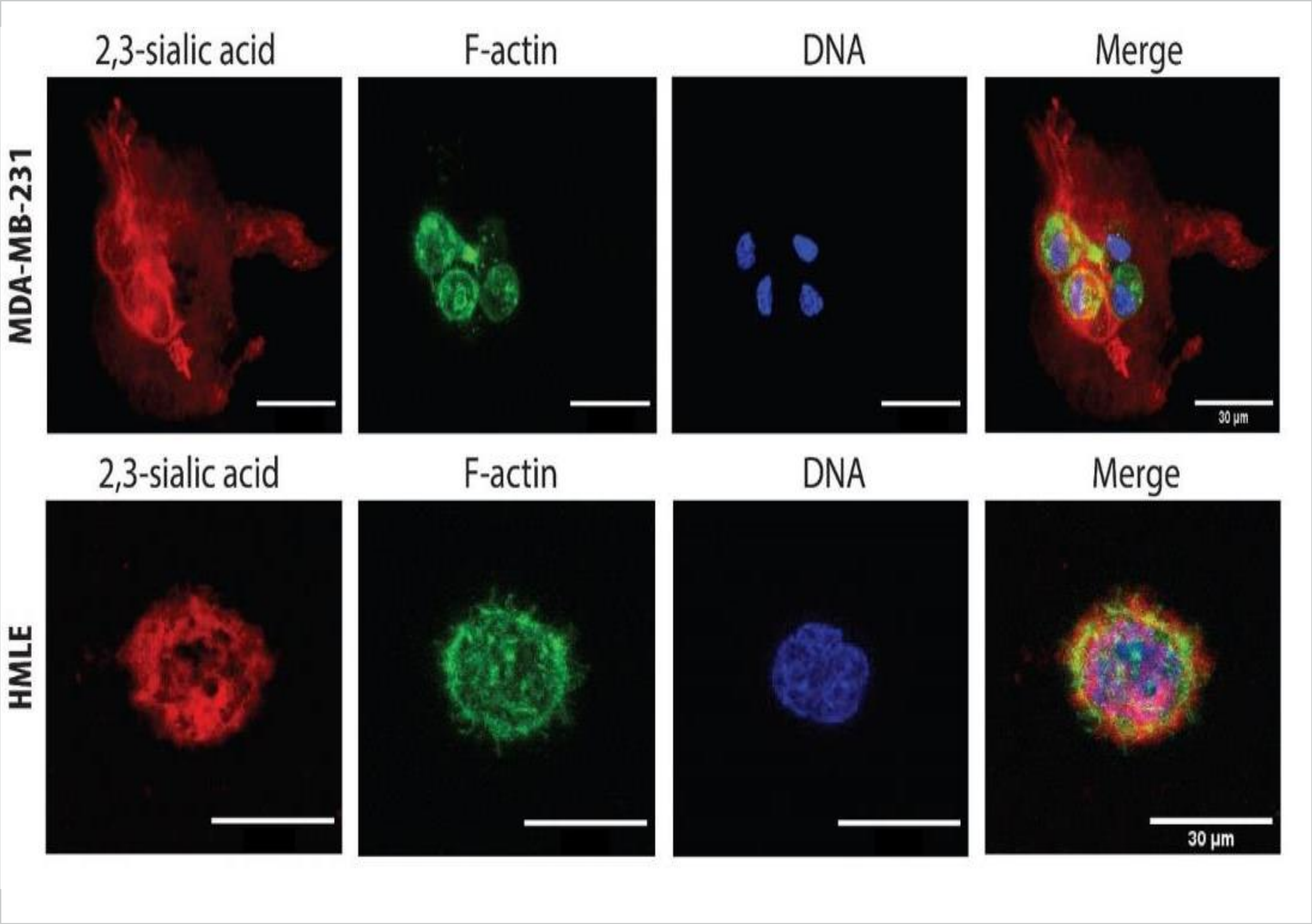
Movie 1:
Adhesion of a nanomotor near a cancer cell

Movie 2:
No adhesion near normal cells at 50G, 5Hz

Cell Type: HMLE



Cells secrete proteins into the ECM

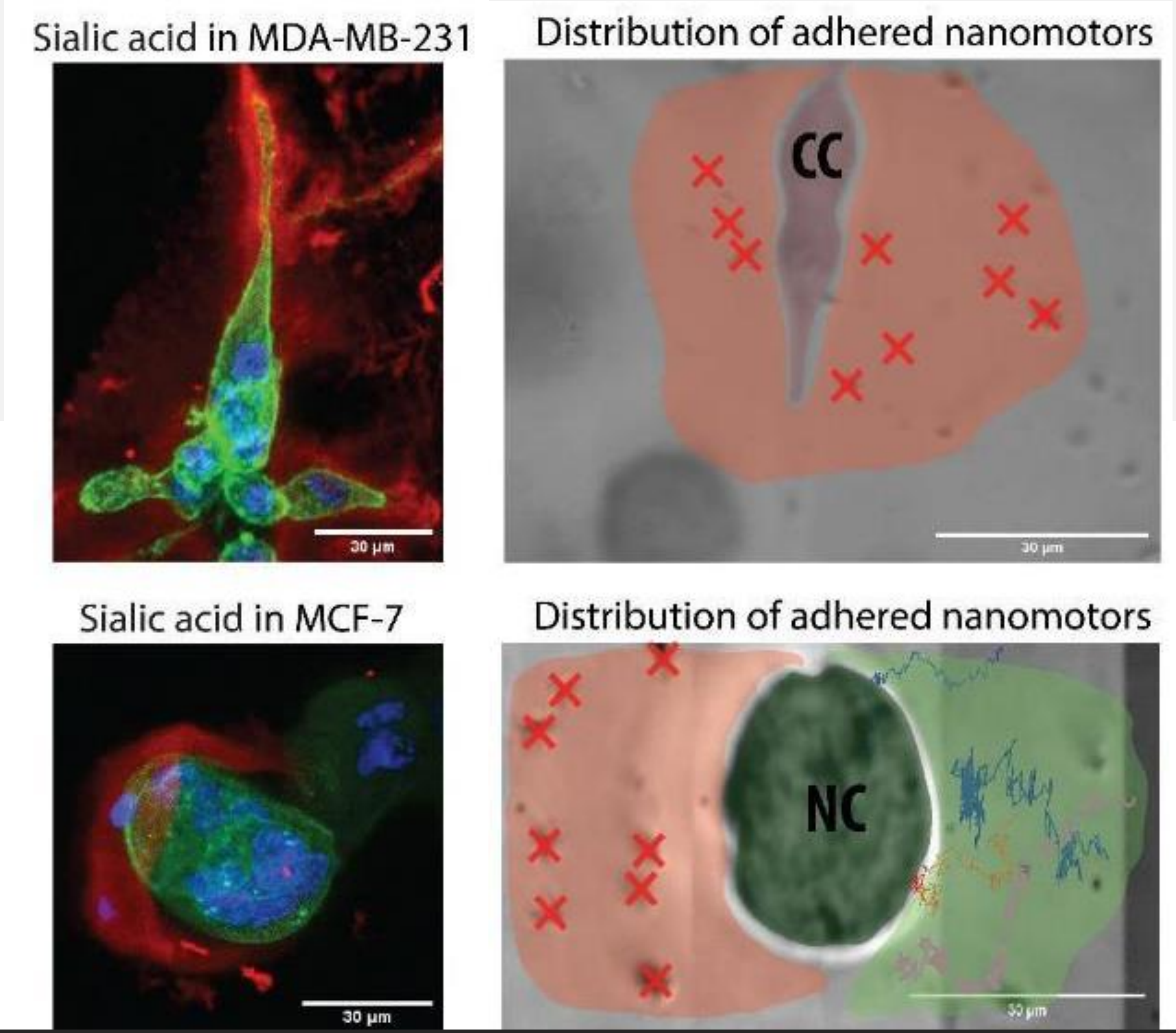


Cancer ECM

and

non-Cancer ECM

Cell-line specific anisotropy



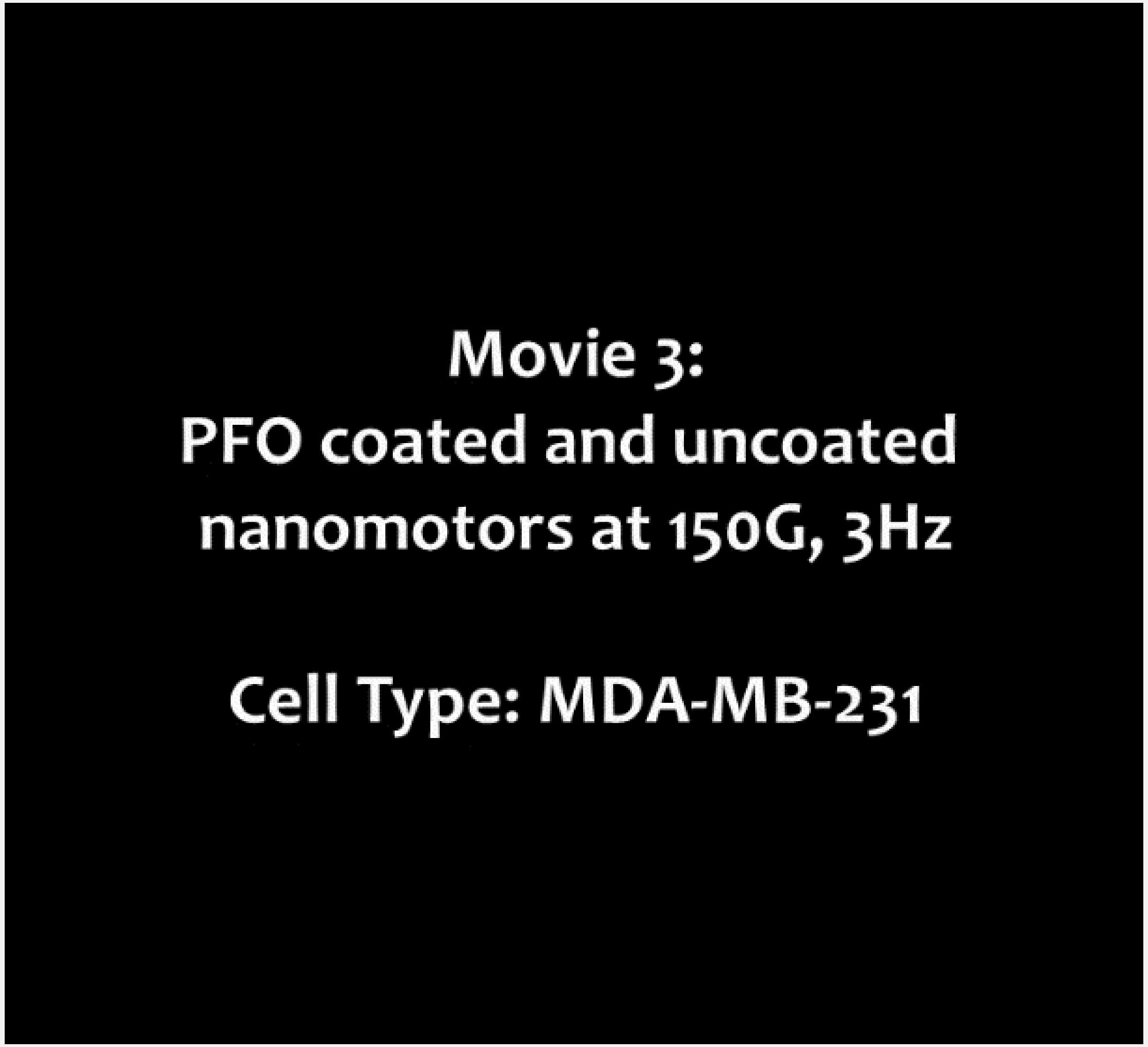
Correlation between sialic acid distribution and nanomotor adhesion

Hypersialated charged ECM secreted by cancer cells contribute to nanomotor adhesion

Differences in Cancer ECM and non-Cancer ECM

Surface modification of nanomotors using PFO

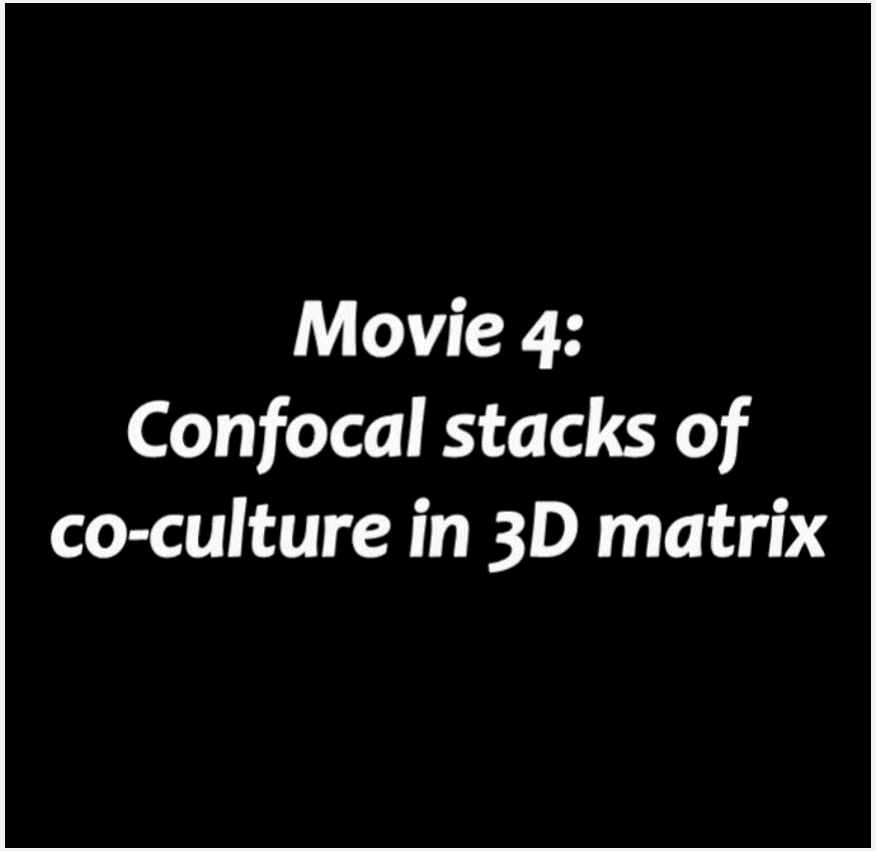
Charge shielding effect of PFO eliminates adhesion

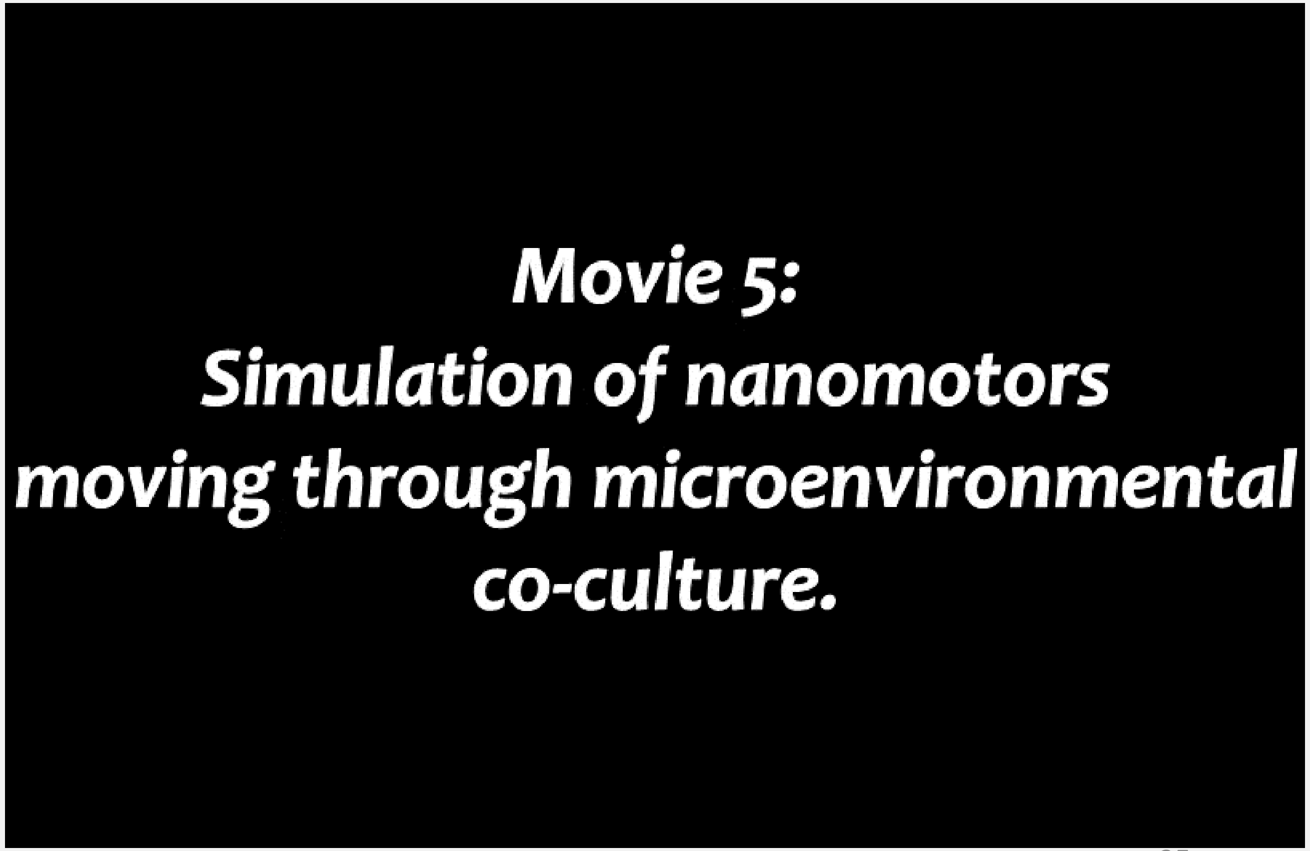


Potential Applications

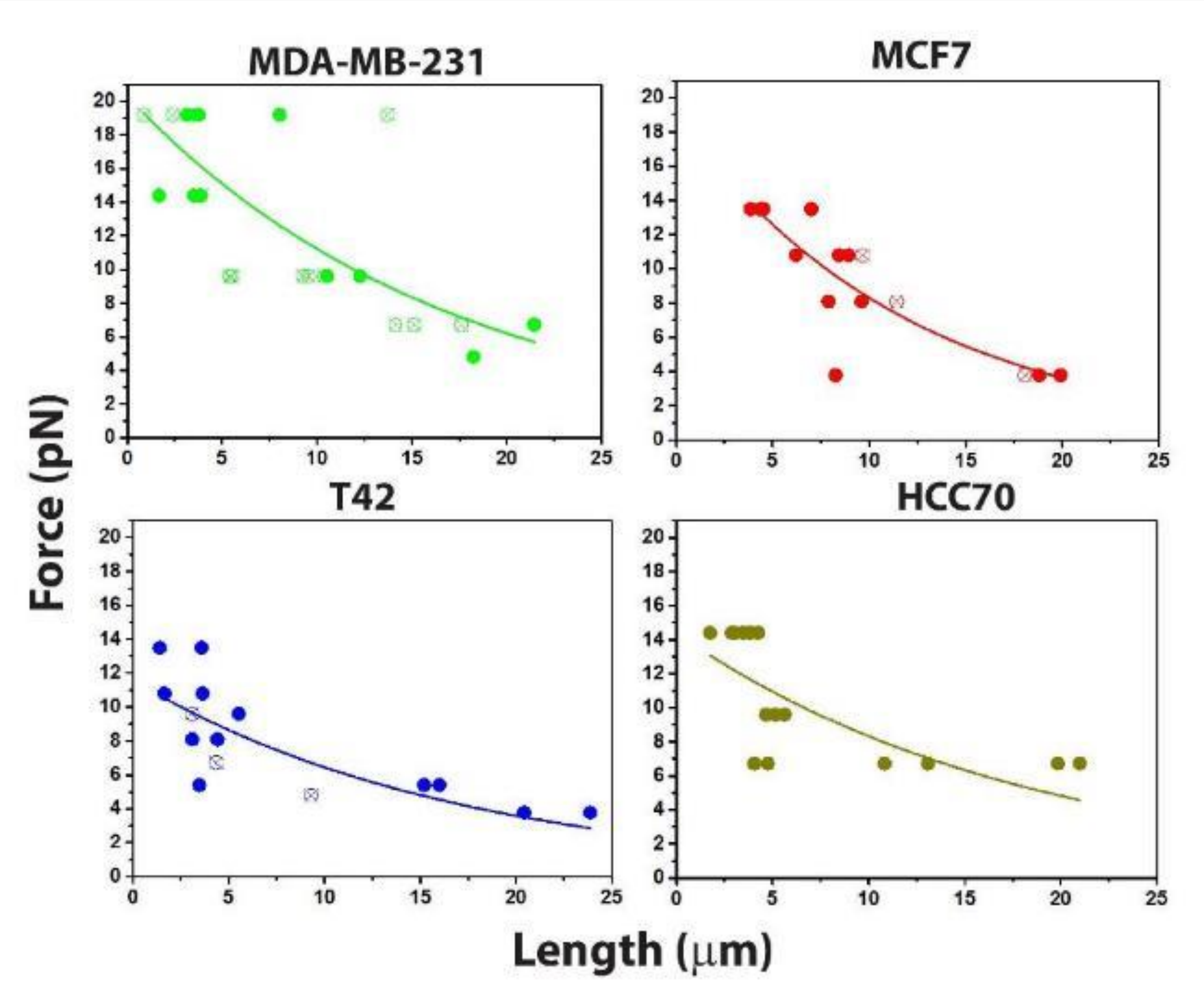
Cancer targeting

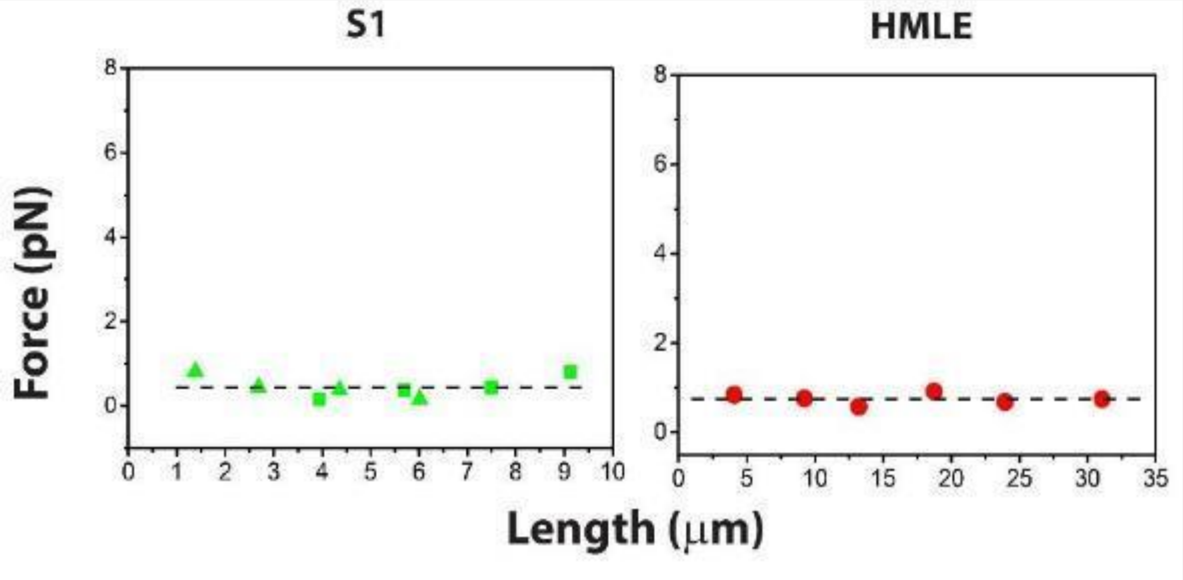
Preferential adhesion near Cancer secreted ECM can be used to target cancerous cells in a tumor

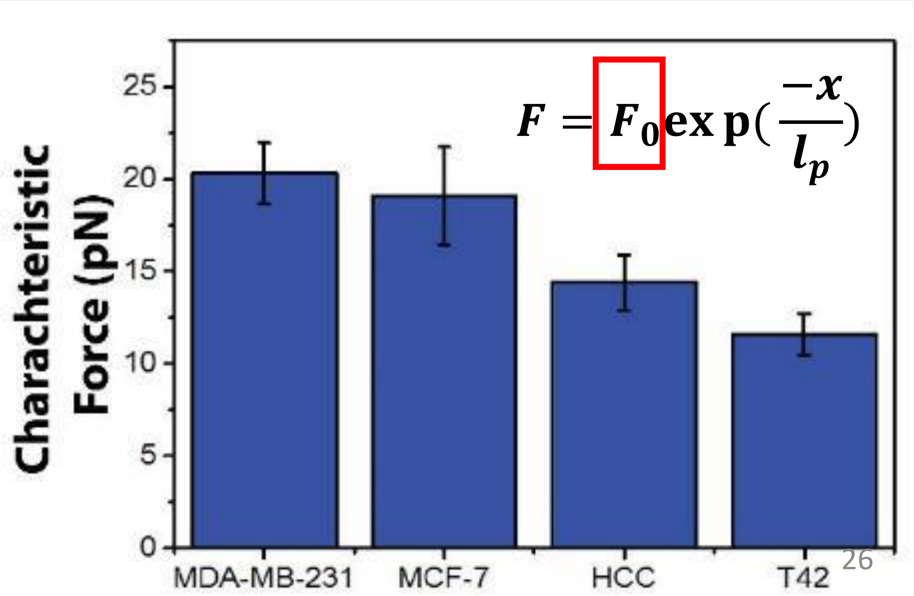




Gauging metastatic potential

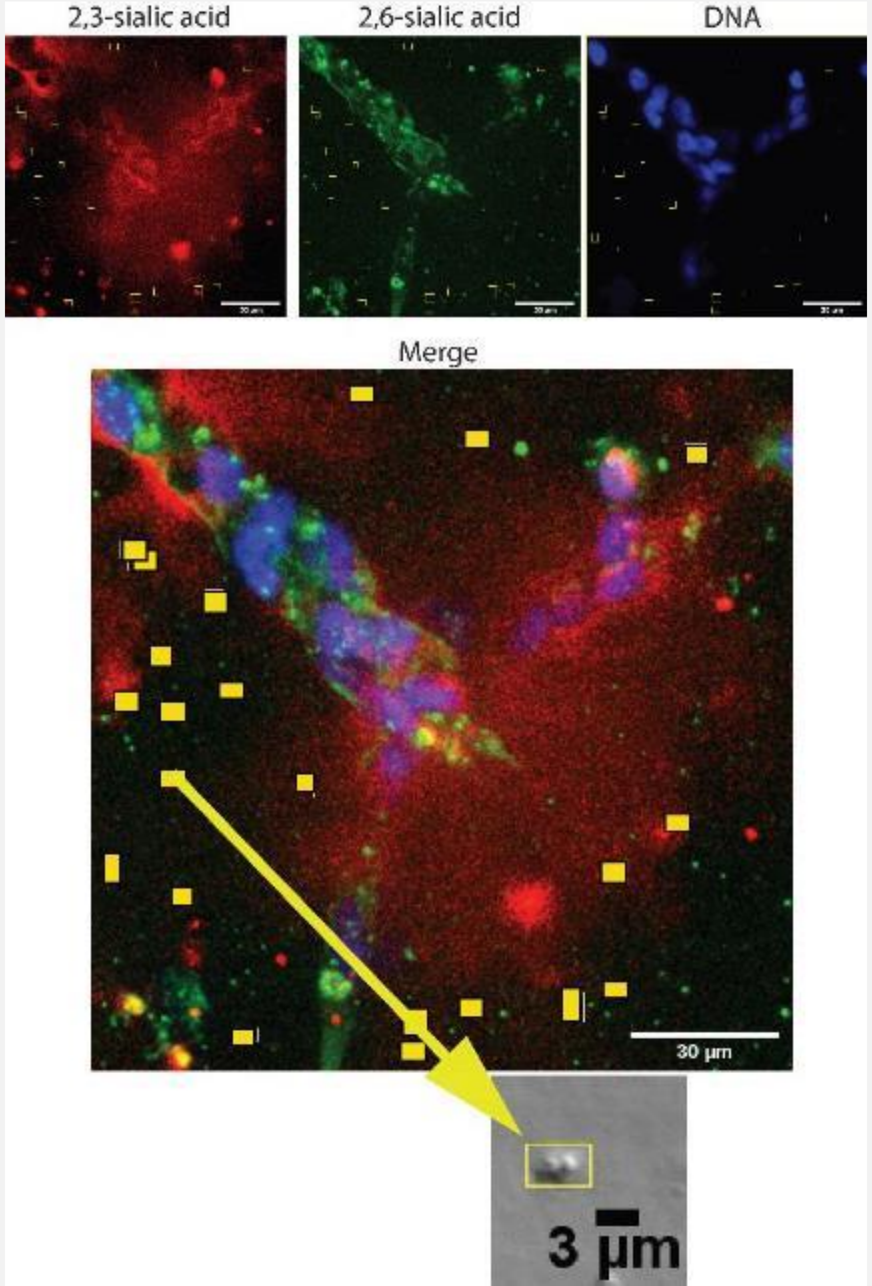




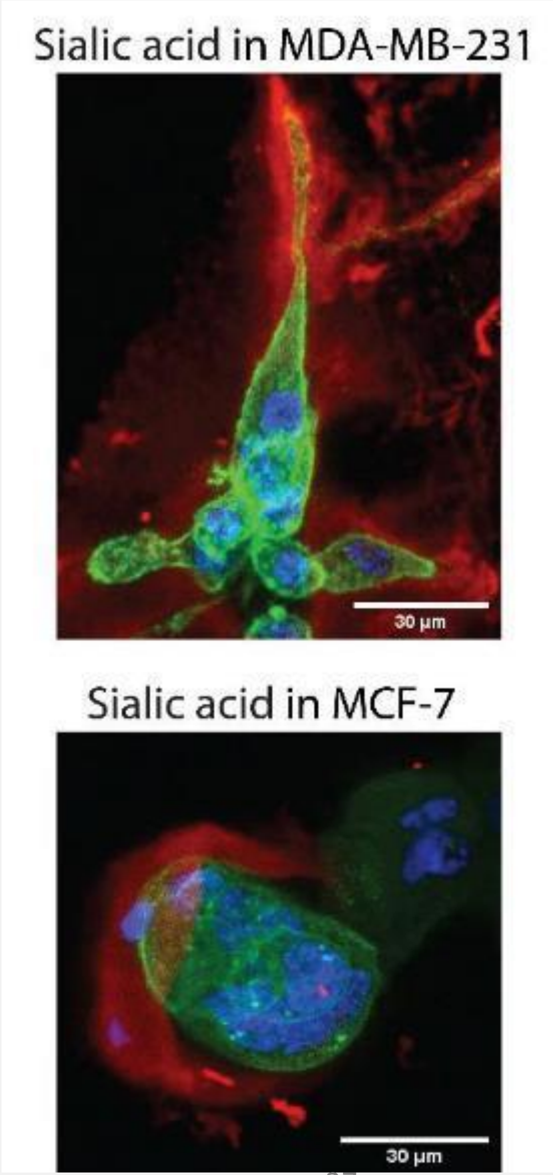


Discovering new phenomenon

The existence of sialylated proteins in cancer-secreted ECM is reported for the first time.



Anisotropic distribution of sialylation in cancer ECM is reported for the first time.



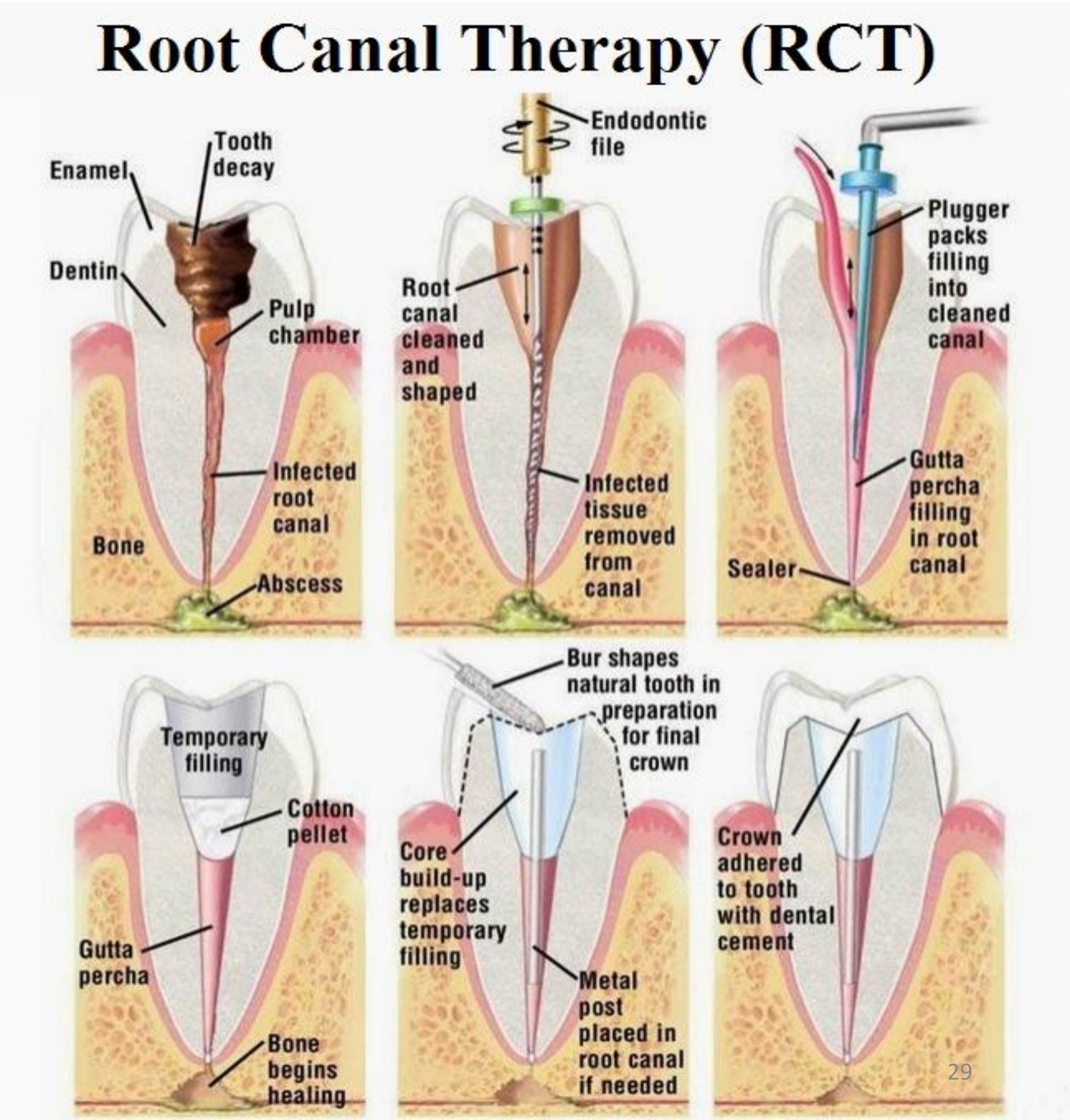
Micro-rheology using nanomotors

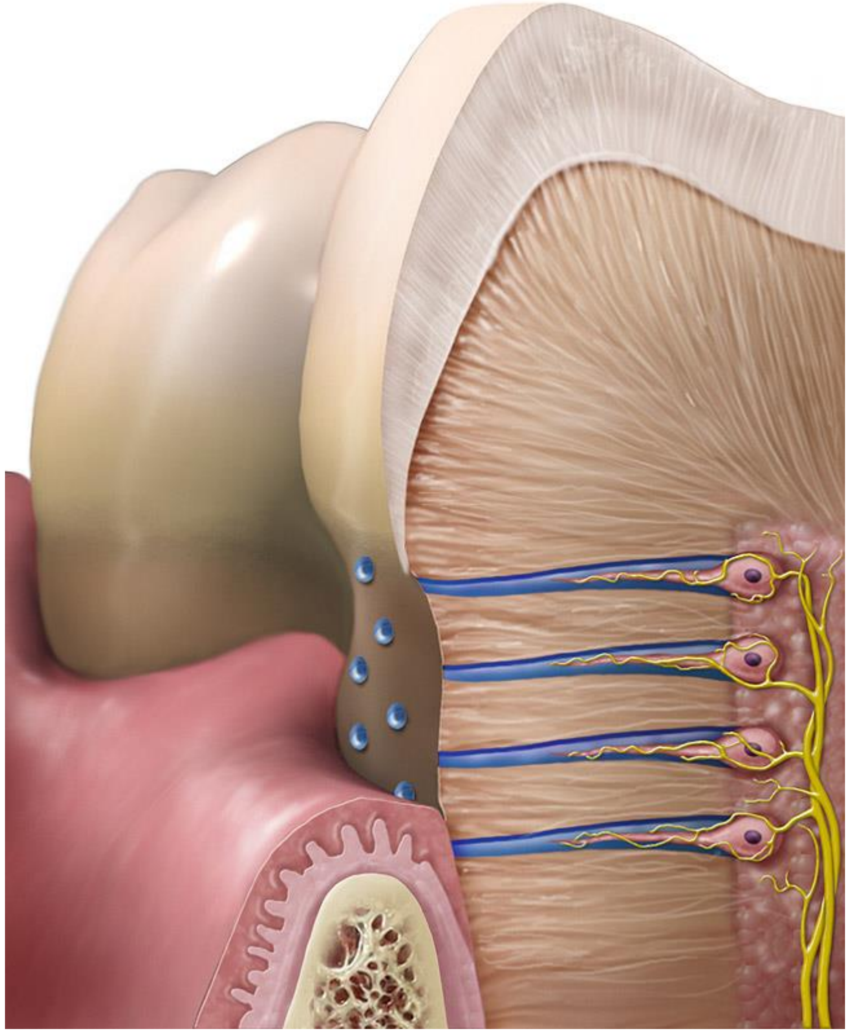
Probing the cancer microenvironment

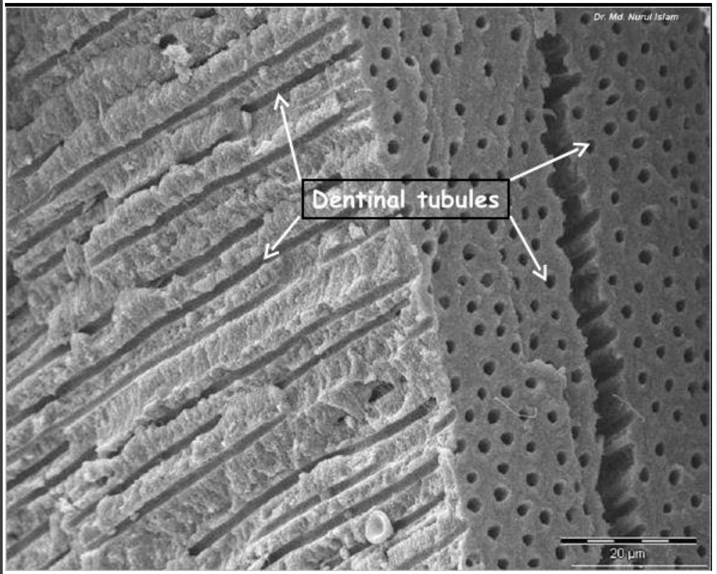
Nanomotors in real world

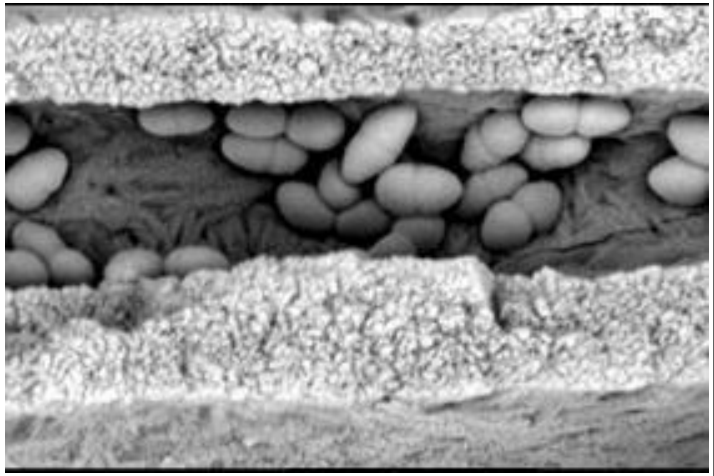
- Endodontic reinfection
- Problems with current treatment procedure
- Solving reinfection with nanomotors

Root canal procedure





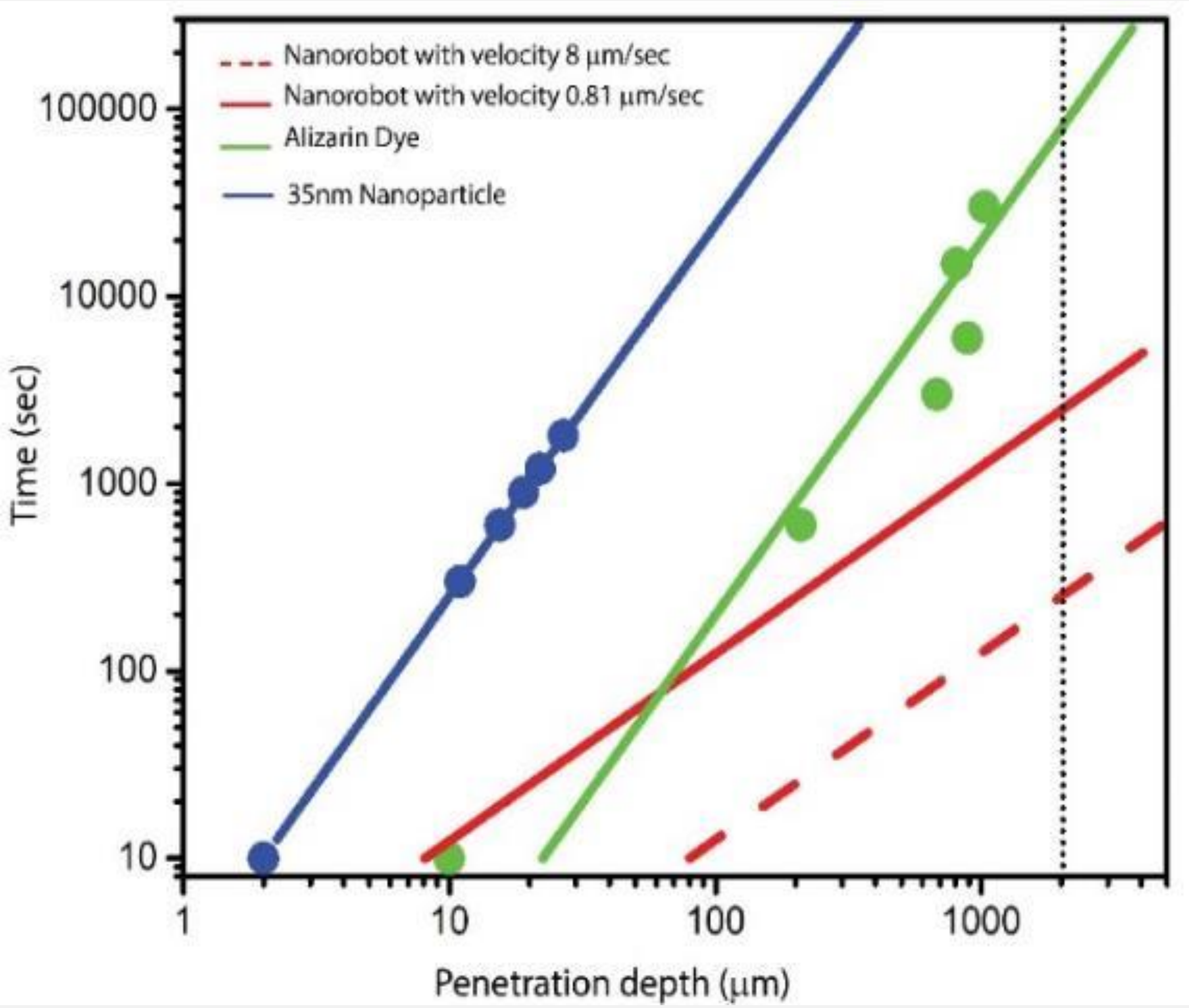




Endodontic Reinfection

Limitations of current technology

Relying on diffusion alone is hopeless



Currently available devices

Depth inside Dentinal Tubules

LASER

Fotona
Ultra Performance Lasers

500µm – 850µm

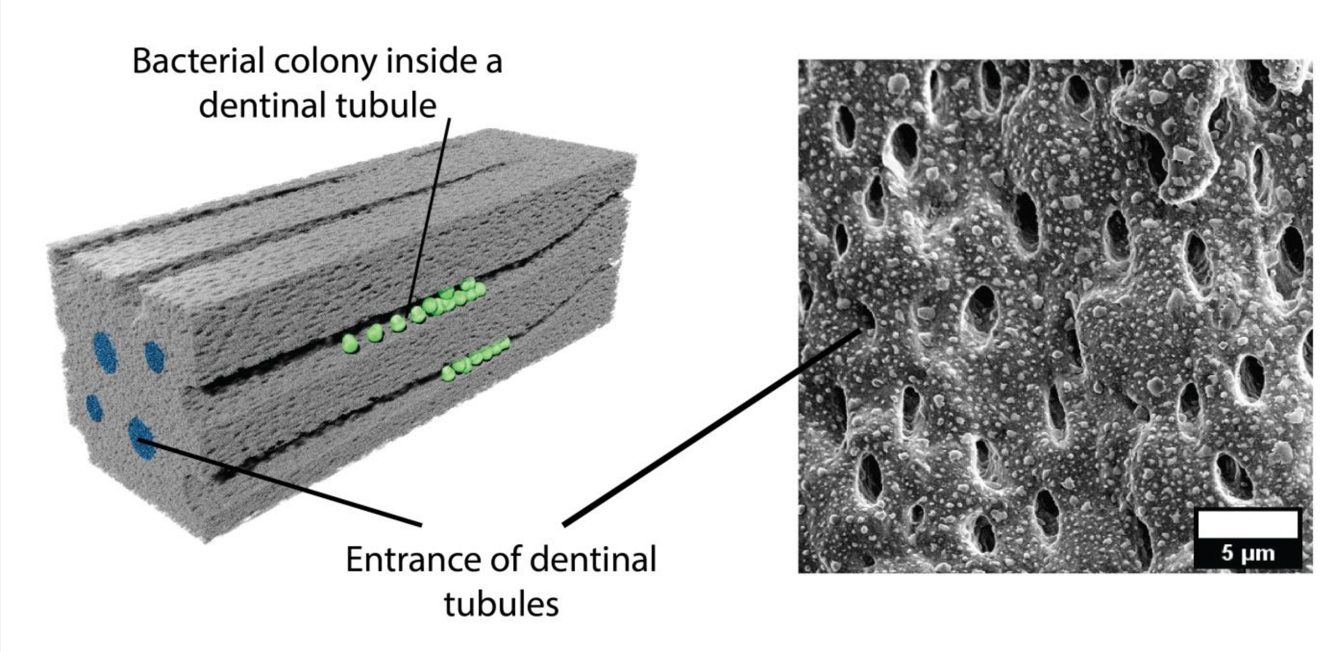
Ultrasound

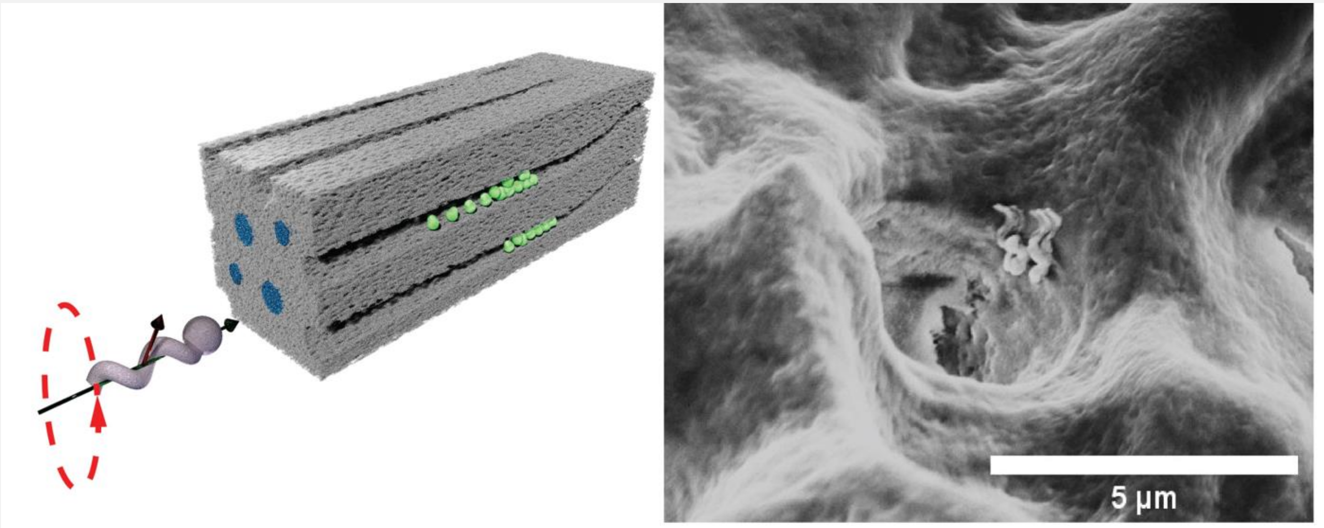
SybronEndo
Dentsply Sirona

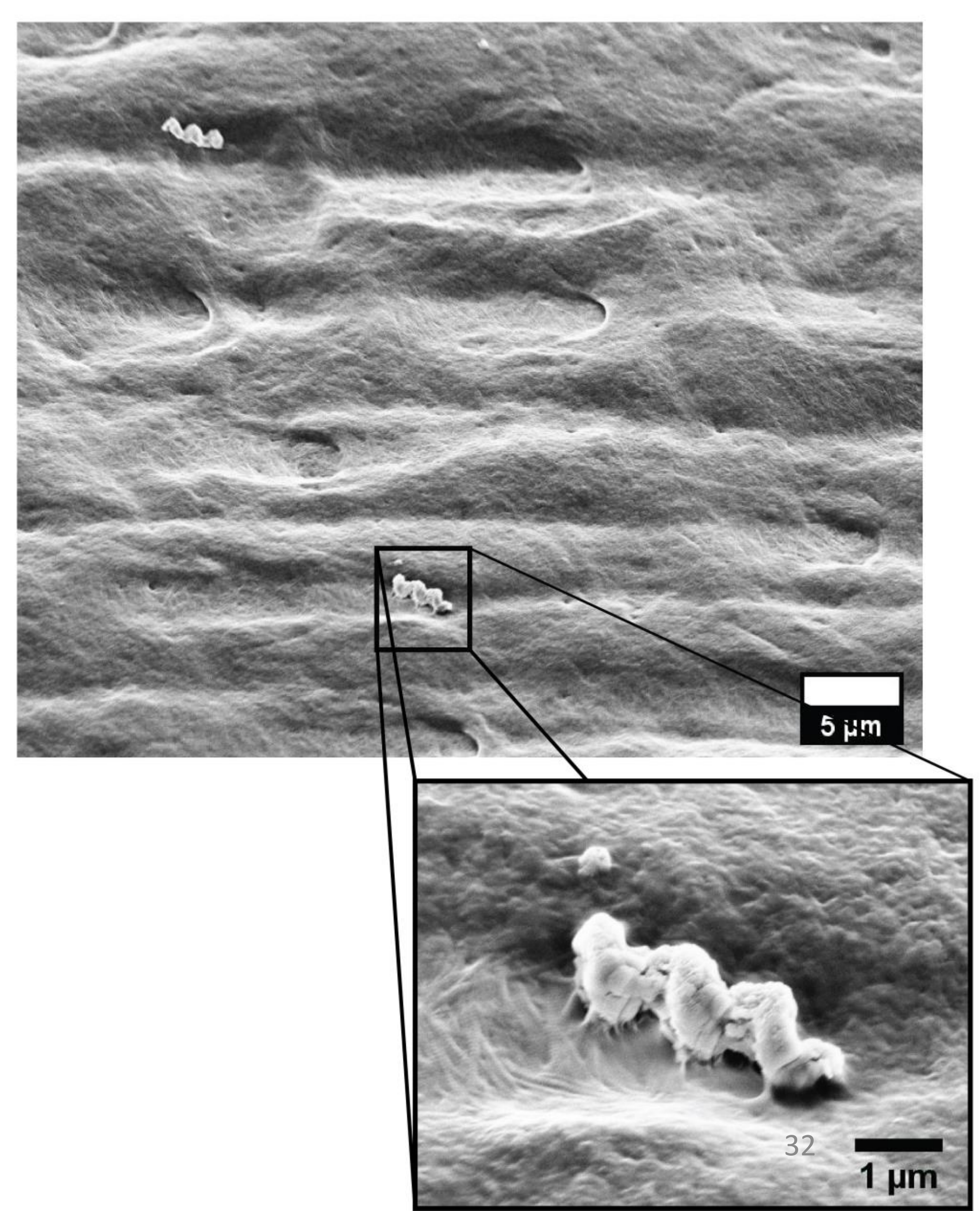
100µm – 250µm

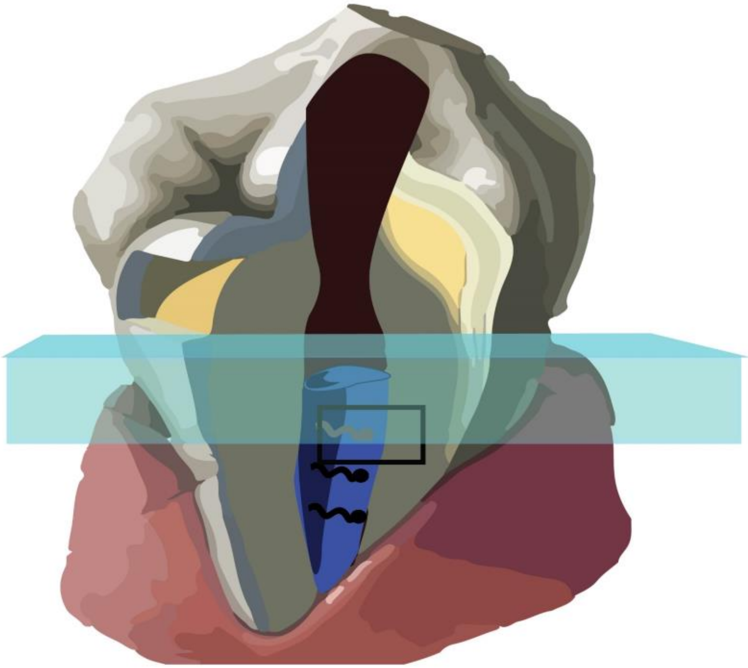
theranautilus

Our solution

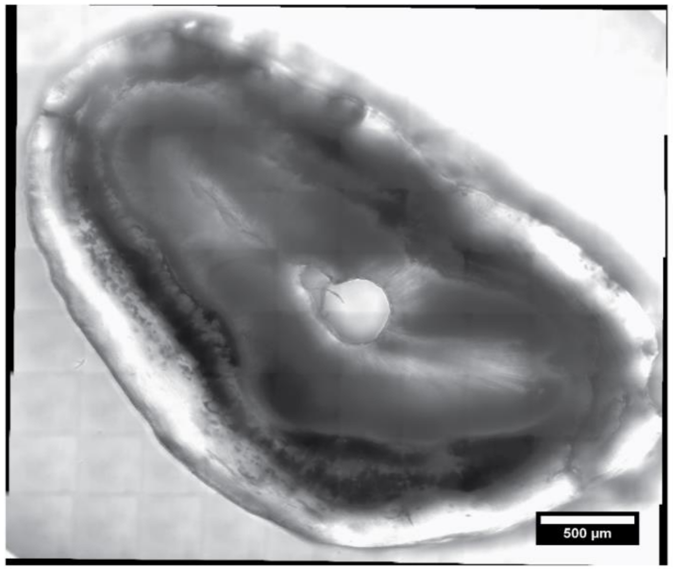


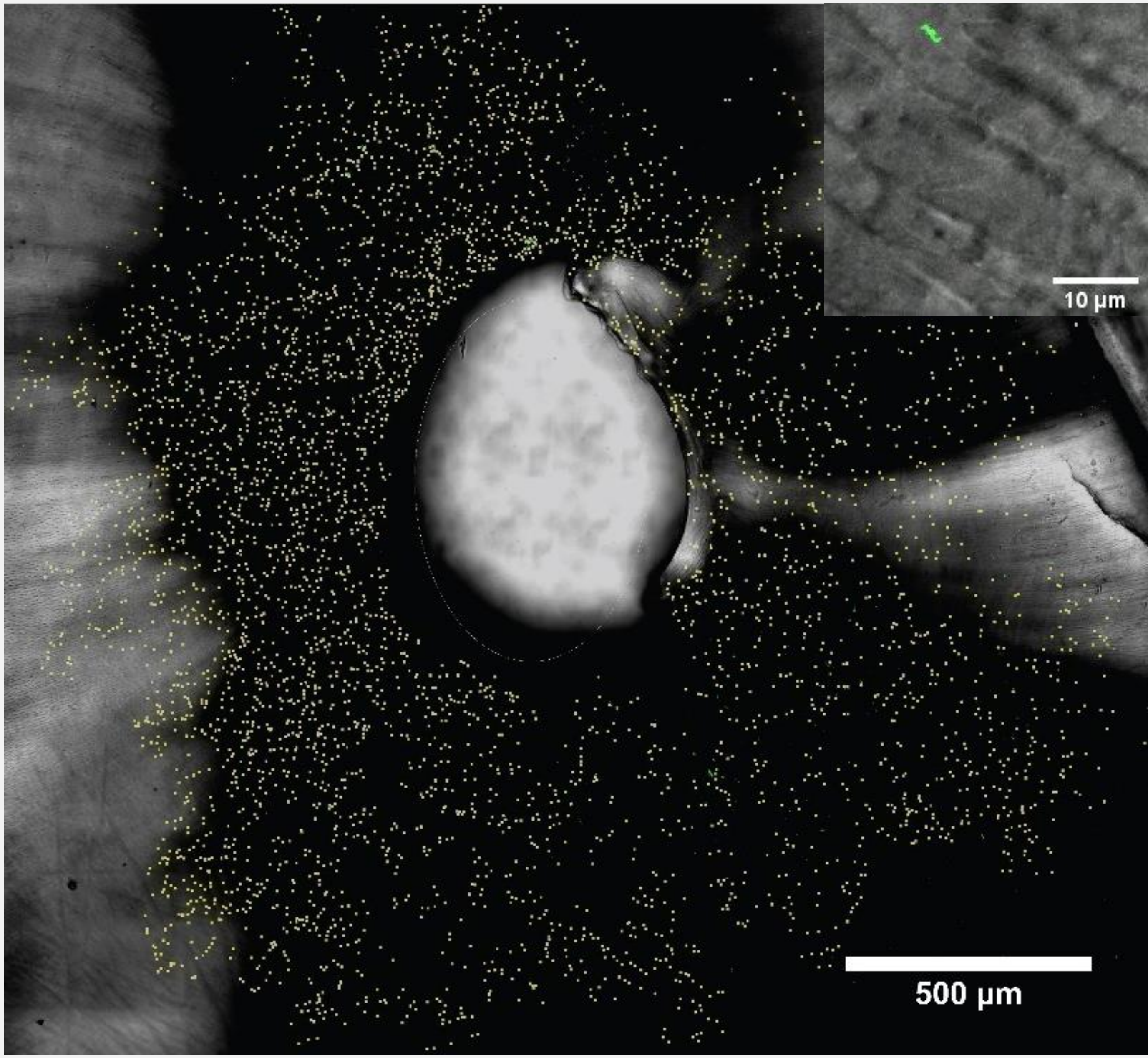




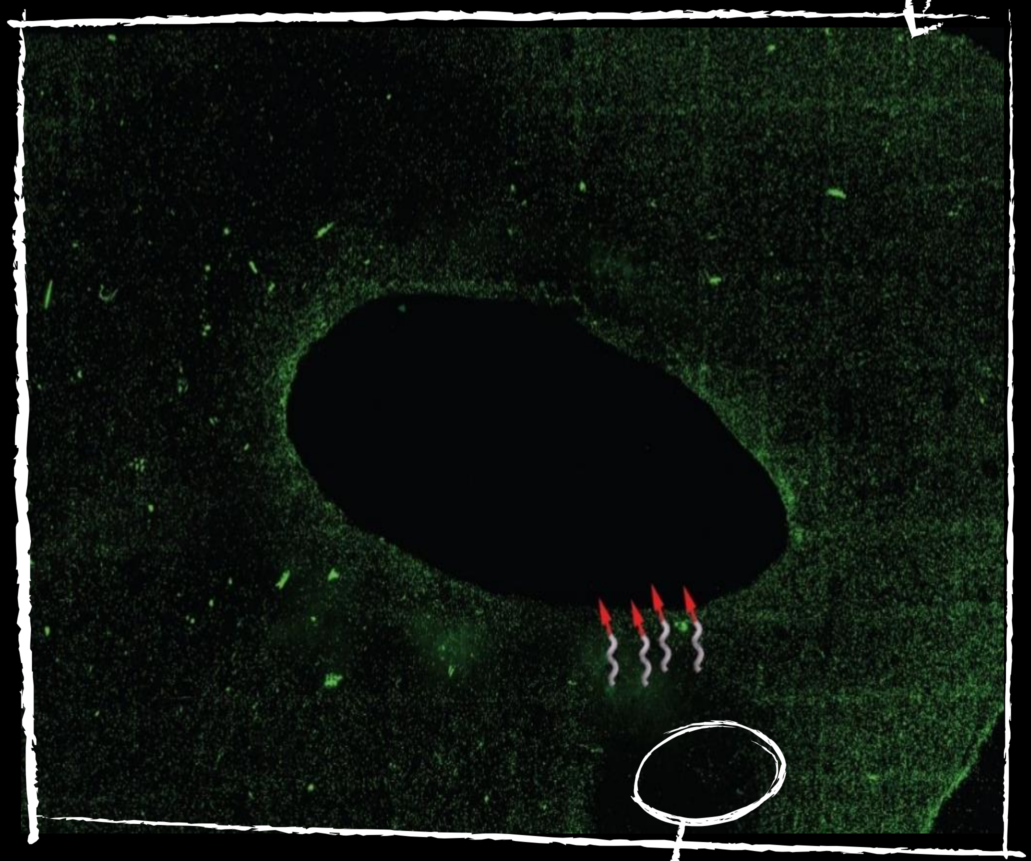


Cross section of human teeth used for experiments

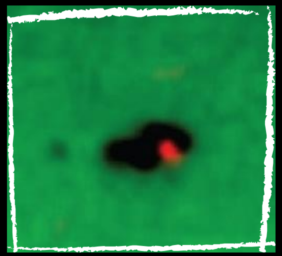


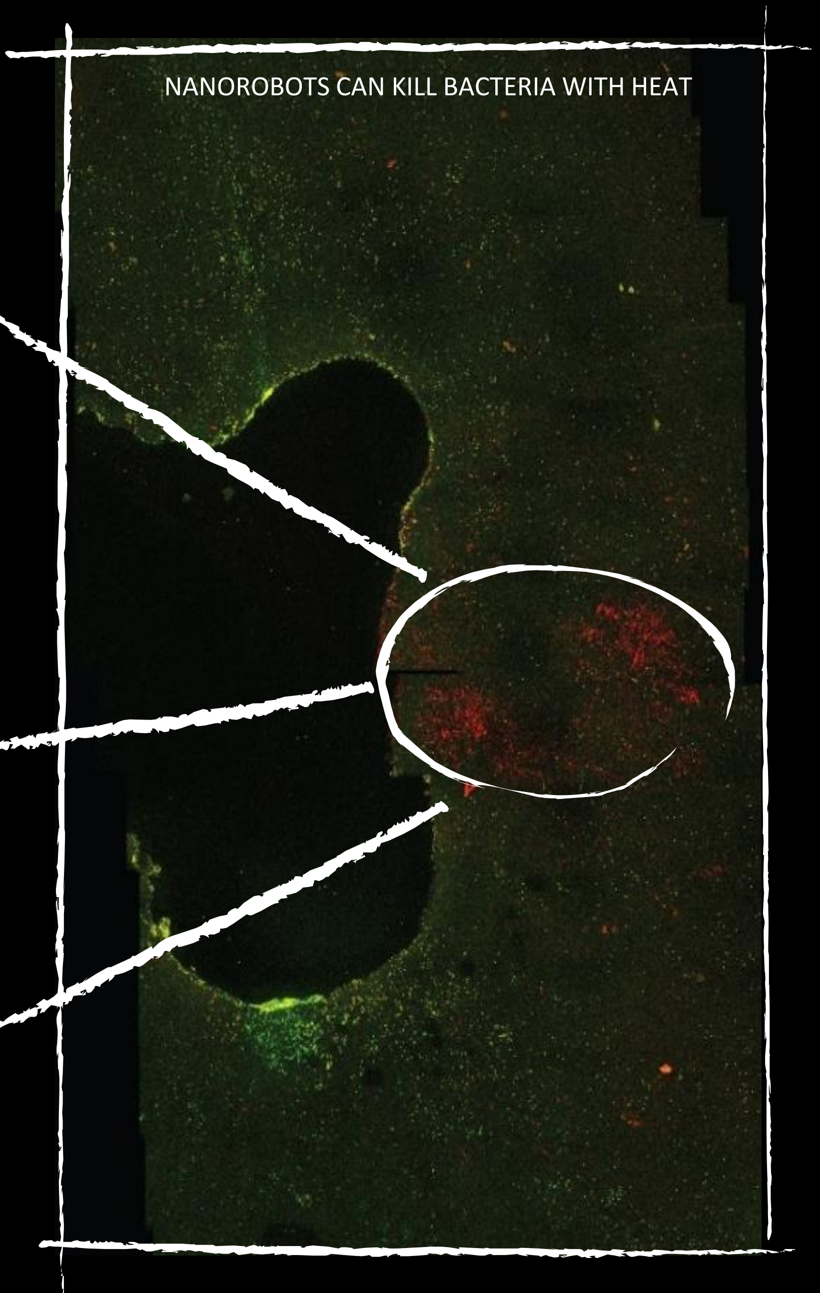


NANOROBOTS CAN BE RETRIEVED WHEN THE JOB IS DONE



Area of retrieved Nanorobots





NANOROBOTS CAN KILL BACTERIA WITH HEAT

Publications

- Helical Nanomachines as Mobile Viscometer,

Advanced Functional Materials, 1705687, 2018

- Helical nanobots as mechanical probes of intra- and extracellular environments

Journal of Physics: Condensed Matter, 224001, 2020

- Nanomotors Sense Local Physicochemical Heterogeneities in Tumor Microenvironments**.

Angewandte Chemie - International Edition (2020) doi:10.1002/anie.202008681.

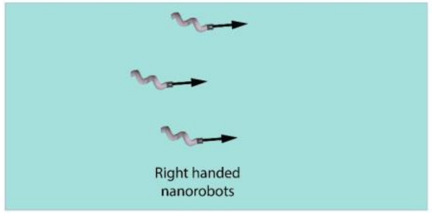
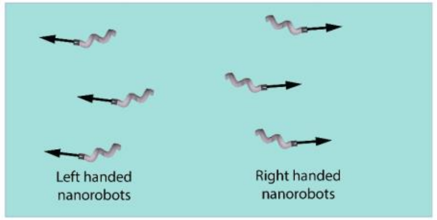
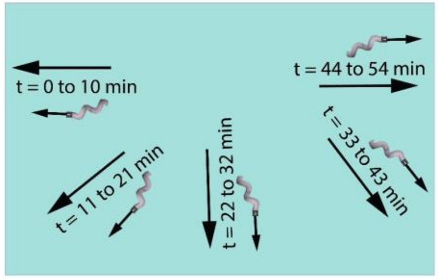
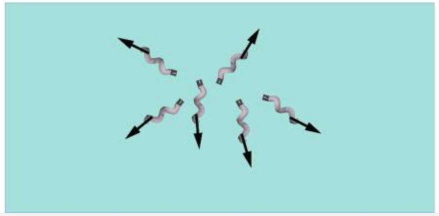
- Nanomotors for treatment of endodontic reinfection

D. Dasgupta*, S. Srinivas*, A. Ghosh
Chemrxiv

Thank You

EXTRAS

Treating Endodontic Reinfection: Comparison

Unidirectional rotating field Single Chirality	Angular Distribution	Area of sector of dentin covered	Experimental time needed to achieve area coverage	Comments
	Gaussian with single peak and FWHM ~ 40^0	~ 11 %	20 minutes	Precisely targeted penetration in one sector of the dentine
Unidirectional rotating field Opposite Chirality 	Bimodal FWHM ~ 50^0	~ 28 %	20 minutes	Precisely targeting diametrically opposite sectors of the dentine
Rotating rotating field 	Uniform distribution	~ 100 %	120 minutes	Uniform sector by sector delivery in dentine
Oscillating field 	Uniform distribution	~ 100 %	20 minutes	Uniform one shot delivery in dentine

magnetic torque on the helix due to the rotating magnetic field is denoted by τ. The dynamics of the helix can be written as: $\tau = \gamma\omega$ where γ is the rotational friction tensor and ω is the angular velocity vector. The torque is related to the magnetic moment m and B as: $\tau = m \times B$.

The magnetic field in the body frame $(x'y'z')$ of a helix is related to a magnetic field rotating in the lab frame by the following equation: $\begin{bmatrix} B_{x'} \\ B_{y'} \\ B_{z'} \end{bmatrix} = R \times \begin{bmatrix} Bcos(\Omega_B t) \\ Bsin(\Omega_B t) \\ 0 \end{bmatrix}$, where R is the transformation matrix and t is the time elapsed. The body frame magnetic field may be used to derive the body frame torque: $\begin{bmatrix} \tau_{x'} \\ \tau_{y'} \\ \tau_{z'} \end{bmatrix} = \begin{vmatrix} \vec{i} & \vec{j} & \vec{k} \\ m\cos\theta_m & 0 & m\sin\theta_m \\ B_{x'} & B_{y'} & B_{z'} \end{vmatrix}$ where m is the magnetic moment projected along the long axis and short axis.

Using standard notations to represent the Euler angles to describe the generalized orientation of a symmetric elongated object we can obtain the angular velocities in the body frame which are: $\omega_{x'} = \dot{\phi}\sin\theta\sin\psi + \dot{\theta}\cos\psi$, $\omega_{y'} = \dot{\phi}\sin\theta\cos\psi - \dot{\theta}\sin\psi$, $\omega_{z'} = \dot{\phi}\cos\theta + \dot{\psi}$.

Equating the two expressions for the torque and solving for $\dot{\phi}, \dot{\psi}, \dot{\theta}$, we get the Euler equations with $\beta = \Omega_B t - \phi$:

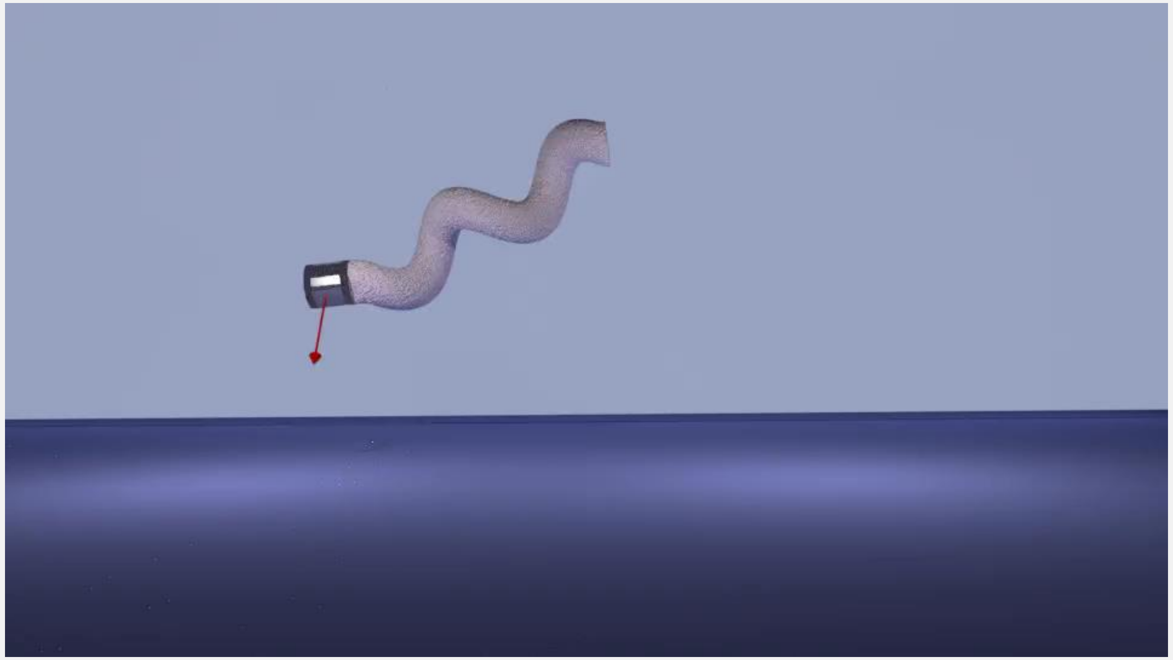
$$\dot{\phi} = \frac{mB}{\gamma_s \sin\theta}(\sin\theta_m cos\,\beta + cos\theta_m \sin\beta\, sin\theta\ \ cos\phi)$$

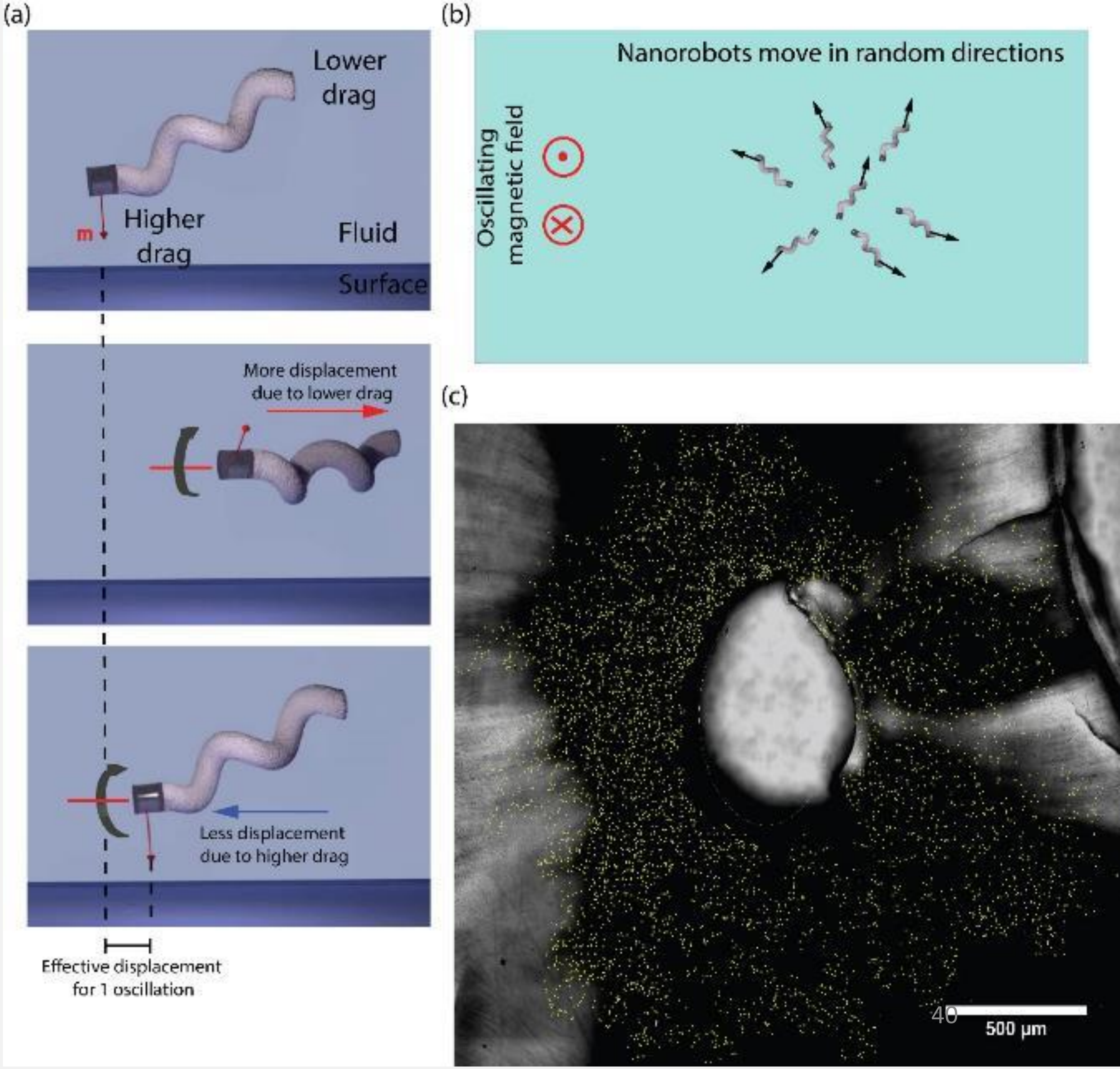
$$\dot{\theta} = -\frac{mB}{\gamma_s}\sin\beta\,(\sin\theta_m\cos\theta + \cos\theta_m\sin\theta\sin\psi)$$

$$\dot{\psi} = \frac{mB\cos\theta_m\,(\sin\beta\cos\theta\cos\psi - \cos\beta\sin\psi)}{\gamma_l} - \dot{\phi}\cos\theta$$

The above equations can be solved for the steady state configurations where θ and ψ remain constant in time. This leads to two different dynamical configurations for an object rotated by an external torque namely 'tumbling' and 'precession'. Tumbling motion means a precession angle $\theta = 90^o$. This occurs for all frequencies below Ω_1 denoted by mB/γ_s. At very low actuating frequencies ($\Omega_B < \Omega_1$), the magnetic moment of the nanomotor can follow the applied magnetic field with a constant phase difference and hence a phase locked tumbling motion of the nanomotor is observed, i.e., the nanomotor shows rotation about its geometric short axis. Above Ω_1, the nanomotor starts to precess about the axis of rotating field. This happens because beyond this frequency the angle between m and B becomes more the 90^o and the moment can no longer follow the magnetic field, thus causing phase slip. Precessional motion ($\theta < 90^o$) is a solution to the Euler angles and the object can show precessional phase locked motion for $\Omega_B > \Omega_1$. Above the critical frequency Ω_2, the magnetic moment of the helix starts to phase slip with the magnetic field.

Treating Endodontic Reinfection: Oscillating field





Differences in Cancer ECM and non-Cancer ECM

Physical differences

MDA-MB-231 HMLE