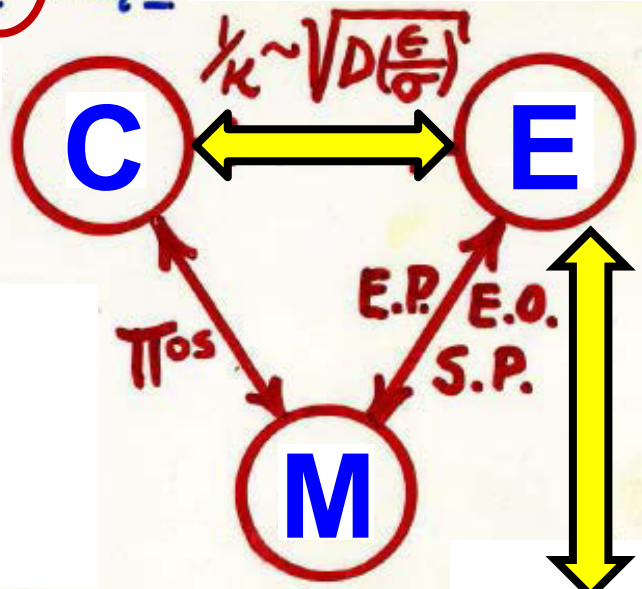
FFF: Complete Description of Coupled Transport and Biomolecular Interactions

$$\underline{N}_i = -D_i \nabla c_i + \frac{z_i}{|z_i|} u_i c_i \underline{E} + c_i \underline{v}$$

$$\frac{\partial c_i}{\partial t} = -\nabla \cdot \underline{N}_i + R_{vi}$$

Diffusion-Reaction



$$\nabla \cdot \epsilon \underline{E} = \rho_e = \sum_i z_i F c_i$$

$$(\underline{E} = -\nabla \Phi)$$

$$\nabla \cdot \underline{J} = -\frac{\partial \rho_e}{\partial t}$$

$$\underline{J} = \sum_i z_i F \underline{N}_i$$

"E.Q.S."

Navier Stokes

$$\rho \frac{D\underline{v}}{Dt} = -\nabla p + \mu \nabla^2 \underline{v} + \rho_e \underline{E}$$

$$\nabla \cdot \underline{v} = 0 \quad \text{(incompressible fluid)}$$

TODAY: start "fully coupled" examples

Term Paper Project

Enzymatic Targeting of the Stroma Ablates Physical Barriers to Treatment of Pancreatic Ductal Adenocarcinoma

Cancer Cell 2012

Paolo P. Provenzano,[1] Carlos Cuevas,[4] Amy E. Chang,[1] Vikas K. Goel,[1] ~~Daniel D. Von~~ Hoff,[5] and Sunil R. Hingorani[1,2,3,*]
v'ant Hoff
[1]Clinical Research Division
[2]Public Health Sciences Division
Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA
[3]Division of Medical Oncology, University of Washington School of Medicine, Seattle, WA 98195, USA
[4]Department of Radiology, University of Washington, Seattle, WA 98195, USA
[5]Clinical Translational Research Division, Translational Genomics Research Institute, Scottsdale, AZ 85259, USA
*Correspondence: srh@fhcrc.org
DOI 10.1016/j.ccr.2012.01.007

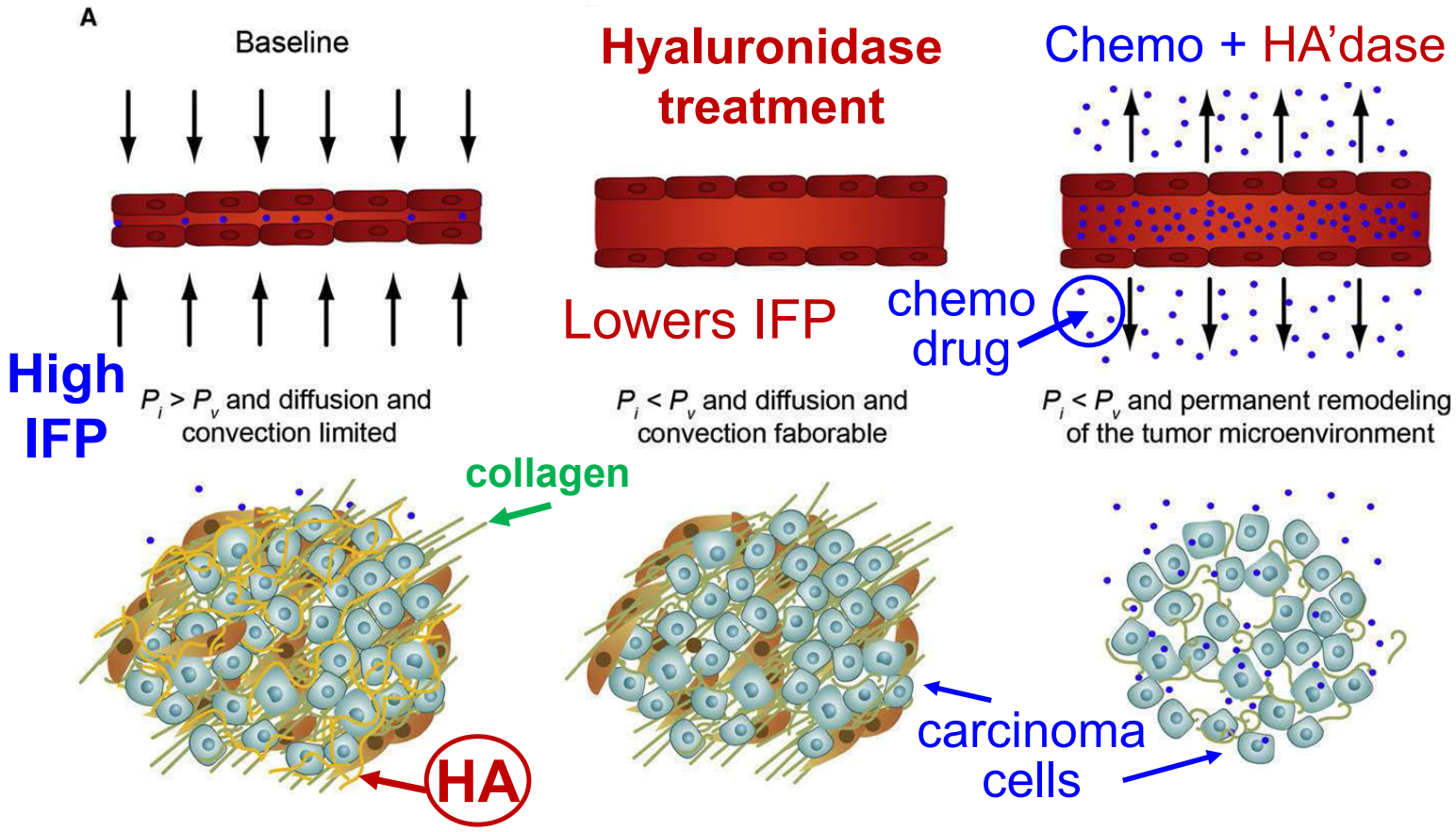
Hyaluronan, fluid pressure, and stromal resistance in pancreas cancer

British J of Cancer 2013

P P Provenzano[1,4] and S R Hingorani*[,1,2,3]

[1]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA; [2]Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA; [3]Division of Medical Oncology, University of Washington School of Medicine, Seattle, WA 98195, USA

Fig. 7: Altering Physicomechanics & Remodeling Stroma in Pancreatic Ductal Adenocarcinoma to Therapeutic Advantage

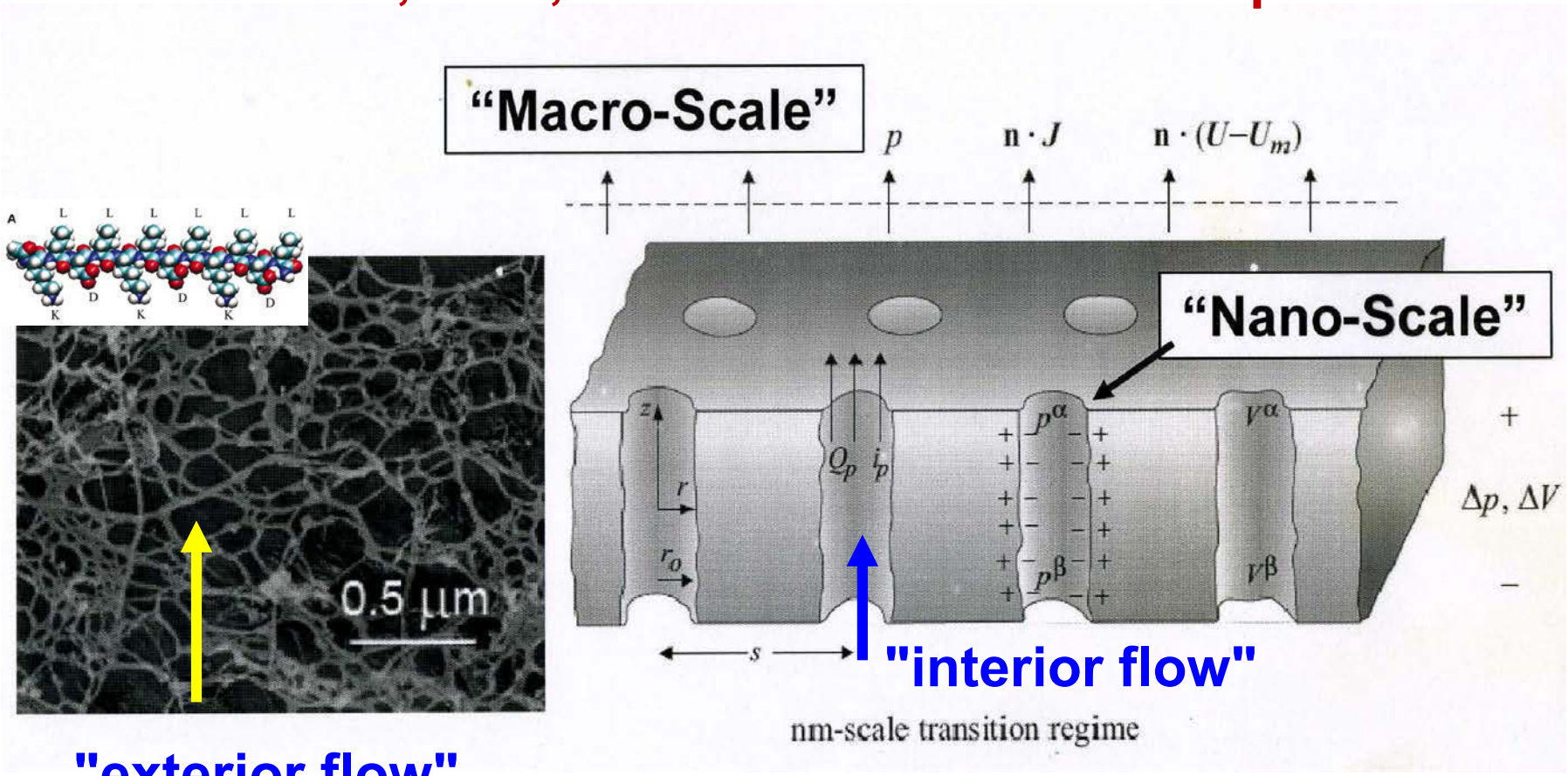


Courtesy of Elsevier, Inc., http://www.sciencedirect.com. Used with permission.
Source: Provenzano, Paolo P. et al. "Enzymatic targeting of the stroma ablates physical barriers to treatment of pancreatic ductal adenocarcinoma." Cancer Cell 21, no. 3 (2012): 418-429.

(A) High **I**nterstitial **F**luid **P**ressure → impedes diffusion & convection of chemo drugs. (B) Enzymatic degradation of stromal HA decreases IFP and relieves physical constraints on small molecule perfusion. (C) Combined enzymatic + cytotoxic therapy permanently remodels the tumor microenvironment to favor drug delivery

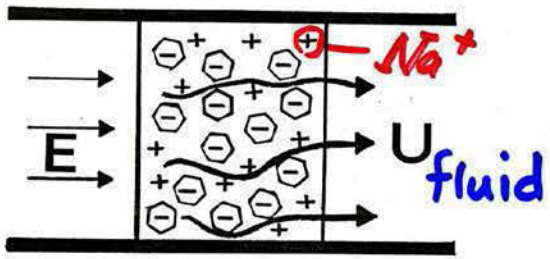
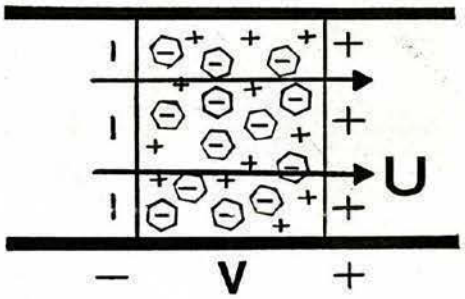
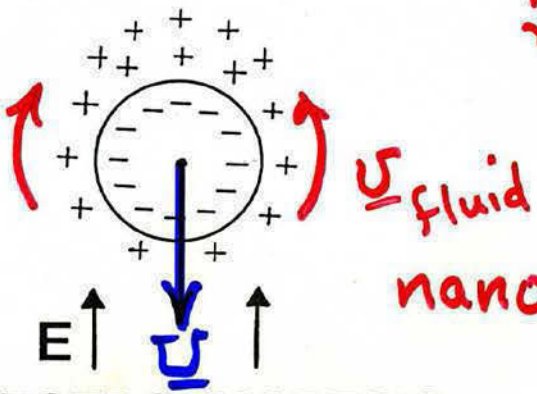
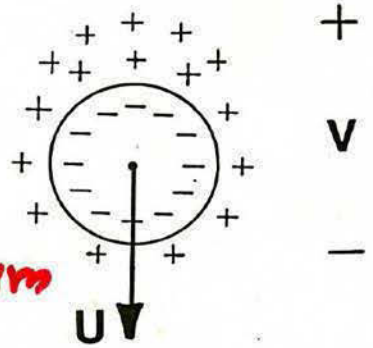
Fluid Flow in and across "Bio Porous Media:

Tissues, Gels, Intra- and Extra-cellular space



Local "nano"interior / exterior flows vs. "macro" Darcy model

ELECTROKINETIC PHENOMENA

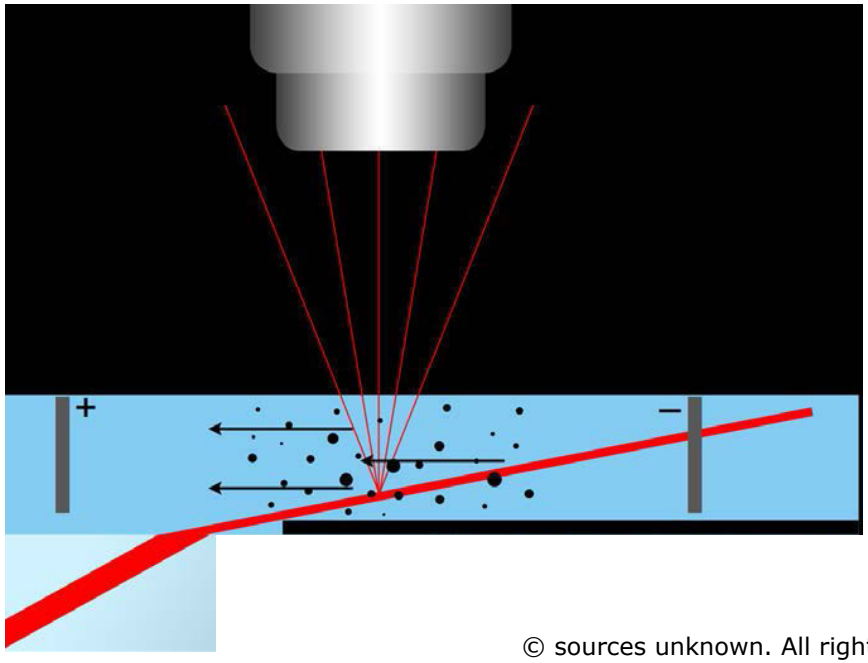
	Electrical → Mechanical	Mechanical → Electrical
Liquid Moves w.r.t. Solid	 **ELECTROOSMOSIS** (Reuss, 1809)	 • **STREAMING POTENTIAL** (Quincke, 1859) CURRENT
Solid Moves w.r.t. Liquid	 **ELECTROPHORESIS** (Reuss, 1809)	 **SEDIMENTATION POTEN.** (Dorn, 1880)

macro-porous media models

U_{fluid}

nano-continuum

Zeta Potential (particle charge) Instruments

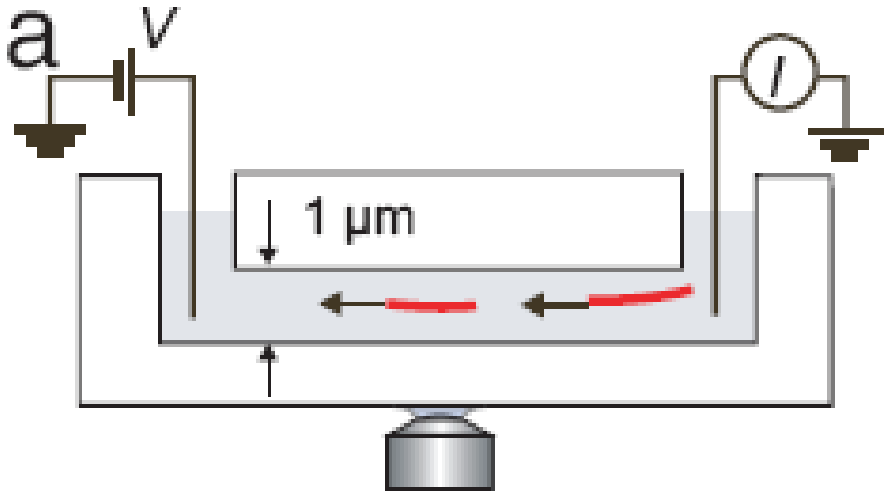


Measure "ζ" → infer "σ_{eff}"

Electrophoresis of individual microtubules in microchannels

PNAS 2007

M. G. L. van den Heuvel, M. P. de Graaff, S. G. Lemay, and C. Dekker*

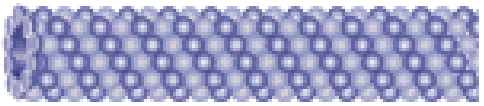


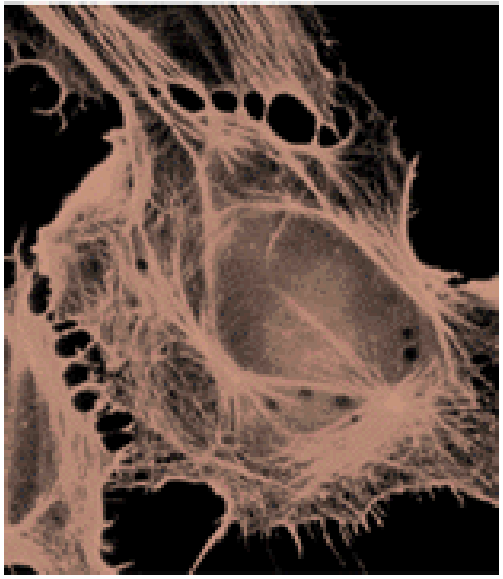
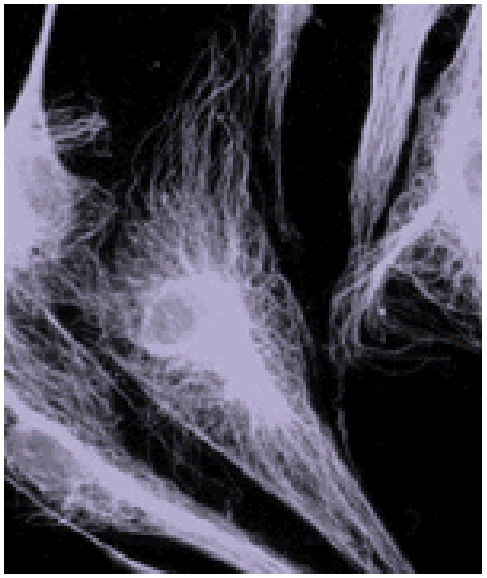
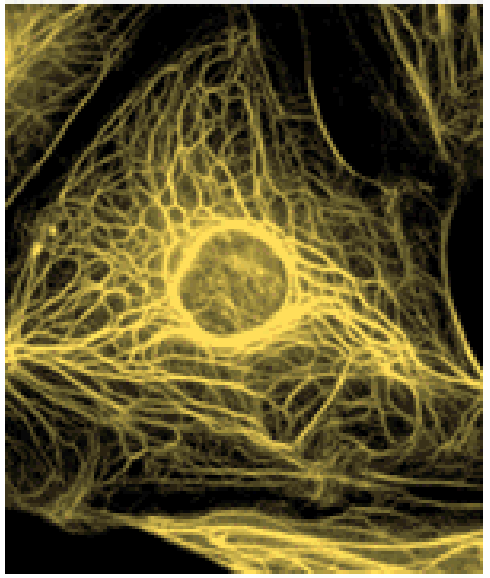
Microfluidic channels were fabricated .....
500 µm thick fused-silica substrates....

Microfabricated slit-like fluidic channels form an excellent system to confine and observe the electrophoretic motion of individual fluorescently labeled biomolecules, such as microtubules, actin filaments, or virus particles.

Primary Structural Filaments of the Cytoskeleton

Microfilaments | **Microtubules** | **Intermediate filaments**

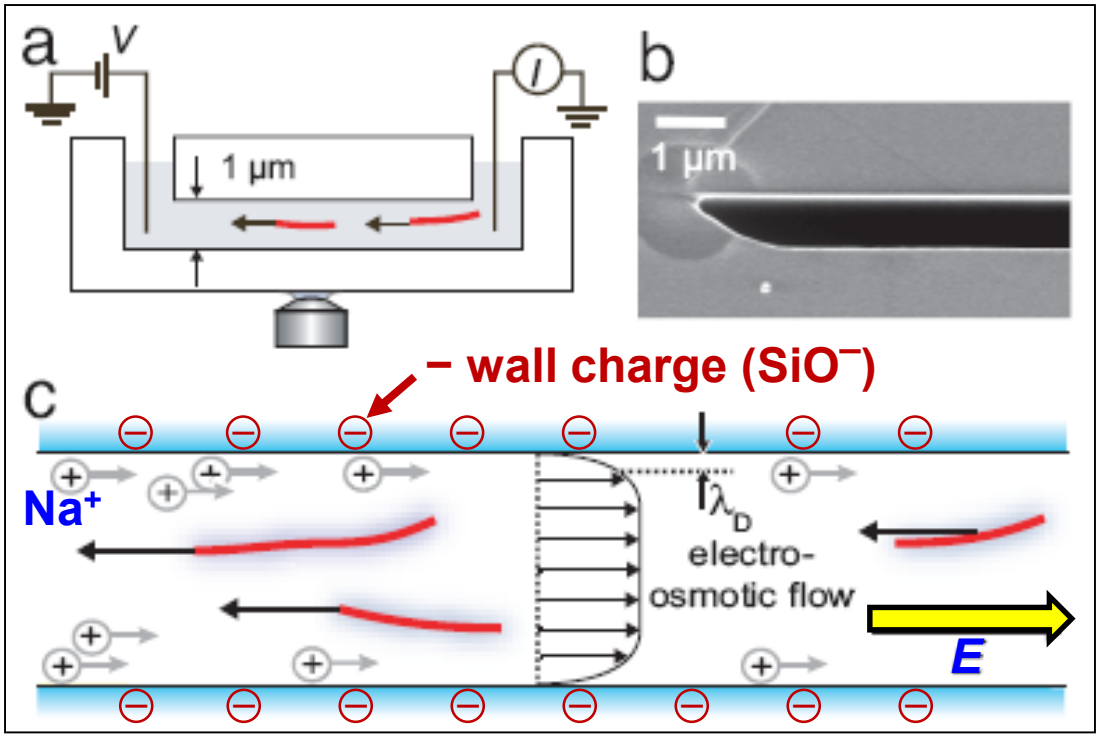
Source: Ingber, Donald E. "The architecture of life." Scientific American 278, no. 1 (1998): 48-57.

Electrophoresis of individual microtubules in microchannels

PNAS 2007

M. G. L. van den Heuvel, M. P. de Graaff, S. G. Lemay, and C. Dekker*

Kavli Institute of Nanoscience, Delft University of Technology, Lorentzweg 1, 2628 CJ, Delft, The Netherlands



The electrophoretic mobility of molecules is a fundamental property.... In ensemble measurements, such as gel electrophoresis or dynamic light scattering, the differences between individual molecules are obscured. Here, **individual microtubules** are visible by fluorescent labeling, and their electrophoretic motion can be imaged using fluorescence microscopy

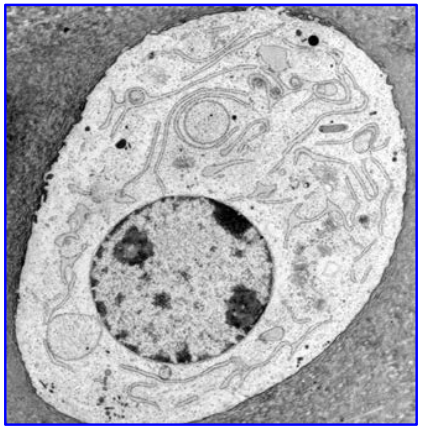
OPEN ACCESS Freely available online 2013 PLOS ONE

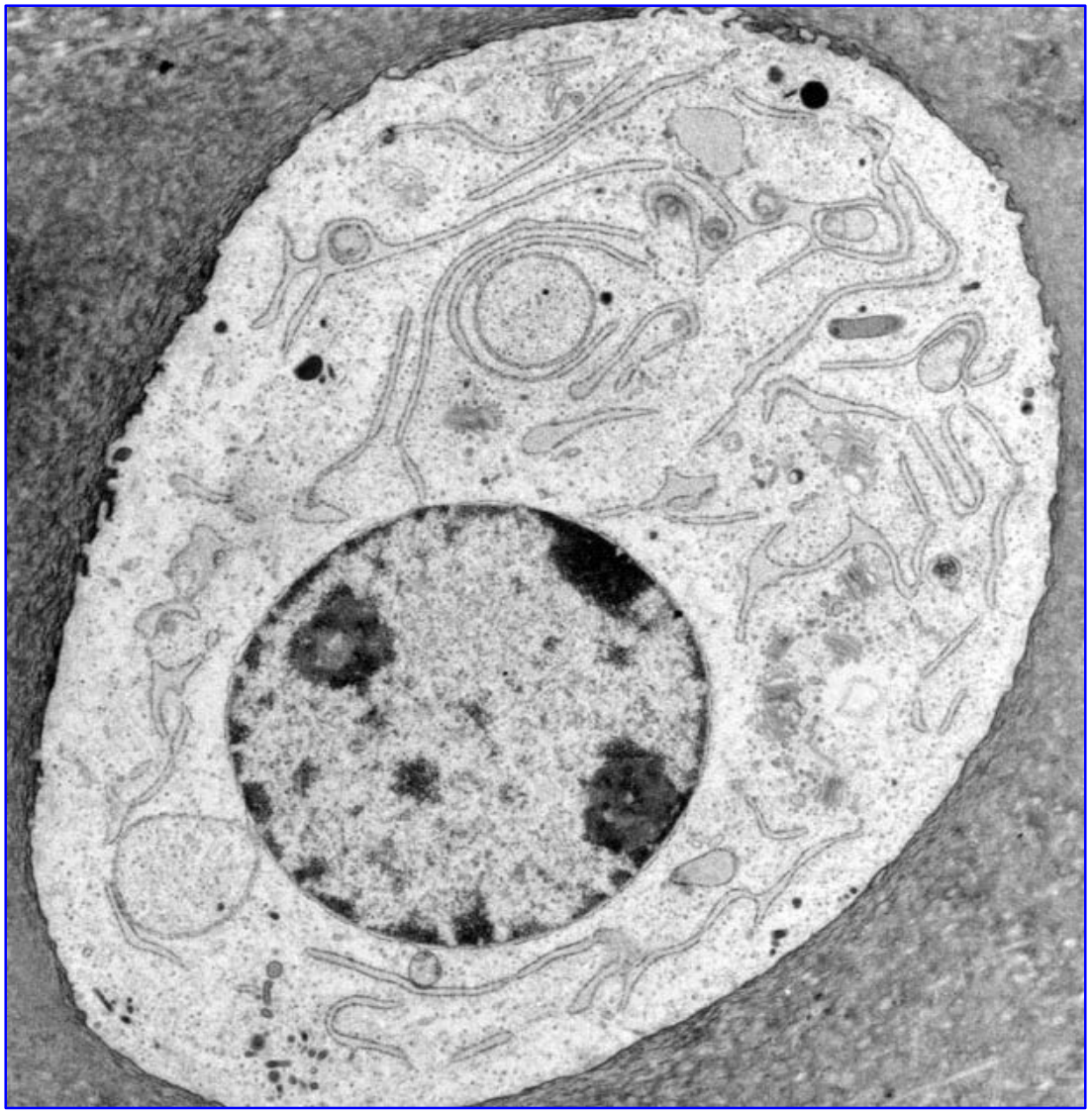
Cytoplasmic Electric Fields and Electroosmosis: Possible Solution for the Paradoxes of the Intracellular Transport of Biomolecules

Victor P. Andreev[1,2,3]*

Abstract

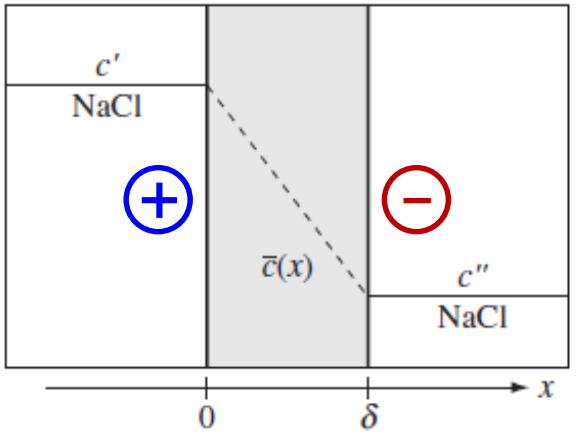
Electroosmotic flow might play an important role in the intracellular transport of biomolecules. The paper presents two mathematical models describing the role of electroosmosis in the transport of negatively charged messenger proteins to the negatively charged nucleus and in the recovery of the fluorescence after photobleaching





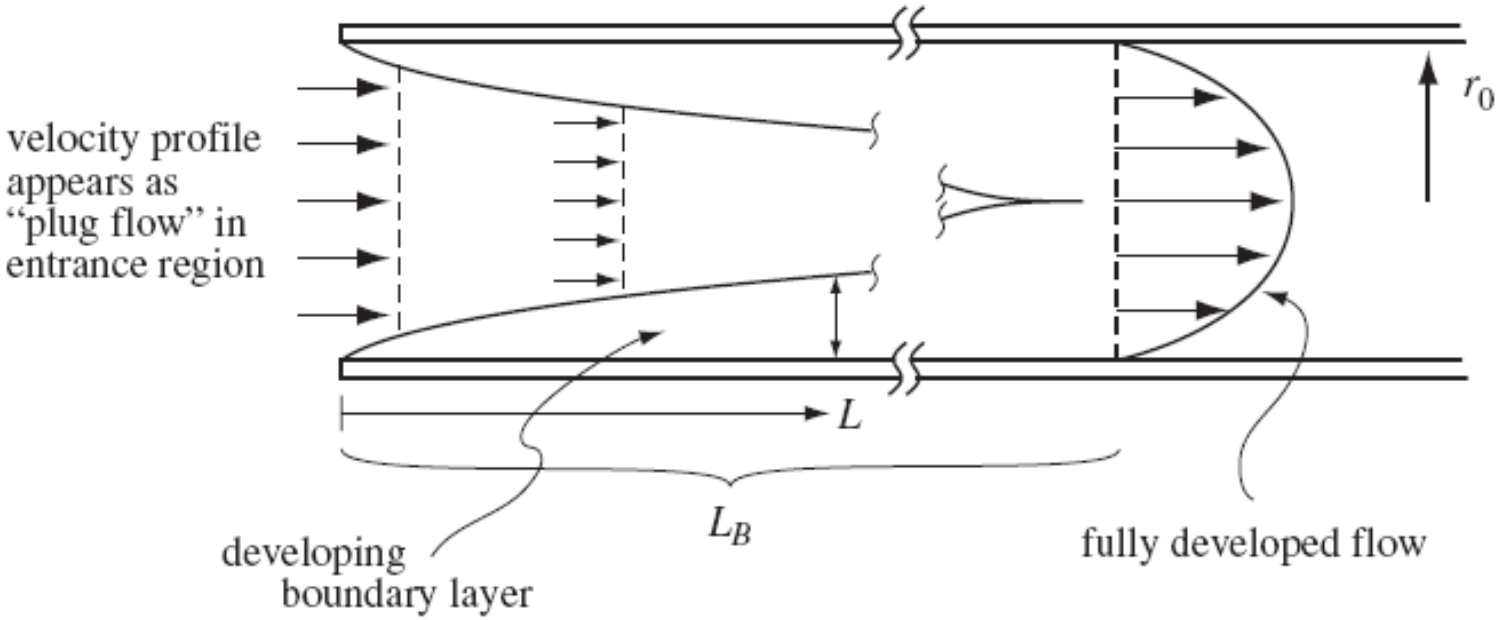
Transmembrane potentials everywhere inside

(ion channels + diffusion potentials)



$D_{Cl} > D_{Na}$

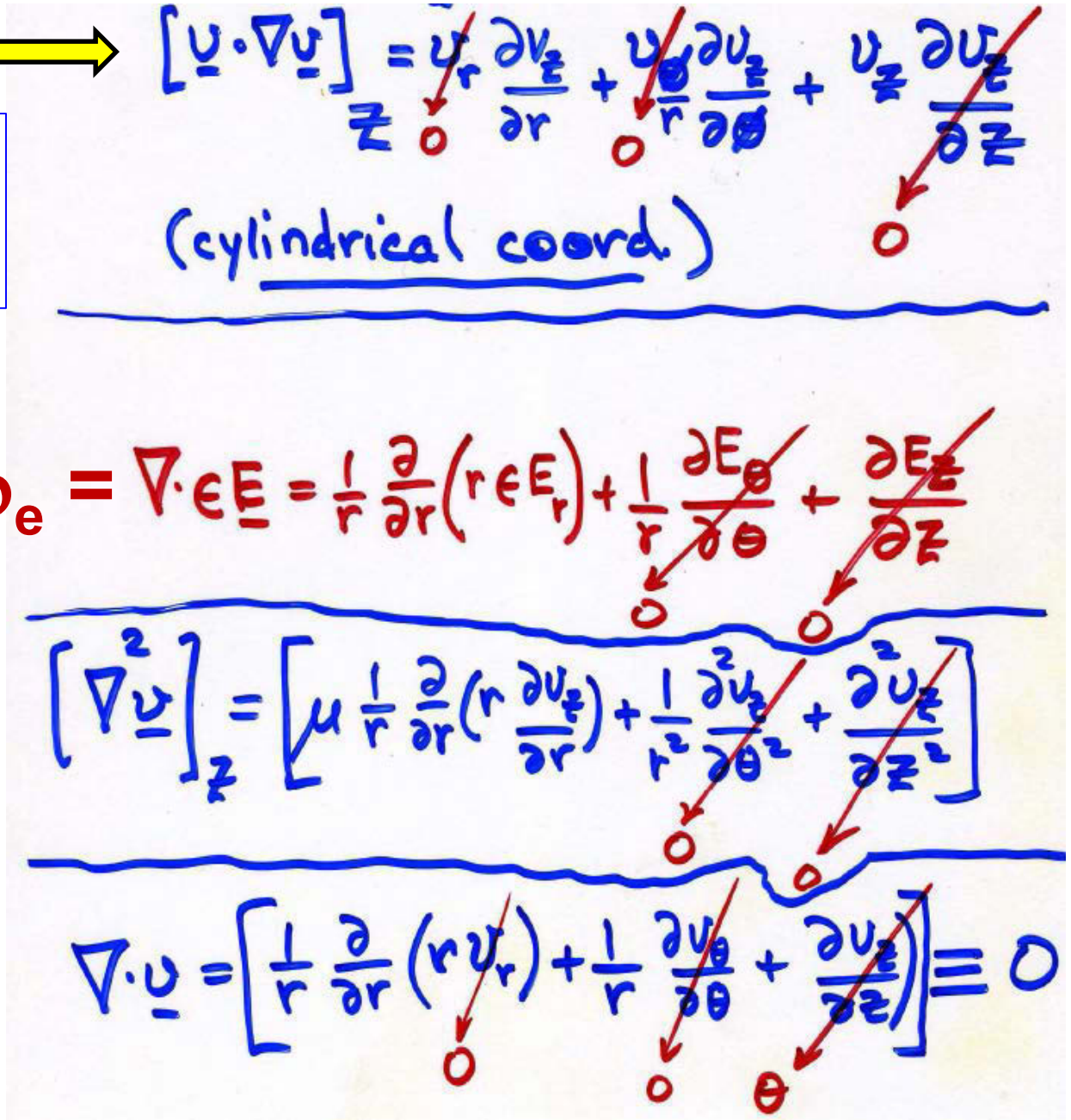
Transition to Fully Developed Flow in Channel



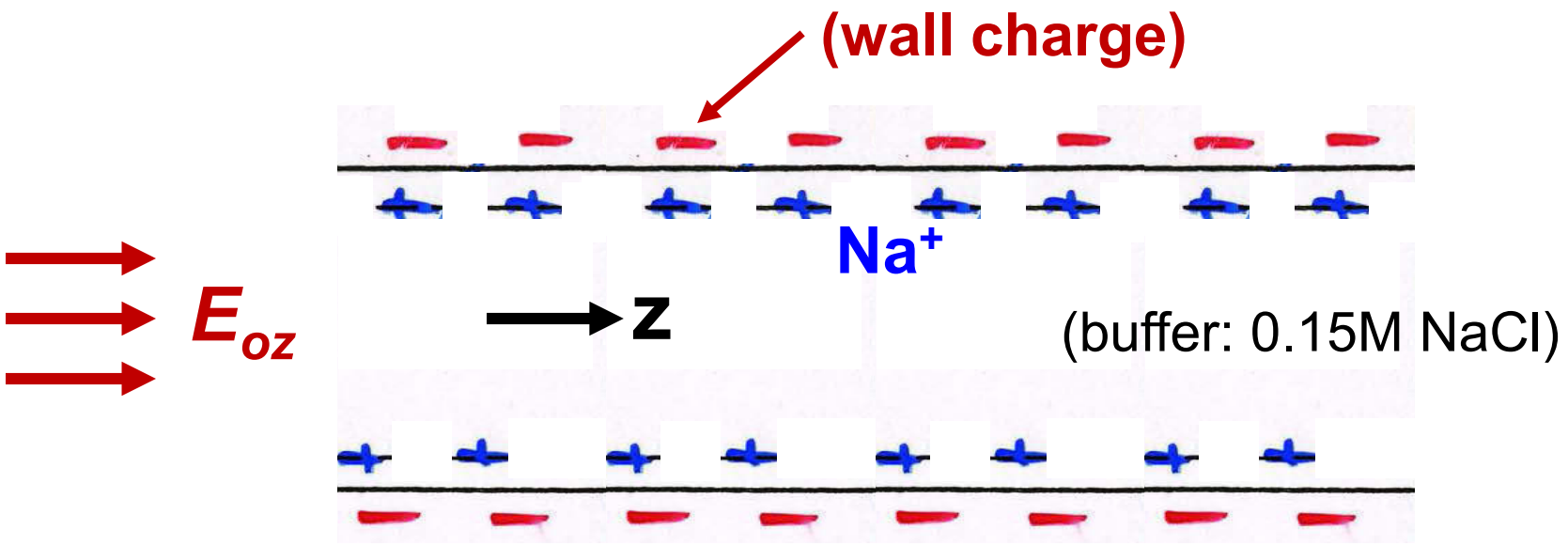
$$\frac{\partial v}{\partial t} = \frac{\mu}{\rho}\nabla^2 v$$

$$\tau_{vd} \sim \frac{R^2}{(\mu/\rho)}$$

Table B.4
p. 294

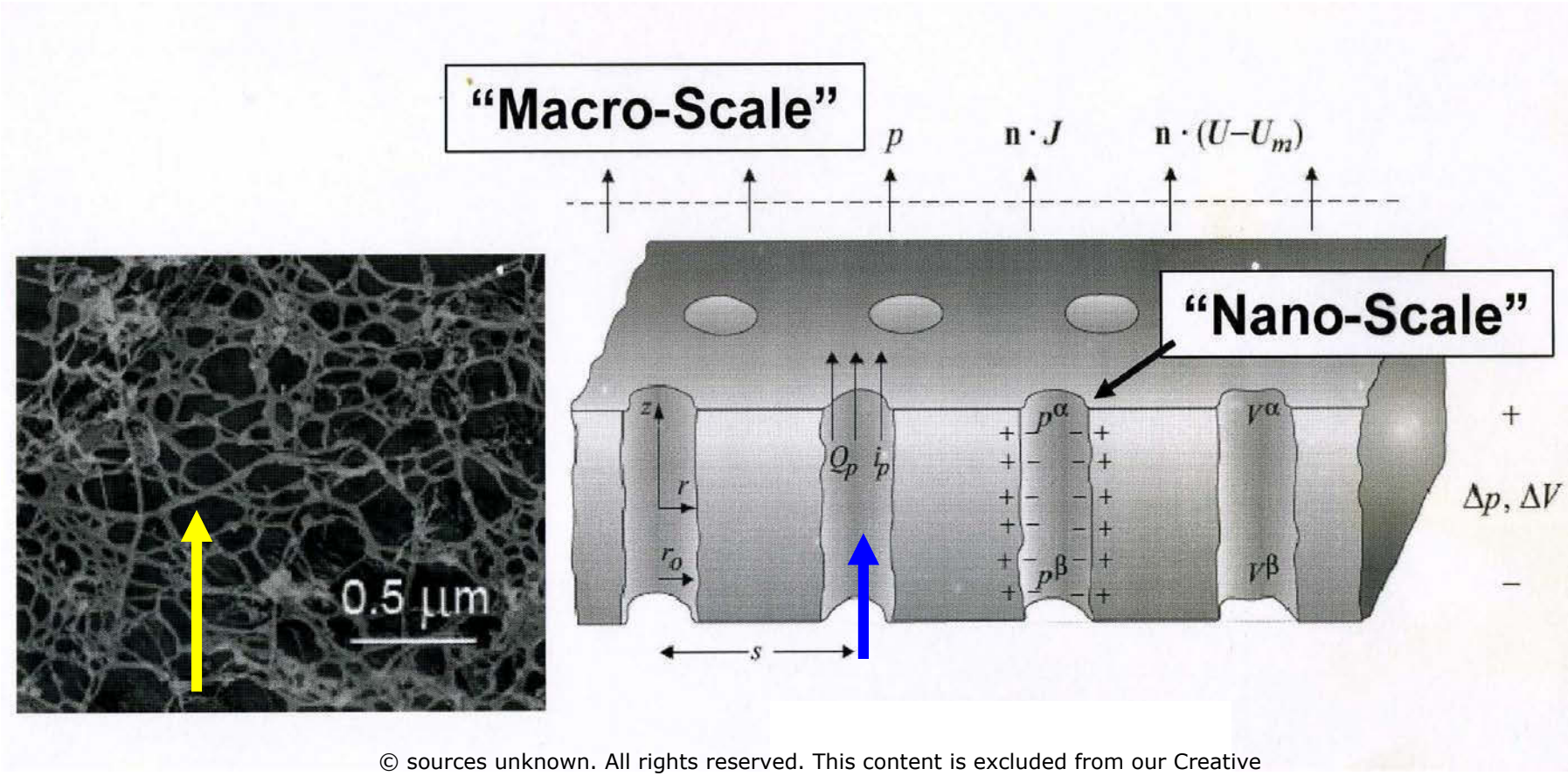


Electroosmosis



Charged fibers and "pores" in Bio-porous Media:

Tissues, Gels, Intra- and Extra-cellular space



Tandon, Kirby et al. *Electrophoresis* 2008, *29*, 1092–1101

Zeta potential and electroosmotic mobility in microfluidic devices fabricated from hydrophobic polymers: The origins of charge

Electroneutrality In bulk

$$\bar{\rho}_m(x) + \sum_i z_{i+} F \bar{c}_{i+}(x) + \sum_j z_{j-} F \bar{c}_{j-}(x) = 0$$

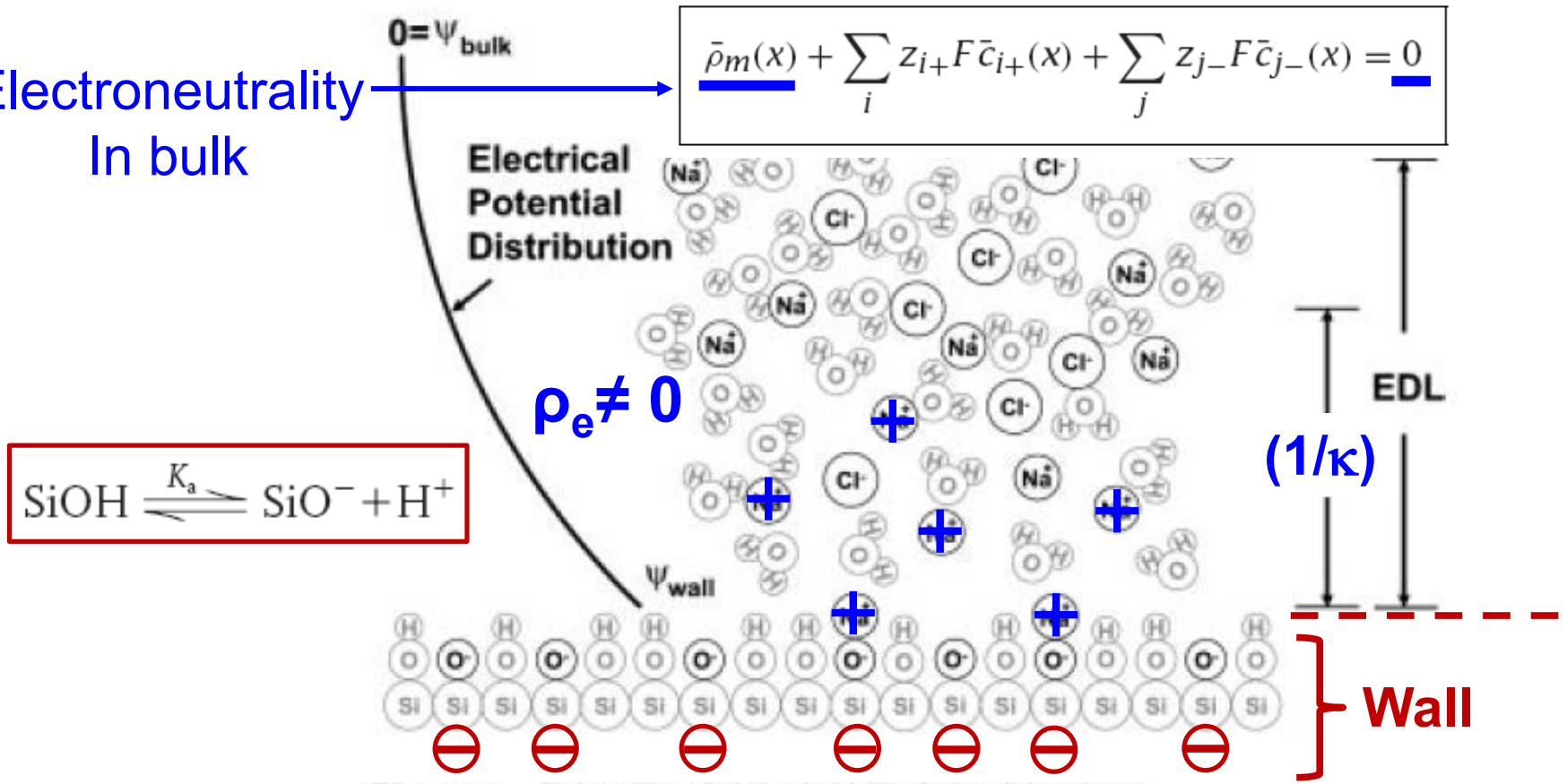
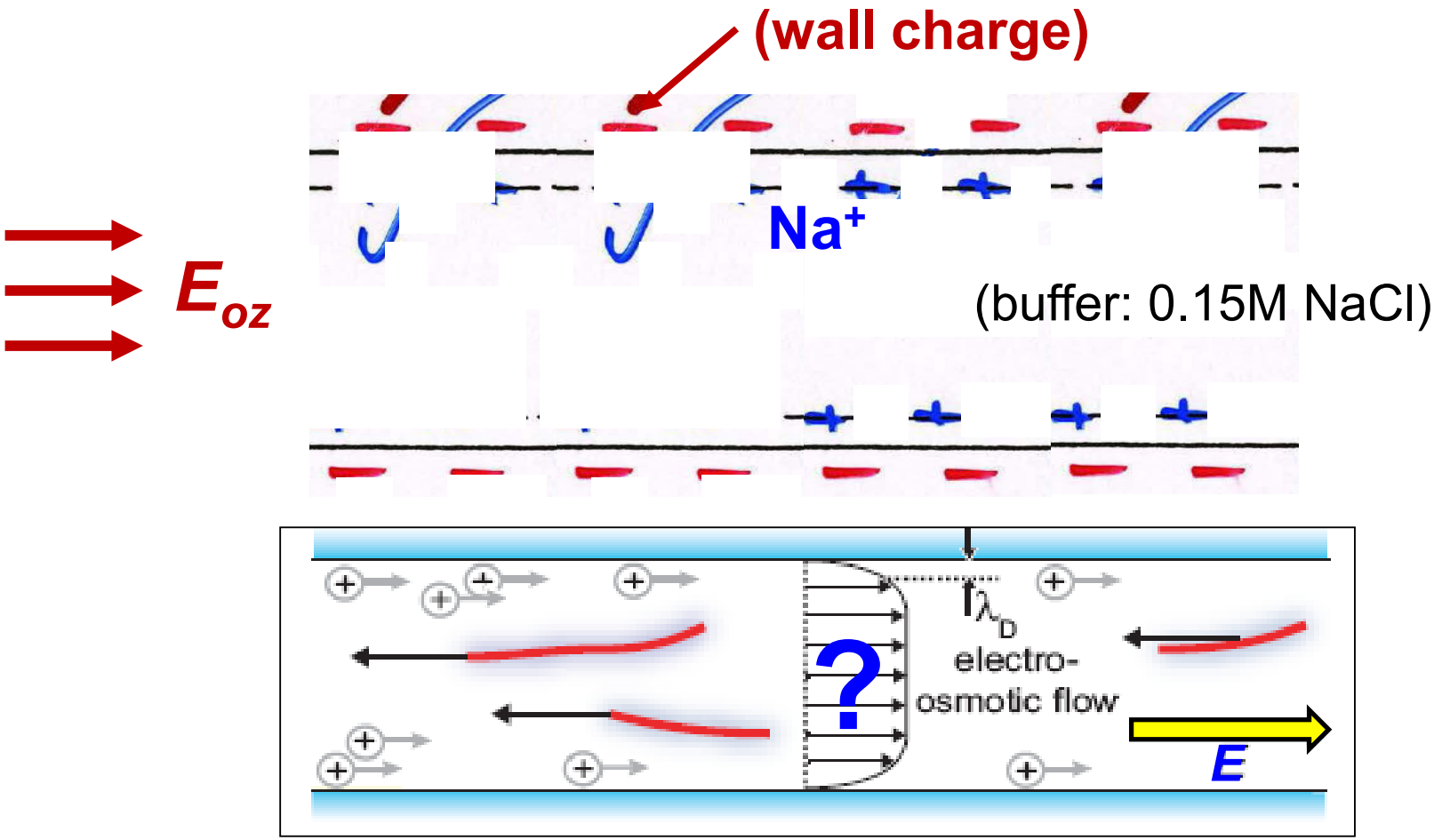


Figure 1. Scheme of the electrical double layer.

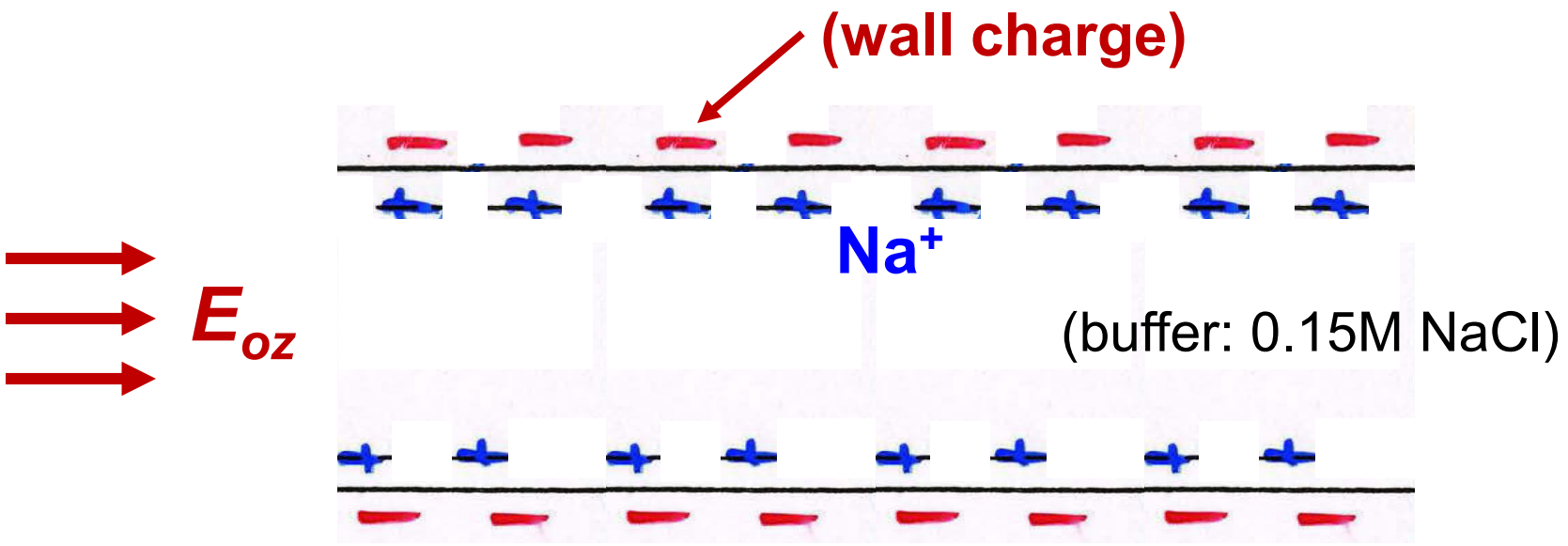
Source: Tandon, Vishal et al. "Zeta potential and electroosmotic mobility in microfluidic devices fabricated from hydrophobic polymers: 1. The origins of charge." Electrophoresis 29, no. 5 (2008): 1092-1101.

Electroosmosis



Courtesy of National Academy of Sciences. Used with permission.
Source: Van den Heuvel, M. G. L. et al. "Electrophoresis of individual microtubules in microchannels." Proceedings of the National Academy of Sciences 104, no. 19 (2007): 7770-7775.

Electroosmosis



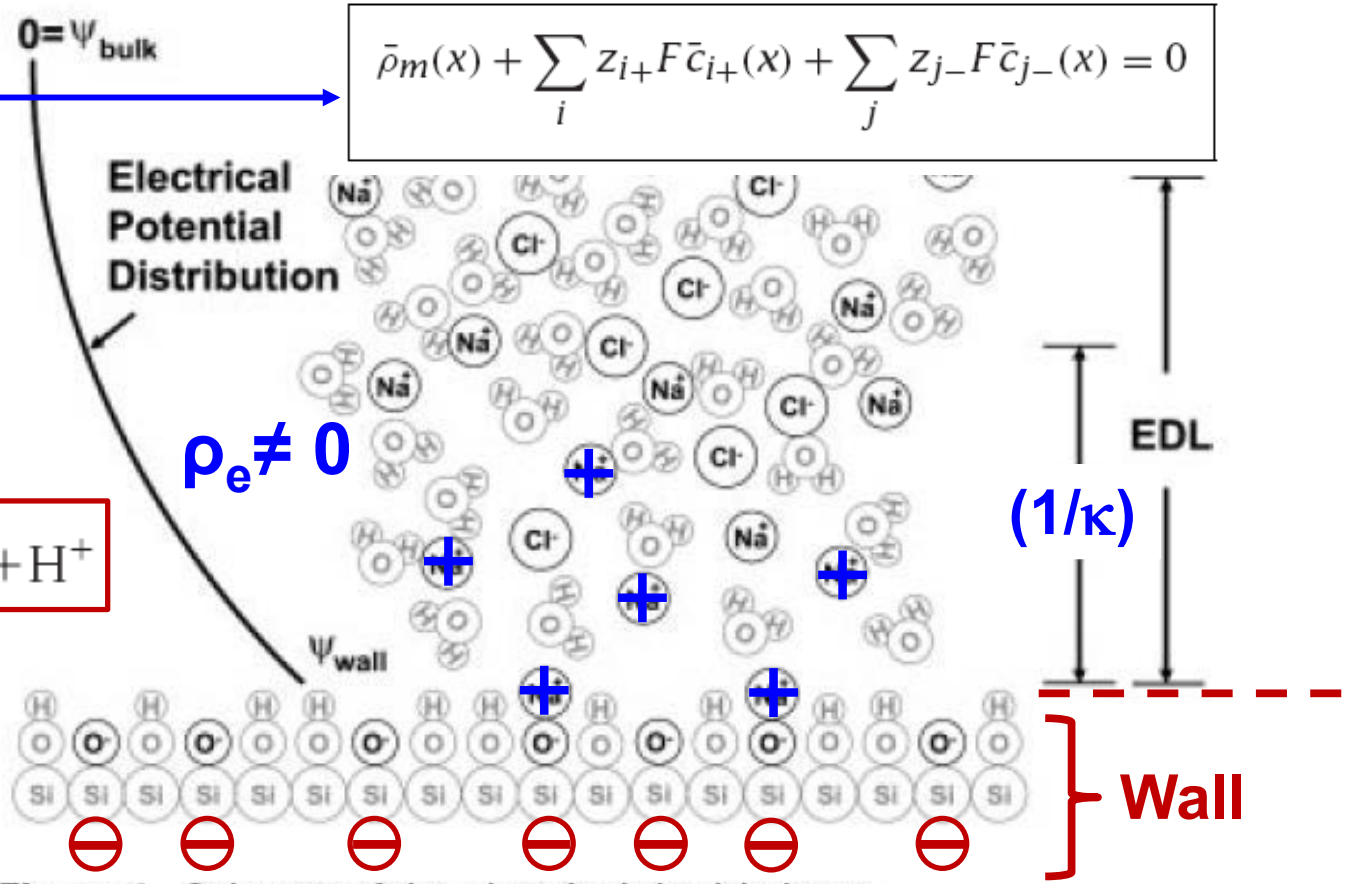
Where is the $\rho_e \underline{E}$ force on the fluid??

Tandon, Kirby et al. *Electrophoresis* 2008, *29*, 1092–1101

Zeta potential and electroosmotic mobility in microfluidic devices fabricated from hydrophobic polymers: The origins of charge

Electroneutrality In bulk

$$\bar{\rho}_m(x) + \sum_i z_{i+} F \bar{c}_{i+}(x) + \sum_j z_{j-} F \bar{c}_{j-}(x) = 0$$



$$SiOH \rightleftharpoons SiO^- + H^+ \quad (K_a)$$

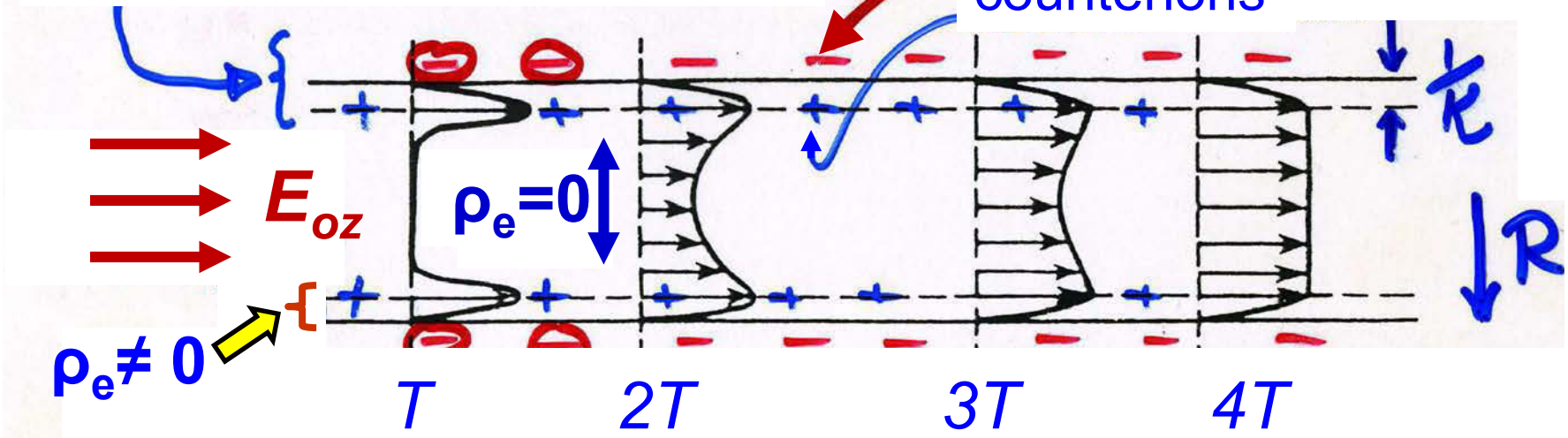
Figure 1. Scheme of the electrical double layer.

Electroosmosis: Turn-on Transient

Electrical Double Layer

Glass, plastic, proteins: surface charge on wall

counterions



$$-\nabla p + \mu \nabla^2 v + \rho_e \boldsymbol{E} = 0$$

$$\tau_{vd} \sim \frac{R^2}{(\mu/\rho)}$$

Superposition

$$v_z(r) = \left(\text{parabolic profile}\right)\frac{\Delta p}{L} + \left(\text{plug profile}\right)\frac{\Delta V}{L}$$

"E_{oz}"

$$0 = -\nabla p + \mu \nabla^2 \underline{v} \qquad 0 = \mu \nabla^2 \underline{v} + \rho_e \underline{E}$$

??

Stokes → (Poiseuille) + (Electroosmosis)

LAWS

C

(1) $\underline{N}_i = -D_i \nabla c_i + \frac{z_i}{|z_i|} u_i c_i \underline{E}^{TOT} + c_i \underline{v}$

(2) $(\partial c_i / \partial t) = -\nabla \cdot \underline{N}_i + R_i$

E

(3) $\nabla \cdot \epsilon \underline{E}^{TOT} = \rho_e = \sum z_i F c_i$

(4) $\underline{E}^{TOT} = -\nabla \Phi^{TOT}$

(5) $\nabla \cdot \underline{J} = -(\partial \rho_e / \partial t)$

(6) $\underline{J} = (\sigma \underline{E}^{TOT} + \rho_e \underline{v} + (\,) \nabla c_i) = \sum z_i F N_i$

M

(7) $\rho \frac{D\underline{v}}{Dt} = (-\nabla p + \mu \nabla^2 \underline{v} + \underbrace{\rho_e \underline{E}}_{\nabla \cdot \epsilon \underline{E}}^{TOT}) \simeq 0$

(8) $\nabla \cdot \underline{v} = 0$

c_+, c_- ; $\underline{N}_+, \underline{N}_-$; $\underline{E}$; $\underline{v}$

14 EQNS. IN 14 unknowns !!

LAWS

C

$$(1)\ \underline{N}_i = -D_i \nabla c_i + \frac{z_i}{|z_i|} u_i c_i \underline{E}^{TOT} + c_i \underline{v}$$

$$(2)\ (\partial c_i/\partial t) = -\nabla \cdot \underline{N}_i + R_i$$

E

$$(3)\ \nabla \cdot \epsilon \underline{E}^{TOT} = \rho_e = \sum z_i F c_i$$

$$(4)\ \underline{E}^{TOT} = -\nabla \Phi^{TOT}$$

$$(5)\ \nabla \cdot \underline{J} = -(\partial \rho_e/\partial t)$$

$$(6)\ \underline{J} = \sigma \underline{E}^{TOT} + \rho_e \underline{v} + (\ )\nabla c_i$$

M

$$(7)\ \rho \frac{D\underline{v}}{Dt} = \left(-\nabla p + \mu \nabla^2 \underline{v} + \rho_e \underline{E}^{TOT}\right) \simeq 0$$

$\nabla^2 \underline{v} \rightarrow 0$

$\rho_e \underline{E}^{TOT} \rightarrow \nabla \cdot \epsilon \underline{E}$

$$(8)\ \nabla \cdot \underline{v} = 0$$

Initial equilibrium (t < 0):

Tissue, tumor, can SWELL due to electrostatic repulsive interactions in ECM

+ $\rho_e \underline{E}$ → Donnan Osmotic Swelling Pressure

$$\text{“}p\text{”} \rightarrow \text{“}\pi^{os}\text{”}$$

20.430J / 2.795J / 6.561J / 10.539J Fields, Forces, and Flows in Biological Systems
Fall 2015