Micro-Scale Engineering –IV

Dielectrophoresis and Single-Cell Encapsulation

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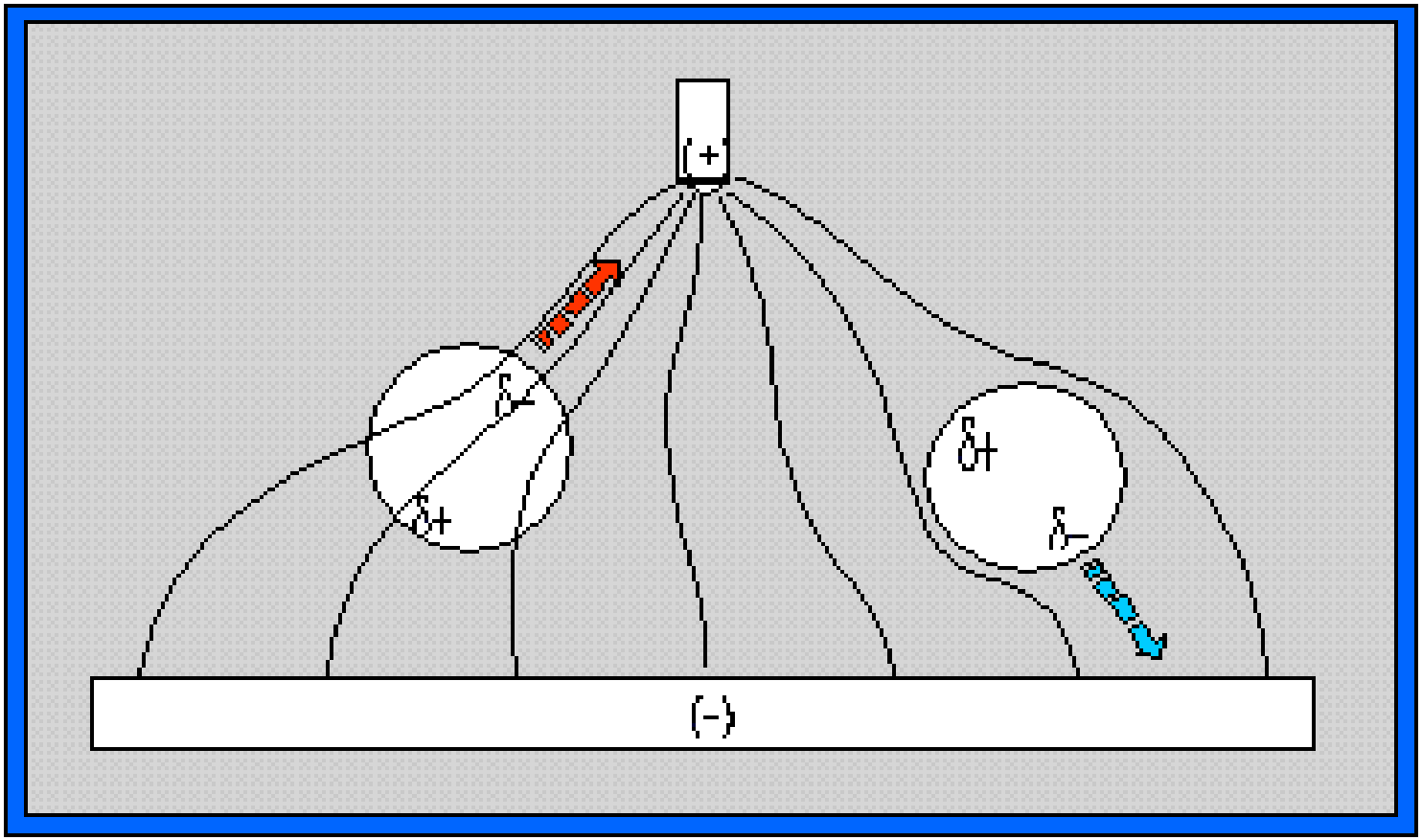
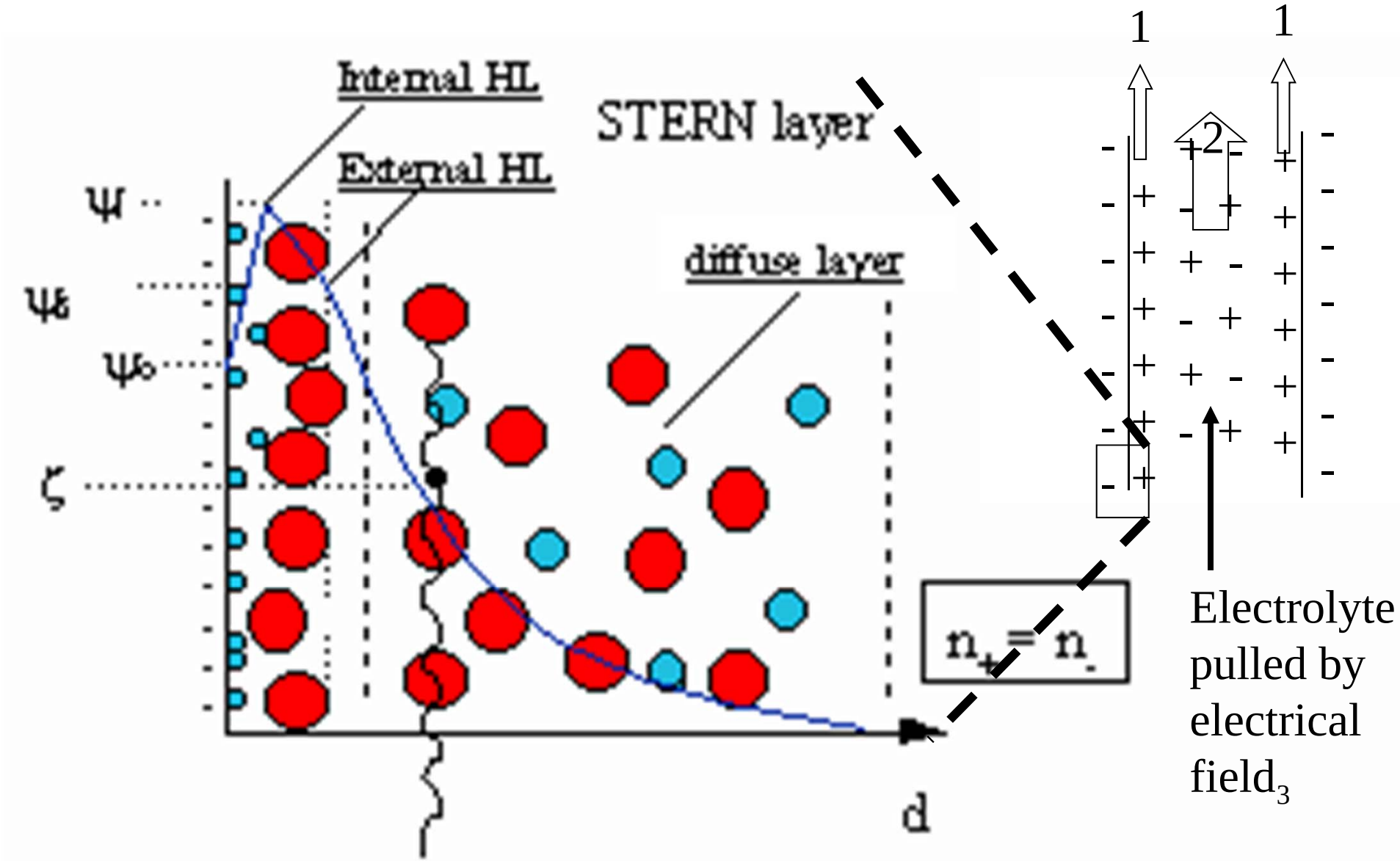
Dielectrophoresis



Two different particles in a non-uniform electric field. The particle on the left is more polarisable than the surrounding medium and is attracted towards the strong field at the pin electrode, whilst the particle of low polarisability on the right is directed away from the strong field region.

Electrochemical double layer → Capacitance



f_{CM} is the Clausium-Mossotti factor which describes the frequency-dependent dielectri characteristics of the particle and its surroundings.

Simulation

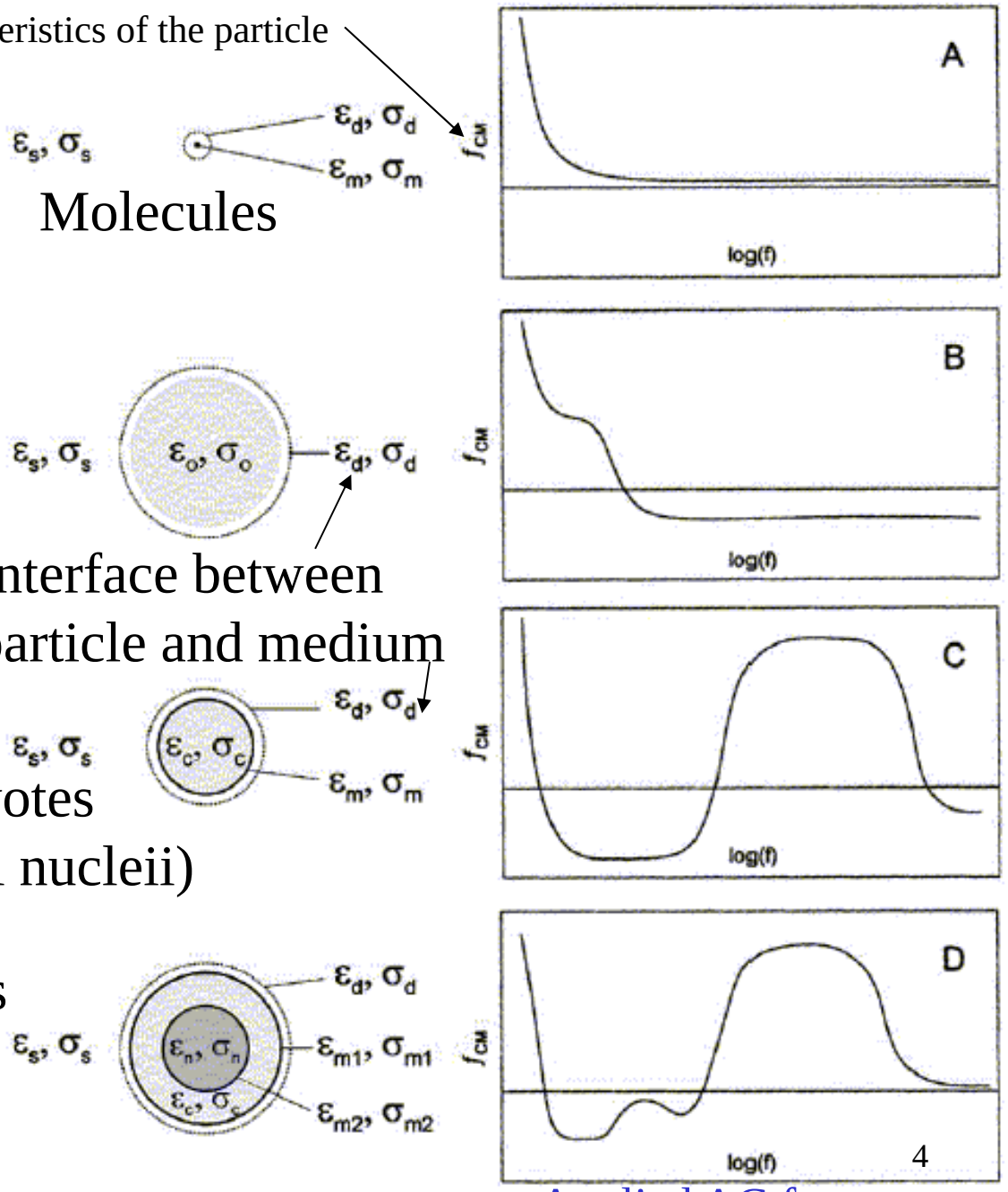
Molecules

Inert particles

Interface between particle and medium

Entities with a single membrane (virus, prokaryotes and eukaryotes with small nucleii)

Complex cells (plant cells or mammalia cells with large nucleii)



Applied AC frequency

Dielectrophoresis Force and Cutoff Frequency

much lower than that of its cytoplasm by an inhomogeneous AC electric field of frequency f may be approximated as:

$$F_{\mathrm{DEP}} = 2\pi\varepsilon_s\varepsilon_0 r^3 \cdot \left(\frac{f^2 - {f_{\mathrm{CO}}}^2}{f^2 + 2{f_{\mathrm{CO}}}^2}\right) \cdot \nabla E^2 \quad (1)$$

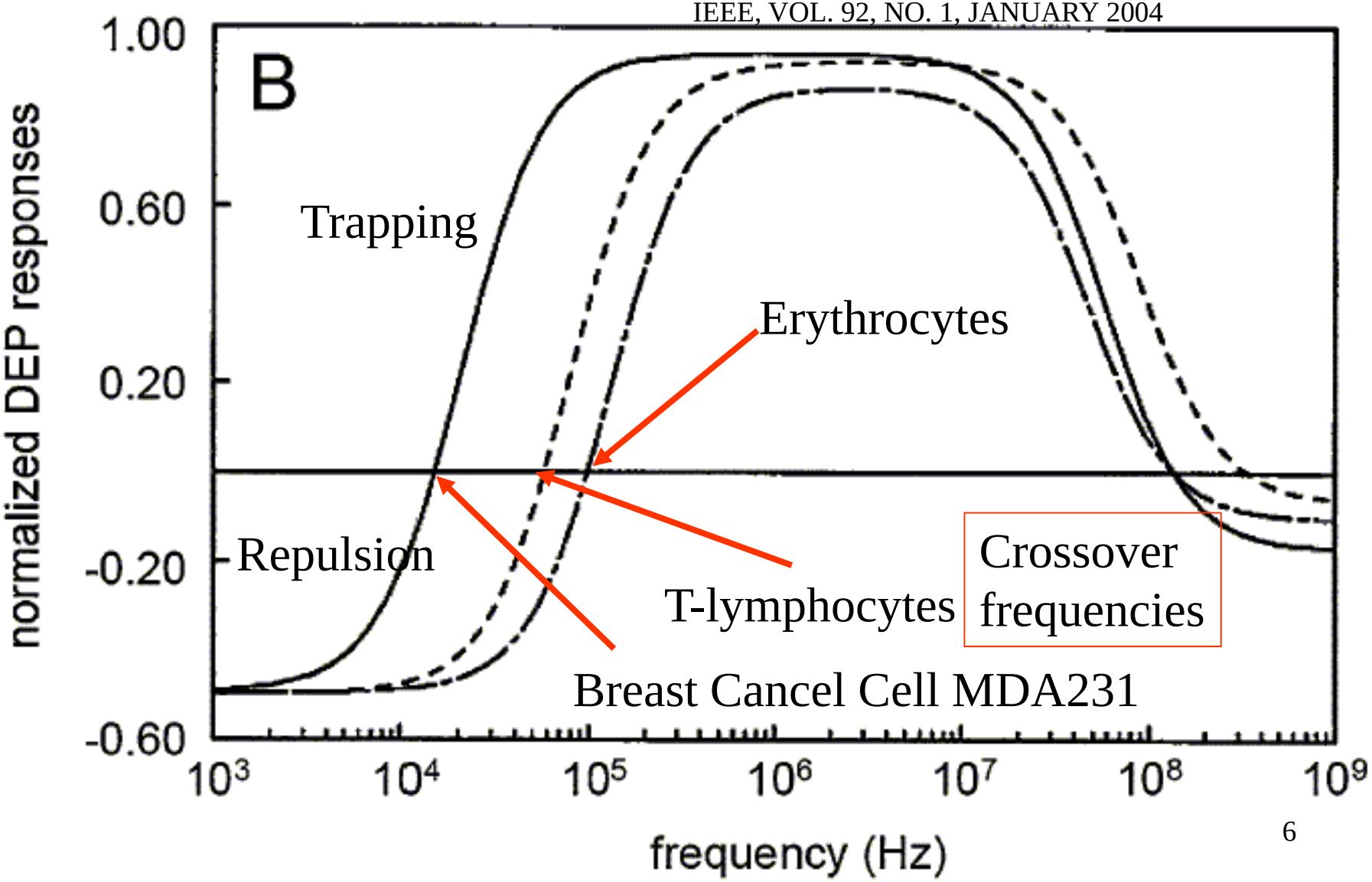
where r is the cell radius, ∇E^2 is the gradient of the mean-squared field strength, $\varepsilon_s\varepsilon_0$ is the electric permittivity of the suspending medium, and f_{CO} is the cell crossover frequency, which is proportional to the rate at which the plasma membrane capacitance (C) can be charged in the ionic milieu of the suspending medium in response to an applied electric field. The DEP force is null and changes direction when the applied electric field frequency is f_{CO}. At DEP frequencies well below 1 MHz, a spherical mammalian cell under these conditions has a crossover frequency that may be approximated by the expression:

$$f_{\mathrm{co}} \approx \frac{\sigma_s}{\sqrt{2}\pi.r.C_{\mathrm{mem}}}, \quad (2)$$

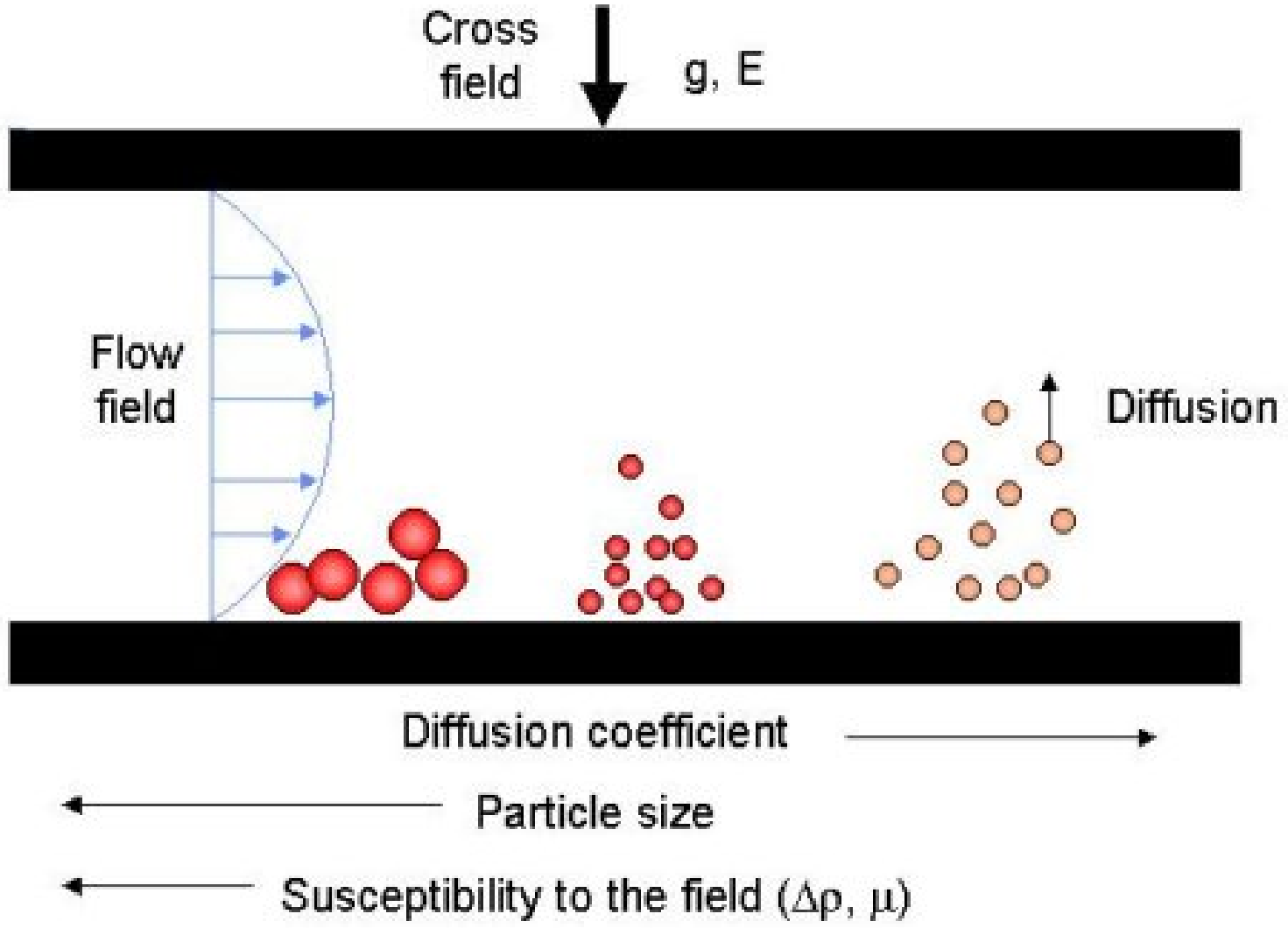
where σ_s is the medium conductivity [27, 29, 30]. We and others have shown that C_{mem}, the capacitance per unit area of the cell plasma membrane, varies substantially between different cell types [31], cells in different states of differentiation [26, 27, 32], in different stages of the cell cycle [33, 34]

Dielectrophoresis-Based Sample Handling in General-Purpose Programmable Diagnostic Instruments

GASCOYNE and VYKOUKAL, PROCEEDINGS OF THE IEEE, VOL. 92, NO. 1, JANUARY 2004



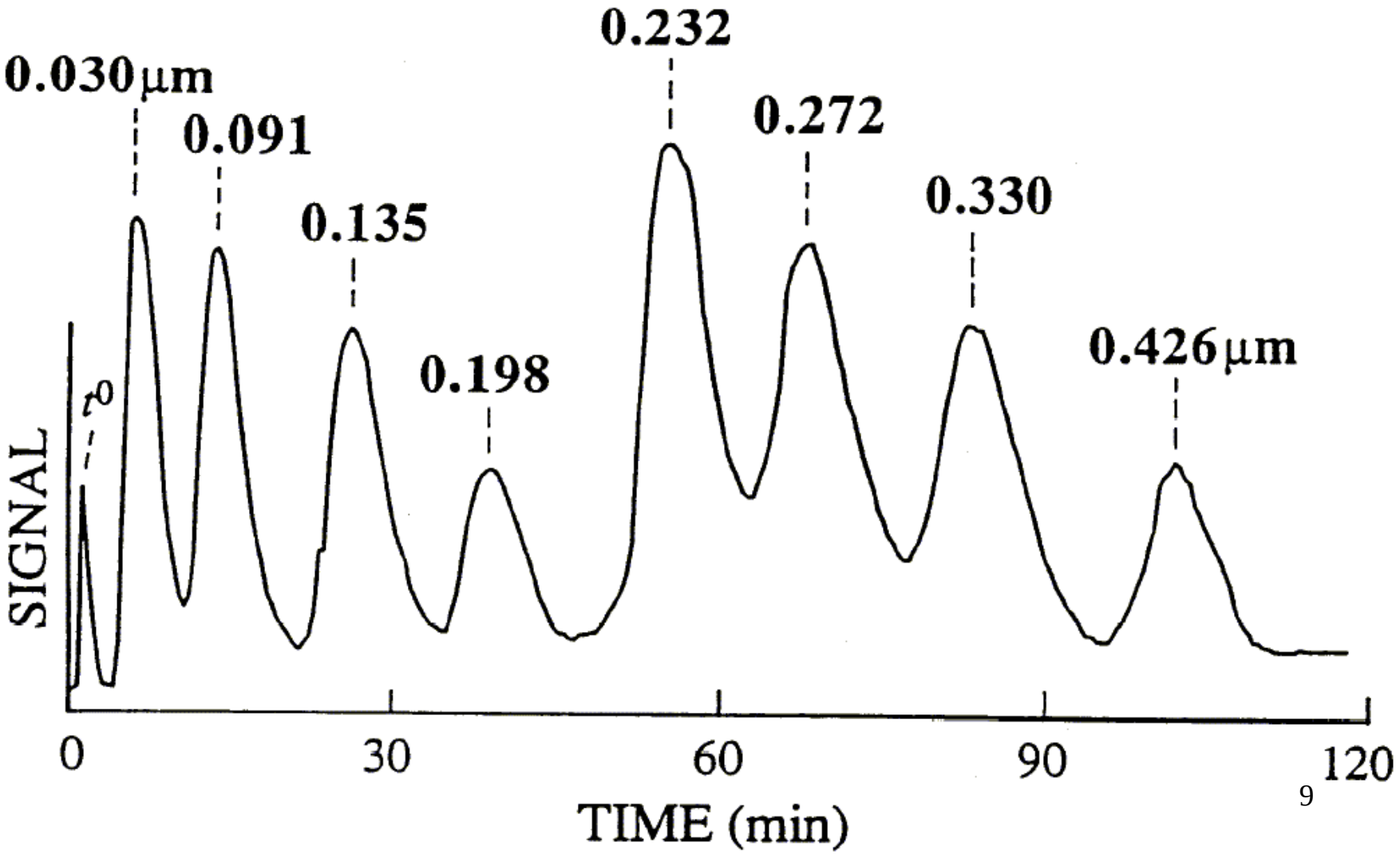
Field Flow Fractionation (FFF)



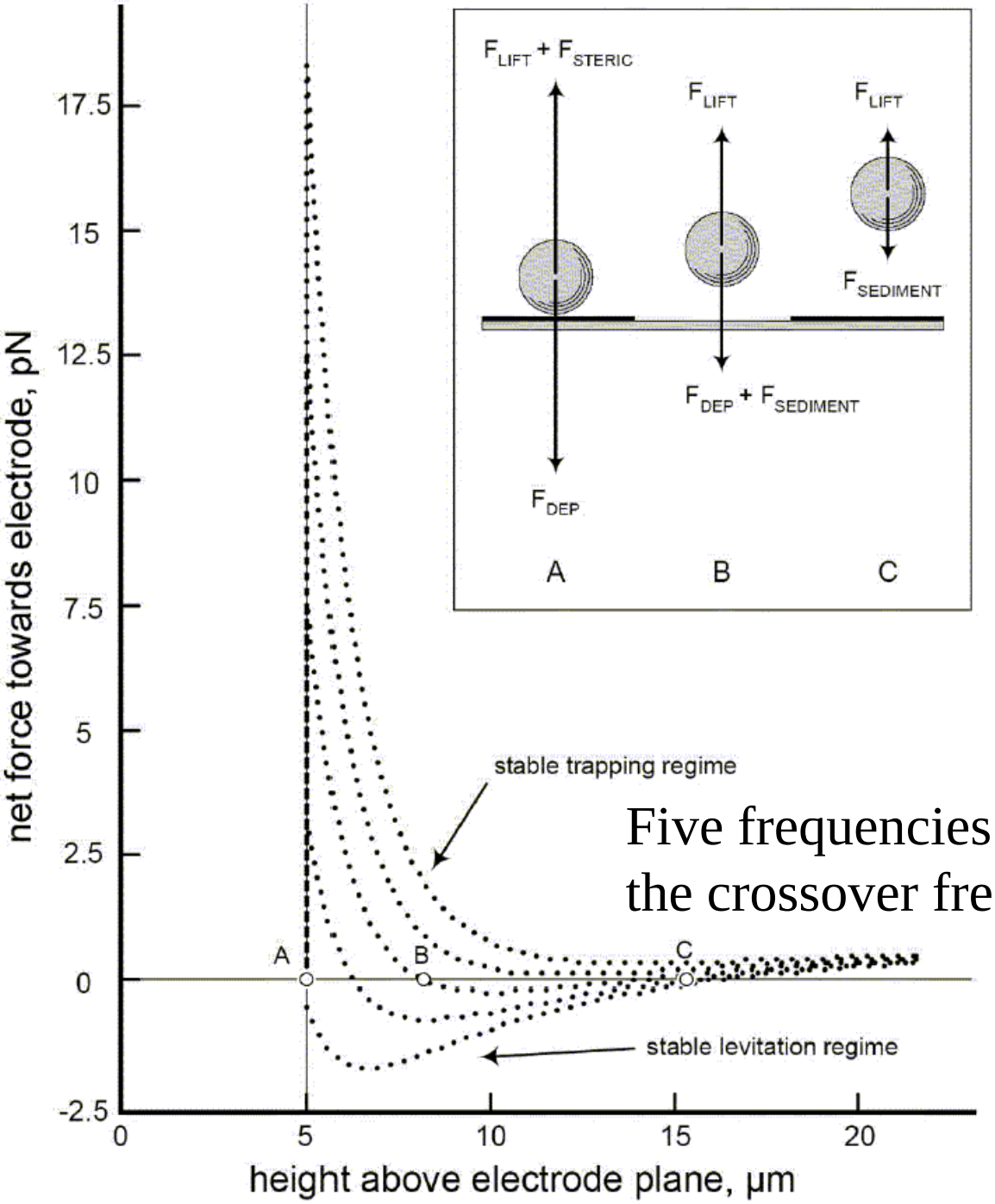
Field Flow Fractionation (FFF)

- Narrow channel with the maximum velocity along the centerline.
- Large particles → Small diffusion coefficients → Closer to the wall → Leave the column late.
- Particles susceptible to the field applied → Closer to the wall → Leave the column late.

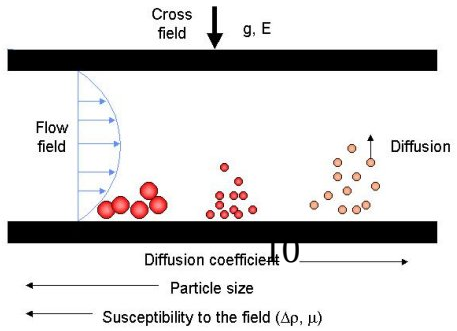
Field Flow Fractionation (FFF)



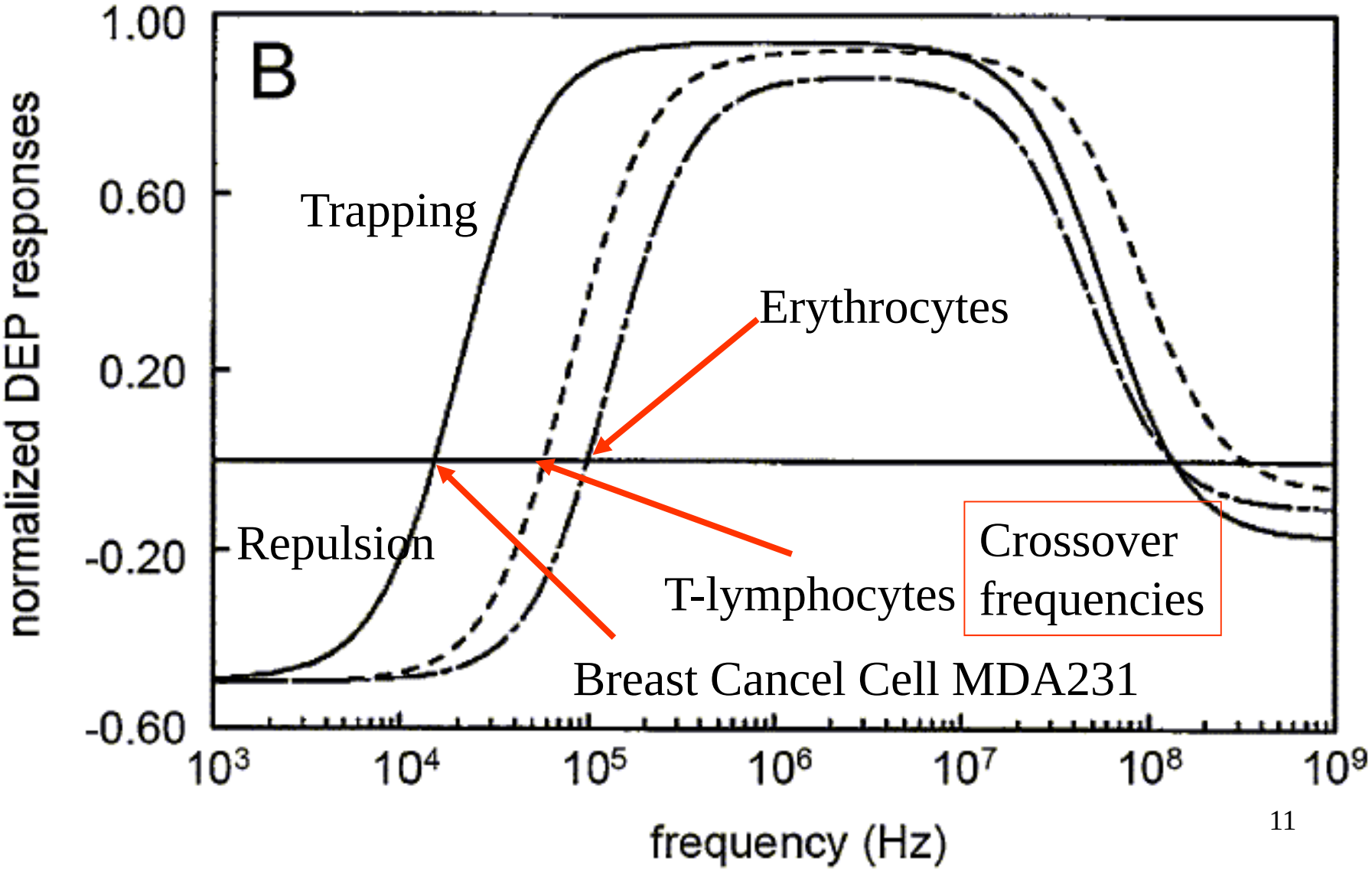
Particles in a Flow Stream with Positive DEP



Five frequencies close to the crossover frequency.

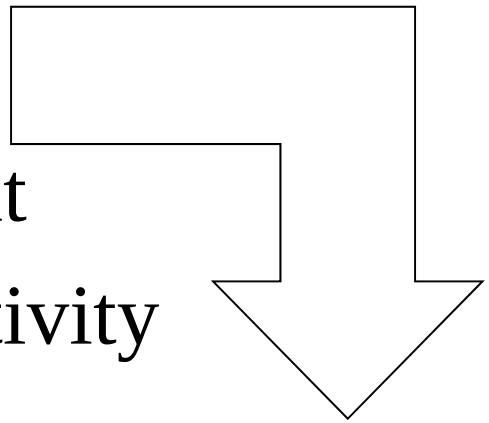


DEP Collection Spectra



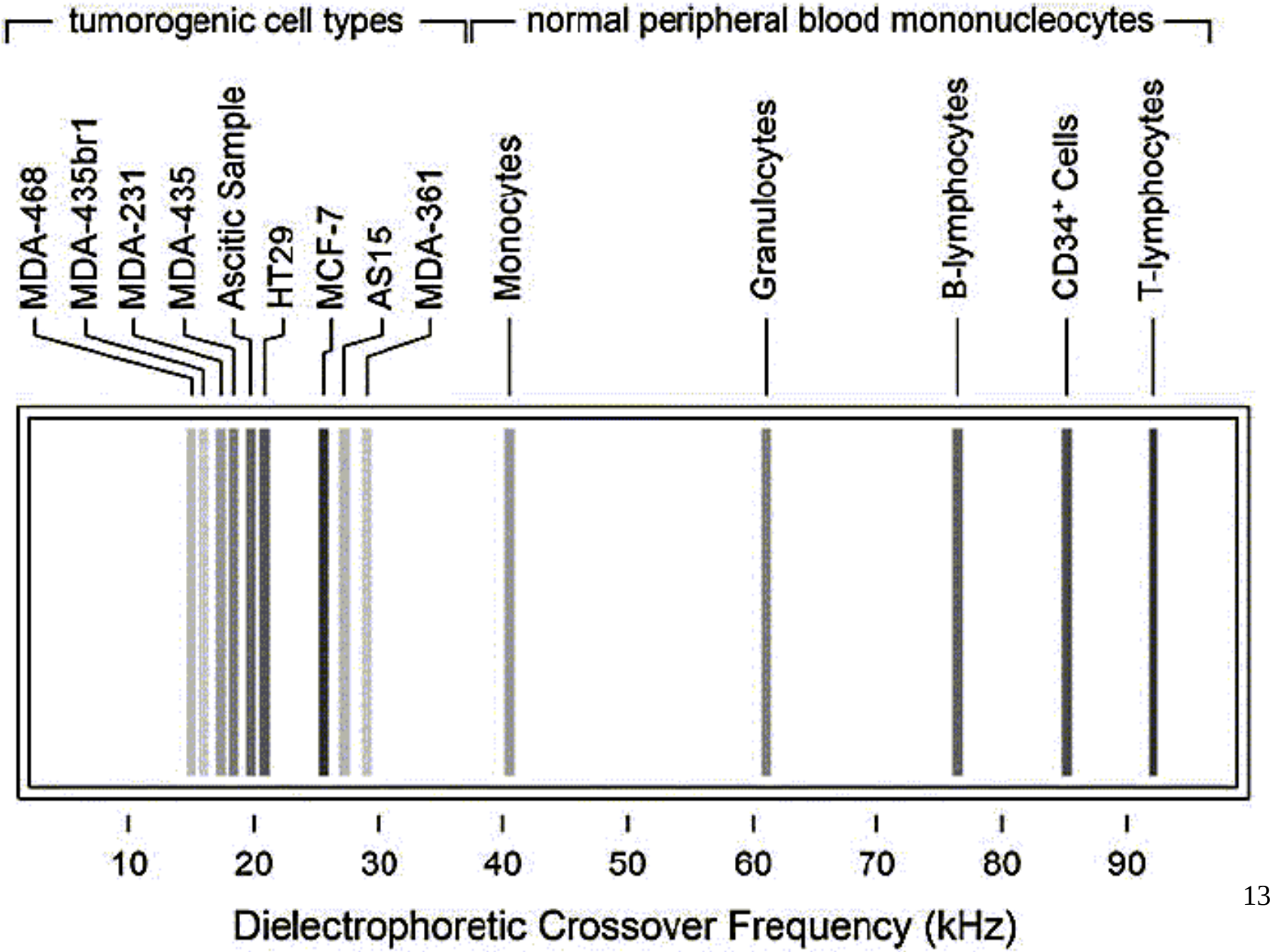
Parameters Affecting Cell Properties

- Membrane thickness
- Effective area
- Dielectric constant
- Electrical conductivity

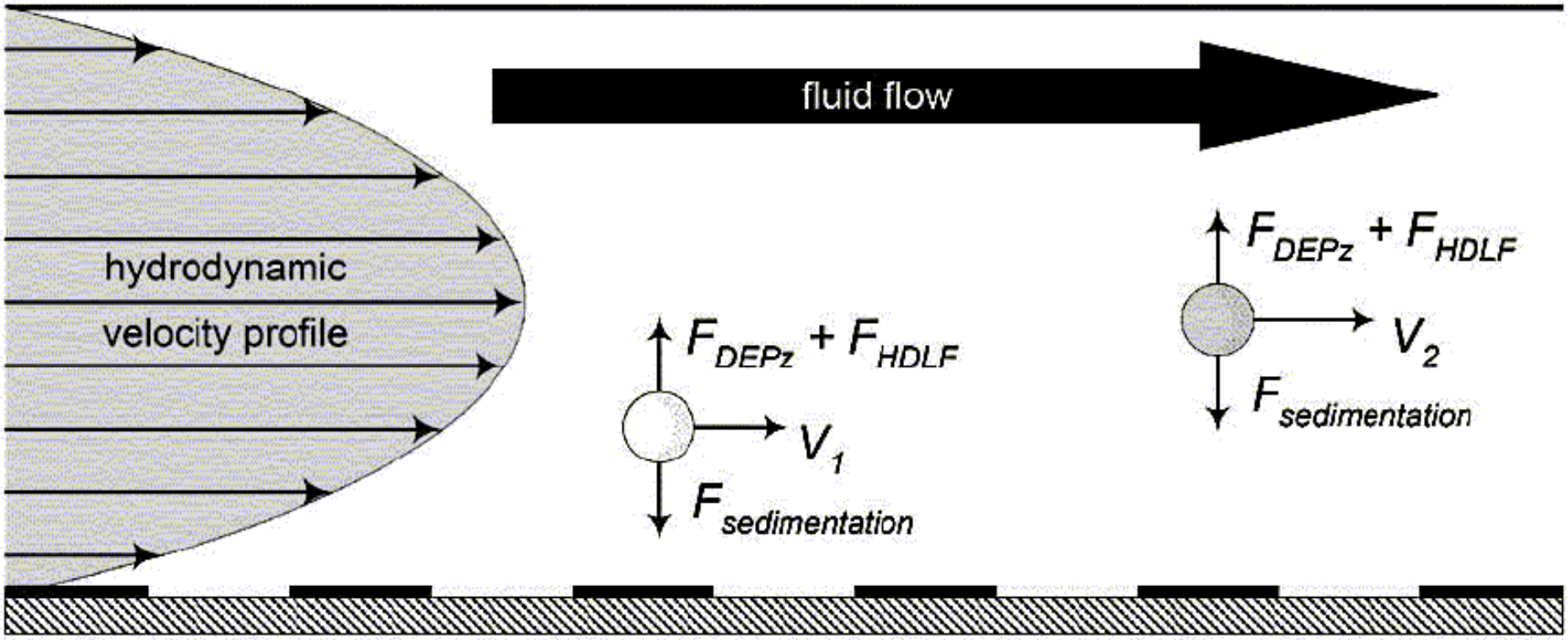


0.8 μF/cm^2 for smooth biological membrane
15 μF/cm^2 for highly convoluted hepatocyte membrane
1.2 to 4 μF/cm^2 are typical for mammalian cells

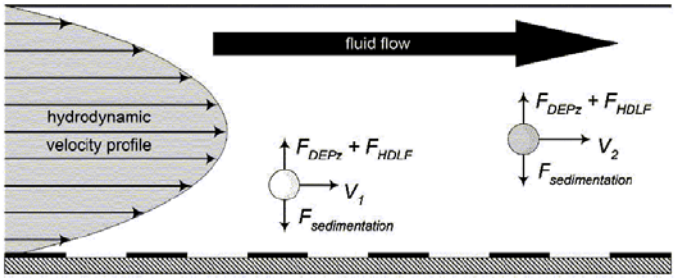
DEP Crossover Data (σ_s = 56 mS/m)



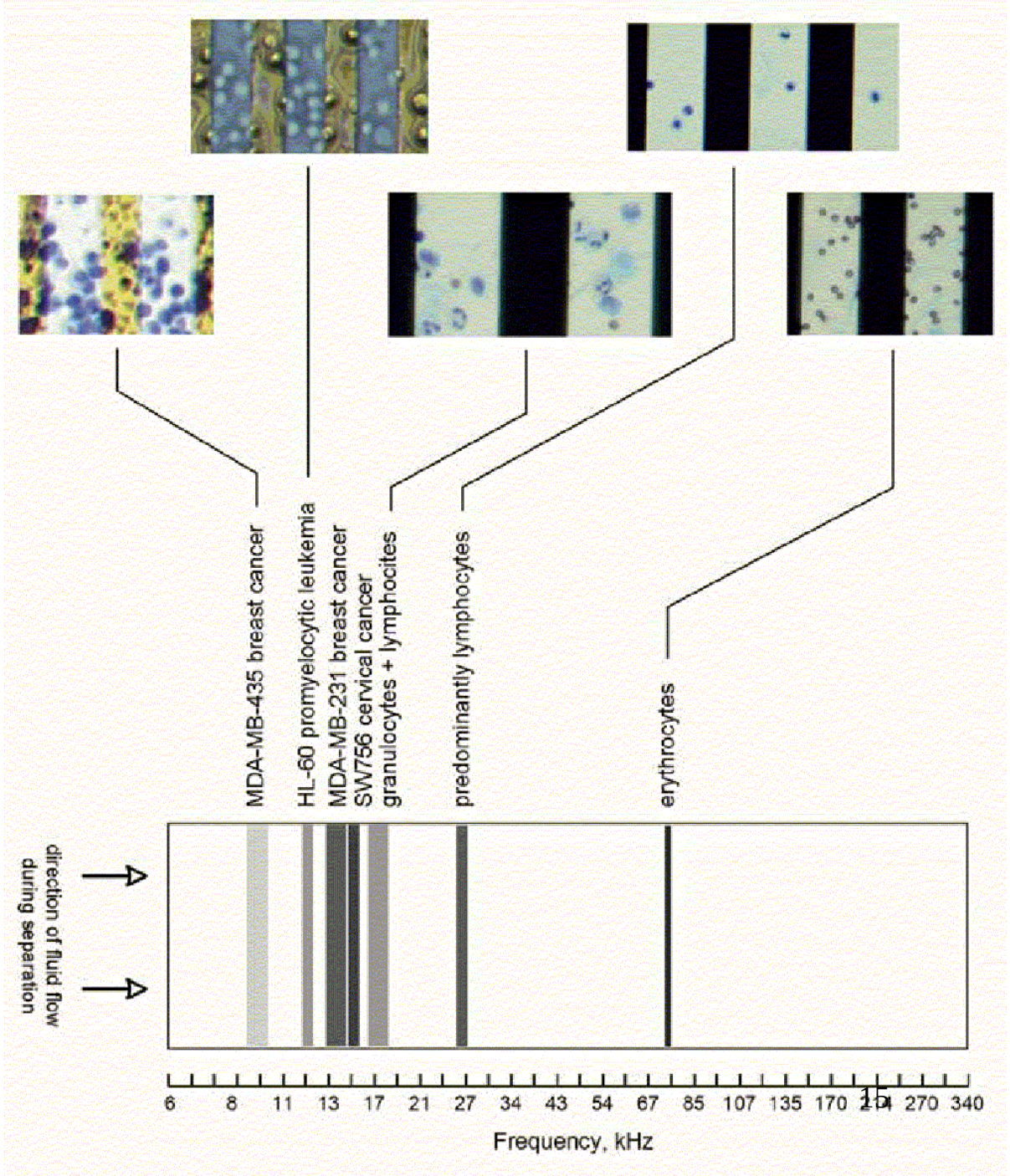
Particles in a Flow Stream with Negative DEP



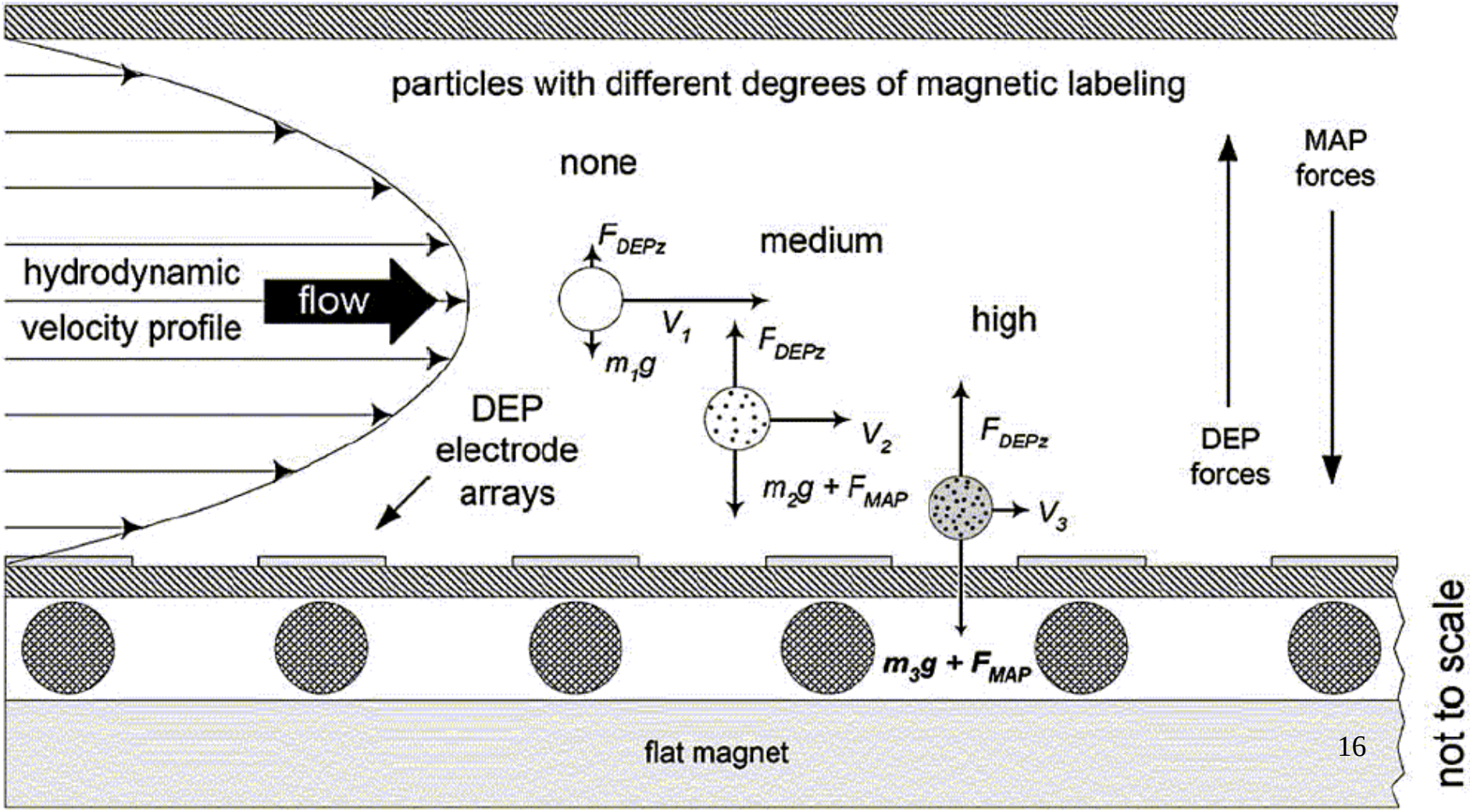
Eletrosmear for normal and cultured tumor cells



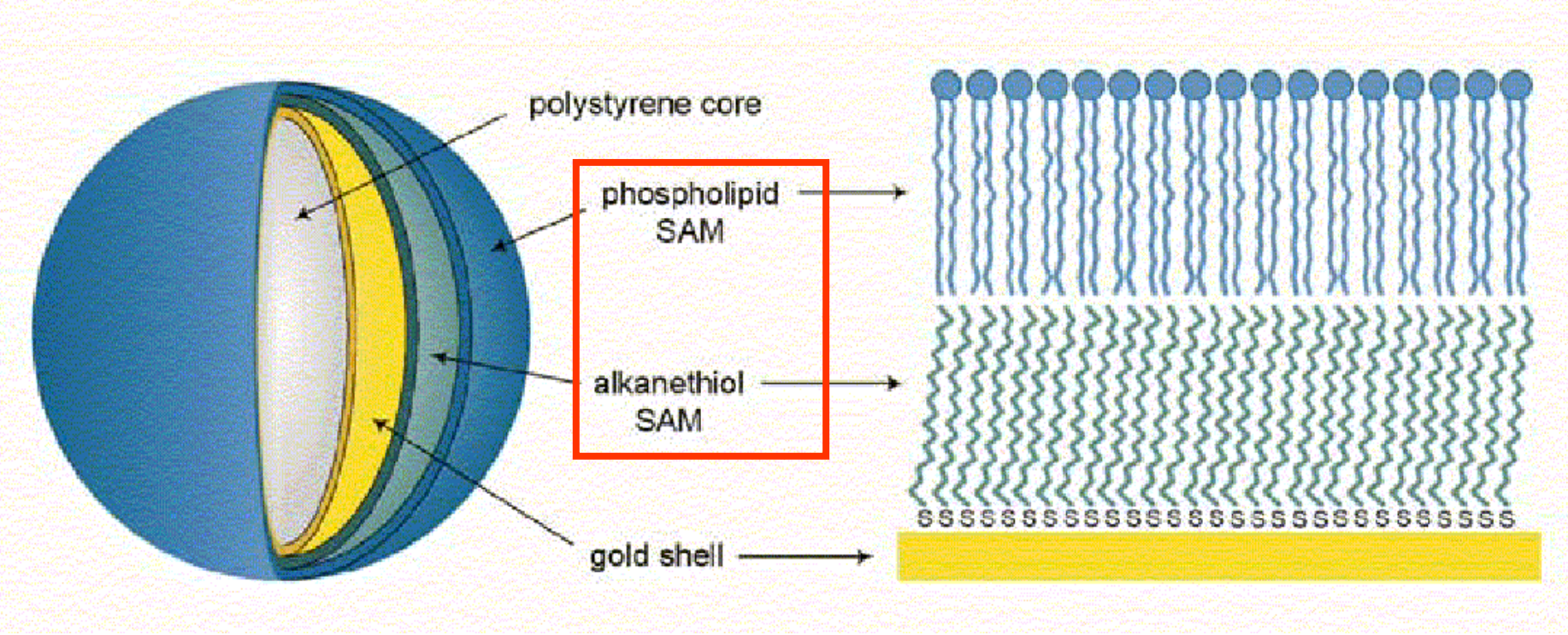
At their crossover frequencies, cells touch down on the slide surface and are captured by the binding agent.



Magnetaphoretic-dielectrophoretic FFF for Cells with Magnetically Labeled Surface Markers

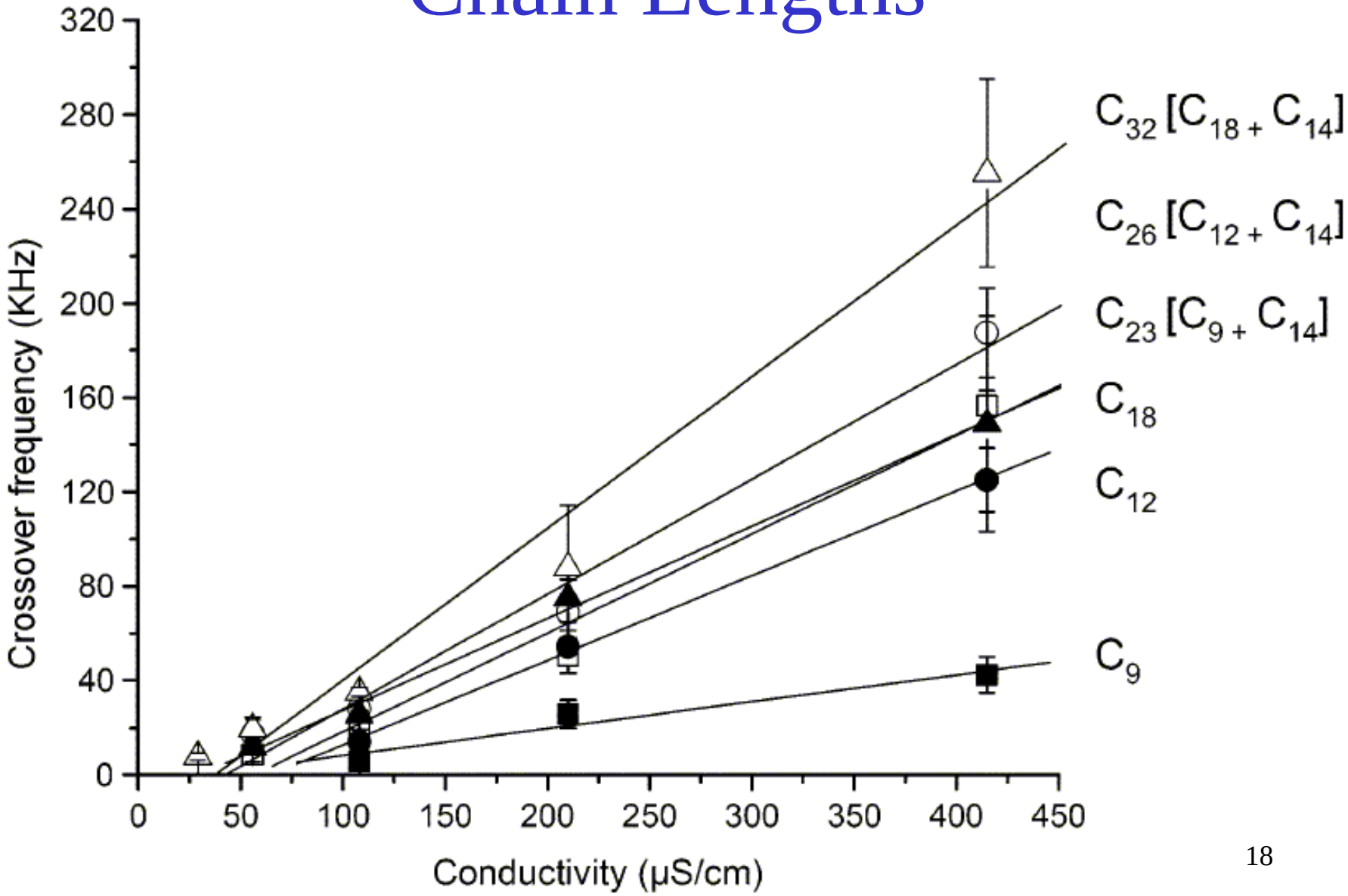


Alternative:
Dielectrically Engineered Carrier Beads



2.5 to 10 um in diameter.

Carrier Beads with Different Chain Lengths



Correlations between the dielectric properties and exterior morphology of cells revealed by dielectrophoretic field-flow fractionation

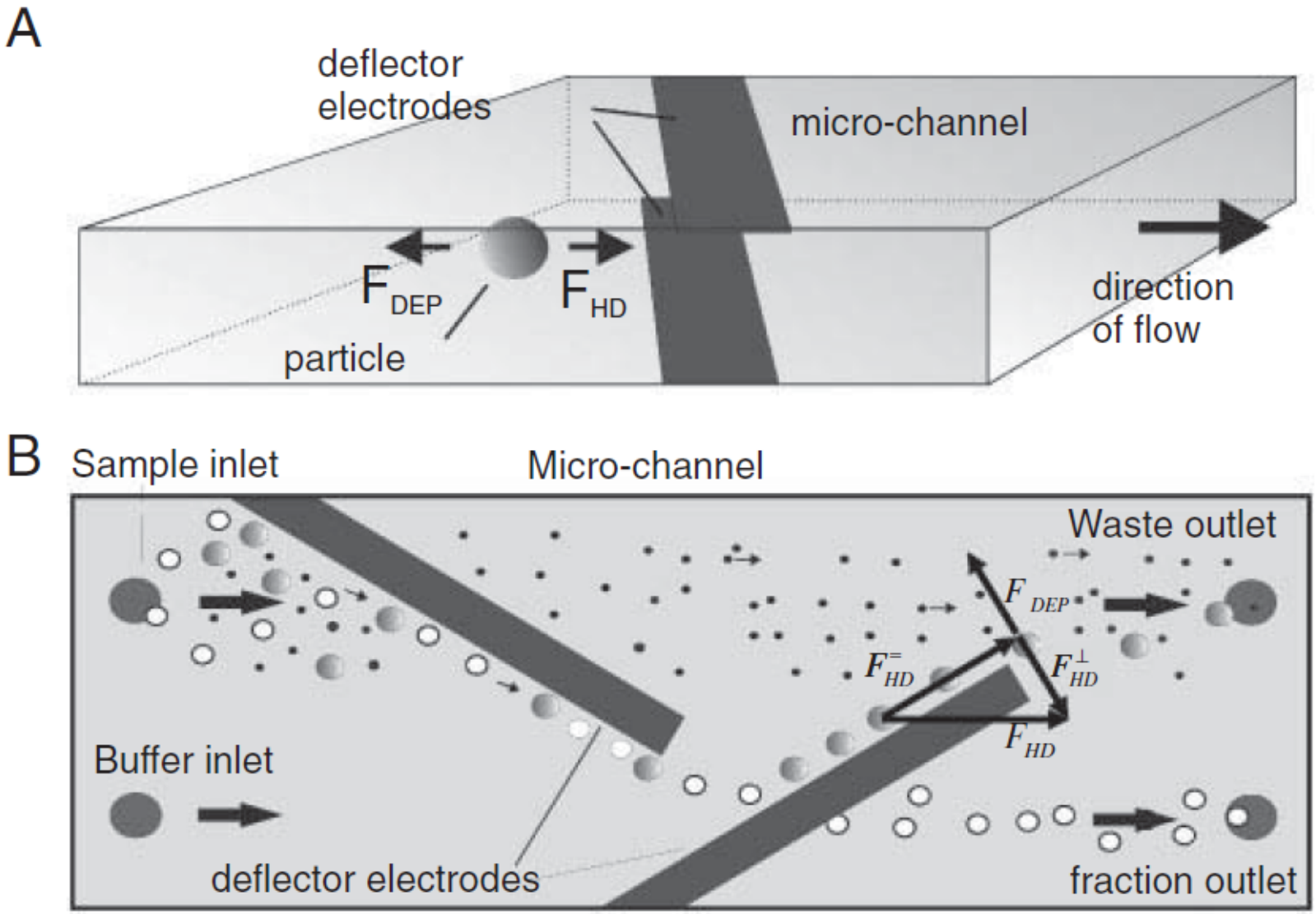
Table 1. Dielectric and exterior morphological parameters for the NCI-60 panel and blood cells

Cell type	Method	Tissue type	$r(\mu m)$	f_{co}(kHz)	C_{mem}(mF/m)	C_{tot}(pF)	Folding(φ)	$M = (F + P + R)/3$
Basophils	DCO [31]	Blood	3.58 ± 0.03	169 ± 18.8	11.2 ± 1.3	1.8 ± 0.2	1.24 ± 0.14	1.38
B-lymphocytes	ROT [49]	Blood	3.29 ± 0.03	163 ± 45.3	12.6 ± 3.5	1.7 ± 0.5	1.40 ± 0.39	1.25
	DCO [31]		3.09 ± 0.22	221 ± 17.8	9.9 ± 0.8	1.2 ± 0.1	1.10 ± 0.09	
$CD34^+$ HSC	ROT [50]	Blood	3.50 ± 0.05	189 ± 27.8	10.2 ± 1.5	1.6 ± 0.2	1.13 ± 0.17	1.25
Eosinophils	DCO [31]	Blood	4.19 ± 0.07	172 ± 7.3	9.4 ± 0.4	2.1 ± 0.1	1.04 ± 0.04	1.13
Erythrocytes	ROT [51]	Blood	3.10 ± 0.02	218 ± 21.8	10 ± 1.0	1.2 ± 0.1	1.11 ± 0.11	1.31
	DCO [51]		3.10 ± 0.02	185 ± 23.5	11.8 ± 1.5	1.4 ± 0.2	1.31 ± 0.17	
	ROT [14]		2.8 ± 0.1	268 ± 23.8	9 ± 0.8	0.9 ± 0.1	1.00 ± 0.09	
Granulocytes (mixed)	ROT [49]	Blood	4.71 ± 0.23	130 ± 37.9	11 ± 3.2	3.1 ± 0.9	1.22 ± 0.36	
	DFF		4.70 ± 0.23	95 ± 13.9	15.1 ± 2.2	4.2 ± 0.6	1.68 ± 0.24	
Lymphocytes-mitototic	ROT	Blood	4.54 ± 0.63	92 ± 17.8	16.1 ± 3.1	4.2 ± 0.8	1.79 ± 0.34	1.80
Monocytes	ROT [49]	Blood	4.63 ± 0.36	95 ± 26.8	15.3 ± 4.3	4.1 ± 1.2	1.70 ± 0.48	1.50
	DCO [31]		4.21 ± 0.05	113 ± 6.4	14.2 ± 0.8	3.2 ± 0.2	1.58 ± 0.09	
Neutrophils	DCO [31]	Blood	4.06 ± 0.06	170 ± 1.2	9.8 ± 0.1	2.0 ± 0.0	1.09 ± 0.01	1.13
T-lymphocytes	ROT [14]	Blood	3.5 ± 0.2	176 ± 17.6	11 ± 1.1	1.7 ± 0.2	1.22 ± 0.12	1.38
	DCO [31]		3.40 ± 0.08	149 ± 20.2	13.3 ± 1.8	1.9 ± 0.3	1.48 ± 0.20	
	ROT [33]		3.04 ± 0.26	184 ± 22.8	12.1 ± 1.5	1.4 ± 0.2	1.34 ± 0.17	
	DFF		3.40 ± 1.29	155 ± 35.2	12.8 ± 2.9	1.9 ± 0.4	1.42 ± 0.32	
BT-549	DFF	Breast	10.36 ± 3.53	45 ± 15.7	14.4 ± 5.0	20 ± 6.8	1.6 ± 0.56	2.00
HS 578T	DFF	Breast	8.88 ± 3.63	40.9 ± 12.4	18.5 ± 5.6	19 ± 5.6	2.05 ± 0.62	

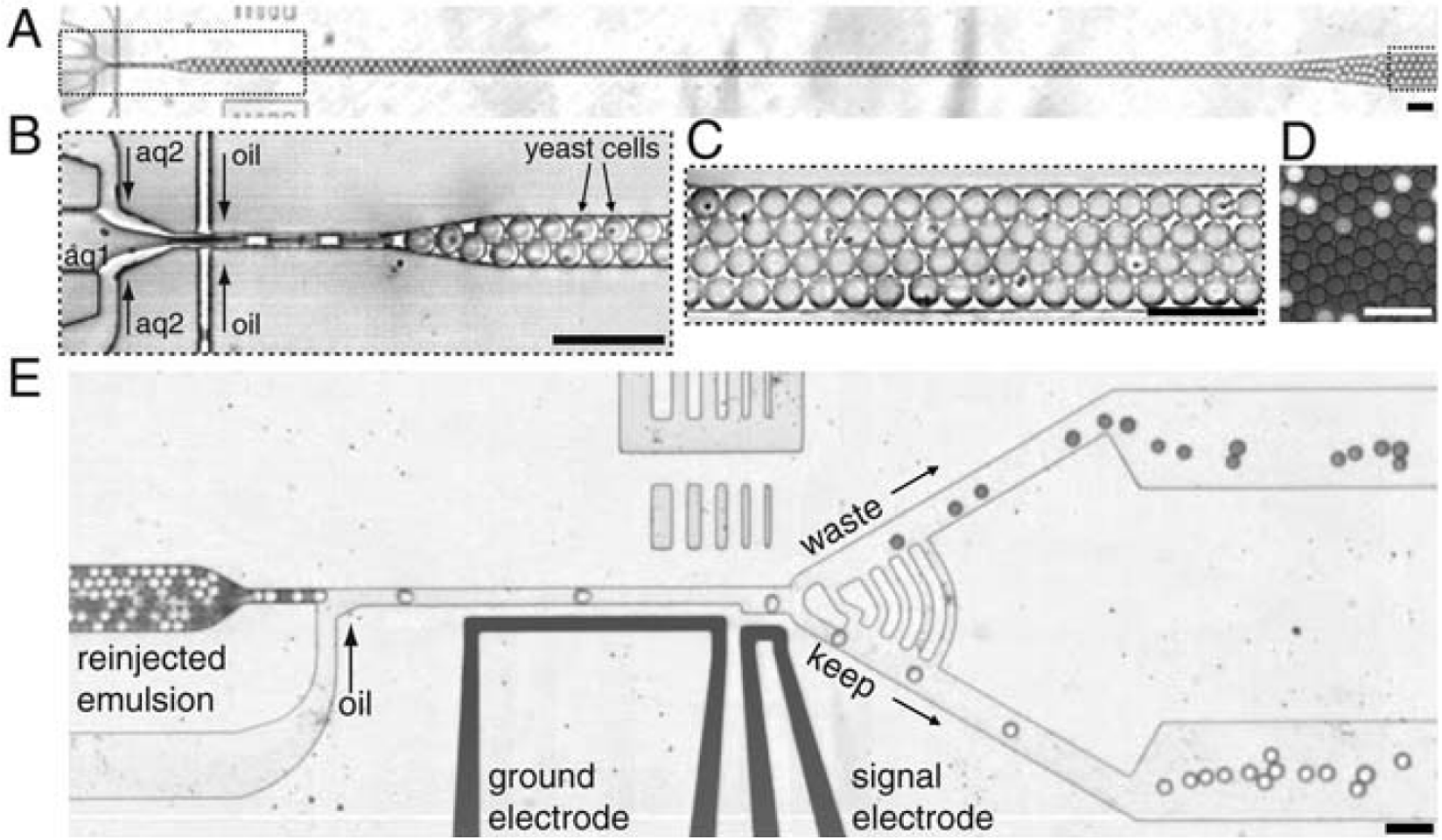
NCI-60 utilizes 60 different human tumor cell lines, representing leukemia, melanoma and cancers of the lung, colon, brain, ovary, breast, prostate, and kidney

MicroPrep: Chip-based dielectrophoretic purification of mitochondria

Electrophoresis 2010, *31*, 2655–2663



Ultrahigh-throughput screening in drop-based microfluidics for directed evolution



Agresti et al., PNAS, 2010; screen ~10^8 individual enzyme reactions in only 10 h, using <150 μL of total reagent volume; compared to robotic screening systems, we perform the entire assay with a 1,000-fold increase in speed and a 1-million-fold reduction in cost.