Peculiarities of living cells interaction with micro- and nanoparticles

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There are some experimental evidence collected more than 20 years ago in different laboratories suggesting that the interactions between living biological cells and micro- and nano-particles depend on their metabolic state and contain long-range component. The early experiments were conducted mostly with micro-particles by reputable groups led by prominent leaders:

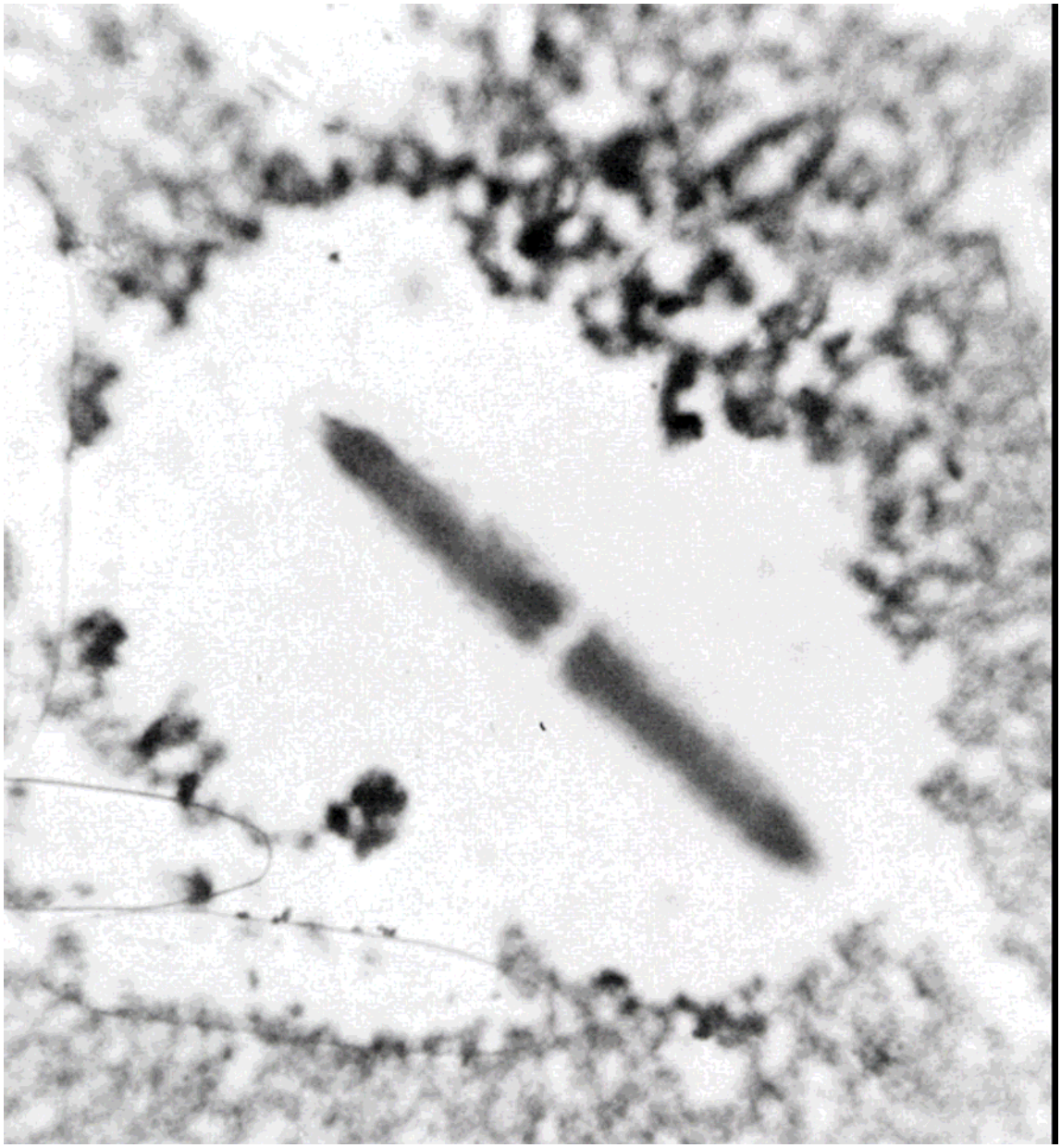
- ***Herbert Pohl*** (MIT, USA) - the inventor of dielectrophoresis, published several papers with co-authors with titles like "**The AC field patterns about living cells**", Cells Biophysics, (**1985**)
- ***Boris Derjaguin*** (Soviet Union) - the leading author of DLVO theory, published papers with titles like "**On long-range forces of repulsion between biological cells**", Colloids Surfaces, (**1984**)
- The next round was conducted in the early **1990s** with **gold nanoparticles**. Their interaction with living cells contains an initial reversible step that also depends on function of **cell ionic pumps**.
- Function of ionic pumps generates **transmembrane potential**, which is measurable and widely used characteristic of cell energetic state. Transmembrane potential, in turn, strongly affect **ζ-potential**, as was experimentally discovered using cell electrophoresis **40 years ago** by several independent groups.

There have been several theories suggested for explaining these four groups of experiments.

- ***Herbert Pohl*** explained observed long-range interaction as particles **micro-dielectrophoresis** in AC field generated by cells;
- ***Boris Derjaguin*** and others instead suggested that it is caused by **diffusiophoresis** generated by cell metabolic exchange (molecules and ions) with exterior solution.
- We suggested theoretical model for explaining relationship between transmembrane and ζ-potential – **biospecific mechanism of Double Layer formation**. Unfortunately it does not explain reversibility of nano-particles interaction.
- **Electrosmotic trap** model can explain such reversibility, however, detail theory is not available yet.

There are illustrations of these experiments and theories given on following pages.

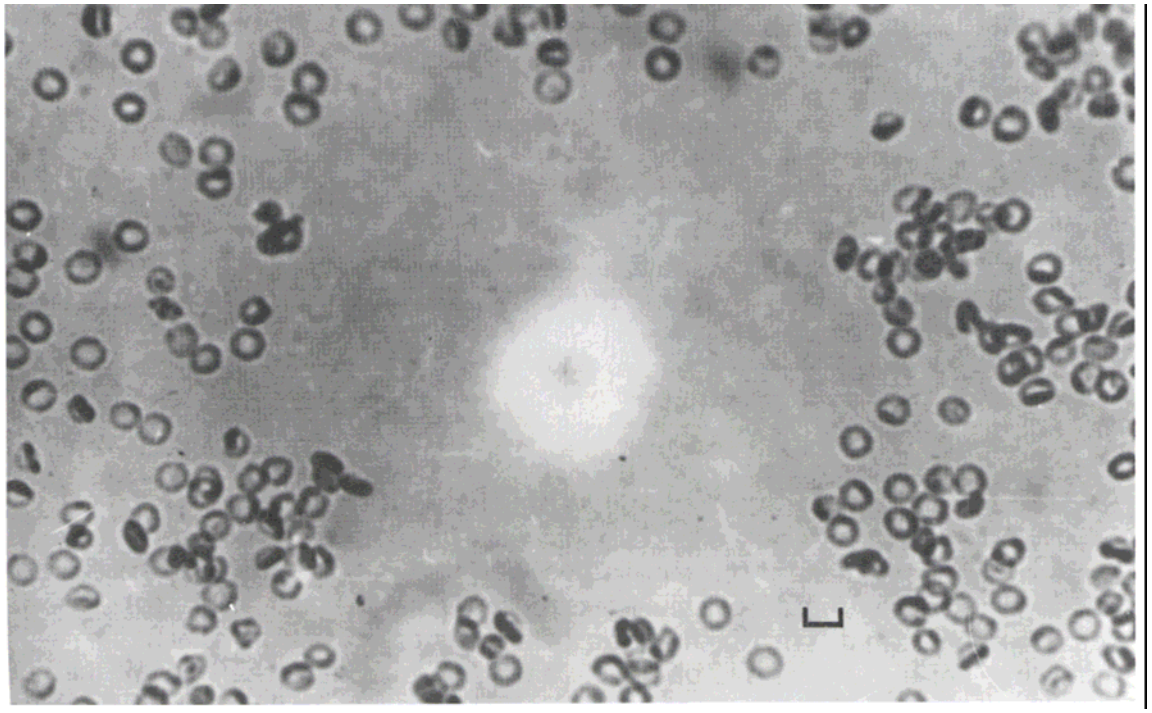
Herbert Pohl (inventor of dielectrophoresis) experiments in 1980th



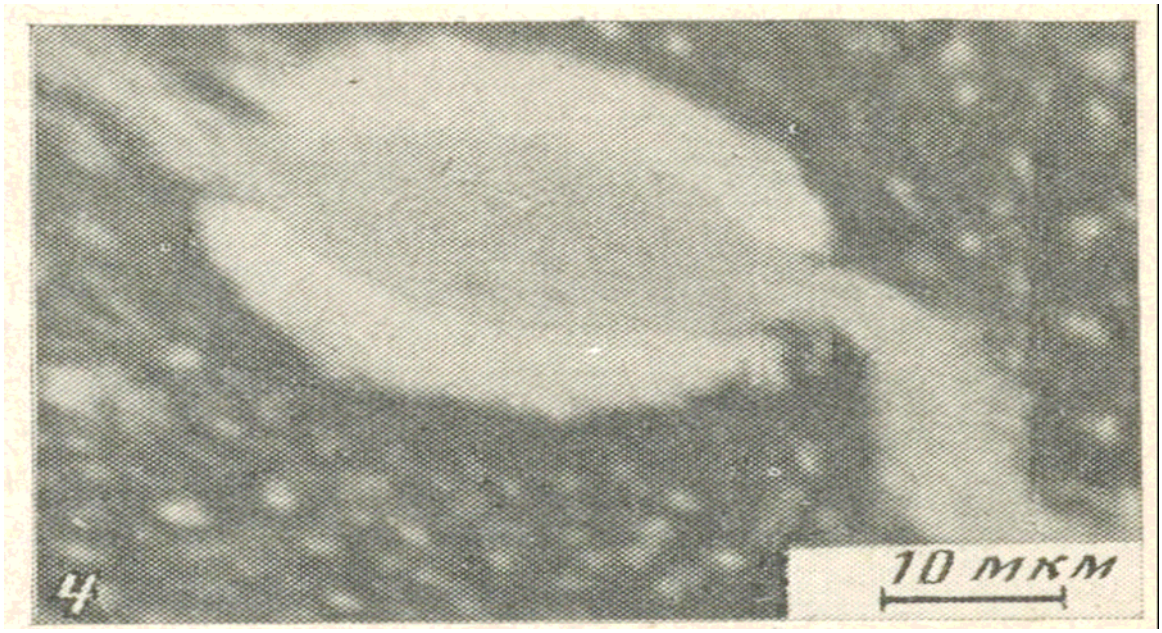
Long range repulsion of barium titanate 2 micron size particles by live *Netrium digitus.*

Rivera, H., Pollock, J.K. and Pohl, H.A. "The AC field patterns about living cells", Cells Biophysics, 7, 43-55 (1985)

Boris Derjaguin (DLVO theory) experiments in 1980-90th



An aureole in the medium consisting of the Indian ink particles, and in the medium of erythrocytes.

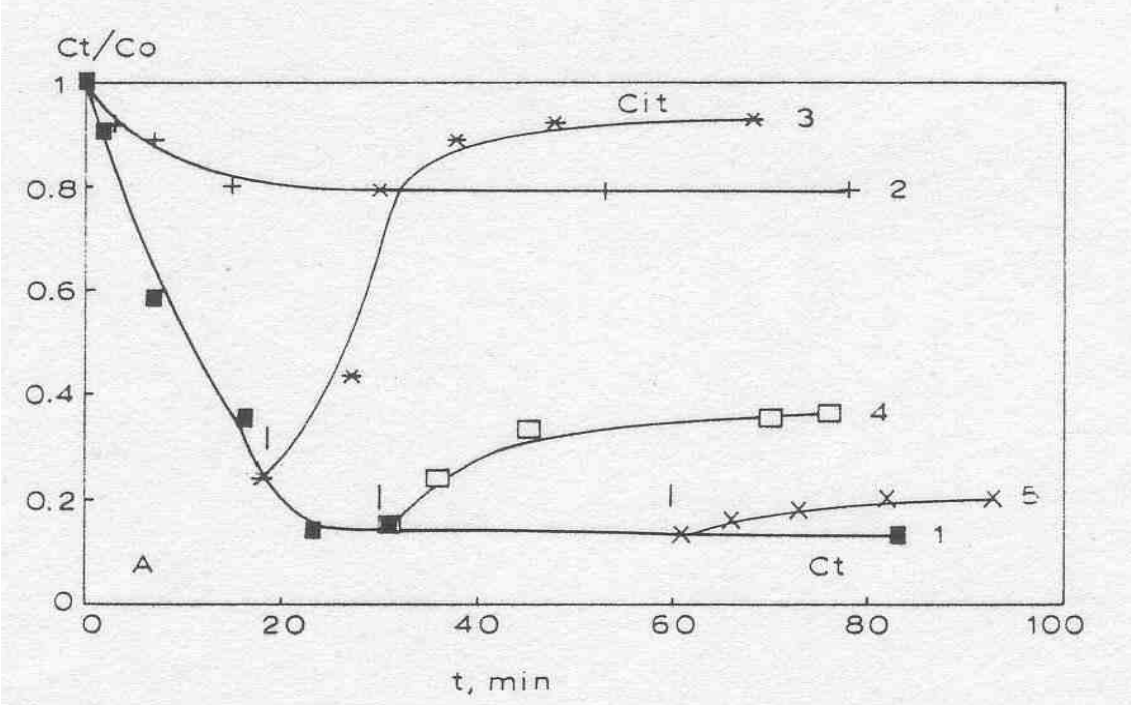


An aureole of the ink particles around cancer cell.

Derjaguin, B.V. and Golovanov, M.V. "On **long-range forces** of repulsion between biological cells", Colloids and Surfaces, 10, 77-84 (1984)

Reversible hetero-coagulation gold sol – living cells. Ukraine 1990th

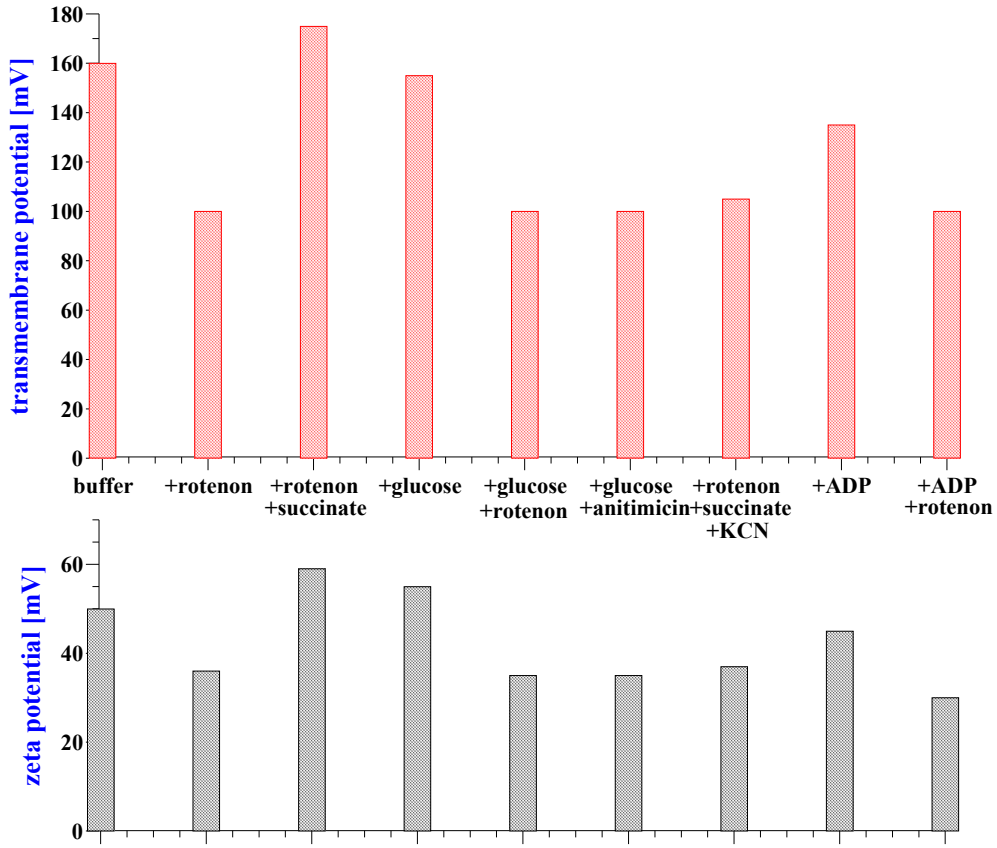
Bacillus subtilis cells in the presence of gold particles. Scale bar 1.8 μm



Kinetic curves of the gold-nanoparticles adsorption by bacteria *Bacillus cereus* B-4368, where C_t is a relative concentration of gold nanoparticles in the solution. Curve 1 is uninterrupted adsorption. Curve 2 is adsorption when pentachlorophenol is initially added to the solution. Curves 3, 4, and 5 represent the kinetics after injection of pentachlorophenol at different time points.

Ulberg, Z.R., Karamushka, V.I., Vidybida, A.K., Serikov, A.A., Dukhin, A.S., Gruzina, T.G. and Pechenaya, V.I. "Interaction of energized bacteria cells with particles of colloidal gold: peculiarities and kinetic model of the process" Biochimica et Biophysica Acta, 1134, pp. 89-95 (1992)

Relationship between ζ-potential and transmembrane potential. Five independent groups in 1970th

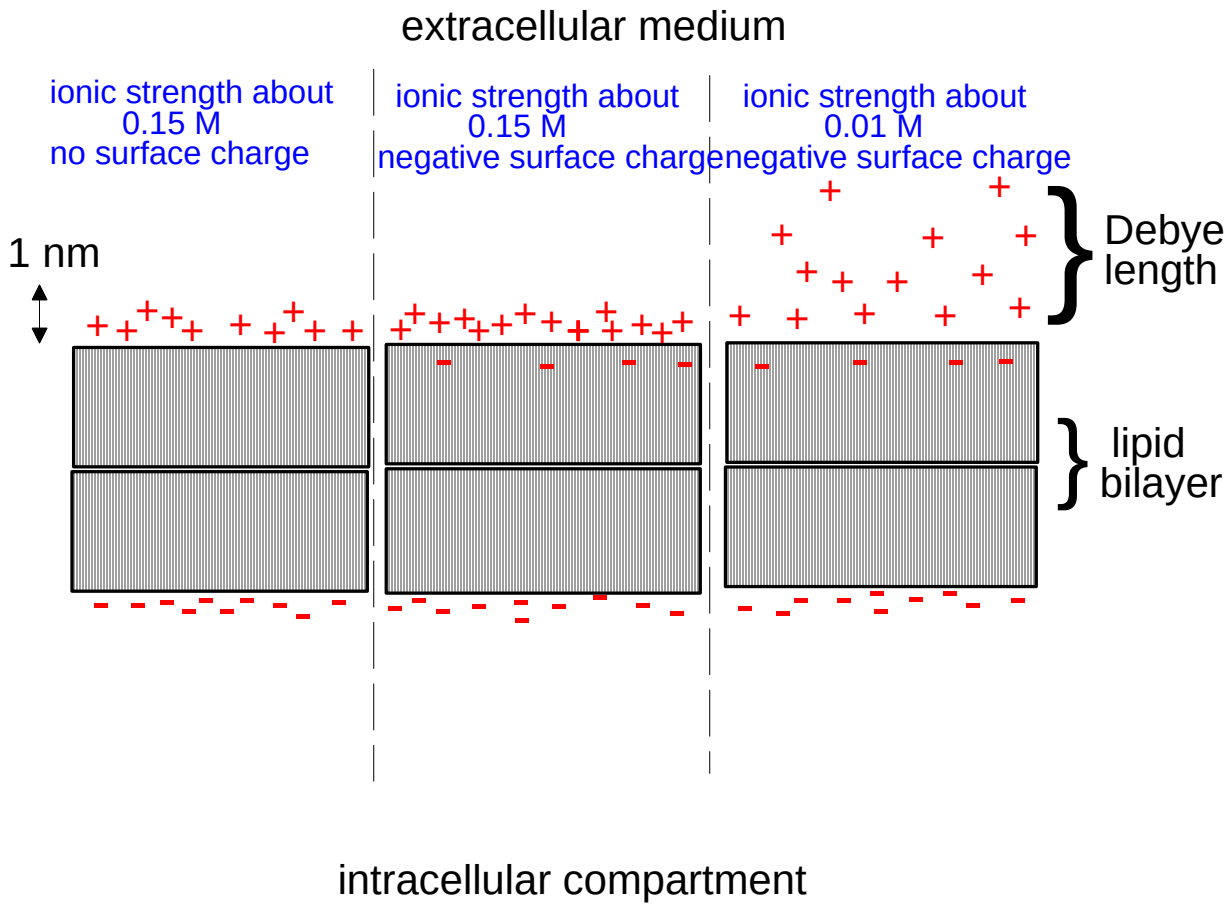


The transmembrane and ζ-potential changes induced by inhibitors and stimulants of mitochondria bioenergetis.

Kamo, N., Muratsugu, M., Kuhinara K., Kobatake, Y. "Change in surface charge density and membrane potential of intact mitochondria during energization", FEBS Letters, 72, 2, 247-250 (1976)

Biospecific mechanism of Double Layer formation.

Dukhin, Ulberg, Karamushka 1990th



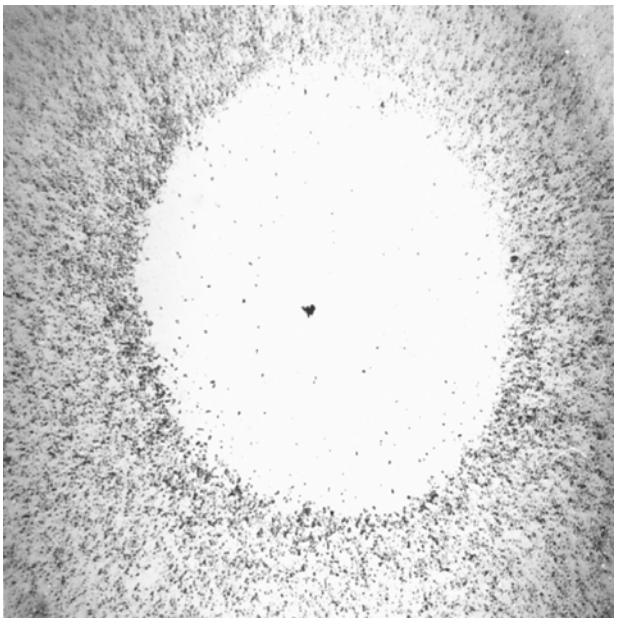
. Illustration of electric charges distribution across lipid bilayer at different ionic strength

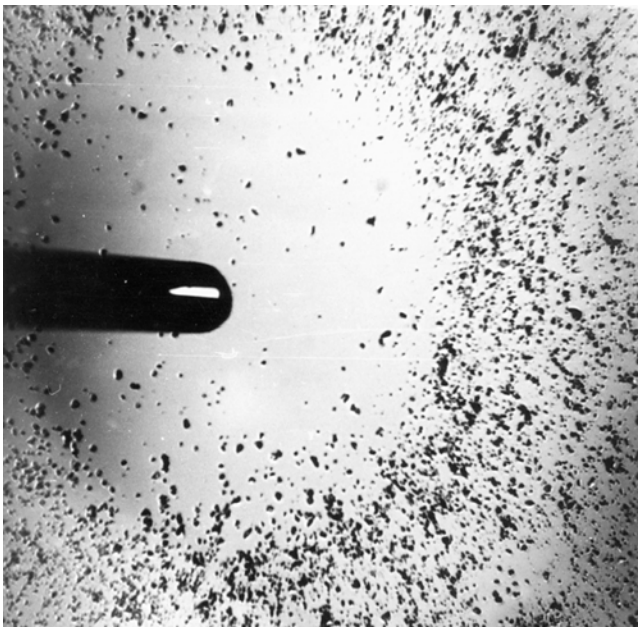
Dukhin, A.S. "Biospecific mechanism of double layer formation and peculiarities of cell electrophoresis" Colloids and Surfaces A, 73, pp. 29-48 (1993)

Pohl's model of micro-dielectrophoresis raises question about origin of the strong AC field, up to 50 V/cm.

That is why Derjaguin preferred model of *diffusiophoresis*. Question remains – strength of the diffusional field around a cell.

In order to verify this diffusiophoretic model, Murtsovkin performed experiments with dissolving particles – modeling living biological cell (1987). He observed similar long-range repulsion as Pohl and Derjaguin groups. Some photos are below.





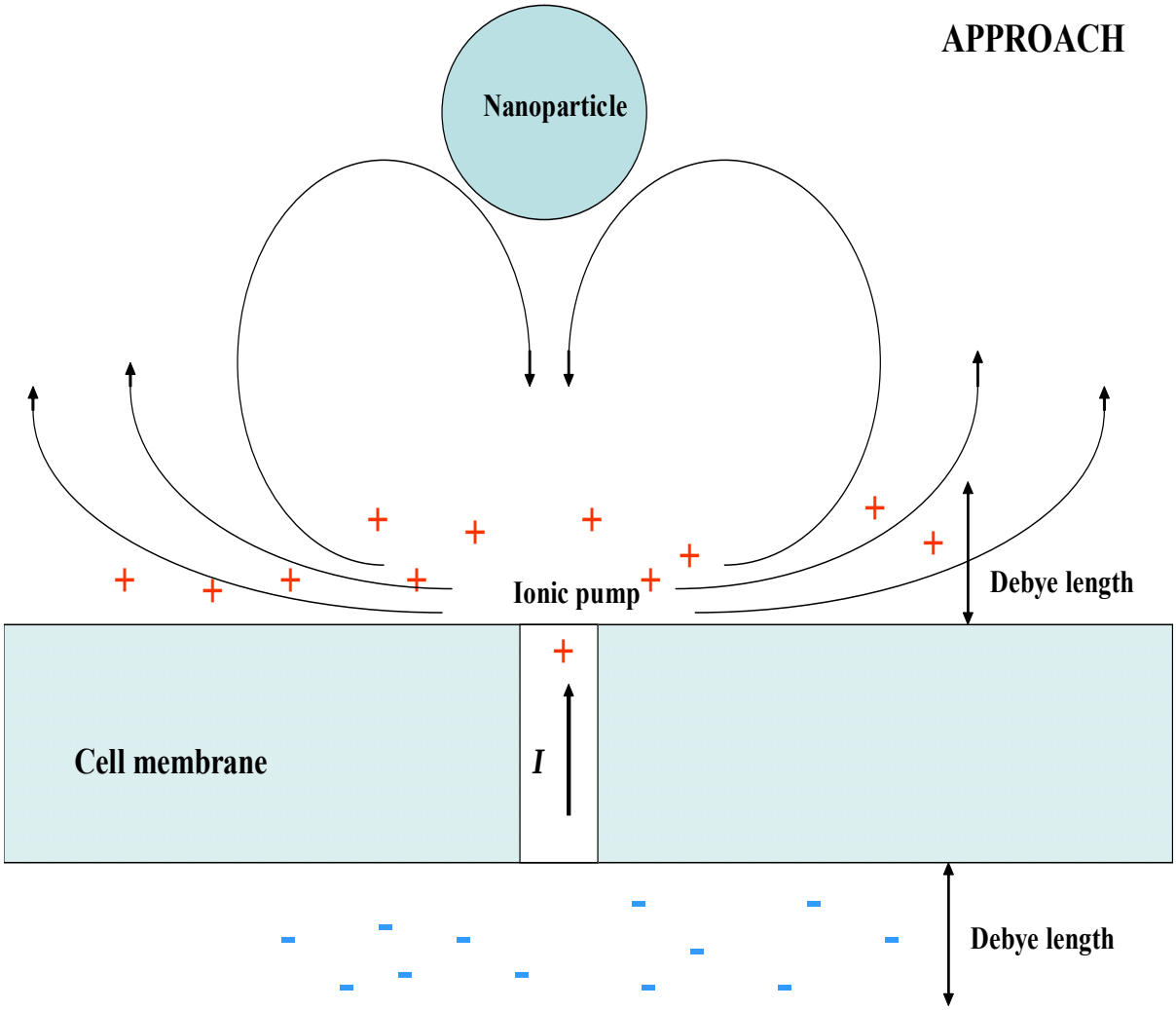
a) repulsion of quartz particles (3 microns) by steel particle dissolving in the center of the circle with approximate diameter 1.2 millimeters;

b) repulsion of similar particles from the tip of capillary filled with KCl solution.

Murtsovkin, V.A. "Long-range interaction of dispersed particles in electrolytes. 1. Experiment", Kolloid. J., 3, 584-588 (1987)

Diffusiophoresis, even if it exists around a cell would be suppressed at high ionic strength. That is why we need another model that would work at high ionic strength and explain reversibility of gold particles adsorption.

Electrosmotic trap.



Cations injected by ionic pump into exterior solution would migrate away from the pump tip under influence of electric field and diffusion. They will migrate along the cell surface within diffuse layer. They cannot leave diffuse layer due to attraction by anions that remain inside of the cell. This surface current would create electrosmotic flow with spherical symmetry around the pump. Continuity of the hydrodynamic flow would require bulk circulation, as shown on Figure above. This circulation could bring nano-particles to the tip of the pump. This would look like adsorption, which can be terminated if pump is turned off – observed reversibility.

Conclusions

There are several independent lines of experimental evidence to suggest that the interaction of some living biological cells with micro- and nano-particles might strongly depends in some cases on cell metabolism and the functioning of ionic pumps. This dependence shows up at very large distances, on scale of microns, between particles and a cell. There is also an additional interaction mechanism that causes reversible aggregation of nano-particles with some living cells. This mechanism is controlled by the function of ionic pumps.

This experimental facts could be related to peculiarities of cell electrophoresis, in particular relationship between transmembrane and ζ-potential. This relationship was established independently by several groups in several countries decades ago. There is theoretical model of “biospecific DL formation” that explains this relationship.

Three different theoretical models have been suggested over the last four decades to explain mentioned above peculiarities of living cells interaction with mineral particles: “micro-dielectrophoresis” model, “micro-diffusiophoresis” model and “electrosmotic trap” model. there are some supporting and objecting arguments for all of them.