

## Nanothermodynamics mediates drug delivery

Stefi A., Sarantopoulou E., Kollia Z., Spyropoulos-Antonakakis N., Bourkoula A., Petrou P., Kakabakos S., Soras G., Trohopoulos P., Nizamutdinov A., Semashko V., Cefalas A.  
*Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia*

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### Abstract

© Springer International Publishing Switzerland 2015. The efficiency of penetration of nanodrugs through cell membranes imposes further complexity due to nanothermodynamic and entropic potentials at interfaces. Action of nanodrugs is effective after cell membrane penetration. Contrary to diffusion of water diluted common molecular drugs, nanosize imposes an increasing transport complexity at boundaries and interfaces (e.g., cell membrane). Indeed, tiny dimensional systems brought the concept of “nanothermodynamic potential,” which is proportional to the number of nanoentities in a macroscopic system, from either the presence of surface and edge effects at the boundaries of nanoentities or the restriction of the translational and rotational degrees of freedom of molecules within them. The core element of nanothermodynamic theory is based on the assumption that the contribution of a nanosize ensemble to the free energy of a macroscopic system has its origin at the excess interaction energy between the nanostructured entities. As the size of a system is increasing, the contribution of the nanothermodynamic potential to the free energy of the system becomes negligible. Furthermore, concentration gradients at boundaries, morphological distribution of nanoentities, and restriction of the translational motion from trapping sites are the source of strong entropic potentials at the interfaces. It is evident therefore that nanothermodynamic and entropic potentials either prevent or allow enhanced concentration very close to interfaces and thus strongly modulate nanoparticle penetration within the intracellular region. In this work, it is shown that nano-sized polynuclear iron (III)-hydroxide in sucrose nanoparticles have a nonuniform concentration around the cell membrane of macrophages *in vivo*, compared to uniform concentration at hydrophobic prototype surfaces. The difference is attributed to the presence of entropic and nanothermodynamic potentials at interfaces.

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