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Parametrizing the exposure of superparamagnetic iron oxide nanoparticles in cell cultures at different *in vitro* environments

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Abstract

The response of cells to the exposure of nanomaterials is crucial for determining their safety in their multiple uses; however, the majority of the *in vitro* experiments use monolayered cell cultures instead of comparing the behavior of the cells in 3D, a more realistic environment. Here, we have analyzed how the exposed surface of the cells, as well as the environment where cells grow, can influence the interaction and uptake of superparamagnetic iron oxide nanoparticles (SPIONs). We exposed three different cell lines (MDAMB-231, HL60 and bEnd3), which grow at different environments, to increasing concentrations of SPIONs (0 – 150 $\mu\text{g}\cdot\text{ml}^{-1}$) and we evaluated parameters analyzing the morphological changes of the cell, iron uptake and cell viability. Results showed that upon exposure to SPIONs, cell viability and morphology are more affected when cells are growing in 3D systems, indicating that the increase of exposed surface area of the cells is a strong parameter to take in account when evaluating SPIONs or other materials or drugs. Our results clearly reinforce the use of more realistic environments, such as 3D, for the design of new drug delivery systems.

Keywords: 2D environments, 3D cell culture, suspension cells, *in vitro*, surface exposed, SPIONs, cytotoxicity

1. Introduction

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Abbreviations: SPIONs, superparamagnetic iron oxide nanoparticles; SQUID, superconducting quantum interference device.

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