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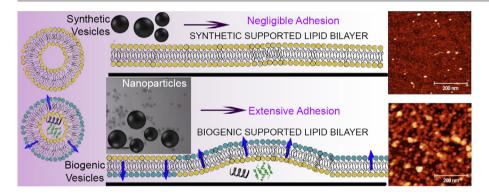
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ABSTRACT

Hypothesis: Extracellular Vesicles (EVs) are natural nanosized lipid vesicles involved in most intercellular communication pathways. Given their nature, they represent natural cell membrane models, with intermediate complexity between real and synthetic lipid membranes. Here we compare EVs-derived (EVSLB) and synthetic Supported Lipid Bilayers (SLBs) in the interaction with cationic superparamagnetic iron oxide nanoparticles (SPIONs). The aim is twofold: (i) exploit SPIONs as nanometric probes to investigate the features of EVSLBs as novel biogenic platforms; (ii) contribute at improving the knowledge on the behavior of SPIONs with biological interfaces. **Experiments:** Quartz Crystal Microbalance, X-ray Reflectivity, Grazing-incidence Small-angle X-ray Scattering, Atomic Force Microscopy, Confocal Microscopy data on SPIONs-EVSLB were systematically compared to those on SPIONs challenging synthetic SLBs, taken as references. **Findings:** The ensemble of experimental results highlights the much stronger interaction of SPIONs with EVSLBs with respect to synthetic SLBs. This evidence strongly supports the hypotheses on the peculiar structure of EVSLBs, with cushioned non-flat areas and extended

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