

Highly-ordered microgel monolayers for precise and localized biomolecule capture: towards diagnostic and biosensing platforms

G. Sánchez-Balderas ^{a,b}, C.L. Moraila-Martínez ^{c,d}, J. G. Guerrero-Félix ^{b,c}, M. Hurtado-López ^e, A. Dorigo ^b, Sarita Montaña ^{a,f}, M. Bramini ^g, P. Sánchez-Moreno ^b, and M.A. Fernandez-Rodriguez ^b

^a Faculty of Chemical-Biological Sciences, Autonomous University of Sinaloa, Culiacan, 80030, Sinaloa, Mexico

^b Department of Applied Physics, Faculty of Sciences, University of Granada, Granada, 18071, Granada, Spain

^c Faculty of Biology, Autonomous University of Sinaloa, Culiacan, 80040, Sinaloa, Mexico

^d Department of Electronics and Computer Technology, Faculty of Sciences, University of Granada, Granada, 18071, Granada, Spain

^e Institute of Parasitology and Biomedicine Lopez-Neyra, CSIC, Granada, 18016, Granada, Spain

^f Department of Pathology, University of Michigan, Ann Arbor, 48109, Michigan, USA

^g Department of Cell Biology, Faculty of Sciences, University of Granada, Granada, 18071, Granada, Spain

inv.gbalderas@ugr.es

Thermoresponsive microgels composed of poly(N-isopropylacrylamide) (pNIPAM) and poly(N-vinylcaprolactam) (pVCL) are self-assembled into ordered monolayers at liquid interfaces and transferred onto glass substrates via Langmuir-Blodgett deposition. Their colloidal stability and morphological changes under different liquid media, including phosphate-buffered saline (PBS), Dulbecco's Modified Eagle Medium (DMEM), supplemented DMEM (cDMEM), and HEK-293 cell culture, are evaluated via in-situ fluid-cell atomic force microscopy (AFM). Although both microgels show biocompatibility, only the softer pVCL ones remain structurally stable after incubation and cell removal, enabling reproducible microscopic characterization. Irreversible protein adsorption and exosome capture by pVCL microgels are confirmed by fluorescence microscopy, AFM and FTIR spectroscopy, and quantitatively estimated through AFM-based volumetric analysis and UV-vis microplate reader measurements. These findings establish that soft, low-crosslinked pVCL microgels are promising candidates for bioactive surfaces with high molecular uptake capacity for biosensing, diagnostics, and biomedical applications.

Keywords:

Thermoresponsive microgel, pNIPAM, pVCL, Fluid atomic force microscopy, Biointeractions, Biomolecules

Acknowledgements:

This work was supported by projects PID2020-116615RA-I00, PCI2020-112045, and RYC 2019-027692-I, funded by MCIN/AEI/10.13039/501100011033, EU Next Generation EU/ PRTR, and the European Social Found “El FSE invierte en tu futuro”. MAFR acknowledges support from the EMERGIA grant EMC21_00008 and project C-ING-208-UGR23 funded by Consejería de Universidad, Investigación e Innovación de la Junta de Andalucía, and by FEDER “Andalucía 2021-2027”. Also, by projects PID2023-149387OB-I00 and PID2023-147135OB-I00 funded by MICIU/AEI/10.13039/501100011033 and by FEDER, EU. CLMM acknowledges support from project B-RNM-486-UGR20 funded by Consejería de Universidad, Investigación e Innovación de la Junta de Andalucía, and “ERDF A way of making Europe”. GSB acknowledge support from PostDoc grant associate to CVU 659625 by SECIHTI México.