

Plasmonic hydrogels; enabling 3d sensing and imaging in breast cancer models

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The transition from traditional two-dimensional (2D) cell cultures to three-dimensional (3D) cell models has emerged as a pivotal bridge between in vitro research outcomes and their clinical applications. 3D cell models more accurately mimic the complex in vivo cellular microenvironments, offering valuable insights into cell behavior, disease monitoring or drug testing.

However, the adoption of 3D cell models has brought forth the need for improved imaging and sensing techniques capable of monitoring cellular events in these intricate 3D environments [1]. Traditional imaging techniques designed for 2D cell cultures often fall short when applied to 3D cell models due to their increased complexity and spatial arrangement. One promising solution is Surface Enhanced Raman Scattering (SERS), that allows for the spatiotemporal detection of biologically relevant molecules, the study of drug diffusion profiles or 3D imaging [2,3,4]. This technique utilizes the remarkable optical properties of noble metal nanoparticles (NP), which exhibit Localized Surface Plasmon Resonances (LSPR) that enable them to absorb and scatter light at specific wavelengths, generating high local electric fields on the surface [5]. These electric fields enhance the Raman scattering of molecules near the metal surface, permit extremely low detection limits, and multiplex detection ability. Additionally, the excitation wavelength can be tuned to the near infrared range (NIR) that corresponds to the biological transparency window (650-1350 nm), enhancing light penetration into tissues [6].

In this talk, different 3D models using biopolymers, synthetic polymers or decellularized extracellular matrix-based hydrogels containing plasmonic NPs for in vitro sensing and imaging will be presented. For sensing applications, bare gold NPs were employed for detection of cell-secreted metabolites whereas SERS imaging was performed using gold NPs decorated with SERS tags that can be also internalized by cells. Different material compositions, model configurations and NP combinations were explored in order to perform sensing as well as

multiplex imaging of different cell populations in a 3D fashion.

References

- [1] C. S. Hansel, M. N. Holme, S. Gopal, M. M. Stevens. *Biomaterials*, 226 (2020), 119406.
- [2] C. García-Astrain, E. Lenzi, D. Jimenez de Aberasturi, M. Henriksen-Lacey, M. Binelli, M. Liz-Marzán. *Advanced Functional Materials*, 30 (2020), 2005407.
- [3] J. Plou, B. Molina-Martinez, C. García-Astrain, J. Langer, I. García, A. Ercilla, G. Perumal, A. Carracedo, L. M. Liz-Marzán. *Nano Letters*, 21 (2021), 8785.
- [4] P. González-Callejo, C. García-Astrain, A. Herrero-Ruiz, M. Henriksen-Lacey, J. Seras-Franzozo, I. Abasolo, L. M. Liz-Marzán. *ACS Applied Materials and Interfaces*, 16 (2024), 27151.
- [5] J. Langer et al. *ACS Nano*, 14 (2020), 28.
- [6] E. Lenzi, M. Henriksen-Lacey, B. Molina, J. Langer, C. de Albuquerque, D. Jimenez de Aberasturi, L. M. Liz-Marzán. *ACS Sensors*, 4 (2019), 1126.

Figures

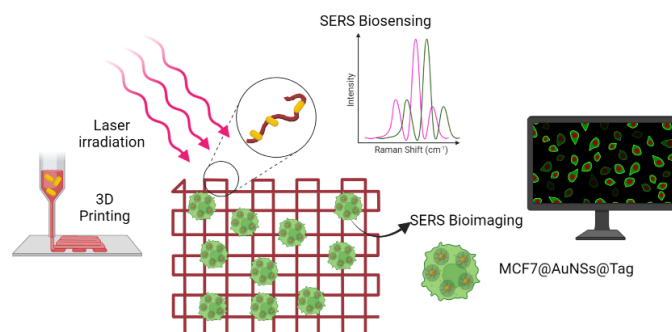


Figure 1. Schematic of 3D printed plasmonic scaffolds for label-free SERS sensing or containing SERS-tag decorated NP for SERS imaging of 3D breast cancer cell cultures.