



Contribution ID: 24

Type: **Keynote**

It is just a matter of surfaces: how multidimensional (nano)modifications can modulate neuronal network activity

Thursday, 15 September 2022 10:45 (30 minutes)

In the past decade, (nano)technology applications to the central nervous system have often involved studying and using novel materials to modulate neuronal activity. The ability to govern neuronal excitability could have a significant impact not only on fundamental neurophysiology but in developing therapeutic approaches to treat neurological diseases. Surface (nano)modification via carbon-based nanomaterials (CBNs) was demonstrated to have a pivotal role in neuromodulation. In particular, we have shown that 2D and 3D materials functionalized with graphene [1] or carbon nanotubes [2,3] are fully biocompatible and, remarkably, able to induce in cultured neurons an increased network synaptic activity via the combined effect of their physico-chemical and morphological properties.

In this regard, we discovered that neuronal network activity is modulated by the synergic contribution of the nanomorphology, chemical activity, and local mechanical compliance possessed by the surface interfacing the neuronal cells. This multimodal surface modification could be used to recapitulate the different cues provided by the extra-cellular matrix (ECM) to neurons within the central nervous system. By growing neuronal cells on/within 2D/3D supports and measuring the electrical activity by patch-clamp recordings, we demonstrated how neuronal activity could be modulated by different surface modifications opening the possibility of orchestrating the firing activity of the entire neuronal network.

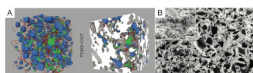


Figure 1:

Figure 1. (A) μ CT volumetric reconstructions of a nanomodified porous scaffold. In blue and green, the maximal filling sphere for pores and throats, in red the interconnection path, and in white the scaffold's matrix. (B) SEM image of a PDMS+CNT scaffold slice showing macroscopic porous morphology. In the top-left inset, the carpet of MWCNTs decorating pores' walls. Scale bars: 100 μ m and 1 μ m, respectively.

[1] Pampaloni NP, Lottner M, Giugliano M, Matruggio A, D'Amico F, Prato M, Garrido JA, Ballerini L, Scaini D., Single-layer graphene modulates neuronal communication and augments membrane ion currents. *Nat Nanotechnol.* 2018, 13, 755-764.

[2] Rago, I., Rauti, R., Bevilacqua, M., Calaresu, I., Pozzato, A., Cibinel, M., Dalmiglio, M., Tavagnacco, C., Goldoni, A., Scaini, D., Carbon Nanotubes, Directly Grown on Supporting Surfaces, Improve Neuronal Activity in Hippocampal Neuronal Networks. *Adv. Biosys.* 2019, 3, 1800286.

[3] Pampaloni NP, Rago I, Calaresu I, Cozzarini L, Casalis L, Goldoni A, Ballerini L, Scaini D. Transparent carbon nanotubes promote the outgrowth of entorhino-dentate projections in lesioned organ slice cultures. *Dev Neurobiol.* 2019, 80, 316-331.

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Session Classification: MS

Track Classification: Nanostructured Materials