

## **A bio-electronic memristive interface for real-time and adaptive coupling of neuronal populations**

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Significant efforts are being made to develop nanoscale electronic devices integrated into neuromorphic circuits capable of emulating the dynamics of natural synapses. The coupling between neuronal populations via artificial synapses bears great potential for therapeutic strategies focused on the monitoring and control of neuronal electrical activity. Such hybrid systems, effectively coupling biological and electrical components, are important milestones for the development of a new generation of neuroprosthetic devices aimed to address a number of challenging neurologic disorders. Memristors have gained attention as a core component in these hybrid systems, mainly because of their neuromorphic properties, small size and low power signature. Relevant proofs of concept have already been presented in the literature, but we argue that crucial aspects have not yet been demonstrated on how these memristor-based hybrid systems can effectively operate in a meaningful way. Here we show, for the first time, how biological *in vitro* neuronal populations can be dynamically coupled with a memristive device acting as a synapse, forming a hybrid bio-electronic system. We demonstrate that the conductance state of a memristor can be changed by the electrical activity of biological neurons and mediate a dynamic connection between isolated spiking neuronal populations. Our system connects biological neurons to microelectrodes, amplifier, memristor, stimulator, microelectrodes, and back to biological neurons, in an effective real-time configuration that does not use software nor simulations. Using our system, we can have neuronal population B being effectively activated if, and only if, there is a consistent firing pattern of activity in population A (network bursting activity). Importantly, we demonstrate that our artificial synapse is capable of short-term plasticity, dynamically changing its conductance level in both directions. Our results pave the way for further implementation of elements able to perform more complex modulatory operations in neuronal populations.