Artificial Neural Network–Assisted Electrochemical Sensors for Reliable Biomarker Analysis in Complex Fluids

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The development of advanced sensors for the analysis of biomarkers in biological fluids such as **saliva, blood, and sweat** is of critical importance for modern healthcare, personalized medicine, and continuous health monitoring. These fluids provide rich diagnostic information in a minimally invasive manner, and enable point-of-care and wearable sensing technologies. However, **accurate sensing in real biological matrices remains challenging** due to their intrinsic complexity; biological fluids contain thousands of proteins, small molecules and ions, whose simultaneous presence can introduce strong matrix effects such as cross interference and signal drift, ultimately leading to sensing artifacts and reduced analytical reliability.
Conventional strategies rely on highly selective sensing elements to minimize these issues such as highly specific "lock-and-key" recognition elements, but selectivity is often difficult to achieve and may limit sensor versatility. An emerging alternative is the use of data-driven approaches based on **artificial neural networks (ANNs)**, which can learn complex, non-linear relationships between sensor signals and analyte concentrations. By processing large, multivariate datasets, ANNs can mitigate matrix induced artifacts, compensate for sensor variability and aging, and significantly improve quantitative accuracy.
In this contribution, we discuss the use of **composite nanomaterials as sensing elements for ANN assisted electrochemical analysis**. Such materials, combining different nanostructured components, exhibit diversified and ion-dependent electrochemical responses rather than strict selectivity. When arranged in multi sensor configurations, they generate **rich and informative datasets that are ideally suited for training neural networks**. This synergistic combination of composite nanomaterials and artificial intelligence opens new avenues for robust biomarker quantification in complex biological fluids, paving the way for next generation chemical sensors capable of reliable operation in real world conditions.

References

[1] Malavolta, L. *et al. Multivariate sensing of ions using machine learning and composite 2D-3D graphene oxide-hexacyanoferrate electrodes. **SENSORS AND ACTUATORS B-CHEMICAL*** 2025, 427, 137194.
[2] Lancellotti, *et al. Selective ion transport in large-area graphene oxide membrane filters driven by the ionic radius and electrostatic interactions. **NANOSCALE*** 2024, 16, 7123–7133.
[3] Poletti, F. *et al. Graphene-Paper-Based Electrodes on Plastic and Textile Supports as New Platforms for Amperometric Biosensing.* ***ADVANCED FUNCTIONAL MATERIALS*** 2022, 32

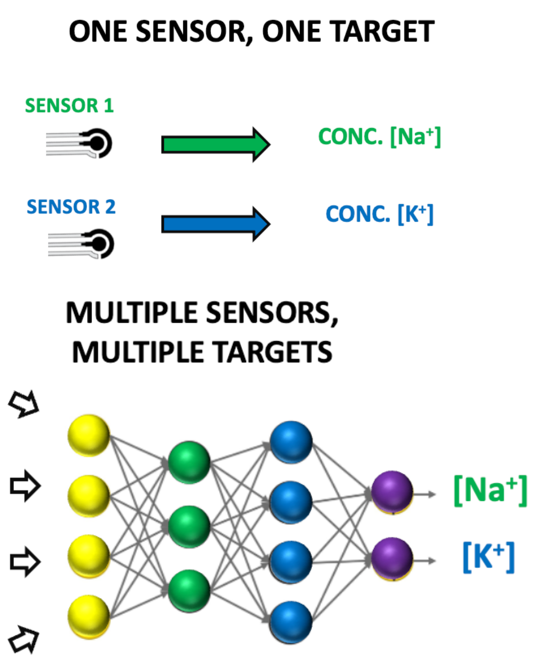

Figure 1. Schematic representation of ANN approach applied to electro- chemical sensors.

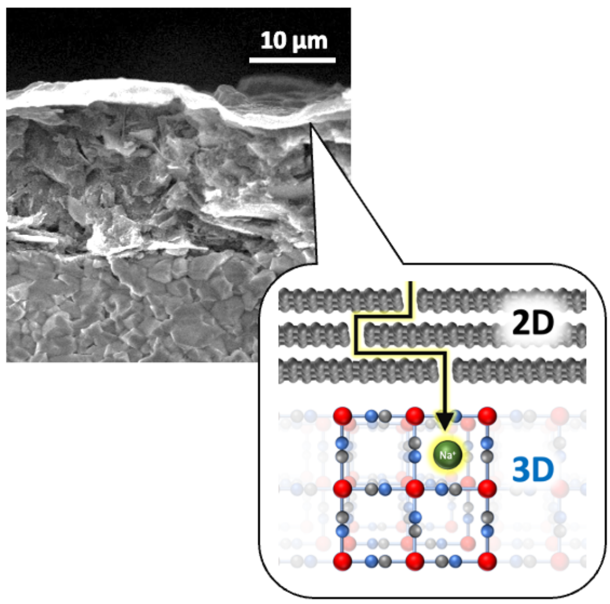

Figure 2. SEM image of a tunable composite material able to sense selectively small ions in a biological matrix, thanks to selective ion diffusion and intercalation in 2-dimensional and 3-dimensional nano-architectures.