



# Electrochemical sensors between the academic world and harsh reality: a few thoughts on the past, present, and future

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“There are three sides to every story. Yours, mine, and the cold hard truth.”  
Unknown author

The development of electrochemical sensors and electroanalytical methods had a strong impact on the development of electrochemistry but also on other fields of science. The discovery of polarography has influenced the development of electrochemistry for a few decades. The invention of pH electrode was the main motivation in the formulation and development of the whole concept of chemical sensors. However, either due to geniality of Fritz Haber or because of the sarcasm of nature, even after over 100 years of the development, no single sensor with so unique analytical properties (selectivity, dynamic range, long-time stability) as pH electrode was developed. Although many types of chemical sensors became necessary components of our usual life or industrial processes, the real progress measured in the number of new devices and concepts realized as a commercial product is relatively slow.

Not all unsolved problems of electrochemical sensors have an electrochemical nature. For example, the development of ion-selective electrodes is strongly dependent on the progress in molecular design and organic synthesis of corresponding ionophores. Very similar limitations define the development of selective electrocatalytical sensors and especially electrochemical affinity sensors, and also in these cases, there is a lack of chemical receptors with high affinity and selectivity. But in general, the number of known chemical receptors is very limited, and only very few of them possess high values

of the binding constant [1]. A promising approach in this field is the implementation of cyclic molecular evolution consisting of (i) a combinatorial organic synthesis, (ii) a high-throughput screening of the property to optimize, and (iii) data analysis (usually by using of neuronal networks) to design the next evolution cycle [2]. We tried to apply such approach for the development of affinity sensors based on conducting polymers [3], but an effective implementation of this strategy requires a formation of large scientific consortiums with extensive funding.

Obviously, each general combinatorial approach for development of new materials with high affinity using standard protocols and allowing one to be realized without large investments always is the goal of intensive investigation. Two such concepts were suggested. The first one is the concept of molecularly imprinted polymerization [4], first mentioned in the 1930s, rediscovered in the 1980s, and being intensively studied since the end of the 1990s. The technology is based on the following steps: (i) formation of complexes between a template (analyte) molecule and complementary monomers, (ii) cross-linking polymerization of these monomers in the presence of porogens, and (iii) extraction of the template molecules. However, such problems like a relatively poor affinity (in most cases below  $10^7$  L/mol [1]) and strong heterogeneity of the binding sites compromising the binding selectivity, complicate applications of molecularly imprinted polymers in sensor devices. The second concept is based on the exploitation of affinity of nucleic acids (DNA or RNA), sometimes with terminal modification by other chemical groups. The development of such molecules (aptamers) is performed by the procedure of systematic evolution of ligands by exponential enrichment (SELEX) which includes a synthesis of randomized oligonucleotide sequences, selection of the molecules with highest affinity, and their further biosynthesis using polymerase chain reaction. Recently, this approach was extended to peptides, and here, the complexes of peptides with corresponding oligonucleotides were used for PCR

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amplification of the selected peptides [5]. However, also by this technology, it is really challenging to obtain aptamers with high affinity [6]. But the development continues, and one can hope for new ideas and further increase of optimism.

Another problem in the development of selective and sensitive affinity sensors is a very slow sensor recovery. This drawback may be sound to be too academic, but actually, this is the only reason why many highly sensitive (electro)chemical sensors did not find practical applications. Physically, the affinity is defined by the ratio of kinetic constants of analyte binding and dissociation. Therefore, in many cases, a high affinity to the analyte (which is required not only for a high sensitivity but also for a high selectivity of the sensor device) is achieved by minimization of the kinetic constant of the analyte dissociation. The sensor recovery can be accelerated by heating but it is hardly applicable for liquid analytes. A novel approach is based on electrochemical control of the redox state of the sensor layer [7, 8]. Currently, an application of this approach was limited only to chemical sensors based on conducting polymers, but it can be certainly extended to other redox-active receptors. One can expect further progress in this field by introducing of redox-active groups into other receptor molecules (various chemical receptors, nucleic acids, aptamers, or even native antibodies): this may be a way to achieve electrochemically controlled affinity of these receptors.

Due to the strong pressure of the market and costs, the development of sensors was almost focused on a single measurement technology. This led to competitive consideration of different approaches, and during the last decade, we always observed such competitions, for example, Clark electrode vs. fluorescence quenching in oxygen sensing. Simultaneous application of two or more different measurement technologies was used only in science but was not typical for final devices. The cost decrease of the measurement technologies leads to the change of this paradigm, and we observe now such sensors where a high synergetic potential of application of different technologies (usually optical and electrochemical) is exploited. One example of this friendship is the establishing of electroluminescent techniques. Recently, this trend was extended to the new challenge in electrochemical analytics—detection of nanoparticles. Using microelectrodes, it was possible to perform electrochemical analysis of individual nanoparticles [9], and this resulted in the concept of “impact electrochemistry.” However, the requirement to measure fast current kinetics leads to the necessity to have a small electrode capacitance (this capacitance is included into the feedback of the current amplifier, thus limiting time resolution). This leads to the fundamental limitation of the electrode area and requires a high particle concentration for the analysis. The use of optical reading of electrochemical conversions of metallic nanoparticles allows one to

make an electrochemical analysis of individual nanoparticles on macroscopic electrode surface where hundreds thousands of nanoparticles are present [10]. Notably, this reading of the electrochemical conversion is performed simultaneously for all nanoparticles adsorbed on the electrode surface. Another example of successful implementation of optical techniques in electrochemical sensors is a photomodulation of electrochemical processes using quantum dots [11]. Certainly, the synergetic combination of optical and electrochemical measurement technologies has a high potential for further development of electrochemical (or more exactly - optoelectrochemical) sensors.

Finally, one has to mention a specific problem in the publications on electrochemical sensors. The huge amount of submitted manuscripts in this field describes “new sensors” obtained by an application of a cocktail from some “hot” materials (like nanoparticles, graphene, nanotubes, quantum dots) for electrocatalytical detection of any (typically-relatively exotic) analyte. Only very few of these manuscripts are based on scientific ideas exploiting unique properties of nanomaterials, while the majority presents rather phenomenological observations without any electrochemical study of the effect or/and constructive and systematic comparison of different composites. Unfortunately, many such manuscripts pass through peer-reviewed filter. Let us hope that this non-scientific problem of modern science will be solved already in the near future.

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