Investigating the detection limit of electrochemistry

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In electrochemical measurements, every detail matters. By cutting away the noise, the researchers created order out of chaos. And all this to increase the sensitivity of the study of even single molecules. Credit: Grzegorz Krzyzewski/IPC PAS

With recent improvements in instrumentation and confinement techniques, the detection of molecules using electrochemical techniques has become easier than ever before; however, there are still many conditions which restrict the electrochemical detection of single molecules and ultra-fast processes at the molecular level.

All of this is due to the presence of a limit of detection, which is set by the minimum number of electrons that can be observed passing through an electrochemical system during a measurement. This is a serious problem for diagnostic devices based on electrochemistry, so many efforts are being made to find alternatives to overcome the electrochemical detection limit.

Recently, scientists from the Institute of Physical Chemistry of the Polish Academy of Sciences (IPC PAS) provided insight into electrochemistry performed below the limit of detection and into the prospects for applying the proposed solution in fields where that limit is still an issue.

Electrochemistry is a branch of science concerned with the relationship between chemical changes and electrical charges. Electrochemical processes have significant practical applications in many areas of science and everyday life. There are several electroanalytical methods, each of which can be used to study numerous processes.

Corrosion? Electrochemical techniques can be used to detect the formation of pits as small as several nanometers under environmental conditions.

What about energy storage? Batteries for portable electronics and electric cars, fuel cells, and even photovoltaics are based on electrochemical processes.

The detection of certain molecules in food samples, pharmaceutical mixtures, wastewater, and even biological fluids can be performed by capturing certain electrochemical signals. Through this, it is possible to accurately assess the content of molecules of interest in a sample under investigation.

The electrochemical methods used to detect molecules with high sensitivity have been greatly updated since the methods used by Michael Faraday almost two centuries ago. Researchers are constantly trying to make our lives easier by increasing the sensitivity of electrochemical techniques towards the detection limit of such chemicals.

However, despite the broad use of electrochemical methods in everyday life, the detection of single molecules, particles, and redox processes at a molecular level is still challenging and needs an amplification approach to deal with the low numbers of electrons passed during the measurement.

Furthermore, the thermal and statistical motion of electrons in electrical circuits adds some background noise which means more than 2,100 electrons are required in order to even see an electrochemical event. This translates to thousands of molecules reacting at the electrode, far from the dream of single molecule detection. However, this limit can be overcome by converting electrochemical charges into photons, which can be detected even if only one photon is present.

Analytical Chemistry recently published an article on this very topic written by researchers from the Nanoelectrochemistry group at the Institute of Physical Chemistry of the Polish Academy of Sciences (IPC PAS). An increased sensitivity towards the detection of charge-transfer processes was demonstrated through the measurement of fluorescence induced in a closed bipolar electrochemical setup. In this unique setup, the oxidation of an analyte in one cell was used to concurrently drive the oxidation of fluorogenic redox compound, Amplex Red, in another cell.

"We demonstrated the use of a luminescent molecule to measure charges close to the electrochemical limit of quantification and compared the efficiencies of the reaction under different experimental timescales. This is a large step toward the quantitative conversion of sub-detection limit electrochemical signals into more sensitive photon signals. This advancement will improve the sensitivity of single-entity electrochemistry and sensing applications that use remote optical reporting, allowing smaller nanoparticles and lower concentrations of analyte to be detected," explained Dr. Steven Linfield, one of the researchers behind the publication.

The integrated fluorescence signal caused by the passage of charge was measured, and the results revealed a linear relationship between the charge passed and the fluorescence signal, depending on the experiment's timeframe. Microelectrodes were used for their low capacitance and rapid establishment of a steady-state diffusion field, which allowed the researchers to approach the electrochemical limits of quantification without appreciable capacitive current.

"In our work, we presented an alternative system for remote reporting in which fluorescence is induced through microelectrodes in a closed bipolar electrochemical cell in three-electrode driving mode. To report on electrochemistry measured in the detection cell, we need an understanding of the processes which may occur in the reporting cell and how the design of the closed bipolar cell can influence the reporting process," states Dr. Wojciech Nogala, the principal investigator of the project.

This alternative system not only provides the possibility for the direct thermodynamic control of electrochemical processes, but also enables observation of the fluorogenic reaction induced by either reduction or oxidation processes. Thanks to these experiments, it is now possible to see currents that are close to the limit of quantification. This outcome could revolutionize the detection of discrete signals given by many molecules that are normally not detectable using classical electrochemical setups and opens up the possibility of sensing molecules at ultralow concentrations.

So, where might the results of these studies be applied? Well, one application is in the sensing of clinically relevant biomolecules at low concentrations, which may bring us closer to earlier diagnosis and treatment of various diseases. Another can be detection of particular chemicals in food or environment with higher sensitivity than before. Detecting molecules with a higher sensitivity can enhance the analytical capabilities of various sectors and can aid in the development of novel sensors in many aspects of life.

More information: Steven Linfield et al, Toward the Detection Limit of Electrochemistry: Studying Anodic Processes with a Fluorogenic Reporting Reaction, *Analytical Chemistry* (2023). DOI: 10.1021/acs.analchem.3c00694

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