Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Electrochemistry

Review Article

Critical reviews on recent states and challenges in spectroelectrochemistry with applications to microfluidic systems

Zhenglong Li[1], Maryom Rahman[1], Sreerag Kaaliveetil[1], Niranjan Haridas[1], Yu-Hsuan Cheng[1], Charmi Chande[1] and Sagnik Basuray[1,2]

Abstract

Spectroelectrochemistry (SEC) is an integrated technique that marries the best of electrochemistry and spectroscopy during the electron transfer process. The review presents the recent developments in two not-frequently used but promising techniques (nuclear magnetic resonance (NMR) SEC and dark field microscopy (DFM) SEC). The dissemination of these two SEC techniques is required for their future widespread applications. The research challenges and development perspectives of NMR and DFM SEC are elaborated. Furthermore, it is found that employing SEC techniques in microfluidics is becoming a research hotspot. Therefore, Raman and ultraviolet-Visiblevisible-based SEC techniques in microfluidics are discussed. The last section summarizes and elaborates on the inherent challenges with SEC.

Addresses

[1] Department of Chemical and Materials Engineering, New Jersey Institute of Technology, Newark, NJ 07102, United States

[2] Department of Biomedical Engineering, New Jersey Institute of Technology, Newark, NJ 07102, United States

Corresponding author: Basuray, Sagnik (sbasuray@njit.edu)

Current Opinion in Electrochemistry 2023, **41**:101357

This review comes from a themed issue on **Innovative Methods in Electrochemistry (2023)**

Edited by **Emmanuel Maisonhaute** and **Jay D.Wadhawan**

For a complete overview see the Issue and the Editorial

Available online 20 July 2023

https://doi.org/10.1016/j.coelec.2023.101357

Keywords:

Spectroelectrochemistry, Nuclear magnetic resonance SEC, Dark field microscopy SEC, Microfluidics.

Introduction

As a composite technology, spectroelectrochemistry (SEC) is attracting increasing attention from fields ranging from inorganic, organics, electrodeposition, and even radiological analytes [1,2]. The integration of electrochemistry and spectroscopy allows SEC techniques to offer a detailed and comprehensive study of the electron transfer kinetics and vibrational spectroscopic fingerprint of analytes during electrochemical reactions [3–5]. Specificity and anti-interference properties are inherent to SEC experiments due to the impossibility of finding two compounds that exhibit identical electrochemical behavior and spectroscopic properties [6]. Well-developed traditional analytical methods in electrochemistry, like cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and differential pulse voltammetry (DPV), have been widely applied in SEC [2]. Ultraviolet-visible (UV-Vis), surface-enhanced Raman spectroscopy (SERS), nuclear magnetic resonance (NMR), and fluorescence spectra are frequently used spectroscopy techniques. Thus, as a composite technology, SEC can offer many theoretical combinations. The SEC "family" is continually expanding by adding other spectroscopy techniques like dark field microscopy SEC (DFM SEC) [2,7].

The past few decades have witnessed the use of SEC techniques in different analysis fields. However, most published literature on SEC techniques concentrates on two relatively mature combinations: UV-Vis and Raman SEC. Very few examples of NMR and DFM SEC are available in the literature. Hence, more dissemination and understanding of NMR and DFM SEC is needed. Through this work, we hope that more people, whether established researchers or beginners, can see, understand, and use those SEC techniques in their respective fields of study. To this end, this article presents, summarizes, and discusses the development of NMR and DFM SEC techniques in recent years. Due to the need for more understanding of which technologies can be used for which applications, this article elaborates on helping researchers carefully understand and utilize the right technologies for their intended applications. In addition, the employment of SEC techniques in microfluidics is gaining significant attention from the scientific community. Therefore, this article presents recent advances in using SEC techniques in microfluidics. Finally, the summary and outlook section

discuss current challenges to each technique and future perspectives.

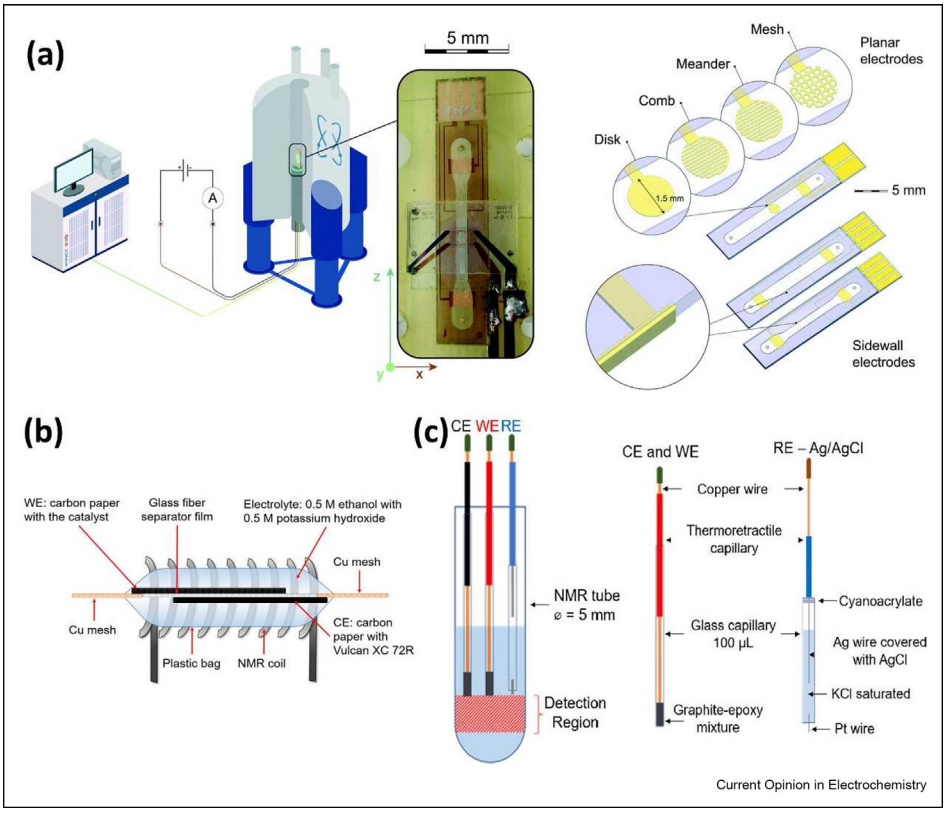
Nuclear Magnetic Resonance SEC (NMR SEC)

For electrochemical systems, obtaining information on the reaction intermediates, reagent concentrations, and reaction products during the reaction are critical to examine the possible reaction pathways. Nuclear magnetic resonance (NMR) is the most popular technique for elucidating molecular structures [8,9]. NMR SEC can obtain comprehensive structural information on the molecules and has been used to investigate electrocatalytic processes, reaction intermediates, reagent and product concentrations [10,11].

NMR SEC usage has been limited since few commercial NMR SEC cells exist. Further, NMR SEC cells are difficult to assemble for routine measurements [10,12]. In most electrochemical NMR cells, the electrodes are placed inside the NMR coil. However, the commonly-used metallic electrodes disrupt the static magnetic field ($\boldsymbol{B_0}$) homogeneity, a critical requirement for NMR to gain a high signal-to-noise ratio (SNR) [13]. Thus, NMR SEC is more complicated than other SECs. Significant efforts have been made to reduce or eliminate the disruption in the magnetic field [7,10]. The approaches are summarized here: (**i**) Using ultra-thin film metallic electrodes [10]; (**ii**) Nonmetallic electrodes like carbon microfibers and polymer electrodes [14]; (**iii**) Placing the electrodes outside the detection region [9].

Thin film metallic electrodes with different electrode geometries have been successfully used to monitor *in-situ* chitosan electrodeposition [10]. It is found that electrodes with ultra-thin thicknesses (tens of nanometers) or placed on the sidewalls of microfluidic channels show better device performance without affecting the homogeneity of the magnetic field $\boldsymbol{B_0}$, as verified by simulations and experiments, as shown in Figure 1(a). Recently, the use of conducting polymer or carbon-based, nonmetallic working electrodes (WE) has become a popular area of research [7,15–18]. Direct alcohol-based fuel cells have attracted tremendous research interest due to their well-recognized advantages [19]. To monitor molecular changes of the reaction products and to reveal the reaction mechanism of

Figure 1



(a) Schematic structure of the electrochemical cell designed for *in-situ* EC-NMR experiment [10]. **(b)** Pouch cell with all components in the solenoid coil [14]. **(c)** Electrochemical cell and electrodes. The WE, CE, and RE are fixated on the glass capillary tube [9].

alcohol oxidation reaction, Jana et al. introduce the *in-situ* real-time setup of electrochemical NMR, as shown in Figure 1(b). Here a carbon-based WE is employed [14].

However, the complex fabrication process usually implies high, time-consuming preparation costs for ultra-thin metal electrodes. Using carbon-based electrodes also has limitations, like weak adhesion between the substrate and carbon nanomaterials, surface preparation dependent-electrochemical performance, and others [20]. Furthermore, nonmetallic polymer electrodes usually have limited electrochemical applications due to the low achievable currents [12]. Instead of focusing on the WE's preparation, the placement of the electrodes is also quite critical [9]. In Figure 1(c), the electrodes (WE and counter electrode) are fixed on a capillary glass tube, inserted into a standard 5 mm NMR tube, and placed 1 mm above the NMR detection region. The magnetohydrodynamic (MHD) effect is an important observation here, arising from the electric field of the electrochemical cell and the magnetic field of the NMR spectrometer [21]. Stirring with MHD force will homogenize the concentration of reagents and products in the NMR detection region, allowing real-time measurement of analytes, even though the electrodes are placed outside the NMR detection region.

Dark field microscopy SEC (DFM SEC)

NMR SEC is a good candidate for elucidating possible reaction pathways in electrochemical redox processes. However, the collected information by NMR SEC mainly relies upon bulk samples rather than individual nanoparticles (NPs). Understanding NPs' electrocatalytic properties and the oxidation process in aqueous suspensions is essential for their applications in sensing and catalysis [22,23]. Since electron-rich metal NPs such as AuNPs and AgNPs can exhibit intrinsic localized surface plasmon resonance (LSPR), the oxidation/reduction process of NPs in aqueous suspension will shift the LSPR frequency. Established in-situ optical methods like fluorescence spectroscopy and SERS, which only monitor the signal intensity, cannot access such information [24]. DFM SEC is gaining significant attention due to its ability to observe such changes/chemical reactions at a single-entity/nanoscale level [25]. The LSPR changes are tracked using an electron-multiplying charge-coupled device (EMCCD) camera.

For example, a recent work by Hui et al. has successfully shown the applicability of DFM SEC to track the synthesis of multi-metallic Au@MNPs (M = Pt, Pd, and Rh), which are candidate catalysts for the methanol oxidation reaction (Figure 2(a)) [26]. In addition, the shape of NPs is one of the critical factors affecting the LSPR intensity. Therefore, different nanostructures of NPs have been used in the DFM SEC technique. Among them, Au nanocubes (AuNCs) stand out in their sharp vertices, providing electric-field-enhanced hotspots [27]. A recent article by Kim et al. shows the successful observation of distinct electrochromic behaviors of AuNCs via an *in-situ* DFM SCE technology (Figure 2(b)) [28]. One more recent interesting work by Jazlynn et al. shows us the feasibility of using redox MHD-DFM as an efficient tool to evaluate the NP sizes while simultaneously differentiating between mixtures of different nanomaterials (AgNPs and Au-coated-silicaNPs) [29]. Figure 2(c) shows that a permanent magnet parallels the electrochemical cell. The introduced MHD force allows a controllable flow within the cell. However, for most of the reported DFM SEC setups, the requirement for optically transparent electrodes (OTEs, like Indium tin oxide and Fluorine-doped tin oxide) has limited its widespread use due to the limited natural source and less negative inert potential window [30].

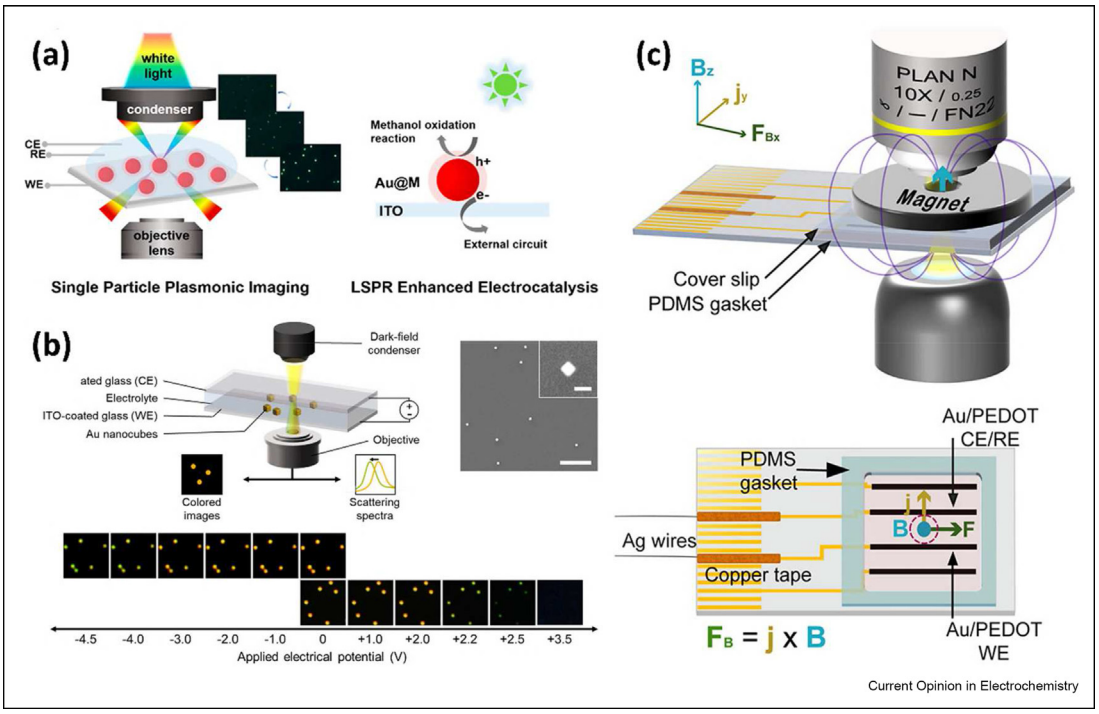
SEC techniques' applications in microfluidics

Due to the often-cited characteristics of microfluidics, the combination of microfluidics and SEC is receiving more and more attention [31–33]. However, due to the stringent requirements on the NMR cell structure and the limited use of DFM techniques, the current research chiefly relies on the SERS/Raman- or UV-Vis-based SEC combined with microfluidics.

The excellent compatibility between the SERS technique and microfluidic chips has triggered quantities of scientific research in the last decades [34,35]. For example, in quantitative assays, cells, and droplets sorting and biomolecules [36,37]. Although the sensitivity of SERS in microfluidic devices is relatively low compared to conventional SERS measurements, the repeatability of SERS measurements in microfluidic systems is somewhat higher due to the continuous flow of analyte molecules [38]. Preparing reliable SERS substrates is critical to realize microfluidic SERS chips with fast detection, high sensitivity, and good repeatability [39]. SERS substrates can be broadly classified into two categories: mobile SERS substrates and fixed SERS substrates. The mobile SERS substrates use metal colloids like Ag or Au colloids as the substrates [36]. However, the main drawback of metal colloids is their poor reproducibility. In addition, there is the possibility of clogging the microchannels. The main advantage of fixed SERS substrates with defined metal nanostructures is the higher morphological control of the nanostructures [40].

For SERS-based analytical transducers, reusability is critical to decreasing variation between measurements and the manufacturing time. For fixed SERS substrates,

Figure 2



(a) Experimental setup of the DFM-guided electrochemical synthesis of Au@MNPs and plasmonic accelerated MOR [26]. **(b)** Top Right: Electrochromic behavior of AuNCs measured under DFM. Top Left: SEM images of the AuNCs loaded on the ITO-coated glass substrate. Scale bars are 5 μm for the main image and 100 nm for the inset. Bottom: DFM images of the AuNCs under applied potentials ranging from 0 V to −4.5 V (cathodic) and 0 V−3.5 V (anodic), respectively [28]. **(c)** Electrochemical cell/magnet assembly used for RMHD–DFM is located between the illuminating system and the microscope objective. Top-down view of the electrochemical portion of the RMHD assembly [29].

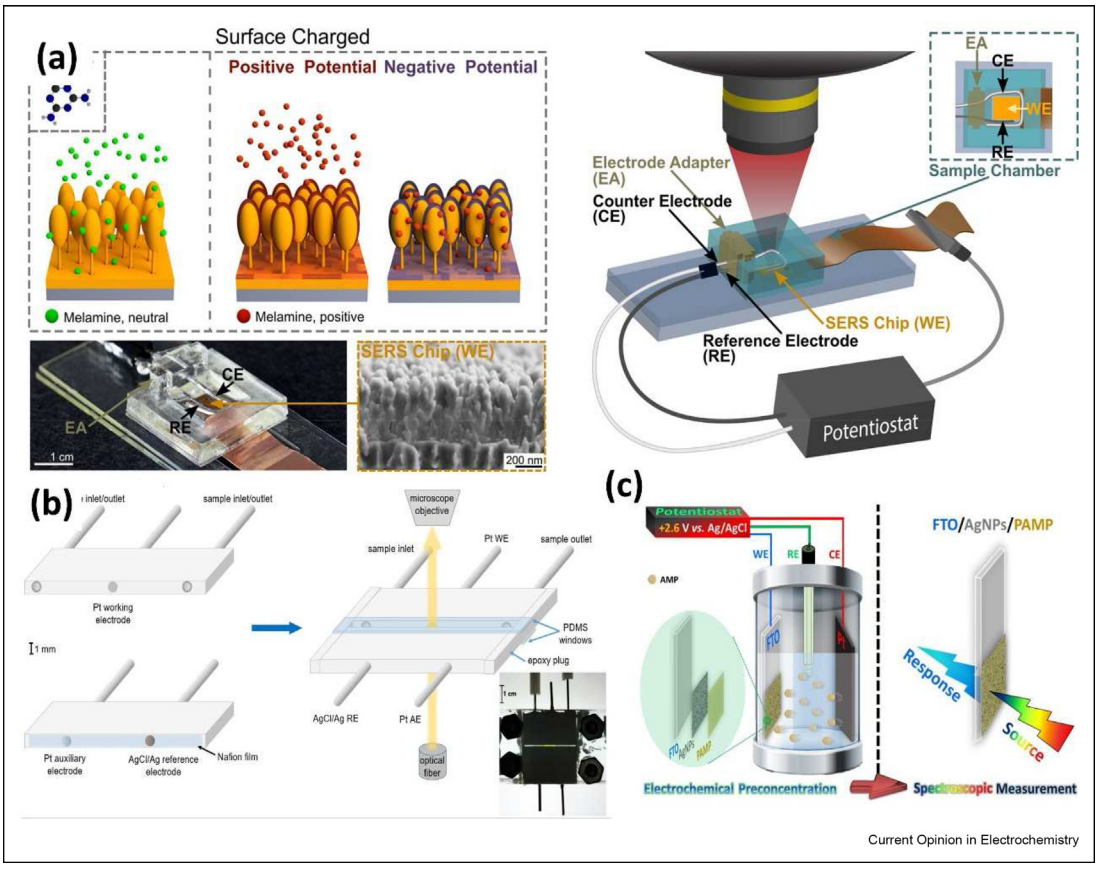
the frequently used methods include harsh reagents, UV irradiation, and high-temperature treatment [41,42]. These processes rely on drastic surface treatments, specialized equipment, and time-consuming reversion processes. Marlitt et al. proposed one possible way to prepare a standard/practical analytical tool with excellent reusability [42]. The structure of the SERS SEC setup is shown in Figure 3(a). The forest of Au-capped silicon nanopillars is applied as the SERS-active substrate and the WE. The substrate recycling is obtained by applying a small positive voltage to remove the positively charged Melamine. However, the requirements of substrates with defined nanostructure morphologies (like NPs, nanopillar forest, and nanodot arrays, among others) complicate the preparation process and increase the cost. Unlike SERS SEC in microfluidics, Raman SEC is relatively flexible for substrates, like laser-induced graphene or reduced graphene-modified paper, which are well suited for scalable production [43,44].

UV-Vis SEC and Microfluidics have been widely used in biotechnology, catalysis, environmental protection, and others [45,46]. However, compared with the SERS/Raman SEC, the employment of UV-Vis SEC in Microfluidics is more, probably because the electrode substrate can be prepared easily. In Figure 3(b), an interesting microfluidic device for UV-Vis SEC is proposed by Wang et al. [47] Spectral measurements are made using an "in-house" constructed visible micro spectrometer which consists of a deuterium/tungsten-halogen light source and a CCD spectrometer. In addition, electrochemical preconcentration is one of the most frequently discussed preconcentration techniques at a controlled potential [48]. Hybrid SEC techniques also often involve this method to assist the goal of quantifying ultra-trace aqueous target analytes. Arash et al., in this work, monitor a potassium-channel blocking agent, Ampyra (AMP) (Figure 3(c)) [49].

Summary and outlook

We have detailed the recent development in DFM and NMR SEC and recent progress in combining SEC techniques and microfluidics. A detailed analysis of the working principles, challenges, and intended application directions in the selected recent applications is summarized in Table 1. For each SEC technique, some limitations from lab-scale to widespread practical use are summarized below.

Figure 3



(a) Left Top: Schematic diagram of the electrochemically assisted SERS-based detection working principle. Left Bottom: Photo of the assembled detection chamber and SEM image of Au-capped nanopillar structures for SERS detection. Right: Illustration of the custom-made electrochemical-SERS platform and its respective system interfacing. Inset shows the placement of the electrodes. Here, a platinum wire is applied as the counter electrode. A silver/silver chloride reference electrode is involved. The Au-capped Si nanopillar substrate is used as the working electrode [42]. **(b)** Illustration of the microfluidic setup for UV-Vis SEC measurements [47]. **(c)** Schematic illustration of the sensing procedure developed to determine ampyra [49].

NMR SEC

The NMR SEC technique seems to be one of the most versatile techniques for identifying the molecular signatures of the captured chemical moieties or small biomolecules. However, considering the low sensitivity of NMR, most of the NMR SEC is mainly focused on information about reaction intermediates or revealing possible reaction pathways [50]. The applications of NMR SEC are limited due to a few points: (**i**) The conducting electrode will lead to severe disruption in the homogeneity of $\boldsymbol{B_0}$, a critical requirement for NMR (**ii**) The design of suitable electrode materials (e.g., conducting polymers, thin metal films) and electrode configurations will increase the cost and difficulty of applying the technology and discourage rapid adoption by researchers.

DFM SEC

Instead of studying structural characteristics and activities from bulk samples or NP ensembles level, the DFM SEC technique can directly explore the structure-activity relationship from the individual NP level [51]. The understanding from the nanoscale level is critical to designing and producing stable, high-performance catalysts [52]. However, there is a considerable gap for this technology to cross. Reasons are: (**i**) Limited by the light source arrangement, the technology has high requirements on the material and structure of the electrode. In addition, OTEs are frequently involved in DFM SEC. As well as (**ii**) tedious coupling procedures of the light and electric paths. (**iii**) Further, DFM SEC setups require extensive optics and might not be easy to incorporate into a sensor system. (**iv**) The reliability and device-to-device variation in DFM SEC are also concerns.

In addition, using SEC techniques in microfluidics is becoming an exciting trend within research fields, ranging from biotechnology to catalysis, environmental protection, and others. Although there are many

Table 1

Summary of desired applications for different SEC techniques.

SEC technologies	Desired general applications	Limitations
UV-Vis SEC	Quantitative analysis	Requirements on the optically transparent electrode; difficulty in the alignment of light beams, etc.
SERS SEC	Structural study; reaction intermediates; quantitative analysis, etc.	Preparation of SERS-active nanostructured substrate; low reusability, low reproducibility, etc.
NMR SEC	Quantitative analysis; reaction intermediates; reaction mechanism study, etc.	Critical requirement on the homogeneity of the magnetic field; suitable electrode materials; NMR cell structure, etc.
DFM SEC	Structural characteristics of individual NP; designing stable and high-performance catalysts.	Requirements on the optically transparent electrode, compatibility between different techniques, etc.

compatibility problems, mutual interference, optical road layout, and so on, this will be one of the promising development directions in the future. As more researchers familiarize themselves with the SEC techniques and new materials continue to be developed, these current problems, such as the OTEs problem in DFM SEC and the inhomogeneity of the magnetic field in NMR SEC, will be solved. In the end, we hope that through this article, researchers will see and get familiar with different SEC techniques, including the know-how on building SEC systems and using them to obtain and analyze the information they want.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper article.

Data availability

Data will be made available on request.

Acknowledgments

This manuscript is supported by Sagnik Basuray's NSF grant # 1751759, Career: "ASSURED" electrochemical platform for multiplexed detection of Cancer Biomarker Panel using Shear Enhanced Nanoporous Capacitive Electrodes and a New Jersey Health Foundation Grant, # PC 54-20, "ESSENCE - A Selective and Sensitive Electrochemical POC Platform for Liquid Biopsy."

References

Papers of particular interest, published within the period of review, have been highlighted as:

* of special interest

1. Gomes B, Nunes L, Lobo C, Carvalho A, Cabeça L, Colnago L: **In situ analysis of copper electrodeposition reaction using unilateral NMR sensor**. *J Magn Reson* 2015, **261**:83–86.

2. Chatterjee S, Fujimoto MS, Cheng YH, Kargupta R, Soltis JA, Motkuri RK, Basuray S: **Improving the sensitivity of electrochemical sensors through a complementary luminescent mode: a new spectroelectrochemical approach**. *Sensor Actuator B Chem* 2019, **284**:663–674.

3. Hernandez S, Perales-Rondon JV, Heras A, Colina A: **Simultaneous Raman and reflection UV/Vis absorption spectroelectrochemistry**. *Nano Res* 2022, **15**:5340–5346.

4. Amatore C, Da Mota N, Sella C, Thouin L: **Theory and transport experiments at channel microband electrodes under laminar flow. 3. Electrochemical detection at electrode arrays under steady state**. *Anal Chem* 2010, **82**:2434–2440.

5. Horny M-C, Lazerges M, Siaugue J-M, Pallandre A, Rose D, Bedioui F, Deslouis C, Haghiri-Gosnet A-M, Gamby J: **Electrochemical DNA biosensors based on long-range electron transfer: investigating the efficiency of a fluidic channel microelectrode compared to an ultramicroelectrode in a two-electrode setup**. *Lab Chip* 2016, **16**:4373–4381.

6. Garoz-Ruiz J, Heras A, Colina A: **Direct determination of ascorbic acid in a grapefruit: paving the way for in vivo spectroelectrochemistry**. *Anal Chem* 2017, **89**:1815–1822.

7. Zhang X-P, Jiang W-L, Cao S-H, Sun H-J, You X-Q, Cai S-H, Wang J-L, Zhao C-S, Wang X, Chen Z: **NMR spectroelectrochemistry in studies of hydroquinone oxidation by polyaniline thin films**. *Electrochim Acta* 2018, **273**:300–306.

8. Lobo CM, Gomes BF, Bouzouma H, Danieli E, Blümich B, Colnago LA: **Improving in operando low field NMR copper electrodeposition analyses using inductively coupled coils**. *Electrochim Acta* 2019, **298**:844–851.

9. * Ferreira da Silva P, Ferreira Gomes B, Silva Lobo CM, Carmo M, Roth C, Colnago LA: **Composite graphite–epoxy electrodes for in situ electrochemistry coupling with high resolution NMR**. *ACS Omega* 2022, **7**:4991–5000.
In this article, the introduction of magnetohydrodynamic (MHD) effect to homogenize the reagent and and generated products in the NMR detection region for real-time measurements are detailed.

10. * Davoodi H, Nordin N, Bordonali L, Korvink JG, MacKinnon N, Badilita V: **An NMR-compatible microfluidic platform enabling in situ electrochemistry**. *Lab Chip* 2020, **20**:3202–3212.
The NMR SEC technique for in-situ Chitosan electrodeposition is studied in this work. The combination of simulation and experimental validation is introduced to identify the optimized electrode geometry for NMR SEC experiments, which provides an instructive approach for further works.

11. Dong H, Su H, Chen Z, Yu H, Yu H: **Fabrication of electrochemically reduced graphene oxide modified gas diffusion electrode for in-situ electrochemical advanced oxidation process under mild conditions**. *Electrochim Acta* 2016, **222**:1501–1509.

12. Da Silva PF, Gomes BF, Lobo CMS, Júnior LHKQ, Danieli E, Carmo M, Blümich B, Colnago LA: **Electrochemical NMR spectroscopy: electrode construction and magnetic sample stirring**. *Microchem J* 2019, **146**:658–663.

13. Bussy U, Boujtita M: **Review of advances in coupling electrochemistry and liquid state NMR**. *Talanta* 2015, **136**:155–160.

14. Fritzke JB, Eßbach C, Wollmann P, Khan AH, Senkovska I, Weidinger IM, Kaskel S, Brunner E: **The role of metal–organic frameworks in moderating platinum-based ethanol electrooxidation catalysts**. *J Phys Chem C* 2021, **125**:14263–14274.

15. Klunder KJ, Clark KM, McCord C, Berg KE, Minteer SD, Henry CS: **Polycaprolactone-enabled sealing and carbon**

composite electrode integration into electrochemical microfluidics. *Lab Chip* 2019, **19**:2589–2597.

16. Horny M-C, Billon F, Deslouis C, Dupuis V, Siaugue J-M, Pailleret A, Gamby J: **Amorphous carbon nitride microband integrated in a microfluidic device for DNA biosensors applications**. *J Electroanal Chem* 2021, **895**:115395.

17. Neckel IT, de Castro LF, Callefo F, Teixeira VC, Gobbi AL, Piazzetta MH, de Oliveira RA, Lima RS, Vicente RA, Galante D: **Development of a sticker sealed microfluidic device for in situ analytical measurements using synchrotron radiation**. *Sci Rep* 2021, **11**:23671.

18. Renault C, Scida K, Knust KN, Fosdick SE, Crooks RM: **Based bipolar electrochemistry**. *J Electroche Sci Technol* 2013, **4**: 146–152.

19. Dolle C, Neha N, Coutanceau C: **Electrochemical hydrogen production from biomass**. *Curr Opin Electrochem* 2022, **31**: 100841.

20. López-Naranjo EJ, González-Ortiz LJ, Apátiga LM, Rivera-Muñoz EM, Manzano-Ramírez A: **Transparent electrodes: a review of the use of carbon-based nanomaterials**. *J Nanomater* 2016, **2016**.

21. Monzon LM, Coey JMD: **Magnetic fields in electrochemistry: the Lorentz force. A mini-review**. *Electrochem Commun* 2014, **42**:38–41.

22. Li Z, Ni J, Zhang S, Li C, Du Y, Zhang Y, Cai H, Li J, Zhang J: **Effect of incorporation of highly-ordered a-Ge: H nanoparticles on the performance of perovskite solar cells**. *Micro & Nano Lett* 2018, **13**:1111–1116.

23. Schopf C, Wahl AI, Martín A, O'Riordan A, Iacopino D: **Direct observation of mercury amalgamation on individual gold nanorods using spectroelectrochemistry**. *J Phys Chem C* 2016, **120**:19295–19301.

24. Wonner K, Evers MV, Tschulik K: **The electrochemical dissolution of single silver nanoparticles enlightened by hyperspectral dark-field microscopy**. *Electrochim Acta* 2019, **301**: 458–464.

25. Wonner K, Evers MV, Tschulik K: **Simultaneous opto-and spectro-electrochemistry: reactions of individual nanoparticles uncovered by dark-field microscopy**. *J Am Chem Soc* 2018, **140**:12658–12661.

26. Wang H, Zhao W, Zhao Y, Xu C-H, Xu J-J, Chen H-Y: **Real-time tracking the electrochemical synthesis of Au@ metal core–shell nanoparticles toward photo enhanced methanol oxidation**. *Anal Chem* 2020, **92**:14006–14011.

27. Gu XY, Gao PF, Zou HY, Liu JH, Li YF, Huang CZ: **The localized surface plasmon resonance induced edge effect of gold regular hexagonal nanoplates for reaction progress monitoring**. *Chem Commun* 2018, **54**:13359–13362.

28. Kim J-H, Cha S, Kim Y, Son J, Park J-E, Oh J-W, Nam J-M: **Nontrivial, unconventional electrochromic behaviors of plasmonic nanocubes**. *Nano Lett* 2021, **21**:7512–7518.

29. * Sikes JC, Wonner K, Nicholson A, Cignoni P, Fritsch I, Tschulik K: **Characterization of nanoparticles in diverse mixtures using localized surface plasmon resonance and nanoparticle tracking by dark-field microscopy with redox magnetohydrodynamics microfluidics**. *ACS Phys Chem Au* 2022, **2**: 289–298.

In this paper, the introduction of MHD-DFM enables the simultaneous determination of nanoparticle size and differentiates nanoparticles with different components, which is quite interesting.

30. Zhou H, Ma X, Sailjoi A, Zou Y, Lin X, Yan F, Su B, Liu J: **Vertical silica nanochannels supported by nanocarbon composite for simultaneous detection of serotonin and melatonin in biological fluids**. *Sensor Actuator B Chem* 2022, **353**:131101.

31. Höhn E-M, Panneerselvam R, Das A, Belder D: **Raman spectroscopic detection in continuous microflow using a chip-integrated silver electrode as an electrically regenerable surface-enhanced Raman spectroscopy substrate**. *Anal Chem* 2019, **91**:9844–9851.

32. Bogdanowicz R, Jönsson-Niedziolka M, Vereshchagina E, Dettlaff A, Boonkaew S, Pierpaoli M, Wittendorp P, Jain S, Tyholdt F, Thomas J: **Microfluidic devices for photo-and pectroelectrochemical applications**. *Curr Opin Electrochem* 2022, **36**, 101138.

33. Lin Q: **A primer to in-situ opto-and spectro-electrochemistry**. *Curr Opin Electrochem* 2022, **37**, 101201.

34. Ngo L, Tukova A, Hassanzadeh-Barforoushi A, Zhang W, Wang Y: **Emerging integrated SERS-microfluidic devices for analysis of cancer-derived small extracellular vesicles**. *Lab on a Chip* 2023, **23**:2899–2921.

35. Zhang Y, Wu L, Yang K, Zong S, Wang Z, Cui Y: **2D profiling of tumor chemotactic and molecular phenotype at single cell resolution using a SERS-microfluidic chip**. *Nano Res* 2022, **15**:4357–4365.

36. Yue S, Fang J, Xu Z: **Advances in droplet microfluidics for SERS and Raman analysis**. *Biosens Bioelectron* 2022, **198**: 113822.

37. Sun J, Wang R, Wang L, Wang X, Wang J, Shi Z, Chen Z, Wang M, Xu C: **Visual/quantitative SERS biosensing chip based on Au-decorated polystyrene sphere microcavity arrays**. *Sensor Actuator B Chem* 2023, **388**:133869.

38. Panneerselvam R, Sadat H, Höhn E-M, Das A, Noothalapati H, Belder D: **Microfluidics and surface-enhanced Raman spectroscopy, a win–win combination?** *Lab Chip* 2022, **22**:665–682.

39. Guo J, Zeng F, Guo J, Ma X: **Preparation and application of microfluidic SERS substrate: challenges and future perspectives**. *J Mater Sci Technol* 2020, **37**:96–103.

40. Moldovan R, Vereshchagina E, Milenko K, Iacob B-C, Bodoki AE, Falamas A, Tosa N, Muntean CM, Farcău C, Bodoki E: **Review on combining surface-enhanced Raman spectroscopy and electrochemistry for analytical applications**. *Anal Chim Acta* 2022, **1209**:339250.

41. Weng X, Feng Z, Guo Y, Feng J-J, Hudson SP, Zheng J, Ruan Y, Laffir F, Pita I: **Recyclable SERS substrates based on Fe 2 O 3–Ag hybrid hollow microspheres with crumpled surfaces**. *New J Chem* 2016, **40**:5238–5244.

42. * Viehrig M, Rajendran ST, Sanger K, Schmidt MS, Alstrøm TS, Rindzevicius T, Zór K, Boisen A: **Quantitative SERS assay on a single chip enabled by electrochemically assisted regeneration: a method for detection of melamine in milk**. *Anal Chem* 2020, **92**:4317–4325.

To keep the reusability and repeatability of SERS-active substrates, instead of conventional harsh reagents, UV irradiation, and among others, one relatively easy way of applying an opposite voltage to remove attached analytes is employed in this work. One crucial point is that this work shows the promising potential to work as a detector to monitor the level of Melamine in actual powdered infant formula.

43. Griesche C, Hoecherl K, Baeumner AJ: **Substrate-independent laser-induced graphene electrodes for microfluidic electroanalytical systems**. *ACS Appl Nano Mater* 2021, **4**:3114–3121.

44. * Cao L, Han G-C, Xiao H, Chen Z, Fang C: **A novel 3D paper-based microfluidic electrochemical glucose biosensor based on rGO-TEPA/PB sensitive film**. *Anal Chim Acta* 2020, **1096**: 34–43.

This work proposes novel three-dimensional paper-based microfluidic devices to sense glucose. The structure is quite interesting and new, and the device has been proven with good repeatability, stability, and anti-interference properties, which are crucial to mass production.

45. Ko E, Tran V-K, Son SE, Hur W, Choi H, Seong GH: **Characterization of Au@ PtNP/GO nanozyme and its application to electrochemical microfluidic devices for quantification of hydrogen peroxide**. *Sensor Actuator B Chem* 2019, **294**:166–176.

46. Huang Y, Han Y, Gao Y, Gao J, Ji H, He Q, Tu J, Xu G, Zhang Y, Han L: **Electrochemical sensor array with nanoporous gold nanolayer and ceria@ gold corona-nanocomposites enhancer integrated into microfluidic for simultaneous ultrasensitive lead ion detection**. *Electrochim Acta* 2021, **373**: 137921.

47. Wang W, Grace HM, Flowers PA: **Simple microfluidic device for spectroelectrochemistry**. *Microchem J* 2022, **181**:107718.

48. Arduini F: **Electrochemical paper-based devices: when the simple replacement of the support to print ecodesigned electrodes radically improves the features of the electrochemical devices**. *Curr Opin Electrochem* 2022, **35**, 101090.

49. * Ghoorchian A, Afkhami A, Madrakian T, Rameshan R, Rameshan C, Hajian A: **Absorbance-based spectroelectrochemical sensor for determination of ampyra based on electrochemical preconcentration**. *Sensor Actuator B Chem* 2020, **324**:128723.
In this paper, the low detection limit (~5.77 μmol/L) of ampyra (AMP) and excellent anti-interference properties demonstrate the proposed setup has the potential to monitor the AMP levels in actual pharmaceutical samples, which is vital from lab-scale work to widespread practical use.

50. Wang J, You X, Xiao C, Zhang X, Cai S, Jiang W, Guo S, Cao S, Chen Z: **Small-sized Pt nanoparticles supported on hybrid structures of MoS2 nanoflowers/graphene nanosheets: highly active composite catalyst toward efficient ethanol oxidation reaction studied by in situ electrochemical NMR spectroscopy**. *Appl Catal B Environ* 2019, **259**:118060.

51. Wang H, Zhang T, Zhou X: **Dark-field spectroscopy: development, applications and perspectives in single nanoparticle catalysis**. *J Phys Condens Matter* 2019, **31**:473001.

52. Ma Y, Highsmith AL, Hill CM, Pan S: **Dark-field scattering spectroelectrochemistry analysis of hydrazine oxidation at Au nanoparticle-modified transparent electrodes**. *J Phys Chem C* 2018, **122**:18603–18614.