Molecularly Imprinted Polymer-Based Electrochemical Sensing in Protein Detection

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Abstract. Protein detection is paramount across various scientific, clinical, and industrial domains. Accurate and sensitive detection of proteins is pivotal for understanding biological processes, diagnosing diseases, drug development, environmental monitoring, and ensuring food safety. Traditional protein detection methods encounter sensitivity, specificity, and ease of use challenges. Molecularly imprinted polymers (MIPs), with their tailored molecular recognition sites, offer a novel approach to address these limitations. When combined with electrochemical techniques, MIP-based electrochemical methods have emerged as a revolutionary technology, showcasing enhanced sensitivity and selectivity. This article provides a comprehensive overview of MIP-based electrochemical methods for protein detection, including the principles, engineering aspects, advantages, and potential applications. The aim is to elucidate the potential of this cutting-edge technology in reshaping protein detection and its promising role in advancing biosensing technologies.

Keywords: proteins; biomolecular recognition; analytical methods; sensitivity; specificity.

INTRODUCTION

In the expansive landscape of biotechnology and biosensing, the accurate detection and analysis of proteins stand as a foundational pillar, wielding immense significance across scientific, clinical, and industrial domains. Proteins, as fundamental biomolecules, play a critical role in various biological processes and are integral to disease diagnosis and therapeutic interventions [1, 2]. Accurate protein detection is essential for deciphering complex biological mechanisms and identifying potential disease biomarkers. Traditional protein detection methodologies, such as enzyme-linked immunosorbent assays (ELISAs) and mass spectrometry, have limitations related to sensitivity, specificity, and complexity of operation [3]. MIPs offer a viable alternative with their ability to provide high specificity and binding affinity towards target proteins. When integrated with electrochemical techniques, MIP-based electrochemical sensors provide a potent platform for precise and reliable protein detection [4, 5].

Traditional protein detection methods, while invaluable, encounter persistent challenges, ranging from sensitivity limitations to cross-reactivity issues and the need for complex protocols. Addressing these challenges head-on, molecularly imprinted polymers (MIPs) have emerged as a revolutionary technology in analytical chemistry, offering a new dimension to biosensing [6].

MIPs, synthetic polymers with particular molecular recognition sites, have been intricately designed to selectively bind with target proteins, providing a robust foundation for developing sophisticated protein sensors. When coupled with electrochemical techniques, these MIP-based electrochemical methods usher in a new era of protein detection characterised by enhanced sensitivity, selectivity, and ease of use [7].

This article will explore protein detection, focusing on the innovative utilisation of MIP-based electrochemical methods. We will delve into the foundational principles and intricate mechanisms that govern MIP-based electrochemical sensing, illuminating the science behind the precise engineering of these polymers to recognise and bind a diverse range of proteins [8, 9].

Furthermore, we will unravel the multitude of advantages that MIP-based electrochemical sensors bring to the fore, including heightened sensitivity, exceptional selectivity, and the potential for miniaturisation, positioning them as promising candidates for applications in point-of-care diagnostics and field-based monitoring [10–12].

Through this comprehensive journey, our objective is to showcase the expansive potential of MIP-based electrochemical methods in revolutionising protein detection. By highlighting their capacity to push the boundaries of biosensing technologies, we envision a future where these innovative techniques significantly impact diverse domains, paving the way for advancements that rely on precise protein analysis [13–15].

In doing so, we anticipate a world where health, safety, and quality are underpinned by accurate biomolecular scrutiny. This will empower us to forge ahead into a future of remarkable scientific discoveries and societal well-being. As we delve deeper, we will unfold the intricacies of MIP-based electrochemical sensing, elucidating real-world applications, foreseeing the trajectory of this promising field in the years to come, and discussing the challenges that lie ahead.

RESULTS AND DISCUSSION

MIP-Based Electrochemical Sensors: Principles and Mechanisms

Molecular Imprinting Process. The molecular imprinting process involves arranging molecules within a reaction vessel to create a polymer matrix. The functional monomer is responsible for specificity and reactivity, the cross-linking agent provides stability and structure, and the target protein contributes its form and characteristics. Chemical reactions result in a polymer matrix of intricate patterns and connections [16, 17].

The functional monomer conforms to the target protein's shape and chemical properties, creating precise binding sites. The cross-linking agent reinforces the polymer structure[18,19]. The resulting polymer matrix accurately replicates the target protein's structure and behaviour.

Molecular imprinting finds applications in drug delivery, biosensors, and environmental monitoring. It enables precise molecular recognition and promises scientific exploration and technological advancement [20–22].

Electrochemical Transduction. Electrochemical transduction is a pivotal link between the molecular recognition capabilities of MIP-based sensors and the ability to interpret these interactions in terms of electrical response. The foundation of this process lies in the precise molecular imprinting technique, where the polymer matrix is strategically designed to contain cavities or imprinted sites that possess a solid binding affinity for the target analyte, often a specific protein [23].

Upon exposure to the target protein, the imprinted sites within the polymer undergo a binding event, creating a unique interaction that alters the electronic properties of the polymer. This interaction can affect the flow of electrons, manifesting as current, voltage, or impedance changes. More specifically, the binding event can either hinder or enhance the movement of charge carriers, thereby modifying the electrical conductivity or resistance of the polymer. These alterations in electrical parameters are directly proportional to the concentration of the target protein in the sample [20, 21, 23–25].

The electrochemical signal generated by these changes is then meticulously measured and analysed. The distinct signal patterns provide valuable insights into the target protein's presence, concentration, or structural changes. Advanced electrochemical techniques, such as cyclic voltammetry [26, 27], electrochemical impedance spectroscopy, or chronoamperometry, characterise and quantify these electrical changes precisely.

In practical applications, this electrochemical transduction process offers numerous advantages. It enables real-time and rapid detection of target analytes with high sensitivity and selectivity, making it ideal for applications in healthcare [28–30], environmental monitoring [31–41], food safety [42–49], and pharmaceutical research [50–55]. This field's continuous research and development strives to further optimise the electrochemical transduction process, aiming for enhanced performance, increased versatility and expanded applications across a broad spectrum of analytical domains.

Engineering MIPs for Protein Detection

Rational Design and Synthesis. Crafting the properties of a MIP involves a comprehensive and strategic design approach encompassing several vital elements. The choice of monomers, pivotal building blocks of the polymer, is a critical aspect, as it dictates the structure, functional groups, and rigidity of the resulting polymer network. The selection of monomers is influenced by their ability to interact with the template molecules and form complementary binding sites. These binding sites are carefully orchestrated to mimic the template proteins' specific spatial and chemical arrangement, optimising binding affinity and ensuring high selectivity for the target molecules [56, 57].

Template proteins play a crucial role in guiding the imprinting process. They act as molecular templates around which the polymer forms, imparting their unique structure and molecular information to the monomers. This molecular memory then guides the creation of complementary binding sites within the polymer, ensuring it can selectively recognise and bind to the target molecules of interest [58].

Incorporating suitable cross-linkers is another essential aspect of tailoring MIP properties. Cross-linkers link the monomers, forming a three-dimensional network that gives the polymer stability and structural integrity. The choice of cross-linkers influences the polymer's porosity, flexibility, and overall mechanical properties. A reasonable selection ensures that the resulting MIP exhibits the desired stability and robustness, making it suitable for various applications [59].

Integrating these components using a rational design approach achieves a Molecularly Imprinted Polymer with finely tuned properties. This tailored MIP exhibits exceptional binding affinity and specificity for the target molecules and enhanced stability, ensuring its effectiveness and reliability in diverse applications such as molecular recognition, drug delivery, environmental remediation, and biosensing [60, 61].

Surface Modification and Immobilisation. Achieving the optimal performance of MIPs in protein sensors and biosensing platforms necessitates a thorough understanding of the significance of surface modification and immobilisation techniques. The surface modification involves altering the electrode surface's physical and chemical properties to create a favourable substrate for MIP attachment. This alteration is crucial to ensure a robust interface between the electrode and the MIP, enhancing the stability and durability of the MIP structure [62, 63].

Various surface modification techniques can be employed to facilitate the effective immobilisation of MIPs. Physical adsorption involves the adsorption of MIPs onto the electrode surface through van der Waals forces, hydrogen bonding, or electrostatic interactions. Conversely, covalent bonding entails forming strong chemical bonds between the functional groups of the MIP and the modified electrode surface, resulting in a more secure and lasting attachment. Layer-by-layer deposition involves the sequential deposition of alternating layers of oppositely charged materials onto the electrode surface, providing a structured and organised platform for MIP immobilisation [64, 65].

Proper immobilisation of MIPs ensures their orientation and accessibility, allowing efficient binding interactions with the target proteins. It prevents random exposure or aggregation of the MIPs, thus maintaining their structural integrity and, consequently, their recognition capabilities. The oriented and stable MIPs on the electrode surface are poised to exhibit a high affinity and specificity toward the target proteins, enhancing the overall binding efficiency and sensitivity of the biosensing platform [66, 67].

In summary, meticulous surface modification and immobilisation of MIPs are fundamental steps in harnessing their potential for protein sensing applications. These processes contribute to the stability and structural integrity of MIPs, paving the way for particular and efficient protein recognition – an essential aspect in the design and development of advanced biosensing technologies [68, 69].

Advantages of MIP-Based Electrochemical Sensors for Protein Detection

Enhanced Sensitivity and Selectivity. MIP-based electrochemical sensors represent a groundbreaking advancement in sensing technology, showcasing exceptional sensitivity and selectivity. The distinct advantage of MIPs lies in their ability to meticulously engineer specific and high-affinity binding sites during the imprinting process, which involves carefully selecting functional monomers and cross-linkers [70]. This strategic selection allows for the creation a molecular framework with precisely tailored recognition sites that mimic the target analyte's molecular structure. These sophisticated imprinted sites possess high specificity and selectivity, ensuring optimal binding affinity for the target molecules, even in complex sample matrices [71].

MIP-based electrochemical sensors' precise and deliberate design involves intricate steps, including forming a template-analyte complex, polymerisation, and subsequent template removal, leaving behind complementary binding sites [72]. The resulting MIPs boast an impressive level of molecular recognition, enabling them to selectively capture the target analytes, even amidst many potentially interfering compounds. This targeted selectivity significantly minimises false positives and negatives, enhancing the accuracy and reliability of the sensor's output [73].

MIP-based electrochemical sensors find extensive use in practical applications across various fields. In environmental monitoring, these sensors detect pollutants, toxins, and heavy metals in air, water, and soil samples. Their outstanding selectivity ensures precise measurements, allowing for timely and informed environmental management and preservation decision-making [74]. Moreover, these sensors are vital in medical diagnostics, facilitating the early detection of biomarkers associated with various diseases, such as cancer, diabetes, and cardiovascular disorders. The tailored imprinting process enables the sensors to identify subtle changes in analyte concentrations, aiding in early intervention and improved patient outcomes [75].

Furthermore, MIP-based electrochemical sensors play a pivotal role in the pharmaceutical industry, assisting in drug development, quality control, and pharmacokinetic studies. The high-affinity binding sites allow for accurate quantification of pharmaceutical compounds in complex matrices, ensuring compliance with regulatory standards and guaranteeing the safety and efficacy of medicinal products [76, 77]. As technology evolves, ongoing research and advancements in molecular imprinting techniques promise even greater precision and efficiency in designing MIP-based electrochemical sensors, further propelling their application and impact across diverse scientific and industrial domains [78, 79].

Potential for Miniaturization and Portability. The advent of these sophisticated sensors, designed with a focus on miniaturisation and precision, heralds a transformative wave in medical diagnostics. Their compact form factor and efficiency empower healthcare professionals to perform tests at the bedside, in rural or underserved areas, and even in resource-constrained environments. This decentralisation of diagnostic capabilities ensures quicker results, enabling immediate intervention and personalised patient care [80–83].

In a scenario where time is of the essence, such as during a medical emergency or disease outbreak, these sensors prove invaluable. A healthcare worker can swiftly obtain vital protein-level data without needing a specialised laboratory, leading to timely diagnoses and tailored treatment strategies. Furthermore, these sensors' ease of use and rapid results make them indispensable in the arsenal against emerging infectious diseases and other health crises [84].

Beyond healthcare, these sensors offer game-changing potential in environmental monitoring. They can be deployed in various locations, including remote ecosystems or urban centres, providing real-time monitoring of protein markers relevant to ecological health. This real-time data collection not only aids in detecting environmental pollutants but also supports research and policy decisions to preserve our ecosystems and public health [85, 86].

As research continues to refine and expand the capabilities of these sensors, we anticipate a cascade of innovations. These innovations could include enhanced multiplexing capabilities, allowing for the simultaneous detection of a broader range of proteins, thus amplifying the scope and applications of these sensors. Integrating these advanced sensors in diagnostics epitomises a new paradigm in healthcare and scientific advancements, promising a brighter and more efficient future [85–87].

Applications and Future Prospects. MIP-based electrochemical sensors have showcased substantial promise across a spectrum of crucial applications, underpinning pivotal areas such as clinical diagnostics, environmental monitoring, and food safety – their potential lies in their ability to detect specific target molecules with high sensitivity and precision selectively. In clinical diagnostics, MIP-based sensors show promise for revolutionising disease detection by enabling multi-target detection, allowing for a comprehensive analysis of biomarkers associated with various diseases. This capability is crucial for early disease identification and monitoring complex conditions, enhancing the effectiveness and efficiency of healthcare systems [88].

In environmental monitoring, MIP-based electrochemical sensors demonstrate their versatility by enabling the detection of pollutants, toxins, and hazardous substances in air, water, and soil. Their high selectivity allows for precise measurements, aiding in enforcing environmental regulations and policies. Moreover, the potential integration of these sensors with remote monitoring systems can provide real-time data, facilitating rapid response and mitigation strategies in environmental emergencies [89].

In the context of food safety, MIP-based electrochemical sensors offer a reliable means to detect contaminants, pollutants, and pathogens in food products. This is essential for maintaining food quality and safety standards ensuring consumer well-being. With the advancements in nanotechnology, these sensors could become even more sensitive and selective, paving the way for better traceability and control throughout the food supply chain [90, 91].

Future advancements in MIP-based electrochemical sensors are anticipated to drive their capabilities further. Multi-target detection, where a single sensor can detect multiple analytes simultaneously, is an area of active research and holds immense promise for enhancing sensing efficiency and reducing overall costs. Real-time monitoring capabilities will evolve, enabling continuous data collection and analysis, thereby supporting timely decision-making and intervention [92-93].

Integrating MIP-based electrochemical sensors with emerging technologies such as wearable devices is a frontier with great potential. This integration could lead to wearable sensors capable of real-time monitoring of various biomarkers, providing individuals with personalised health insights and enabling proactive healthcare management. The resulting data could be seamlessly integrated into healthcare systems, empowering individuals and healthcare professionals with a comprehensive view of health status and trends [92, 93].

In summary, the trajectory of MIP-based electrochemical sensors is on the cusp of a transformative phase, moving towards a more sophisticated, integrated, and impactful future. These sensors are set to play a pivotal role in revolutionising how we perceive and interact with critical aspects of our lives, health, environment, and overall well-being.

Protein detection through MIP-based electrochemical sensors

Monomer and template mixture. The development of MIP for the electrochemical sensing of proteins has been achieved through several methods, such as *in situ* bulk polymerisation of monomer-template mixtures andol-gel; precipitation, emulsion and suspension chaining of monomers [94]. Although each of these approaches targets specific goals, such as improved electrostatic interactions between templates and the MIP, it is acknowledged that the susceptibility of proteins to denaturation upon sudden shifts of pH and temperature hinders some polymerisation strategies [95, 96]. Therefore, several authors relied on the bulk electro-polymerisation of monomer-template mixtures to assemble MIPs for protein electroanalysis to keep the conformational integrity of peptide chains [97].

Figure 1 showcases the basic outline of bulk polymerisation of a monomer-template mixture on the surface of an electrode.

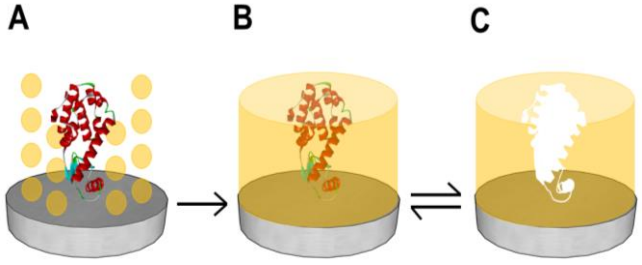

Figure 1 – Schematic of the bulk polymerisation of a monomer-template mixture

A – wherein the embedding of the protein template is promoted by the polymerisation of monomers (orange);

B – followed by the removal of the template, thereby yielding the cavities

C – the protein structure is lysozyme, stored under the code 4LZM at the Protein Data Bank.

The versatility of bulk electro-polymerisation allows this method to be used in the facile modification of working electrodes. Several electrode platforms based on carbon and gold were proven modifiable through this technology. For instance, in a particularly recent outreach, a screen-printed carbon electrode was quickly and reliably modified through bulk electro-polymerisation with pyrrole as functional monomer and interleukin-6 as template, thence yielding a sensor with a meagre limit of detection of 0.02 pg ml^{-1} [98]. Similarly, other authors used a screen-printed gold electrode which had its surface modified by bulk electro-polymerisation with phenol and human epidermal growth factor to develop an MIP-based electrochemical sensor for breast cancer, which yielded a detection limit that rivalled that of standard techniques, being the sensibility of the sensor of 1.6 ng l^{-1} [99].

Nonetheless, the success of bulk electro-polymerisation in protein electroanalysis is attributed to the possibility of crafting and tuning the sensitivity and selectivity of sensors by optimising the electrostatic interactions between the MIP and the template. In this regard, it has been reported that the biomimetic properties of MIP allow interaction sites that mimic the behaviour of natural ligand-macromolecule systems, thereby involving Van der Walls and π-π stacking interactions [100]. These hydrophobic sites seal off water molecules in the interaction site and lead to a solventless environment of low dielectric constant, which promotes a strong bond effect [100], such as showcased in a recently published MIP-based sensor for prostate-specific antigen that achieved an optimal equilibrium dissociation constant of about $1.02 \pm 0.54\ 10^{-14}$ mol l^{-1}. This sensor yielded a detection limit that surpassed the golden standard methods for this cancer biomarker, reaching as low as $3.0\ 10^{-8}$ ng ml^{-1} [101]. At the same time, the exploitation of electrostatic interactions between MIP-template was used to craft highly sensible sensors for cancer-related inflammatory biomarkers such as interleukin-8. In a particularly recent outreach, this biomarker was determined through a poly (3,4-ethylenedioxythiophene) polystyrene sulfonate/ 4-aminothiophenol/ eriochrome black T ensemble, which led to a limit of detection of 1.5 pmol l^{-1} [102].

Notwithstanding, bulk electro-polymerisation is known to have limitations regarding the imprinting of more significant and less flexible proteins due to the difficulty in controlling the orientation of the template during MIP formation, which, therefore, can also impair selectivity and sensibility for sensing applications [103]. It is known that binding sites for protein recognition occur in defined contact points which cover surfaces between 500 and 3500 $Å^2$ [100]. In this regard, more homogenous binding sites in the MIP increase the contact area, decreasing the free energy change by a measurement unit, culminating in stronger interactions and higher stability [100]. As such, alternative methods like surface imprinting have been used to improve the selectivity and sensibility of MIP-sensors for protein detection to address the need to establish more controlled imprinting.

Overall, bulk polymerisation is advantageous because it usually requiresess strenuous protocols to develop electroanalytical sensors for protein detection whilst yielding adequate performance for a wide range of templates [104]. Nevertheless, alternatives to bulk electro-polymerisation, such as surface imprinting technologies, are becoming more common due to the need for more control of the imprinting process and more selective and sensible platforms for protein electroanalysis.

Surface imprinting of proteins. The surface imprinting approach for MIP synthesis relies on embedding the template on the working electrode surface. This process can be achieved by anchoring agents that showcase terminal moieties with affinity to the electrode surface and the template [105]. The functionalisation of electrode surfaces with anchoring agents before MIP assembly is frequently achieved through chemoadsorption, with self-assembled monolayer (SAM) formation being the most common approach [106].

The anchoring of the template on the electrode surface allows better control of the imprinting process, as the template orientation can be optimised according to the anchoring protocol used to develop the sensor. In fact, as aforementioned, several researchers have proven that surface imprinting leads to more homogenous binding sites

[107, 108]. For instance, a recent report compared the analytical performance of sensors built through bulk electro-polymerisation or surface imprinting of lysozyme with scopoletin as a monomer. The results evidenced that the surface functionalisation with the template before MIP assembly led to an increase in the imprinting factor of almost 3-fold, thereby leading to a more reliable quantification [109].

The most common material for surface imprinting in MIP-sensor development is gold due to the possibility of spontaneous SAM formation, which leads to simpler surface modification protocols and more straightforward manufacturing of highly sensible sensing platforms. For instance, a recent work reported the facile anchoring of SARS-CoV-2 nucleoprotein onto a thin-film-based gold electrode through a self-assembled 4-amino thiophenol monolayer, thereby yielding a meagre limit of detection of 15 fmol l^{-1} [110].

On the other hand, although not providing spontaneous monolayer formation, carbon materials have also been used in the surface imprinting of proteins by exploiting π-π stacking interactions between anchoring agents bearing aromatic moieties or by forcing the genesis of polar anchoring sites through oxidative treatments such as electrochemical activation [111]. For instance, the surface imprinting of troponin T was reported on electrodeposited polyethene blue at multiwalled carbon nanotubes, whilst Dengue virus non-structural protein was surface-imprinted on screen-printed carbon electrodes coated with electrospun nanofibers of polysulfone to develop MIP-based electrochemical sensors for biomedical applications which yielded limits of detection of 0.04 pg ml^{-1} for troponin T and 0.30 ng ml^{-1} for Dengue virus protein, respectively [112, 113].

Regarding the surface imprinting of proteins on gold electrodes, it is well reported that anchoring agents bearing hydroxyl, thiol, and amino motifs allow the spontaneous formation of monolayers of conserved geometric orientation that favour biosensing design. For instance, a recent outreach described the quick and easy functionalisation of gold electrodes with prostate-specific antigen, followed by the polymerisation of dopamine for MIP formation. The resulting electrochemical sensor was very sensible, with a detection limitf 1.0 pg ml^{-1}, and showcased a highly ordered topology, which contributed to an optimal selectivity towards the antigenic analyte [114].

The affinity of selected functional groups to gold surfaces allowed researchers to immobilise proteins onto outer layers of electrode materials, promote the in vitro carbamylation of amino acid residues, and provide antifouling interfaces for MIP-based electrochemical biosensors [115]. Nonetheless, the versatile assembly of SAMs on gold electrodes for surface imprinting has also given rise to multi-analyte point-of-care biosensors for healthcare applications, such as the concomitant use of prostate-specific antigen and myoglobin as surface imprinted templates for poly-acrylamide MIP assembly in a dual-sensing impedimetric biosensor; leading to detection limits of 5.40 pg ml^{-1} and 0.83 ng ml^{-1}, respectively [116].

Concerning the length of SAM-forming anchoring agents, it has been shown that short-chained SAM-forming units allowed the development of highly sensible biosensors for the detection of peptides such as oxytocin, whose anchoring on a gold electrode surface was mediated by allyl mercaptan, followed by MIP synthesis through 2-hydroxyethyl methacrylate-methacryloyl amidoglutamic acid; which yielded the sensor with a limit of detection of 0.0030 ng ml^{-1} [117]. Nevertheless, the use of lengthier-chained thiol-bearing residues has also been reported to produce reliable sensors, as evidenced by the use of 11-mercaptoundecanoic in many sensing platforms, as well as the immobilisation of double-cysteine-modified peptide nanofilms onto gold surfaces for neuron-specific enolase imprinting on polyscopoletin-based MIP, which yielded a detection limit of 0.25 μmol l^{-1} [118].

Overall, surface imprinting technology in protein electroanalysis is conditioned by the intrinsic features of the electrode surface and those of the anchoring agent and the template. Therefore, the appropriate protocol must consider the surface material, the chemical structure and topology of the anchoring agent, and their compatibility with the template. Nevertheless, overly bulky templates may hinder the application of surface imprinting for whole-protein sensing, which led to the development of alternative imprinting approaches such as epitope imprinting.

Epitope Imprinting. The advance of imprinting techniques in biosensor development allowed researchers to standardise the topology of tem-

plated cavities to tune sensor selectivity better and bypass the intrinsic limitations of whole protein imprinting. This, in turn, resulted in the possibility of developing precise sensors by solely imprinting the recognition motifs of proteins, known as epitopes, onto polymer structures [119].

The process of epitope imprinting for MIP-based electrochemical sensors has been extensively exploited in literature to use only the recognition sites of proteins as pseudo-templates. This bypasses the hindrances of whole protein imprinting due to bulkiness and the use of short and stable oligopeptide chains for imprinting purposes [120].

Figure 2 depicts how epitope imprinting can selectively detect proteins through their recognition motifs.

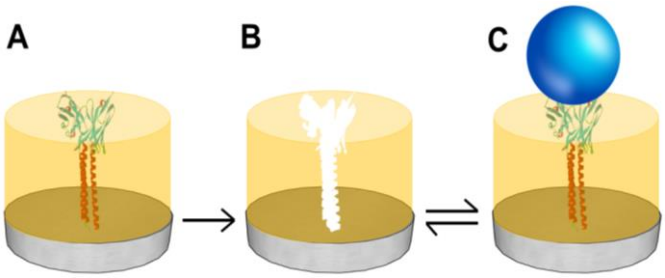

Figure 2 – Schematic of epitope imprinting technique, wherein the epitope is imprinted in the polymer (orange) A and then removed B. After that, recognising peptides and proteins (blue sphere) is feasible through rebinding the epitope motif C. The epitope structure depicted is the human immunodeficiency virus epitope scaffold, which is stored under the code 3LHP at the Protein Data Bank

Epitopes can be obtained through their extraction and isolation from their biological source and faster synthetic approaches, which produce only the peptide chain required for biosensor development instead of the whole protein analyte [121]. Moreover, owing to their shorter length than entire proteins, epitopes have predictable primary and/or secondary conformation, unlike complete proteins' complex coiled tertiary structures whose recognition sites may not be adequately exposed for molecular imprinting applications [122].

Nonetheless, epitope imprinting has allowed the development of tailored MIP-based sensors for considerably rare or hard-to-obtain biomarkers and bypassing the imprinting hindrances of whole proteins attributed to size and conformational flexibility [123]. In this sense, even when taking into consideration that the contact area required for low-energy binding of whole proteins to receptor cavities ranges between 500-3500 $Å^2$ as previously commented[100], the binding of epitopes comprised of oligopeptide chains, short α-helixes and β-strands often exhibit optimal values bellow 2000 $Å^2$, thence contributing to their acknowledged selectivity[120]. Furthermore, given the sheer diversity of recognition motifs such as peptides, glycans, monosaccharides, His and FLAG-tags, this technology is up-and-coming for biosensing applications [124].

Considering the exposed nature of the binding sites of epitopes and the possibility of achieving optimal electrostatic interactions between these small templates and MIPs, some researchers have exploited this technology to gain very low dissociation constants in protein electroanalysis. For instance, in a recent report, epitopes of human atrial natriuretic peptide underwent detection through a MIP-sensor with a dissociation constant as low as 5.3 μmol l^{-1}, thereby suggesting outstanding binding affinity and highlighting the possibility of using epitope imprinting for enhancing the sensor performance [125]. On the other hand, it must be noted that oligopeptides accounting for up to 30 amino acid units may not be compatible with all polymerisation strategies, and many epitope chains are known to undergo aggregation in aqueous environments. What must also be considered when using these biomaterials in molecular imprinting technologies [120, 122].

Their use in crafting sensible and selective MIP-based sensors for electroanalysis has been reported in several fields, ranging from healthcare to foodstuff quality control. For instance, in a recent report, ovalbumin was imprinted on a gold nanoparticle-coated carbon screen-printed electrode, followed by dopamine electropolymerisation. The resulting sensor yielded a meagre detection limit of 10.76 nmol l^{-1}, reaching a sensibility level of .46 parts per million in wine samples [126]. Other authors also achieved shallow detection limits by imprinting cytochrome c epitope on poly-3-aminopropyltriethoxysilane; which determinedinute concentrations of this biomarker (*i.e.*, 3.6 ng ml^{-1}). Nonetheless, these detection levels were among the lowest reported

in the literature, which highlights the effectiveness of epitope imprinting in several applications [127].

Literature states that the imprinting of epitopes can be achieved through grafted or constrained approaches since grafted methodologies are often more reported in developing electrochemical immunosensors, the straightforward embedding of epitopes onto electrode surfaces [128]. Grafted epitope imprinting follows the direct modification of the electrode surfaces with the epitope through direct chemisorption or anchoring agents such as SAM-forming units, followed by MIP formation and template removal [128].

On the other hand, constraint epitope imprinting requires the immobilisation of the template on a matrix, followed by MIP formation and removal of both template and matrix. Roving the substrate with the template yields MIP nanoparticles, which can be employed in electrochemical sensing using surface-functionalisation protocols [120]. This technology has been used to craft MIP nanoparticles that dramatically enhance the analytical performance of immunosensors, and is a promising approach in protein electroanalysis [129]. For instance, a recent report showcased the use of cysteine-modified epitopes of neuron-specific enolase as templates in the synthesis of MIP nanoparticles onto gold nanoparticles, thereby yielding an electrochemical sensor with an imprinting factor of 4.2 and a detection range in the picogram level of 25–4000 pg mL^{-1} [130].

Although epitopes may have limitations for molecular imprinting applications due to possible compatibility issues with solvents and particular morphology, this technology is undeniably an intelligent approach to tackle molecular imprinting while avoiding the drawbacks of whole-protein imprinting.

CONCLUSIONS

Molecularly imprinted polymer-based electrochemical methods have emerged as a powerful tool for precise protein detection. The amalgamation of molecular imprinting and electrochemical transduction provides a versatile platform with exceptional sensitivity, selectivity, and potential for miniaturisation. Future advancements in this field promise to revolutionise biosensing technologies and foster applications in diverse domains, ultimately contributing to enhanced healthcare, environmental sustainability, and food security. Further research and development in this burgeoning field are imperative to unlock the full potential of MIP-based electrochemical sensors in protein detection.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

1. Antipchik, M., Reut, J., Ayankojo, A. G., Öpik, A., & Syritski, V. (2022). MIP-based electrochemical sensor for direct detection of hepatitis C virus via E2 envelope protein. Talanta, 250, 123737. doi: 10.1016/j.talanta.2022.123737

2. Bueno, L., El-Sharif, H. F., Salles, M. O., Boehm, R. D., Narayan, R. J., Paixão, T. R. L. C., & Reddy, S. M. (2014). MIP-based electrochemical protein profiling. *Sensors and Actuators B: Chemical, 204*, 88–95. doi: 10.1016/j.snb.2014.07.100

3. Mazouz, Z., Mokni, M., Fourati, N., Zerrouki, C., Barbault, F., Seydou, M., Kalfat, R., Yaakoubi, N., Omezzine, A., Bouslema, A., & Othmane, A. (2020). Computational approach and electrochemical measurements for protein detection with MIP-based sensor. *Biosensors and Bioelectronics, 151*, 111978. doi: 10.1016/j.bios.2019.111978

4. Di Giulio, T., Mazzotta, E., & Malitesta, C. (2020). Molecularly Imprinted Polyscopoletin for the Electrochemical Detection of the Chronic Disease Marker Lysozyme. *Biosensors, 11*(1), 3. doi: 10.3390/bios11010003

5. Ratautaite, V., Boguzaite, R., Brazys, E., Ramanaviciene, A., Ciplys, E., Juozapaitis, M., Slibinskas, R., Bechelany, M., & Ramanavicius, A. (2022). Molecularly imprinted polypyrrole based sensor for the

detection of SARS-CoV-2 spike glycoprotein. *Electrochimica Acta, 403*, 139581. doi: 10.1016/j.electacta.2021.139581

6. Mazzotta, E., Di Giulio, T., & Malitesta, C. (2022). Electrochemical sensing of macromolecules based on molecularly imprinted polymers: challenges, successful strategies, and opportunities. *Analytical and Bioanalytical Chemistry, 414*(18), 5165–5200. doi: 10.1007/s00216-022-03981-0

7. Thomaz, D. V., Goldoni, R., Tartaglia, G. M., Malitesta, C., & Mazzotta, E. (2022). Effect of Recombinant Antibodies and MIP Nanoparticles on the Electrical Behavior of Impedimetric Biorecognition Surfaces for SARS-CoV-2 Spike Glycoprotein: A Short Report. *Electrochem, 3*(3), 538–548. doi: 10.3390/electrochem3030037

8. Liu, Y., & Dykstra, G. (2022). Recent progress on electrochemical (bio)sensors based on aptamer-molecularly imprinted polymer dual recognition. *Sensors and Actuators Reports, 4*, 100112. doi: 10.1016/j.snr.2022.100112

9. Ben Hassine, A., Raouafi, N., & Moreira, F. T. C. (2021). Novel Electrochemical Molecularly Imprinted Polymer-Based Biosensor for Tau Protein Detection. *Chemosensors, 9*(9), 238. doi: 10.3390/chemosensors9090238

10. Choi, D. Y., Yang, J. C., Hong, S. W., & Park, J. (2022). Molecularly imprinted polymer-based electrochemical impedimetric sensors on screen-printed carbon electrodes for the detection of trace cytokine IL-1β. *Biosensors and Bioelectronics, 204*, 114073. doi: 10.1016/j.bios.2022.114073

11. Lee, M.-H., Thomas, J. L., Chang, Y.-C., Tsai, Y.-S., Liu, B.-D., & Lin, H.-Y. (2016). Electrochemical sensing of nuclear matrix protein 22 in urine with molecularly imprinted poly(ethylene-co-vinyl alcohol) coated zinc oxide nanorod arrays for clinical studies of bladder cancer diagnosis. *Biosensors and Bioelectronics, 79*, 789–795. doi: 10.1016/j.bios.2016.01.005

12. Pacheco, J. G., Silva, M. S. V., Freitas, M., Nouws, H. P. A., & Delerue-Matos, C. (2018). Molecularly imprinted electrochemical sensor for the point-of-care detection of a breast cancer biomarker (CA 15-3). *Sensors and Actuators B: Chemical, 256*, 905–912. doi: 10.1016/j.snb.2017.10.027

13. Zidarič, T., Finšgar, M., Maver, U., & Maver, T. (2022). Artificial Biomimetic Electrochemical Assemblies. *Biosensors, 12*(1), 44. doi: 10.3390/bios12010044

14. Hasseb, A. A., Abdel Ghani, N. din T., Shehab, O. R., & El Nashar, R. M. (2022). Application of molecularly imprinted polymers for electrochemical detection of some important biomedical markers and pathogens. *Current Opinion in Electrochemistry, 31*, 100848. doi: 10.1016/j.coelec.2021.100848

15. Li, R., Feng, Y., Pan, G., & Liu, L. (2019). Advances in Molecularly Imprinting Technology for Bioanalytical Applications. *Sensors, 19*(1), 177. doi: 10.3390/s19010177

16. Dykstra, G., Reynolds, B., Smith, R., Zhou, K., & Liu, Y. (2022). Electropolymerized Molecularly Imprinted Polymer Synthesis Guided by an Integrated Data-Driven Framework for Cortisol Detection. *ACS Applied Materials & Interfaces, 14*(22), 25972–25983. doi: 10.1021/acsami.2c02474

17. Meskher, H., Ragdi, T., Thakur, A. K., Ha, S., Khelfaoui, I., Sathyamurthy, R., Sharshir, S. W., Pandey, A. K., Saidur, R., Singh, P., Sharifian jazi, F., & Lynch, I. (2023). A Review on CNTs-Based Electrochemical Sensors and Biosensors: Unique Properties and Potential Applications. *Critical Reviews in Analytical Chemistry*, 1–24. doi: 10.1080/10408347.2023.2171277

18. Brambilla, E., Locarno, S., Gallo, S., Orsini, F., Pini, C., Farronato, M., Thomaz, D. V., Lenardi, C., Piazzoni, M., & Tartaglia, G. (2022). Poloxamer-Based Hydrogel as Drug Delivery System: How Polymeric Excipients Influence the Chemical-Physical Properties. Polymers, 14(17), 3624. doi: 10.3390/polym14173624

19. Goldoni, R., Thomaz, D. V., Di Giulio, T., Malitesta, C., & Mazzotta, E. (2022). An insight into polyscopoletin electrosynthesis by a quality-by-design approach. *Journal of Materials Science, 57*(25), 12161–12175. doi: 10.1007/s10853-022-07349-8

20. Rajpal, S., & Mishra, P. (2022). Next generation biosensors employing molecularly imprinted polymers as sensing elements for in vitro diagnostics. *Biosensors and Bioelectronics: X, 11*, 100201. doi: 10.1016/j.biosx.2022.100201

21. Li, Y., Luo, L., Nie, M., Davenport, A., Li, Y., Li, B., & Choy, K.-L. (2022). A graphene nanoplatelet-polydopamine molecularly imprinted biosensor for Ultratrace creatinine detection. *Biosensors and Bioelectronics, 216*, 114638. doi: 10.1016/j.bios.2022.114638

22. Zhang, J., Wang, Y., & Lu, X. (2021). Molecular imprinting technology for sensing foodborne pathogenic bacteria. Analytical and Bioanalytical Chemistry, 413(18), 4581–4598. doi: 10.1007/s00216-020-03138-x

23. Lu, Z., Du, X., Sun, M., Zhang, Y., Li, Y., Wang, X., Wang, Y., Du, H., Yin, H., & Rao, H. (2021). Novel dual-template molecular imprinted electrochemical sensor for simultaneous detection of CA and TPH based on peanut twin-like NiFe2O4/CoFe2O4/NCDs nanospheres: Fabrication, application and DFT theoretical study. *Biosensors and Bioelectronics, 190*, 113408. doi: 10.1016/j.bios.2021.113408

24. Shao, Y., Duan, J., Wang, M., Cao, J., She, Y., Cao, Z., Li, G., Jin, F., Wang, J., & Abd El-Aty, A. M. (2022). Application of Molecularly Imprinted Electrochemical Biomimetic Sensors for Detecting Small Molecule Food Contaminants. *Polymers, 15*(1), 187. doi: 10.3390/polym15010187

25. Li, W., Zhang, X., Li, T., Ji, Y., & Li, R. (2021). Molecularly imprinted polymer-enhanced biomimetic paper-based analytical devices: A review. *Analytica Chimica Acta, 1148*, 238196. doi: 10.1016/j.aca.2020.12.071

26. Thomaz, D. V., Couto, R. O., de Oliveira Roberth, A., Oliveira, L. A. R., de Siqueira Leite, K. C., de Freitas Bara, M. T., Ghedini, P. C., Bozinis, M. C. V., Lobón, G. S., de Souza Gil, E., & Machado, F. B. (2018). Assessment of Noni (Morinda citrifolia L.) Product Authenticity by Solid State Voltammetry. *International Journal of Electrochemical Science, 13*(9), 8983–8994. doi: 10.20964/2018.09.390

27. Macêdo, I. Y. L. de, Alecrim, M. F., Oliveira Neto, J. R., Torres, I. M. S., Thomaz, D. V., & Gil, E. de S. (2020). Piroxicam voltammetric determination by ultra low cost pencil graphite electrode. *Brazilian Journal of Pharmaceutical Sciences, 56*. doi: 10.1590/s2175-97902019000317344

28. Goldoni, R., Thomaz, D. V., Strambini, L., Tumedei, M., Dongiovanni, P., Isola, G., & Tartaglia, G. (2023). Quality-by-Design R&D of a Novel Nanozyme-Based Sensor for Saliva Antioxidant Capacity Evaluation. *Antioxidants, 12*(5), 1120. doi: 10.3390/antiox12051120

29. Dongiovanni, P., Meroni, M., Casati, S., Goldoni, R., Thomaz, D. V., Kehr, N. S., Galimberti, D., Del Fabbro, M., & Tartaglia, G. M. (2023). Salivary biomarkers: novel noninvasive tools to diagnose chronic inflammation. *International Journal of Oral Science, 15*(1). doi: 10.1038/s41368-023-00231-6

30. Contardi, U. A., Morikawa, M., Brunelli, B., & Thomaz, D. V. (2021). MAX30102 Photometric Biosensor Coupled to ESP32-Webserver Capabilities for Continuous Point of Care Oxygen Saturation and Heartrate Monitoring. *The 2nd International Electronic Conference on Biosensors*. doi: 10.3390/iecb2022-11114

31. Ferraz, D., Thomaz, D. V., Antunes, R. S., & Lopes, F. M. (2021). Development of a low-cost colorimetric paper-based spot test for the environmental monitoring of phenolic pollutants. Environmental Challenges, 4, 100128. doi: 10.1016/j.envc.2021.100128

32. Thomaz, D. V., de Oliveira, M. T., Lobón, G. S., da Cunha, C. E. P., Machado, F. B., Moreno, E. K. G., de Siqueira Leite, K. C., Ballaminut, N., Alecrim, M. F., de Carvalho, M. F., Isecke, B. G., de Macêdo, I. Y. L., do Couto, R. O., Rodrigues, E. S. B., de Faria Carvalho, L. A., & Ávila, L. F. (2018). Development of Laccase-TiO2@Carbon Paste Biosensor for Voltammetric Determination of Paracetamol. *International Journal of Electrochemical Science, 13*(11), 10884–10893. doi: 10.20964/2018.11.61

33. Lima Morais, R., Ferreira Garcia, L., Kussmaul Gonçalves Moreno, E., Vieira Thomaz, D., De Brito Rodrigues, L., Barroso Brito, L., Sanz Lobón, G., Augusto Rodrigues de Oliveira, G., Ferreira Rodrigues, M., Gontijo Vaz, B., & Gil, E. D. S. (2019). Electrochemical remediation of industrial

pharmaceutical wastewater containing hormones in a pilot scale treatment system. *Eclética Química Journal, 44*(1), 40. doi: 10.26850/1678-4618eqj.v44.1.2019.p40-52

34. Garcia, L. F., Lacerda, M. F. A. R., Thomaz, D. V., de Souza Golveia, J. C., Pereira, M. das G. C., de Souza Gil, E., Schimidt, F., & Santiago, M. F. (2019). Optimisation of laccase–alginate–chitosan-based matrix toward 17 α-ethinylestradiol removal. *Preparative Biochemistry and Biotechnology, 49*(4), 375–383. doi: 10.1080/10826068.2019.1573195

35. Morais, R. L., Garcia, L. F., Thomaz, D. V., Lobón, G. S., Rodrigues, M. F., Vaz, B. G., Caetano, M. P., de Lacerda Medrado, L. C., Nunes, E. S., dos Santos, C. G., Ávila, L. F., de Souza, K. M., Vieira, R. P., & de Souza Gil, E. (2019). Electrochemical Removal of Algestone Acetophenide and Estradiol Enanthate in Real Industrial Wastewater. *International Journal of Electrochemical Science, 14*(6), 5856–5867. doi: 10.20964/2019.04.42

36. Lacerda, M. F. A. R., Lopes, F. M., Sartoratto, A., Ponezi, A. N., Thomaz, D. V., Schimidt, F., & Santiago, M. F. (2018). Stability of immobilised laccase on Luffa Cylindrica fibers and assessment of synthetic hormone degradation. *Preparative Biochemistry and Biotechnology, 49*(1), 58–63. doi: 10.1080/10826068.2018.1525568

37. Golveia, J. C. S., Santiago, M. F., Sales, P. T. F., Sartoratto, A., Ponezi, A. N., Thomaz, D. V., Gil, E. de S., & F. Bara, M. T. (2018). Cupuaçu (Theobroma grandiflorum) residue and its potential application in the bioremediation of 17-A-ethinylestradiol as a Pycnoporus sanguineus laccase inducer. *Preparative Biochemistry & Biotechnology, 48*(6), 541–548. doi: 10.1080/10826068.2018.1466161

38. Coelho, G. D., Silva, K. K. S., Silva, D. P. D., Soares, J. K. N. C., Ballaminut, N., & Thomaz, D. V. (2020). Biodegradation of Synthetic Effluent Containing CI Direct Red 28 (Congo Red) by Lentinus sp. Laccase Leads to Low Ecotoxicity. *Current Biotechnology, 9*(2), 127–133. doi: 10.2174/2211550109999200720162021

39. Coelho, G. D., Ballaminut, N., Thomaz, D. V., & Gomes Machado, K. M. (2019). Characterisation of a thermostable Deconica castanella Laccase and application toward pentachlorophenol degradation. *Preparative Biochemistry & Biotechnology, 49*(9), 908–915. doi: 10.1080/10826068.2019.1636280

40. Silva, M. A., Nascimento Júnior, J. C. do, Thomaz, D. V., Maia, R. T., Costa Amador, V., Tommaso, G., & Coelho, G. D. (2022). Comparative homology of Pleurotus ostreatus laccase enzyme: Swiss model or Modeller? *Journal of Biomolecular Structure and Dynamics, 41*(18), 8927–8940. doi: 10.1080/07391102.2022.2138975

41. Neto, S. L. M., Coelho, G. D., Ballaminut, N., Matheus, D. R., Thomaz, D. V., & Machado, K. M. G. (2021). Application of Deconica castanella ligninolytic enzymatic system in the degradation of hexachlorobenzene in soil. *Biotechnology and Applied Biochemistry, 69*(6), 2437–2444. doi: 10.1002/bab.2293

42. Vieira Thomaz, D. (2021). Thermodynamics and Kinetics of Camellia sinensis Extracts and Constituents: An Untamed Antioxidant Potential. *Bioactive Compounds in Nutraceutical and Functional Food for Good Human Health*. doi: 10.5772/intechopen.92813

43. Alves, C. B., Rodrigues, E. S. B., Thomaz, D. V., Aguiar Filho, A. M. de, Gil, E. de S., & Couto, R. O. do. (2020). Correlation of polyphenol content and antioxidant capacity of selected teas and tisanes from Brazilian market. *Brazilian Journal of Food Technology, 23*. doi: 10.1590/1981-6723.03620

44. Batista, R. D., de Cássia Sousa Mendes, D., Morais, C. C., Thomaz, D. V., Ramirez Ascheri, D. P., Damiani, C., & Asquieri, E. R. (2020). Physicochemical, functional and rheological properties of fermented and non-fermented starch from canary seed (Phalaris canariensis). *Food Hydrocolloids, 99*, 105346. doi: 10.1016/j.foodhyd.2019.105346

45. Moreno, E. K. G., Thomaz, D. V., Machado, F. B., Leite, K. C. S., Rodrigues, E. S. B., Fernandes, M. A., Carvalho, M. F., de Oliveira, M. T., Caetano, M. P., da Cunha Peixoto, C. E., Isecke, B. G., de Souza Gil, E., & de Macêdo, I. Y. L. (2019). Antioxidant Study and Electroanalytical Investigation of Selected

Herbal Samples Used in Folk Medicine. *International Journal of Electrochemical Science, 14*(1), 838–847. doi: 10.20964/2019.01.82

46. Leite, K. C. de S., Garcia, L. F., Lobón, G. S., Thomaz, D. V., Moreno, E. K. G., Carvalho, M. F. de, Rocha, M. L., Santos, W. T. P. dos, & Gil, E. de S. (2018). Antioxidant activity evaluation of dried herbal extracts: an electroanalytical approach. *Revista Brasileira de Farmacognosia, 28*(3), 325–332. doi: 10.1016/j.bjp.2018.04.004

47. Thomaz, D. V., Peixoto, L. F., de Oliveira, T. S., Fajemiroye, J. O., da Silva Neri, H. F., Xavier, C. H., Costa, E. A., dos Santos, F. C. A., de Souza Gil, E., & Ghedini, P. C. (2018). Antioxidant and Neuroprotective Properties of Eugenia dysentericaLeaves. *Oxidative Medicine and Cellular Longevity, 2018*, 1–9. doi: 10.1155/2018/3250908

48. de Oliveira, T. S., Thomaz, D. V., da Silva Neri, H. F., Cerqueira, L. B., Garcia, L. F., Gil, H. P. V., Pontarolo, R., Campos, F. R., Costa, E. A., dos Santos, F. C. A., de Souza Gil, E., & Ghedini, P. C. (2018). Neuroprotective Effect of Caryocar brasiliense Camb. Leaves Is Associated with Anticholinesterase and Antioxidant Properties. *Oxidative Medicine and Cellular Longevity, 2018*, 1–12. doi: 10.1155/2018/9842908

49. Thomaz, D. V., do Couto, R. O., Goldoni, R., Malitesta, C., Mazzotta, E., & Tartaglia, G. M. (2022). Redox Profiling of Selected Apulian Red Wines in a Single Minute. *Antioxidants, 11*(5), 859. doi: 10.3390/antiox11050859

50. Garcia, L. F., da Cunha, C. E. P., Moreno, E. K. G., Vieira Thomaz, D., Lobón, G. S., Luque, R., Somerset, V., & de Souza Gil, E. (2018). Nanostructured TiO2 Carbon Paste Based Sensor for Determination of Methyldopa. *Pharmaceuticals, 11*(4), 99. doi: 10.3390/ph11040099

51. da Cunha, C. E. P., Rodrigues, E. S. B., Fernandes Alecrim, M., Thomaz, D. V., Macêdo, I. Y. L., Garcia, L. F., de Oliveira Neto, J. R., Moreno, E. K. G., Ballaminut, N., & de Souza Gil, E. (2019). Voltammetric Evaluation of Diclofenac Tablets Samples through Carbon Black-Based Electrodes. *Pharmaceuticals, 12*(2), 83. doi: 10.3390/ph12020083

52. Antunes, R. S., Thomaz, D. V., Garcia, L. F., Gil, E. de S., & Lopes, F. M. (2020). Development and Optimisation of Solanum Lycocarpum Polyphenol Oxidase-Based Biosensor and Application towards Paracetamol Detection. *Advanced Pharmaceutical Bulletin, 11*(3), 469–476. doi: 10.34172/apb.2021.054

53. Moreira, L. K. da S., Turones, L. C., Campos, H. M., Nazareth, A. M., Thomaz, D. V., Gil, E. de S., Ghedini, P. C., Rocha, F. F. da, Menegatti, R., Fajemiroye, J. O., & Costa, E. A. (2023). LQFM212, a piperazine derivative, exhibits potential antioxidant effect as well as ameliorates LPS-induced behavioral, inflammatory and oxidative changes. *Life Sciences, 312*, 121199. doi: 10.1016/j.lfs.2022.121199

54. Moreira, L. K. da S., Silva, R. R., da Silva, D. M., Mendes, M. A. S., de Brito, A. F., de Carvalho, F. S., Sanz, G., Rodrigues, M. F., da Silva, A. C. G., Thomaz, D. V., de Oliveira, V., Vaz, B. G., Lião, L. M., Valadares, M. C., Gil, E. de S., Costa, E. A., Noël, F., & Menegatti, R. (2022). Anxiolytic- and antidepressant-like effects of new phenylpiperazine derivative LQFM005 and its hydroxylated metabolite in mice. *Behavioural Brain Research, 417*, 113582. doi: 10.1016/j.bbr.2021.113582

55. Thomaz, D. V., de Oliveira, M. G., Rodrigues, E. S. B., da Silva, V. B., & dos Santos, P. A. (2020). Physicochemical Investigation of Psoralen Binding to Double Stranded DNA through Electroanalytical and Cheminformatic Approaches. *Pharmaceuticals, 13*(6), 108. doi: 10.3390/ph13060108

56. Murdaya, N., Triadenda, A. L., Rahayu, D., & Hasanah, A. N. (2022). A Review: Using Multiple Templates for Molecular Imprinted Polymer: Is It Good? *Polymers, 14*(20), 4441. doi: 10.3390/polym14204441

57. Furtado, A. I., Viveiros, R., & Casimiro, T. (2021). MIP Synthesis and Processing Using Supercritical Fluids. *Methods in Molecular Biology*, 19–42. doi: 10.1007/978-1-0716-1629-1_3

58. Lowdon, J. W., Diliën, H., Singla, P., Peeters, M., Cleij, T. J., van Grinsven, B., & Eersels, K. (2020). MIPs for commercial application in low-cost sensors and assays – An overview of the current status quo. *Sensors and Actuators B: Chemical, 325*, 128973. doi: 10.1016/j.snb.2020.128973

59. Silva, C. F., Menezes, L. F., Pereira, A. C., & Nascimento, C. S. (2021). Molecularly Imprinted Polymer (MIP) for thiamethoxam: A theoretical and experimental study. *Journal of Molecular Structure, 1231*, 129980. doi: 10.1016/j.molstruc.2021.129980

60. El-Schich, Z., Zhang, Y., Feith, M., Beyer, S., Sternbæk, L., Ohlsson, L., Stollenwerk, M., & Wingren, A. G. (2020). Molecularly imprinted polymers in biological applications. *BioTechniques, 69*(6), 406–419. doi: 10.2144/btn-2020-0091

61. Piletsky, S., Canfarotta, F., Poma, A., Bossi, A. M., & Piletsky, S. (2020). Molecularly Imprinted Polymers for Cell Recognition. *Trends in Biotechnology, 38*(4), 368–387. doi: 10.1016/j.tibtech.2019.10.002

62. Iskierko, Z., Sharma, P. S., Prochowicz, D., Fronc, K., D'Souza, F., Toczydłowska, D., Stefaniak, F., & Noworyta, K. (2016). Molecularly Imprinted Polymer (MIP) Film with Improved Surface Area Developed by Using Metal–Organic Framework (MOF) for Sensitive Lipocalin (NGAL) Determination. *ACS Applied Materials & Interfaces, 8*(31), 19860–19865. doi: 10.1021/acsami.6b05515

63. Jolly, P., Tamboli, V., Harniman, R. L., Estrela, P., Allender, C. J., & Bowen, J. L. (2016). Aptamer–MIP hybrid receptor for highly sensitive electrochemical detection of prostate specific antigen. *Biosensors and Bioelectronics, 75*, 188–195. doi: 10.1016/j.bios.2015.08.043

64. Nottelet, P., Bataille, L., Gourgues, G., Anger, R., Lartigue, C., Sirand-Pugnet, P., Marza, E., Fronzes, R., & Arfi, Y. (2021). The mycoplasma surface proteins MIB and MIP promote the dissociation of the antibody-antigen interaction. *Science Advances, 7*(10). doi: 10.1126/sciadv.abf2403

65. De Middeleer, G., Dubruel, P., & De Saeger, S. (2016). Characterisation of MIP and MIP functionalised surfaces: Current state-of-the-art. *TrAC Trends in Analytical Chemistry, 76*, 71–85. doi: 10.1016/j.trac.2015.11.007

66. Zhang, H. (2019). Molecularly Imprinted Nanoparticles for Biomedical Applications. *Advanced Materials, 32*(3). doi: 10.1002/adma.201806328

67. Preda, D., David, I. G., Popa, D.-E., Buleandra, M., & Radu, G. L. (2022). Recent Trends in the Development of Carbon-Based Electrodes Modified with Molecularly Imprinted Polymers for Antibiotic Electroanalysis. *Chemosensors, 10*(7), 243. doi: 10.3390/chemosensors10070243

68. Dong, X., Zhang, C., Du, X., & Zhang, Z. (2022). Recent Advances of Nanomaterials-Based Molecularly Imprinted Electrochemical Sensors. *Nanomaterials, 12*(11), 1913. doi: 10.3390/nano12111913

69. He, S., Zhang, L., Bai, S., Yang, H., Cui, Z., Zhang, X., & Li, Y. (2021). Advances of molecularly imprinted polymers (MIP) and the application in drug delivery. *European Polymer Journal, 143*, 110179. doi: 10.1016/j.eurpolymj.2020.110179

70. Mostafiz, B., Bigdeli, S. A., Banan, K., Afsharara, H., Hatamabadi, D., Mousavi, P., Hussain, C. M., Keçili, R., & Ghorbani-Bidkorbeh, F. (2021). Molecularly imprinted polymer-carbon paste electrode (MIP-CPE)-based sensors for the sensitive detection of organic and inorganic environmental pollutants: A review. *Trends in Environmental Analytical Chemistry, 32*, e00144. doi: 10.1016/j.teac.2021.e00144

71. Afsharara, H., Asadian, E., Mostafiz, B., Banan, K., Bigdeli, S. A., Hatamabadi, D., Keshavarz, A., Hussain, C. M., Keçili, R., & Ghorbani-Bidkorpeh, F. (2023). Molecularly imprinted polymer-modified carbon paste electrodes (MIP-CPE): A review on sensitive electrochemical sensors for pharmaceutical determinations. *TrAC Trends in Analytical Chemistry, 160*, 116949. doi: 10.1016/j.trac.2023.116949

72. Dabrowski, M., Lach, P., Cieplak, M., & Kutner, W. (2018). Nanostructured molecularly imprinted polymers for protein chemosensing. *Biosensors and Bioelectronics, 102*, 17–26. doi: 10.1016/j.bios.2017.10.045

73. Mustafa, Y. L., Keirouz, A., & Leese, H. S. (2022). Molecularly imprinted polymers in diagnostics: accessing analytes in biofluids. *Journal of Materials Chemistry B, 10*(37), 7418–7449. doi: 10.1039/d2tb00703g

74. Suzaei, F. M., Daryanavard, S. M., Abdel-Rehim, A., Bassyouni, F., & Abdel-Rehim, M. (2022). Recent molecularly imprinted polymers applications in bioanalysis. *Chemical Papers, 77*(2), 619–655. doi: 10.1007/s11696-022-02488-3

75. Fauzi, D., & saputri, F. A. (2019). Molecularly imprinted polymer nanoparticles (MIP-NPs) applications in electrochemical sensors. International *Journal of Applied Pharmaceutics*, 1–6. doi: 10.22159/ijap.2019v11i6.35088

76. Ali, G. K., & Omer, K. M. (2022). Molecular imprinted polymer combined with aptamer (MIP-aptamer) as a hybrid dual recognition element for bio(chemical) sensing applications. Review. *Talanta, 236*, 122878. doi: 10.1016/j.talanta.2021.122878

77. Refaat, D., Aggour, M. G., Farghali, A. A., Mahajan, R., Wiklander, J. G., Nicholls, I. A., & Piletsky, S. A. (2019). Strategies for Molecular Imprinting and the Evolution of MIP Nanoparticles as Plastic Antibodies—Synthesis and Applications. *International Journal of Molecular Sciences, 20*(24), 6304. doi: 10.3390/ijms20246304

78. Wisnuwardhani, H. A., Ibrahim, S., Mukti, R. R., & Damayanti, S. (2022). Molecularly-Imprinted SERS: A Potential Method for Bioanalysis. *Scientia Pharmaceutica, 90*(3), 54. doi: 10.3390/scipharm90030054

79. Karimi Baker, Z., & sardari, S. (2021). Molecularly Imprinted Polymer (MIP) Applications in Natural Product Studies Based on Medicinal Plant and Secondary Metabolite Analysis. *Iranian Biomedical Journal, 25*(2), 68–77. doi: 10.29252/ibj.25.2.68

80. Harito, C., Khalil, M., Septiani, N. L. W., Dewi, K. K., Hardiansyah, A., Yuliarto, B., & Walsh, F. C. (2022). Trends in nanomaterial-based biosensors for viral detection. *Nano Futures, 6*(2), 022005. doi: 10.1088/2399-1984/ac701d

81. Wang, L., Pagett, M., & Zhang, W. (2023). Molecularly imprinted polymer (MIP) based electrochemical sensors and their recent advances in health applications. *Sensors and Actuators Reports, 5*, 100153. doi: 10.1016/j.snr.2023.100153

82. Sun, P.-X., Cai, J., Chen, L.-J., Wang, J., & Yang, C. (2022). MIP-Based Portable Sensors for the Simultaneous Analysis of Multiple Food Additives. *Food Analytical Methods, 15*(8), 2335–2345. doi: 10.1007/s12161-022-02273-8

83. Raziq, A., Kidakova, A., Boroznjak, R., Reut, J., Öpik, A., & Syritski, V. (2021). Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen. *Biosensors and Bioelectronics, 178*, 113029. doi: 10.1016/j.bios.2021.113029

84. Ramanavičius, S., Morkvėnaitė-Vilkončienė, I., Samukaitė-Bubnienė, U., Ratautaitė, V., Plikusienė, I., Viter, R., & Ramanavičius, A. (2022). Electrochemically Deposited Molecularly Imprinted Polymer-Based Sensors. *Sensors, 22*(3), 1282. doi: 10.3390/s22031282

85. Park, R., Jeon, S., Jeong, J., Park, S.-Y., Han, D.-W., & Hong, S. W. (2022). Recent Advances of Point-of-Care Devices Integrated with Molecularly Imprinted Polymers-Based Biosensors: From Biomolecule Sensing Design to Intraoral Fluid Testing. *Biosensors, 12*(3), 136. doi: 10.3390/bios12030136

86. Henry, O. Y. F., Cullen, D. C., & Piletsky, S. A. (2005). Optical interrogation of molecularly imprinted polymers and development of MIP sensors: a review. *Analytical and Bioanalytical Chemistry, 382*(4), 947–956. doi: 10.1007/s00216-005-3255-8

87. Shahhoseini, F., Azizi, A., & Bottaro, C. S. (2022). A critical evaluation of molecularly imprinted polymer (MIP) coatings in solid phase microextraction devices. *TrAC Trends in Analytical Chemistry, 156*, 116695. doi: 10.1016/j.trac.2022.116695

88. Cardoso, A. R., de Sá, M. H., & Sales, M. G. F. (2019). An impedimetric molecularly-imprinted biosensor for Interleukin-1β determination, prepared by in-situ electropolymerisation on carbon screen-printed electrodes. *Bioelectrochemistry, 130*, 107287. doi: 10.1016/j.bioelechem.2019.04.017

89. Rebelo, T. S. C. R., Miranda, I. M., Brandão, A. T. S. C., Sousa, L. I. G., Ribeiro, J. A., Silva, A. F., & Pereira, C. M. (2021). A Disposable Saliva Electrochemical MIP-Based Biosensor for Detection of the Stress Biomarker α-Amylase in Point-of-Care Applications. *Electrochem, 2*(3), 427–438. doi: 10.3390/electrochem2030028

90. Uzun, L., & Turner, A. P. F. (2016). Molecularly-imprinted polymer sensors: realising their potential. *Biosensors and Bioelectronics, 76*, 131–144. doi: 10.1016/j.bios.2015.07.013

91. Kongintr, U., Lertanantawong, B., & Promptmas, C. (2023). A Label-Free Electrochemical Biosensor for Homocysteine Detection Using Molecularly Imprinted Polymer and Nanocomposite-Modified Electrodes. *Polymers, 15*(10), 2241. doi: 10.3390/polym15102241

92. Guan, G., Liu, B., Wang, Z., & Zhang, Z. (2008). Imprinting of Molecular Recognition Sites on Nanostructures and Its Applications in Chemosensors. *Sensors, 8*(12), 8291–8320. doi: 10.3390/s8128291

93. Liu, Y., Huang, S., Li, Z., & Zhao, M. (2015). Molecularly Imprinted Polymers as Tools for Bioassays and Biotransformation. *Advances in Biochemical Engineering/Biotechnology*, 207–226. doi: 10.1007/10_2015_315

94. Villa, C. C., Sánchez, L. T., Valencia, G. A., Ahmed, S., & Gutiérrez, T. J. (2021). Molecularly imprinted polymers for food applications: A review. *Trends in Food Science & Technology, 111*, 642–669. doi: 10.1016/j.tifs.2021.03.003

95. Sasaki, S., Ooya, T., Kitayama, Y., & Takeuchi, T. (2015). Molecularly imprinted protein recognition thin films constructed by controlled/living radical polymerisation. *Journal of Bioscience and Bioengineering, 119*(2), 200–205. doi: 10.1016/j.jbiosc.2014.06.019

96. Pratiwi, R., Megantara, S., Rahayu, D., Pitaloka, I., & Hasanah, A. N. (2018). Comparison of Bulk and Precipitation Polymerization Method of Synthesis Molecular Imprinted Solid Phase Extraction for Atenolol using Methacrylic Acid. *Journal of Young Pharmacists, 11*(1), 12–16. doi: 10.5530/jyp.2019.11.3

97. Wei, S., Jakusch, M., & Mizaikoff, B. (2006). Capturing molecules with templated materials—Analysis and rational design of molecularly imprinted polymers. *Analytica Chimica Acta, 578*(1), 50–58. doi: 10.1016/j.aca.2006.06.077

98. Gonçalves, M. de L., Truta, L. A. N., Sales, M. G. F., & Moreira, F. T. C. (2021). Electrochemical Point-of Care (PoC) Determination of Interleukin-6 (IL-6) Using a Pyrrole (Py) Molecularly Imprinted Polymer (MIP) on a Carbon-Screen Printed Electrode (C-SPE). *Analytical Letters, 54*(16), 2611–2623. doi: 10.1080/00032719.2021.1879108

99. Pacheco, J. G., Rebelo, P., Freitas, M., Nouws, H. P. A., & Delerue-Matos, C. (2018). Breast cancer biomarker (HER2-ECD) detection using a molecularly imprinted electrochemical sensor. *Sensors and Actuators B: Chemical, 273*, 1008–1014. doi: 10.1016/j.snb.2018.06.113

100. Pasquardini, L., & Bossi, A. M. (2021). Molecularly imprinted polymers by epitope imprinting: a journey from molecular interactions to the available bioinformatics resources to scout for epitope templates. *Analytical and Bioanalytical Chemistry, 413*(24), 6101–6115. doi: 10.1007/s00216-021-03409-1

101. Mazouz, Z., Mokni, M., Fourati, N., Zerrouki, C., Barbault, F., Seydou, M., Kalfat, R., Yaakoubi, N., Omezzine, A., Bouslema, A., & Othmane, A. (2020). Computational approach and electrochemical

measurements for protein detection with MIP-based sensor. *Biosensors and Bioelectronics, 151*, 111978. doi: 10.1016/j.bios.2019.111978

102. Cardoso, A. R., de Sá, M. H., & Sales, M. G. F. (2019). An impedimetric molecularly-imprinted biosensor for Interleukin-1β determination, prepared by in-situ electropolymerisation on carbon screen-printed electrodes. *Bioelectrochemistry, 130*, 107287. doi: 10.1016/j.bioelechem.2019.04.017

103. Yarman, A., Turner, A. P. F., & Scheller, F. W. (2014). Electropolymers for (nano-)imprinted biomimetic biosensors. *Nanosensors for Chemical and Biological Applications*, 125–149. doi: 10.1533/9780857096722.1.125

104. Abbasy, L., Mohammadzadeh, A., Hasanzadeh, M., & Razmi, N. (2020). Development of a reliable bioanalytical method based on prostate specific antigen trapping on the cavity of molecular imprinted polymer towards sensing of PSA using binding affinity of PSA-MIP receptor: A novel biosensor. *Journal of Pharmaceutical and Biomedical Analysis, 188*, 113447. doi: 10.1016/j.jpba.2020.113447

105. Kalecki, J., Iskierko, Z., Cieplak, M., & Sharma, P. S. (2020). Oriented Immobilization of Protein Templates: A New Trend in Surface Imprinting. *ACS Sensors, 5*(12), 3710–3720. doi: 10.1021/acssensors.0c01634

106. Pan, M., Hong, L., Xie, X., Liu, K., Yang, J., & Wang, S. (2020). Nanomaterials-Based Surface Protein Imprinted Polymers: Synthesis and Medical Applications. *Macromolecular Chemistry and Physics, 222*(1). doi: 10.1002/macp.202000222

107. Kato, M., Masuda, Y., Yoshida, N., Tosha, T., Shiro, Y., & Yagi, I. (2021). Impact of membrane protein-lipid interactions on formation of bilayer lipid membranes on SAM-modified gold electrode. *Electrochimica Acta, 373*, 137888. doi: 10.1016/j.electacta.2021.137888

108. Yan, X., Tang, J., Tanner, D., Ulstrup, J., & Xiao, X. (2020). Direct Electrochemical Enzyme Electron Transfer on Electrodes Modified by Self-Assembled Molecular Monolayers. *Catalysts, 10*(12), 1458. doi: 10.3390/catal10121458

109. Di Giulio, T., Mazzotta, E., & Malitesta, C. (2020). Molecularly Imprinted Polyscopoletin for the Electrochemical Detection of the Chronic Disease Marker Lysozyme. *Biosensors, 11*(1), 3. doi: 10.3390/bios11010003

110. Raziq, A., Kidakova, A., Boroznjak, R., Reut, J., Öpik, A., & Syritski, V. (2021). Development of a portable MIP-based electrochemical sensor for detection of SARS-CoV-2 antigen. *Biosensors and Bioelectronics, 178*, 113029. doi: 10.1016/j.bios.2021.113029

111. Wang, X., Li, J., & Chen, L. (2019). Advanced preparation technologies and strategies for molecularly imprinted materials. *Chinese Science Bulletin, 64*(13), 1352–1367. doi: 10.1360/n972018-00964

112. Phonklam, K., Wannapob, R., Sriwimol, W., Thavarungkul, P., & Phairatana, T. (2020). A novel molecularly imprinted polymer PMB/MWCNTs sensor for highly-sensitive cardiac troponin T detection. *Sensors and Actuators B: Chemical, 308*, 127630. doi: 10.1016/j.snb.2019.127630

113. Arshad, R., Rhouati, A., Hayat, A., Nawaz, M. H., Yameen, M. A., Mujahid, A., & Latif, U. (2020). MIP-Based Impedimetric Sensor for Detecting Dengue Fever Biomarker. *Applied Biochemistry and Biotechnology, 191*(4), 1384–1394. doi: 10.1007/s12010-020-03285-y

114. Jolly, P., Tamboli, V., Harniman, R. L., Estrela, P., Allender, C. J., & Bowen, J. L. (2016). Aptamer–MIP hybrid receptor for highly sensitive electrochemical detection of prostate specific antigen. *Biosensors and Bioelectronics, 75*, 188–195. doi: 10.1016/j.bios.2015.08.043

115. Tan, D., Li, F., & Zhou, B. (2020). Antifouling Self-Assembled Monolayers for Designing of Electrochemical Biosensors. *International Journal of Electrochemical Science, 15*(9), 9446–9458. doi: 10.20964/2020.09.56

116. Karami, P., Bagheri, H., Johari-Ahar, M., Khoshsafar, H., Arduini, F., & Afkhami, A. (2019). Dual-modality impedimetric immunosensor for early detection of prostate-specific antigen and myoglobin markers based on antibody-molecularly imprinted polymer. *Talanta, 202*, 111–122. doi: 10.1016/j.talanta.2019.04.061

117. Yola, M. L., Atar, N., & Erdem, A. (2015). Oxytocin imprinted polymer based surface plasmon resonance sensor and its application to milk sample. *Sensors and Actuators B: Chemical, 221*, 842–848. doi: 10.1016/j.snb.2015.07.004

118. Drzazgowska, J., Schmid, B., Süssmuth, R. D., & Altintas, Z. (2020). Self-Assembled Monolayer Epitope Bridges for Molecular Imprinting and Cancer Biomarker Sensing. *Analytical Chemistry, 92*(7), 4798–4806. doi: 10.1021/acs.analchem.9b03813

119. Yang, K., Li, S., Liu, L., Chen, Y., Zhou, W., Pei, J., Liang, Z., Zhang, L., & Zhang, Y. (2019). Epitope Imprinting Technology: Progress, Applications, and Perspectives toward Artificial Antibodies. *Advanced Materials, 31*(50). doi: 10.1002/adma.201902048

120. Wang, X., Chen, G., Zhang, P., & Jia, Q. (2021). Advances in epitope molecularly imprinted polymers for protein detection: a review. *Analytical Methods, 13*(14), 1660–1671. doi: 10.1039/d1ay00067e

121. Caserta, G., Zhang, X., Yarman, A., Supala, E., Wollenberger, U., Gyurcsányi, R. E., Zebger, I., & Scheller, F. W. (2021). Insights in electrosynthesis, target binding, and stability of peptide-imprinted polymer nanofilms. *Electrochimica Acta, 381*, 138236. doi: 10.1016/j.electacta.2021.138236

122. Dietl, S., Sobek, H., & Mizaikoff, B. (2021). Epitope-imprinted polymers for biomacromolecules: Recent strategies, future challenges and selected applications. *TrAC Trends in Analytical Chemistry, 143*, 116414. doi: 10.1016/j.trac.2021.116414

123. Khumsap, T., Corpuz, A., & Nguyen, L. T. (2021). Epitope-imprinted polymers: applications in protein recognition and separation. *RSC Advances, 11*(19), 11403–11414. doi: 10.1039/d0ra10742e

124. Zhao, Y., Simon, C., Daoud Attieh, M., Haupt, K., & Falcimaigne-Cordin, A. (2020). Reduction-responsive molecularly imprinted nanogels for drug delivery applications. *RSC Advances, 10*(10), 5978–5987. doi: 10.1039/c9ra07512g

125. Hou, H., Jin, Y., Xu, K., Sheng, L., Huang, Y., & Zhao, R. (2021). Selective recognition of a cyclic peptide hormone in human plasma by hydrazone bond-oriented surface imprinted nanoparticles. *Analytica Chimica Acta, 1154*, 338301. doi: 10.1016/j.aca.2021.338301

126. Khumsap, T., Bamrungsap, S., Thu, V. T., & Nguyen, L. T. (2021). Epitope-imprinted polydopamine electrochemical sensor for ovalbumin detection. *Bioelectrochemistry, 140*, 107805. doi: 10.1016/j.bioelechem.2021.107805

127. Ma, X.-T., He, X.-W., Li, W.-Y., & Zhang, Y.-K. (2019). Oriented surface epitope imprinted polymer-based quartz crystal microbalance sensor for cytochrome c. *Talanta, 191*, 222–228. doi: 10.1016/j.talanta.2018.08.079

128. Yang, K., Li, S., Liu, L., Chen, Y., Zhou, W., Pei, J., Liang, Z., Zhang, L., & Zhang, Y. (2019). Epitope Imprinting Technology: Progress, Applications, and Perspectives toward Artificial Antibodies. *Advanced Materials, 31*(50). doi: 10.1002/adma.201902048

129. Haupt, K., Medina Rangel, P. X., & Bui, B. T. S. (2020). Molecularly Imprinted Polymers: Antibody Mimics for Bioimaging and Therapy. *Chemical Reviews, 120*(17), 9554–9582. doi: 10.1021/acs.chemrev.0c00428

130. Pirzada, M., Sehit, E., & Altintas, Z. (2020). Cancer biomarker detection in human serum samples using nanoparticle decorated epitope-mediated hybrid MIP. *Biosensors and Bioelectronics, 166*, 112464. doi: 10.1016/j.bios.2020.112464