ISSN 2582-6441 [Online]
RESEARCH JOURNAL OF PHARMACY AND LIFE SCIENCES
LET OTHERS KNOW YOUR RESEARCH
RJPLS
An International Peer Reviewed Journal

Review Article

Biosensors in Drug Discovery, Development, and Delivery: A Concurrent Review

Goutam Kumar Jena*, Supriyo Satapathy, AvipsaMohapatra, Ch Niranjan Patra, J Sruti

Department of Pharmaceutics, Roland Institute of Pharmaceutical Sciences, Berhampur, Odisha-760002

ARTICLE INFO

Date of submission: 23-05-2025
Date of Revision: 28-06-2025
Date of acceptance: 03-07-2025

Key Words:
Biosensors, Drug Discovery, Drug Development, Drug Delivery, Electrochemical Biosensors

ABSTRACT

Background: Biosensors have emerged as pivotal tools in the pharmaceutical industry, offering real-time, sensitive, and specific insights that span the entire drug lifecycle. These devices integrate biological recognition elements with transducers, facilitating the rapid detection of target analytes, which is crucial for drug discovery, development, and delivery. **Objective**: This review aims to elucidate the role of biosensors in the drug discovery and development process, focusing on their applications from target identification to patient monitoring. The integration of biosensors into drug delivery systems is also explored, with an emphasis on their potential to enhance therapeutic outcomes. **Methods**: A comprehensive literature review was conducted, analyzing the latest advancements in biosensor technology, including electrochemical, optical, and nanomaterial-based sensors. Studies were selected based on their relevance to the pharmaceutical applications of biosensors. **Results**: Biosensors have shown significant utility in various stages of the drug lifecycle. In drug discovery, they aid in target identification and lead optimization. In drug development, they contribute to preclinical testing by providing real-time data on

drug interactions and toxicology. In drug delivery, biosensors are integrated into smart systems that enable controlled release and monitoring of therapeutic agents, enhancing treatment efficacy. Notably, electrochemical biosensors offer high sensitivity and low detection limits, while optical sensors provide label-free analysis. Nanomaterial-based biosensors demonstrate increased surface area and functionalization capabilities, making them suitable for complex biological environments. **Conclusion:** Biosensors hold immense potential in transforming drug discovery, development, and delivery by offering precise, rapid, and non-invasive analysis. However, challenges such as standardization, scalability, and regulatory approval need to be addressed to fully realize their impact. Future research should focus on enhancing biosensor sensitivity, integrating artificial intelligence for data interpretation, and developing personalized drug delivery systems.

[*]**Corresponding author:**
Dr. Goutam Kumar Jena,
Professor, Roland Institute of Pharmaceutical Sciences, Brahmapur, Odisha-760002
E-mail: Email: goutam2902@gmail.com

Introduction

Drug discovery and development is a complex and multifaceted process, typically involving a series of steps that span over several years and require substantial financial investment[1, 2]. The process begins with the identification of potential drug targets and the screening of thousands of compounds, eventually narrowing down to a few candidates that show promise for clinical development[3, 4]. Despite the advances in technology and science, the journey from a promising compound to an approved drug remains fraught with challenges, including high attrition rates, lengthy timelines, and escalating costs[5, 6].

One of the critical needs in drug discovery is the ability to accurately monitor biological and chemical interactions in real time[7]. Traditional methods, such as cell-based assays and biochemical techniques, often fall short in providing the sensitivity, specificity, and speed required for modern drug development[8]. Furthermore, these methods may not always capture the dynamic nature of biological systems, leading to missed opportunities for identifying potential drug candidates or understanding their mechanisms of action[9].

Biosensors have emerged as powerful tools that address many of these challenges. A biosensor is a device that combines a biological recognition element with a physicochemical transducer to convert a biological response into a measurable signal[10]. The biological recognition element could be an enzyme, antibody, nucleic acid, or other biomolecule, while the transducer could be electrochemical, optical, piezoelectric, or thermal in nature[11]. The working principle of biosensors is presented in Figure 1.

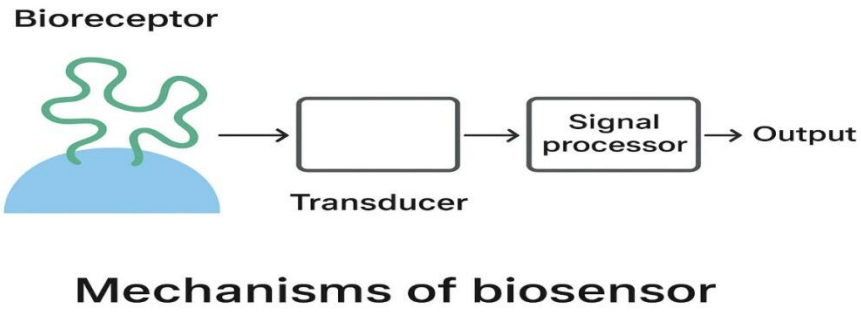

Figure 1: General mechanism of biosensors

The key advantages of biosensors include their ability to provide real-time monitoring, high sensitivity, and specificity[12]. They can detect minute changes in biological systems, enabling the early identification of potential drug candidates and the precise evaluation of drug effects[7]. Additionally, biosensors can be miniaturized and integrated into high-throughput screening platforms, making them ideal for use in early-stage drug discovery[13, 14].

Moreover, biosensors offer the potential for continuous monitoring of biological processes, which is particularly valuable in preclinical and clinical stages of drug development[15, 16]. For example, wearable biosensors can be used to track physiological parameters in real time, providing continuous data on drug effects and patient responses[17, 18].

The application of biosensors in drug discovery is not limited to a single stage of the process. They play a role in target identification, lead optimization, preclinical testing, and even clinical trials[19, 20]. By providing real-time data on drug-target interactions, pharmacokinetics, and biomarker levels, biosensors contribute to more informed decision-making and can help accelerate the drug development timeline[21, 22].

In the drug delivery phase, biosensors contribute to the development of advanced delivery systems that ensure precise and controlled release of therapeutics [22-24]. They facilitate the design of smart drug delivery systems that can respond to physiological changes and target specific tissues or cells, enhancing therapeutic efficacy and minimizing side effects[25].

In recent years, the field of biosensors has witnessed significant advancements, particularly with the integration of nanotechnology and microfluidics [10, 25, 26]. These innovations have further enhanced the performance of biosensors, making them more sensitive, selective, and capable of multiplexed detection[27]. As a result, biosensors are increasingly being recognized as indispensable tools in the pharmaceutical industry.

However, the adoption of biosensors in drug discovery is not without its challenges. Issues related to validation, standardization, and integration into existing workflows must be addressed to fully realize the potential of biosensors in this field. Despite these challenges, the future of biosensors in drug discovery looks promising, with ongoing research and development efforts focused on overcoming these hurdles and expanding their applications[28, 29].

Overall, the integration of biosensors into the pharmaceutical industry represents a significant advancement, offering a range of benefits from improved drug discovery

and development processes to innovative delivery solutions[23]. This review aims to provide a comprehensive overview of the role of biosensors in these areas, highlighting recent advancements, current applications, and future prospects.

Types of Biosensors in Drug Discovery

1. Electrochemical Biosensors

Electrochemical biosensors detect biological events by measuring changes in electrical properties such as current, voltage, or impedance[30, 31]. These sensors are widely used due to their high sensitivity, low cost, and ease of miniaturization. In drug discovery, they are employed for monitoring enzyme activity, detecting biomarker levels, and screening potential drug candidates[31, 32].

2. Optical Biosensors

Optical biosensors utilize light-based methods, such as fluorescence, surface plasmon resonance (SPR), and bioluminescence, to detect biological interactions[33, 34]. These sensors offer high specificity and are non-invasive, making them suitable for real-time monitoring of molecular interactions, drug-target binding, and cellular responses[35]. Optical biosensors are particularly useful in high-throughput screening (HTS) and early-stage drug discovery[14, 36].

3. Nanomaterial-based Biosensors

Nanomaterials, including nanoparticles, carbon nanotubes, and quantum dots, have unique properties that enhance the sensitivity and selectivity of biosensors[36, 37]. Nanomaterial-based biosensors can detect low-abundance biomarkers and provide insights into drug mechanisms at the molecular level[38]. These biosensors are increasingly being integrated into drug development pipelines to identify potential drug candidates and evaluate their efficacy[39].

Applications of Biosensors in Drug Discovery

1. Target Identification and Validation

Biosensors play a crucial role in identifying and validating biological targets for drug development[40]. By monitoring the interaction between potential drug targets and ligands, biosensors can help identify the most promising targets for therapeutic intervention[41]. For example, SPR-based biosensors can be used to study protein-protein interactions, providing valuable information for target validation[42, 43]. The application of biosensors is presented in Figure 2.

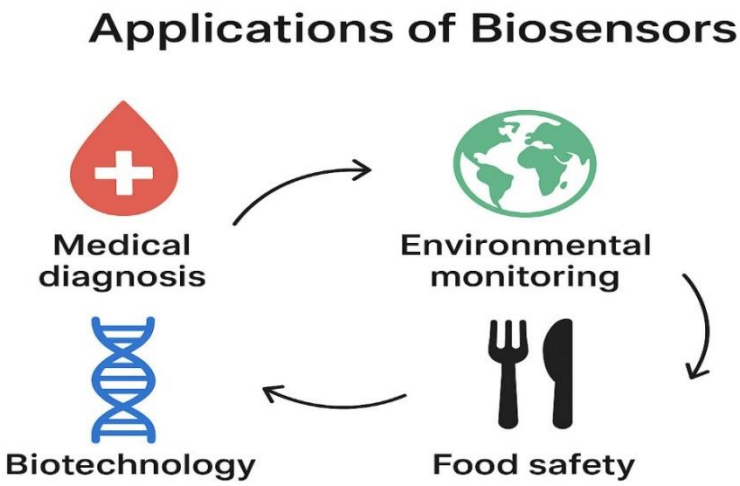

Figure 2: Applications of Biosensors in different fields

2. Lead Optimization

During lead optimization, biosensors can be used to assess the binding affinity, specificity, and toxicity of lead compounds[44]. Electrochemical and optical biosensors enable the real-time monitoring of drug-target interactions, allowing researchers to optimize lead compounds more efficiently[36]. Additionally, biosensors can be employed to detect off-target effects, reducing the likelihood of adverse side effects in later stages of development[36, 45].

3. Preclinical Testing

In preclinical testing, biosensors are utilized to monitor the pharmacokinetics and pharmacodynamics of drug candidates[46]. By providing real-time data on drug absorption, distribution, metabolism, and excretion (ADME), biosensors help predict the in vivo behaviour of drugs[47, 48]. Nanomaterial-based biosensors, in particular, offer high sensitivity for detecting drug concentrations in biological fluids, aiding in the evaluation of drug efficacy and safety[49, 50].

4. Clinical Trials

Biosensors are increasingly being integrated into clinical trials to monitor patient responses to drugs in real-time[51]. Wearable biosensors, for example, can continuously measure physiological parameters such as glucose levels, heart rate, and oxygen saturation, providing valuable data for assessing drug efficacy and safety[17]. Moreover, biosensors can be used to detect biomarkers of disease progression, enabling personalized medicine approaches in clinical trials[52].

Applications in Drug Development

Biosensors have significantly advanced the drug development process by providing

precise, real-time data and facilitating more efficient and effective development workflows. Here's how biosensors are applied in various stages of drug development:

1. Pharmacokinetics and Pharmacodynamics

Real-Time Drug Monitoring: Biosensors enable real-time monitoring of drug levels in biological fluids such as blood, plasma, and urine[53]. For example, implantable biosensors can track drug concentrations continuously, providing insights into the drug's pharmacokinetics (ADME: Absorption, Distribution, Metabolism, Excretion)[54]. This data helps optimize dosing schedules and improve drug efficacy while minimizing adverse effects.

Dynamic Response Assessment: Biosensors can assess the pharmacodynamics of a drug by monitoring its interaction with biological targets or cellular responses[55]. For instance, surface plasmon resonance (SPR) and quartz crystal microbalance (QCM) technologies measure the binding kinetics between drugs and their targets, providing crucial data on drug efficacy and mechanism of action[56].

2. Biomarker Detection

Disease Biomarker Identification: Biosensors are used to identify and quantify biomarkers associated with diseases, which can guide drug development[56]. For example, biosensors that detect cancer biomarkers like PSA (Prostate-Specific Antigen) or HER2 (Human Epidermal Growth Factor Receptor 2) help in evaluating the effectiveness of new cancer therapies[57, 58].

Therapeutic Monitoring: Biosensors help track changes in biomarker levels in response to drug treatment[41]. This allows researchers to assess how well a drug is working and make necessary adjustments. For example, biosensors can monitor cytokine levels in inflammatory diseases to gauge the effectiveness of anti-inflammatory drugs[59].

3. Toxicity Assessment

Early Toxicity Screening: Biosensors are employed to screen for potential toxicity early in the drug development process[36]. For example, biosensors can detect changes in cellular behaviour or biomarkers indicative of toxicity[60]. Techniques like electrochemical biosensors can assess oxidative stress or changes in enzyme activity that signal potential adverse effects[61].

Cellular and Tissue-Level Monitoring: Biosensors can be used to monitor cellular responses to drug candidates in real-time, providing insights into potential toxic effects[36]. For instance, biosensors integrated into cell culture systems can measure changes in cellular metabolism,

proliferation, or viability in response to drug exposure[62].

4. High-Throughput Screening

Automated Screening Platforms: Biosensors enable high-throughput screening (HTS) by automating the process of testing large libraries of compounds[63]. For example, fluorescence-based biosensors can rapidly assess the interaction between compounds and biological targets, allowing researchers to identify promising drug candidates more efficiently[64].

Cell-Based Assays: Biosensors integrated into cell-based assays facilitate the high-throughput evaluation of drug candidates by monitoring cellular responses such as changes in intracellular calcium levels, pH, or other biomarkers[16, 62]. This provides valuable data on drug efficacy and potential side effects.

5. Pharmacogenomics

Genotype-Phenotype Correlations: Biosensors are used to study the relationship between genetic variations and drug responses, known as pharmacogenomics[65]. For example, biosensors can detect specific genetic markers or mutations that influence how individuals metabolize or respond to drugs, guiding the development of personalized therapies[52].

Customized Drug Regimens: By integrating biosensor data with genetic information, researchers can develop customized drug regimens tailored to individual patients' genetic profiles[52]. This approach aims to enhance drug efficacy and minimize adverse effects, leading to more personalized and effective treatments.

6. Clinical Trials

Real-Time Data Collection: During clinical trials, biosensors provide real-time data on patients' physiological parameters, drug levels, and biomarkers[51, 66]. This data helps monitor patient responses, adjust treatment protocols, and ensure safety and efficacy throughout the trial.

Remote Monitoring: Wearable biosensors enable remote monitoring of patients during clinical trials, allowing for continuous data collection without frequent hospital visits[67]. This is particularly useful for trials involving chronic conditions or long-term treatment regimens, improving patient compliance and data accuracy.

Drug Delivery

The integration of biosensors into drug delivery systems allows for precise control and monitoring of drug administration, adapting to the specific needs of patients and their physiological conditions[68]. Here are some real-world applications:

1. Smart Drug Delivery Systems

Glucose-Sensing Insulin Pumps: One of the most well-known applications is the

glucose-sensing insulin pump used by diabetic patients[68, 69]. These systems incorporate glucose biosensors to continuously monitor blood glucose levels. When the sensor detects elevated glucose, the insulin pump automatically administers the appropriate dose of insulin[70]. This real-time feedback mechanism helps maintain optimal glucose control and reduces the risk of hypo- or hyperglycemia [71].

PH-Responsive Drug Delivery: pH-sensitive drug delivery systems use biosensors to detect changes in pH levels within the body, such as in the gastrointestinal tract or tumor microenvironment [72]. For example, nanoparticles or polymer-based carriers can be designed to release their payload in response to acidic or basic pH changes[73]. This approach is used to target drugs to specific areas, like delivering chemotherapeutic agents directly to tumors while minimizing systemic side effects [73, 74].

2. In Vivo Monitoring

Implantable Biosensors: Implantable biosensors provide continuous, real-time monitoring of physiological parameters[75]. For instance, biosensors can be implanted to track drug levels in the bloodstream, allowing for adjustments in drug delivery rates based on current therapeutic needs[76]. This technology is particularly useful for drugs with narrow therapeutic windows, such as certain anticoagulants or pain medications, where precise dosing is crucial[68, 77].

Wearable Biosensors: Wearable biosensors, such as those embedded in smart patches or bracelets, monitor various biomarkers or physiological parameters non-invasively[78, 79]. These devices can track factors like hydration levels, skin temperature, or drug levels, providing feedback to adjust drug delivery systems dynamically[80]. For example, smart patches can release medication in response to changes in skin temperature or pH, offering a personalized approach to managing chronic conditions[81].

3. Personalized Medicine

Tailored Drug Delivery: Biosensors enable the development of personalized drug delivery systems that adapt to individual patient profiles[52]. For instance, biosensors can monitor biomarkers specific to a patient's condition, such as hormone levels or disease markers, and adjust drug delivery accordingly[82]. This approach is increasingly used in oncology, where personalized drug regimens are designed based on the genetic and molecular profile of tumors[83].

Customized Dosage Adjustments: In chronic disease management, biosensors can help fine-tune medication dosages

based on real-time data[52, 84]. For example, in the treatment of hypertension, biosensors can monitor blood pressure continuously and adjust medication delivery in response to fluctuations, ensuring optimal blood pressure control while minimizing side effects[85].

4. Advanced Drug Delivery Platforms

Nanoparticle-Based Delivery: Biosensors integrated into nanoparticles can provide targeted drug delivery and real-time monitoring of therapeutic effects[86]. For example, nanoparticles engineered with biosensors can release drugs in response to specific cellular signals or environmental conditions, such as changes in pH or enzyme activity[87]. This approach enhances the precision of drug delivery and reduces off-target effects.

Microelectromechanical Systems (MEMS): MEMS-based drug delivery systems use miniature biosensors and actuators to control drug release at the micro or nanoscale [77]. These systems can be implanted or wearable and offer highly controlled and precise drug delivery[88]. Applications include targeted cancer therapies, where MEMS devices release drugs directly at the tumor site based on detected biological signals[89].

Challenges and Limitations

Despite their potential, biosensors face several challenges in drug discovery and development. One major limitation is the need for extensive validation and standardization to ensure accuracy and reproducibility[90]. Additionally, the integration of biosensors into existing workflows can be complex and may require significant investment in infrastructure and training[91]. Furthermore, the sensitivity of biosensors can be affected by factors such as sample matrix interference and environmental conditions, which must be carefully controlled[92].

Future Perspectives

The future of biosensors in drug discovery is promising, with ongoing advancements in nanotechnology, microfluidics, and artificial intelligence[93]. These innovations are expected to enhance the sensitivity, specificity, and automation of biosensors, making them even more valuable tools in drug development[94]. Additionally, the growing trend toward personalized medicine and the use of biosensors in point-of-care diagnostics will likely drive further integration of biosensors into clinical practice[95].

Real-World Examples of Biosensors in Drug Discovery and Development

Surface Plasma Resonance (SPR) in Target Identification

Surface Plasmon Resonance (SPR) biosensors have been extensively used in drug discovery to study protein-ligand interactions[96]. One notable example is

the use of SPR in identifying inhibitors for the kinase enzyme, which plays a role in cancer progression[44]. SPR was employed to screen a library of compounds, providing real-time data on binding affinities and kinetics[97]. This enabled the identification of several potent kinase inhibitors that later advanced into clinical trials.

Glucose Biosensors in Diabetes Drug Development

Glucose biosensors, commonly used in continuous glucose monitoring (CGM) systems, have been pivotal in the development of antidiabetic drugs[98]. These biosensors enable real-time monitoring of blood glucose levels, allowing researchers to evaluate the efficacy of insulin analogs and other glucose-lowering therapies[99]. The data from these biosensors have been critical in optimizing drug dosing and improving patient outcomes in clinical trials.

Electrochemical Biosensors in Antibiotic Discovery

Electrochemical biosensors have been utilized in the discovery of new antibiotics, particularly in identifying compounds that target bacterial biofilms[100]. For example, researchers used electrochemical sensors to monitor the disruption of biofilms by potential antibiotic candidates[101]. This approach provided rapid feedback on the effectiveness of different compounds, accelerating the identification of novel antibiotics[102].

Quartz Crystal Microbalance (QCM) for Drug-Target Interaction Studies

Quartz Crystal Microbalance (QCM) biosensors measure mass changes on a sensor surface in real time and have been used to study drug-target interactions[103]. In one instance, QCM was used to analyze the binding of small-molecule inhibitors to the HIV-1 protease enzyme[104]. The data obtained from QCM helped researchers understand the binding mechanisms, which informed the optimization of these inhibitors as potential antiretroviral drugs[105].

Nanoparticle-Based Biosensors in Cancer Drug Development

Nanoparticle-based biosensors have been employed in cancer drug development, particularly in the detection of cancer biomarkers and drug efficacy studies[106]. For example, gold nanoparticles functionalized with specific antibodies have been used to detect circulating tumor cells (CTCs) in blood samples[107]. These biosensors provided highly sensitive detection of CTCs, aiding in the evaluation of cancer immunotherapies and targeted therapies in clinical trials[108].

Label-Free Biosensors in Lead Optimizations

Label-free biosensors, such as those using impedance or mass spectrometry, have

been utilized in lead optimization during drug discovery[109]. These biosensors allow for the direct measurement of drug-binding events without the need for fluorescent or radioactive labels[110]. For example, label-free biosensors have been used to optimize small-molecule inhibitors targeting G-protein-coupled receptors (GPCRs), a common drug target[111]. This approach provided more accurate data on binding kinetics and affinities, improving the selection of lead compounds for further development.

Microfluidic Biosensors in Drug Screening

Microfluidic biosensors have been integrated into high-throughput screening platforms to evaluate large libraries of drug candidates[112, 113]. In one example, a microfluidic-based biosensor system was used to screen potential inhibitors of the SARS-CoV-2 virus during the COVID-19 pandemic[114]. This system allowed for the rapid and simultaneous testing of multiple compounds, accelerating the identification of antiviral drugs[115].

Impedance Biosensors in Toxicity Testing

Impedance biosensors have been employed in preclinical toxicity testing to monitor cell viability and cytotoxicity in response to drug candidates[116]. For instance, these biosensors have been used to assess the cardiotoxicity of chemotherapy drugs by measuring the impedance changes in cardiac cells exposed to the drugs[117]. This real-time monitoring helped identify compounds with lower toxicity profiles, improving the safety of drug candidates before clinical trials[118]

Bioluminescence Biosensors in Mechanism of Action Studies

Bioluminescent biosensors, which emit light in response to specific biological events, have been used to study the mechanism of action of drugs[119]. For example, a bioluminescent biosensor was developed to detect the activation of caspases, enzymes involved in apoptosis (programmed cell death)[120]. This biosensor was used to evaluate the efficacy of anticancer drugs that induce apoptosis, providing insights into their mechanisms and effectiveness in killing cancer cells[121].

Wearable Biosensors in Clinical Trials

Wearable biosensors, such as smart watches and patches, have been increasingly integrated into clinical trials to monitor patient responses to drugs in real time[78]. For instance, wearable biosensors that track heart rate, physical activity, and sleep patterns have been used in trials for cardiovascular drugs[122]. These biosensors provide continuous data, allowing researchers to assess the effects

of the drugs on patients' overall health and well-being, leading to more personalized treatment plans [123].

Conclusion

Biosensors are pivotal in the pharmaceutical industry, impacting drug discovery, development, and delivery by providing real-time, sensitive, and accurate data. In drug discovery, they accelerate lead identification by enabling high-throughput screening of drug-receptor interactions. During development, biosensors optimize formulations by monitoring drug stability, bioavailability, and release profiles. In delivery, they ensure precise, controlled release through smart systems and wearable devices, enhancing therapeutic efficacy and patient outcomes. While challenges like sensor stability and integration remain, the future of biosensors, particularly when combined with AI and machine learning, promises to revolutionize personalized medicine and expedite drug development processes.

References

1. Petrova, E., Innovation in the pharmaceutical industry: The process of drug discovery and development, in Innovation and Marketing in the Pharmaceutical Industry: Emerging Practices, Research, and Policies. 2013, Springer. p. 19-81.
2. Blass, B.E., Basic principles of drug discovery and development. 2015: Elsevier.
3. Berdigaliyev, N. and M. Aljofan, An overview of drug discovery and development. Future medicinal chemistry, 2020. 12(10): p. 939-947.
4. Mohs, R.C. and N.H. Greig, Drug discovery and development: Role of basic biological research. Alzheimer's & Dementia: Translational Research & Clinical Interventions, 2017. 3(4): p. 651-657.
5. Dickson, M. and J.P. Gagnon, The cost of new drug discovery and development. Discovery medicine, 2009. 4(22): p. 172-179.
6. Mak, K.-K., Y.-H. Wong, and M.R. Pichika, Artificial intelligence in drug discovery and development. Drug Discovery and Evaluation: Safety and Pharmacokinetic Assays, 2023: p. 1-38.
7. Schneider, G., Automating drug discovery. Nature reviews drug discovery, 2018. 17(2): p. 97-113.
8. Wu, G., Assay development: fundamentals and practices. 2010: John Wiley & Sons.
9. Renaud, J.-P., et al., Biophysics in drug discovery: impact, challenges and opportunities. Nature reviews Drug discovery, 2016. 15(10): p. 679-698.
10. Kulkarni, M.B., N.H. Ayachit, and T.M. Aminabhavi, Biosensors and microfluidic biosensors: from

fabrication to application. Biosensors, 2022. 12(7): p. 543.

11. Parmin, N., et al., Biosensor recognizes the receptor molecules, in Nanobiosensors for biomolecular targeting. 2019, Elsevier. p. 195-210.
12. Turner, A.P., Biosensors--sense and sensitivity. Science, 2000. 290(5495): p. 1315-1317.
13. Szymański, P., M. Markowicz, and E. Mikiciuk-Olasik, Adaptation of high-throughput screening in drug discovery—toxicological screening tests. International journal of molecular sciences, 2011. 13(1): p. 427-452.
14. Matthew, A., Current biosensor technologies in drug discovery. Drug discovery, 2006. 69.
15. Rong, G., S.R. Corrie, and H.A. Clark, In vivo biosensing: progress and perspectives. ACS sensors, 2017. 2(3): p. 327-338.
16. Koo, K.-M., et al., Recent advances in electrochemical biosensors for monitoring animal cell function and viability. Biosensors, 2022. 12(12): p. 1162.
17. Kim, J., et al., Wearable biosensors for healthcare monitoring. Nature biotechnology, 2019. 37(4): p. 389-406.
18. Carreiro, S., et al., Real-time mobile detection of drug use with wearable biosensors: a pilot study. Journal of Medical Toxicology, 2015. 11: p. 73-79.
19. Danese, S., C. Fiocchi, and J. Panés, Drug development in IBD: from novel target identification to early clinical trials. Gut, 2016. 65(8): p. 1233-1239.
20. Colburn, W.A., Biomarkers in drug discovery and development: from target identification through drug marketing. The Journal of Clinical Pharmacology, 2003. 43(4): p. 329-341.
21. Brees, D., et al., Recent Advances in the Development of Novel Biomarkers of Toxicity. Current Topics in Nonclinical Drug Development, 2020: p. 81-120.
22. Adepu, S. and S. Ramakrishna, Controlled drug delivery systems: current status and future directions. Molecules, 2021. 26(19): p. 5905.
23. Ngoepe, M., et al., Integration of biosensors and drug delivery technologies for early detection and chronic management of illness. Sensors, 2013. 13(6): p. 7680-7713.
24. Akolpoglu, M.B., et al., Biosensing–drug delivery systems for in vivo applications, in Advanced biosensors for health care applications. 2019, Elsevier. p. 249-262.
25. Alvarez-Lorenzo, C. and A. Concheiro, Smart drug delivery systems: from fundamentals to the clinic. Chemical communications, 2014. 50(58): p. 7743-7765.
26. Luka, G., et al., Microfluidics integrated biosensors: A leading

technology towards lab-on-a-chip and sensing applications. Sensors, 2015. 15(12): p. 30011-30031.
27. Chadha, U., et al., Recent progress and growth in biosensors technology: A critical review. Journal of Industrial and Engineering Chemistry, 2022. 109: p. 21-51.
28. Kirsch, J., et al., Biosensor technology: recent advances in threat agent detection and medicine. Chemical Society Reviews, 2013. 42(22): p. 8733-8768.
29. Sin, M.L., et al., Advances and challenges in biosensor-based diagnosis of infectious diseases. Expert review of molecular diagnostics, 2014. 14(2): p. 225-244.
30. Brett, C.M., Electrochemical impedance spectroscopy in the characterisation and application of modified electrodes for electrochemical sensors and biosensors. Molecules, 2022. 27(5): p. 1497.
31. Huang, X., Y. Zhu, and E. Kianfar, Nano biosensors: properties, applications and electrochemical techniques. Journal of Materials Research and Technology, 2021. 12: p. 1649-1672.
32. Grieshaber, D., et al., Electrochemical biosensors-sensor principles and architectures. Sensors, 2008. 8(3): p. 1400-1458.
33. Shrikrishna, N.S., et al., Navigating the landscape of optical biosensors. Chemical Engineering Journal, 2024: p. 151661.
34. Khan, R., A. Mohammad, and A.M. Asiri, Advanced biosensors for health care applications. 2019: Elsevier.
35. Pan, S., et al., Small-molecule probes from bench to bedside: advancing molecular analysis of drug–target interactions toward precision medicine. Chemical Society Reviews, 2023. 52(16): p. 5706-5743.
36. Tao, Y., et al., Tailored biosensors for drug screening, efficacy assessment, and toxicity evaluation. ACS sensors, 2021. 6(9): p. 3146-3162.
37. Zhang, X., Q. Guo, and D. Cui, Recent advances in nanotechnology applied to biosensors. Sensors, 2009. 9(02): p. 1033-1053.
38. Chen, Y., et al., Engineering micro–nanomaterials for biomedical translation. Advanced NanoBiomed Research, 2021. 1(9): p. 2100002.
39. Chen, Y., Upconversion nanoparticle based optical biosensor for the detection of molecular biomarkers. 2019.
40. Rasooly, A. and J. Jacobson, Development of biosensors for cancer clinical testing. Biosensors and Bioelectronics, 2006. 21(10): p. 1851-1858.
41. McKeating, K.S., A. Aubé, and J.-F. Masson, Biosensors and

nanobiosensors for therapeutic drug and response monitoring. Analyst, 2016. 141(2): p. 429-449.

42. Nikolovska-Coleska, Z., Studying protein-protein interactions using surface plasmon resonance. Protein-Protein Interactions: Methods and Applications, 2015: p. 109-138.
43. Florinskaya, A., et al., SPR biosensors in direct molecular fishing: implications for protein interactomics. Sensors, 2018. 18(5): p. 1616.
44. Danielson, U.H., Integrating surface plasmon resonance biosensor-based interaction kinetic analyses into the lead discovery and optimization process. Future Medicinal Chemistry, 2009. 1(8): p. 1399-1414.
45. Pettersen, E.O., et al., Targeting tumour hypoxia to prevent cancer metastasis. From biology, biosensing and technology to drug development: the METOXIA consortium. Journal of enzyme inhibition and medicinal chemistry, 2015. 30(5): p. 689-721.
46. Conway, J.R., N.O. Carragher, and P. Timpson, Developments in preclinical cancer imaging: innovating the discovery of therapeutics. Nature reviews cancer, 2014. 14(5): p. 314-328.
47. Ramadan, Q., et al., Pharmacokinetics-on-a-chip: in vitro microphysiological models for emulating of drugs ADME. Advanced Biology, 2021. 5(9): p. 2100775.
48. Zhang, A., et al., Absorption, distribution, metabolism, and excretion of nanocarriers in vivo and their influences. Advances in Colloid and Interface Science, 2020. 284: p. 102261.
49. Qian, L., et al., Nanomaterial-based electrochemical sensors and biosensors for the detection of pharmaceutical compounds. Biosensors and Bioelectronics, 2021. 175: p. 112836.
50. Tripathi, A. and J. Bonilla-Cruz, Review on healthcare biosensing nanomaterials. ACS Applied Nano Materials, 2023. 6(7): p. 5042-5074.
51. Haleem, A., et al., Biosensors applications in medical field: A brief review. Sensors International, 2021. 2: p. 100100.
52. Ahmed, M.U., et al., Personalized diagnostics and biosensors: a review of the biology and technology needed for personalized medicine. Critical Reviews in Biotechnology, 2014. 34(2): p. 180-196.
53. Ates, H.C., et al., Biosensor-Enabled Multiplexed On-Site Therapeutic Drug Monitoring of Antibiotics. Advanced Materials, 2022. 34(2): p. 2104555.
54. Cavallini, A., An implantable biosensor array for personalized therapy applications. 2013, EPFL.
55. Meneghello, A., et al., Biosensing technologies for therapeutic drug monitoring. Current medicinal chemistry, 2018. 25(34): p. 4354-4377.

56. Das, S., et al., Surface plasmon resonance as a fascinating approach in target-based drug discovery and development. TrAC Trends in Analytical Chemistry, 2023: p. 117501.
57. Topkaya, S.N., M. Azimzadeh, and M. Ozsoz, Electrochemical biosensors for cancer biomarkers detection: recent advances and challenges. Electroanalysis, 2016. 28(7): p. 1402-1419.
58. Ramirez-Valles, E.G., et al., A quest for new cancer diagnosis, prognosis and prediction biomarkers and their use in biosensors development. Technology in Cancer Research & Treatment, 2020. 19: p. 1533033820957033.
59. Chen, P., et al., Label-free cytokine micro-and nano-biosensing towards personalized medicine of systemic inflammatory disorders. Advanced drug delivery reviews, 2015. 95: p. 90-103.
60. de Oliveira, W.F., et al., Biomarkers, biosensors and biomedicine. Current Medicinal Chemistry, 2020. 27(21): p. 3519-3533.
61. Wang, L., et al., Highly sensitive electrochemical biosensor for evaluation of oxidative stress based on the nanointerface of graphene nanocomposites blended with gold, Fe3O4, and platinum nanoparticles. ACS applied materials & interfaces, 2015. 7(33): p. 18441-18449.
62. Edmondson, R., et al., Three-dimensional cell culture systems and their applications in drug discovery and cell-based biosensors. Assay and drug development technologies, 2014. 12(4): p. 207-218.
63. Cronk, D. and J. Shearer, High-throughput screening. Drug Discovery and Development-E-Book: Drug Discovery and Development-E-Book, 2012: p. 95.
64. Prével, C., et al., Fluorescent biosensors for drug discovery new tools for old targets–Screening for inhibitors of cyclin-dependent kinases. European Journal of Medicinal Chemistry, 2014. 88: p. 74-88.
65. Jain, K., Applications of biochip and microarray systems in pharmacogenomics. Pharmacogenomics, 2000. 1(3): p. 289-307.
66. Brothers, M.C., et al., Achievements and challenges for real-time sensing of analytes in sweat within wearable platforms. Accounts of chemical research, 2019. 52(2): p. 297-306.
67. Lee, S.P., et al., Highly flexible, wearable, and disposable cardiac biosensors for remote and ambulatory monitoring. NPJ digital medicine, 2018. 1(1): p. 2.
68. Pandey, P.C., et al., Current advancements in transdermal

biosensing and targeted drug delivery. Sensors, 2019. 19(5): p. 1028.

69. Bruen, D., et al., Glucose sensing for diabetes monitoring: recent developments. Sensors, 2017. 17(8): p. 1866.
70. Marks, B.E., et al., Practical aspects of diabetes technology use: Continuous glucose monitors, insulin pumps, and automated insulin delivery systems. Journal of clinical & translational endocrinology, 2022. 27: p. 100282.
71. Ly, T.T., et al., Effect of sensor-augmented insulin pump therapy and automated insulin suspension vs standard insulin pump therapy on hypoglycemia in patients with type 1 diabetes: a randomized clinical trial. Jama, 2013. 310(12): p. 1240-1247.
72. Mu, Y., et al., Advances in pH-responsive drug delivery systems. OpenNano, 2021. 5: p. 100031.
73. Das, S.S., et al., Stimuli-responsive polymeric nanocarriers for drug delivery, imaging, and theragnosis. Polymers, 2020. 12(6): p. 1397.
74. Crucho, C.I., Stimuli-responsive polymeric nanoparticles for nanomedicine. ChemMedChem, 2015. 10(1): p. 24-38.
75. Wilson, G.S. and R. Gifford, Biosensors for real-time in vivo measurements. Biosensors and Bioelectronics, 2005. 20(12): p. 2388-2403.
76. Bian, S., et al., Towards wearable and implantable continuous drug monitoring: A review. Journal of pharmaceutical analysis, 2021. 11(1): p. 1-14.
77. Coffel, J. and E. Nuxoll, BioMEMS for biosensors and closed-loop drug delivery. International journal of pharmaceutics, 2018. 544(2): p. 335-349.
78. Sharma, A., et al., Wearable biosensors: an alternative and practical approach in healthcare and disease monitoring. Molecules, 2021. 26(3): p. 748.
79. Xu, J., Y. Fang, and J. Chen, Wearable biosensors for non-invasive sweat diagnostics. Biosensors, 2021. 11(8): p. 245.
80. Lee, H., et al., Device-assisted transdermal drug delivery. Advanced drug delivery reviews, 2018. 127: p. 35-45.
81. Wong, S.H.D., et al., Smart skin-adhesive patches: from design to biomedical applications. Advanced Functional Materials, 2023. 33(14): p. 2213560.
82. Sim, D., et al., Biomarkers and detection platforms for human health and performance monitoring: a review. Advanced Science, 2022. 9(7): p. 2104426.
83. Gambardella, V., et al., Personalized medicine: recent progress in cancer therapy. Cancers, 2020. 12(4): p. 1009.

84. Wang, J., In vivo glucose monitoring: Towards 'Sense and Act'feedback-loop individualized medical systems. Talanta, 2008. 75(3): p. 636-641.
85. Kario, K., Management of hypertension in the digital era: small wearable monitoring devices for remote blood pressure monitoring. Hypertension, 2020. 76(3): p. 640-650.
86. Cicha, I., et al., Biosensor-integrated drug delivery systems as new materials for biomedical applications. Biomolecules, 2022. 12(9): p. 1198.
87. De La Rica, R., D. Aili, and M.M. Stevens, Enzyme-responsive nanoparticles for drug release and diagnostics. Advanced drug delivery reviews, 2012. 64(11): p. 967-978.
88. Song, Y., J. Min, and W. Gao, Wearable and implantable electronics: moving toward precision therapy. ACS nano, 2019. 13(11): p. 12280-12286.
89. Lee, H.J., et al., MEMS devices for drug delivery. Advanced drug delivery reviews, 2018. 128: p. 132-147.
90. Sardini, E., M. Serpelloni, and S. Tonello, Printed electrochemical biosensors: Opportunities and metrological challenges. Biosensors, 2020. 10(11): p. 166.
91. Dixon, T.A., T.C. Williams, and I.S. Pretorius, Sensing the future of bio-informational engineering. Nature Communications, 2021. 12(1): p. 388.
92. Gavrilaș, S., et al., Recent trends in biosensors for environmental quality monitoring. Sensors, 2022. 22(4): p. 1513.
93. Jin, X., et al., Artificial intelligence biosensors: Challenges and prospects. Biosensors and Bioelectronics, 2020. 165: p. 112412.
94. Ramalingam, M., et al., Impact of nanotechnology on conventional and artificial intelligence-based biosensing strategies for the detection of viruses. Discover Nano, 2023. 18(1): p. 58.
95. Gaba, S., et al., Future advances of artificial biosensor technology in biomedical applications. Talanta Open, 2024. 9: p. 100301.
96. Fang, Y., Ligand–receptor interaction platforms and their applications for drug discovery. Expert opinion on drug discovery, 2012. 7(10): p. 969-988.
97. Huber, W., A new strategy for improved secondary screening and lead optimization using high-resolution SPR characterization of compound–target interactions. Journal of Molecular Recognition: An Interdisciplinary Journal, 2005. 18(4): p. 273-281.
98. Lee, I., et al., Continuous glucose monitoring systems-Current status and future perspectives of the flagship technologies in biosensor research. Biosensors and Bioelectronics, 2021. 181: p. 113054.
99. Zou, Y., et al., Minimally invasive electrochemical continuous glucose monitoring sensors: Recent progress

and perspective. Biosensors and Bioelectronics, 2023. 225: p. 115103.

100. Funari, R. and A.Q. Shen, Detection and characterization of bacterial biofilms and biofilm-based sensors. ACS sensors, 2022. 7(2): p. 347-357.
101. Darvishi, S., et al., Advances in the sensing and treatment of wound biofilms. Angewandte Chemie, 2022. 134(13): p. e202112218.
102. Miethke, M., et al., Towards the sustainable discovery and development of new antibiotics. Nature Reviews Chemistry, 2021. 5(10): p. 726-749.
103. Marx, K.A., Quartz crystal microbalance: a useful tool for studying thin polymer films and complex biomolecular systems at the solution− surface interface. Biomacromolecules, 2003. 4(5): p. 1099-1120.
104. Becker, B. and M.A. Cooper, A survey of the 2006–2009 quartz crystal microbalance biosensor literature. Journal of Molecular Recognition, 2011. 24(5): p. 754-787.
105. Cheng, C.I., Y.-P. Chang, and Y.-H. Chu, Biomolecular interactions and tools for their recognition: focus on the quartz crystal microbalance and its diverse surface chemistries and applications. Chemical Society Reviews, 2012. 41(5): p. 1947-1971.
106. Farka, Z., et al., Nanoparticle-based immunochemical biosensors and assays: recent advances and challenges. Chemical reviews, 2017. 117(15): p. 9973-10042.
107. Huang, X., et al., Triple-enhanced surface plasmon resonance spectroscopy based on cell membrane and folic acid functionalized gold nanoparticles for dual-selective circulating tumor cell sensing. Sensors and Actuators B: Chemical, 2020. 305: p. 127543.
108. Mummareddy, S., et al., On demand biosensors for early diagnosis of cancer and immune checkpoints blockade therapy monitoring from liquid biopsy. Biosensors, 2021. 11(12): p. 500.
109. Lundstrom, K., Cell-impedance-based label-free technology for the identification of new drugs. Expert opinion on drug discovery, 2017. 12(4): p. 335-343.
110. Cooper, M.A., Optical biosensors in drug discovery. Nature reviews Drug discovery, 2002. 1(7): p. 515-528.
111. Lee, P.H., Label-free optical biosensor: a tool for G protein-coupled receptors pharmacology profiling and inverse agonists identification. Journal of Receptors and Signal Transduction, 2009. 29(3-4): p. 146-153.
112. Pereira, S.A., P.J. Dyson, and M.L.M. Saraiva, Miniaturized technologies for high-throughput drug screening enzymatic assays and

diagnostics–A review. TrAC Trends in Analytical Chemistry, 2020. 126: p. 115862.

113. Barata, D., C. van Blitterswijk, and P. Habibovic, High-throughput screening approaches and combinatorial development of biomaterials using microfluidics. Acta biomaterialia, 2016. 34: p. 1-20.
114. Flores-Contreras, E.A., et al., Microfluidics-based biosensing platforms: Emerging frontiers in point-of-care testing SARS-CoV-2 and seroprevalence. Biosensors, 2022. 12(3): p. 179.
115. Tarim, E.A., et al., Microfluidic-based virus detection methods for respiratory diseases. Emergent Materials, 2021. 4: p. 143-168.
116. Pan, Y., et al., 3D cell-based biosensor for cell viability and drug assessment by 3D electric cell/matrigel-substrate impedance sensing. Biosensors and Bioelectronics, 2019. 130: p. 344-351.
117. Wei, X., et al., Efficacy and cardiotoxicity integrated assessment of anticancer drugs by a dual functional cell-based biosensor. Sensors and Actuators B: Chemical, 2019. 283: p. 881-889.
118. Loiodice, S., A. Nogueira da Costa, and F. Atienzar, Current trends in in silico, in vitro toxicology, and safety biomarkers in early drug development. Drug and chemical toxicology, 2019. 42(2): p. 113-121.
119. Love, A.C. and J.A. Prescher, Seeing (and using) the light: recent developments in bioluminescence technology. Cell Chemical Biology, 2020. 27(8): p. 904-920.
120. Torkzadeh-Mahani, M., et al., Design and development of a whole-cell luminescent biosensor for detection of early-stage of apoptosis. Biosensors and Bioelectronics, 2012. 38(1): p. 362-368.
121. Akçapınar, R., et al., Designing of various biosensor devices for determination of apoptosis: A comprehensive review. Biochemical and Biophysical Research Communications, 2021. 578: p. 42-62.
122. Kuehn, B.M., Wearable biosensors studied for clinical monitoring and treatment. Jama, 2016. 316(3): p. 255-257.
123. Bhatia, D., et al., Biosensors and their widespread impact on human health. Sensors International, 2024. 5: p. 100257.