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Employing nano-enabled artificial intelligence (AI)-based smart technologies for prediction, screening, and detection of cancer

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Cancer has been classified as a diverse illness with a wide range of subgroups. Its early identification and prognosis, which have become a requirement of cancer research, are essential for clinical treatment. Patients have already benefited greatly from the use of artificial intelligence (AI), machine learning (ML), and deep learning (DL) algorithms in the field of healthcare. AI simulates and combines data, pre-programmed rules, and knowledge to produce predictions. Data are used to improve efficiency across several pursuits and tasks through the art of ML. DL is a larger family of ML methods based on representational learning and simulated neural networks. Support vector machines, convulsion neural networks, and artificial neural networks, among others, have been widely used in cancer research to construct prediction models that enable precise and effective decision-making. Although using these innovative methods can enhance our comprehension of how cancer progresses, further validation is required before these techniques can be used in routine clinical practice. We cover contemporary methods used in the modelling of cancer development in this article. The presented prediction models are built using a variety of guided ML approaches, as well as numerous input attributes and data collections. Early identification and cost-effective detection of cancer's progression are equally necessary for successful treatment of the disease. Smart material-based detection techniques can give end consumers a portable, affordable instrument to easily detect and monitor their health issues without the need for specialized knowledge. Owing to their cost-effectiveness, excellent sensitivity, multimodal detection capacity, and miniaturization aptitude, two-dimensional (2D) materials have a lot of prospects for clinical examination of various compounds as well as cancer biomarkers. The effectiveness of traditional devices is moving faster towards more useful techniques thanks to developments in 2D material-based biosensors/sensors. The most current developments in the design of 2D material-based biosensors/sensors—the next wave of cancer screening instruments—are also outlined in this article.

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1 Introduction

According to WHO (World Health Organization) data from 2018, cancer was the only factor in 9.6 million deaths, making it the most prevalent cause of death.[1] On a global scale, cancer is said to be the sixth leading cause of mortality. This highlights the critical need to develop fresher, more targeted treatment plans for cancer. Cancer is a broad concept; it describes the sickness that develops after biological alterations that lead to unchecked cell proliferation and division. The majority of cells in the human body have set lifespans and specific functions. Apoptosis, a natural event, is programmed cell death. A cell perishes so that our bodies can replace it with a healthier, more functional one. Cancerous cells are not equipped with the processes necessary for inducing them to cease proliferating and die. Due to their growth within the body, they have the potential to produce tumors, harm the immune system, and lead to other abnormalities that impede the body from operating normally.[2] Early cancer diagnosis is challenging, and patients who have undergone treatment for it frequently relapse. Additionally, it is quite difficult to make precise forecasts about disease prognosis with great certainty. Due to their hazy symptoms and illegible warning indications on scans, some malignancies can be challenging to identify in their

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early stages. Therefore, it is critical to improve predictive models in clinical cancer research by employing multivariate data and high-resolution diagnostic technologies. AI and ML have been speculated to have major implications in medical technology for the detection, progression, and management of diseases. This creative synergy, as shown in Fig. 1, transforms disease detection, monitoring, and therapy by fusing advanced imaging technologies with artificial intelligence algorithms. AI enhances precision medicine by evaluating large datasets, spotting minute patterns, and making previously unheard-of predictions about the course of diseases. AI-enabled imaging technology offers a proactive approach for healthcare by accelerating medical advances from early diagnosis to personalized therapies. This dynamic integration creates the groundwork for a future in which personalized medicine and predictive insights completely transform the current state of healthcare. It also improves diagnostic skills. These technologies are gradually expanding their influence on daily life. By utilizing massive data sets, breakthroughs in AI and ML have paved the way for autonomous illness diagnosis tools that will help to address the hurdles of detecting human diseases at an early stage, particularly in the case of cancer.

The development of neural network based algorithms for ML, a subset of AI, enables computers to learn and solve problems similarly to the human brain.[3,4] In turn, DL is a subset of ML that replicates the human brain's capacity for data processing to recognize objects and images, comprehend languages, find new drugs, advance precision medicine, enhance diagnosis, and support human decision-making. Without human oversight, it can also function and provide suggestions.[5] With the use of an artificial neural network, which is made up of inputs, outputs, and numerous hidden multi-layer networks to improve machine learning handling capabilities, DL can process data, including medical images. Clinical oncology research is now more heavily concentrated on unravelling the molecular basis of cancer by comprehending the intricate biological framework of cell proliferation. To address the current situation of an increasing number of cancer fatalities worldwide, it also concentrates on processing the millions of pertinent instances in big data and cognitive biology. Additionally, the likelihood of early disease prognosis and identification using next-generation sequencing and high-resolution imaging techniques is thought to be improved using AI in clinical decision-making. Creating sizable datasets and utilizing specialized bioinformatic tools could additionally lead to the introduction of novel biomarkers for determining the presence of cancer, the design of novel personalized medications, and the administration of prospective treatment regimens.[6]

Early cancer detection remains a pipe dream, necessitating the creation of cutting-edge, smart materials. Traditional methods, such as physical examinations, biopsies, and blood tests, are laborious to perform and time-consuming. Modern sensors/biosensors have thus been implemented in the field of oncology, and current research has demonstrated that their use has led to the development of more effective detection alternatives and further molecular data. Large-scale data collection has gotten simpler and more affordable as sensors have become more widely available.

Research on the creation of innovative diagnostic and therapeutic approaches for cancer treatments is centered on the swiftly growing field of nanotechnology. It encourages the creation of tools for the treatment of cancer, including ablation, medication delivery, and detection and diagnostics. Early

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Fig. 1 AI-enabled imaging technology advances disease diagnosis and monitoring, transforming healthcare by enhancing precision, early detection, and personalized treatment through sophisticated analysis and interpretation of medical images.

illness detection is essential for providing successful cancer treatment. The early identification of biomarkers is therefore necessary for the effectiveness of cancer treatment. Biomarkers are natural moieties present in tissues, blood, and other bodily fluids that change during pathological processes, such as cancer, and can be tracked to distinguish an infected patient from a healthy individual. Meanwhile, 2D materials, like graphene and MXenes, show potential in biosensing applications, enabling ultra-sensitive detection of cancer biomarkers. Modern-day 2D-nanomaterial advancements have

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given researchers new tools for combating cancer-related problems.[7] Compared to other inorganic materials, 2D materials have the capability to improve selectivity, by coupling with an aptamer, antibody, or cell-specific targeting peptide. 2D materials have the ability to increase deep tissue penetrability, chemical structure and moieties can be adjusted by varying their excitation and emission owing to their exceptional properties. A hydrophilic polymer surface coating can improve their solubility in aqueous solution, thereby increasing their efficacy on the transducer surface. The fact that 2D materials are environmentally benign and sustainable is crucial. Novel functional nanomaterial-based systems for detection with prospective medical applications have been successful because of enhanced methods for completing the surface modification of nanomaterials and control over the preparation of these materials at the nanoscale.

Modern nanomaterial-based platforms for detection, monitoring, and prompt diagnosis enable the quantitative identification of cancer biomarkers with increased precision and specificity.[8] Although several aspects have seen tremendous improvement, healthcare sensors still have major shortcomings. Intuitive health monitoring is now possible because of the growth of artificial intelligence, which has also made it possible to make very accurate forecasts and judgments. A closed-loop system with the capabilities of real-time monitoring, data gathering, digital evaluation, diagnosis, and treatment suggestions may be realized by fusing the internet of things (IoT), AI, and healthcare sensors. AI and its subsets, ML and DL, offer sophisticated data analysis, enhancing diagnostic precision and tailoring treatments. These techniques excel in image recognition, enabling swift and accurate analysis of radiology scans, and facilitating early prediction and detection of cancer. Together, these advancements are revolutionizing early diagnosis and the personalization of therapeutic strategies, promising improved outcomes for cancer patients. This article discusses the recent state-of-art in the prediction of cancer based on artificial intelligence, machine learning, deep learning strategies, and quantum technologies. We have also incorporated a thorough study of advanced 2D nanomaterials employed in the detection of biomarkers for different types of cancers.

2 Artificial intelligence to support health wellness

AI describes computer algorithms or programs that use information to arrive at judgments or predictions. For the computer to assess data and reach a particular judgment, scientists may develop a set of rules, or directions, for the system to follow. John McCarthy first used the phrase "artificial intelligence" in 1956 to refer to "the science and engineering of creating intelligent machines".[9,10] Beginning as a straightforward set of "if, then" principles, AI has developed over the years to include complex, hybrid algorithms that function comparably to the brain of a person.[9] Today, AI is an innovative and quickly developing paradigm that takes into account various scientific domains, including those concerned with handling the affairs of patients with cancer.[10,11] AI can be viewed as a generic term to describe computer algorithms that demonstrate a machine's capacity to discover trends and correlations from an adequate number of realistic representations and to apply this knowl-

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edge to enhance the prevailing strategy for the procedure of making decisions in a particular field.[11]

AI-powered forecasting algorithms are now a vital part of cancer treatment. By recognizing the risk variables, predictive models can determine a person's likelihood of developing a specific cancer. AI can identify people who are at a greater risk of catching the disease ahead of it spreading. This makes it possible for medical experts to closely monitor these patients and take prompt action as and when required.[12] Intelligent tools for early disease prediction, effective screening, and ongoing monitoring are made possible by the application of AI, ML, and DL approaches, as shown in Fig. 2. These techniques make use of data patterns to predict possible health hazards, expedite the diagnostic procedure, and offer patient monitoring in real time. The combination of AI, ML, and DL provides proactive insights for healthcare professionals, leading to a paradigm shift in the field towards personalised and preventive medicine and ultimately improving the overall effectiveness of illness management.

In comparison with other ailments, cancer has the greatest number of clinically significant variations and numerous multi-modal therapeutic choices, in part due to developments in translational studies and the execution of clinical trials.[13] Given the broad spectrum of malignancies and the diversity of observed manifestations, oncology may have the highest demand for individualized therapy. To take advantage of inherent data richness of the cancer sector, AI developers rely on the trifecta of computational methods, databases, and computing resources. To achieve the degree of precision that oncology strives for, each of these AI principles must be expanded beyond existing limitations. AI algorithms have been used to detect circulating tumor cells (CTCs) in patients with esophageal cancer, and the results showed that the use of a convolutional neural network (CNN)-based AI for CTC detection was effective.[14] In addition, further molecular characterization of the CTCs might enhance the possibility of using these cells to distinguish clinically significant and non-significant, indolent cancers. Identifying different subsets of CTCs, for example, distinguishing between dormant and proliferative CTCs and CTCs associated with different immune cells, might be clinically useful.[15]

The simulation algorithms used in medicine are as diverse as the issues they were individually created to address. Since most algorithms are not tied to any one application, significant efforts are being made in both industry and academia to advance the discipline. In several cancer applications, artificial intelligence has already surpassed the crucial barrier of exceeding professional opinion-based assessment platforms, increasing the likelihood that it will be used in therapeutic settings. With this momentum, it is anticipated that approaches based on AI will be further researched and eventually incorporated into practice.[16] It is vital to anticipate how gradual advancement might lead to the shared objective of genuine precision oncology, even although doing so runs the danger of escalating the years of criticism that have offset the field's usually bold promises. Diverse technologies are included in AI,

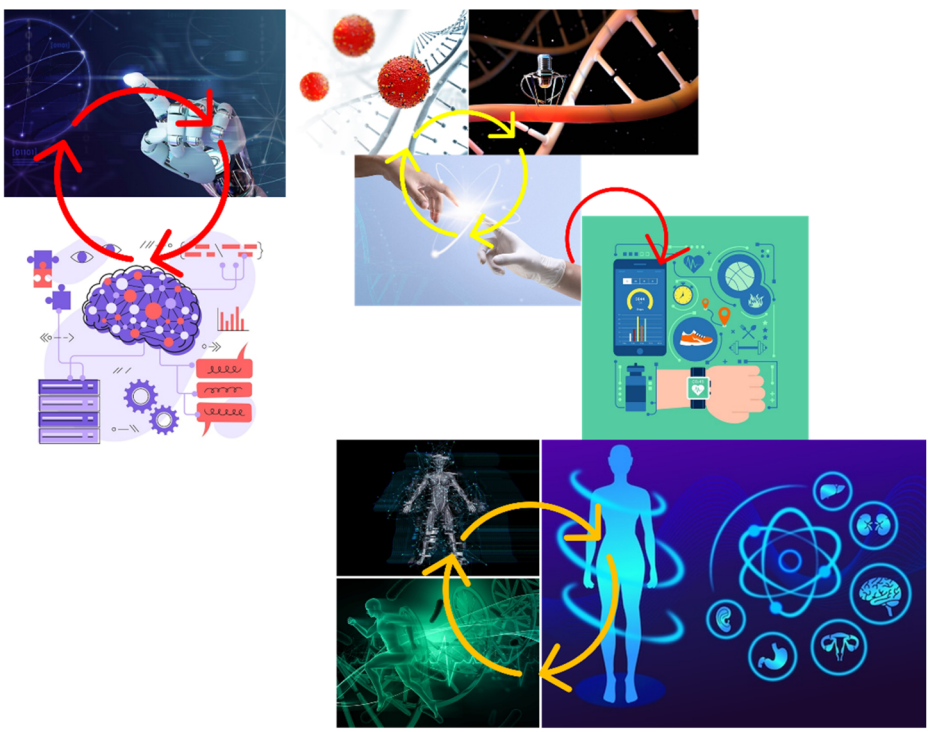

Fig. 2 Utilizing AI, ML, and DL techniques for early disease prediction, efficient screening, and continuous monitoring, advancing healthcare through innovative, data-driven approaches.

which has the unifying goal of computationally simulating human intellect. The internet of things (IoT) has developed over the past ten years, embracing new technologies like ML, DL, supply chains, cloud computing, security, and datasets. This evolution has expanded its industrial acceptance, primarily in the healthcare sector. The goal of ML, a branch of AI, is to find patterns in data and make predictions.

Using ML techniques, the IoT assists in providing an analysis of real-time data and historical data. A branch of ML known as DL involves generating predictions by employing multi-layered neural network algorithms that are motivated by the brain's neurological structure. The neural network design of DL enables the simulations to be scaled linearly with the increasing amount and complexity of data, in contrast to other ML approaches like logistic regression. Difficult computational problems including large-scale picture categorization, natural speech manufacturing, speech recognition, and translation may be solved using DL in this way, which makes it extremely helpful.

2.1 Support vector machine (SVM): a machine learning approach

Support vector machine (SVM) learning, a type of machine learning that maximizes the separation margin (vector), is a potent classification method that has been applied to the categorization or subtyping of cancer genomics.[17] The decision boundary of an SVM, a binary linear classification, is specifically designed to reduce generalization error. It is a very strong and adaptable machine learning model capable of conducting regression, outlier identification, and linear or nonlinear segmentation.

The categorizing feature of SVM has expanded its application in cancer genomics as improvements in high-throughput methods result in the generation of enormous quantities of genomic and epigenomic data. This has led to the exploration of fresh biomarkers, unfamiliar drug targets, and improved comprehension of cancer driver genes.

SVM provides the following benefits:

- Efficient for spaces with multiple dimensions.
- Beneficial for instances in which the number of parameters exceeds the quantity of samples.
- It is also memory viable since it only uses a portion of the learning points (known as support vectors) in the selection function.
- Different kernel functions can be declared for the decision activity, making it customizable. There are common kernels available, but one can also define the kernels.

An increasingly used tool for machine learning problems requiring classification, regression, or novelty detection is the support vector machine. To train a support vector machine, an extremely complicated quadratic programming issue must be solved. Memory limitations prevent the straightforward application of conventional optimization techniques.[18]

There are currently several effective methods for getting around the aforementioned problems for use in the detection, diagnosis, and prognosis of cancer. Particle swarm optimization, also known as quantum-behaved particle swarm, is a new learning algorithm that has been introduced. The active set strategy and least-squares support vector machine (LSSVM) are two further methods that are being explored.[19] These approaches' outputs are evaluated on a dataset related to breast cancer and contrasted with the precise solution model issue.

Fig. 3 illustrates the numerous steps taken in the construction of a system for categorization. The feedback arrows make it clear that these processes are interdependent. They are interconnected, and based on the outcomes, one may go back and rebuild earlier stages to enhance the performance.

Support vector machines have several drawbacks, including over-fitting when selecting kernel functions and regularisation terms if the total amount of parameters is much more than the quantity of samples. It also limits the probabilistic anticipation that is not directly provided by SVMs; instead, they are computed *via* a costly five-fold cross-validation method.[20] Three challenges must be overcome when utilizing the SVM for cancer screening: selecting the best kernel function, selecting the ideal input feature subset, and determining the ideal kernel parameters. These difficulties are important since selecting a feature subset affects the appropriate kernel settings and *vice versa*.

The choice of features is a crucial consideration when creating categorization systems. To have a decent prediction model with a less computationally exorbitant model, it is preferable to restrict the amount of input characteristics in a classifier for a more profound manner of prediction. The development of a model that can manage all three challenges at once is a crucial challenge that will require more study in the field of cancer.[21]

2.2 Neural networks: a deep learning approach

Like the neural networks of humans, artificial neural networks (ANNs) provide a solid method for addressing the problem of categorization and predicting issues. An ANN is a mathematical framework inspired by the structure and functionality of natural neural networks. In neural networks, there are input and output layers in addition to hidden layers that (in the majority of situations) convert the input into something the output layer can utilize. A neural network that is used to detect cancer goes through two stages: training and validation. The network is first trained with the help of a pre-determined dataset. The network is then evaluated to identify the categories of a new dataset after the relative weights of the links between neurons are adjusted.[22]

To derive non-linear, entwined, and relevant characteristics from enormous and high-dimensional data, DL uses ANNs. Millions of tightly coupled computational neurons grouped into successive layers make up a deep neural network. A neuron is linked to neurons in the layer beneath it, which is where it obtains its data, and neurons in the layer above it, to which it transmits data, throughout every layer.[23] A neural network supplies every training specimen with an established ground truth to its layer of input when given data then passes the knowledge down to all subsequent layers (sometimes

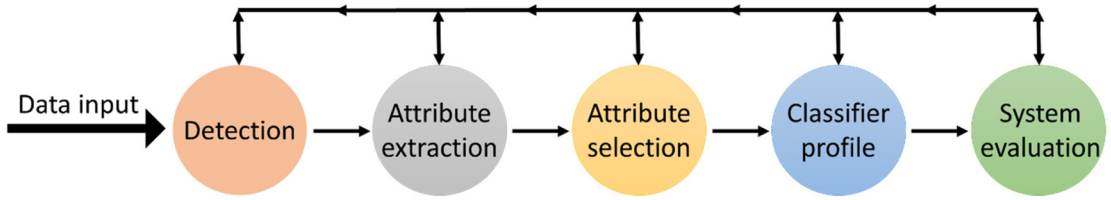

Fig. 3 The fundamental steps in creating a classification system, namely, a support vector machine.

referred to as hidden layers). The forecast is then created by multiplying, dividing, adding, and subtracting these data millions of times until it gets to the output layer.[24]

Every training and label pair sample is passed through a neural network in guided DL datasets while the network's weights and cutoffs are changed to bring the predicted value closer to the given label. These learned cutoffs and weights are thawed and applied to forecast the unknown (test) data (Fig. 4). By identifying patterns throughout the whole transcriptome, ML/DL algorithms can go beyond the limits of conventional computational techniques.[25] For example, an ML approach employing whole-transcriptome RNA sequencing data and multiple tumor histories has been found to correctly recognize a cancerous condition and distinguish it from normal cells; it additionally worked well for extremely uncommon cancer types and showed utility for identifying the site of tumor formation.[26]

Screening efforts have increased survival in several cancer groupings but choosing patients and risk differentiation remain major obstacles. Additionally, there are worries that the COVID-19 pandemic may put pressure on pathologists and radiologists owing to the shortage of diagnostic staff.[27] The use of neural networks powered by artificial intelligence algorithms may help doctors better diagnose cancer recurrence, investigate, and assess those with symptoms, and screen asymptomatic people at potential risk of cancer.

For instance, Mostafa *et al.* developed multiple convolutional neural network (CNN) models that categorized tumor and non-tumor specimens into their respective cancer kinds or identified them as normal using unorganized gene expression inputs. They constructed three CNN models, namely, 1D-CNN, 2D-Vanilla-CNN, and 2D-Hybrid-CNN, based on various gene anchoring architectures and convolution algorithms. The Cancer Genome Atlas (TCGA) aggregated 10 340 samples from 33 different cancer types and 713 matched normal tissues were used for training and validation of the models. Their models successfully predicted 34 classes (33 malignancies and normal) with great prediction accuracies (93.9–95.0%). Additionally, the research group used a guided saliency approach to interpret one of the models, the 1D-CNN model, and discovered a total of 2090 cancer indicators (108 on average per class). The codes are accessible on

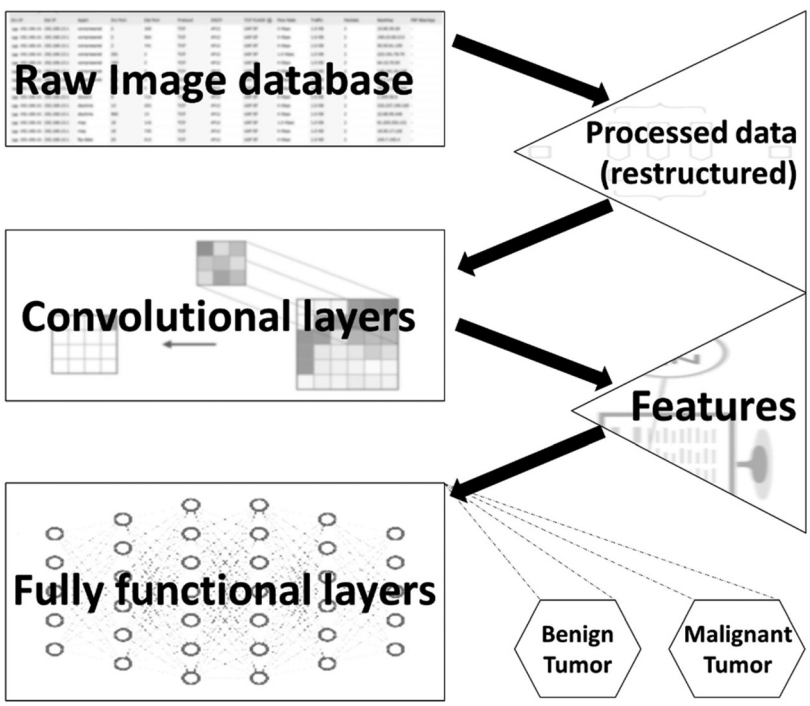

Fig. 4 Flow chart for an artificial neural network for cancer prediction.

the internet. It can be seen that innovative CNN designs can be modulated for precise and concurrent forecasting of cancer/normal and cancer kinds according to gene expression patterns, as well as a novel model interpretation strategy to clarify the biological significance of cancer biomarker genes once tissue-of-origin effects have been considered. Future detection of cancer will be facilitated by the suggested model's simple adaptation because it includes minimal parameters that can be further tuned.

2.3 Transfer learning

It ought to be emphasized that techniques involving assessment at the pixel or patch level frequently call for labelled training sets, wherein the malignant lesions are either highlighted in the pictures or the images only contain the image patches where the lesions are present. Since the annotation of photographs is a time-consuming, laborious procedure that must be carried out by subject-matter specialists and is still rife with inter-reader fluctuation, this significantly adds to the challenge of acquiring acceptable training datasets.[28] Therefore, it is important to reduce the quantity of training these algorithms take and, thus, the quantity of necessary sets. Transfer learning is an efficient strategy for doing this. Transfer learning entails employing a DL-based CNN that has already been trained, maintaining a substantial amount of the underlying CNN parameter tenets, and only tweaking parameters in each of the network's final levels for the new purpose. As a result, it is possible to train a CNN that is focused on analyzing mammograms using input from unrelated, extremely big data sets, such as the natural picture set ImageNet, which contains over a million images.[29–31]

3 Prediction of different types of cancer using artificial intelligence

Cancer has been classified as a varied illness with several different subgroups. Because it promotes potential medical therapy of patients, prompt cancer screening and treatment are essential prerequisites in early cancer research. Numerous research teams investigated the use of ML and DL techniques in the fields of biology and bioinformatics to categorize patients suffering from different types of cancer into high- or low-risk groups. Therefore, the growth and treatment of different cancer types have been modeled after these methods. It is crucial that ML tools can identify essential characteristics in complicated datasets. ANN, SVMs, and DTs are a few of the technologies that are often used to construct prediction models to anticipate a cure for various cancer types.[32] While ML approaches may be used to understand how cancer progresses, a sufficient validity level is required to apply these methods regularly in clinical practice. The ML and DL techniques utilized in the modeling of cancer progression are discussed further. The majority of predictions discussed are associated with certain ML, input, and data management.[33] To predict outcomes for long-term cognitive function and cancer survival, many research teams have developed random-forest-ML and DL models. Understanding the biological processes involved in healthy growth and their impact on the condition of learning tissues is essential in this case.[34] It is consequently extremely difficult for a person to assess the change, but a computer may holistically examine millions of these photographs from numerous modalities to make inferences.[35] The ability to forecast overall survival, relapse risk, or additional results for those with cancer would be beneficial for more individualized treatment plans and patient counselling, as shown in Fig. 5. Various kinds of cancer prevail in society today. Fig. 6 describes certain instances reported by the National Institutes of Health (NIH) where AI models have been used to predict tumours.[36] Discussed further are recent state-of-the-art implementations of AI-ML in the prediction of some of the most pervasive types of cancer.

3.1 Colorectal cancer

A lot of emphasis is currently being paid to the broad application of AI technology in the diagnosis and treatment of, particularly colorectal cancer (CRC), which is the third most prevalent malignancy in both males and females. CRC is regarded as one of the main causes of cancer-related deaths worldwide.[37] Based on recent research, various studies seek to offer in-depth comprehension and evaluation of AI applications in CRC screening, diagnosis, and therapy. With several encouraging findings, current developments in AI systems related to medical diagnosis and therapy are discussed further. CRC is a highly avoidable illness, and frequent screening with AI-assisted methods is a critical first step in reducing the occurrence of this cancer. To boost the identification rate of adenomas, computer-aided detection, and characterization techniques have so far been created. Additionally, robotic surgery and cutting-edge computer-assisted medication administration methods usher in a new era in CRC therapy. Personalized or precision medicine is rapidly advancing in the medical field at the same time. Machine learning systems can change the face of medicine and help with individualized cancer therapy.

A study by Zhi *et al.* sought to find possible biomarkers for CRC metastases and elucidate the pathophysiological processes driving the illness.[38] The study used the five datasets GSE62321, GSE68468, GSE14297, GSE22834, and GSE6988, which all comprised samples of CRC with and without metastatic disease. To determine the differentially expressed genes (DEGs) across the types of samples, three datasets were combined using meta-analysis. For these DEGs, a network based on the interaction between proteins was built. The SVM classifier was then used to choose the prospective genes relying on the centrality of the betweenness technique. The Cancer Genome Atlas database's CRC dataset was utilized to test the SVM classifier's precision. Evaluation of pathway enrichment was done for the SVM-classified gene profiles, through meta-analysis, and 358 DEGs were discovered in total. Signal sequence receptor 3 (SSR3), cullin 7 (CUL7), and cAMP response element binding protein 1 (CREB1) were among the best ten nodes in the network with the most elevated BC

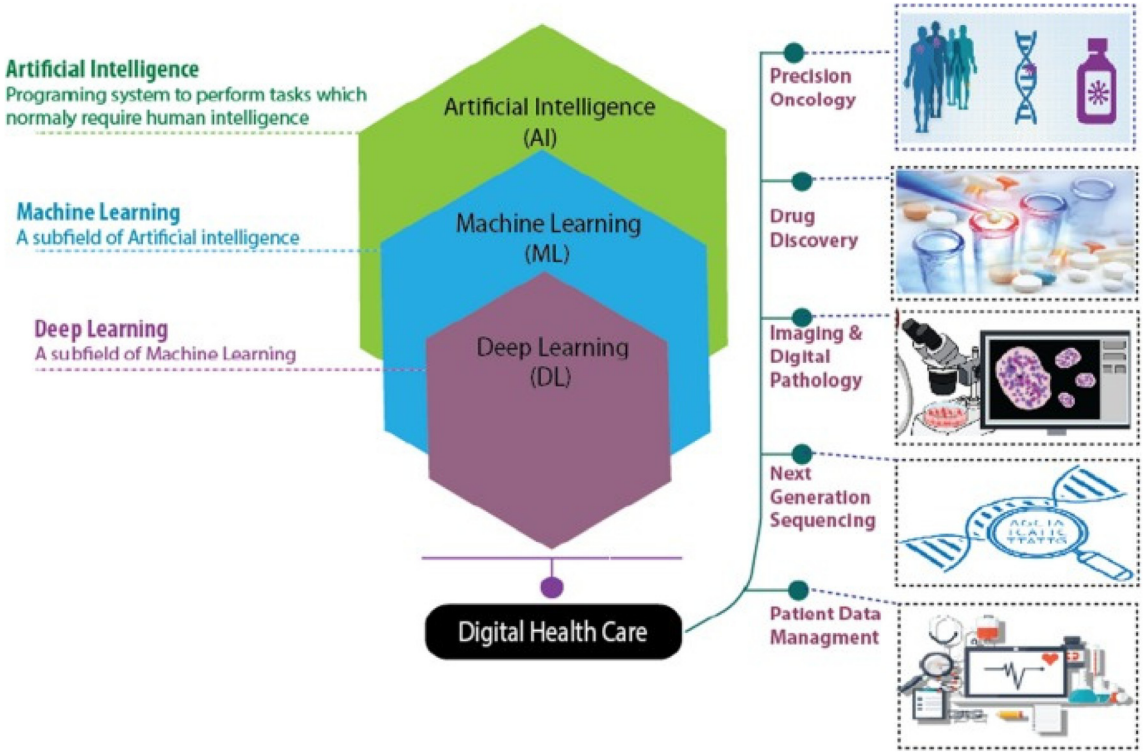

Fig. 5 Applications of AI, ML, and DL in oncology and virtual healthcare to address health-related problems and forecast the best course of action.

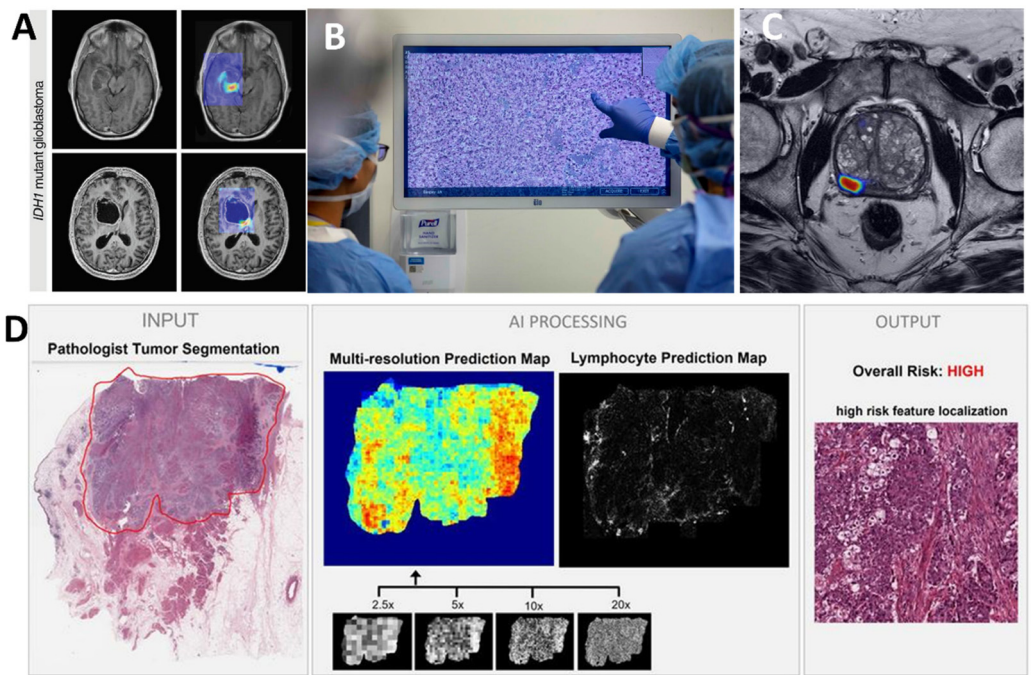

Fig. 6 (a) DL algorithm predicted the existence of *IDH1* in brain tumor; (b) AI-based approach detected cancer within 3 min; (c) AI model highlighted the tumour site of prostate cancer; (d) AI model predicted the spread of a tumor to the lymph nodes (right) based on digital images of a bladder tumor.

values. It was possible to choose between metastatic samples and those that were not by creating the best SVM categorization model. Based on this SVM algorithm, 40 signature genes were found; these were particularly concentrated in different pathways of the body, *e.g.*, SSR3 (processing of proteins in the endoplasmic reticulum), CUL7, FBXO2, UBE2D3 (ubiquitin-

ligase proteolysis), and CREB1 (AMPK signalling system). After successfully establishing the datasets and algorithms, the research groups were successfully able to find the correlation with the SVM-classified genes, such as CUL7, CREB1, and SSR3, and accurately separated the metastatic CRC samples from the normal ones. The identification of these genes, which directly correspond to CRC biomarkers, is a potential breakthrough in the prognosis of the disease.

Using cell-free DNA from tumors, Wan *et al.* suggested a machine-learning technique that had good specificity as well as sensitivity.[39] Their approach could represent a fruitful future line of inquiry for early-stage CRC detection studies. In a different study, Kel *et al.* developed a procedure known as "walking pathways" to find possible methylation DNA biomarkers and then used AI methods to examine cancer-specific regulators.[40]

Bychkov *et al.* used pictures of tumor tissue samples, and mixed convolutional and recursive topologies to create a deep network that could forecast the course of colorectal cancer.[41] Their method is unique in that patient outcomes are predicted without using any intermediary tissue categorization. They examined 420 colorectal cancer patients' digitalized tumor tissue microarray (TMA) data with accessible pathological and prognosis information. The findings demonstrate that in the differentiation of patients into low- and high-risk groups, DL-assisted forecasting of outcomes outperforms the visual histological evaluation conducted by human experts on both TMA and whole-slide data. Their findings imply that cutting-edge DL-based approaches are better able than skilled human observers to glean predictive data regarding the tissue shape of colorectal cancer. With just one TMA spot picture per patient as the input, the research group has created and programmed an ML model to accurately anticipate the five-year disease-specific fate. In this situation, the model resolves to a binary categorization job and generates a survival chance five years after the initial CRC diagnosis. Using the same collection of TMA spot pictures, an identical task was given to three expert pathologists, urging them to predict the probability of survival five years following the CRC diagnoses. The visual risk score was created by the three pathologists with a majority vote. The performances of the pathologists and the automated response were compared thoroughly by the group, and it was found that the automated ML-based approach outperformed the analysis of the experts. The histological evaluation, which was determined by a traditional microscope inspection of the whole-slide cancer sample, was likewise surpassed by the ML-based approach. In a multifaceted survival model, it was found that the digital risk score was unaffected by the histology grade or stage of the illness. This finding suggests that even a little tissue sample from a TMA site can provide important details about the tumor's morphology and the course of the illness. The recommended model can potentially be trained on whole-slide samples and assessed on a comprehensive case series using data from several hospitals and diagnostic labs to create a therapeutically relevant prognostic prediction.

Late diagnosis is a common occurrence with colorectal cancer. The malignancy is typically well-advanced when colorectal cancer is discovered. Early colorectal cancer detection is possible through ML, which is an integral component of AI as discussed before. A twin SVM approach, together with kernel functions, such as polynomial kernels, linear kernels, RBF kernels, and Gaussian kernels, are all addressed in research by Rustam *et al.* as ways to diagnose colorectal cancer.[42] They validated the technique performed for categorizing the colorectal cancer dataset obtained from Al-Islam Hospital in Bandung, Indonesia, by assessing precision and processing times. Results indicated that polynomial kernels had higher precision and longer operating times. With the twin SVM's highest precision, 86% kernels and 0.502 s of computation time are recorded. Rapid diagnosis of colorectal cancer is crucial for treating it as soon as possible before it spreads to different organs of the body. This is challenging, though, as colorectal cancer does not have any distinct symptoms. Utilizing blood tests and age, the twin SVM approach can aid in the detection of colorectal cancer. The polynomial kernel, which generates an accuracy of 86% and requires 0.502 s to execute, is the most suitable kernel for the twin SVM approach in diagnosing colorectal cancer.

Hornbrook *et al.* used ML methods that were capable of recognizing people whose blood counts pointed to a higher risk of colorectal cancer and who should be referred for a colonoscopy.[43] The research aimed to test a colorectal cancer screening model using ML on an insured adult group in the US. 439 female and 461 male eligible colorectal cancer patients with full blood counts before diagnosis were found. The precision of the predictions was assessed using the area under the curve, specificity, and likelihood ratios. The colorectal cancer detection area under the recipient operator feature curve was 0.80 ± 0.01. The odds ratio for linking a high-risk detection score with colorectal cancer was 34.7 (95% CI 28.9–40.4) with 99% specificity. The detection model was more accurate at spotting colorectal tumors appearing on the right side compared to tumors on the left side.

In a study using SVM analysis, Kaul *et al.*[9] sought to classify patients with a significant likelihood of colon cancer resurgence by locating DEGs.[44] Interestingly, they discovered a 15-gene profile that could help predict the prognosis and risk of recurring for those with colon cancer. A reliable and affordable technique for identifying the B-rapidly accelerated fibrosarcoma (BRAF) mutation in the gene, which comprises a valine to glutamic acid substitution at codon 600 (V600E), was proposed by Zhang *et al.* in 2019.[45] The model achieved 100% sensitivity, 87.5% diagnostic selectivity, and 93.8% diagnostic accuracy when used to test for the v-raf murine sarcoma viral oncogene homolog B1 (BRAF) V600E mutation in colorectal carcinomas. This innovative method, which combines a counter propagation artificial neural network (CP-ANN) with near-infrared (NIR) spectroscopy, can assist in discriminating between the BRAF V600E mutant and the unmodified type.

3.2 Breast cancer

The second most frequent cause of death for women worldwide and the most prevalent malignancy among women is breast cancer. Breast cancer develops when the breast's tissues experience aberrant and uncontrollable cell division. These

aberrant cells aggregate into a sizable mass of tissues, which later develops into a tumor. In 2012, 1.7 million new instances of breast cancer were discovered worldwide. With a standard rate of mortality of 12.9 per 100 000, breast cancer is the second leading cause of cancer death, and its prevalence has increased over time. Breast cancer might be effectively handled if found early. Therefore, it is crucial to have effective techniques for identifying the first indications of the disease. The three most crucial imaging techniques for the detection and identification of breast cancer are mammography, ultrasonography, and thermography. One of the most crucial early detection techniques for breast cancer is mammography. The mammography technique is not particularly effective on thick breasts; instead, diagnostic sonography or ultrasound procedures are advised. Thermography can be more effective than ultrasonography for identifying tiny malignant tumors, taking into consideration that small masses of muscle/fat may pass radiographic radiation effectively.

The examination of clinical data and expert opinion is without a doubt the most crucial aspect of image-based diagnosis, but several other aspects might affect such a type of diagnosis. The appearance of noise in pictures, the radiologist's sense of sight skills, insufficient clarity, low contrast, and the radiologist's lack of prior experience are some of the variables impacting image-based diagnosis. Technologies have been designed to build and develop image processing due to inherent issues with images, such as low contrast, disturbances, and lack of identification with the eye. One of the sectors of the healthcare industry with the highest growth right now is medical image processing. The goal of processing images is to employ methods for creating accurate human body pictures that are credible for utilization in diagnostic and treatment procedures. The application of neural networks to image and signal processing increased in the early 1980s. Given how challenging it is to diagnose breast cancer, statistical tools and AI-based techniques could be crucial in this area.

In the past few years, the field of autonomous breast cancer diagnosis in digital mammography and digital breasts has been thoroughly transformed by the AI revolution in computing; this is primarily driven by DL and CNN. Comparing the capabilities of this new technology to those of traditional computer-aided design methods was the first step in the investigation in this field and rapidly illustrated its enormous potential. In recent years, studies of the efficacy of sophisticated, and some commercial, digital-mammography and digital-tomosynthesis breast systems in the field of autonomous breast cancer diagnosis, in contrast to that of skilled breast radiologists, demonstrate that these methods are on par with naturally performing levels in retrospective data sets. It is increasingly obvious that AI will play a significant role in the field of breast cancer screening in the future, despite the need for more research, particularly prospective assessments carried out in the actual screening setting. Although it is unclear how exactly this new contender would change the field, current studies have begun to look at several approaches for its deployment.

In work by Shen *et al.*, it is shown that end-to-end DL models may be extremely precise and possibly easily transferrable across various mammography platforms.[46] As training datasets and computer resources become more readily available, DL techniques offer tremendous potential to significantly increase the reliability of breast cancer diagnosis through screening mammography. Their method is capable of aiding in the eventual creation of better computer-aided design systems that might be utilized as an automatic second reader after producing an initial independent diagnosis, or to help prioritize the most worrisome cases to be reviewed by a radiologist. Other medical imaging issues with a dearth of ROI annotations can be solved using the end-to-end methodology proposed by the group.

Research on breast cancer risk also includes studies on the disease's origin and models for predicting risk based on past data. An essential area of contemporary computational intelligence technology is data-based statistical learning. An innovative concept for the detection of breast cancer is the use of machine learning techniques to forecast and evaluate unknown data. The SVM, combined with the genetic approach, particle swarm optimization, and artificial annealing, creates the enhanced optimization method (GSP_SVM), which is suggested in a study by Dou *et al.*[47] The outcomes demonstrate a very high degree of achievement in categorization, accuracy, *etc*., and other measures. When compared to previous optimization algorithms, it is clear that this technique may effectively help decision-making in auxiliary breast cancer diagnosis, greatly enhancing the diagnostic effectiveness of medical institutions. Subsequently, by contrasting it to alternative algorithms, this research analyses the use of this algorithm in several categories and preliminarily investigates the impact of using it to identify and classify breast cancer in various stages.

Furthermore, a study on the integration of more sophisticated kernel functions for various categories can be done from the standpoint of medical risk to maximize the precision of the identification of malignant tumors. To avoid a major disparity between the two similar types of sample data, medical organizations must simultaneously gather typical sample data for the intended use. Of course, more study of additional high-risk diseases is necessary if we hope to significantly raise the standard of computer-aided disease diagnosis in healthcare facilities. Both soft tissue lesions and calcifications need to be looked for by algorithms for breast cancer diagnosis. For every one of these types of spots, often distinct independent detection algorithms are utilized, and the findings are pooled at the last phase of evaluation, given their extremely varied properties and the generally still-limited datasets used for training. For instance, Lotter *et al.* created a two-stage algorithm in which the image was first scanned and analyzed in patches using two distinct multi-scale CNNs. The production of these CNNs is then gathered to pool jointly across both lesion types and evaluation scales, producing a final categorization estimate.[48] For instance, Samala *et al.* successfully optimized the network for breast cancer detection in both analog and digital mammography with only about 1500 lesion image adjustments, out of which only 500 were analog images and 96 were digital images containing malignancies, beginning from the pre-trained DL-

based CNN AlexNet.[29] The capacity of transfer learning is enormous, especially because more than 1.2 million non-medical natural photos were used in AlexNet's first training.

Becker *et al.* employed a DL-based commercialized image analysis algorithm meant for industry usage, which is not licensed for use in medicine, in other early research, but with comparisons of performance *versus* radiologists rather than against traditional computer-aided design.[49] While the incidence of cancer is still about ten times larger than in a real evaluation set, the algorithm was trained and tested using two distinct datasets: one clinical set with a 50–50% ratio of malignant/control cases, and a second set with a roughly 10%/90% percentage of cases. It was demonstrated that DL algorithms could be taught to identify breast cancer in DM even though they were created for non-medical imaging reasons. Two of the three readers greatly outperformed the algorithm for the highly prevalent set, whereas the algorithm performed on par with radiologists for the low-frequency set.

As previously mentioned, Kooi *et al.*[50] created an AI system for DM assessment that combined hand-crafted characteristics with a DL-CNN. In that study, they evaluated how well the novel system performed in comparison with both a traditional computer-aided design algorithm and how well people performed while analyzing identical DM pictures. The proposed CNN produced a significant improvement in the region under the recipient operating characteristics (ROC) curve (AUC) about the conventional computer-aided design under circumstances where it was granted access to just the image patch and no outside data. The addition of customized features, however, improved the CNN's efficiency.

3.3 Lung cancer

The leading cause of cancer-related mortality both domestically and internationally is lung cancer. Because of their intense daily demands, radiologists and doctors are particularly vulnerable to burnout. Lung cancer also has one of the largest global financial burdens on society. The expenditures of healthcare for Medicare participants were examined; the largest costs, roughly $30 000 over a 15-year time frame, were associated with surgeries. This section analyses the effectiveness of distinct AI models in lung nodule cancer diagnosis, as well as their effectiveness relative to doctors and radiologists, to lessen this cost and reading proficiency. Patients undergoing chemotherapy treatment and radiation therapy paid between $4000 and $8000 per month, with a median longevity of 14 months after diagnosis.[51] Lung cancer is thought to affect 60 people in every 100 000 people in Europe. Its annual healthcare and handling of patients' expenses are anticipated to be 17 000 Euros. In a high-risk group, low-dose computed tomography (LDCT) examination was found to result in a 20% lower death rate than routine chest X-rays, according to the National Lung Screening Trial (NLST).[5] Additionally, low-dose CT has a rate of detection for lung cancer screening that is 2.6 to 10 times higher than chest radiography. The key to lowering lung cancer-related fatalities is early identification, which depends on quick and reliable lung nodule identification and meticulous chest CT scan inspection to confirm the malignancy as this procedure takes a lot of time and effort from radiologists and doctors.

A model with a hybrid approach using LeNet, AlexNet, and VGG-16 was proposed by Toğaçar *et al.*[52] The features from this model—the final fully-connected layer of CNNs—were then fed into several ML-categorization models: SVM, *k*-nearest neighbor (*k*NN), LR, linear discriminate analysis (LDA) and softmax function. Following testing, each model performance indicator associated with these machine learning classifications was compared to the others. Whilst the computational models were being trained, picture augmentation methods were used to increase the classification accuracy of the models. From the dataset, twenty more photos were retrieved. The effective features were then found using the minimal redundancy maximum relevance (mRMR) choice of features approach, which served as the input for the aforementioned hybrid model.

In this study by Nasser *et al.*, the research group created an ANN to determine whether lung cancer existed in the human body.[53] Yellow fingers, stress, chronic illness, exhaustion, allergies, snorting, coughing, difficulty in breathing, trouble swallowing, and chest discomfort were a few of the signs that were utilized to identify lung cancer. They served as input parameters for their ANN, along with other pieces of information regarding that individual. Their ANN was created, trained, and verified using a dataset, namely, "survey lung cancer". An algorithm evaluation revealed that the model had a 96.67% accuracy rate for detecting the existence or nonexistence of lung cancer.

Automated malignant lesion identification, division, and computer-assisted diagnostics all heavily rely on AI techniques. Radiomics and DL-based algorithms seem to hold the greatest potential among the ones now in use. Several indicators have been effectively produced, but the clinical validation and repeatability of the results are still significant issues for contemporary approaches. Other rapidly-developing technology involves DL algorithms, which are acknowledged as an important tool in the discipline of medical imaging research for the identification, classification, and evaluation of lesions.[54] Therefore, a substantial level of classification accuracy is maintained while designing the structure of an artificial neural network.

In their study, Chassagnon *et al.* emphasized the necessity for radiologists to make use of modern technical developments like AI in the field of chest CT for widespread cancer screening and pave the way for the most recent advances in radiology.[1] According to Nasrullah *et al.*'s hypothesis, clinical criteria for the identification of nodules may be integrated with a DL based on employing customized mixed-link network (CMixNet) topologies to lower the rate of inaccurate findings and incorrect diagnoses in the initial phases of lung cancer.[55] It was discovered to have greater sensitivity as well as specificity.

By combining handmade features (HF) with features from a three-dimensional (3D) deep CNN, Shulong Li *et al.* developed an algorithm to identify lung nodule malignancies with a higher level of specificity and sensitivity. This fusion approach

addressed the drawback of HF and proved to have the greatest AUC, specificity, sensitivity, and correctness when compared to the other competing classification models.[56] The amalgamated-convolutional neural network (A-CNN), a framework for fused neural networks created by Wenkai Huang *et al.*, was tested using the Lung Nodule Analysis 16 (LUNA) and Ali Tianchi datasets.[57] With A-CNN, high sensitivity of 81.7% and 85.1% per scan was attained with a mean of 0.125 and 0.25, respectively, of false positives per scan. Wookjin Choi *et al.* created a radionics predictive system for nodules in the lungs with low-dose CT for the early diagnosis of lung cancer.[58] This predictive model's precision was 84.6%, which was greater than that of the lung CT screening reporting and data system (Lung-RADS) and had two CT radiomic characteristics.

Artificial intelligence continues to show promise as a development. Nearly all of the research came to the same conclusion: the use of AI in radiography would enhance patient care by enabling earlier and more precise illness identification and, consequently, a better prognosis. Cancers being overlooked can be decreased thanks to improved classification and examination of a wider range of lung nodules. Thoracic imaging has benefited from the advancement of several artificial intelligence algorithms for a range of diseases. AI algorithms may perform as well as or better than radiologists, but working alongside them to create a more effective system is a more practical option. For AI algorithms to be used in ordinary clinical practice, the absence of retrospective clinical evaluation of these algorithms has to be examined, and appropriate validation methods need to be done in the future.

3.4 Pancreatic cancer

One of the most prevalent malignant tumors of the digestive tract is pancreatic cancer. Pancreatic cancer has been called the "king of cancer" because of its quick development, early metastases, high mortality, and dismal prognosis.[3,4] Surgery is the primary treatment option for people with pancreatic cancer, and its prevalence has recently started to rise. However, some individuals have advanced to late-stage pancreatic cancer at the moment of identification and have missed the best window for aggressive surgery because there are not any distinct clinical signs and serological biomarkers. The outlook and cure rate can thus be improved by early diagnosis and precise staging before surgery. The high death rate and late identification of pancreatic cancer are well known. The inability to accurately diagnose from imaging investigations is the primary contributing factor. It might be difficult to distinguish between benign conditions such as chronic pancreatitis and cancer. Radiological imaging can reveal many radiological manifestations of malignant pancreatic disorders, such as intraductal papillary mucinous neoplasms (IPMN), pancreatic ductal carcinoma, and mucinous cystic neoplasm. Endoscopic ultrasonography (EUS), which has a good responsiveness but low selectivity, has proved to be a reliable tool for identifying pancreatic cancer. EUS performed better on small pancreatic tumors than CT scans and MRIs did.

The purpose of this article does not enable a thorough discussion of neural network topologies; however, Muhammad *et al.* described how ANNs could be utilized to demonstrate the general ideas.[59] An ANN was recently utilized, for instance, by the research group to predict the risk of pancreatic cancer using clinical factors such as age, tobacco usage, alcohol consumption, and ethnicity. Based on individual health records, it was revealed that an ANN with a sensitivity of 80.7%, specificity of 80.7%, and AUC of 0.85 might be utilized for predicting pancreatic cancer. Additionally, for more specialized diagnosis and risk mitigation, the created ANN was able to categorize people into mild, moderate, and severe cancer risk groups. This ANN, which uses easily accessible personal health data, is non-invasive, affordable, and simple to adopt in comparison with current screening methods. It would be easier to apply the ANN in the clinic if its efficacy could be enhanced by further datasets and testing.

In other work by Liu *et al.*, the goal was to create a fast and accurate imaging processing system that could interpret computed tomography (CT) pictures accurately and diagnose pancreatic cancer more quickly.[60] 4385 CT scans from 238 individuals with pancreatic cancer in the dataset served as the training dataset for our study's training method. Additionally, the research group utilized VGG16 to initialize the attribute extraction network. VGG16 was trained in the ImageNet dataset and had 13 convolutional strata and 3 fully connected layers. As experimental data for the validation experiment, serial clinical CT scans from 238 pancreatic cancer subjects were used. These pictures were then fed into the trained faster region-based convolution network (Faster R-CNN) model. 100 pancreatic cancer patients' pictures, totalling 1699, were added for clinical verification. One CT picture was automatically processed by the Faster R-CNN AI in around 0.2 s, which was substantially quicker than the time needed for a diagnosis by a human.

Hsieh *et al.* proposed that those with type 2 diabetes (T2DM) had an increased chance of acquiring pancreatic cancer.[61] To estimate the possibility of pancreatic cancer in T2DM patients, they employed two models acquired from the Taiwan research databases. The pancreatic cancer risk variables that were at hand were incorporated into the prediction models. 97.5% of the data were used as the training set, while 2.5% were utilized as the test set. Python 3.7.0 was used to develop the LR and ANN models. The LR and ANN models' F1, accuracy, and recall were compared. Also evaluated were the prediction models' areas under the receiver operating characteristic (ROC) curves. The measures employed in this study showed that the LR model predicted pancreatic cancer more precisely than the ANN model. The area under the ROC curve for the LR model's prediction of pancreatic cancer was 0.727, which denoted a decent match.

In a study by Qiao *et al.*, 68 hospitalized patients with pancreatic cancer served as the experimental group, whereas 68 hospitalized patients with chronic pancreatitis served as the control group.[62] Both groups had CT imaging. Additionally, a 2D–3D CNN segmentation method for CT image enhancement

processing was suggested by the research group, and an analysis of the diagnostic effectiveness of serum tumor biomarkers paired with CT based on smart algorithms for pancreatic cancer was performed. The analysis showed that the image segmentation algorithm developed in this work outperformed FCN and UNet in terms of algorithm stability and image segmentation efficacy. When CT was used in conjunction with tumor marker detection, the diagnosis of pancreatic cancer achieved the greatest degree of sensitivity and selectivity. Other tumor biomarkers for pancreatic cancer than CA-50, CA-199, and CA-242 however, did not have diagnostic performance assessments in the research. It is necessary to further verify the 2D–3D CNN algorithm's performance at thorough segmentation. Overall, the findings of this investigation provide trustworthy information to support medical diagnoses and patient prognoses for the ailment.

4 Constraints of using AI-based ML/DL methods

Multiple techniques are included in AI, which has the unifying goal of computationally simulating human intellect. The goal of ML is to find patterns in data and make predictions. DL is concerned with generating predictions using complicated neural network algorithms that are motivated by the brain's neurological anatomy. The neural network design of DL enables the models to scale rapidly with the increasing quantity and complexity of data, in contrast to other ML approaches like logistic regression. Due to this, DL is especially helpful for tackling challenging computational issues like the categorization of massive amounts of images, the processing of natural language, and the interpreting and recognition of voices. With growing accessibility and integration of many data types, such as transcriptomic, genomic, and histopathologic data, cancer therapy is moving towards precision medicine. It takes a lot of time and experience to use and analyze a variety of multidimensional data formats for clinical or translational research jobs. Additionally, understanding the meaning of many data types requires more computational resources than understanding a single data type, and training algorithms that are capable of learning from a vast array of detailed properties are required. ML algorithms are increasingly being used to automate these processes and help in cancer detection (identification of the existence of cancer) and diagnosis (characterization of the disease). Excitingly, DL models may be able to make use of this complexity to offer insightful information and find pertinent granular characteristics from a variety of sources.

The potential of artificial intelligence in healthcare is accompanied by several difficulties, such as ethical issues, governance, algorithmic impartiality, data bias, and safety. Significant continuing efforts regarding medical AI are focused on creating ethical guidelines and norms. Healthcare AI developers have been urged by the WHO to make sure that the latest innovations put morality and human rights at the forefront of their development and application. Issues include the black-box nature of AI predictions, their effect on patient encounters and collaborative decision-making, and who is responsible if AI malfunctions and makes inaccurate predictions; an in-depth examination of ethical issues is outside the purview of this review. AI models have special legal and ethical constraints that restrict their widespread use and reliability, including their innate bias when developed on datasets that preferentially leave out underrepresented people. Process and ideological issues, as well as a lack of prospective validating studies, are deterrents to the general deployment of AI; nevertheless, as healthcare reform proceeds, these obstacles are eroding more and more. Living libraries of multi-modal datasets utilized iteratively to enhance clinical simulations in precision oncology by making use of AI may also produce previously unheard-of results.

Creating a sensitive, user-friendly, and cost-effective diagnostic system that effectively distinguishes between false negatives and false positives is a significant hurdle in disease diagnosis. The integration of AI can mitigate error rates by minimizing human bias. Additionally, AI-based systems excel in efficiently managing vast datasets, a task that is challenging for humans, leading to more accurate diagnostic outcomes. With the aid of AI, clinicians may now make appropriate clinical judgments that result in effective and efficient treatment plans; yet, patient data security must always be the first priority.[63] As a result, there should be strong regulations governing the use of patient medical records when implementing AI models in the healthcare industry. In a similar vein, medical professionals have employed AI technology to process and analyse cancer picture data in order to accurately diagnose, characterize, and track cancers—all the while keeping patient data privacy concerns in mind.[64]

Clinicians have benefited from providing a suitable clinical decision to make efficient and efficacious treatment decisions with the help of AI and IoT, however, it is very important to keep an eye on patient data safety. Therefore, the implementation of an AI model in the healthcare sector should have strict laws regarding the handling of healthcare records of patients. Similarly, clinicians have used AI technology for processing and analysis of cancer images for accurate detection, characterization, and monitoring of cancers, while bearing in mind privacy issues regarding patient data.

It is challenging, in reality, to ensure that the characteristics of the training and testing data come from the same distribution since the machine learning approach is data-driven. This is because the data source may differ from the training dataset in a real-world application. A growing number of academics, healthcare experts, scientists and prominent professionals from relevant fields are focusing on the solution to many such issues, which involves changing the computing framework to online perpetual learning, which gives the model the capacity to learn continuously, much like a human being.[14] The integrated working of experts from different fields is important in order to consider any possible aspect of their respective fields in order to develop an efficient model based on AI-driven technologies.

Regulatory limitations regarding data security and privacy, the lack of tagged data, data bias, and unbalanced data prevent AI from being properly used for cancer research. We cannot incorporate a human verification component in the process until a human medical expert collaborates with the AI system. No one believes that AI will ever completely replace the need for medical experts. Future cancer treatments will rely heavily on AI-based precision healthcare. Extremely complicated models that can tailor therapy selection, dosage calculation, monitoring modality and time frame, *etc*., will be powered by living databases. The majority of cancer diagnosis, treatment, and prognosis operations will be automated when artificial general intelligence (AGI) replaces artificial narrow intelligence (ANI).

5 Next generation 2D materials for effective screening of cancer biomarkers

A wide range of sensor applications in medicine, wearable electronics, security, the environment, defence, and agriculture have been transformed by the integration of 2D nanomaterials with IoTs, AI, and ML. The development of graphene, borophene, and MXene as advanced 2D materials (A2M) for the construction of next-generation sensors is due to their distinctive physicochemical properties and surface functions.[65] By cutting down on costs, labor requirements, and contamination, ML-AI-based theoretical modelling has effectively directed the study and development of A2M sensors. A2M sensors provide several advantages over traditional sensing techniques, including being adaptable, portable, intelligent, bio-compatible, mobile, energy-efficient, self-sustaining, point-of-care, and affordable.[66,67] It is rapidly becoming apparent that 2D materials enhance sensors' analytical capabilities by boosting their electrical conductivity and active surface area and/or by offering novel means of interacting with the intended analyte.[68] A2M sensors, which are state-of-the-art and effectively identify cancer biomarkers, are discussed further in this section. In addition to the fundamental issues causing a discrepancy between theoretical forecasts, empirical assessments, in-lab technology, the profitability of their potential solutions, and field-deployable customers are dealt with to realize marketing, ensuring the capacity of future generations to uphold sustainable communities.

5.1 Graphene spectrum materials

Owing to their planar honeycomb nanostructures, high surface-area-to-volume ratio, simplicity of modification, and distinctive chemical and physical characteristics, the bioanalysis use of graphene-based materials (graphene, GO, and rGO) is quickly being extending to microfluidic systems.[69] By immobilizing the antigen, preventing biofouling, boosting the effective surface area, allowing the exchange of electrons across the electrode or the molecule of interest, or simply acting as an electrode, they are frequently utilized to improve the effectiveness of detection.[70,71]

A new nanostructure-based microfluidic device was created by Mata *et al.* for the ultrasensitive monitoring of H_2O_2 produced from cancer cells.[72] The direct drop-casting of exfoliated graphene solution onto the top of the metal-deposited platform done by the research group enabled the integration of the graphene nanosheets into the microfluidic system, as shown in Fig. 7(a). The instrument successfully measured H_2O_2 that was released into human plasma by breast cancer (MCF-7) and prostate cancer (PC3) cells. An excellent LOD of 1 pM in the linear range of 1 pM–10 μM was achieved with simulated visible light conditions; this opens the door for the creation of electrochemical sensors that are non-intrusive and plasmon-aided for fluid biopsies.

The oxidized form of graphene is called graphene oxide (GO), and it contains a lot of oxygen atoms in different shapes, such as carboxyl, hydroxyl, and epoxy groups. To easily and evenly attach antibodies to the surface of the electrode, graphene oxide can be deposited onto the electrode. By merely drop-casting an aqueous solution of graphene oxide onto paper electrodes, Prasad *et al.* created an inexpensive paper-based electrochemical microfluidic system incorporating a composite electrode based on a biomarker for pancreatic cancer, pseudopodium-enriched atypical kinase one (SGK269), PEAK1, for swift quantitative recognition. With a low LOD of 10 pg mL^{-1} and a wide linear range of 10 pg mL^{-1} to 106 pg mL^{-1}, the immunosensor for PEAK1 showed tremendous potential for quick, accurate, and timely identification of pancreatic cancer at the point of care as well as minimal-resource contexts.[73] Reduced graphene oxide (rGO) is an important part of the graphene family. In most cases, reducing graphene oxide by eliminating a lot of oxygenated functional groups yields rGO. It has attracted attention because it is a special transitional state between graphene oxide and graphene. It has a greater prospect to create rGO-based photoactive materials for photoelectrochemical systems because it can increase the productivity of these artificial biological processes and speed up the conveyance of photoactive moieties, both of which are essential advantages over graphene.

Reduced graphene oxide modified $BiFeO_3$ (rGO–$BiFeO_3$) was used by Zhou *et al.* to create a magnetically driven photoelectrochemical sensing (PEC) system for the sensitive detection of prostate-specific antigen (PSA).[74] By pouring an aqueous suspension of rGO–$BiFeO_3$ onto the surface of the FTO electrode, the rGO–$BiFeO_3$-modified FTO electrode was then immediately fitted into the detection cell for PSA detection (Fig. 7(b)). The addition of rGO significantly improved the absorbance of rGO–$BiFeO_3$ during visible light irradiation, easing charge transport and enabling more efficient segregation of photoexcited carriers of charge. The PEC sensing framework demonstrated good photocurrent responses towards target PSA under ideal conditions with an excellent detection limit of 0.31 pg mL^{-1}, demonstrating that the performance of the PEC was noticeably improved with favorable specificity, good repeatability, and adequate precision.

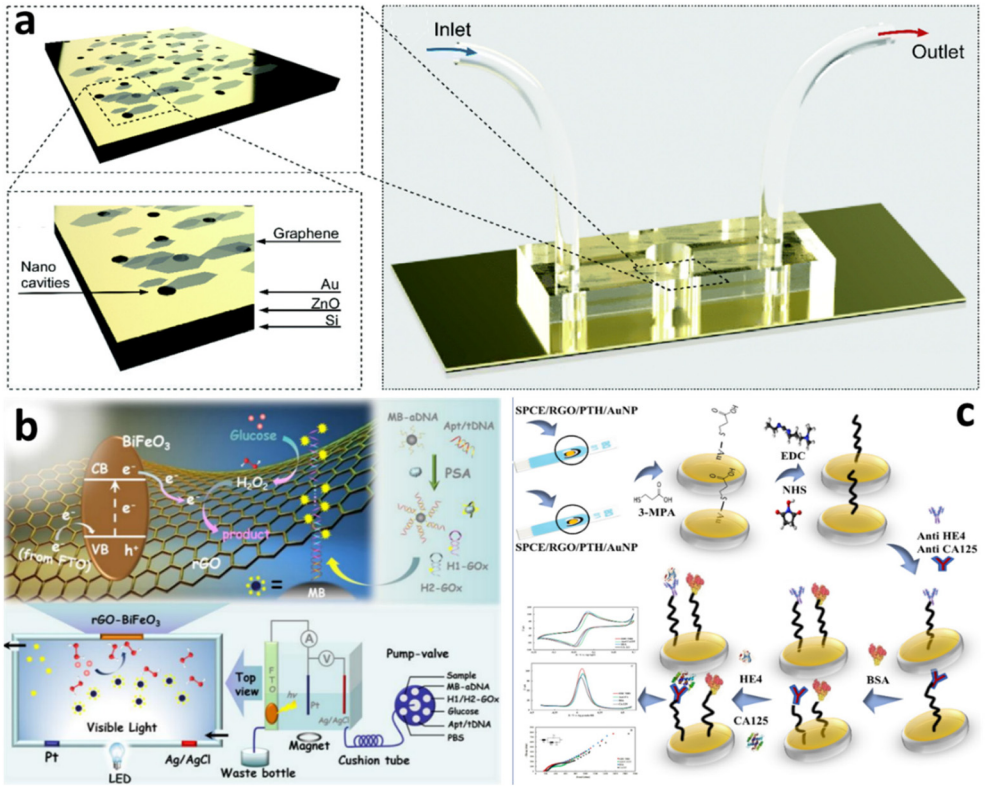

Fig. 7 (a) Schematic of a nanostructured microfluidic device for PEC detection of H_2O_2 (copyright permission RSC 2020); (b) schematic illustration of a magnetically controlled photoelectrochemical (PEC) sensing system (copyright permission Elsevier 2017); (c) the preparation stage of CA125 and HE4 immunosensors.

Human epididymal secretory protein 4 (HE4) and cancer antigen 125 (CA125) are important biomarkers for ovarian cancer diagnosis and advancement screening. In recent work, label-free HE4 and CA125 immunosensors were created by employing reusable screen-printed carbon electrodes modified with reduced graphene oxide, polythionine, and gold nanoparticles for the accurate, quick, and useful measurement of CA125 and HE4.[75] For the electrochemical determination of antigens in different linear ranges, square wave voltammetry (SWV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS) methods were employed by the research group (Fig. 7(c)). For each linear range, significant sensitivity, and a small limit of detection were obtained. The shelf life of the immunosensors was reported to be 16 weeks, while the application durability was 60 days. In nine distinct antigen blends, the immunosensors displayed good selectivity. The sensor's capacity for reuse was tested for up to 9 cycles. The concentrations of HE4 and CA125 in the blood were used to construct the risk of ovarian cancer algorithmic score values, which were then assessed by the research groups in light of ovarian cancer susceptibility. High recuperation was attained using the designed immunosensors and an electrochemical detector to quantify the HE4 and CA125 levels at pg mL^{-1} concentration in blood samples for point-of-care testing. With sensitivity, good specificity, and reliability, these throwaway label-free graphene-based immunosensors can be utilized in point-of-care testing for the quick and pragmatic detection of cancer biomarkers.

The goal of efforts by Singh *et al.* was to create a biosensing platform that was both affordable and expandable for the quick and accurate screening of the cancer biomarker carcinoembryonic antigen (CEA).[76] Here, the research group provided results from the sensitive and focused detection of CEA utilizing biosensing technology based on graphene. On a copper (Cu) substrate, homogeneous, continuous graphene films were produced using the chemical vapor deposition (CVD) process using hexane as a liquid precursor. The films were reported to be large (2.5 1.0 cm^2), single- and few-layers, and single- and continuous-layers. Additionally, CEA antibodies (anti-CEA) were covalently immobilized onto the Cu/PBSE/graphene electrode to further make the sensor specific to CEA. An electrochemical approach enabled the selective and sensitive identification of CEA. The constructed sensor exhibited a linear response under ideal conditions in the physiological range of 1.0–25.0 ng mL^{-1} (normal value 5.0 ng mL^{-1}), displaying a sensitivity of 563.4 ng mL cm^2 with an R^2 of 0.996 and a limit of detection (LOD) of 0.23 ng mL^{-1}. In this approach, one-step electrode manufacturing with a large surface area offers a unique biosensing platform that is light weight, inexpensive, dependable, and scalable for the sensitive

and precise detection of CEA. With the use of this bioelectrode, several other molecules can also be detected successfully as it has recognition components.

For the detection of various types of cancer-affected cells, Patel *et al.* suggested different meta-surface sensor designs, with different kinds of inner and outer gaps by using graphene moieties. When the refractive indices of each of the cell types were examined, it became clear that the cancer-contaminated cell and its respective usual counterparts exhibited considerable changes in optical characteristics. An estimated 80% of the cells in a liquid were cancerous. To create the best design, many construction parameters were used. Several factors, such as the quality factor (Q factor), the sensors' absolute and relative sensitivities, the limit of detection, and the figure of merit (FOM), were examined. For each structural design, the greatest absolute and relative sensitivities were attained. The ideal design of a metasurface with both inner and outer gaps achieves a Q factor and FOM of 13.11 and 3.86 RIU1, respectively, with the lowest limit of detection of 0.17 RIU.

For an accurate early cancer diagnosis, multiplexed biomarkers must be sensitively detected simultaneously. By utilizing an oscillating band-pass filtering array for electrochemiluminescence (ECL) spectrum discrimination, an integrated waveband and potential-resolved ECL platform for multiplexed immunoassay were presented by Xue *et al.*[77] Using nanocomposites of gold nanoparticles/graphene oxide/*N*,*N*′-caproate sodium-3,4,9,10-perylenedicarboximide (AuNPs/GO/PDI), CdSe nanocrystals (NCs), and CdTe NCs as ECL tags, three lung cancer biomarkers—carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and cytokerkeratin 19 fragment antigen (CYFRA21-1)—were detected. The values of intensities from the ECL in the signalling of antibody bio-conjugates were evaluated in one potential scan run with $K_2S_2O_8$ as the co-reactant. The intensity at 649 nm in the waveband-resolved ECL mode was used to rectify the interference from the $O_2/S_2O_8^{2-}$ enriched ECL of the three ECL tags. NSE, CYFRA21-1, and CEA were all measured simultaneously under ideal circumstances with detection limit values of 0.86, 2.6, and 0.53 fg mL^{-1}, respectively.

While graphene-based materials do have significant drawbacks, such as costly synthesis and poor resistance to high temperatures under aerobic circumstances, once the production/integration challenge is addressed, they nevertheless show promising application potential.[69,78] Creating hybrids and composites based on graphene or dotting graphene with nanoparticles are further options for adjusting the electrical characteristics and boosting surface-to-volume ratios for reduced limits of detection.[79]

5.2 MXenes

The optical, electrical, structural, and even biological features of MXenes are just a few of the many traits that distinguish them. The properties of MXenes enable a wide range of applications, with perhaps the most contemporary one becoming in the biomedical industry. Large surface area, hydrophilic functional group metals, and paramagnetic activity are only a few of MXenes' distinctive properties. The rigidity and elasticity of MXenes—both of which are crucial for the creation of thin films as a component of bio-electronic devices—are also influenced by the functional groups on them. The flexibility and variable composition of MXene, a recently discovered multidimensional 2D material, are provided by surface-modified carbide. The typical formula for them is $M_{n+1}X_nT_x$, where n = 1–3. They are composed of strata of early transition metals, interspersed with n layers of carbon or nitrogen (identified as X), and terminating with surface functional groups (denoted as T_x/T_z). High conductance of electricity, exceptional mechanical equilibrium, and great optical characteristics are just a few of the unique qualities that MXenes have to offer. MXenes also have favorable biological characteristics, including a high surface area for drug holding and administration, favorable hydrophilicity for biocompatibility, and additional electronic characteristics for CT and MRI scans. The innovative 2D materials have sparked an increase in research interest due to their appealing physico-chemical and biological compatibility features for use in biomedicine and advanced biotechnology.

Using a platelet membrane, a gold nanomaterial/delaminated V2C nano-sheet (PM/AuNPs/d-V2C)-amended electrode as a substrate of the sensing connection and a methylene blue/aminated metal–organic framework (MB@NH_2-Fe-MOF-Zn) as an electrochemical signaling probe, Lian *et al.* presented a facile and sensitive sandwich-type antifouling immunoassay (Fig. 8(a)).[80] The biosensor has successfully combined the outstanding loading property of NH_2-Fe-MOF-Zn with the high permeability of AuNP-loaded V2C MXene to enhance the sensing efficiency. Additionally, the uniform cell membrane's outstanding antifouling qualities could successfully stop the adsorption of modeled proteins. The acquired anti-fouling biosensor demonstrates outstanding analytical accuracy for the examination of CD44 with a linear range from 0.5 ng mL^{-1} to 500 ng mL^{-1} and is capable of ultrasensitive screening of CD44 and CD44-positive cancer cells in convoluted solutions. The development of additional complicated biosensors using this approach of creating cell membrane-based detection platforms with improved antifouling capability is simple, and the use of cutting-edge biological probes and analytical techniques makes it possible to precisely quantify the biomarkers linked to tumor advancement.

The ECL sensor created by Nie *et al.* is an innovative MXene-derived quantum dot (MQD)@gold nanobone (Au NB) heterostructure (Fig. 8(b)).[81] First, MXene and MQDs were created using a green preparation method that prevented hydrofluoric acid's negative effects on both people and the planet. The MQD@Au NB heterogeneous structure led to a significant increase in the ECL signal. To limit the excess influx of electrons to the conduction band of MQDs, Au NBs could transfer them to themselves owing to the surface plasmon resonance (SPR) effect, which functioned as an "electronic regulator". In the ECL sensing technique, the bright signal of MQDs can be effectively produced and enhanced. The work function of MQDs in the heterogeneous structure with good conductivity was reported to be quite similar to that of Au

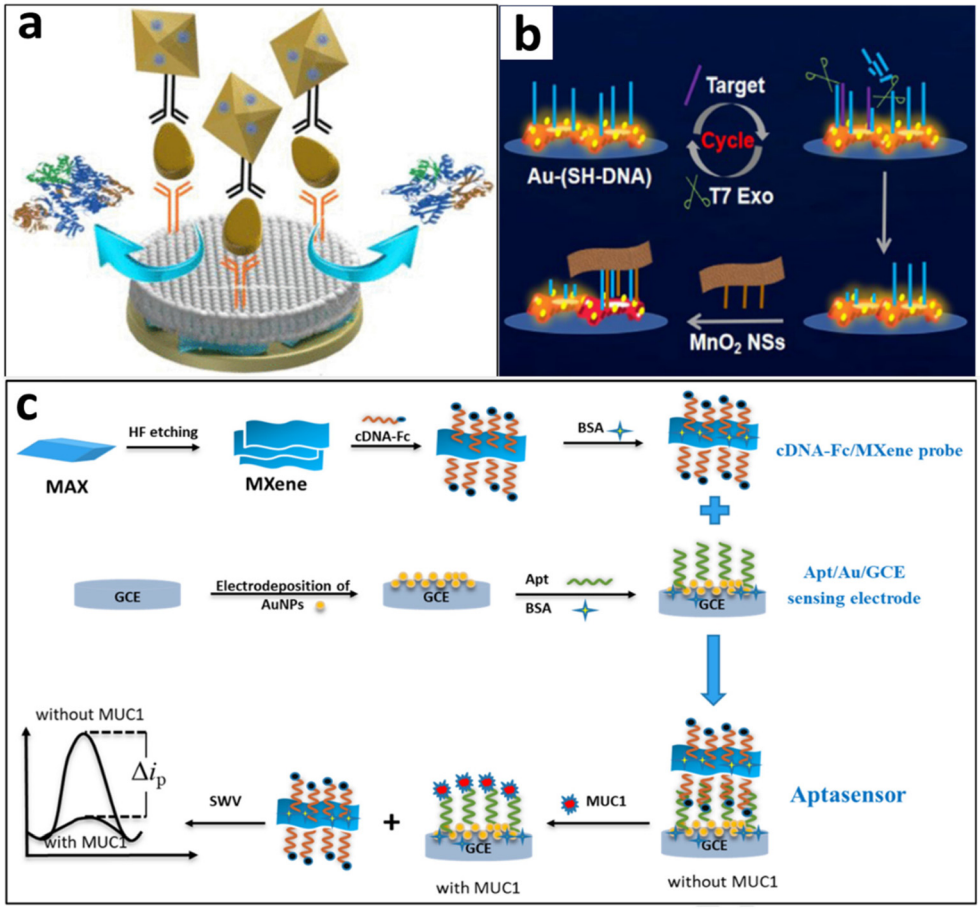

Fig. 8 (a) Sandwich-type anti-fouling immunoassay, reprinted with permission from ref. 80 copyright 2022 American Chemical Society; (b) MQDs based gold nanobone. reprinted with permission from ref. 81 copyright 2022 American Chemical Society; (c) preparation of an electrochemical apta-sensor (copyright permission Elsevier 2020).

NBs. This efficiently suppresses ECL quenching brought on by short-range electron transport between the luminophore and the gold nanomaterial. With the help of the ECL sensing device, miRNA-26a levels in the samples of individuals with triple-negative breast cancer were found. The research group not only offers suggestions for environmentally friendly MXene synthesis but also provides a manual for using the MQD@Au NB heterostructure in the context of ECL detection.

To identify the breast cancer biomarker Mucin1 (MUC1), an adversarial electrochemical apta-sensor built around a cDNA-ferrocene/MXene probe was developed by Wang *et al.* MXene (Ti_3C_2) nano-sheets with a high specific surface area and outstanding electrical conductivity are used as aptamer probe bearers (Fig. 8(c)).[82] To create a cDNA-Fc/MXene probe, ferrocene-labeled DNA that is complementary (cDNA-Fc) was first coupled to the exterior of MXene. After that, Au–S bonds hold the MUC1 aptamer to the electrode. The Apt/Au/GCE sensing electrode carries this designation. An aptasensor made of cDNA-Fc/MXene/Apt/Au/GCE is created once the probe and aptamer are comparable to one another. When MUC1 is detected with the aptasensor, antagonism between the cDNA-ferrocene/MXene probe and MUC1 causes the cDNA-Fc/MXene probe to separate from the detecting electrode, which, in turn, lowers the electrical signal. To determine the quantitative change in bound MUC1, a comparison of the equivalent redox peak current before and following detection was done by the research group. The competitive electrochemical aptasensor that has been proposed has a promising linear range of 1.0 pM to 10 M and a low detection limit of 0.33 pM (S/N = 3).

For the electrochemical detection of tumor cells, gold electrodes were augmented with MXene nanosheets by Vajhadin *et al.*[83] Electrostatic interactions were used to immobilize an HB5 aptamer with remarkable specificity for HER-2-positive cells on the MXene sheets. HER-2 positive flowing tumor cells were magnetically separated using $CoFe_2O_4$@Ag magnetic nano-hybrids attached to HB5 to reduce biofouling with blood components. To properly screen the transfer of electrons of a redox probe and enable accurate cell screening utilizing an alteration in current, sandwich-like arrangements are formed between the magnetically trapped cells and the functionalized MXene electrodes. This label-free MXene-based cytosensor device produced excellent selectivity and sensitivity in the detection of HER2-positive cells in blood samples, as well as a broad linear range of 10^2–10^6 cells per mL and a low limit of

detection of 47 cells per mL. Using $CoFe_2O_4$@Ag magnetic nanohybrids and MXenes for monitoring cancer growth *via* circulating tumor cells in the blood at an affordable price has a lot of potential, as shown by the sensor presented by the group.

In a study by Kumar *et al.*, label-free, extremely sensitive recognition of the cancer marker carcinoembryonic antigen (CEA) was achieved using ultrathin Ti_3C_2-MXene nanosheets that had been systematically enriched with aminosilane (f-Ti_3C_2-MXene) and synthesized using minimally labor-intensive layer delamination techniques.[84] Hexaammineruthenium ($[Ru(NH_3)_6]^{3+}$), which was studied by the research group as a result of the impact of several redox probes on the electrochemical behavior of f-Ti_3C_2-MXene, was determined to be the most effective redox probe for biological sensing. The biomodified Ti_3C_2-MXene that was manufactured had a linear detection range of 0.0001–2000 ng mL^{-1} and a sensitivity of 37.9 A ng mL cm^2 per decade. f-Ti_3C_2-MXene's greater linear range of detection was reported to be higher than that of previously reported pristine 2D nanomaterials by the research group and even it was indicated to be on par with other hybrid 2D nanomaterials. This research opens new possibilities for the creation of MXene-based highly sensitive DNA, enzyme, antibody, aptamer, and cell-based biosensors, which may also have applications in drug administration.

Sharifuzzaman *et al.* reported, for the first time, a one-pot electroplating method for depositing 2D MXene-$Ti_3C_2T_x$ nanosheets (MXNSs) onto conducting electrodes within a short period—termed electroMXenition.[85] Under the influence of a constant applied voltage, the redox process in the colloidal solution produces a charged field that directs the nanoparticles toward a particular electrode interface where they get electroplated. 4-Amino-1-(4-formyl-benzyl) pyridinium bromide (AFBPB), a task-driven ionic liquid, is used as a multiplexed substrate for the significant immobilization of MXNSs and the covalent attachment of antibodies. By examining the advantages of AFBPB coated on MXNSs, a dual interdigitated microelectrode (DIDE), which was micro-prepared and single-masked, was provided by the research group. Due to homogeneous accumulation, the resulting MXNS-AFBPB-film-functionalized biosensor displayed a 7 times greater redox peak current than untreated electrodes. This newly created dual immunosensor displayed accurate and wide linear ranges over five orders of magnitude with detection limit values as low as 0.3 and 0.7 pg mL^{-1}, respectively, for Apo-A1 and NMP 22 as model bladder cancer biomarkers.

5.3 Borophene

The scientific community has paid close attention to 2D nanomaterials because of their exceptional and distinctive features. The higher surface areas, greater chemical and physical activity, and quantum-confinement implications of ultrathin 2D nano-sheets mean that almost all of their atoms are subjected to exterior photonic, catalytic, electronic, and magnetic properties.[86] These ultrathin 2D nanosheets have a wide range of potential applications in biosensors, bio-mimicking resources, carriers of drugs, gadgets, and other fields. The discovery of graphene sparked a significant reaction from the materials world and significantly boosted the use of 2D materials in a variety of industries.

However, many of the material's uses in photodynamic treatment, medical imaging, and electronics are hampered by its zero bandgap. Scientists have been looking for 2D materials with a honeycomb structure resembling graphene, or mono-elemental 2D nano-sheets that are near or in the same group as the carbon element, to create materials with superior qualities that are similar to graphene. Fortunately, the emergence of materials with graphene-like structures, such as square boron nitride (h-BN), transition metal disulphides (TMDs), and mono-elemental 2D materials like stanene, germanene, silicene and borophene may not only overcome the drawback of the graphene's zero bandgap but also possess additional unique attributes that will contribute to new application possibilities. Borophene is generally synthesized using etching methods (Fig. 9).

Mono-elemental nanoparticles have three distinct benefits over conventional 2D materials. (I) They are better suited to current semiconductor innovation. For instance, the primary building blocks for conventional semiconductor substances are silicon and germanium. (II) Because they only contain one element, it is fairly trivial to synthesize high-grade nanoparticles. (III) They are simple for biological systems to break down and metabolize. Another of the mono-elemental 2D nano-materials with high bio-compatibility is black phosphorus. As a starting point for ATP and DNA, it can be broken down to phosphate *in vivo* and contribute to preserving many crucial biological processes.

The mono-elemental 2D materials are also better possibilities application in electron devices, drug administration, optical treatment, biological imaging, and other sectors due to their extremely large specific surface areas and varied levels of reactivity to light, pH, electricity, *etc*.[87] As a mono-elemental 2D material, borophene is comparable to black phosphorus and graphene in that it not only has a substantial surface area and drug-placing ability (borophene: 114%, black phosphorus: 108%, graphene oxide: 200%, other nanomaterials: 10–30%) but also responds to optical, pH, and heat stimuli by responsively releasing drugs. One of the most enigmatic mono-elemental 2D nanomaterials is borophene, whose versatility sets it apart from other mono-elemental 2D materials.[88]

The geometries and attributes of the many allotropes of borophene produced under various settings and processes are diverse. One such fascinating Dirac material, projected to have Dirac cones and unique electrical properties, is *Pmmn* borophene. Since some are extremely anisotropic whereas others are isotropic, there are differences between their properties. This implies that we can govern and manage the conditions of processing to synthesize borophene to satisfy application specifications.[87] There have not been many reports regarding borophene in recent years, and the unique characteristics that have been discovered are only the tip of the iceberg. There remain a lot of subtleties that scientists can investigate further.

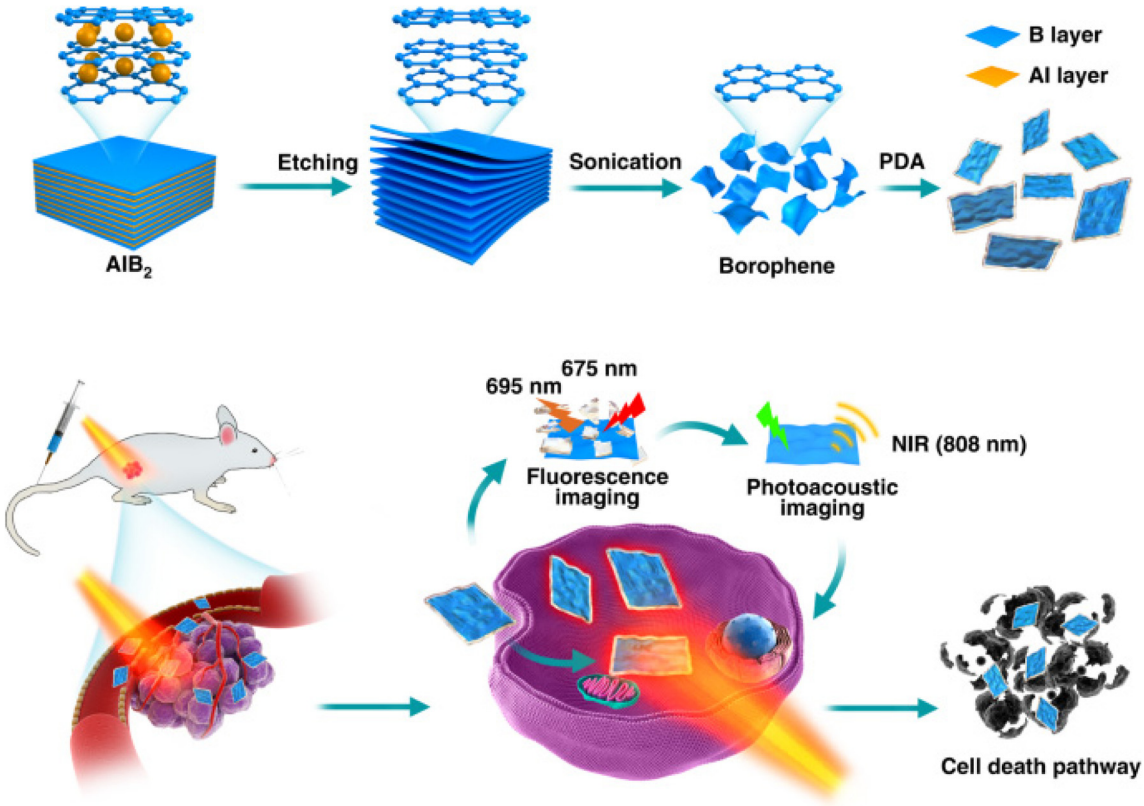

Fig. 9 Borophene obtained by an etching process for guided photothermal therapy.

The extraordinary transverse nano-material 2D borophene is now making an appearance, replacing its forebears in the fields of diagnostic tools, biomedical sensors, energy storage devices, high-performance medical equipment, and supercapacitors. In comparison with other 2D nanomaterials, borophene has powerful attributes and controlled mechanical, optical, thermal, magnetic, and electrical properties, which make it s distinct material. However, efforts to transform conceptual and empirical understanding into practical systems are ongoing. Computational and analytical chemistry investigations are required to optimize borophene with desirable traits to fill the related knowledge gap.

The extraordinary transverse nano-material 2D borophene is now making an appearance, replacing its forebears in diverse fields. In comparison with other 2D nanomaterials, borophene has powerful attributes, and controlled optical, magnetic, thermal, mechanical, and electrical properties. High electrical conductivity brought on by HOMO (highest occupied molecular orbital) destabilization, monolayer nano-engineering, chemistry-focused biological compatibility, and photo-induced characteristics makes borophene suitable for use in sensing, imaging, and treatment of cancer and other theragnostic applications.[89] In addition, the morphs of borophene have helped enable particular binding for DNA sequencing and the construction of powerful medical equipment. The development of efficient biomedical systems using borophene-based futuristic biomedical applications, such as AI, the IoT, and the internet of medical things (IoMT), as well as challenges and opportunities, are extensively being explored. So, based on the investigated properties of borophene for future biomedical uses, this material will be a crucial supporting platform.

5.4 Quantum dots

Quantum dots (QDs) are semiconducting nano-sized crystals with an inter-molecular spacing of roughly 2 to 10 nm. From everyday products like photovoltaic systems, lights, or sign boards to more complex, sensitive, and precise medications intended for human administration, QDs are used in a variety of applications. When utilized as drug carriers for medications, QDs can also be used as diagnostic instruments for ailments when viewed under specific wavelengths of light. The distinctiveness of QDs comes from the fact that distinct QDs exhibit unique emission bands when stimulated under a wavelength of the same range. QDs can be synthesized using a variety of well-established, documented processes that are based on the components employed in their production and the resulting particles are luminous dots.[90] The application of such luminescent nano-dots in the field of nanomedicine is made possible by the simplicity of conjugating QDs with drug delivery carriers, which include micelles, liposomes, polymers, solid lipid nanomaterials, and carbon-based nanomaterials. In

recent years, the use of nanoparticles has been observed in the detection and management of even complex problems such as cancer, diabetes, cardiovascular disease, and neurological disorders. QDs are employed in a variety of nano-biomedical tests for chronic illnesses, including cancer, to determine the severity and location of the disease because of their ability to excite light.

The ability of graphene quantum dots (GQDs) to detect biomarkers using electrochemical biosensing systems has shown promise as a cancer diagnostic tool, particularly for spotting early tumorigenic changes and detecting ultra-low levels of indicators that differentiate between benign and malignant cells. The study by Kalkal illustrates the construction and use of a fluorescence turn-on biosensor for extremely sensitive detection of a small cell lung cancer biomarker using gold nanoparticles (AuNPs) as the energy recipient and biofunctionalized graphene quantum dots as the energy provider (Fig. 10(a)).[91] To detect neuron-specific enolase (NSE), a label-free and effective luminous biosensor that utilizes nano-surface energy transfer (NSET) between anti-NSE/amine-N-GQDs and AuNPs was created. As a result of the NSE antigen, fluorescence turnaround investigations of the anti-NSE/amine-N-GQDs@AuNPs nanoprobe showed a quick reaction time of 16 min, a wide range of linear detection of 0.1 pg mL^{-1} to 1000 ng mL^{-1}, and an incredibly small limit of detection of 0.09 pg mL^{-1}. Additionally, with a median recovery value of 94.69% in real samples, the luminous biosensor demonstrated exceptional performance.

In situ hybridization (ISH) and immunohistochemistry are now the two main test modalities approved for the assessment of HER2, which is a biomarker for breast cancer; these tests are not suitable for point-of-care diagnostics. As a result, a lot of work has been put into creating new alternative approaches. The field of point-of-care device analysis is currently made possible by amazing instruments made possible by "lab-on-a-chip" and contemporary biosensor technology.[92] Different sensing technologies have been applied to detect cancer biomarkers like sensing techniques based on antibody/affibody screening,[93] sensors based on molecularly imprinted polymers (MIPs),[94] magnetic immunoassays, ensembles of nanoelectrodes, cellulose-based assays,[95] polycytosine-based immunosensors,[96] and a nano-shearing based microfluidic device.[97] Each of these approaches is shown to have adequate empirical accomplishments, but owing to their lengthy and arduous procedures, their applicability is still constrained.

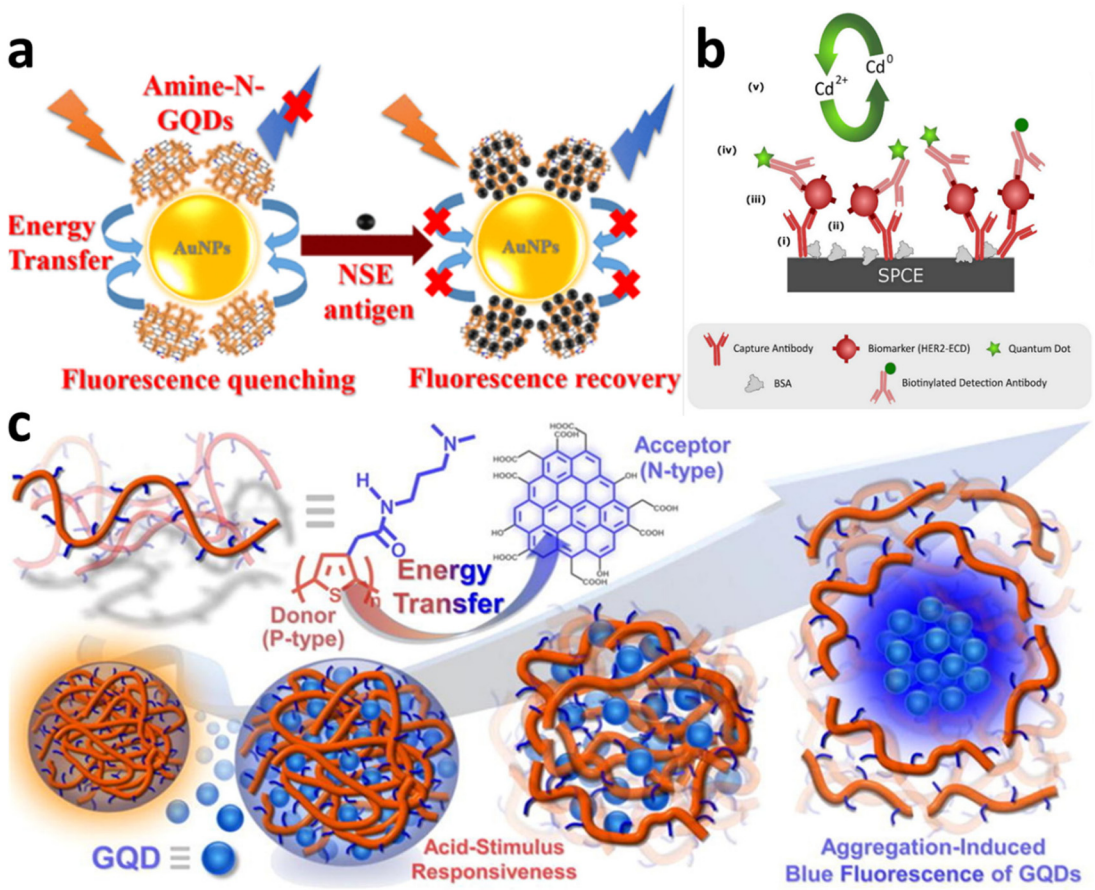

Fig. 10 (a) Mechanism for the detection of cancer biomarkers through gold quantum dots, reprinted with permission from ref. 91 copyright 2020 American Chemical Society; (b) representation of the immunosensor construction and detection strategy (copyright permission Elsevier 2020); (c) energy transfer in quantum dots (copyright permission Elsevier 2023).

The extracellular domain of the human epidermal growth factor receptor 2 (HER2-ECD), a biomarker for breast cancer, is easily and effectively detected using an environmentally friendly immunosensor electrochemically developed by Freitas *et al.*[92] A sandwiched immunoassay was created as a transducer on bare carbon electrodes that had been screen-printed (Fig. 10(b)). Core/shell CdSe@ZnS quantum dots were used as the electro-active tag to monitor the binding process using differential pulse voltammetry (DPV) throughout a 2-h test, with the functional time being less than 30 min. The reported immunosensor displayed acceptable precision and a limit of detection (2.1 ng mL^{-1}, corresponding to a detected amount (sample volume = 40 L) of 1.18 fmol) that was roughly 7 times lower than the established cut-off value (15 ng mL^{-1}). The proposed immunosensor responded linearly to HER2-ECD concentration over a wide range (10–150 ng mL^{-1}). Samples of spiked human serum were used to gauge the effectiveness of the suggested technology. By examining a different biomarker for breast cancer (CA15-3) and various human serum proteins, the validity of the proposed biosensor for the specific screening of HER2-ECD was validated. Another bioassay for the detection of HER2-ECD was reported by the same research group in which they did a thorough evaluation and further investigation of (ultimately) HER2-positive breast cancer based upon the identification of HER2-ECD and cancer cells in samples.[98] MBs and SPCE were used as the transducer surface, core/shell CdSe@ZnS QDs were used as the electro-active labels, and an efficacious immuno-magnetic test with an assay duration of 90 min was created by the research group. DPV was used to assess the Cd^{2+} ions released by the breakdown of the QDs' acid. Utilizing human serum samples, the device's usability was evaluated, and its specificity was verified by examining potential interferent serum components and other cancer indicators. Additionally, the HER2-positive SK-BR-3 breast cancer cell line, HER2-negative MDA-MB-231, and less expressive HER2 (MCF-7) breast cancer cell lines could all be identified using the immuno-magnetic test developed by the group. A signal dependent on the concentration from the SK-BR-3 cell lines was greater than 12.5 times stronger than the signal from the other cells. The bioassay was successful in evaluating tumor markers in cancer patients' serum in a quick, accurate, and focused manner.

Chang *et al.* provided a fresh, clever donor–acceptor (D–A) energy transfer-based method for making water-soluble multimodal pH-responsive hetero-junction nanomaterials as shown in Fig. 10(c).[99] Co-assembled nanomaterials made of fluorescent blue-colored GQD as the recipient with spontaneously formed water-loving tertiary amine-grafted polythiophene (WPT) as the source of energy serve as a very sensitive and effective sensor for the identification of cancer cells. These WPT/GQD nanoparticles show a variety of distinctive physical properties, including a wide range of configurable GQD-loading materials and morphology of particles, very little cytotoxicity in healthy and cancerous cells, and highly receptive pH-responsiveness and swift acid-triggered fluorescent behavior under aqueous acidic conditions. The research group has demonstrated that these characteristics are brought about by GQD's self-agglomeration within the nanomaterials and GQD's consequent agglomeration-induced fluorescence after the nanoparticles are disassembled and the D–A contacts are broken in an acidic environment. An important finding was that WPT/GQD nanomaterials were progressively absorbed by both healthy and malignant cells *in vitro*, as indicated by *in vitro* fluorescent imaging tests. Later, in the acidic microenvironment of the cancer cells, GQD aggregates were specifically formed, and the inside of the cancer cells fluoresced strongly blue; similar events did not happen in healthy cells. Conversely, in cancer or normal cell lines, immaculate WPT or GQD did not show cellular microenvironment-triggered fluorescence shifts. As a result, the recently found water-soluble heterojunction combination could serve as an extremely precise and fluorescent bio-probe for quick screening of cancer cells.

5.5 Transition metal dichalcogenides

Transition metal dichalcogenides (TMDs) have become more prevalent in 2D nanomaterials in recent years. TMDs consist of a surface of transition metal atoms wedged between two strata of chalcogen atoms that interact by inept van der Waals interactions to form a hexagonal lattice, such as MoS_2, NbS_2, WS_2, $TiSe_2$, VSe_2, and WTe_2. TMDs, which resemble graphene in many ways, are less strong and thinner than graphene but have superior electrical conductance due to the presence of a direct gap band. TMDs are semiconductors, hence their bandgap is dependent on their thickness and widens as the thickness narrows. TMDs offer good electrical, optical, and photoluminescence capabilities; TMDs have garnered a lot of interest from a variety of energy, materials, catalysis, electronics, and bio-analysis disciplines.

Because of its better capabilities, MoS_2 is the TMD that is most frequently employed in microfluidic devices. Instead of simply using MoS_2 nano-sheets, metal nanomaterial-decorated MoS_2 nanosheets are typically synthesized and incorporated into microfluidic systems to further improve the electrochemical properties of these materials. These materials not only maintain the unique properties of both MoS_2 nanosheets and metal nanomaterials but also convey novel properties as an outcome of their arrangement. As a new family of 2D materials with intriguing features, TMDs are suited for a wide range of applications in optoelectronics, materials science, electronics, and even biomedical technology. These materials are effective for a variety of applications due to their ease of exfoliation and potential for surface alteration. Modern-day biological applications seem exciting even though they have strong candidates in the fields of materials, electronics, and optoelectronics. They are suitable for dual-model cancer diagnosis due to their comparatively high photothermal coefficients.

Due to their biocompatibility, variety and multifunctionality, tunable bandgap, and superior photoelectric properties, TMDCs are widely exploited for chemical detection, and biosensing, specifically for tumor detection. TMDs have been

intensively explored due to their high quenching efficacy, great dispersion, and simple large-scale preparation. They have a weak quenching capacity and a propensity to agglomerate, which could result in a decline in electrochemical performance. TMDs and other materials in combination are a potential research avenue that can address this deficiency. Microfluidic chips using TMD-based nanocomposites have high surface areas, better electrical conductivity, and catalytic abilities that are projected to become increasingly popular in the future.

TMD-based field-effect sensors are attracting significant interest due to their promising properties, but due to their biocompatibility, variety, and high electrical performance, stability deterioration in liquid environments is essential for FET biosensors to function practically. Ji *et al.* reported the detection of the CA125 biomarker in samples from patients by using a high-performance, self-prepared InSe-FET biosensor.[100] Due to the passivation effect on the InSe channel, the InSe-FET is merged with a homemade microfluidic channel and displays remarkable electrical constancy. InSe-FET biosensors have a detection time of 20 min and are capable of quantitatively detecting the CA125 biomarker in breast cancer in the range of 0.01–1000 U mL^{-1}. For the detection of protein biomarkers, this work offers a generic identification technique (Fig. 11(a)). The indicated biosensor has reported a standard error of <8.78% and can detect a broad range of the antigen CA125, from 0.01 to 1000 U mL^{-1}. Clinical sample recognition has revealed that InSe-FET bio-

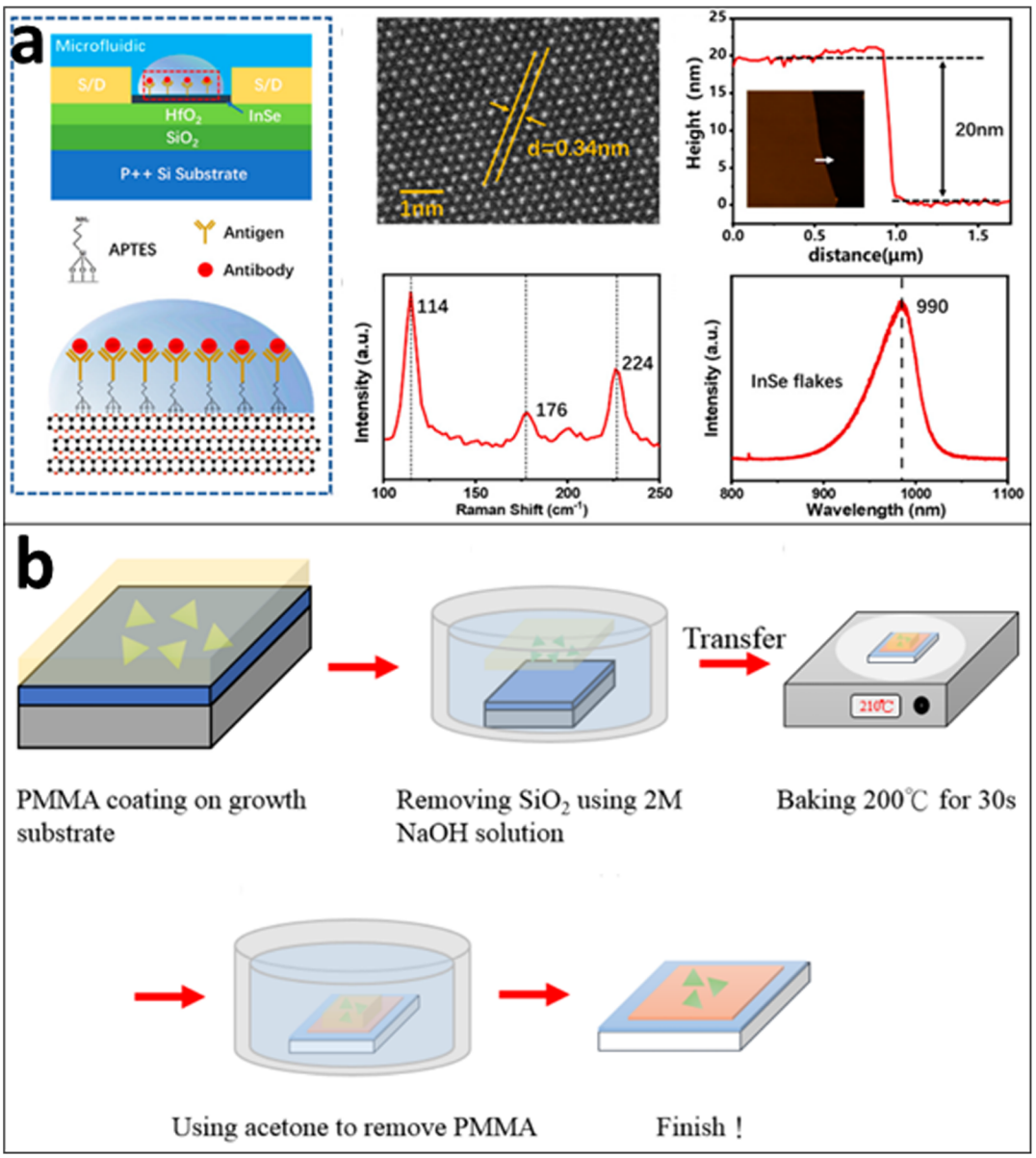

Fig. 11 (a) Schematic of the InSe-FET biosensor for CA125 biomarker detection (copyright permission 2023); (b) preparation of a sensing platform for biomarker detection (copyright permission 2023).

sensors have a lot of potential for real-world uses, including the early detection and prognostic of cancer, the investigation of the pathophysiology of serious ailments, and smart monitoring of health. A low-cost, extremely sensitive PEC biosensor, which may be used to quickly identify different types of lung cancer cell types in hydrologic atmosphere (Fig. 11(b)), was also successfully created. The MoS_2/Cu_2O biochip material created by electrochemical deposition was used by the research group to evaluate the photocurrent response. The amount of oxidized characteristic materials, glutathione and glutathione disulfide, grows along with the detected cancer cell count, and as a result, the photocurrent is reduced. Di-electrophoresis can also be used to detect un-labelled cancer cells, assemble cancer cells into pearl strings, and mould lung cancer cells by using the slope of the admittance values. Different types of cancer cells in the pleural fluid are identified by comparing the coefficients of the linear regression curve with the admittance result and the photocurrent assessment values.

6 Quantum technology for cancer management: a revolution in precision medicine

Cancer continues to be one of the most challenging and prevalent diseases worldwide, with millions of lives affected every year. Despite significant advancements in conventional cancer treatment methods, the need for more effective, precise, and less invasive approaches remains paramount. In this pursuit, the emerging field of quantum technology has begun to offer remarkable potential for revolutionizing cancer management. Quantum technology leverages the principles of quantum mechanics to create innovative tools and techniques with unprecedented capabilities. These quantum-enabled advancements hold promise across various facets of cancer management, from early detection and accurate diagnosis to personalized treatment strategies.

One of the most exciting applications of quantum technology in cancer management lies in early detection. T cells are a type of white blood cell that play a crucial role in the immune response to cancer. Quantum technology has been used to develop T cell-based therapies for cancer management. For example, researchers have used quantum dots to track T cells *in vivo* and monitor their migration to tumors.[101] Quantum sensors, such as superconducting qubit-based detectors and nitrogen-vacancy (NV) centers in diamonds, offer unparalleled sensitivity and precision in detecting minute changes in biomarkers associated with cancer.[102] These sensors can identify cancer-related molecules and genetic mutations at their earliest stages, facilitating timely intervention and significantly improving survival rates. Quantum computing's immense computational power is poised to transform the field of cancer treatment. Traditional algorithms struggle to process the vast amount of genomic and clinical data required for personalized therapies. Quantum computers, with their ability to perform complex calculations exponentially faster, can analyze this data swiftly, helping oncologists tailor treatments to each patient's unique genetic profile. This promises more effective therapies with fewer side effects.

Imaging techniques have long been crucial in cancer diagnosis and monitoring. Quantum-enhanced imaging methods, such as quantum-enhanced MRI and quantum dot-based imaging agents, offer higher resolution, sensitivity, and specificity. These innovations enable non-invasive, real-time tracking of tumor growth, response to treatment, and the detection of metastasis, enhancing our ability to manage cancer progression effectively. Protecting patient data privacy is of utmost importance in cancer management. Quantum communication, utilizing the principles of quantum cryptography, offers unbreakable encryption methods that ensure the security of sensitive medical information.[103] This technology is particularly crucial when sharing patient data for collaborative research and treatment planning.

7 Challenges for 2D materials in effective screening of cancer biomarkers

Next-generation 2D materials, like graphene and transition metal dichalcogenides, present transformative possibilities for the biomedical field, especially in the realm of cancer diagnostics.[104] Their unique electronic, mechanical, and optical properties provide an attractive platform for biosensing applications. However, harnessing their full potential for effective screening of cancer biomarkers presents several challenges:

7.1 Sensitivity and specificity in biomarker detection

2D materials, such as graphene, have displayed enhanced electronic properties, which can potentially aid in the detection of biomolecules. However, tailoring these materials to have a high binding affinity exclusively for specific cancer biomarkers is complex.[105] Ensuring they bind selectively and efficiently without unnecessary interactions with other molecules is crucial for accurate diagnostic outputs. Biological samples, especially fluids like blood or urine, are intricate mixtures teeming with various molecules. For a 2D material-based sensor to be effective, it must pinpoint target biomarkers with remarkable specificity, even when these biomarkers are present in extremely low concentrations amidst this vast molecular landscape.[106]

7.2 Stability in biological environments

Biological matrices present a multifaceted challenge for any diagnostic material. The presence of diverse proteins, salts, and other bio-molecules can lead to unintended interactions, potentially altering the structure or function of 2D materials. Over time, this can degrade the material or diminish its diagnostic efficacy.[107] Ensuring that 2D materials retain their desired properties in such intricate environments is a signifi-

cant hurdle. To enhance their selectivity for specific biomarkers, 2D materials often require functionalization—a process where certain molecules or groups are attached to their surface. However, functionalizing these materials uniformly and efficiently, without compromising their intrinsic properties or introducing defects, remains technically challenging.[108] Moreover, ensuring that these functional groups remain stable and active in biological settings further complicates the matter.

7.3 Economic and scalability concerns

While 2D materials offer promising novel properties, seamlessly integrating them into existing diagnostic technologies is not straightforward. Whether it is embedding them into microfluidic devices, biosensor arrays, or other platforms, achieving optimal compatibility and performance is a meticulous task. This involves not only the physical integration of the material but also ensuring that data acquisition, processing, and interpretation align with the platform's standards.[109] Beyond the intrinsic scientific and technical challenges, the practical aspects of producing and implementing 2D materials in diagnostic settings cannot be overlooked. Scalable production of high-quality, defect-free 2D materials suitable for medical applications is non-trivial. Variations in material quality across batches can significantly impact diagnostic reliability.[110] Furthermore, the costs associated with developing, validating, and deploying 2D material-based diagnostic platforms might be substantial, raising questions about their economic viability and accessibility.

Whilst next-generation 2D materials hold immense promise for revolutionizing the early detection of cancer biomarkers, several multifaceted challenges lie ahead. Addressing these challenges necessitates an interdisciplinary approach, bringing together expertise from materials science, oncology, nanotechnology, and quantum technology. The potential benefits, in terms of enhanced cancer detection and patient outcomes, underscore the importance of continued research and innovation in this domain.

8 Conclusion and future perspectives

The medical field is experiencing a seismic shift with the integration of AI, and nowhere is this more palpable than in cancer imaging. As it stands, most radiologists have recognized the transformative potential of AI-driven therapeutic applications, making it an exciting frontier for innovation and research. Cancer imaging is undergoing rapid evolution. Advancements in AI, especially those rooted in ML, are paving the way for more accurate, efficient, and timely diagnostic procedures. However, as with any technological leap, there are challenges to overcome. One primary constraint is the availability of vast amounts of high-quality imaging data, which are crucial for training and refining ML algorithms. In the absence of such data, the development of new ML techniques may be stymied. However, the silver lining here is the emergence and accessibility of biobanks and open-source repositories. These platforms offer a treasure trove of well-curated, real-world imaging data. By leveraging these data, researchers can bypass some of the data-related limitations that might otherwise impede the development of ML techniques. Additionally, the increasing emphasis on open-source tools presents a democratized approach to algorithm development. Such collaborative platforms can foster greater accessibility and promote collaborations across centers, transcending geographical and institutional barriers. Despite palpable excitement in the field, a note of caution is warranted. The long-term viability and impact of these AI-driven tools in terms of clinical outcomes and cost-effectiveness remain topics of debate. While many algorithms demonstrate high diagnostic accuracy in controlled settings, their real-world effectiveness, scalability, and return on investment remain to be conclusively established. Furthermore, the regulatory landscape for AI in healthcare remains fluid and somewhat nebulous. As AI-driven solutions burgeon, the need for a robust regulatory framework becomes paramount. It is essential to ensure that these tools undergo rigorous scrutiny before clinical deployment, safeguarding patient interests and ensuring clinical efficacy. Education plays a pivotal role in this AI-driven transformation. Radiologists, being at the forefront of this revolution, need a deep understanding of these technologies. They must be equipped with the knowledge to critically assess, validate, and integrate AI solutions into their practice. This is not just about understanding the algorithms but also about appreciating their implications, potential biases, and limitations. It is crucial to incorporate AI for effective prediction, screening and detection in designed systems. We hope that this review can be used as a starting point to address the issues that can arise with the incorporation of AI into the field biosensors for cancer monitoring. AI biosensors have the potential to revolutionize almost every facet of healthcare and hold promising potential for future innovations in the field of oncology. The foreseeable prospects of biomedicine and healthcare are quite promising when it comes to the incorporation of AI into sensor technology. The achievement of tailored healthcare is one of the main advantages of AI-escalated sensor systems. AI algorithms may produce individualized suggestions for illness prevention, early prediction, and management by continually monitoring physiological indicators and unimpeded merging of them with a person's medical history. Additionally, AI-enabled sensors can provide instantaneous tracking of vital signs, allowing for the quick discovery of anomalies and prompt action, which could potentially save lives.

The choice of the 2D material incorporated into the sensing platform is crucial for applications involving chemical and physical sensors. The specificity of the device may change if only perfect and defect-less materials are used. In order to facilitate analyte absorption, anchoring groups may be included on the surface. Although various 2D material-based biomedical devices have shown *in vitro* biocompatibility, the fundamental obstacle to their practical usage lies in their *in vivo* biological

Fig. 12 Revolutionizing cancer care through personalized monitoring with advanced smart technologies such as AI, ML, and DL, enhancing patient-centric approaches for comprehensive and proactive management.

compatibility. It has been demonstrated that mechanical elements with biomimetic qualities or coatings made of biocompatible moieties can lower immune reactions and inflammation. With a few notable exceptions, the majority of 2D sensing derivatives require biomolecule modifications since they are typically unable to detect the target analytes on their own. This feature restricts their applicability in addition to raising production costs due to their unstable nature. Despite these obstacles, a large body of research indicates that 2D nanomaterials have the potential to be effective at cancer detection.

Finally, the integration of AI into cancer imaging, detection, and the emerging realm of circulating tumor cells (CTCs) is not a solitary journey. It necessitates a multidisciplinary approach, bringing together radiologists, oncologists, pathologists, computer scientists, engineers, and data scientists. As CTCs offer a real-time snapshot of a patient's tumor profile, combining their analysis with AI-driven tools can lead to unprecedented accuracy and insights. Cancer management embraces cutting-edge smart technologies, including ML, AI, and DL, to revolutionize personalized monitoring, as shown in Fig. 12. By analyzing vast datasets, these technologies enable precise diagnostics, therapy optimization, risk assessment, and optimized diagnostics. Real-time monitoring, coupled with intelligent algorithms, ensures timely adjustments for optimized therapy outcomes. This synergistic integration of advanced technologies empowers healthcare professionals with data-driven insights, offering personalized care that is adaptive, efficient, and minimizes potential side effects. The fusion of healthcare and smart technologies marks a transformative era in cancer management, fostering tailored, high-precision approaches for improved patient outcomes. In the past, people have made practically all healthcare choices. Using intelligent devices to help or make judgments raises questions about privacy, consent, responsibility, and openness.

The combination of smart technology and nano-enabled AI promises to revolutionize cancer care in the next years. Early cancer detection through non-invasive screenings is made possible by nano-scale sensors that are precisely calibrated for molecular interactions. By incorporating AI algorithms into this nano-framework, cancer risk may be accurately and quickly predicted using extensive data analysis. Connectivity is improved by smart technologies, which can provide individualized insights for customized treatment regimens. With a focus on early identification and individualized therapy, this comprehensive strategy represents a significant turn toward proactive and accurate cancer management. With AI in healthcare, there will probably be a lot of ethical, technological, medicinal, and vocational changes. Healthcare organizations, together with governmental and regulatory agencies, should set up systems to keep an eye on crucial concerns, respond responsibly when necessary, and implement governance procedures to minimize unfavorable effects. Since this is one of the more potent and significant technologies to affect human society, it will take years of careful policymaking and ongoing attention.[28] The convergence of AI and CTCs has the potential to revolutionize early detection, monitor treatment efficacy, and even predict recurrence with more precision than ever before. As the landscape of healthcare monitoring continues its rapid evolution, driven in part by AI and innovative methodologies centered on CTCs, the onus is on these stakeholders to embrace, understand, and guide this transformation in a manner that prioritizes patient welfare above all.

Conflicts of interest

The authors declare that there is no conflict of interest.

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