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Application of artificial intelligence in disease diagnosis

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Abstract
Artificial intelligence plays enormous role in field of disease diagnosis both human and veterinary science. In digital pathology the journey of a glass slides starts to create a virtual image. Telepathology makes this image available to view at any workstation. This saves time and increases accuracy significantly. Virtual reality (VR) is feeling the imaginary world i.e. simulation running in computer in a 3D manner with a collection of technological devices. In recent years Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI TOF MS) has emerged as a potential tool for microbial identification and diagnosis in less time.

Keywords: Disease diagnosis, digital pathology, MALDI TOF MS, telepathology, virtual reality

Introduction
Artificial intelligence (AI) is the simulation of human intelligence processes by machines, especially computer systems. In computer science, sometimes it called machine intelligence, which menace intelligence demonstrated by machines, in contrast to the natural intelligence displayed by humans. Leading AI textbooks define the field as the study of "intelligent agents": any device that perceives its environment and takes actions that maximize its chance of successfully achieving its goals. Colloquially, the term "artificial intelligence" is often used to describe machines (or computers) that mimic "cognitive" functions that humans associate with the human mind. These processes include learning (the acquisition of information and rules for using the information), reasoning (using rules to reach approximate or definite conclusions) and self-correction. Particular applications of AI include expert systems, speech recognition and machine vision and also considered to be as a components of AI [1, 2].

Components of Artificial Intelligence
Learning: There are a number of different forms of learning as applied to artificial intelligence. The simplest is learning by trial and error. For example, a simple computer program for solving mate-in-one chess problems might try moves at random until mate is found. The program might then store the solution with the position so that the next time the computer encountered the same position it would recall the solution. This simple memorizing of individual items and procedures—known as *rote learning*—is relatively easy to implement on a computer [3].

Reasoning: This is to draw inferences appropriate to the situation. Inferences are classified as either deductive or inductive. An example of the former is, "Fred must be in either the museum or the café. He is not in the café; therefore he is in the museum," and of the latter, "Previous accidents of this sort were caused by instrument failure; therefore this accident was caused by instrument failure." The most significant difference between these forms of reasoning is that in the deductive case the truth of the premises guarantees the truth of the conclusion, whereas in the inductive case the truth of the premise lends support to the conclusion without giving absolute assurance. Inductive reasoning is common in science, where data are collected and tentative models are developed to describe and predict future behaviour—until the appearance of anomalous data forces the model to be revised. Deductive reasoning is common in mathematics and logic, where elaborate structures of irrefutable theorems are built up from a small set of basic axioms and rules [1, 4].

Self correction: Problem solving, particularly in artificial intelligence, may be characterized as a systematic search through a range of possible actions in order to reach some predefined goal or solution. Problem-solving methods divide into special purpose and general purpose. A general-purpose method is applicable to a wide variety of problems. One general-purpose technique used in AI is means-end analysis—a step-by-step, or incremental, reduction of the difference between the current state and the final goal. The program selects actions from a list of means-in the case of a simple robot this might consist of Pickup, Putdown, Moveforward, Moveback, Moveleft, and Moveright-until the goal is reached [2, 3].

Types of Artificial Intelligence

Theoretical AI says that Intelligence (be it natural or artificial) has two types

1. Weak/Narrow Artificial Intelligence
2. Strong/ Artificial General Intelligence

1. Weak/Narrow Artificial Intelligence: The principle of Weak AI is that the machines behave as if they are intelligent. Weak AI proves that virtual abilities like thinking, talking, moving can be done by machine if they are programmed in that manner and they lack self-awareness. E.g. In the chess game, the computer can play and move players automatically. The computer does not have thinking ability but in actual it is programmed so that the computer always takes right step. Narrow AI is often focused on performing a single task extremely well and while these machines may seem intelligent, they are operating under far more constraints and limitations than even the most basic human intelligence. Narrow AI is all around us and is easily the most successful realization of artificial intelligence to date. Every sort of machine intelligence that surrounds us today is Narrow AI. Image recognition software, Siri, Alexa (speech recognition devices) and other personal assistants, Self-driving cars, smart phones are some excellent and well known examples of narrow artificial intelligence [2, 4-6].

2. Strong/ Artificial General Intelligence: is an AI system with generalized human cognitive abilities. When presented with an unfamiliar task, a strong AI system is able to find a solution without human intervention. This is the kind of artificial intelligence we see in the movies, like t "Robot" a famous Indian movie or "Her" a award winning Hollywood movie. AGI is a machine with general intelligence and, much like a human being; it can apply that intelligence to solve any problem. The principle of Strong AI is that the machines will do calculations and think itself and will predict the answer in future. Currently, machines are able to process data faster than we can. But as human beings, we have the ability to think abstractly, strategize, and tap into our thoughts and memories to make informed decisions or come up with creative ideas. This type of intelligence makes us superior to machines, it is hard to define because it's primarily driven by our ability to be sentient creatures. Therefore, it's something that is very difficult to replicate in machines [1, 2, 4].

Artificial Intelligence in Disease Diagnosis

The healthcare industry has always been a leader in innovation. The constant mutating of diseases and viruses makes it difficult to stay ahead of the curve, but with the help of artificial intelligence and machine learning algorithms, it continues to advance, creating new treatments and helping humans and animals live longer and healthier lives. This article covers the four basic methods of AI which plays significant role in disease diagnosis [6, 32].

Digital Pathology

Modern pathology practice is moving toward a digital workflow, cumulating in utilizing computer screens to view scanned pathology slides. The term is often assumed to imply or include the processing, compression, storage, printing, and display of such images. A key advantage of a digital image, versus an analogue image such as a film photograph, is the ability make copies and copies of copies digitally indefinitely without any loss of image quality. This process of digitization of glass slides, in combination with the development of specialized software tools to identify and measure events previously observed via a microscope, has brought about the ability for pathologists to utilize digital image analysis on tissue sections. Tissue image analysis, when performed correctly, can result in the generation of tissue-derived readouts that are precise and highly reproducible. It is a subfield of pathology that focuses on data management based on information generated from specimen slides. Digital imaging can be done by three basic camera imaging systems [7-10].

Digital imaging can be classified by the type of electromagnetic radiation or other waves whose variable attenuation, as they pass through or reflect off objects, conveys the information that constitutes the image. In all classes of digital imaging, the information is converted by image sensors into digital signals that are processed by a computer and made output as a visible-light image. For example, the medium of visible light allows digital photography (including digital videography) with various kinds of digital cameras (including digital video cameras). X-rays allow digital X-ray imaging (digital radiography, fluoroscopy, and CT), and gamma rays allow digital gamma ray imaging (digital scintigraphy and PET). Sound allows ultrasonography (such as medical ultrasonography) and sonar, and radio waves allow radar. Digital imaging lends itself well to image analysis by software, as well as to image editing (including image manipulation) [9, 10].

A digital image is represented in a computer by a two dimensional array of numbers, each element of which represents a pixel (picture element). A digital image composed of pixels represents an analogue image converted to numerical form using ones and zeros (binary) so that it can be stored and used in a computer. The digital imaging process includes four key steps: image acquisition (capture), storage and management (saving), manipulation and annotation (editing), and viewing, display or transmission (sharing) of images. Before digital images become widely used for routine clinical work, standards are needed and the entire imaging process needs to be validated. Multiple types of devices are used to acquire digital images. Microscopic digital images can be static (still images), viewed live (real-time robotic microscopy), or virtual images viewed after scanning of the glass using specified microscope and computer setup [8, 11].

Whole slide scanning/ Virtual imaging and image analysis

Traditional glass histology slide is digitized via a slide scanner and can be viewed on a computer screen or handheld device at a similar resolution as light microscopy. Compared to the general workflow of how tissue sections are prepared

and viewed under a microscope, this digital workflow requires additional equipment i.e. slide scanner, image storage, digital pathology workstation for viewing, trained personnel, and specific quality control steps (e.g., quality control of scans).
All of which require increased information technology and departmental resources. However, there are multiple advantages of transitioning to a digital workflow, including ease of slides and cases sharing (consulting with other pathologists, or collaborating within interdisciplinary research teams), standardization of teaching, organization of archived digitized slides, and extraction of complex data in a highly reproducible fashion via specialized software. The pathologist plays a key role both in the process of slide digitization and in the subsequent data generation via the use of appropriate image analysis algorithms [12-14, 33].

Digital workflow of Whole Slide Scanning: Before being scanned, all glass slides received a two-dimensional (2D) tracking barcode on their label that is read by the WSI scanner. By reading the 2D barcode, each e-slide was automatically assigned to the correct case. The scanning station situated in the same room used to house the staining and coverslipping machine (Sakura Tissue-Tek Prisma and Coverslipper). Stained and coverslipped glass slides were loaded into scanner slide racks after they were dried at 60°C in an oven for an hour. After scanning, glass slides were still assembled onto trays and physically delivered to the assigned pathologist. Each pathologist could also access their assigned cases directly from the computer, thus supporting the hybrid possibility to access and consult digital slides from the virtual tray on a monitor or to render a diagnosis with glass slides using a conventional microscope [14, 15, 24].

Image Analysis: One of the most fundamental units in a typical histology image is the cell. In H and E-stained slides, in particular, cell nuclei are prominently visible structures. Other cellular compartments are often visible as well and the cell's cytoplasm has its own characteristic staining attributes. Second-order structures formed from arrangements of cells are readily observed in microscopic images and provide important cues that support several scoring and grading systems in cancer. A common theme for computational image analysis is to achieve a quantitative representation of cell staining, morphology, and architecture that can ultimately be used to support diagnosis and prediction. Therefore, demarcating cells or subcellular structures are among the first and most important steps of many image analysis routines. Image analysis has long been promised as a way to remove the subjectivity and variability in pathology diagnosis. A number of image analysis tasks in DP involve some sort of quantification (e.g., cell or mitosis counting) or tissue grading (classification). These tasks invariably require identification of histologic primitives (e.g., nuclei, mitosis, tubules, epithelium, etc.) [15, 16].

Telepathology

Telepathology refers to practicing pathology from a distance. Telecommunications technology is used for facilitating the transmission of pathology image-rich data between two distant locations for diagnosis, research and education purposes. In order to perform telepathology, a pathologist must choose the video images that need to be analyzed and then render a diagnosis [13, 17].

Telepathology is the practice of pathology at a distance, transmitting macroscopic and/or microscopic images using telecommunication links for remote interpretations (telediagnosis), second opinions or consultations (teleconsultation), and/ or for educational purposes. The original material (eg, glass slide) is spatially separated from the remote consultant (telepathologist) who will interpret a representative image of the material. The digital or analog image is remotely viewed on a computer monitor or cell phone screen. Ubiquitous access to the Internet, or to other broadband telecommunications linkages, facilitates nearly global image sharing. As a result, telepathology has been used to aid a growing number of laboratories around the world to deliver pathology and diagnosis services by allowing them to easily connect with experts. Telepathology has even been used to enhance the efficiency of pathology services between hospitals less than a mile apart. With increasing subspecialization in pathology, the use of telepathology to access subspecialists (eg, neuropathologists) has been extremely beneficial. The practice of telepathology, however, is not only limited to diagnostic work but can be used in quality assurance (eg, re review of cases), education, and research [13, 18, 19].
The various modes of telepathology like static, dynamic and WSI are present. Static telepathology involves the examination of precaptured still digital images (snapshots) that can be transmitted via e-mail or stored on a shared server. Dynamic telepathology involves the examination of live images or a sequence of images in real time using a live telecommunications link. In general, dynamic systems offer greater accuracy because the user can interpret images in real time without limited focus. WSI involves digitization (scanning) of glass slides to produce high-resolution digital slides. Hybrid technology combines robotics with high-resolution imaging [19, 20].

Static Telepathology: Static (store-and-forward) telepathology can be used to share digital images of just about anything in pathology, such as gross specimens, parasites, microbiology culture plates, histopathology, blood smears, and electrophoresis gels. These images may be shared with others via e-mail, social networking sites like WhatsApp, Facebook and Telegram or can be stored on a shared server. The person sending the image and the pathologist receiving it do not need to do so simultaneously (asynchronous telepathology). In addition to still images, other types of information that can be transferred with this technique include audio, text, and video files. Static images can be viewed by a single telepathologist or simultaneously by multiple clients during an online discussion (Figure 2) [19].

Robotic Telepathology: This form of telepathology involves a robotically controlled microscope with a digital camera attached and linked to a networked computer. Robotic systems allow one to perform dynamic (real-time) telepathology. The telepathologist has software controls on his or her computer to remotely "drive" (i.e. pan and zoom around a slide) and focus the microscope. Advantages of robotic telepathology include access to the entire slide, user control of the microscope and image with respect to fields (panning) and magnification, good image quality along with fast driving speed [13].

Whole Slide Imaging: WSI Telepathology offers another means to view an entirely digitized (scanned) slide. Whole-slide scanners typically include a slide loader, microscope with different objectives, digital camera, robotics, and software. Slide loaders range from trays that hold 1 to 4 slides to large racks or hotels that can stack up to 400 slides. For recently mounted slides (eg, frozen section slides with a movable coverslip), it is better to use horizontal loading rather than vertical placement. Slide scanning can be automated or done manually. Slides can be scanned using an objective lens magnification of 20, 40, or higher depending on the telepathology need. For routine surgical pathology work, 20 should use; however, for hematopathology cases, 40 may be preferred, and for telemicrobiology even higher magnification. WSI has been shown to be remarkably suitable for telepathology, because digital slides are of high resolution and permit access to an entire slide or set of slides at various magnifications. Once the scanned slide is ready, viewing the digital image to render a diagnosis can be faster than using a robotic microscope, especially if performed on a computer with a high-speed network connection. The length of time required to prepare slides for scanning and conduct previsualization quality checks should be taken into account when using WSI for rapid telepathology, such as during frozen section [18, 20].

Virtual Reality

Virtual reality is best described as a collection of technologies that allow people to interact efficiently with 3D computerised databases in real time using their natural senses and skills. New technologies, in particular virtual reality and robotics, will have a major impact on health care in the next decade. Clinically validated, powerful medical simulators are now available and in use across the world. General surgery leads in the use of simulators, and neurosurgery leads with augmented reality and image guided surgery. Robotics is used in orthopaedics and cardiology. Other virtual reality applications are being used in mental health, anaesthetics, emergency medicine and disease diagnosis. Rapid developments in the internet and "e-learning" domains have accelerated the dissemination of simulation techniques, interactive 3D images, and structured courseware. Although this so called immersive technology is still evident today, only 10% of virtual reality applications warrant its use. The key strength of virtual reality, be it in design or training, is that it supports and enhances real time interaction on the part of the user (Figure 3) [21, 22].

A number of benefits can be gained through using models within immersive 3D environments. For example, trainees, educators and/or practitioners do not need to be in the same physical environment to view and interact with the model. A demonstrator for example, can be in a remote location working via a virtual interface whilst sharing their model(s) with students or other practitioners who are located somewhere else. Interaction with models in the immersive environment may also be more intuitive than that with traditional 2-D models and they may also allow the user greater freedom of movement and ability to explore structures from multiple viewpoints. Simulation, modelling and visualization are the main techniques that can be employed and a number of immersive virtual training applications have been developed, each one offering unique characteristics [23, 24].

Typically, a VR system is composed of following things -

1. A database construction and virtual object modelling software
2. An input tool (trackers, gloves or user interface)
3. A graphic rendering system
4. An output tool (visual, aural and haptic): actually, less than 20% of VR healthcare applications in medicine are using any immersive equipment
5. A VR sensory stimuli delivery: using various forms of visual display technology that integrate real-time computer graphics and/or photographic images/video with a variety of other sensory (audio, force-feedback haptic/touch sensations and even olfactory) output devices. Other methods employ 3D displays that project on a single wall or on a multiple wall space (multiwall projection rooms are known as CAVES). Other gadgets are: a helmet or head-mounted display in high-resolution, 3D sights and sounds, head and/or limb-tracking hardware, and specialized software to reproduce an interactive virtual environment [21, 25].

The wide acceptance of high tech surgery and disease diagnosis, such as using videos in laparoscopic procedures, has overcome many surgical prejudices, but virtual reality and robots are still viewed as gimmicks or potentially dangerous by most surgeons. More multidisciplinary teams will be required to develop the use of these new technologies in surgery. As with so many advances in health care, however, these new technologies are likely to increase costs, against which must be weighed the potential for improved surgical competence and reduced medical error, with reduced morbidity and mortality. Evidence for these benefits is likely to take at least 5-10 years to accumulate [22, 25].

Matrix-Assisted Laser Desorption Ionization Time of Flight - Mass Spectrometry (Maldi Tof Ms)

The genomic information within a microbial cell translates into more than 2000 proteins, a substantial number of which can be studied using proteomics. It is estimated that for genomes which contain less than 1000 genes, more than 50% of predicted proteome may be identified from the genome. Similarly 30 and 10% predicted proteome may be identified from genomes which carry ca. 2500 and ca. 4000 genes respectively. Thus, a microbial genome containing 600–7000 predicted genes represents a medium-sized complex system where application of proteomics may provide knowledge of a substantial part of the microbe's proteome [26, 27].

Mass spectrometry is an analytical technique in which chemical compounds are ionized into charged molecules and ratio of their mass to charge (m/z) is measured. Though MS was discovered in the early 1900s, its scope was limited to the chemical sciences. However, the development of electron spray ionization (ESI) and matrix assisted laser desorption ionization (MALDI) in 1980s increased the applicability of MS to large biological molecules like proteins. In both ESI and MALDI, peptides are converted into ions by either addition or loss of one or more than one protons. Both are based on "soft ionization" methods where ion formation does not lead to a significant loss of sample integrity. The high throughput and speed associated with complete automation has made MALDI-TOF mass spectrometer an obvious choice for proteomics work on large-scale [29, 30].

Principle and Methodology: The sample for analysis by MALDI MS is prepared by mixing or coating with solution of an energy-absorbent, organic compound called matrix. When the matrix crystallizes on drying, the sample entrapped within the matrix also co-crystallizes. The sample within the matrix is ionized in an automated mode with a laser beam. Desorption and ionization with the laser beam generates singly protonated ions from analytes in the sample. The protonated ions are then accelerated at a fixed potential, where these separate from each other on the basis of their mass-tocharge ratio (m/z). The charged analytes are then detected and measured using different types of mass analyzers like quadrupole mass analyzers, ion trap analyzers, time of flight (TOF) analyzers etc. For microbiological applications mainly TOF mass analyzers are used. During MALDI-TOF analysis, the m/z ratio of an ion is measured by determining the time required for it to travel the length of the flight tube. A few TOF analyzers incorporate an ion mirror at the rear end of the flight tube, which serves to reflect back ions through the flight tube to a detector. Thus, the ion mirror not only increases the length of the flight tube, it also corrects small differences in energy among ions. Based on the TOF information, a characteristic spectrum called peptide mass fingerprint (PMF) is generated for analytes in the sample. Identification of microbes by MALDI-TOF MS is done by either comparing the PMF of unknown organism with the PMFs contained in the database, or by matching the masses of biomarkers of unknown organism with the proteome database [26, 27, 29, 30].

Disadvantage of Artificial Intelligence

It requires high cost to arrange the whole setup as whole setup is complicated, thus require professional expertise. It decreases demand of human labour. The storage and access is not efficient as human brain. No improvement with experience as it is a only machine thus has no power of self learning. It may programmed to do something devastation.Virtual world can simulate, but can not provide the real experience in order to get experties in surgical interventions.

Conclusion

Artificial intelligence plays enormous role in field of disease diagnosis both in human and veterinary science. In digital pathology the journey of a glass slide would finish in the laboratory after scanning. Telepathology makes this virtual slide available to view at any workstation. This saves time spent by experts and increases accuracy significantly**.** Virtual reality (VR) is feeling the imaginary world, rather than the real one. This imaginary world is simulation running in computer in a 3D manner with a collection of technological devices *i.e.* a computer capable of interactive 3D visualization, a head-mounted display and data gloves equipped with one or more position trackers. In recent years matrix assisted laser desorption ionization mass spectrometry (MALDI MS) has emerged as a potential tool for microbial identification and diagnosis. The process is rapid, sensitive, and economical in terms of both labour and costs involved. Pathology is the motor that drives healthcare to understand diseases. While it does the job via the same methods that it has been using for the last 150 years, it's time to change. Artificial intelligence could push the field of disease diagnosis to be well-organized, effective and precise.

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