Therapeutic Screening Software for Vessel Normalization in Melanoma
(Technical Paper)

Impact of Machine Learning on the Healthcare Industry
(STS Paper)

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

Introduction

The theme of humans versus technology is one that is pervasive within the collective conscious due to the human penchant for dystopian scripts. Is this theme all but a work of imagination, or is it slowly taking hold of society and becoming more accurate than ever? Technological unemployment, technology replacing jobs previously held by humans, is an issue that has created fears against the implementation of innovative technologies within various workspaces (Chuang & Graham, 2018). Common examples of this theme include the replacement of retail cashiers with self-service checkout kiosks and the displacement of manual labor with robotic equipment in manufacturing. Although automation has historically been limited to low-skill jobs, more recently, this trend has seen an increase in automation within specialty fields such as medicine and healthcare through machine learning and artificial intelligence (AI). As such, the proposed research study aims to focus on how AI will shape medicine in the coming years and how this technology may impact the job description of doctors and their relationships with patients.

On a similar note, medical research has seen a rapid increase in the implementation of machine learning algorithms to both decrease the time required for analysis, as well as decrease any analyst-specific variation introduced through manual methods. These computational methods tend to be extremely useful in studying various pathological states, such as different cancers. The proposed technical study focuses on melanoma research, which is extremely important as there are over 100,000 new diagnoses each year (*Melanoma Skin Cancer Statistics*, n.d.). Many current therapeutics are anti-angiogenic, focusing on the vasculature as cancer promotes the formation of new blood and lymphatic vessels to cope with the high nutrient and oxygen demand. Recently, a compensatory angiogenic pathway regulated by the protein hornerin has been identified (Gutknecht et al., 2017). The technical study focuses on optimizing an existing vessel analysis software to understand the effect of hornerin knockdown on vessel normalization and its subsequent impact on T-cell entry into the tumor region.

Technical

The human body is an incredibly complex system, which presents a challenge in investigating pathological conditions such as cancer. Cancer is one of the leading causes of death in the United States, with approximately two million new diagnoses and 600,000 associated deaths each year (*Cancer Statistics - National Cancer Institute*, 2015). In particular, there are about 100,000 diagnoses and 7,000 deaths each year due to melanoma, a form of skin cancer (*Melanoma Skin Cancer Statistics*, n.d.). Cancer treatments aim to target cancerous cells and related pathways to halt cancer progression. One such pathway involves the coexistence of cancer cells with the surrounding blood and lymphatic vessel network. The generation and maintenance of this vascular network, known as angiogenesis, is essential for tumor growth and favors the spread of cancer or cancer metastasis. The vessels promote this growth and spread by compensating for the tumor's high oxygen and nutrient demand (Folkman, 2010). Also, the cancer cells secrete high levels of pro-angiogenic factors, which contribute to the creation of a disordered vascular network characterized by immature and permeable blood vessels. The abnormal vascular network then further limits the subsequent immune response, as vessels are one factor that modulate T-cell, a type of immune cell, trafficking (Viallard & Larrivée, 2017).

As such, tumor blood vessels are a key target for cancer therapeutic management, as anti-angiogenic therapies can normalize tumor vasculature to ultimately restore immune function and decrease tumor progression. Many current therapeutics target a pro-angiogenic factor named vascular endothelial growth factor (VEGF) (Melincovici et al., 2018). These current cancer therapeutics have demonstrated effective results, but often yield temporary remission as the possibility of recurrence following treatment is highly likely with most cancers. Therefore, additional pathways that lead to vessel growth are crucial in effectively targeting the vascular network. Previous studies have identified a protein called hornerin, which is located on cells that line blood vessels and is independent of VEGF. Hornerin is part of a compensatory pathway in angiogenesis. Hornerin knockdown using silencing RNA (siRNA) results in a reduction of protein expression, allowing researchers to study the impact on the tumor microenvironment. In studies concerning pancreatic cancer, hornerin knockdown resulted in normalization of the vessels and reduced tumor burden (Gutknecht et al., 2017). Additionally, hornerin is expressed in psoriatic and wounded skin, elucidating its potential in melanoma treatment (Takaishi et al., 2005).

For analysis of therapeutics, such as those that result in hornerin knockdown, comparing the characteristics of tumor vasculature to normal vasculature can provide an understanding of the drug efficacy. The Rapid Analysis Vessel Element (RAVE) software is a vessel analysis software that was introduced almost a decade ago (Seaman et al., 2011). RAVE performs analysis of vascular environment images with a few variations. An image is uploaded to the software, which performs several operations to compile and output vessel parameters such as vessel volume fraction, vessel length density, vessel radius and fractal dimension. Although operational, RAVE only has the ability to analyze one image at a time, limiting the efficacy of large scale analysis due to the time consuming nature of the program. Additionally, the software lacks a single data output function as well as the capacity to copy and paste. Therefore, by the end of the academic year, the capstone team will deliver an optimized RAVE software. The deliverable will include characteristics such as batch processing and a more user-friendly output, including a single, exportable file containing all the vessel parameter data. Further, the technical research project will upgrade the existing RAVE software by incorporating an algorithm to automatically set appropriate thresholds for individual images. This algorithm will reduce the processing time for multiple images and reduce potential variations produced by manual threshold entry. The proposed research project will offer an optimized therapeutic screening software that presents an effective way to screen new therapeutics directly targeting the tumor vasculature. The software will specifically be used to test the effect of a hornerin targeting therapeutic in melanoma; however, it has the potential to serve as a tool for vascular network analysis in a wide range of cancers.

STS Topic

Today, technology is hailed as humanity's savior. Every innovation is looked at with excitement and approached with an eagerness to see it implemented as soon as possible. With the advent and more comprehensive application of machine learning in many spheres, both rational and irrational fears have been brought forth in the debate for whether such technologies should be implemented within the healthcare industry. The proposed research paper will focus on these fears and explore the possibilities of how this innovative technology may be perceived by doctors, patients, researchers, and other actors in the medical field as its popularity increases. The paper will also discuss how machine learning and AI may impact the future of the medical field as an increasing number of institutions start using these technologies as an aid to diagnosis.

Although technologies increase the ease with which tasks can be completed through automation, there are very credible fears to automation's widescale implementation in workspaces. For example, the use of robots in workplaces has seen a massive increase, with current estimates stating that there are about 1.5-1.75 million robots in operation, which is expected to increase to 4-6 million by 2025 (Sirkin et al., n.d.). Moreover, current estimates state that in the next one to two decades, approximately 47 per cent of all human jobs will be lost to robots, machines, automations, or computerizations that have the capability to not only do the work faster but to also cost less in the long run (Frey & Osborne, 2017). This phenomenon of automation replacing human jobs is the prime argument against the implementation of machine learning and various other types of automation within workspaces. It is termed technological unemployment and will be examined further within the research paper.

AI, at its core, is the branch of computer science that seeks to answer Alan Turing's question of "Can machines think?" It is an endeavor to replicate or simulate human intelligence within machines. In their seminal work, *Artificial Intelligence: A Modern Approach,* authors Stuart Russell and Peter Norvig divide the study of AI into four approaches: thinking humanly, thinking rationally, acting humanly, and acting rationally (Russell & Norvig, 2009). Although machine learning and AI are used synonymously, they are not one and the same. Machine learning is but a subset of Artificial Intelligence. It is one of many approaches that can be taken to power artificially intelligent systems, with other approaches being deep learning and simpler algorithms (*What Is Artificial Intelligence? How Does AI Work? | Built In*, n.d.). Machine learning refers to computer algorithms that improve performance automatically through experience. They require some training data, which needs to be representative of the whole set of data that can be provided as input to the algorithm. The efficiency of the algorithm is usually measured on a test data set after it has been trained.

The most promising use of machine learning is in aid of diagnosis. Currently, due to the ambiguous nature of medical issues and the vast number of treatments present, different doctors with varying levels of exposure and experience can provide starkly different treatments for the same diagnosis. Additionally, in some cases where the issue itself is hard to diagnose, differential diagnosis can be both expensive and time-consuming, especially when doctors are lost as to what underlying issue is causing symptoms. Machine learning can encompass the wisdom of multiple doctors depending on the training data and can also aid in diagnosis, especially in medical specialties that rely on image-based diagnosis (Rajkomar et al., 2019) ("Ascent of Machine Learning in Medicine," 2019).

To analyze how the healthcare system is impacted by the incorporation of machine learning both on a macro and micro level, it is necessary to chart who all the different actors are and how they impact each other. The actor network theory (ANT), thus provides a framework that analyzes the interplay between the different actors, be they human or non-human, as is the case with the artifact of Machine learning (Cressman, 2009). This framework allows for investigation into how networks come into being, what associations exist, how actors are enrolled into a network, how power is established and how networks gain temporary stability (Cresswell et al., 2010). Although ANT offers a broad analysis of interactions between both human and non-human elements, some critiques have been raised. Even though there may be differences in status between all the actors, equal importance is ascribed to all actors within the network, which can lead to incorrect attributions of an actor's true impact over another actor within the network. Additionally, actors in the network are defined by the author themselves, which can leave a lot of room for subjectivity in the analysis. If the author incorrectly chooses a very narrow list of actors, the analysis may completely miss or incorrectly attribute the impact of an invisible actor over the entire network. Despite these intrinsic limitations, ANT provides an excellent framework to employ when analyzing how a network such as the healthcare industry attains stability when a new actor (Machine learning) is added into the network.

Methodologies

Research Question: How will AI reshape the landscape of medicine in the coming years, and what barriers are to be expected for widescale implementation of such a technology?

To address the research question, the discussion will be organized using discourse analysis and historical case studies, concluding with a network analysis of the healthcare industry to provide a comprehensive understanding of the potential impact of implementing machine learning algorithms. The proposed research project will start by providing a background into what machine learning is and its potential within medicine. Here, discourse analysis will be employed by bringing in representative viewpoints of doctors, researchers, and patients on how this revolutionary technology can impact the field of medicine. These viewpoints will be critically examined to understand whether they are based on well-founded information, dispelling certain myths in the process. This section will also allow for a discussion on both the pros and cons of introducing machine learning as an aid to medical diagnosis. Additionally, historical case studies will be utilized to analyze the similarities between the introduction of machine learning and other medical innovations, such as laparoscopic surgery procedures. Examining previous breakthrough medical technologies will allow for a better understanding of the expected barriers that AI may face before its use as a diagnostic aid is accepted by the majority of doctors and patients (Kelley, 2008). Lastly, network analysis will be conducted using the Actor Network Theory STS framework. The different actors that comprise the healthcare network that is directly impacted by the addition of machine learning algorithms will be outlined. A summary of the previous section's research will follow, where discourse analysis will be employed to chart how machine learning may impact various actors in a unique but related manner. For the different sections mentioned above, the research scope will be limited using the following keywords: Diagnostic machine learning, healthcare, patients, physicians, and laparoscopic surgery. These keywords will help focus the research on best answering the research questions and will hopefully give better insight into how this innovative technology of machine learning will shape the field of medicine in the coming years.

Conclusion

With many cancer treatments ending in the recurrence of disease, novel therapeutics are continually being developed. One valuable target in the tumor microenvironment is the vasculature, using anti-angiogenic therapies. The recent identification of hornerin as a protein involved in tumor growth presents promising clinical applications. As such, characterization and comparison between tumor and normal vasculature warrants a software with such capability. The Rapid Analysis Vessel Software, optimized for batch processing with a user-friendly output, will allow researchers to screen novel drugs to test their efficacy in a broad spectrum of cancers.

As with any other field that encounters substantial change, the field of medicine is bound to face resistance from the various actors that comprise the network as it evolves and adapts to current technologies. One such technology that has the potential of redefining the roles of doctors as well as how patients and physicians will interact is that of machine learning. With a proper understanding of how this technology can impact the medical field as a whole, the transition into integrating this technology can be made much smoother, with a more conscious redefinition of physician roles and minimal loss in quality of care to patients.

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