

able to analyze complex phenotypes, risk factors, and outcomes only further highlights this issue. Limitations of classical computing are contributing to a tremendous lag in pioneering genetic and/or molecular epidemiology research on spine disorders^{6,7)}. Fortunately, advanced computing techniques, such as parallel processing and supercomputing methods, are being designed to circumvent the constraints of today's modern computers. Research investigating optimization theory and quantum phenomena has also promoted theoretical advancements in computing that are beginning to be realized today. As the spine community continues to drive the development and processing of Big Data, familiarization and understanding of emerging technologies is of great importance.

Classical Computing

Modern transistors and their limitations

An understanding of how our current computing technology functions is relevant to any discussion of quantum computing. The most basic unit of data processing in modern microchips is the transistor, which is nothing more than a switch that either permits or blocks the flow of information in the form of an electrical current. A current flowing through a transistor is interpreted as "on," or 1, and the absence of current is read as "off," or 0 (i.e., binary operators). Combinations of 1's and 0's, referred to as "bits," are used to represent more complicated information, forming the basis of *Classical Computing*. The arrangement of transistors into higher order structures, called logic gates (Fig. 1), is what confers the ability to perform complex computations.

Since their initial development, transistors have become vastly smaller through time. In 1965, Gordon Moore, co-founder of Intel, predicted that the density of transistors on microchips would double every two years. By 1975, his prediction held true and has since been referred to as *Moore's Law* (Fig. 2). Numerous technological innovations made over the past 70 years have miniaturized transistors from 40 micrometers in 1947 down to the roughly 5-nanometer transistors of today, representing a reduction in size of four orders of magnitude without compromising processing power. One of the first fully transistorized computers developed in the late 1950s, the IBM 7090, contained over 50,000 transistors and could perform roughly 229,000 operations per second⁸⁾. Alternatively, Apple's new high-performance M1 processor holds 16 billion transistors, each measuring a mere 5 nanometers in length, and performs more than 11 trillion operations each second⁹⁾. Despite the great superiority in capability, the M1 processor costs only \$50 and is easily housed within the modern laptop, whereas the IBM 7090, which sold for \$2.9 million in 1960 (equivalent to \$20 million in 2020), required an entire room to contain the computer, electrical, and cooling equipment. As transistors continue to shrink, however, the behavior of fundamental particles on such microscopic scales begins violating the very

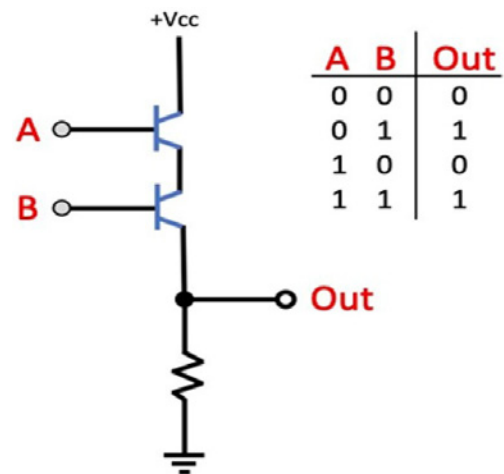


Figure 1. AND Logic Gate. The arrangement of transistors (blue) in the AND logic gate is such that both transistors must be open to allow current originating from the positive voltage at common collected (+Vcc) to flow through them for the output (Out) bit to read "1." If at least one of the transistors is closed the output will instead read "0." "A" and "B" are the gates, or input bits, that control their respective transistors.

principles of classic mechanics.

Determining the exact location of incredibly small particles, such as the an electron, is problematic. Over small enough scales, subatomic particles may appear anywhere within a probability distribution, allowing them to behave in a manner not in accordance with classical mechanics. One phenomenon, called *quantum tunneling*, occurs when waveforms, like the electron that is both a particle and wave, propagate through potential barriers such as a closed tiny transistor, making their binary outputs unreliable. As transistors approach the size of the atom, the likelihood of an electron passing through a closed transistor per unit time ultimately increases. Effects of *quantum tunneling* likely indicate that the size limit of modern transistors has been reached, and increasing the density of transistors per unit size, which has been our main method for improving CPU performance for nearly 70 years, will not be possible. As such, current technology will not be able to meet the processing needs required to incorporate the wealth of patient data necessary to personalize spine care, despite the incredible computation speed of modern transistorized computers.

Quantum Computing

A brief history

The conception of quantum computing is often incorrectly attributed to the early 1980s, either to Paul Benioff¹⁰⁾—for his quantum mechanical model of the infamous Turing machine—or Richard Feynman¹¹⁾—for his paper that postulated future problems that classical computers may not be able to

tum entanglement. The implications of these two phenomena, *superposition* and *quantum entanglement*, are that we can store exponentially more information in the same number of qubits and can access that stored information much more efficiently than in traditional circuitry.

Superposition, quantum entanglement, and quantum mechanics are complex and difficult theoretical topics to understand. Therefore, interdisciplinary collaborative efforts among physicists, computer scientists, and spine researchers are necessary to drive innovation in neuroradiological applications, clinical simulations, computational optimization, and the IBSC approach.

Applications in non-spine fields

As the transition from bits to qubits heralds a new era in computing, the potential implications largely remain to be elucidated. While scientists continue to grapple with scientific and engineering challenges associated with quantum computing, numerous large companies, such as Google, IBM, Microsoft, and Amazon, in addition to several startups, have begun exploring this emerging field and have made significant progress toward establishing commercial applications²³. One field particularly shaken by the rise of quantum computing is Cybersecurity. Because quantum algorithms can be applied to many cryptographic calculations, modern encryption algorithms can effectively be reduced from exponential complexities to polynomial problems, significantly decreasing the time and computational cost required to break them¹⁶. Recognizing the possibility that modern cybersecurity may soon be obsolete, the U.S. government passed the Quantum Initiative Act²⁴ in 2018 to allocate funding and effectively join the quantum computing race. Addressing combinatoric challenges through quantum computing has also demonstrated value in the financial sector by optimizing derivatives pricing and risk assessment²⁵, as well as in advanced manufacturing, where identifying faults in systems despite a paucity of data from prior failures can reduce the likelihood of future failure and translate to enormous savings²³.

Healthcare represents a particular field of promise for applications of quantum computing. One of its main advantages is the theorized ability to simulate molecular systems with a high degree of fidelity. In 2019, Google's quantum computer (Fig. 3) accurately simulated the isomerization of diazene, which is a molecule consisting of two nitrogen and two hydrogen atoms. Although relatively simple, this achievement demonstrates that simulating higher order structures, as is currently done on classical computers with extensive applications in biochemical research, is feasible with quantum computing. However, there are limits to what can be studied on classical computers. For instance, simulating protein folding is too computationally expensive for processors that rely on current technology²⁶. Quantum computing may allow us to simulate molecular structures as it leverages the same tenets of physics that we attribute to biological structures²⁷. Cheng et al.²⁷ recently detailed why three bio-



Figure 3. Stearns F. Artist's rendition of the Sycamore processor mounted in the cryostat. Available at: <https://ai.googleblog.com/2019/10/quantum-supremacy-using-programmable.html> (Accessed December 10, 2021).

chemical systems—histone demethylase, telomerase, and biotin-avidin binding—are challenging to simulate for current computational methods. A quantum computer may therefore one day be able to simulate the entire inner workings of a cell, a tissue colony of those cells, an organ comprised of multiple types of tissues, and even complete organ systems, all based on variations of that original simulated cell.

Whereas drug discovery has a history filled with luck and chance, the application of quantum computing to modern R&D may allow scientists to better understand the structure and properties of their products while simultaneously minimizing cost and maximizing efficacy. Perhaps even more impressive is the speed with which new drugs can be discovered. During the height of the Ebola outbreak in 2015, Atomwise, a company using supercomputers to discover novel drug therapies from an extensive database of molecular structures, conducted a search using its deep convolutional network and successfully identified two drug candidates to treat the virus in less than one day, a feat that would otherwise take several months²⁸. Translated directly to patient care, quantum computing can assist physicians in their clinical practices. By improving precision and interpretation of imaging, guiding radiation therapy and targeting of malignant cells in the treatment of various cancers, and interpreting large amounts of patient data, healthcare providers will be better able to determine truly personalized approaches to the preventative and therapeutic management of their patients²⁹⁻³¹. Moreover, the incorporation of quantum computing into implantable and prosthetic devices may di-

rectly affect patient quality of life. For example, quantum-enabled neural devices can be used to establish a brain-computer interface that records and decodes brain signaling concerning motor intention and planning and translates this information to movement of prosthetic or robotic limbs³²⁻³⁴. The BrainGate group has already successfully demonstrated the ability of neural interface technology to enable robotic prostheses to perform three-dimensional reach and grasp movements³⁵, indicating profound implications for patients with mobility limitations due to paralysis or stroke.

Applications for spine care and research

The ability of quantum computers to collect and analyze vast amounts of patient data using pattern recognition generates extensive potential applications in the field of spine care, specifically. Koebbe et al.³⁶ demonstrated how quantum-mechanically entangled light augments the utility of imaging in the diagnosis and treatment of spinal conditions when paired with AI and the precision-based spine care approach^{37,38}. In fact, quantum sensors may improve imaging technology by enabling visualization to the molecular level, providing clinicians with substantially more accurate imagery to guide them in identifying the pain source, mapping treatment efficacy, and even identifying high-risk candidates for disease development and progression. The age of Big Data has introduced a wealth of platforms worthy of investigation in relation to spinal disorders, such as those of genomics, metabolomics, transcriptomics, lipidomics, proteomics, interactomics, epigenomics, and so on³⁹⁻⁴². A “panomics” or “integrative omics” approach is most likely a necessity considering the complex disease states and conditions that are inherent to human variation and associated with spine disorders/pathologies. Implications of the microbiome and its effects on human health and disease further add to the complexity of understanding why we develop certain spine conditions, their severity, and resolution^{43,44}. Similarly, pain genes have shed light on questions surrounding which patients may develop a symptomatic herniated disc as well as pain severity, resolution, and outcomes among other conditions⁴⁵.

Integration of the above platforms will surely introduce new dimensions to spine conditions and their management options. Initiatives, such as the multicenter National Institutes of Health-supported Back Pain Consortium Research Project⁴⁶, among others, may ultimately address the aforementioned data platforms by using quantum computing, allowing for robust conclusions regarding mechanisms of disease, provide guidelines for treatment options, and thus facilitating more precise approaches for patients with chronic low back pain. Phenotyping clinical profiles and maximizing outcomes are critical and demand intensive analytical scrutiny and applications. Quantum computing will further fuse the cellular, molecular, structural, and overall histopathological sub-tissue elements with various “panomic” domains into high fidelity simulations, allowing us to better understand disease development and progression, develop targeted thera-

peutics, improve and optimize existing treatments, and discover new markers for prevention. For example, near-exact simulated spines may allow researchers to elaborate upon the natural history of disc degeneration and its severity as well as explain who may develop symptomatic disease, recurrent herniation following discectomy, or adjacent segment disease following fusion. Furthermore, such simulations built upon these integrations will also allow us to identify which patients may develop intra- and/or postoperative complications, improve patient stratifications, develop risk profile calculators, and refine algorithmic modeling of spine conditions to optimize outcomes, inevitably paving the way for translational findings from the bench to the bedside. Moreover, regenerative biologics of the spine is a field that has encountered numerous barriers and challenges, with advances that remain controversial; however, quantum computing may add value to refined patient and dose selection as well as algorithmic modeling of outcomes and the regenerative process from the molecular to structural level with greater certainty. Finally, the interaction of a given reconstituted motion segment with the whole spine and the entire body as a functional, interactive unit may be better understood and incorporated into more elaborative and precise predictive modeling through a quantum computing approach. With the explosion of new data platforms and the need for data-driven science, quantum computing may one day become commonplace and instrumental in every facet of patient care.

Conclusion

Considering the great potential quantum computing carries to provide personalized patient care³⁸, incorporated with the IBSC model¹, the traction and support it has gained recently within the spine community is well-warranted. Harnessing advanced computational algorithms in conjunction with extensive patient datasets, optimization of patient care using quantum computing is here to stay. In a time of abundance of data, complexities that may seem impossible to tackle today can be addressed tomorrow with the emergence of quantum computing. To achieve such goals, a team-based approach involving multicenter and multidisciplinary collaboration is mandatory. The data scientist and the clinician must work together to find solutions and map the way forward for the spine field to evolve.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

Acknowledgement: The authors wish to thank Zakariah Siyaji for his insights towards this topic.

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