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Enabling Precision Medicine via Contemporary and Future Communication Technologies: *A Survey*

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ABSTRACT Precision medicine (PM) is an innovative medical approach that considers differences in the individuals' omics, medical histories, lifestyles, and environmental information in treating diseases. To fully achieve the envisaged gains of PM, various contemporary and future technologies have to be employed, among which are nanotechnology, sensor network, big data, and artificial intelligence. These technologies and other applications require a communication network that will enable them to work in tandem for the benefit of PM. Hence, communication technology serves as the nervous system of PM, without which the entire system collapses. Therefore, it is essential to explore and determine the candidate communication technology requirements that can guarantee the envisioned gains of PM. To the best of our knowledge, no work exploring how communication technology directly impacts the development and deployment of PM solutions exists. This survey paper is designed to stimulate discussions on PM from the communication engineering perspective. We introduce the fundamentals of PM and the demands in terms of quality of service that each of the enabling technologies of PM places on the communication network. We explore the information in the literature to suggest the ideal metric values of the key performance indicators for the implementation of the different components of PM. The comparative analysis of the suitability of the contemporary and future communication technologies for PM implementation is discussed. Finally, some open research challenges for the candidate communication technologies that will enable the full implementation of PM solutions are highlighted.

INDEX TERMS Precision medicine, fourth industrial revolution (4IR) technologies, communication technologies, 5G, 6G.

I. INTRODUCTION

The goals of medicine [1], [2] include the provision of a timely and accurate diagnosis and the effective treatment of all diseases to enable the satisfactory improvement of the health conditions of the global population. These goals conform to the third United Nations (UN) Sustainable Development Goal (SDG), which emphasizes the need to guarantee healthy lives and promote well-being. The third SDG goal has not been met as many diseases such as cancer, Alzheimer's disease, diabetes, Crohn's disease, and cardiovascular diseases do not have clear-cut permanent cures. More also, in the course of applying various therapeutics for the treatment of many diseases, it has been observed that different individuals respond differently to the same treatment for the same disease. And in some cases, physiological conditions associated with a disease in an individual often change with time [3], thereby making treatment ineffective. For instance, the emergence of inherent anticancer drug resistance before chemotherapy, as well as the acquisition of resistance due to drug treatment, has remained the dominant impediment to the treatment of cancer [4]. The same applies to the treatment of Alzheimer's disease, where the vast heterogeneity in the disease etiology involves very complex and divergent pathways [5]. This phenomenon is also observed in the treatment of cardiovascular diseases [6] and other diseases [7], [8].

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A common factor associated with the lack of clear-cut treatment for the diseases mentioned above and the divergent responses by individuals to medicines is the high complexity and the systemic nature of the conditions. This level of complexity makes obtaining a complete understanding of the molecular characteristics and mechanisms of these diseases in connection with the mechanism of the entire human body, which is pivotal to effective treatment, challenging. Insufficient knowledge influences the accuracy of disease diagnosis, efficacy, and attrition rates of drugs/other therapeutics. Consequently, the effectiveness and timeliness of treatments are affected. Contemporarily, there exist fragmented knowledge of the characteristics and mechanisms of many diseases, which are obtained from tests and experiments carried out discreetly in many laboratories and clinical settings across the globe. These tests and experiments result in the generation of massive medical data. The data generated from high-throughput biological assays and screening are often grouped under the term ‘omics’. In the context of this paper, omics data include data associated with genomics, transcriptomics, proteomics, metabolomics, viromics, and microbiomics.

The omics data and other types of medical data can be stratified and analyzed to individualize diagnosis and therapy to address the variability in the individual’s response to treatments. This approach is termed *precision medicine* (PM). Succinctly put, PM takes advantage of the personalized information of patients to tailor the practice of medicine to an individual. The contemporary idea of PM [9], [10] focuses on classifying persons into subpopulations that vary in their predisposition to a particular disease and do not include the creation of drugs or therapeutic modalities exclusive to a patient. However, medicine and its concern for the well-being of patients, in general, encompasses many subjects, including diagnosis, drug discovery and development (DDD), surgery, therapy, and care. Therefore, tailoring these subjects to address health challenges using personalized information is crucial to achieving the goal of medicine. In this paper, we employ the term PM to define the generalized platform engaging personalized medical data to guide all aspects of medicine, pharmacology, and biotechnology towards addressing individuals’ medical challenges.

A. MOTIVATION

The enabling technologies that are pivotal to the implementation of PM include nanotechnology [11], automation/robotics [12], [13], artificial intelligence (AI) [14], 3D printing [15], big data [16], high-speed computation [17], internet of everything (IoE) [18], extended reality (XR) (includes virtual reality (VR), augmented reality (AR)) [19], holographic display [20], digital twin [21], blockchain [22], [23], and advanced communication technologies [24]. Integrating these technologies into PM processes puts PM in the category of a cyber-physical system. By cyber-physical systems, we mean an engineered system built from and depends upon the seamless integration of computational algorithms and physical components [25], [26]. Indeed, PM presents scenarios for the application of systems that are a true representation of a cyber-physical system (CPS) [27], [28] based on the level of integration of almost all the enabling technologies (mentioned above) of the Fourth Industrial Revolution (4IR).

And like in any use case of a cyber-physical system, the communication technology in use defines the extent to which the system expectations are realizable. Many contemporary works have presented discussions on PM, as is shown in Section II. However, to the best of our knowledge, no work exists that explores how communication technology directly impacts the development and deployment of PM solutions and applications. Indeed, communication technology serves as the nervous system of PM, without which the entire system collapses. The contemporary communication technologies available for use in PM process include the 4G and 5G technologies. The question is, **1)** *how do these technologies perform in enabling PM*? **2)** *What are required of future communication technologies such as 6G and beyond-6G in enabling PM should the contemporary technologies not meet the needs of PM*? It is, therefore, necessary to deliberate on these questions to determine the optimized communication technology required for a reliable and full PM deployment.

B. PAPER CONTRIBUTION

The 4G and 5G communication technologies are currently available, and 6G is expected in less than a decade. As shown in Fig. 1, these communication technologies evolved from the older generation communication technologies where the design consideration is such that each generation meets the needs of end-users, depending on the techniques available to the network operators. The first generation (1G) provides voice communication using analog technology. The second-generation (2G) supports basic short message signaling in addition to voice communication using digital technology. The third-generation (3G) introduced mobile broadband access that opens the door to multimedia services and applications such as Internet access, mobile television, and video calls. In the 4G communication era, improvements in mobile broadband services, all-IP communication, and Voice Over IP were introduced, providing capabilities such as ultra-high-definition video streaming and online gaming. The 5G launched in 2020 presents a significant improvement in data rate, latency, and other key performance indicators compared to the previous generations of mobile communication. These improvements enable 5G to support three generic services with vastly heterogeneous requirements, namely, enhanced mobile broadband (eMBB), massive machine-type communications (mMTCs), and ultra-reliable low-latency communications (URLLCs). These generic services enable massive broadband services such as the internet of things (IoT), VR, AR, autonomous vehicular systems, and the digital transformation of manufacturing/production. It is expected that by 2030, the 6G will be introduced with an expected massive improvement over 5G. And as we move into the 4IR era, various advanced technologies will need to be synergized to provide new and unprecedented services and solutions.

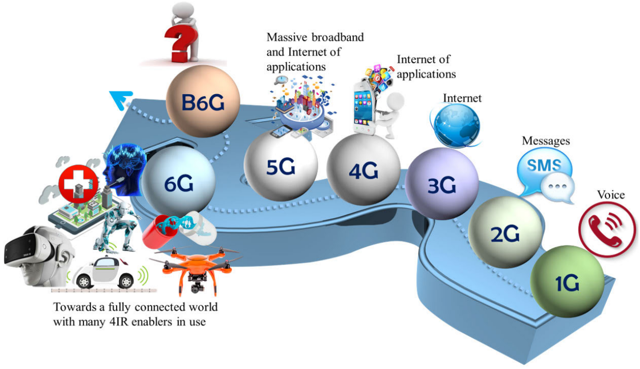


FIGURE 1. Evolution of mobile communication technologies from 1G to beyond 6G.

The requirement for such synergy will put huge pressure on the communication network to enable the desired connectivity. PM is a typical example of a 4IR-driven solution that is envisaged to have the capacity to put enormous demands on the communication network.

In this survey paper, we explore how the contemporary (4G and 5G) and future (6G) communication technologies excel in providing a network that supports PM and its goals. Firstly, some background on PM and its taxonomy are presented. Then, the various enabling technologies of PM are discussed with particular focus on underlining the demands each of the technology places on the communication network in terms of some key performance indicators (KPI). The KPIs considered here are given in Table 1 [29], [30]. The choice of these indicators is informed by the fact that they mirror the overlap between the quality of service (QoS) and quality of experience (QoE) in an explicitly quantifiable manner for the analysis presented in this survey.

The definitions of the KPI metrics employed for this survey are as follows

- *Peak Data Rate (bps)*: This is the maximum achievable data rate for a user in a real network environment.
- *User Experienced (UE) Data Rate (bps)*: This is the minimum achievable data rate for a user in a real network environment.
- *Area Traffic Capacity (bps/km^2)*: This is the traffic volume density (bps/km^2).
- *Connectivity Density (Device/km^2)*: This is the total number of connected devices per unit area.
- *Latency (ms):* This is the delay from the time a packet is sent from the transmitter until it is received at the receiver.
- *Reliability (PER):* This is the success probability of transmitting a given byte within a certain delay.
- *Energy Efficiency (bpJ):* This is the ratio of the total number of packets received to the total energy spent by the network to deliver the packets.
- *Mobility (km/h):* This is the relative speed between receiver and transmitter under certain performance requirements.

TABLE 1. Comparison among the KPIs of the communication technologies.

Key Performance Indicator for True PM experience	4G	5G	6G
Peak Data Rate (Gbps)	1	20	1000
User Experienced Data Rate (Gbps)	Up to 0.0125	0.1	1
Area Traffic Capacity (Mbps/km^2)	Up to 3.7	10	100
Spectrum efficiency (bp/Hz)	15-30	30	60
Connectivity Density (Device/km^2)	10^5	10^6	10^7
Maximum Channel Bandwidth (GHz)	20	1	100
Reliability (PER)	10^{-2}	10^{-5}	10^{-9}
End-to-End Latency (ms)	10-50	1-10	0.1
Mobility (kmph)	350	500	1000
Energy Efficiency (TbpJ)	NS	NS	1

NS = not specified

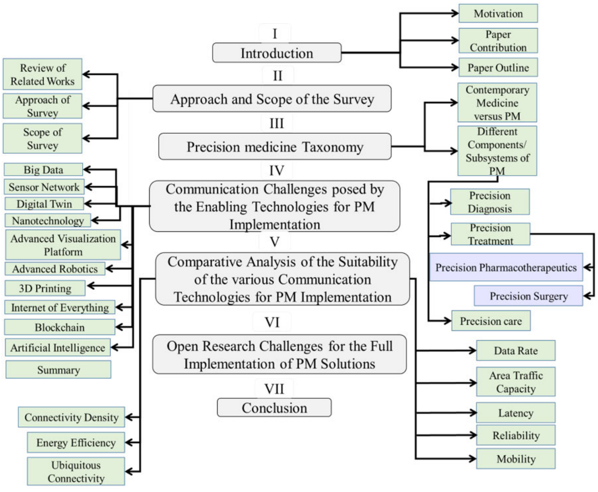


FIGURE 2. Illustration of the survey outline.

Secondly, the estimated range of the candidate communication systems requirement for reliable PM implementation is provided. Thirdly, we discuss the possible communication techniques that can be employed or improved to achieve the target KPI for PM implementation. Finally, we highlight some open communication network problems for each of the enabling technologies of PM that need to be addressed to ensure that the aims and objectives of PM can be fully achieved.

We also provided a comparative analysis of the suitability of the various communication technologies for PM implementation. A list of the essential acronyms used in this paper is given in Table 2.

C. PAPER OUTLINE

This survey is organized as shown in Fig. 2.

II. APPROACH AND SCOPE OF THE SURVEY

A. REVIEW OF RELATED WORKS

In the past two decades, research activities relating to PM have relatively increased, which is evident from the number of publications that have PM in their titles according to Web of science®(Fig. 3a). Comparatively, the number of

TABLE 2. List of some acronyms used in this paper.

Acronym	Definition
4G	4th generation mobile communication technology
5G	5th generation mobile communication technology
6G	6th generation mobile communication technology
ADR	Adverse drug reaction
AI	Artificial intelligence
APSK	Amplitude phase-shift keying
AR	Augmented reality
CoMP	coordinated multi-point
CRN	Cognitive radio network
D2D	Device-to-device
DDD	Drug design and development
eMBB	Enhanced mobile broadband
FDA	Food and drug agency
HCA	Human cell atlas
HCA-WC	Human cell atlas-Whole-cell model
IoBNT	Internet of Bio-nano Things
IoE	Internet of Everything
IoT	Internet of Things
MIMO	Multiple-input multiple-output
MISO	Multiple-input single-output
mMIMO	Massive MIMO
mMTC	Massive machine-type communications
NFV	Network function virtualization
NOMA	Non-orthogonal multiple access
OFDM	Orthogonal frequency-division multiplexing
OFDMA	Orthogonal frequency-division multiple access
PDDD	Precision drug discovery and development
PM	Precision medicine
QoE	Quality of experience
QoS	Quality of service
RAN	Radio access network
SDN	Software-defined network
SIMO	Single-input multiple-output
SON	Self-organizing network
TDD	Targeted drug delivery
UE	User experience
uMIMO	Ultra-massive MIMO
URLLC	Ultra-reliable low-latency communications
VR	Virtual reality
WC	Whole-cell
*X*G	Arbitrary generation of mobile communication technology
XR	Extended reality

publications with PM in the title for IEEE Xplore®is much lower (Fig. 3b). The high margin of discrepancy may be attributed to the lack of clear identification of PM's connectedness and open problems for many engineering research fields. Narrowing the discussion down to communication engineering, it can be seen from Fig. 4 that there are shallow research activities in PM under communication engineering. Yet, the goals of PM cannot be achieved without an efficient and robust communication technology. The thin level of research activities on PM from a communication engineering perspective can be attributed to the lack of clear identification of the connectedness of PM to communication engineering in terms of addressing the technical challenges of PM. Therefore, we hope that this survey will energize the efforts in increasing research activities in PM under the umbrella of communication engineering.

B. APPROACH TO THE SURVEY

In this paper, we employ Fig. 5 to give a clear picture of the problem statement and approach to this survey.

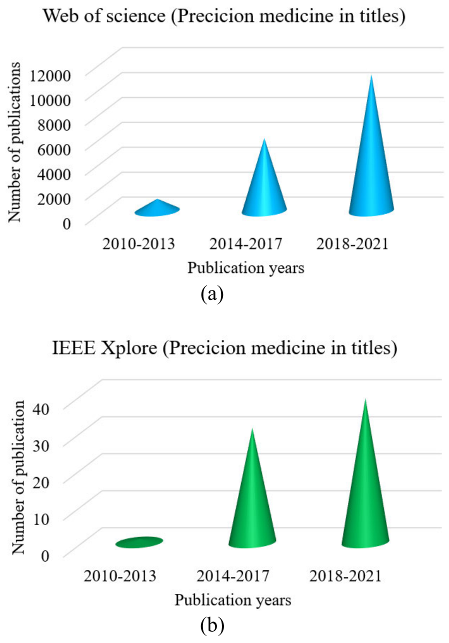


FIGURE 3. Publications with PM in their titles from 2010 to April 2021 in (a) Web of Science® (b) IEEE Xplore®.

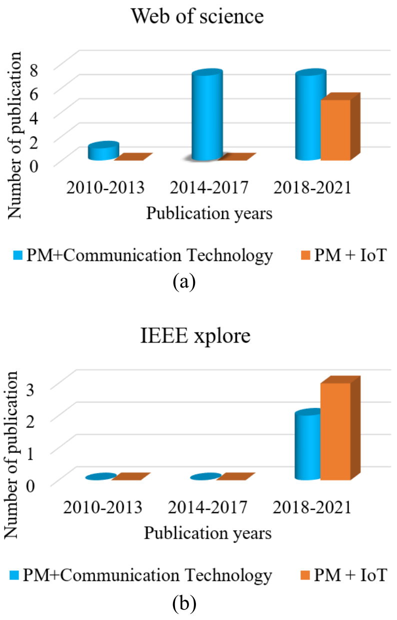


FIGURE 4. Publications with PM and communication technology in their titles from 2010 to April 2021 in (a) Web of Science® (b) IEEE Xplore®.

The problem statement is inclined toward identifying the adequacy of the various contemporary and future communication technologies to enable PM implementation. Specifically, the survey aims to determine the suitability of the contemporary and future communication technologies, namely, 4G, 5G, and 6G to support PM implementation that is enabled by technologies such as big data, robotics, XR, digital twin, and sensor network. This challenge is addressed by looking at various research papers on PM concepts, PM enablers, and communication engineering. And based on the review,

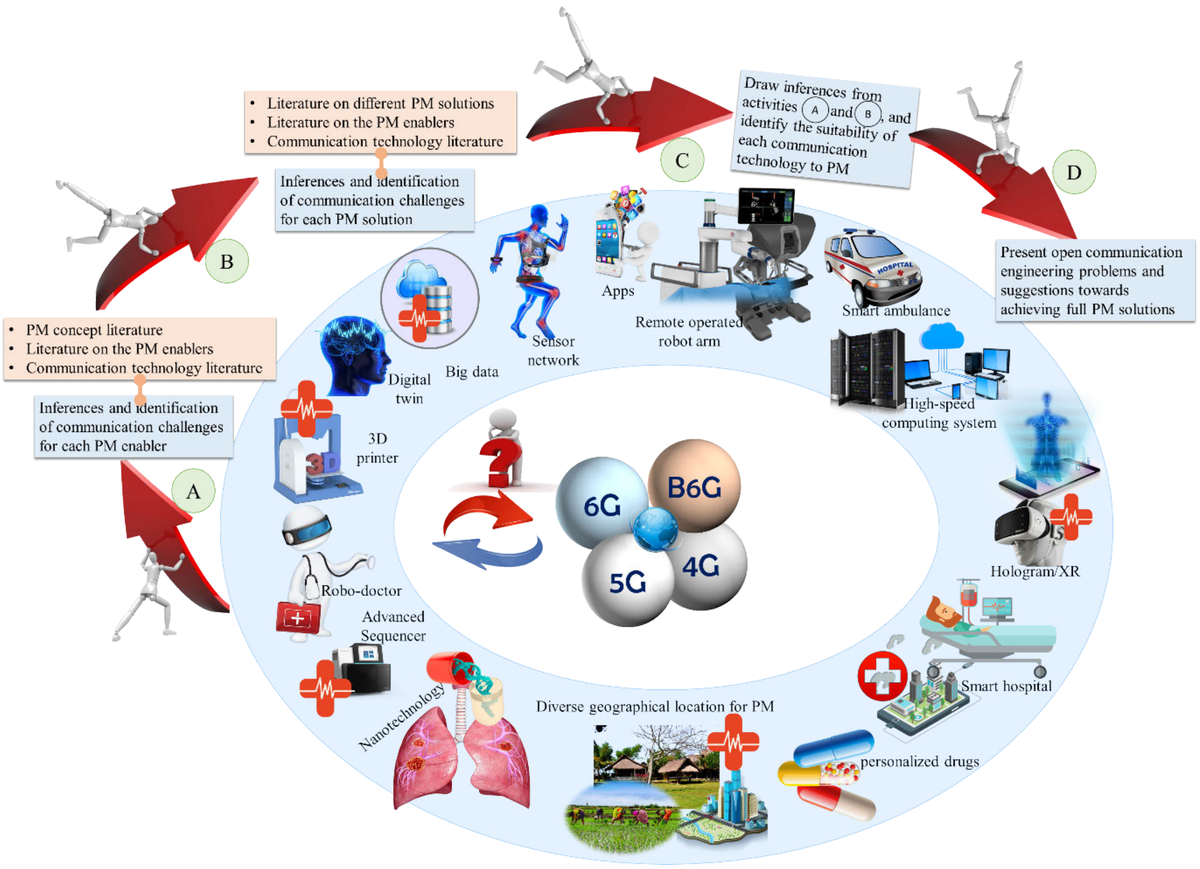


FIGURE 5. Illustration of the problem statement and methodology of this paper.

we draw inference on the critical requirements of these technologies in terms of data rate, latency, area traffic capacity, reliability, energy efficiency, connectivity density, ubiquitous connectivity, and mobility. We also provide suggestions on the approaches that can be used to improve the performance of the existing/future communication technologies to provide the required QoS for effective PM implementation.

C. SCOPE OF THE SURVEY

The scope of our work mainly covers aspects related to PM concepts, considering PM in the context of communication engineering impacts, clearly identifying the challenges PM implementation will pose to communication networks, and positing possible solutions where we can. The deep technicalities of PM operations are not discussed in this paper. Some of the recurrent acronyms are given, and some existing papers on PM and communication technologies are compared with the current survey paper in Table 3.

III. PRECISION MEDICINE TAXONOMY

A. CONTEMPORARY MEDICINE versus PM

Contemporary (traditional) medicine such as the intuition and evidence-based medicine [40] consider a 'one-size-fits-all' (1-of-n) approach. This implies that pharmacotherapy and other therapies are designed to address the medical challenges of large groups of people with similar diseases. This approach often undesirably results in the variability of the efficacy and ADR of a given therapeutic method for different individuals with the same disease, as is illustrated in Fig. 6a. On the other hand, PM considers a 'one-size-fits-one' (n-of-1) approach, which ensures that individuals with the same disease are provided with individualized treatment that gives a better outcome, as is illustrated in Fig. 6b. In PM, personalized information such as the patient's omics data, lifestyle, medical history, family medical history, and environment data is employed in therapies.

B. TAXONOMY OF PM

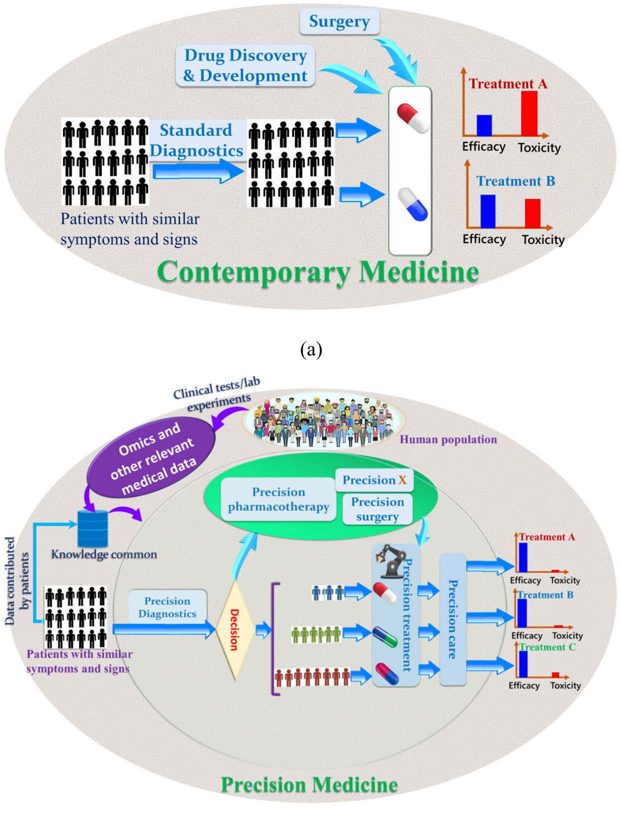
As the popularity of PM keeps increasing, the prospect of more personalized treatment that can be grouped under it is accelerating. Hence, it is necessary to provide the taxonomy of PM. As depicted in Fig. 7, PM can be taxonomized into various aspects of medicine and other related medical fields guided by personalized data toward addressing the health challenges of individuals. The principal subsets of PM include precision diagnostics, precision treatment, precision DDD, precision pharmacotherapeutics, precision surgery, precision care, and precision X (where X stands for other primary fields of medicine).

Looking at Fig. 7, it can be observed that the various subsets of PM have to collaborate very closely to deliver PM promises. Each of the subsets/subsystems of PM will require

TABLE 3. Summary of some related review, survey, and technical papers on PM and communication technologies.

Ref.	PM	*XG*	4IR enabler	Remark
[21]	o	x	Digital twin	Proposes the use of the digital twin model as a PM solution.
[12]	✓	x	Advanced robotics	This review discusses the current trends of medical micro and nanorobotics for therapy, surgery, diagnosis, and medical imaging for PM application.
[11]	o	x	Advanced Sensor/sense network	Highlights key breakthroughs in the development of enabling technologies for PM implementation.
[31]	o	o	Sensor (*mentioned*)	Discusses how the 5G capabilities can enable PM.
[32]	x	o	Big data, IoT, and Cloud computing	Discusses the role of emerging technologies such as cloud computing, fog computing, Big Data analytics, IoT, and mobile-based applications in realizing the benefits of PM.
[33]	✓	x	Big data and AI	Considers the informatics viewpoint to review the enabling tools and techniques for PM applications.
[34]	o	o	3D printing	The overall goal of this progress report is to highlight recent advances in 3D printing technologies that are helping to enable advances important in precision medicine.
[35]	o	x	Big data	Presents demonstrate how big data analytics enables PM.
[36]	o	x	Advanced Sensor/sense network	Reviews the role of implantable biosensors in PM.
[37]	✓	x	Nanotechnology, Big data (*mentioned*), Sensors(*mentioned*)	Explored how innovations and new technologies in precision medicine are paving a new era in patient-centric care
[38]	o	x	IoT and sensors	Explores how IoT will enable precision medicine
[39]	✓	x	Advanced visualization platform	A review of the current progress and impact of AR on precision medicine
This survey	✓	✓	Big data, nanotechnology, sensors/sensor network, Digital twin, Advanced visualization platform, advanced robotics, IoE, High-speed computational platform, Blockchain	Explores whether the contemporary and future communication technologies can provide the needed network to support PM.

{*XG* = 4**G**, 5**G**, 6**G**}; ✓ = extensively discussed ; o = limited discussion ; x = not discussed.



(a)

(b)

FIGURE 6. Illustrative comparison between contemporary medicine and PM.

the integration of a number of the 4IR enabling technologies in its operation. Hence, a network built on the premise of a communication technology capable of delivering specific performance requirements in terms of QoS and QoE is crucial to realizing the goals of PM. Therefore, these requirements must be identified and considered in modifying contemporary communication technologies and developing future ones. Let us briefly discuss some of the principal subsets of PM.

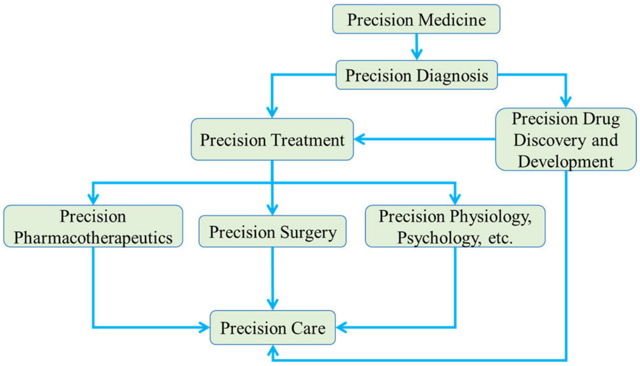


FIGURE 7. Taxonomy of PM.

1) PRECISION DIAGNOSIS

Precision diagnosis determines which disease or health condition explains a person's symptomatic and phenotypic state by taking advantage of the gains of molecular diagnosis and the pool of medical data associated with the individual. It is pivotal to implementing PM and has become a predominant practice in oncology [41], [42]. The precision diagnostic procedure involves the patient's physical examination, molecular testing, and omics/medical data-informed analysis, classification, and decision making.

The precision physical examination entails using a sensor or a network of advanced biosensors to obtain accurate body vital functions that are important in determining the disease under observation in a patient. In some cases, robots (macro/micro/nano-robots) embedded with these sensors can be employed in physical examination to achieve more sensitivity [43], remote examination [44], [45], and safer practice [46] in the event of contagious diseases. Not only will a robot-embedded sensor network provide accurate and safe measurement, but a wide range of measurements can also be taken simultaneously, transmitted in real-time, and stored in the desired format. For remote examination, the use of tactile internet and advanced visualization systems are required [47], [48].

The next procedure in precision diagnostics is detecting and measuring the genetic and proteins variants associated with the health condition or disease to aid in exposing the underlying mechanisms of the disease. This procedure enables the clinicians to tailor medication and care to the individual. Advanced molecular biological techniques such as molecular diagnosis [49], [50] and molecular imaging [49], [50] and molecular imaging [51], [52] are crucial for the precision diagnostic process. Techniques that are often employed in precision diagnostics include single-cell RNA sequencing [53], whole-genome sequencing [54], polymerase chain reaction (PCR) [55], in situ hybridization [56], and mass spectrometry [57]. To reduce the risk of infection transmission and errors in diagnosis, the collection of samples, the biobank storage, and assays of samples can be handled by robots with precision and speed [58]. It is also possible to deploy biosensors [36] and nano biosensors [59] inside the body to provide continuous diagnostics, which can be observed in real-time when the *in vivo* sensor network is interfaced with the internet [60]. The molecular imaging techniques for precision diagnosis include Positron Emission Tomography – Computed Tomography (PET-CT) [61], single-photon emission computed tomography (SPECT) [62], magnetic resonance imaging (MRI) [63], optical imaging [64], and ultrasound molecular imaging [65].

The final precision diagnostic procedure is to make an informed decision on the best therapeutic approach given the capability to analyze and classify the results from the precision diagnostic procedure in combination with the omics data, molecular imaging data, and other medical data related to the patient. The decision-making process is a crucial procedure that will typically employ AI and high-end computation platforms. The AI deployed in high-end computational platforms is instrumental to the data classification and pattern outlining. For instance, in [150], AI is employed to develop a sensitive and specific early warning system to predict necrotizing enterocolitis (NEC) in premature infants. In the analytical and decision-making stage, the use of the digital twin model of the patient will be essential. The model will be developed from the patient's omics data and serve as a virtual model. Various tests and validations can be made to determine the optimum therapeutic intervention needed.

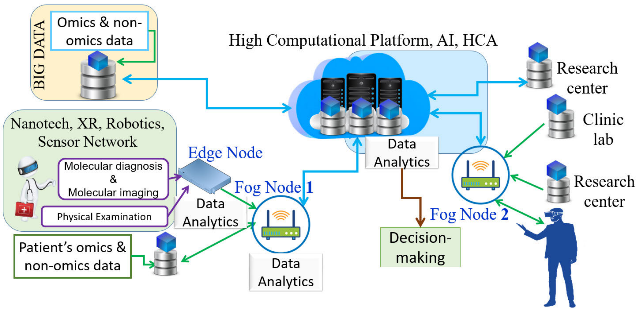


FIGURE 8. The illustrative communication network of the precision diagnostic system.

Each procedure involves different enabling technologies of PM, which make multiple demands on the communication network, as illustrated in Fig. 8. The ability to interconnect the various components and procedures of precision diagnosis depends on the capabilities of the communication network.

2) PRECISION TREATMENT

The outcome of precision diagnosis provides information on the optimal treatment procedure for a patient. The optimal treatment procedure will include one or a combination of precision pharmacotherapy, precision surgery, or other types of therapy. Precision pharmacotherapy and precision surgery as typical examples of precision treatment procedures will be deliberated in the ensuing discussion.

a: PRECISION THERAPEUTICS

Precision pharmacotherapeutics[66] encompasses the use of the right therapeutic drugs at the right dose for the right duration tailored to the treatment of an individual. To realize such a level of treatment, the subject of precision drug discovery and development (PDDD) [67]–[69] is vital. In traditional medicine, precision therapeutics and PDDD processes illustrated in Fig. 9 are normally disjoint. In this sense, drugs are produced in a ‘one-size-fits-all approach with no particular patient in mind. In pharmacotherapy, a given patient is administered a drug from the relevant set of drugs produced in the ‘one-size-fits-all approach of the conventional DDD process. Finding the right drug for a patient often depends on the availability of a large set of related drugs and generalized evidence of the efficacy and toxicity of the set, which is then extrapolated to the patient in a trial and error way. The precision pharmacotherapeutics approach integrates DDD and pharmacotherapy into one process. In this sense, the gap between precision pharmacotherapeutics and PDDD is tight.

The goal of the PDDD is to significantly improve the therapeutic ratio of drug products in a given patient population. This can be achieved by increasing the probability of efficacy and decreasing the likelihood of toxicity. The PDDD process includes precision drug target identification (DTI), the precision design of putative drug molecules, and precision drug development. In the precision DTI process, the use of the digital twin [70], [21] will be at the heart of its operation to provide the needed in silico replica of a patient for the process. The generation of the digital twin model will employ

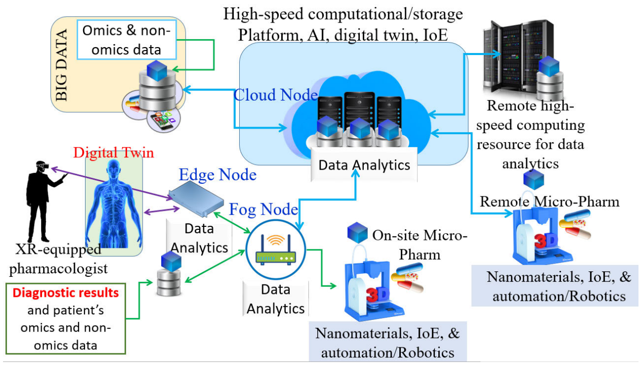


FIGURE 9. Illustrative communication network of the PDDD system.

high-speed computation-enabled AI-based data analytics of the personalized big data [71] and data from nanotechnology tools such as high-throughput assay and molecular imaging. The analysis and interrogation of the virtual patient will be done using tools that include XR and holographic displays to provide the needed high-resolution and immersive experiences to the specialists. The in silico precision DTI results will, in most cases, be further verified and validated experimentally.

The next stage in the PDDD process will be the precision design of the drugs. Here again, big data [72]–[74], and the patient's personalized omics data will be computationally and experimentally curated using AI-enabled high-speed computational platforms. The PDDD process ensures the identification of potent personalized drug molecules and compounds that can bind to the optimally identified target proteins in the body of an individual patient with low ADR. Here, the usefulness of the digital twin and nanotechnology will come into play. Nanotechnology will provide insights into the molecular and sub-molecular behaviors of the drug targets and the candidate drug molecules in a way that takes the systemic view of the patient's body composition into perspective. The molecular information geneared will be digitally projected onto the digital twin model of the patient to provide a wholesome analytical perspective on the drug efficacy and ADR. The precision drug design process can benefit from the gains of using advanced visualization tools such as XR and holographic displays to provide high resolution and immersive virtual experience in data analytics. The entire precision drug design process will typically be looped through the precision DTI stage for optimal results.

The last stage in the PDDD process will be the precision drug development stage. The contemporary drug development stage includes the Phase I-III clinical trial, food and drug administration (FDA) review and approval, and the drug manufacturing processes. In the case of PDDD, the accuracy and the duration of clinical trials are optimized by a much deeper and distributed efficacy and ADR evaluation across the DTI and drug design stages with the aid of the virtual patient model. Here distributed efficacy and ADR evaluation implies that the processes are evaluated at multiple phases in the entire PDDD process. The individualized focus of this process forces an n-of-1 trial approach, which decreases the duration of the drug design and development process. The drug approval in the PDDD process will typically be left in the hand of the patient, specialist, and relatives. Irrespective of that, the FDA approval may still be needed, in which case the development of automated blockchain smart contract platforms that are synergized with AI-enabled big data analytic systems to ensure near-zero-delay processing time and that patients take responsibility in the approval process will be incorporated. The 3D printing technology (and integrated IoE platform), automation, and advances in nanomaterial for drug manufacturing will provide on-site manufacturing of the drug, which will usher in the creation of many micro-pharm industries [75], [76].

b: PRECISION SURGERY

One of the treatment procedure options in medicine is surgery. Rather than performing surgery on many to benefit a few, as is the case in contemporary surgery, precision surgery aims to apply surgical therapy to those most likely to benefit and avoid surgery in those doomed to fail [77]. To achieve this, the surgical procedure should be patient-specific, accurate, and accessible anywhere and anytime. And to achieve these aims, the complete medical information about the patient must be available before (for planning) and during the procedure (for execution). Also, a high-precision surgical system must be available, and the entire system should have the capability of being remotely operated. Precision surgery will employ data/XR/hologram-driven [78], [79] digital twin model [80] of the patient to avail adequate information for the procedure. As depicted in Fig. 10, advanced robotic, automation, advanced sensor network, AI, IoE, big data [81], [82], and advanced visualization systems are required to ensure high precision in the procedure.

3) PRECISION CARE

Precision care aims to plan and tailor the path of care to an individual patient's need based on data from the individual's precision diagnostic and precision X results, where X stands for the therapeutic approach recommended for treatment. The framework of precision care includes components and processes such as patient-centric drug delivery modalities and X delivery procedure, which will ideally be enabled by technologies such as advanced sensor networks, IoE, automation/robotics, and AI.

The precision care workflow and framework ideally act on the precision X system's output to provide a patient with the right care and management based on PM recommended procedure until full recovery is achieved, as is illustrated in Fig. 11. The precision care cycle starts from the point of referral of the patient. It goes through the administration of the actual therapeutic measure to the patient, the patient/procedure progress monitoring and data analysis, and the decision-making process on the procedure's progress. If the resultant analysis and the ensuing decision points to a satisfactory outcome, PM is deemed completed; else, the

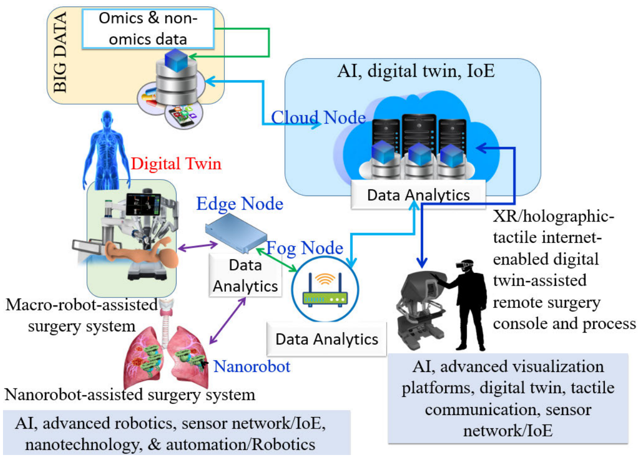


FIGURE 10. **Illustrative communication network of precision surgery system.**

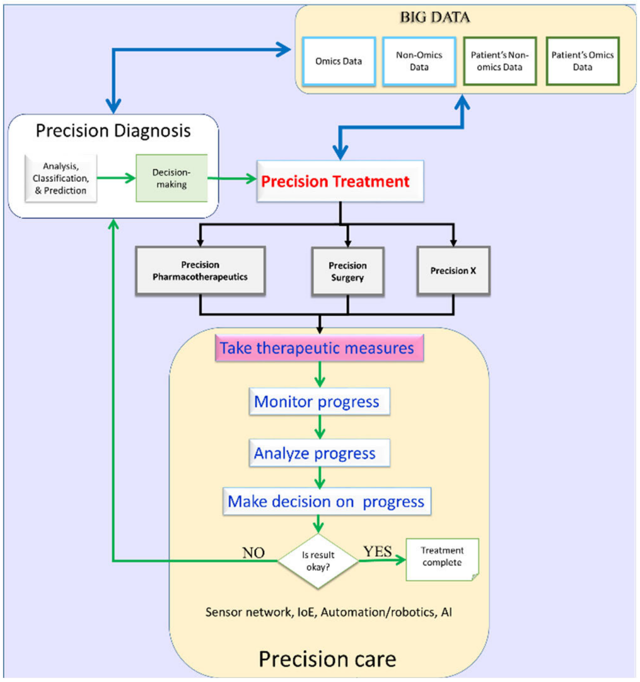


FIGURE 11. **Precision care workflow.**

analytical data is looped back to the previous systems, especially the precision diagnosis stage, for more action.

Sensor networks serve to constantly and robustly monitor the patient's condition throughout the care period to ensure that dose parameters, vital signs, and physiological signals [83] are at their optimal level. The sensor network comprise in-body sensors, intra-body sensors, on-body sensors, and environmental sensors. These sensors can be used to monitor electrophysiological signals, oxygenation and heart rate, analysis of body fluids. For more on the sensor types for the precision care application, readers can refer to [11]. AI is required to analyze data from the sensors, which will be ideally automated to inform the line of actions required in the care process. The required line of actions may include a change in the patient-centric drug delivery modality and the regulation of food intake and the adjustment of the environmental conditions. The entire system can be accessed and controlled over the IoE. There may also be the need to 3D-print some components that will be required in the care process. These components will mostly be the replacement parts for the systems required for the successful execution of the care procedure.

IV. COMMUNICATION CHALLENGES POSED BY THE ENABLING TECHNOLOGIES FOR PM IMPLEMENTATION

PM is a data-driven medical solution. In this sense, data acquisition, exchange/sharing, analysis, informed decisions, and implementations are pivotal to the operation and delivery of the promises of PM. The coordination of the data acquisition from multiple sensors/sensor networks, data exchange/sharing among numerous databases, multi-platform analysis of data, and decision-making operations require a communication network. Hence, it is logical to state that the expectations of PM cannot be fully met without the availability of an exemplary communication network. This section discusses the communication technology challenges and basic performance requirements for the effective implementation of PM. Expressly, the communication challenges individually posed by the various enabling technologies of PM, namely, big data, nanotechnology, digital twin, sensor network, internet of everything, artificial intelligence, XR, Holographic display, advanced robotics, 3D printing, and blockchain, are discussed.

A. *BIG DATA*

In the era of PM, it is expected that billions of people will be generating PM-related data from individualized vital sign sensing activities, assays, and tests carried out by many research and medical laboratories across the globe. The high volume, velocity, variety, and veracity of the data acquisition and processing present a 'big data' challenge to the communication system for PM implementation [84], [85]. Among the many big data generators globally, PM-related data such as omics data will likely supersede all of the others by a wide margin in terms of volume, velocity, variety, and veracity. This assertion is supported by the fact that when we compare the major generators of big data such as astronomy, YouTube, and Twitter to only genomic data, the genomic data comes second only to astronomical data [86]. However, genomics is just a portion of the omics data. Other slices of the omics data, which include transcriptomics, proteomics, metabolomics, metabolites, viromics, and micobiomics data, are not factored into the above comparison.

To further substantiate the claim that the omics data will supersede all other big data generators by a wide margin, we note that the genome that encodes roughly 19,000-23,000 genes [87] is static and only changes when a mutation, methylation, or translocation occurs [88]. By comparison, the proteome is far more dynamic, complex, and larger [88]. This implies that proteomic data will be much larger than genomic data. Suppose we extend this argument to the other omics data types, whose dynamism and variability are linked to genetic and proteomic variations. In that case, we will be having more of a combinatorial complexity scenario that indicates that omics data volume will be so large and exceeds astronomical data. Now, if we include viromics, micobiomics, other medical data, and the fact that only a tiny fraction of the global population currently has their omics data available, then the enormity of the 'Big data' requirement and challenges of PM solution will be much higher than any big data generator in years to come.

The distribution and analysis of PM big data will place high data rates and computational demands on contemporary and future communication systems. Unlike other big data that usually contain many redundancies, which are usually sieved out during processing at the source of the data generation, the individual nature of the data analytics implies that the sieving takes place at the point of need. Hence, the omics data for PM will be distributed in units spanning a wide range of sizes that is dependent on the individual need of whom the solution is meant. Informed by [86] and following the argument above, we project that the data rate requirement for the transmission of a few bases or gene sequences will be greater than 10Mbps and up to 100Mbps, and for massive bulk downloads from central repositories, the data rate will be $>$10Tbps [86].

The reliability of the data transfer network that can support the big data service for PM applications will be up to 10^{-9} [24] due to the sensitivity of the data and the intended application. When you consider the distributed nature of the sources of the data required for PM application, the need in some cases for real-time data analysis, and the requirement for real-time responses to addressing a medical condition, then will be the need for a low latency communication network that can offer seamless coordination of these activities. More also, in a case where distributed and cloud computing are employed for big data analytics, the protocol at the big data sources, the geographical locations of the computing sources, the amount of data being shared for a given job within a mean job processing timeframe, will impact the latency requirement [89]. A pervasive communication network is also required so that big data resources can be accessed from anywhere in the world where they are needed. Therefore, the communication network challenges for PM applications include very high reliability, high data rate, low latency, and ubiquity.

B. SENSOR NETWORK

Sensor and sensor networks play crucial roles in PM. These sensors include those that are used for on-body [90], intra-body [91], and in vivo [92] data acquisitions and those embedded in other systems employed in PM for functions such as automation and control. The wide range and diversities of PM applications and systems require a wide range of different types of sensors and sensor networks that are vertically and horizontally heterogeneous. Vertically, the network can comprise sensors of different technologies such as macro-sensors, micro-sensors, and nanosensors. Horizontally, the network can comprise sensors for different functions such as those for measuring biosignals like temperature, pressure, and blood sugar level. While communication between macro-sensors can be achieved using conventional electronic communication, communications among micro-sensors and nanosensors require a nanocommunication technology [93]–[95]. For example, some nanosensors can function as precision biomarker identifiers [96], which can be integrated into an *in vivo* nanonetwork [60] to relay discoveries to a remote system. If such *in vivo* nanosensors are employed, nanocommunication capability will likely be a requirement for the full implementation of a PM system.

It is estimated that by 2020, the 5G network will support 50 billion connected devices and 212 billion connected sensors [97], which is six times what it was in 2011. Taking PM scenarios into consideration, these numbers will surely exceed the factor of six projected for the period 2011-2020. For instance, *in vivo* targeted drug delivery (TDD) application nanonetworks will likely contain hundreds to millions of nanosystems within the space of a human body, say, 1 m^2 [98], and some wearable devices will be used per person for personalized vital sign data acquisition. Hence, a much higher number of sensors is projected than what is projected in [97]. The existence of a very large number of devices/sensors in PM solution environments in the coming years and the fact that more and more people will be wearing sensors to keep a record of their health conditions will result in the need for very high connectivity density communication network. Even people in rural areas will have sensors to acquire and transmit their medical data for PM applications; hence, there is a need for pervasive coverage of the communication network. In some scenarios like in the stadium and other high-capacity event places, there may be a momentary surge in data traffic, which will necessitate the need for a high area traffic capacity. And the sensitivity of the sensor data implies the need for high-reliability communications. Moreover, the billions of sensors for PM application will need to be energy efficient, which also translated to the requirement of an energy-efficient communication system.

Therefore, the sensor network challenge for PM requires energy-efficient, ultra-reliable, and low latency communication technology that is pervasive and supports very high connectivity density. And where nanosensor networks will be employed to enable *in vivo* communication among nanosensors, nanocommuniations [99] will be a requirement.

C. DIGITAL TWIN

The primary aim of PM is the provision of timely and effective treatment of all diseases, which entails timeliness in diagnosis, determining the suitable therapeutics, and administering the same to a given patient at any location in the world. However, the process of obtaining a patient's tissue sample, conducting omics experiments/assays, determining the putative therapeutic modality, and conducting the assessment of the effect of therapeutic interventions will usually take a long time Indeed the process can possibly take months/years, which negates the timeliness factor required for on-the-spot therapeutic intervention. And, conducting an extensive assessment of the effect of therapeutic interventions directly on the patient under observation is very risky and typically unacceptable. Therefore, that begs the question of how to address the challenges mentioned above.

An option to address the above challenges is using the digital twin of a patient to conduct the various assessment required to determine the effect of therapeutic interventions on the patient before administering them to the individual. The digital twin concept comes from engineering and has been applied to complex structures. The digital twin for PM purposes [21], [100], [101] is a computational system that is a replica of a given patient and allows for in silico tests and assessment of therapeutic modalities before the same is administered to the patient in reality. The use of a virtual patient model that replicates the patient's body system under medical investigation and therapy is crucial to PM to ensure the provision of timely and accurate diagnosis as well as the effective treatment of all diseases irrespective of where the patient is located. The digital twin model has also found application considerations in combating viral infection [102] and Multiple Sclerosis [103].

While the digital twin is important to implementing PM, its development is not an easy task due to the complexity of the human system and the current state of the unavailability of a complete understanding of the molecular characteristics and mechanisms of many diseases in connection with the entire body system. This assertion translates to the lack of complete understanding of how a trigger in one part of the body influences the entire molecular mechanisms of the whole body. To obtain a complete knowledge of the human body's molecular mechanics, it is the opinion of this paper that the complete knowledge of all the different cells in the body, which are the fundamental units of organisms, and their interactions with one another, are crucial. With such knowledge, it is possible to integrate the models of the cells into a whole community that can mimic the human system, at least within a reasonable margin.

The genome project [104] leads in the quest to achieve the goal of complete knowledge of the human body by taking up the challenge of obtaining the human genome sequence. However, despite the decades of accumulation of massive genomics data, we still do not fully understand how genotypes give rise to phenotypes. Other grand projects such as the whole-cell computational (WC) model project [105] and the human cell atlas (HCA) initiative [106] have also been initiated. The WC model aims to develop the computational abstraction of human cells for understanding and predicting how phenotypes arise from genotypes [107]. The HCA project seeks to define all human cell types in terms of distinctive molecular profiles and connect this information with classical cellular descriptions as the basis for understanding human health and diagnosing, monitoring and treating disease. However, while these fragmented efforts are going on, the idea of a human digital twin for PM implementation is still far-fetched.

Recently, [108] presented a conceptual approach to digital twin for PM implementation in which the integration of HCA and WC projects is considered in developing a virtual patient model. While the conceptual model presented in [108] considered a few sparsely modeled cells, it is yet to be seen how such a model can be used to implement a realistic virtual patient model taking the many cells in the human body into consideration. If such a model is realizable, it will expectedly be an extremely complex network that presents a huge computational challenge. Even with other models that will emerge in the future, there will be a huge computation burden associated with their practical implementation. Consequently, this will translate to communication challenges where very high data rates and low latency networks will be required for the exchange/update of the virtual patient models across the network. Also, the sensitivity of the human digital twin-component data requires that the network will have a high level of reliability. Additionally, the digital twin models should be accessible from anywhere across the world where they are needed, which requires pervasive communication networks.

D. HIGH-SPEED COMPUTATIONAL PLATFORMS

The acquisition of massive omics and medical data makes no sense if we do not have the fast analytical capability to interpret these data for effective tailoring to patients' therapeutic processes. Hence, not only is PM data-driven, but it is also computation-driven. The computational demand of PM stems from the need to handle at record time the analyses of the massive data that is generated for the process. For instance, in the course of employing the digital twin in PM solutions, the computational burdens involve so many simultaneous computations that require the initiation of both distributed and parallel computations. The computing task can be accomplished using a dedicated local distributed (or parallel) computing network, fog/edge distributed (or parallel) computing network, distributed (or parallel) cloud computing infrastructures, or the integration of two or more of the platforms [109]. Irrespective of the platform of choice, the computing nodes will communicate with one another to share tasks and resources. Hence, the ratio of the computation latency of the participating computing nodes to the latency of the communication network is crucial. Computation latency relates to the mean average delay in executing a computational task. A high computation-to-communication latency ratio is desirable so that a large time will not be spent on communication between computing nodes. Hence, the task allocation protocol must consider the average of this ratio while allocating computational tasks to each computing node. And since computation speed is usually very high for most modern processors, this implies a low computation latency, hence, it is required that the communication latency be as low as possible to keep the ratio high enough. Consequently, for the use of a high-speed computational platform, an ultra-low latency communication network is a requirement. If mobile computing nodes [110] are included in the distributed system, issues relating to high mobility and how they affect the computational performance of the system have to be considered. More also, almost all contemporary computing systems consume lots of energy; therefore, the use of high-speed computational platforms will necessitate energy-efficient communication technology.

E. NANOTECHNOLOGY

PM entails the interrogation of the human body system at the nano-scale level; hence, it will benefit a lot from the basics and gains of nanoscience/nanotechnology [111]. Nanoscience is the study of the properties and characteristics of things at the nano-scale level. And nanotechnology is concerned with the engineering of nano-scale size things using different techniques and knowledge from nanoscience. There are various contemporary nanotechnology tools and techniques currently being developed that will be crucial to deploying PM solutions. These tools and techniques include single-cell sequencing, molecular-level sensing/detection techniques/ devices, nanosystems design and fabrication, and gene editing tools. The gene-editing tools include the clustered regularly interspaced short palindromic repeats (CRISPR), transcription activator-like effector nucleases (TALEN), and zinc finger nucleases (ZFN). The techniques can alter specific components of a genome, thereby opening new doors to precision editing/repair of defective genes associated with diseases [112]–[114]. Other nanotechnology tools for use in PM include nanoparticles and nanocarrier designs [115], [116] for targeted drug delivery (TDD) [98], [117]. Nanotechnology also offers the possibility of developing nanorobots for very minimal invasive localized surgery [12], [118], [119]. In the case of precision diagnostics, nanotechnology tools such as those for single-cell RNA sequencing [120], single-cell proteomics sequencing [121], single-cell metabolomics sequencing [122], biomarker discovery [123], and molecular in-vivo imaging aided by nanoparticles [124], [125], are available. These molecular-level diagnostics and discovery tools are essential to the implementation of PM.

The nanotechnology-based PM enablers mentioned above present communication challenges that the current and future communication systems have to address to ensure the delivery of the gains of PM. Firstly, nano-scale devices are used to explore and acquire data from locations and for phenomena that are hitherto not accessible. This results in the exacerbation of the 'big data' challenge already discussed. A challenge that the exploration and use of nanotechnology concepts and tools may pose to the communication networks is the integration of nano-scale signaling capability if communication among nanodevices [93], [126] is required for PM purposes.

F. ADVANCED VISUALIZATION PLATFORMS

To visualize the various processes, stages, and outcomes of PM procedure, there is a need for a visualization system/platform. The visualization systems provide a graphical representation of information and data. As shown in Fig. 12, examples of typical visualization types include texts, images, videos, extended reality(XR), and holograms. The term extended reality is used here as the generalization of virtual reality (VR), augmented reality (AR), and mixed reality (MR). Each of the display types mentioned above provides the user with its own peculiar experience and level of immersion. While text, images, and video displays are the typically used visualization systems in contemporary medicine, PM additionally requires true immersion in visualization by employing XR and holograms. In fact, for a truly immersive visualization experience, it is expected that PM solution will take full advantage of advances in sensing, imaging, AI, video, 3D display, and hyper-connectivity to provide the ultimate multimedia experience required for diagnosis, data analytics, and monitoring. The visualization systems for PM ought to be highly interactive, immersive, and create a kind of reality that allows multiple analysts to manipulate/zoom into the virtual digital object or system under examination for improved analytical results. The use of the VR [19], [127], AR, [128], [129], MR [130], and holographic display [131], [132] technologies are increasingly gaining attention in medical practice. For instance, specialists can examine the virtual anatomy or the digital model of a patient that is thousands of miles away on an XR or 3D holographic display and make some changes to the models as a pre-therapeutic procedure. This scenario can be extended to multiple specialists that are miles apart interacting simultaneously with the same patient's virtual anatomy model. Such procedure can be used in different aspects of PM including, diagnosis, therapy, surgery, drug discovery, and even medical education.

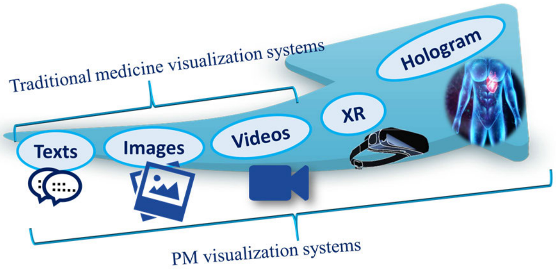


FIGURE 12. Various visualization platforms for use in PM applications.

However, to transmit and render the required very high-quality displays interactively requires a tremendous depth of information and extremely low delay. This implies the need for a communication technology with ultra-high data rate, ultra-low latency, and high-reliability capabilities [133]. While the XR experience for the contemporary VR systems with 3840 × 1920 (4K Video) requires 25Mbps, the XR experience for PM solution will require much higher video resolution and higher bandwidth. A data rate of 100 Mbps is required to live-stream sub-4K resolutions with full immersion for more than 15 min without nausea [134]. The expected visual perception for PM-suitable XR system will be within and above the human perception quality, which is from 16K Video and above. For such perception, the XR experience for multimedia with a lossy compression ratio of 400:1 will require 0.9 Gbps, multimedia with a lossy compression ratio of 300:1 will require 3.36Gbps, and the rate can be up to 1Tbps for an uncompressed media [135]. In the case of a holographic display system, it is expected that the bandwidth requirement will be more than the requirement for XR. For instance, a digital twin full length, raw data, and 30fps holographic interactive display will require up to 5Tbps [136], [137]. The latency requirement for XR is about 1-10ms [135], and for the holographic display, a sub-ms [137] is required.

A very high area traffic capacity is also required if there is a burst in using these technologies for PM solutions in a given area. In such a scenario, the traffic capacity can be as high as 12.5 Tbps/km^2 [135]. A typical packet error rate of the XR technology is about 10^{-6} [135]. However, a very low error rate is important in using XR to render the digital twin of a PM solution. For instance, a 0.01% packet error rate in a virtual patient model transmission may present less credible diagnostic results when such an error occurs in rendering the implicated disease cell model. Hence, lag spike and packet dropouts need to be kept extremely low the sensitivity of the medical procedure requires very high reliability in the range from 10^{-9}.

G. ADVANCED ROBOTICS

The rising use of robots in many facets of human engagements significantly shapes the way we live. Along with other enabling technologies of PM, robotics will play a significant role. Robots can be employed in the acquisition process, processing, and storage of personalized omics and other medical data with high precision. They can also be used in precision/remote surgery [138], [139] tailored to an individual procedure and driven by personalized data. Robots can help to accelerate drug discovery by improving the throughput of tests and doing so with high precision. In the area of precision therapy, robots can also assist especially, in drug delivery [140], [141], rehabilitation [142], and delivering medical procedures in a highly infectious environment [143].

To employ robots in the delivery of the functions/tasks mentioned above for PM purposes, the integrated communication technology should meet specific requirements. For instance, in the remote hologram/XR/robot-assisted surgical imaging systems [79], [144], [145], a high data rate communication system imposed by the integrated advanced visualization system is required. A crucial challenge that is particular to the use of robotics in PM procedures is the need for ultra-low latency communication platforms to implement the robot-assisted surgical imaging system, where tactile internet [146] is a requirement. This requirement stems from the need for delay-sensitive control of the robots' operations in real-time, where sub-millisecond latency will be required in most cases. When nanorobot becomes operationally and practically available to assist in surgery operations [147], the additional requirements associated with nanoscale signaling will need to be achieved. And given the very low network error tolerance of the surgery operation, a communication system with high reliability in the order of 10^{-9} is required [148], [149].

H. 3D PRINTING

The 3D printing technology is a technology of importance in facilitating PM. It is expected that this technology will enable the production of patient-specific models of body parts and medical devices. For instance, the 3D printed body parts can be used in tissue engineering [150], [151], and medical education [152]. In this sense, surgeons and other medical personnel will be able to 3D-print personalized models of the patients' tissues and organs and create medical devices, prosthetics, and implants tailored to a specific patient's therapeutic use. 3D printing will also revolutionize drug discovery and development in PM era. In this sense, a personalized drug discovery process conducted in a specialized facility using a patient's medical data can be printed and administered remotely to the patient far away from the specialized facility, as illustrated in Fig. 16. This will be made possible by advances in bio-printing [153], [154] and IoT-integrated 3D printing [39], [155] technologies. This 3D printing-enabled conceptual DDD approach will eventually change the face of the entire pharmaceutical industry and encourage the establishment of micro pharmaceutical industries across the globe.

The challenges that the 3D printing capability will impose on the communication network are reliability and data rate. Due to the delicacy of the objects that are to be printed, a very reliable communication network is required. For instance, the complexity of the structure and working operation of an organ or tissue implies that what may be assumed to be a minor error in the received STD file for the 3D printing may result in the production of a defective model. Hence, a reliable communication network is required for the faithful transmission of files for 3D printing in PM. Additionally, files for the printing of the organs and other body parts will usually be developed in specialized facilities. These files may then be required at the patient's remote location. Hence, the file must be sent over a communication network probably, within the IoE scenario, to be printed close to the patient's location. Therefore, to transfer such high-resolution 3D printing files requires a high data rate communication network.

I. INTERNET OF EVERYTHING

The IoE defines the seamless interconnection of many living things and non-living things, systems, and processes, using the internet infrastructure [156]. PM can tap into the capabilities of the IoE to tackle medical challenges in unprecedented ways, as is illustrated in Fig. 13. The data available from the plethora of 'things' connected will significantly help drive PM solutions, which are typically data-centric. Researchers conducting clinical trials for precision medicine will directly benefit from this technology. More also, research effort is going on to achieve the capability to query and alter the states of the living and non-living systems at the nanoscale level. In this case, the futuristic concept of the internet of bio-nano things (IoBNT) [60], [157], an offshoot of the Internet of

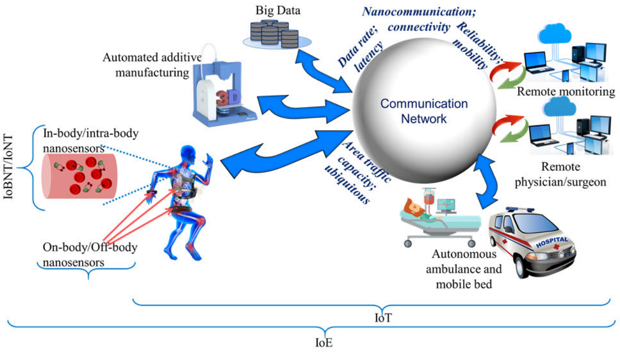


FIGURE 13. **Communication requirements for IoE application to PM.**

Things (IoT), which is still far from a practical realization, can be employed. Additionally, remote diagnosis/sensing, robot-assisted surgery, and remote additive manufacturing are other PM use cases of the IoE for which the sensor network and tactile internet are integral parts. Hence, the communication technology challenges that were mentioned earlier in association with the sensor network, advanced robotics, big data, 3D printing, and tactile capabilities are obtainable on the IoE platform. Hence, virtually all the communication technology challenges associated with the enablers of PM suffice for the IoE.

Consequently, IoE in PM context requires high-data-rate, ultra-low latency, high area traffic capacity, massive connectivity density, pervasive connectivity, ultra-reliable, nanocommunication capable, high mobility, and high energy-efficient communication technology.

J. BLOCKCHAIN

Blockchain is an immutable digitally distributed ledger technology that is characteristically transparent and operates on the peer-to-peer network architecture. Its decentralized and immutable characteristics offer huge potential to address challenges across platforms that deal with trust issues, such as the financial sectors, information exchange, and other sectors that deal in the exchange of values/valuables/services. PM can also benefit from blockchain. For instance, many entities will be involved in data generation, processing/computation, and storage in PM. These processes will be conducted on a decentralized platform. This calls for a secure and privacy-protected decentralized platform for the resource (data, computing resource, and storage space) sharing and allocation among PM solution providers/users (patients, medical personnel, researchers, device/drug manufacturers, and application developers). Blockchain technology is ideal for providing such a platform [158]. For example, so many research centers are scattered across the globe, and millions of sensor networks will generate patients' medical data for PM purposes that demand privacy and security. Blockchain is ideal for such an application scenario. More also, blockchain can provide the platform to engage in token-based value/information sharing. The idea of getting some tokens for data acquisition and secure sharing will increase participation in the project [159]. Additionally, many computers connected to the internet are often idle many hours a day. These idle computers can volunteer to rent out their computing and storage resources for distributed computing on a token-based appropriation protocol.

The major challenge imposed on the communication network by the integration of blockchain to PM is the issue of energy consumption and efficiency. While there is no clearly defined energy efficiency target for the 5G and 4G, future technologies will require a defined energy efficiency target due to the envisaged increase in data traffic and associated deployment of energy-demanding components in the network. Additionally, blockchain being a well-known huge energy consumer (due to the energy-intensive activities of the mining process) requires a very efficient energy consumption protocol for communication networks with its integration into PM process.

K. ARTIFICIAL INTELLIGENCE

AI algorithms employ learning strategies to define patterns in a data set and make meaning of a given data. It is becoming a pervasive technology present in many aspects of human lives. In PM, AI applies to the intelligent coordination of sensor data collection, data analytics, predicting risk in certain diseases from available multidimensional medical, DDD process, treatment response optimization, automated surgical operations, automated diagnostic procedure, and so on. Indeed, AI finds usage in virtually all aspects of PM [41], [42] and other base technologies that will enable PM implementation, as illustrated in Fig. 14. Hence, as many of PM nodes, systems, and processes become AI-enabled, their operations become interdependent and interconnected. This will impose the need for a communication technology capable of seamlessly connecting these intelligent systems – the connected intelligence - as is illustrated in Fig. 14. The connected-intelligent initiative is primarily challenged by the reliability and latency of the information exchange across the communication network. In some cases, huge data transfer across the communication may be required, hence, the need for high data rate communication. Other communication requirements include high area capacity, high connectivity density, ubiquitous connectivity, the possibility of high mobility of the intelligent nodes, and energy efficiency.

V. COMPARATIVE ANALYSIS OF THE SUITABILITY OF THE VARIOUS COMMUNICATION TECHNOLOGIES FOR PM IMPLEMENTATION

This section provides a comparative summary of the requirements and performance of the various communication technologies such as 4G, 5G, and 6G for PM. Specifically, in Table 4, we presented a comparison table for 4G, 5G, 6G, and the target candidate communication technology that can offer the QoS expected for PM applications. A close look at Table 4 shows that the communication resources demand of PM will stretch the contemporary communication technologies and 6G communication technology. Therefore, to meet

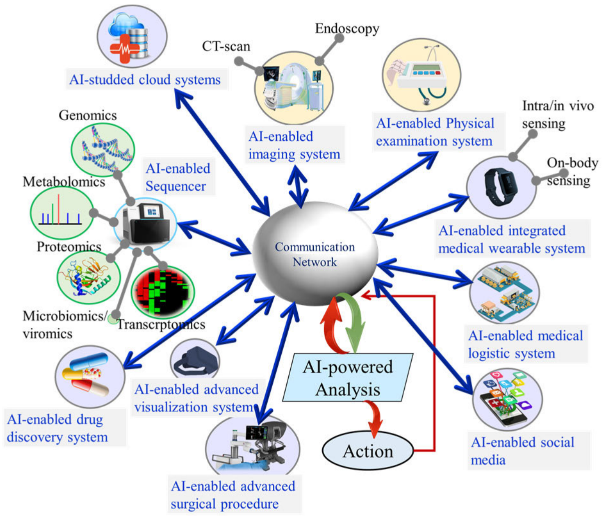


FIGURE 14. **Communication requirements for artificial intelligence application to PM.**

the communication technology demands for the deployment of PM solutions, the rest of this section is devoted to discussing the possible techniques that can be employed or improved to achieve the target communication technology KPI for PM.

A. DATA RATE

The data rate requirement for PM is primarily set by the need for big data, advanced visualization platforms, and digital twin in PM procedure. In particular, the digital twin model rendered using XR/holographic display system is crucial to many PM processes. Hence, the data rate requirement for PM is set from 10 Mbps to the Tbps range. It can be seen from Table 4 that the 4G and 5G communication technologies will be unable to accommodate the data rate range demands for PM applications. The 6G technology on the other hand may marginally handle much of the demands of big data for PM applications (except for massive data transfer) when the communication technology is operated at the proposed peak data rate value (Tbps). Therefore, novel communication strategies have to be explored to be able to achieve over 1 Tbps data rate for the beyond-6G communication technologies.

To obtain data rates in the order of Tbps implies developing techniques that will increase the capacity of the communication system as is illustrated in Fig. 15. Following Shannon's Capacity formula (1), achieving data rates in the order of Tbps is classically possible by increasing the system bandwidth and spectral efficiency. Various advanced techniques for increasing the two variables are typically one of the fundamental focuses considered in the development of contemporary and future communication technologies. To increase the communication bandwidth (BW) to target the Tbps data rate range, the natural approach is to explore the use of spectrum in the ranges of millimeter-wave, Terahertz (THz), and the optical spectrum. And the typical approach to increasing the spectral density includes using high-level modulation techniques, signal multiplexing, beamforming, and increasing the signal-to-noise (SNR) ratio.

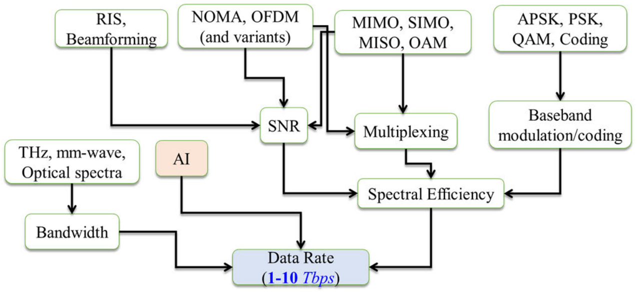


FIGURE 15. **Envisioned key techniques for achieving the target data rate for PM application.**

$$Capacity \rightarrow BW\,.\,\log(Spectral\ Efficiency) \qquad (1)$$

While there is the availability of large system bandwidth in the millimeter-wave and Terahertz band that can be used to greatly increase the data rate, there are several factors that impact the choice of bandwidth size and the frequency range of the bandwidth. Firstly, the use of large bandwidth increases data rate and, at the same time, degrades the spectral efficiency gain of the system by increasing the noise floor of the channel. Secondly, the varying channel propagation characteristics, the frequency-specific atmospheric attenuation, and time-selective phenomena significantly impact signal propagation at the millimeter and THz frequencies. In particular, communication in THz and millimeter-wave bands suffer from poor propagation characteristics, high attenuation, blockage and scattering losses, and high Doppler spread. For an in-depth discussion on the effect of wave propagation channel on the millimeter-wave and THz frequencies, the reader is referred to [170]–[173]. The use of the unlicensed optical frequency range of 400-800 THz, which forms the basis of the visible light communication (VLC) technology [174]–[176] with its inherent huge bandwidth gain, can push the data rate possibility to many Tbps; however, VLC has its challenges [174], [177]. Therefore, to achieve the high data rate required by PM application, large bandwidths, which are available at the millimeter-wave, THz frequencies, must be utilized for communication. The choice of frequency ranges for the bandwidth must consider the impact of the wireless channel and the resultant effect on the spectral efficiency as the function of the noise floor level.

An additional gain in data rate can be obtained by increasing the spectral efficiency. This can be done by increasing the overall number of pulse levels (high-level modulation techniques) for message transmission. Such modulation techniques should be robust against channel impairments. Modulation techniques such as PSK, QAM, and APSK are candidates for achieving the desired PM data rate. The APSK has the edge over the other two because of its robustness against nonlinear distortions that may be introduced by receiver amplifiers [178]. Another approach to increasing

TABLE 4. Comparison of the capabilities of the contemporary communication technologies to support PM implementation.

KPI for True PM experience	Critical Requirements	Estimated Value Range for Implementing PM		4G	5G	6G	B6G
User Experienced Data Rate	Digital Twin, Big data, Advanced visualization platform, Advanced robotics, IoE	Big data (non-bulk) Sensor network	**10 - 100 Mbps** [86], [160]	o	✓	✓	✓
		Big data (bulk) Digital twin Adv. visualization Adv. Robotics IoE	**100 Mbps - 1 Tbps (and maybe more)** [86], [136], [161]	x	o	✓	✓
Area Traffic Capacity (Mbps/m^2)	Advanced visualization platform, IoE	Advanced visualization platform, IoE	**> 12.5 Tbps/km^2** [135]	x	o	o	✓
Connectivity Density (Device/km^2)	Sensor Network, IoE, Advanced visualization platform, Advanced robotics, High-speed computational platform, and 3D printing	Sensor Network, IoE, Advanced visualization platform, Advanced robotics, High-speed computational platform, and 3D printing	**> 10^6 Devices/ km^2**	x	o	✓	✓
Ubiquitous Connectivity	Sensor Network, IoE	Sensor Network, IoE	**Pervasive connectivity is crucial to achieving the 'health for all' global initiative**	x	o	✓	✓
Reliability (PER)	Sensor Network, IoE, Digital Twin, Big data, Advanced visualization platform, Advanced robotics, High-speed computational platform, and 3D printing	Sensor Network and IoE	**10^{-3} - 10^{-10} PER** [24], [160], [162]	x	o	o	✓
		Digital Twin, Big data, Advanced visualization platform, Advanced robotics, and High-speed computational platform	**10^{-6} to 10^{-9} PER** [32], [174]	x	o	✓	✓
End-to-End Latency (ms)	Advanced visualization platform, Advanced robotics, High-speed computational platform, Big data, Nanocommunication, and IoE	Sensor network and Big data	**10 – 20 ms** [160], [163], [164]	x	✓	✓	✓
		Advanced visualization platform	**1 – 5 ms** [135], [165], [137]	x	✓	✓	✓
		Advanced robotics High-speed computational platform, and IoE	**0.1 – 1 ms** [166], [167], [168],[169]	x	x	✓	✓
Mobility (kmph)	Advanced robotics, High-speed computational platform, and IoE	Advanced robotics, High-speed computational platform, and IoE	**Up to 1000 kmph may be required**	o	o	✓	✓
Energy Efficiency (TbpJ)	Sensor Network, Blockchain, IoE	Sensor Network, Blockchain, and IoE	**Not specified, but very crucial. Values above 1 TbpJ are considerable**	x	x	o	✓
Nanocommunication Capability	Nanotechnology, Sensor Network, Advanced Robotics, and IoE	Nanotechnology, Sensor Network, Advanced Robotics, and IoE	**Capability may be required in the future**	x	x	o	✓

✓ = Fully support PM applications ; o = limited support for PM applications ; x = cannot support PM applications.

the spectral efficiency and subsequently the data rate is by implementing signal multiplexing. Typical examples of the multiplexing techniques that can be implemented to address the data rate challenge posed by PM. Techniques based on waveform design and spatial multiplexing where orthogonal frequency division multiplexing (OFDM), non-orthogonal multiple access (NOMA), multiple antenna system, and orbital angular momentum (OAM) can be considered for implementing frequency multiplexing, power multiplexing, spatial multiplexing, and polarization multiplexing/phase shifting, respectively.

OFDM has become the prevailing waveform for mobile communication. It employs orthogonal signals that occupy the same frequency band to convey data simultaneously to a receiver, where they are combined in a way that either increases the SNR or increases the overall spectral efficiency. However, OFDM is known to have a high peak to average power ratio (PAPR), which results in nonlinear distortion when amplified with nonlinear amplifiers. Different variants of OFDM [179], have been proposed to address this challenge. However, transmission at a very high frequency, such as the Terahertz frequency requires nonlinear amplifiers, which will be a big challenge to OFDM. Hence, novel waveforms such as NOMA will be highly considered for PM communication technology. NOMA exploits different power levels to serve multiple users using the same time and frequency [180], leading to improved spectral efficiency when compared with OFDM [181]. Additionally, aside from the spectral efficiency and PAPR performance, several other factors such as processing delay, robustness to time and frequency-selective channels, massive asynchronous transmission, filtering/windowing, complexity, high flexibility, reliability, and MIMO friendless make NOMA a good candidate for PM communication network.

Multiple antennas systems such as SIMO, MISO, and MIMO can be implemented to increase the data rate by utilizing spatial multiplexing. By implementing maximum ratio combining for SIMO (signaling between base station serving multiple users with a single antenna, and a user with multiple antennae) and maximum ratio transmission for MISO (signaling between base station serving multiple users with multiple antennae and a user with single antenna), the SNR can be increased by a factor defined by the number of the user antenna and the base station antenna, respectively. If, on the other hand, MIMO is implemented, this will provide a two-thronged approach to increasing the data rate. The first consequence is that it will increase the spectral efficiency, and the second is that it will scale the bandwidth by the number of the receiving antenna. Hence, MIMO implementation is crucial to achieving the desired data rate for PM implementation. The use of a high spectrum other than the millimeter-wave will enable the transition from massive MIMO (mMIMO) [182] to ultra-massive MIMO (uMIMO) [183]. Also, more antennas can be integrated into a mobile system and other devices for PM applications due to the equivalent smaller size of the antenna element and antenna spacing. Notwithstanding, high capacity gain with MIMO requires a high scattering channel, which may not be common when using the millimeter-wave and THz spectrum since small cell sizes will be adopted to increase area traffic capacity and avoid signal attenuation. In this case, there may be a need to create scatterers for the MIMO operation artificially. The reconfigurable intelligent surface (RIS) may come in handy in the scenario to be used to artificially create a high scattering environment[184], [185].

To further satisfy the capacity demand of PM applications, the use of the orbital angular momentum (OAM) can be explored [186], [187]. It is reported that in certain scenarios, the achievable capacity for OAM is greater or equal to that of MIMO [188]. To satisfactorily and fully implement the OAM technique in this scenario, issues such as the limited number of available OAM-Modes, joint OAM-Mode and Frequency/Time Partitioning, and channel estimation for different OAM-Modes, should be addressed [189]. More also, it is possible to combine the gains of OAM with that of MIMO [190], [191], as well as NOMA, OAM, and MIMO [192] to provide a huge gain in channel capacity that will help achieve high data rate demand of PM.

B. AREA TRAFFIC CAPACITY

With the ever-increasing number of nodes, smart products, services, and applications that need to be connected coupled with the varying/high data rate demands of these systems, it is expected that the total throughput served by a communication network of the present and the future per geographical location will increase. And with the demand for PM applications in terms of data rate and the foreseeable ubiquitous use of the application, the area traffic capacity requirement for candidate communication technology that will fully enable PM will be much higher than that offered by 4G, 5G, and 6G. The expression for the area traffic capacity is given by

$$\begin{aligned} \mathit{Area\ Traffic\ Capacity} \rightarrow\ & BW \times .N \\ & \times (\mathit{Spectral\ Efficiency})/K \qquad (2) \end{aligned}$$

where K is the cell/site cluster size, and N is the number of cells per m^2.

It can be seen from (2) that the area traffic capacity is the data rate scaled by variables such as the cluster size of the cells and the number of cells in a defined area of interest. Therefore, as the data rate demand increases, the area traffic capacity should increase to ensure high reliability of network access and low blocking probability (good grade of service). And the desired QoS has to be delivered considering the possibility of having to deliver a burst of PM solutions in a given geographical area while simultaneously delivering communication services to many other data rate-demanding verticals and horizontals in the same geographical area. Hence, the required area traffic capacity of about 12.5 Tbps/km^2 [135], which can ensure the fulfillment of the area traffic capacity requirement of PM, exceeds that of the 4G, 5G, and 6G.

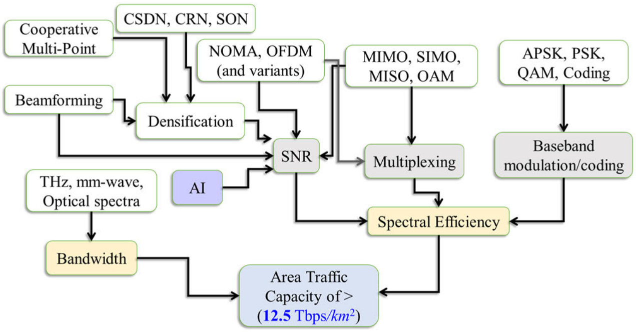


FIGURE 16. **Envisioned key techniques for achieving the target area traffic capacity for PM application.**

To address the challenge of the area traffic capacity requirement, the same argument presented previously for a data rate increase has to be followed while taking the frequency reuse factor and number of sites in the area of interest into consideration. Figure 16 illustrates the possible approaches to the area traffic capacity challenge for the candidate communication technology for PM implementation. Based on (2), aside from increasing bandwidth and spectral efficiency, which have been discussed earlier, we need to increase the number of sites in the area while keeping the number of cells in a cluster low. A way to increase the number of sites is by considering densification [193]. However, as the cell densification factor increases (more cells in an area), inter-cell interference increases and the performance of the network becomes degraded, resulting in lower system capacity. To address this challenge, beamforming techniques [194] and interference mitigation methods such as coordinated multi-point (CoMP) [195], [196] can be employed. Beamforming is crucial to optimizing densification by using antennas with beamforming capabilities [197], [198] to focus the transmitted power to the receivers within a cell, thereby reducing interference. Other network management systems such as Software Defined Networking (SDN), Cognitive Radio Networks (CRNs), and Self Organizing Networks (SONs) can be employed as complementary techniques to address the densification of the network.

C. LATENCY

PM demands not only a high data rate but also low latency. The latency range goes from about 20 ms to zero ms can be seen in Table 4. PM enablers such as big data, and sensor networks will demand latency within the range of 20-10 ms, while advanced visualization platforms will demand latency of about 5-1 ms. Technologies such as advanced robotics and high-speed computational platform, require latency much lower than 1 ms [199]. By comparing these latency figures with that of 4G, 5G, and 6G, it is clear that 4G cannot support PM in the context of the latency requirement. 5G on the other hand, can support the latency requirement of PM solutions except where the use of advanced robotics (like in tactile communication [199]) and high-speed computational systems. The 6G technology will support the latency requirement of PM solutions.

One of the most limiting factors for latency is the fact that the propagation delay is limited by the speed of light. Hence, latency is a function of distance. The longer the distance, the larger the latency. Therefore, short-distance communication is necessary to edge towards the extremely low latency required by many PM applications. As shown in Fig. 17, several approaches are being investigated to reduce the latency of data transmissions in mobile networks, which can be applied to reduce the communication latency for PM solutions. These approaches include reducing processing time, medium access time, queuing time, and routing time [200], as depicted in Fig. 17. To reduce the processing time, grant-free access and device-to-device (D2D) communication can be employed. The grant-free access [201] is proposed as a feasible and promising technology for effective time saving of requesting/waiting, (especially for uplink transmissions), thereby reducing processing time. The processing time and the medium access time can also be reduced by employing D2D [202], which summarily reduces the number of processing nodes and medium access options required in a transmission. The D2D communication approach will significantly reduce latency and is an ideal solution when extreme low latency is the target like in the case of real-time monitoring and control of *in vivo* nanomachine applications that require nanocommunication. Other ways of reducing processing time, such as the use of different subcarrier spacing (when OFDM is in use), Transmission Time Intervals (TTIs) [203], [204], and adaptive modulation and coding [205], can also be employed to reduce latency further.

The latency challenge can also be tackled by reducing the medium access time. This can be technically done by encouraging on-device AI capabilities, using simpler processing algorithms for medium access by nodes, caching/edge processing, deploying mobility management systems, and the use SDN and NVF [206]. Typically, reducing latency implies moving away from the cloud infrastructure and taking computation as close as possible to PM solution location. Here, the computation can be moved to the fog computing platform [207]–[209] or to the edge computing device [210], [211] to reduce latency. Also, if computing is mandated to be done in the cloud, federated learning [212], [213] can be integrated into the fog/edge platform to reduce the amount of data sent to the cloud, thereby, reducing latency. Of course, the computational burden can be taken further back to the source device to reduce latency. However, as the computational capability of many user equipment is limited, simpler computational algorithms, protocols, and AI capabilities can be enabled in the user devices to be able to process as much data as possible and substantially reduce latency. Caching [214], [215], is also important in reducing access time and latency. Another strategy for latency reduction is the optimized management of the terminal's mobility. Mobility management is essential to maintaining a connection for a mobile device. The mobility management burden is exacerbated in a highly densified communication system, which is typical with THz communication as we described earlier. Densification implies the rapid movement of mobile devices from one cell to another over a small area. Reducing the cumulative time required for handover over many cells in an area will considerably reduce the overall network latency. The implementation of adaptive [216] and AI-based [217] handover algorithms will also be of benefit to realizing the latency goal of the candidate communication technology for PM applications.

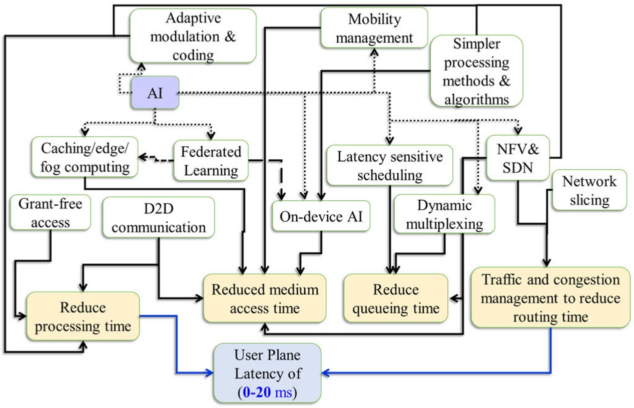


FIGURE 17. Envisioned key techniques for achieving the target latency for PM applications.

To target the extremely low latency requirement of PM applications, the reduction of the queueing time of packets should also be considered. This can be done by considering latency-sensitive scheduling and dynamic multiplexing [218]. Latency-sensitive scheduling includes resource scheduling such as adaptive scheduling [219] and the approach based on machine learning [220]. These techniques ensure that low latency packets are given some level of priority in traffic scheduling and multiplexing. The latency-sensitive traffic scheduling and multiplexing operation can be optimized using the routing layer softwarization capabilities such as network slicing [221], NFV [222], and SDN, [223], [222] with some touch of AI.

Another approach to minimizing network latency is to target the management of traffic and congestion at the routing and transportation layers. Aside from the use of techniques in the routing and transport layer [224], [225], softwarization and virtualization systems such SDN and NFV can also help in reducing latency. However, we note that the softwarization and virtualization techniques like network slicing, SDN, and

NFV do not directly reduce latency by themselves along, but allow for the management of network resources and services flexibly and dynamically to meet the latency demands of the network [206], [226], [227]. For instance, by applying NFV, which typically works together with SDN, transmission time can be reduced by combining different modulation schemes to generate different asynchronous waveforms [228]. Also, these softwarization and virtualization architectures offer the scalability that can guarantee low medium access by enabling on-demand caching, switching, and reducing routing time, queuing time, and processing time [229].

D. RELIABILITY

The reliability metric is specified by the probability that data of a given size is successfully delivered to a destination within a defined latency. As can be inferred from Table 4, the target reliability requirement for a candidate communication technology that can fully aid in realizing the potential of PM is about 10^{-9}. This value has to be achieved without very significant compromise on the data rate and latency targets. The different approaches that can be collectively or individually considered to achieve the reliability target of the candidate communication technology for PM applications are given in Fig. 18. These approaches include 1) the use of techniques that mitigate the effects of channel impairments like time selectivity, frequency selectivity, and interference, 2) choosing an appropriate modulation technique that suits the channel condition, 3) choosing an appropriate channel coding technique that is robust again a given channel condition, 4) reduction of network jitter, 5) the use of retransmission schemes that effectively ensures that any incorrect data received by the user is properly communicated to the sender within the ideal time, and 6) provide coordinated channel access to all users.

Typically, the channel state crucially defines the reliability of the information transfer. Different channel impairments such as frequency selectivity, time selectivity, and interferences impact the error performance of the system. Frequency selectivity impacts inter-symbol interference, and the time selectivity influences the choice of packet size as well as the pilot symbol size, all of which are factors that determine the reliability of the received packet. Also, factors such as interference from other users can affect the reliability of the received packet. Therefore, techniques that mitigate the effect of frequency selectivity, time-selectivity, and interference will help in achieving the targeted reliability value for PM. Techniques such as MIMO, multiple-carrier modulation, and adaptive schemes can be employed to achieve reliable communication. And based on the channel condition, informed decisions on the optimal modulation scheme and channel coding techniques such as space-time coding and forward error correction (FEC) that can achieve the targeted reliability requirement can be employed.

Other approaches such as the coordination of channel access by users using multi-connectivity [230] and mMIMO (and uMIMO) techniques [231], [232] can be employed to increase reliability. More also, the protocols that support the retransmission of packets at the radio link and transport layers to correct data errors at the receiver are required to increase reliability. The hybrid automatic repeat request (HARQ) protocol and its variants [233], [234] are ideal candidates for achieving the targeted reliability for PM. Such protocols include HARQ-chase combining (HARQ-CC) [235], NOMA-HARQ [236], and HARQ-incremental redundancy (HARQ-IR) [237]. Other techniques such as network slicing [238], [239], network coding [240], [241], and control channel design [242], [243], can be beneficial to ensuring efficient retransmission and increasing the reliability of the network for PM applications.

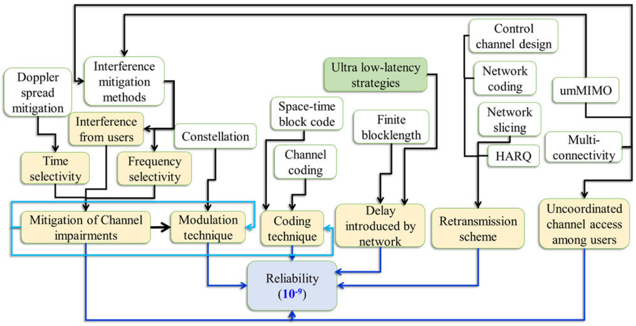


FIGURE 18. **Envisioned key techniques for achieving the target reliability for PM application.**

The requests and acknowledge protocols have to be done within a stipulated delay margin, which is defined by the latency requirement of the system. Therefore, the techniques we suggested for the achievement of the required latency for PM have to be considered simultaneously with the schemes shown in Fig. 18 for achieving the targeted reliability. Alongside, the use of finite-blocklength coding (FBC) can help to guarantee reliability [244].

E. MOBILITY

The mobility metric is associated with the speed at which a defined QoS can be achieved when particular communication technology is employed. This metric is typically defined by the characteristic speeds of the platforms on which the communicating terminals are positioned. For PM applications, the allowable speed of every vehicle that can carry patients should be within the mobility range for the candidate communication that will enable PM, which is crucial to providing the desired QoS. This can be achieved by ensuring that the effect of channel time selectivity introduced by the Doppler effect is mitigated and an optimal mobility management system deployed.

The effect of time selectivity introduced by the Doppler shift/spread manifest in the form of co-channel interference, which is very prominent given that the Doppler shift is directly proportional to the vehicle speed and the carrier frequency, both of which are very high in this case. Several mitigation techniques for the time selectivity challenges are discussed in [245], [246]. Mobility management in this case involves location management and call routing. Location management approaches [247], [248] can aid in achieving the desired mobility target for the candidate communication technology for PM applications. And different techniques and algorithms such as the combination of fast handover and soft handover can be implemented to address the challenge [249]–[251].

F. CONNECTIVITY DENSITY

The connectivity density metric refers to the total number of communication devices fulfilling a target QoS per unit area. The expected connectivity density requirement for PM applications will be over the 10^7 devices/km^2 requirement that is targeted for 6G and much more than the targets for 5G and 4G. And with the expected deployment of nanonetworks and other new networks and devices for many verticals including PM applications, higher connectivity density should be targeted for full implementation of PM solutions.

G. ENERGY EFFICIENCY

Another factor that is crucial to the implementation of PM is the energy consumption of the component systems. The ever increasing demand for connectivity and data rate by the billions of devices worldwide impacts the ability of contemporary and future communication networks to limit the total communications energy consumption and associated carbon footprint. For the candidate PM communication technology, the vision of IoE, pervasive sensing, transmission over mmWave and THz, network densification, high-speed computing, blockchain, and control functionalities will put considerable pressure on the energy efficiency of the network [252]. The expected network energy efficiency for PM application will be much more than the energy efficiency of 1TbpJ targeted for 6G.

To meet the energy efficiency target that is ideal for the candidate PM communication technology, the use of alternative energy sources to power the communication network and the reduction of dependence on the main power grid is required. Also, there is the need to reduce energy consumption by optimizing the network load as is shown in Fig. 19. Methods such as physical components design and optimization, radio resource management, link adaptation, network management, and topology-related methods can be employed to achieve network load optimization. It is important to design physical components [253], [254] that are energy efficient for use in the candidate communication network for PM applications. Energy-efficient radio resource management strategies that allow the system to have control of parameters such as transmit power, and spectrum/channel allocation, can help to reduce energy consumption [255]–[258]. And the various techniques for the link adaptation [259], [260] that allow for adaptive control of parameters such as modulation order and error coding technique, can be employed for the adaptive implementation of radio resource management to reduce energy consumption. Network layer techniques such as network slicing, [261]–[263], NFV [264], [265], and SDN [264], [266], can also aid in reducing the energy consumption of the network. More also, the topology of a network typically defined its energy consumption level, hence, topology design and infrastructural use optimization can be considered to improve the energy efficiency of the network [267], [268].

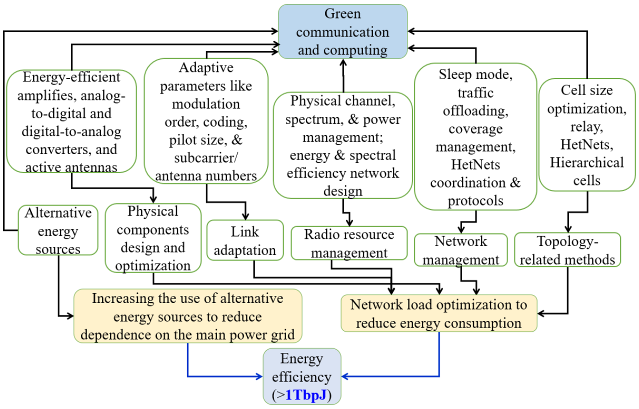


FIGURE 19. **Envisioned key techniques for achieving the target energy efficiency for PM application.**

While we consider the reduction of energy consumption of the candidate network for PM application, it is also important to note that much energy is still needed to power the network and other supporting systems. PM enablers such as blockchain and high-speed computational platforms are known to consume a very large amount of energy [269]. Hence, since the use of these technologies are important in PM, and are also being considered integral parts of future communication systems [270]–[272], there is the need to also consider the use of alternative energy sources to power PM system and reduce carbon emission and footprint.

Artificial intelligence (AI) and machine learning techniques can also be employed to optimally improved all the techniques mentioned above for the reduction of energy consumption [273]–[276], and alternative energy sourcing, prediction, and management [277]. And all the system-level energy provision and consumption optimization methods mentioned above gear towards the realization of Green communications and computing [278].

H. UBIQUITOUS CONNECTIVITY

Another factor that is important for the full implementation of PM solution is the need for ubiquitous and pervasive communication. This implies that the candidate communication network that can support PM needs to be accessible and provide the desired QoS anytime and anywhere. Such a level of 3D pervasiveness in connectivity can only be achieved by the integration of terrestrial and satellite communication networks [279], [280]. Currently, 5G and the earlier communication technologies have networks that primarily operate over terrestrial space, hence, will be unable to provide the desired pervasive connectivity for PM applications. On the other hand, the 6G network is defined based on an aerospace-ground-ocean integrated information network [281], hence, will be able to meet the communication ubiquity required for PM application. Other technologies that can help network coverage and ubiquity include the cell-free massive antenna configuration [282]. This antenna configuration helps great more pervasive delivery of communication signals in environments where attenuation by obstacles is predominant in signal propagation.

VI. OPEN CHALLENGES FOR ENABLING THE FULL IMPLEMENTATION OF PM SOLUTIONS USING COMMUNICATION TECHNOLOGIES

PM aims to provide a timely and accurate diagnosis and effective treatment of all diseases by using personalized medical and lifestyle data. To achieve these aims, emerging and contemporary technologies such as AI, big data, digital twin, nanotechnology, XR, holographic display, blockchain, robotics, IoE, high-speed computational platform, and sensor network are vital to its operation. These technologies will work in tandem to achieve the aims of PM, hence, advanced communication technology is required to connect these technologies to seamlessly and effectively provide the desired PM services and solutions. We have discussed the communication challenges that the integration of these technologies into PM platform possesses to any candidate communication technology that can support PM process. We highlighted the ideal performance indicator values that are required for the communication metrics such as data rate, latency, area traffic capacity, connectivity density, energy efficiency, and mobility. The possible approaches to achieving the target values for these metrics in a candidate PM communication technology are also discussed. In this section, we employ Fig. 20 and Table 5 to highlight and summarize some of the communication network challenges that need to be addressed to ensure that the aims and objectives of PM can be fully achieved.

It can be seen from our discussion that contemporary communication technologies will be unable to offer the infrastructure and operational connectivity that can guarantee the full implementation of PM. It is, therefore, necessary to develop future communication technologies that can handle PM demands. In general, the main target for future communication technology for full PM implementation is to develop an ultra-reliable, very low latency, and energy-efficient secure communication network. Such a network should be capable of delivering a wide dynamic range of data rates (Mbps to Tbps) and handle high traffic volume from millions of intelligent devices over a small area, and billions of devices across the globe. Specifically, the generalized open challenge in PM for communication engineering researchers is to develop a technology that can offer Tbps data rate user experience, sub-millisecond latency, high spectra efficiency, ultra-reliability of one billionth, the energy efficiency of more than 1TbpJ, ubiquitous connectivity, hundreds of km/hour mobility, and connectivity of over 1 million devices per km^2. To achieve these high-end targets, we suggest the approach of addressing the various open challenges that are considered from the perspective of each of the enabling technologies of PM while having an eagle-eye view of the entire communication system. For added clarity, some expanded discussion on the open problems regarding the use of the sensor network, big data, digital twin, and advanced visualization techniques are provided below.

A. SENSOR NETWORK

The sensor network challenge for PM implementation is about the design and development of energy-efficient and reliable sensors and sensor networks that will help in generating the required personalized medical and lifestyle data for PM. In this sense, and among other open problems, there is the need to develop accurate patient-centered information-driven sensor data aggregation strategy for various PM use cases. Such strategies should also address the need for ultra-reliable low latency and energy-efficient sensor/communication networks that will also guarantee ubiquitous coverage and accessibility of the communication network. We can summarize the communication challenges as follows.

1) Addressing the latency challenge by reducing the processing, medium access, queuing and routing time of sensor data for PM applications. Edge computing will play a crucial role in addressing the latency challenge for a sensor network in PM applications.
2) Development of effective channel impairment mitigation techniques, adaptive modulation techniques, robust channel coding techniques, network jitter reduction methods, retransmission schemes, and coordination of channel access to address the challenge of high reliability.
3) Research in satellite communication, underwater communication, airborne communication platforms, and cell-free antennas to address the ubiquitous communication service demands without compromising the latency and reliability of PM solutions.

B. BIG DATA

The main target for PM application is the efficient management of the massive individualized medical and lifestyle data generated globally. To achieve this target, there is the need to develop and aggregate communication techniques that will offer Tbps data rate. More also, the dynamic range of the data rate required for PM and other verticals will entail more research into efficient network slicing and SDN. The possibility of designing incentivized data sharing protocols over the communication networks for PM applications should be explored, and the blockchain technology with more energy-efficient protocols holds the ace. More also, the design of communication networks and systematic approaches that enable easy medical data sharing while keeping the data secured and the patients' rights protected is a challenge to address. We can summarize the communication challenges as follows.

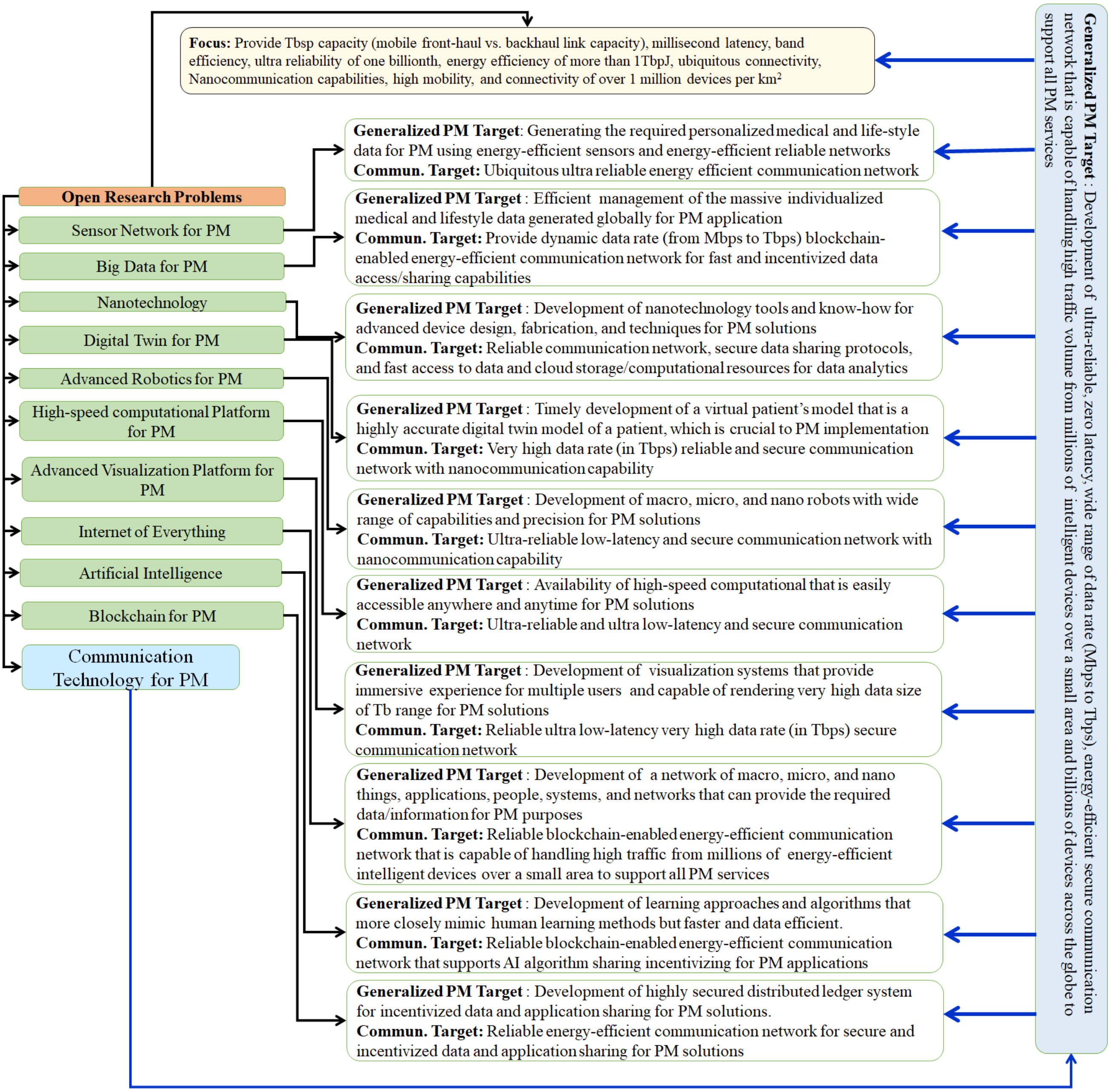


FIGURE 20. Generalized open problems in communication technology for PM application.

1) Addressing the challenge of effective massive data exchange and access using efficient network slicing, SDN, and NFV.
2) Design of efficient energy management protocols to address the impact of deploying contemporary blockchain technology to secure PM data exchange.

C. DIGITAL TWIN

Here, the timely development of the digital twin accurately models patients' biological systems. The exchange of such models requires the development of communication technologies that can offer a Tbps data rate with high reliability. Such a network may likely have nanocommunication capability to enable the exchange of molecular information among the component subsystems of the digital twin and other systems. Hence, the development of a method for designing the digital twin model of a patient is one of the most important open problems for the realization of PM initiative. Various approaches to the design and development of sparse but accurate digital twin models should be explored. We can summarize the challenges as follows.

1) Addressing the challenge of the very high data rate demand of PM by considering THz communication and its, challenges, ultra-massive MIMO, and increasing the spectral efficiency of communication systems.

TABLE 5. Summary of some open problems and issues in enabling PM using communication technology.

System	Some Open Problems for the development of candidate communication technology for PM implementation
Advanced Sensor Technology, Sensor	**1.** New sensor designs for nano, micro, and macro-level sensing that are less invasive, easy to deploy, and less energy demanding.
Network/Design, and Sensing Strategy	**2.** In vivo nanosensor network design and validation for early vital signs detection in various use cases. **3.** Novel and more accurate patient-centered information-driven sensor data aggregation strategy for various medical use cases. **4.** Efficient wide-range and integrated sensing capability for everyday mobile devices with increased computational and intelligent capabilities. **5.** Bandwidth-efficient and low-latency data processing capabilities at the network edge devices. **6.** Ultra-reliable sensor network design with the target of 1/billionth error margin.
Big Data Innovative Data Collection, Access, and Analytics	**1.** The design of suitable strategies/protocols to aggregate data from billions of individualized sensor networks in ways that make informed accessibility easy, timely, and personalized. **2.** Implementation of pilot studies to establish a practical framework to discover relationships between molecular and other patient-specific data, patient diagnoses, and clinical outcomes. **3.** Network slicing procedure for dynamic data rate allocation for different data size access from Big data resources **4.** Development of blockchain-enabled energy-efficient incentivized data sharing protocols and communication networks for PM applications. **5.** Network design and systematic approach to removing the barriers to widespread sharing of the medical data (molecular profiles, lifestyle information, and medical histories) of individuals, while keeping the data secured and the patients' rights protected.
Nanotechnology Innovations	**1.** Novel nanocommunication techniques for targeted drug delivery, biomarker identification, whole-cell modeling, and drug discovery for PM applications. **2.** Nanonetwork modeling and design for various PM use cases. **3.** Secure and fast data/resource sharing protocols for nanotechnology research in PM. **4.** Fast and easy access to data and cloud storage/computational resources for data analytics.
Patients' Digital Twins Development	**1.** The availability of a digital twin model of a patient is pivotal to the realization of the promises of PM. Hence, the development of digital twins must start, and be pursued vigorously/extensively as a global project. **2.** Various approaches to the design and development of sparse but accurate digital twin models should be explored. Research in nanocommunication that considers the sparse model of the whole-cell and the network of such modular structure to develop a digital twin is suggested. **3.** Development of innovative methods for the timely development and real-time update of a digital twin model of a patient is crucial. **4.** Research into communication techniques that can offer a very high data rate (in Tbps) and secure communication
Advanced Robotics Design	**1.** Development of energy-efficient precision robots (macro-, micro-, and nano-robots) for a wide range of capabilities and precision for PM solutions 2. Ultra-reliable very low-latency and secure communication network with nanocommunication capability for robot-assisted PM processes.
High-speed Computational Platforms	**1.** Design of ultra-reliable and ultra-low latency communication network for accessing the computational and storage infrastructures of cloud computing from anywhere and at any time. **2.** Design and development of better computing capabilities at the edge of the communication network **3.** Development of secure protocols for D2D-based distributed computing protocols for very low latency PM activities. **4.** More activities into quantum and molecular computing to increase the computational capabilities of edge devices to promote a very low latency quest for PM.
Advanced Visualization Platforms	**1.** Designing Tbps data rate, ultra-reliable, and low latency communication network for rendering high-resolution XR and hologram in PM. **2.** Designing compressed but informative content for XR PM applications to reduce bandwidth demand. **3.** Designing edge-based video caching and analytics methods to address latency challenge
Internet of Everything	**1.** Designing and developing an energy-efficient IoE platform for PM applications with ultra-reliability, high data rate, ultra-low latency, and security capabilities. **2.** Developing communication technology with pervasive coverage
Artificial Intelligence	**1.** Designing and developing integrated AI and machine learning algorithms and solutions to address the data rate, latency, reliability, mobility, and energy efficiency challenges of the candidate communication technologies for PM applications.
Blockchain	**1.** Designing and developing ultra-energy-efficient communication technology for PM to handle the pervasive integration of blockchain technology. **2.** Developing blockchain protocols that will guarantee reduced energy consumption by PM platform. **3.** Development of alternative energy sources for PM enabling communication technology

2) Address the challenge of high reliability discussed earlier.
3) While considering the various possible solutions for addressing the very high data and reliability challenges, research on the development of a digital twin with a low data size for PM implementation is crucial.

D. ADVANCED VISUALIZATION PLATFORMS

The two main open problems to the communication network in the use of advanced visualization systems in PM are the development of techniques that can offer the required Tbps data rate and low latency for PM application. Research into the approaches outlined in Fig. 16 and 18 will be beneficial to address these challenges. For instance, the design of compressed but informative content for XR PM applications to reduce the bandwidth demand, and the design of edge-based video caching and analytics methods to address latency challenges can be pursued. We can summarize the challenges as follows.

1) Research in THz communication, ultra-massive MIMO, and increasing the spectral efficiency of communication systems are required to address the high data rate demand of PM.
2) Addressing the ultra-low latency challenge by considering edge computing for XR PM application and possibly, D2D computing. Research into the use of federated learning to reduce the volume of data exchange in PM solutions will be beneficial.
3) Addressing the challenge of high reliability by considering the research into techniques for effective THZ channel impairment mitigation, adaptive modulation, and robust channel coding.

Table 5 provides an extended summary of the communication challenges by looking at each of the enabling technologies of PM.

VII. CONCLUSION

In this survey, we have explored how contemporary and future communication technologies fair in providing communication networks that can support PM. Specifically, we addressed the following question. What is required of the future communication technologies such as 6G and beyond-6G in enabling PM should the contemporary technologies not meet the needs of PM? In answering this question, we have provided some background on PM and its taxonomy. We went further to discuss the various enabling technologies of PM and focused on the underlining communication metrics demands introduced by the use of the enabling technologies in PM solutions. We have also provided a comparative survey of how the theoretical KPIs of the various contemporary and future communication technologies measure up to the KPI demands of PM solutions. Further, we explicitly highlighted the communication challenges that need to be surmounted for PM implementation and suggested the possible approach and techniques that can be used to address the challenges. Communication challenges such as very high throughput, ultra-low latency, ubiquitous connectivity, and high reliability are dominant communication challenges for the implementation of PM. By associating these dominant communication challenges to some of PM's exemplary enabling technologies such as sensor networks, big data, digital twin, and advanced visualization techniques some open problems are presented.

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