The utilization of perspective quantum technologies in biomedicine

P A Tarasov¹, E A Isaev¹, A A Grigoriev¹, A F Morgunov¹

¹National Research University "Higher School of Economics"

Abstract. Currently, there is a widespread introduction of quantum technologies in human activity. The prospects of quantum technologies use for the needs of biomedicine are considered. The necessity of the development of new quantum technologies and methods for organizing the processing and analysis of large biomedical data is substantiated. Opportunities and prospects of using modern quantum computers for the needs of biomedicine are being analyzed. The prospects for the use of quantum sensors in biomedicine are discussed. The possibility of using quantum communication lines in the near future to transmit confidential personalized biomedical information is being considered. Prospects for using quantum dots for the purpose of killing both multidrug-resistant bacteria and cancer cells are discussed.

1. Introduction
Biomedicine is a branch of medicine that studies the human body, its structure and function in normal and pathological conditions, methods for their diagnosis, correction and treatment [1]. Currently biomedicine makes extensive use of modern technical means for solving its various tasks related to the collection, storage and analysis of data, the modeling of processes.

Recently, it became possible to massively carry out the most complex research in biomedicine thanks to modern advances in various fields of electrical engineering and informatization.

Currently, the following areas of biomedicine process large volumes of digital information: radiotherapy, machine learning to help diagnose patients, mathematical and computer modeling of living and ecological systems, mathematical and computer modeling of the prevalence and structure of diseases, solving problems of medical diagnostics, predicting disease outcomes, evaluation of the effectiveness of medical interventions, systems for collecting, storing and rapid analysis of patient data, computer genomics, proteomics, immunomika, information management systems and support for biological and medical research, development of new drugs, cell therapy [2].

However, the current computing capacity is not enough due to the avalanche-like growth of the data received. It is necessary not only to significantly increase the capacity for storing large amounts of data, but also to significantly speed up their processing to process the necessary amounts of information. For example, it is necessary not only to process a large amount of data obtained from various devices in the conditions of large networks of body sensors. It is also necessary to store large amounts of information, both received from these sensors, and those arising during processing.

The US National Center for Biotechnology Information (NCBI) provides a large set of online resources for accessing biological information and data, including the GenBank nucleic acid sequence database, PubMed database of published biology journals, the European Nucleotide Archive Database EMBLEBI, and the DNA database Japan, etc. [3]. The amount of data provided already in 2014 exceeded 15 petabytes [4].
The European Molecular Biological Laboratory, one of the world's largest repositories of biological information, currently contains more than 150 petabytes of data [5] and backup copies of genes, proteins, and molecules. More than 38 million requests go to the EMBL-EBI websites every day, and more than 140 gigabytes of information is needed to store information about the genome of one person.

It should be understood that the processing of such amounts of information is difficult or physically impossible using modern classical computers. Thus, in the near future there is a need to move to perspective, higher-speed quantum data processing systems. Their development is actively underway at the present time.

2. Perspective quantum technological possibilities for processing large volumes of data

Currently, a new direction of computers is actively developing. It can significantly improve the efficiency of complex calculations in the near future. Quantum computers operate with a special type of data that differs from standard storage media, bits, namely, so-called qubits. These logic elements can be simultaneously in the “zero” and “one” states, in contrast to the classical bits. They give the measurement of one of them with a certain probability under certain conditions. This allows you to store in one binary bit more than one bit of information from a mathematical point of view. The dimension of a qubit is theoretically unlimited, and this allows us today to create computers with a dimension of more than 1000 qubit when organizing eight-qubit modules into clusters. Quantum computers use the phenomena of quantum superposition and entanglement directly in their algorithms. This allows them to solve completely new classes of problems. And it also allows you to develop fundamentally new computational algorithms, which in some cases turn out to be much more productive than the classical ones. However, it should be noted that the computational capabilities of modern quantum computers do not yet allow surpassing the already existing computers of the classical type. Nevertheless, there are serious prospects for highly specialized quantum computing devices that allow using quantum algorithms to provide a multiple increase in performance in solving some special tasks.

In 2017, it was announced that a so-called boson sampler, a quantum calculator, was created that could find a probability distribution for bosons in a given system. Entangled photons are sent to a special optical network in such devices, and also interfere with it and form an arrangement at the output. The main task of the sampler is to determine the type of this arrangement. With it, you can simulate specific systems, selecting installation parameters and setting up a network. For example, a researcher can calculate the vibrational spectra of molecules [6].

The commercially available D-Wave One and D-Wave Two X quantum computers from D-Wave should be noted. They have already achieved quantum supremacy in solving problems using a quantum annealing algorithm [7]. In March 2018, employees of the US Center for Quantum Informatics and Technology demonstrated that D-Wave can be used in predicting the assessment of a fundamental process in biology,- the binding of proteins of a gene regulator with the genome. A human cell may need more or less of a certain protein to perform its function depending on its molecular environment. This complex process of controlling protein production is known as gene regulation. Auxiliary proteins that regulate gene expression are called transcription factors (TFs). TFs must be able to find and attach to specific places in the genome to perform their function. The algorithm, developed specifically for the D-Wave Two X, allowed making predictions consistent with real experimental data.

Modeling the properties of chemicals is a promising task for quantum systems. Many scientists hope that quantum computers will simplify the calculation of the properties of individual molecules (for example, their spectra), as well as the search for new drugs and materials. For example, an experiment was conducted on scalable quantum modeling of a hydrogen molecule in order to study the process of changing the energy of a hydrogen molecule (H2) depending on the distance between atoms in it [8]. The paper presented the successful results of modeling the evolution of two primitive creatures on the IBM ibmqx4 cloud quantum computer [9]. This service (IBM Cloud platform) is
available to developers, researchers and programmers to study quantum computing using a real quantum processor since 2016 [10]. A 20-qubit IBM Q cloud access system is currently available. In March 2018, Google announced that it was able to create a computing device consisting of 72 superconducting qubits [11]. In early 2019, IBM announced the release of IBM Q System One, the “first integrated universal commercial quantum computer” [12].

3. Quantum sensors
Quantum sensors use the quantum nature of matter, namely the quantum mechanical behavior of atoms or ions, to measure physical quantities such as frequency, acceleration, rotational speeds, electric and magnetic fields, radiation, or temperature with the highest relative and absolute accuracy. In biomedicine, it is promising to use such sensors to detect defects in complex-molecular proteins in the body, which lead to metabolic disorders and induce defects in neighboring proteins. An example would be defective prions that cause brain damage in case of mad cow disease (BSE) or Creutzfeld-Jakob disease. Currently, the problem is to determine the structure of a single biomolecule, to determine the first defective prions in the body with an irregular structure (fig.1). In [13] a method was presented that can be used in the future for reliable studies of individual biomolecules.

The presented quantum sensor (diamond with a nitrogen atom embedded in its carbon lattice near the surface of the crystal) allows nuclear magnetic resonance scanning to be used to investigate the structure of an atom of individual proteins. The advantage of this technology is that it works even at room temperature.

![Figure 1. Schematic representation of a nanoscale NMR probe based on a diamond NV. The probes used in this study had a distance to the sample from 34 to 95 nm.[13]](image)

In [14] it is also proposed to use nitrogen-substituted vacancies (NV) in diamond as a magnetic field sensor, which can detect, polarize and control individual nuclear spins in its locality. NV-vacancy consists of a single electron spin, with the possibility of polarization and optical reading of its state, and which is controlled by magnetic resonance methods. NV-based magnetometers can determine separate electron and nuclear spins in biological samples and allow the molecular structure and functionality to be revealed at the level of a single biomolecule. They can also detect magnetic fields created by ionic activity in neurons. It is argued that this type of magnetometers will lead to a breakthrough in understanding how microscopic communication affects the macroscopic functions of the entire brain.

The new kind of quantum sensor, presented in March 2019 by the Institute of Quantum Computing of the University of Waterloo (IQC), consists of semiconductor nanowires of indium phosphide (InP), and can detect high-speed radiation at a single-photon level, which allows for observations at long
distances. In perspective, detection of singlet oxygen for dose control in the treatment of cancer is indicated as its scope [15].

4. Personalized medicine

The use of quantum computers in the near future can help the rapid development of personalized medicine. It is a medical discipline that offers an individual approach to the prevention and treatment of diseases for humans through in-depth analysis of its genome data, epigenetic modifications, other biomarkers, as well as clinical symptoms and environmental exposure [16].

Personalized medicine is based on the conviction that each individual has unique characteristics at the molecular, physiological, and behavioral levels. If necessary, intervention is possible to prevent diseases that are adapted to these unique characteristics. This statement was to some extent confirmed by the use of new technologies, such as DNA sequencing, proteomics, as well as the processing of large amounts of data from wireless health monitoring devices, which revealed large interpersonal differences in disease processes [17]. DNA sequencing will require a sharp increase not only in the storage of information, but also in its processing capabilities. Since the comparison of different chains of DNA is possible only with a significant increase in computing resources. Due to the huge amount of information received from various monitoring devices, there is a need for its timely processing in order to ensure the stability of the patient's condition.

Thus, from the point of view of modern biomedicine, it is necessary not only to ensure the possibility of processing and storing large amounts of information, but also to guarantee the impossibility of its substitution, which can create a serious threat to the patient's health.

For the storage of medical information about patients, it is necessary to provide mandatory online access to large-sized information containers.

For effective management of biomedical information files, a mandatory requirement is the use of a single standard of clinical reference terminology, for example, SNOMED CT (Systematic Medical Nomenclature - Clinical Terms). SNOMED CT is the most comprehensive multilingual terminology in the field of clinical health in the world. It provides a consistent, processed presentation of clinical content in electronic medical records. It complies with other international standards (for example, LOINC (Logical Observation Identifiers Names and Codes) standard for identifying medical and laboratory observations) has been integrated with SNOMED CT since 1998 and has been used in more than fifty countries. SNOMED CT's comprehensive coverage includes terminology in areas such as: clinical data, symptoms, diagnoses, procedures, body structures, organisms, substances, pharmaceuticals, devices [18].

The clinical data files will have to comply with the international standard ISO / HL7 27932-2015 of the CCD (Continuity of Care Document) electronic medical documents. It is based on XML and is aimed at coding the structure and semantics of a patient's medical record, which makes it possible to ensure the semantic compatibility of medical systems in the exchange of information. The document contains information about the patient's personal data, diagnoses and a list of diseases, prescribed drugs, possible allergic reactions, treatment plans, data on medical insurance [19].

The national standard of the Russian Federation GOST R ISO / HL7 27932-2015 "Architecture of clinical documents HL7. Release 2" was created based on the ISO / HL7 standard, and entered into force on 11/01/2016 [20]. For example, the application solution "1C: Medicine. Hospital" from the company 1C, serves to automate such processes as maintaining an electronic medical record of the patient, managing the provision of outpatient medical care, managing the admission of patients in the hospital and managing the medical staff. It is the so-called EHR-application (Electronic Health Record), and has the ability to save medical documents in external files in the format HL7 CDA R2 [21]. Already at the moment, the rules of data mining of previous visits to patients to fill in the gaps of current medical data of the patient are widely used to store CCD files.
5. Existing non-quantum technologies of analysis and work with big data in biomedicine

Thus, modern biomedicine is faced with a huge amount of heterogeneous data, with a huge variety of methods for their processing and presentation, with the simultaneous existence of various software tools and data formats [22]. Consequently, there is an urgent need for scalable and powerful distributed computing tools to solve these problems.

In the field of information technology, Google’s MapReduce is a distributed parallel programming model and methodology for processing large-scale data sets. The freely distributed Apache Hadoop framework can provide distributed processing of large amounts of data in a reliable, efficient and scalable way. It combines the capabilities of the Hadoop distributed file system (HDFS) for distributed storage of massive data sets distributed between nodes of a computing cluster and MapReduce [23]. Therefore Apache Hadoop is widely used in many areas of biomedicine [24].

However, due to the peculiarities of the work of Apache Hadoop in disk I/O system, intermediate results of calculations are not cached. Therefore, Apache Hadoop is only suitable for batch processing and shows poor performance for iterative processing. Apache Spark is used in biomedicine to solve this problem; a faster, versatile computing environment specifically designed to handle huge amounts of data. Unlike Hadoop disk computing, Spark performs in-memory calculations and stores intermediate results in RAM, which is very efficient for iterative operations. In terms of performance, Apache Spark can be 100 times faster in terms of memory access than Apache Hadoop. [23]. Many technological tools of biomedicine are implemented on the basis of Apache Spark, for example, HiGene platform [25] or the SparkSW scalable distributed computer system [26].

Apache Spark and Apache Hadoop platforms use the project of the National Institute of Health of the USA Big Data to Knowledge (BD2K). His team develops and distributes an integrated open source toolkit that supports causal modeling and the discovery of biomedical knowledge from large and complex biomedical data sets [27].

It should be noted that at present the leading players in the market of commercial corporate enterprise software offer their solutions for the input and processing of large volumes of biomedical data.

For example, SAP offers the SAP Connected Health Platform product, which is based on the SAP HANA platform. It is an analytical platform for hosting data from a variety of disparate sources in the form of a development stack for creating a data warehouse. The platform implements fast data processing by parallelizing processes and storing data in accordance with in-memory technology, which allows storing data in rows and columns [28]. This solution is intended both for integration, storage and analysis of medical data of patients, and for performing a number of specialized functions: analysis and comparison of genotypes; platform for building other applications; integration of research and patient genetic information and evaluation based on their genetic susceptibility, including, for example, the type of mutation responsible for a particular type of cancer, and appropriate personalized treatment. Based on the SAP Connected Health Platform, the CancerLinQ Platform of the American Society of Clinical Oncology and Cancer was built [29]. Also in collaboration with the American Center for Tumor Diseases (National Center for Tumor Diseases, NCT), SAP Medical Research Insights platform based on the SAP Foundation for Health was created. Using this platform, doctors and researchers can access patient data in real time and compare profiles from different sources [29].

In 2015, Salesforce unveiled its large biomedical data management solution, Salesforce Health Cloud. The platform is a medical CRM system, which includes individual relationship management through the patient-to-patient profile of the patient. A profile combines information from several data sources, including electronic medical records (EMR), medical and wearable devices [30].

6. Quantum communication lines and secure bioinformation transfer

Personalized medicine also includes providing protection against unauthorized access to patient biometric information. It is proposed to ensure confidentiality through various quantum cryptography mechanisms that use the principles of quantum physics to protect the communication line. The main property of a quantum communication line is instantaneous listening detection. At the moment, the
market for quantum cryptography is close to the practical level of use, and the span of quantum commercial communication lines, as a rule, is no more than 10–30 km due to the existing hardware-independent limits of the throughput of quantum communication over a wired communication channel.

Most of the existing quantum communication protocols use binary key coding with a photon information capacity of no more than 1 bit per photon [31]. The reason for this size of the photon information capacity is the use of the polarization value of the photon in two bases, orthogonal and diagonal, as the information carrier. In prospective studies, in order to increase the capacity of a quantum communication channel, it is proposed to use as one of the basis the photon “twisted” property (its orbital angular momentum). The “twisted” property is characterized by the fact that it takes only integer values. The light waves, twisted with a different period, can propagate within a single beam without interfering. In 2016, a record quantum number for swirling light was achieved—by special mirrors made of aluminum disks, it was possible to “twist” the light to values in excess of 10,000 [32].

However, the use of such a coding method faces the following problem: the “twist” property is unstable and is lost when the photon is transmitted via wired and wireless communication channels. Currently, the following advances have been made in the transmission of a “swirling” light beam:

- In 2018, it was announced about the transmission of swirling light at a distance of 1.4 km via fiber optic communication channels [33].
- In 2012, a “twisted” light beam was transmitted over a distance of 143 kilometers via a wireless communication channel. The signal was sent from the astronomical observatory of La Palma in the Canary Islands to another observatory—on Mount Teide, on the island of Tenerife [34].

In a promising technology, it is proposed to use two bases, one in the direction of polarization, and the other, in terms of the photon's “twist”. In 2015, it was announced that experiments were conducted in wired communication lines, in which, in the basis corresponding to the “twisted” state, 7 states were used, with values ranging from -3 to 3. As a result, the information capacity of one photon was increased to 2.05 bits information. It is argued that the equipment used in the experiments allows to increase the capacity to values greater than 4 bits/photon [35].

Therefore, at the moment in the commercial lines of quantum communication due to low bandwidth quantum cryptography is used only for key distribution. For example, in August 2018, Toshiba announced the testing of a system for transmitting encrypted genome analysis data between two stations over a distance of 7 km with a record speed of quantum key distribution (10 Mb / s) for one month [36], [37], (fig.2).

![Figure 2. Quantum communication link between the Toshiba Science Center and Tohoku Medical Megabank ([37]).](image-url)
Currently, scientific groups are developing information transfer technologies using the quantum entanglement phenomenon. The property of entanglement is also very unstable. Spreading entangled photons over long distances via wireless and wired communication lines in the conditions of our planet is currently technically difficult. For example, in 2016, it was announced about the achieved speed of 17 photons per minute in the implementation of quantum teleportation of photons at a distance of 6.2 kilometers via conventional fiber optic communication lines with a transmission reliability of 25% [38]. Also, it was announced about conducting successful experiments on quantum teleportation over a distance of 14.7 km with reliability of 50%, but at a lower transmission rate [39]. In 2012, it was announced the implementation of quantum teleportation over the air communication channel for a distance of 143 km between a pair of islands of the Canary archipelago [40].

Therefore, the only available method for transmitting entangled photons over long distances can be the use of a satellite with special equipment. The world's only experimental quantum satellite, Quantum Experiments at Space Scale (QUESS), was launched in 2016. At the beginning of 2018, the experiment was successfully completed on the distribution of quantum keys between the satellite and ground stations in China and Austria, located more than 7,600 km apart. During the experiment, the satellite, as it moved above the Earth, generated a secret key between itself and each of the ground stations. He performed the necessary operations between the two keys and relayed the results to ground stations. The obtained keys were used to implement intercontinental quantum-protected communications for a record distance of more than 5,000 km [41]. The emergence of a fully functional world quantum Internet is planned for 2030.

7. Quantum dots
Quantum dots (QDs) are semiconductor nanocrystals with a size in the range of 2-10 nanometers, consisting of 103 - 105 atoms, created on the basis of inorganic semiconductor materials Si, InP, CdSe, etc., covered with a stabilizer monolayer. Quantum dots are made with a size close to the electron wavelength in this material (usually 1–10 nm in size). Inside QD, the potential energy of an electron is lower than outside it, and, thus, the electron's motion is limited in all three dimensions. The electronic spectrum of an ideal quantum dot is a set of discrete levels separated by regions of forbidden states, and formally corresponds to the electronic spectrum of a single atom. Researchers can easily control transition frequencies, i.e. absorption wavelength or luminescence, changing the size of the quantum dot. This provides the breadth of opportunities for manipulating such objects and gives great potential for practical application, including for the needs of biomedicine. A real quantum dot can consist of hundreds of thousands of atoms [42]. The behavior and properties of these objects are described not by classical physics, but by quantum mechanics. Quantum dots in practical application in biomedicine are used, as a rule, in the form of solutions, or more precisely in the form of sols.

Currently, quantum dots are widely used to visualize the image of a part of the human body, for example, an organ or a tumor, as well as to locate individual molecules expressing in them. These technologies are sufficiently developed at the current time and involve targeted delivery and accession of QD to the targeted cells. With the help of quantum dots, one can see the boundaries of cancerous tumors. It is important in surgical intervention to determine the boundaries of the area being operated on. For example, in 2016, scientists of MISiS synthesized a drug based on alpha neurotoxins derived from the poison of a cobra, and quantum dots. A new drug is able to effectively "mark" the borders of a cancerous tumor in the body [43].

The growth of types of multi-drug resistant bacteria is one of the most serious threats to world food security, to human health in general. New antibiotic classes are needed to treat already common infections. The use of quantum dots in antibiotics can be one of the promising solutions to this problem. In a study presented in 2017, antibiotics equipped with an experimental version of quantum dots proved to be 1000 times more effective in combating bacteria than their “normal” versions. The width of the quantum dots, which were made of cadmium telluride, was 3 nm. The electrons of quantum dots reacted to a green light of a certain frequency, which caused them to bind with oxygen molecules in the body and form superoxide. Bacteria that absorb it can no longer resist antibiotics. At
At the moment, a group of scientists is solving the problem of activating quantum dots inside the body, because the radiation that excites the electrons of QD passes only through a few centimeters of human flesh. In further studies it is proposed to create quantum dots, for the excitation of electrons which require infrared radiation. It passes through the entire human body, and can be used in the treatment of infections with foci inside the soft and bone tissues [44].

![Figure 3. The absorption coefficients for the human epidermis and dermis (left) and the scheme of external light illumination penetrating through two layers of skin (right). The model in the experiments assumed the depth of the epidermis of 0.007 cm [44].](image)

It has also been proven that for some types of cancer tumors, quantum dots can penetrate inside the cancer cells and destroy them. For example, in 2018, a study was presented, according to which quantum dots obtained from tea leaf extract, cadmium sulfate and sodium sulfide prevent the growth of cancer cells in the lungs in case of their malignant tumor. Quantum dots penetrated into the nanopores of A549 cancer cells and destroyed about 80% of them after targeted delivery [45].

In [46] it has been shown that the placement of graphene quantum dots (GQD) in brain tissue seriously disrupts the aggregation of a protein called alpha-synuclein, which is considered the main factor in the loss of neurons and synapses that characterize Parkinson’s disease.

8. Conclusion
The symbiosis of quantum technologies and existing various non-quantum technological solutions has great potential for obtaining the necessary computing power for processing experimental complex-structured data in biology and bioinformatics.

In the near future, it will be possible to use specialized technical quantum solutions for processing and securely transmitting large amounts of information in biomedicine. The possibilities of quantum cryptography in the near future will ensure the necessary level of security in the processing and transmission of biometric information.

Possibilities that quantum dots and quantum sensors can offer in the near future will help to successfully fight many types of malignant tumors.

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