Selected Advances of Quantum Biophotonics – a Short Review

Marcin Lelit, Andrzej Bialecki, Tomasz Gabler, Filip Labaj, Emil Pitula, and Ryszard S. Romaniuk

Abstract—This article discusses four fields of study with the potential to revolutionize our understanding and interaction with biological systems: quantum biophotonics, molecular and supramolecular bioelectronics, quantum-based approaches in gaming, and nano-biophotonics. Quantum biophotonics uses photonics, biochemistry, biophysics, and quantum information technologies to study biological systems at the sub-nanoscale level. Molecular and supramolecular bioelectronics aim to develop biosensors for medical diagnosis, environmental monitoring, and food safety by designing materials and devices that interface with biological systems at the molecular level. Quantum-based approaches in gaming improve modeling of complex systems, while nanomedicine enhances disease diagnosis, treatment, and prevention using nanoscale devices and sensors developed with quantum biophotonics. Lastly, nano-biophotonics studies cellular structures and functions with unprecedented resolution.

Keywords—QBP; ICT; QIT; biomedical engineering; electronics engineering; sensors; quantum Internet; quantum computing

I. INTRODUCTION

QUANTUM Biophotonics is a fascinating field correlated strongly with a number of other partly overlapping research disciplines, Table I. It lies at the crossroads of photonics, biochemistry, biophysics and quantum information technologies [1,2]. In particular, it includes knowledge, from one side, on underlying biological and photonic phenomena, new materials, substances, nano and microobjects, quantum energy efficiency, as well as from the other side, manipulation, measurement technologies and increasingly advanced QBP instrumentation. Some of these metamaterials, laboratory techniques and instrumentation have already been used in preclinical or clinical practice, some are available commercially – like engineered photo-switchable fluorescent proteins, but some still require a lot of effort to be functionalized. The field is very open and awaits for its next discoverers. Perhaps, the best candidates are active young researchers trying to have a fresh glimpse at the QBP from a slightly different perspective.

Quantum biophotonics is related with new methods of observation, measurement, and thus, understanding of physiological and pathological phenomena. New research, diagnostic and therapeutic instruments are born from achievements of the quantum research front of biophotonics. Here, the basic tool is a single, sometimes almost deterministic and isolated photon, or entangled pair of heralding and heralded photons, generated, transmitted, transformed, dressed, and finally absorbed. The wave function of a single photon is transformed, coupled as a result of local interactions at the sub-nanoscale with the components of biological matter. From a photon dressed in this way in a new wave function, after entering a biological system, we can potentially read a lot of information. Today, our possibilities in the field of quantum coherence of a single photon are limited, but it is a huge field of research for QBP. Until now, the information has been read out rather from the scattering or spectral patterns of many photons.

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<td>Biological thermo-dynamics</td>
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<td>Quantum thermo-dynamics</td>
<td>Relations between two nondependent physical theories, here in biological domain, proton motive force, electron transfer chain, ion channels, membrane transport</td>
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<td>Thermo-dynamics of nanostructures</td>
<td>Individual photons, electrons and phonons, electrical, thermal, optical and acoustical conductivity of proteins, bio-nanotubes, thin films</td>
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<th>Theranostics</th>
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<td>Photopharmacology</td>
<td>Photoreactive pharmaceuticals, phototretexate, photostatin, photoswitched molecules, azobenzene, spiropropan, diarylethene, microtubules and ion channel control, optogenetics, photodynamic therapy</td>
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<td>Image bioinformatics</td>
<td>Computational techniques classical and quantum of biomeage acquisition, processing and analysis, knowledge discovery from images, diverse modalities enrichment in images, superresolution fluorescence microscopy and spectrometry</td>
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<td>Bioelectronics</td>
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<td>Supramolecular bioelectronics</td>
<td>Functionalization of intermolecular interactions, electrostatic charges, hydrogen bonds, covalent bonds, energy parameters of functionalized component, porphyrins, phthalocyanines, photochromic and photoisomerizable groups</td>
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<td>Super-resolution technologies</td>
<td>MPM, PTM, ANSOM, NORM, SIM, SMI, with fluorophores, deterministic – STED, GSD, RESOLFT, SSIM; stochastic – SOFI, SMLM/OLM, SPDM, SPDMnp, BALM, PALM, FAPLM, STORM, dSTORM; combination – LIMON, CLEM</td>
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<td>Quantum information technologies</td>
<td>Quantum biotechnologies, ghost bioimaging, nonclassical light illumination and detection in biological imaging, entanglement in photosynthesis, quantum efficiency in artificial biology, quantum enhances superresolution imaging systems, drug discovery.</td>
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A single photon in a biological object is almost always associated with a single electron and its movement, often a quite complex transfer, so conductivity, or more precisely, transduction, of proteins is important. Phonons and the polarization of biological matter are associated with a single photon. Excited phonons in biological matter may remain coupled to the photon or be free in the form of a propagating phonon wave. In general, we deal with energy transfer in protein and DNA at the quantum level, which is one of the fundamental issues of quantum biology. In addition to energy transfer, there are also more subtle phenomena of transformation and transfer of quantum coherence and entanglement in biological objects. Quantum biophotonics is distinguished as a separate discipline because it carries the potential for discovery and application. Quantum biophotonics has a large area in common with the dynamically developed Quantum Information Technologies of ICT, including computing, networks, and sensors [3,4].

Instrumental biophotonics concerns photonic immobilization, imaging, detection and manipulation of biological objects. The challenge in such activities is the fundamental complexity of biological systems and their fragility when interacting with the quantum energy. Fundamental levels of complexity and associated technological barriers arise at all levels of biology, including the molecular, cellular, and tissue and organism levels. Each of these levels requires dedicated, usually very different technologies. The molecular level requires research, observation and measurement of intra-molecular interactions as well as interactions between organic molecules and nanomaterials used for measurements. Measurements take place in a standardized and controlled environment in cooperation with nanomaterials and measurement nanoprobes. Other optical measurement methods are being developed for the cellular level. Molecular interactions and processes in a single cell are being studied using optical methods scalable to the level of a single cell. Standards and validation tests are being created at the single cell level to diagnose diseases at the level of a single cell. At the tissue and organism level, integrated molecular optical imaging techniques are being developed for the optical diagnosis of tissues and organisms. These techniques add to standardized medical clinical imaging [5].

II. MOLECULAR BIO-ELECTRONICS AND SUPRA-MOLECULAR BIOELECTRONICS

Molecular bio-electronics and supra-molecular bioelectronics have emerged as exciting and rapidly growing fields at the interface of biology, chemistry, physics, and engineering. These fields aim to create new materials and devices that can interface with biological systems at the molecular level, and to harness the exquisite functional properties of biomolecules and supramolecular structures for electronic and optoelectronic applications. In this review, we highlight recent advances in the design, synthesis, and characterization of functional molecular nanoblocks, molecular nanomachines, and supra-molecular bio-electronic materials, with a focus on the role of intermolecular interactions, energy transfer, and charge transport in these systems.

One promising approach in molecular bio-electronics is the use of porphyrins and phthalocyanines as building blocks for functional molecular nanoblocks and nanomachines. Porphyrins and phthalocyanines are planar and aromatic macrocycles that can act as electron donors and acceptors, and can be easily functionalized with a variety of chemical groups to tune their electronic and optical properties. The synthesis and characterization of a series of porphyrin-based molecular rotors that can undergo unidirectional rotation in response to light or electric fields, and can be used as switches or motors in molecular electronics [6].
Another area of active research is supra-molecular bioelectronics, which involves the functionalization of intermolecular interactions in biomolecules and supramolecular assemblies to achieve new electronic and optoelectronic functions. One example is the use of hydrogen bonds to control the electronic coupling between molecules in self-assembled monolayers (SAMs) on gold electrodes. The electronic conductance of SAMs can be modulated by changing the strength and orientation of the hydrogen bonds in the SAMs [7], and that this effect can be used to create molecular switches and memory devices.

In addition to hydrogen bonds, electrostatic and covalent interactions can also be used to control the electronic properties of biomolecules and supramolecular assemblies. The design and synthesis of a series of peptide-based molecular wires that can exhibit high charge transport efficiency and conductance modulation through electrostatic interactions with the surrounding environment it is reported in [8]. Moreover, a covalent bonding between graphene and biomolecules can enhance the electronic coupling and energy transfer between the two materials, leading to improved sensing and bioelectronic device performance [9].

Another important aspect of molecular bio-electronics and supra-molecular bioelectronics is the integration of these materials into functional devices and systems. For example, The fabrication of a field-effect transistor (FET) based on a single porphyrin molecule was realized [10], and its potential as a biosensing platform for DNA detection was demonstrated. A nanowire-based biosensor can detect DNA hybridization events with high sensitivity and specificity, using the electronic properties of the nanowires as the sensing mechanism [11].

Recent work has also focused on the use of protein-based materials in bioelectronics. design and synthesis of a conductive protein hydrogel that can be used as a bioelectronic interface for neural recording and stimulation was reported [12]. The hydrogel is composed of a genetically engineered protein that self-assembles into a conductive nanofibrous network, and exhibits excellent biocompatibility and stability in vivo.

Besides the molecular building blocks, the design of supramolecular bioelectronics also involves the control of intermolecular interactions to achieve specific electronic functions. One example of such an application is the development of biomolecular sensing devices, where the electronic properties of a biological recognition element are transduced into an electrical signal that can be readout by a sensor.

Biomolecular sensing devices are widely used in various fields, such as medical diagnosis, environmental monitoring, and food safety. Among different types of biomolecular sensors, electrochemical sensors have attracted significant attention due to their high sensitivity, selectivity, and low cost. Highly sensitive and selective electrochemical biosensor for the detection of dopamine based on the use of self-assembled monolayers (SAMs) of mercaptoundecanoic acid (MUA) on gold electrodes can serve as an example [13]. The MUA SAMs were functionalized with a dopamine-specific recognition element, and the binding of dopamine to the recognition element led to a change in the electrochemical properties of the SAMs, which could be measured by cyclic voltammetry.

In addition to electrochemical sensors, other types of biosensors have also been developed based on molecular bioelectronics and supramolecular bioelectronics. For example, optical biosensors that rely on the modulation of light by biomolecules or supramolecular assemblies have been reported. The use of plasmonic nanocavities as a platform for ultrasensitive detection of biomolecules, such as DNA and proteins, based on the coupling of light with the plasmonic resonances of the nanocavities was demonstrated [14]. The plasmonic nanocavities were functionalized with a specific recognition element, and the binding of the target biomolecule to the recognition element induced a shift in the plasmonic resonance frequency, which could be measured by spectroscopy.

In summary, molecular and supramolecular bioelectronics present a wealth of opportunities for advancing the development of novel materials, devices, and applications across diverse domains. By bridging the knowledge and expertise from biology, chemistry, physics, and engineering, it becomes possible to design and construct sophisticated and functional systems that can seamlessly interact with biological systems at the molecular scale. Despite the remarkable progress achieved in this field, there are still numerous scientific and technological challenges and opportunities that require further exploration, such as the precise control of intermolecular interactions, the elucidation of the fundamental principles that govern their electronic properties, and the discovery of new applications in emerging fields. A comprehensive review article by Berto et al. provides an insightful overview of the recent advancements and perspectives in molecular and supramolecular bioelectronics [15].

III. POSSIBLE APPLICATIONS OF QUANTUM MACHINE LEARNING

Research and development in Artificial Intelligence (AI) and Machine Learning (ML) led to exciting new technologies in various domains. One of these domains is gaming, where applications of AI/ML and Data Mining range from encounter analyses [16], data visualization [17,18], to win prediction [19,20]. While classical computing methods are good enough to solve complex problems, it is yet to be discovered if applying quantum-based approaches might improve the modeling of complex and practical systems.

Quantum computing approaches are different because the user can leverage different logic gates not available in classical computing. One such gate is a “Hadamard Gate” without its classical counterpart. This computational structure differs from a classical computing logic gate by introducing additional states for the programmers to control. Such a solution was required due to the unknown nature of the signal before its measurement called “superposition” [21].

High-level description of ML could be paraphrased as “defining models that learn rules from data”[22]. Ultimately Quantum Machine Learning (QML) is leveraging the properties of quantum computers, or simulated quantum computers, to define models similarly. In related work, authors mention different approaches to applying quantum-based methods: (1) The Classical-Classical approach defines methods using...
classical computing inspired by the quantum phenomena; (2) The Classical-Quantum approach, leveraging classical data with quantum-based methods to port the existing classical methods to QML or find novel quantum methods that can solve classical problems efficiently; (3) The Quantum-Classic approach signifies applying classical methods to quantum data; (4) The Quantum-Quantum approach, where both the data and the method are quantum-based [23].

Due to this modelling computation through quantum theory and its application in information technology can change how people perceive computation. Methods considering uncertainty of environment can bring us closer to simulating and interacting with a new range of systems. For example, representing activities as a signal, dealing with potential loss of signal, perception, and arbitrary evaluation of participants in sports [24]. Viewing sports as an optimization problem could be an interesting venue to apply the QML methods.

IV. NANOPHOTONICS BIOSENSORS IN NANOMEDICINE

Nanomedicine refers to the use of nanotechnology in the diagnosis, treatment, and prevention of diseases. In nanomedicine, quantum biophotonics can be used to develop novel nanoscale devices and sensors that use light–matter interactions to monitor and manipulate biological processes. Photonic biosensors in nanomedicine can revolutionize medical diagnostics and therapy by enabling rapid and accurate detection of diseases, monitoring of disease progression, and targeted delivery of drugs and treatments. Photonic biosensors can detect specific biomolecules such as single proteins [25], DNA [26], and other cellular components, making them useful for point-of-care diagnostics and monitoring [27,28,29].

Several types of photonic biosensors are currently being developed and studied in nanomedicine. These include evanescent-field-based, surface plasmon resonance (SPR) biosensors which use the interaction between light and metal surfaces to detect changes in the refractive index of biological samples. These biosensors are particularly useful for studying protein-protein interactions and can be used for drug discovery and development [30]. Localized surface plasmon resonance (LSMR) biosensors also use metal nanoparticles to detect changes in the refractive index of the surrounding medium. Still, the nanoparticles are smaller, and exhibit localized plasmon resonances [31,32]. Photonic crystal biosensors use the interaction between light and periodic structures to create photonic bandgaps, which can be used to detect changes in the refractive index of biological samples. These biosensors are helpful in detecting small molecules, pathogens, and biomarkers in biological fluids [33]. WGM biosensors use the interaction between light and resonant modes in micro- and nanoscale structures to detect changes in the refractive index of biological samples. These biosensors are particularly useful for detecting biomolecules in low concentrations and can be used for point-of-care diagnostics and monitoring [34].

One example of quantum biophotonics in nanomedicine is the development of quantum dots for imaging and sensing applications. Quantum dots are semiconductor nanocrystals that emit light when excited by an external energy source, such as a laser. They can be engineered to emit light at specific wavelengths, making them useful for fluorescence imaging and biosensing applications. Quantum dots can also be coated with biomolecules, such as antibodies, to target specific biological structures or cells for imaging or therapeutic purposes [35].

Another example of the use of quantum biophotonics in nanomedicine is the development of plasmonic nanoparticles for photothermal therapy (PTT). Plasmonic nanoparticles exhibit unique optical properties due to their interaction with light at the nanoscale. When exposed to light, plasmonic nanoparticles can generate heat, which can be used to kill cancer cells or other disease-causing cells selectively. This approach is known as photothermal therapy and has the potential to provide a minimally invasive and highly targeted alternative to traditional cancer treatments [36].

In summary, photonic biosensors in nanomedicine offer a powerful platform for disease diagnosis, monitoring, and therapy. These biosensors rely on the nanoscale interaction between light and matter to measure the signal and detect biological molecules with high sensitivity and specificity. The continued development and application of photonic biosensors in nanomedicine will undoubtedly significantly impact the field of medical diagnostics and therapy.

V. BIOPHOTONIC WAVEGUIDES, LIGHT SOURCES AND DETECTORS

Photonic integrated circuits (PICs) are photonic systems realized on-chip which, equivalently to the ubiquitous microelectronic chips, can be designed for highly integrated, application-specific purposes. The basic components (so-called Building Blocks – BBs) of PICs can be divided into light sources, passive or active waveguides and photodetectors, as seen in the example of the indium phosphide PIC platform [37]. A promising aspect of the recent developments in biophotonics and especially its newer subset, quantum biophotonics, is the increasing number of varied tools allowing for light generation, guiding, control and detection, corresponding to the basic PIC components [38] and potentially allowing the construction of “bio-PIC” devices in the future.

The main advantage of biophotonic devices and systems is that they can be potentially embedded or even fabricated inside biological systems, while maintaining high biocompatibility, potentially leading to novel in vivo sensing and health monitoring strategies (e.g., early-stage detection of cancer cells [38] inside living tissue) and improved countermeasure delivery methods (e.g., low-intensity light therapy [39] or localized drug delivery methods activated by light such as photodynamic therapy) [40].

Biophotonic light sources developed in recent years are focused on coherent light generation strategies, such as cell-based lasers. These devices can be divided into two types – extracellular and intracellular lasers, dependent on the location of their resonator cavity [38]. Intracellular lasers, more interesting from the point of view of biological, in vivo PIC systems, can be created by exploiting whispering gallery modes (WGM) [41] within the cells themselves. Resonators in WGM’s are typically significantly more compact than in other laser types, additionally they benefit from a very high Q-factor which decreases the lasing threshold. However, their main drawback is intrinsic multi-modal light generation, due to no native mechanism of mode selection [38].

Light sources based on quantum dots (QDs) are also potentially interesting in the context of biocompatible lasers.
However, the biocompatibility of commonly used II-VI elements based QDs (e.g., CdS, CdTe, CdSe) is insufficient [42]. As an alternative, Cd-free QDs using materials such as Si [43] or graphene [44] can be successfully fabricated and potentially applied as light sources in biophotonic systems [45]. Due to being embedded inside biological structures/organisms, light generated by such biophotonic sources can be subject to variations caused by the structures themselves, effectively carrying information about their state.

The generated light can be routed into waveguiding systems, allowing for functionalization and implementation of various detection strategies inside a PICs architecture. Waveguiding strategies in biophotonic systems can be divided into active, usually realized by means of fluorescence inside the waveguide material, excited by an external light source, and passive waveguiding, which can be realized in various ways, e.g., using air-clad, biocompatible spider silk [46] or peptide nanostructures (which could be used either as active or passive waveguides, depending on the fabrication steps taken) [47].

After interacting with measured substances, being subject to different environmental factors during generation and/or being influenced by other mechanisms which change the signal’s parameters, the light is detected and converted into electric signals which can be further processed.

VI. NANO-BIOPHOTONICS

Nano-biophotonics is a highly interdisciplinary field that merges the principles of photonics, nanotechnology, and biotechnology to enable the study of biological systems at the nanoscale. The field is centered around the development, advancement, and application of new technologies and techniques to investigate the fundamental properties of biological molecules, cells, and tissues with sub-cellular resolution and high sensitivity in real-time. The goal is to overcome the limitations of traditional imaging and sensing techniques by harnessing light-matter interactions and quantum effects to obtain in-depth information about biological systems. To achieve this, there is a need to develop optical imaging systems that offer super-resolution with deep penetration capabilities while overcoming fundamental barriers of light diffraction and scattering on biological materials. Moreover, there is a need to find new ways to synthesize functional materials that are biocompatible, offer advanced on-spot mutations or can incorporate chemical modifications with precision and complexity. In this regard, several techniques have been developed in the nano-biophotonic field to advance both photonic and chemical approaches.

One of the approaches/techniques in the nano-biophotonics field is the use of plasmon-enhanced biosensing, which utilizes plasmonics to enhance the signals of biomolecules. Plasmonics is a branch of photonics that focuses on the interaction between light and metallic nanostructures, which can enhance the electromagnetic field at the nanoscale. Since fluorescence-based techniques are among the most widespread in the field of biotechnology, advances in plasmonic nanostructures have the potential to extend the limit of fluorescence detection to the femtomolar level and beyond [48,49,50]. For example, a recent study presented a plasmon-enhanced fluorescence immunosensor for the specific and ultrasensitive detection of Plasmodium falciparum lactate dehydrogenase (PfLDH) in whole blood, which is a malaria marker [51]. Another study demonstrated the detection of single-nucleotide polymorphisms (SNPs) in DNA samples with high sensitivity and specificity using plasmon-enhanced fluorescence [52].

Another important advancement in bio-nanophotonics is super-resolution optical microscopy, which allows for imaging beyond the diffraction limit of light. Super-resolution microscopy has revolutionized the field of cell biology by enabling researchers to study cellular structures and functions with unprecedented resolution. For instance, stimulated emission depletion microscopy (STED) has been used to image synapses in living mice brains with a resolution of up to 30 nanometers [53,54]. The combination of STED with fluorescence lifetime imaging microscopy (FLIM) has created another subdiffraction imaging technique, which has been optimized by using time-correlated single photon counting (TCSPC) to carefully select detected fluorescence photons [55]. STED and FLIM microscopy have been used to study the localization and dynamics of G protein-coupled receptors (GPCRs) in live cells [56]. In addition to STED, other super-resolution microscopy techniques, e.g., Förster Resonance Energy Transfer (FRET) microscopy and structured illumination microscopy (SIM), have been developed [57,58]. FRET microscopy uses the principles of the energy transfer between two fluorophores when they are in close proximity, to measure the distance between molecules. SIM works by projecting a pattern of stripes onto the sample, which generates an interference pattern that is captured by the microscope. By analyzing the interference pattern, high-resolution images can be reconstructed. STED, FRET, or SIM are often combined with FLIM or other techniques to provide more information in single-molecule studies. For example, homoFRET microscopy was used to demonstrate the oligomerization state of the human neurotensin receptor 1 (NTSR1) [59].

Significant progress in chemical methodologies developed in conjunction with photonic techniques is critical for pushing the boundaries of nano-biophotonic research. A notable example is the development of nanosized carbonized polymer dots (CPDs), CPDs-3, which exhibit exceptional efficiency and photostability in emission, enabling super-resolution imaging combined with FLIM techniques [60]. Additionally, click nucleic acid ligation is another powerful tool that enables the precise and rapid synthesis of DNA and RNA molecules with tailored sequences [61]. This approach has led to the development of a DNA aptamer with high affinity for the protein biomarker thrombin, demonstrating the capability of click nucleic acid ligation for synthesizing highly specific biomolecules [61]. The combination of chemical and photonic techniques offers unprecedented resolution for imaging and synthesizing biomolecules, providing new insights into the workings of biological systems.

Lastly, optogenetics is a rapidly evolving field that utilizes light to control the activity of cells and tissues with high spatial and temporal precision. Optogenetics has been revolutionized by the development of genetically encoded light-sensitive
proteins, such as channelrhodopsins and halorhodopsins, which can be selectively activated or inhibited by light of specific wavelengths [62]. Optogenetics has already been used to study various cellular processes, including neuronal signaling, gene expression, and immune cell activation [63, 64, 65]. In addition to genetically encoded proteins, the field of nano-biophotonics has also contributed to the development of new tools for optogenetics. For example, photonic tweezers, which utilize highly focused laser beams to trap and move individual cells and subcellular structures, have been used to deliver light to specific areas of cells and tissues [66]. Furthermore, nano-optical bioantennas, which use plasmonic structures to enhance light absorption and scattering in biological systems, have been developed to improve the efficiency and specificity of optogenetic control [67].

VII. DISCUSSION, CONCLUSIONS

Several distinct fields of study with significant potential to revolutionize our understanding and interaction with biological systems are discussed. Quantum biophotonics is a multidisciplinary field that combines photonics, biochemistry, biophysics, and quantum information technologies to study physiological and pathological phenomena at the sub-nanoscale level. Similarly, molecular and supramolecular bioelectronics involve designing materials and devices that interface with biological systems at the molecular level and have the potential to develop biosensors for medical diagnosis, environmental monitoring, and food safety.

Quantum-based approaches in gaming are also emerging as a novel way of improving modeling of complex systems. Meanwhile, nanomedicine involves using nanotechnology in disease diagnosis, treatment, and prevention and can be enhanced by incorporating quantum biophotonics to develop nanoscale devices and sensors. Lastly, nano-biophotonics combines photonics, nanotechnology, and biotechnology to study cellular structures and functions with unprecedented resolution.

Overall, these fields of study hold significant potential for improving medical diagnostics, therapy, biosensors, computation, and interaction with biological systems. Through innovative research and advancements, quantum biophotonics, molecular and supramolecular bioelectronics, quantum-based approaches in gaming, and nano-biophotonics have the potential to lead to significant discoveries and innovations in various fields, such as medicine, technology, and environmental monitoring.

REFERENCES


