J Nanotechnol Nanomaterials. 2025;6(1):67-75.

Journal of Nanotechnology and Nanomaterials Short Communication

Development of Functional Nano-, Micro-Biostructures with Generation of New Enhanced Light Pathways for Life Science Applications

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Received date: April 28, 2025, **Accepted date:** June 27, 2025

Citation: Quinteros DA, Amé MV, Bracamonte AG. Development of Functional Nano-, Micro-Biostructures with Generation of New Enhanced Light Pathways for Life Science Applications. J Nanotechnol Nanomaterials. 2025;6(1):67-75.

Abstract

Life sciences involve a broad overview of fundamental research of high interest, accompanied by the development of applications based on emerging needs. The generation of non-classical light is a high-impact area of research that could lay the foundation for functional materials, particularly in applications requiring tracking and switchable (on/off) properties. In this regard, the present communication is intended to present and discuss how natural and synthetic bio-structures, along with Nanotechnology, could provide versatile platforms for developing functional and multi-functional structures accompanied by the generation of novel non-classical light pathways. The design involves multidisciplinary research, where the chemistry of nano- and microscale surfaces can be leveraged to tune interactions and enable further functionalization. Moreover, bioconjugation and genetic engineering can be employed to modify material composition and properties. In this context, the biostructure is not merely the target—it becomes an integral part of the functional biomaterial designed to deliver specific, targeted properties. Thus, the design of nano-biostructures requires interdisciplinary knowledge from different research fields such as nanomaterials, nanotechnology, biomaterials, biochemistry, and biotechnology. The targeted functions span a broad range, as highlighted in this short communication, which offers insights and analysis to stimulate discussion on leveraging fundamental knowledge in photonics and biophotonics. New phenomena related to light and electronic interactions—ranging from the nanoscale to the quantum level—are explored through nano–bio interactions, creating new modes of energies, non-classical light generation, and enhanced physical effects.

Enhanced nanomaterials and nanotechnology, particularly in the context biological media with different interests are highlighted. Consequently, life sciences and biomedical developments are central to advancing both fundamental knowledge and practical innovations in areas such as biophotonics, biotechnology, and related fields

Keywords: Nanotechnology, Biotechnology, Nano-biostructures, Micro-machines, Hybrid nano-biostructures, Functional nano-biostructures, Nano-bio-platforms

Development of Nano-Optics for Bioconjugation

The control of the nanoscale and the study of the light interaction with designed nanomaterials should be guided by targeted applications. In this context, nano-optics plays a crucial role in enabling bioconjugation and further functionalization, with an emphasis on biocompatibility and biomedical relevance. Thus, optical nanoplatforms are emerging as powerful tools in biophotonics, attracting significant interest due to their potential impact across the life sciences. The development of hybrids silica nanoparticles with tunable dimensions, surface chemistries, luminescent properties, and bioconjugated surfaces—as nanoplatforms for single nanoparticles analysis based on luminescent nanoimaging is of high interest due to their capability to detect, track and interact within biological media. In this field, there are many synthetic approaches and nanoarchitectures based on fluorescent silica nanoparticles [1] within aqueous media. Notably, highly fluorescent silica nanoparticles have been synthesized via reverse microemulsion methods, incorporating double-layered doping of organic fluorophores to enhance emission efficiency [2]. Moreover, nano-engineered polymeric nanoparticles with quantum dots have been explored for their tunable luminescent properties [3]. All these publications highlighted the importance of the surface chemistry control [4], functionalization [5] and their interactions, which have measurable effects on adjacent biological microstructures [6]. In addition, further developments for the design and fabrication of photonics devices [7,8], and enhanced silica waveguides [9] could be found in current trends toward miniaturized instrumentation and optical active platforms. However, in all these types of prototypes, the signal output in general is too low and it should be amplified [10,11].

In addition, lab-on-particle approaches should be highlighted for their highly tunable functionalities [12]. In this context, the application of fluorescence microscopy is particularly valuable for data analysis, as it enables single nanoparticle tracking—where resolution plays a critical role in capturing detailed and meaningful insights.In addition, the accessibility to this microscopy technique, combined with nano-optics, provide an excellent strategy for enhanced resolutions through precise control of photons emission at the nanoscale. In this way, nano, micro-, and even larger-scale components within optical systems are participating together to produce diverse optical signals depending up on the need. The key challenge lies in integrating optically active materials capable of controlling physical and chemical interactions, with a consistent focus on generating novel non-classical modes of energy and light. To meet these demands, advanced microscopy techniques are continuously evolving such as nanoimaging beyond the diffraction limit using near-field scanning optical microscopy (NSOM) [13], fluorescent silica-nanoparticle probes designed for high-resolution confocal and stimulated emission depletion (STED) microscopy applied for cell Imaging [14]; and hybrid methodologies combining electron microscopy with fluorescence microscopy for enhanced structural and functional analysis [15]. In this regard, it is important to emphasize the impact of all these developments in various applications related to bioimaging [16], cell detection [17], brain cell targeted imaging [18], cancer detection [19], as well as innovations in lab-on chip and lab-on-particle systems. Based on these needs and challenges, this article opens a discussion on recent advances in enhanced optics with nano-resolution capabilities that surpass the diffraction limit—achievable even through techniques such as bright-field microscopy.

From this perspective, the ability to tune the nanoscale by incorporating various materials through diverse techniques and methods provide an open source of optical properties that could generate interest and impact towards the development of new technologies [20]. Thus, by focusing light and various photon sources on nanoparticles, their nano-optical properties can be stimulated under different optical setups. For example, in flow-based methodologies, controlled photonic excitation of single nanoparticles within colloidal media can be achieved and recorded (**Figure 1a**). Alternatively, 3D nanoimaging can be generated within a confined light volume (**Figure 1b**). Further

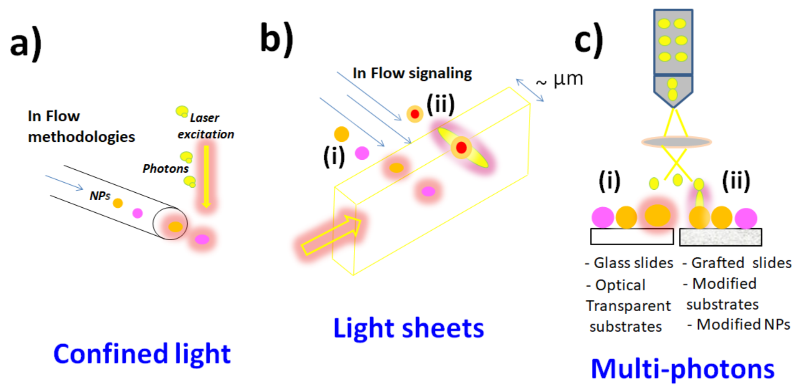

Figure 1. Schema focusing light on reduces sized hot spots. **a**) Laser excitation within micro- and nano-fluidic systems; **b**) In-flow signaling within light sheets to track: (**i**) optically active nanoparticles and (**ii**) enhanced optical nanoplatforms by proper tuning of material components; **c**) Controlled multi-photon delivery on (**i**) glass slides and (**ii**) modified substrates. Reprinted with permission from A. Guillermo Bracamonte *et al.* [20].

developments in optical setups could afford to focus on high irradiance levels to excite single optically active nanoplatforms or generate localized hotspots of reduced size **(Figure 1c)**. In such systems, resolution can be tuned based on the number of photons delivered, the use of pulse controllers, and the specific optical lenses applied (**Figures 1c.i** and **1c.ii**). Consequently, by controlling spectroscopy at the molecular level, different fluorescence microscopy configurations can be employed to achieve tunable resolutions for nanospectroscopy studies.

Thus, nano-optics enables the illumination of biostructures and their surrounding environments with controlled intensities and diverse topological forms of light. This paves the way for the development of novel synthetic non-classical nano-bio light interactions. Similarly, additional multifunctional approaches may emerge by integrating bioelectronics, optoelectronics, and even quantum coupling with natural bio-photosystems.

Insights on Nano-bio-designs for Targeted Functional Structures

The nanoscale is inherently present within living systems in various forms, such as protein structures, enzymes, extracellular vesicles, viruses, and other nanoaggregates and assemblies—many of which are associated with specific biological functions and, in some cases, diseases [21]. Furthermore, the detection of diverse microorganisms is crucial for numerous purposes, particularly in the context of health monitoring and early diagnosis. Therefore, the detection and analysis of microorganisms and related microstructures are of great importance across various disciplines. This is well recognized in fields such as clinical diagnostics, biochemistry, environmental chemistry, and analytical chemistry. These efforts are increasingly supported by ultrasensitive analytical methodologies that employ non-conventional, advanced instrumentation—particularly within biophotonics, ultrasensitive diagnostics [22], genomics [23], and nanomedicine [24]. However, the biological structure is not always the target. In many cases, the biostructure serves as a support platform that enables or delivers the desired function based on specific needs. In this regard, biotechnology and nanobiotechnology are increasingly driving research efforts aimed at developing new functions and applications within the life sciences.

It is important to mention that in recent years, a wide range of research fields have been involved in the development of new technologies such as green nanotechnology and advanced materials and composites, to improve human health, addressing environmental and economic challenges, and advancing clean energy production and storage. In this context, the present article focuses on the design and application of functional nanomaterials integrated with targeted biostructures, highlighting the impact of synthetic hybrid properties and insights drawn from biotechnology and the life sciences. Moreover, environmental remediation, sustainability, sensors, pharmaceutical, medical, and health-cosmetic applications—particularly those utilizing simple and cost-effective methods—are of growing interest. Nanomaterials and biostructures play various critical roles in all these developments. In this regard, the present article focuses on the design and application of functional nanomaterials integrated with targeted biostructures, highlighting the impact of synthetic hybrid properties and insights drawn from biotechnology and the life sciences.

In this regard, biostructures may serve either as the target or as part of the solution for a specific application. This highlights the importance of genetic engineering, which can be used to modify biostructures by introducing desired functional characteristics. Alternatively, such functionality can be achieved through other strategies, including bioconjugation techniques and the application of nanotechnology. Consequently, studying the interactions between novel nanomaterials and bacteria or various microorganisms is of great interest—particularly for their use as nanolabellers to tailor and enhance targeted applications.

From these perspectives, targeted functions and multifunctional natural-, synthetic-, and nano-biostructures could be highlighted. Within this context, the field of synthetic biology plays a pivotal role, enabling the design and modification of structures that mimic natural systems while incorporating custom features based on specific needs. For example, It is mentioned; i) biomachines for genomic material synthesis and repair, such as those developed by CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) [25], ii) cargo loaded biostructures, iii) carriers, iv) bio-catalyzers, v) new functional nano-biostructures composed of pre-designed individual components assembled for synergic effects, vi) nano-enzymatic engines, vii) bioluminescent structures, viii) synthetic nano-biolasers, and ix) other multifunctional structures such as micro-swimmers, drug delivery systems, and bio-captors [26]. As seen, there is a broad and expanding landscape of potential functions and challenges, all deeply interconnected with the life sciences.

Moreover, recent trends in green chemistry are increasingly influencing the fields of photonics and materials design. In these research areas, materials and their associated properties should be biocompatible contemplating their fabrication. Developing green nanomaterials with enhanced conductive and luminescent properties is a great challenge.

These challenges are actively being addressed, with ongoing research focused on the evaluation and optimization of such materials. However, gold-based nanomaterials are offering promising insights within nanotechnology for various bio-applications. From this perspective, and in the pursuit of new optically active materials, it is important to emphasize the design and fabrication of devices from the nanoscale upward. In this context, the synthesis of intermediate reagents and nanostructures via green methods or, in many cases, involving key reagents obtained from natural sources are currently under consideration. In this regard, the design and synthesis of optically active nanocatalysts using green or hybrid methodologies is of growing interest. For example, orange juice provides a renewable and environmentally friendly source for capping photocatalytically active nano-composite; where citric acid and ascorbic acid in orange juice act as natural reducing and capping agents, controlling the size and morphology of the nanostructures [27]. In this development, new nanostructures were designed by modifying nanoplates with electroactive materials, enabling the detection of targeted molecules—such as in the sensing of mesalazine [28]. Additionally, the incorporation of both natural and synthetic minerals has been demonstrated in environmentally friendly methods. One example includes the use of blends composed of wheat starch and *Lepidium perfoliatum* seed mucilage combined with sodium montmorillonite nanoparticles [29]. The composite films were produced through a casting method, combining these components to enhance incorporations of optically active nanomaterials.

In contrast, not only small biomolecules are being utilized; larger biological structures—such as proteins closely related to enzymes—are also being incorporated into nanomaterial design. For example, nano- and microstructured heparin/porous nanocomposites with synergistic catalytic Lewis and Brønsted acid sites have recently been reported for the efficient conversion of monosaccharides [30].

Focusing on the combination of nano- and microscale components—by integrating nanoparticles with biostructures that possess specific properties—offers the potential to achieve synergistic effects and multifunctional capabilities. This underscores the need for the development of strong and stable nano-biostructures. From a nanotechnology perspective, incorporating additional functions into biotechnological systems represents a highly promising and impactful research direction. In this context, recent developments in nano-biotechnology have demonstrated high-impact yet relatively simple approaches for the protection of vaccines and other functional biostructures [31]. From this perspective, the present communication intended to highlight these new trends in research and related publications focused on the generation of nano-biostructures and the development of nano- and micro-biomachines designed for a variety of targeted functions. This research field can be approached through various strategies; however, integrating multidisciplinary fields accelerates progress and serves as a powerful source of knowledge. This is particularly evident when synthetic and modified biostructures are combined with specific bio-optical properties and functional nanomaterials (**Figure 2**).

Biostructures may include tiny viruses, bacteria, unicellular and multicellular organisms, as well as other genetically modified living systems. Meanwhile, nanomaterials contribute essential functionalities—such as nano-optical properties—

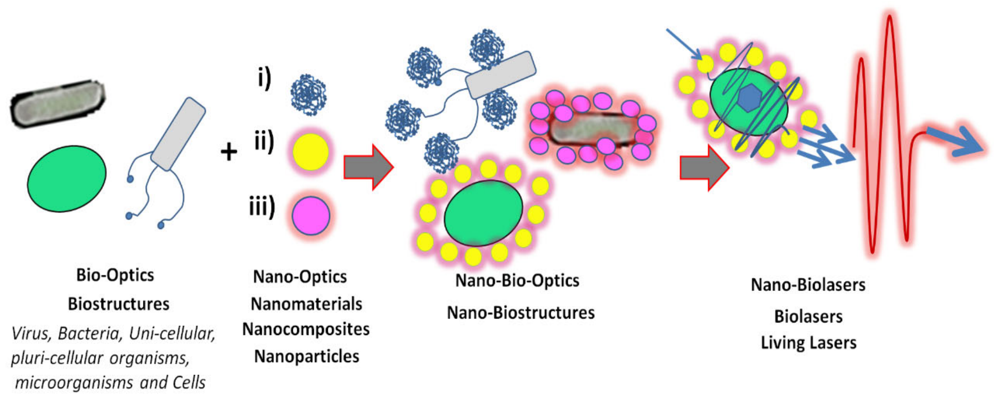

Figure 2. Schematic representation of the design and synthesis of hybrid nano–biostructures, highlighting the integration of various nanomaterials toward the development of nano–bio–optically active materials. (**i**) Nanoassemblies; (**ii**) and (**iii**) Multicolored nanoparticles conjugated with different biostructures, such as viruses, bacteria, and cells.

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enabling the development of optoelectronics, bioelectronics, non-classical light sources, and a variety of physical, chemical, and biophysical phenomena. The integration of these two material classes can be achieved through surface chemical modifications, including wet chemical methods for covalent linking, bioconjugation techniques, and non-covalent interactions for targeted assembly [32,33]. Thus, nano–bio–optical materials can be developed and proposed for tuning enhanced non-classical light emission—functioning as nano–bio–emitters, cargo-loaded nano–bio–emitters, and multifunctional nano–bio materials where light either serves a targeted purpose or contributes to the system's overall versatility.

In this context, it should be noted that there are no limitations in the design or functions of nano–bio systems; rather, the challenge lies in the need to prototype new approaches. This highlights the importance of tuning both nano- and microscale features using organic and inorganic materials. Prototyping serves as a means to conceptualize, design, and characterize systems by hierarchically integrating molecular components at the nanoscale and extending them to the micro- and macroscale. The design process may begin on the drawing board or using 3D imaging software; however, the ability to manipulate real materials that emulate molecular and nanoscale architectures has a profound impact on the design of new Nanomaterials. Prototyping also enables the use of diverse materials to explore and validate nanoscale concepts. Once a design is established and a synthetic methodology is developed, iterative cycles of characterization, evaluation, and optimization can be applied to refine the final product.

From these perspectives, the field of nano-optics emerges as a crucial area for studying and designing optically active nanomaterials, light–matter interactions, quantum phenomena, and metamaterials. In this context, prototyping is not only about shaping the physical structure but also about developing the methodology and know-how needed to create nanomaterials with novel, non-classical optical properties. This process involves conceptual design rooted based on physical and chemical phenomena. To achieve this, a wide range of strategies must be integrated, drawing from diverse material sources and their associated properties. Consequently, a solid understanding of nanochemistry is essential for the bottom-up construction of nanoplatforms, along with foundational knowledge in biology and biochemistry to guide their functional integration in bio-relevant systems.

Advances in Nano-Bio-Optics

As previously introduced, the design of hybrid nano-biostructures represents a current high-impact challenge across various research fields and applications. For example, laser dyes, nanolasers, novel nanomaterials, and quantum laser particles can be integrated with biologically active media—such as viruses, bacteria, and cells.

In this manner, the resulting nano-biostructures can exhibit enhanced lasing properties across various energy modes. The underlying concept is to increase and improve lasing performance either through the integration of nanophotonic materials with optical crystals or by engineering the entire synthetic nano-biostructure to possess lasing capabilities—utilizing the biological component as a structural support, transport vehicle, and optical gain medium. Various challenges must be overcome to successfully develop the proposed prototype, depending on the specific components being integrated. For example, these challenges may include the precise deposition of nanoparticles onto biostructures, achieving targeted interactions, incorporating nanomaterials through cellular membranes or into specific organelles, coupling with photoactive components, and employing bioconjugation techniques. By addressing these factors, it becomes possible to precisely control nano-lasing properties on demand or to modulate the emission characteristics of incorporated materials through their optical interactions with the surrounding biological environment—ultimately enabling the creation of functional biolasers.

In this way, both optically active and non-optically active biostructures can be utilized as functional supports for the design of advanced nano–bio materials. It is important to mention that high-impact applications of nano–bio–optics have been demonstrated in virus detection and also in the identification of larger biostructures [21]. Furthermore, the tuning of enhanced nanoplatforms opens the door to new designs based on the "lab-on-particle" concept, where nanolaser properties play an important role in achieving desired functionalities [34]. For example, a recent study reported the application of laser particles for cell tracking (**Figure 3**) [35]. In this development, controlled spatial emission of high-energy electromagnetic fields was generated using precisely engineered InGaAsP semiconductor microdisks and modified structures that could be incorporated into living cells. Using a modified confocal microscope system [36] for tracking cell-associated lasing emissions, researchers were able to achieve variable signaling and imaging responses depending on the specific nano-biostructure targeted. Laser emissions were distinguishable between non-modified microdisks and nanopatterned structures based on their differing directional outputs. These spatially confined high-energy electromagnetic fields can potentially couple with internal biological components, opening the door to novel approaches in bioimaging and nanomedicine. Notably,

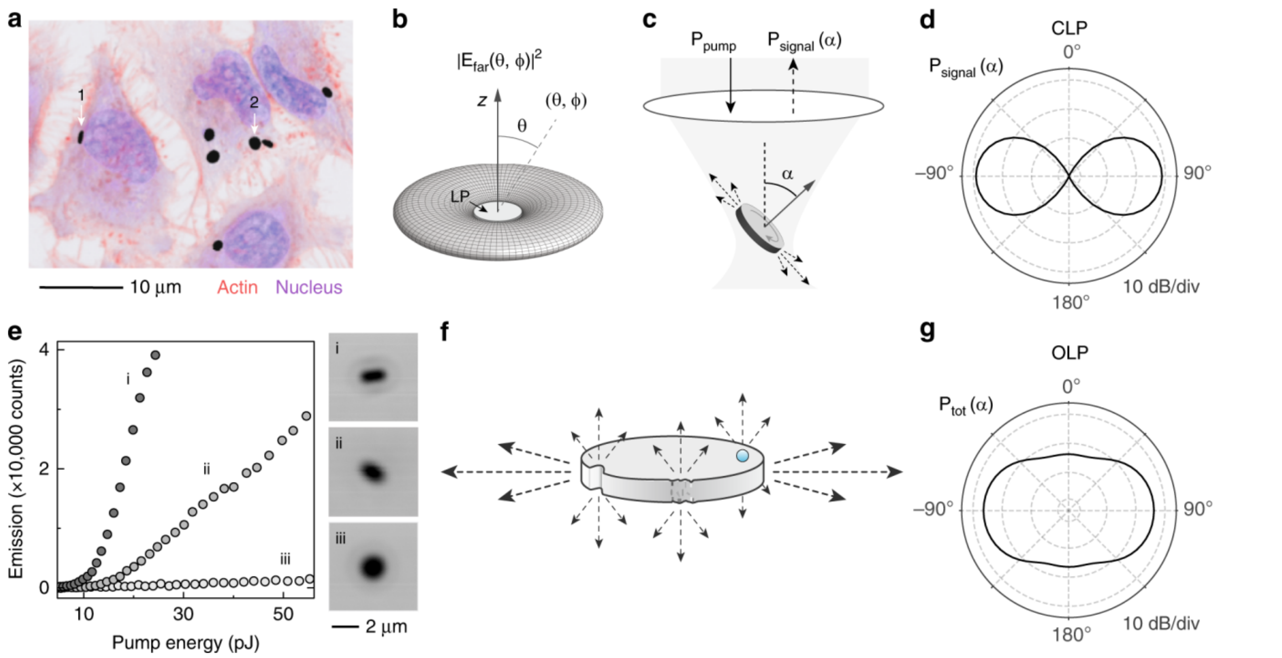

Figure 3. a) Cells tagged with laser particles (LPs). showing two representative disk orientations; **b**) Far-field radiation pattern $|E_{far}(\theta,\phi)|^2$ of the 10th-order transverse electric (TE) whispering gallery mode (WGM) of a conventional microdisk laser; **c**) Schematic of the pumping and collection geometry; **d**) Simulated $P_{signal}(\alpha)$ of a confined laser particle (CLP); **e**) P_{signal} versus pump energy P_{pump} for three CLPs suspended in a hydrogel with different orientations. Insets: Corresponding optical images (**i**, **ii**, **iii**); **f**) Illustration of various strategies for achieving omnidirectional emission: A deformation (notch) on the boundary of the microdisk, surface roughness, or high-index nanoparticles attached to the microdisk can redirect a portion of the lasing emission into the normal direction via elastic scattering; **g**) Simulated $P_{tot}(\alpha)$ of an OLP with a single 200-nm-size notch scatterer. Reprinted with permission from Tang *et al*. [35].

lasing properties were successfully integrated into live cells containing intracellular optical microresonators, enabling barcode-type cell tagging and tracking [37]. As a result, intracellular microlasers operating across different energy modes have demonstrated significant promise and impact in advanced biomedical applications [38].

Building upon the previously discussed results and insights into functional, optically active hybrid nano–biomaterials, a broad framework emerges for future studies and developments across various themes within the life sciences. Thus, the challenge is open to identify high-impact areas and addressing pressing needs by combining diverse material compositions with targeted properties. In particular, the generation of non-classical light within biological systems, biomaterials, and hybrid nano–biomaterials seem to be promising [39].

From an alternative perspective, the optical properties of nanomaterials and biostructures may differ significantly when studied independently compared to when they are assembled. This forms the basis for the development of nano–bio–optics, which can yield either a fully bright nano–bio emitter or enable targeted biomolecular interactions, including those occurring at or across biological membranes. Studies on non-classical light generation by confining laser dyes within silicon-based nanoplatforms have demonstrated tunable wavelength and intensity outputs based on the applied laser excitation. When these silicon-based nano-emitters were combined with optically active unicellular organisms, novel nano–bio–optical effects emerged, influenced by the interaction between both components. Notably, enhanced Fluorescence Resonance Energy Transfer (FRET) was observed—from the nanoscale emitter to the optically active biostructure—resulting in variable bioimaging outcomes depending on the specific bio-optical context. These enhanced nano–bio emissions could be tuned, with both emission characteristics and resolution depending on the species of the biostructure involved [40].

In this manner, it has been demonstrated how nano-biostructures can be strategically designed and developed for a wide range of potential uses and future applications.

A particularly important aspect is the ability to incorporate cargo-loading capabilities and functional tracking, which is highly relevant to emerging technologies such as Next-Generation Sequencing (NGS) and related innovations [41], which increasingly rely on the development and manipulation of non-classical light at both the nano- and bio-scales.

Concluding Remarks

By integrating multidisciplinary research fields and associated knowledge, it is possible to design synthetic or hybrid biostructures that serve as functional biomaterials [26]. In this context, both natural and synthetic biostructure acts not only as a platform or support but also as a functional component—combined with nanoarchitectures that could provide additional properties and enable multi-modal approaches [42,43]. Therefore, the nano–biostructure is not merely the target of study; rather, it becomes the functional device itself [44], capable of delivering and acting through smart, pre-designed mechanisms [45]. This represents a critical challenge and opportunity, calling for thoughtful consideration of such approaches to meet the demands of high-precision life sciences applications—grounded in fundamental research and innovation [46,47]. The design is the fundamental part of the challenge to obtain the targeted functionality. Complex molecular systems placed on Nanosurfaces or confined within the Nanoscale can act as multifunctional smart responsive materials. This is particularly relevant in high-impact research fields such as nanocatalysis, where the nanoscale enables precise interactions for anchoring incoming molecules in optimal positions—either for cleavage or for facilitating new molecular linkages. Such hypothetical nanosystems can also be integrated with bio-structured matter, enhancing biocompatibility while introducing additional functionalities. These principles pave the way for the development of next-generation designs in nano- and bio-robotics, as well as advanced nano- and microdevices [47]. The interactions and underlying mechanisms in these systems are often complex and not immediately evident—representing one of the many challenges in the field. However, these challenges are not limited to mechanical functions or well-defined 3D chemical structures, such as those found in nanoenzymes [48,49]. Other types of interactions can arise from confined matter, where spatial and temporal overlap of various energy modes leads to unique effects. In this context, strong electromagnetic fields—originating from both soft and hard matter systems [50]—can be harnessed to modulate electronic, optoelectronic, and even quantum phenomena within nano- and microdevices [51], opening new avenues for both fundamental studies and technological advancements [52]. These approaches are highly relevant for the development of nanotechnology, but their potential extends further. When integrated into biological systems, they may enable interaction with and modulation of natural biomaterials—even at the quantum level [53].

In this context, a recent study reported the nano-bioconjugation of ultraluminescent gold core–shell nanoparticles with nanostructured human serum albumin (HSA) [45]. These new nano–bio architectures enabled bi-colored, enhanced luminescence imaging through a laser-triggered on/off switching mechanism, based on metal-enhanced fluorescence (MEF) [54]. This approach allowed for the tuning of non-classical light emissions, transitioning from near-field to far-field responses, with spatial resolution dependent on the applied laser excitation. Fundamental research focused on confined matter and the controlled interaction of diverse materials lays the groundwork for the next stages in the bottom-up development of nanotechnology and beyond. These efforts aim toward the creation of new synthetic and hybrid functional nano–biomaterials with potential impact across both soft and hard technologies. For all these developments, it is essential to emphasize the critical need for multidisciplinary fundamental studies—not only to continue advancing scientific knowledge but also to enable the design and realization of novel, functional materials.

Finally, this work has highlighted a broad overview of topics related to the development of nano–biostructures. From a fundamental knowledge perspective, the controlled interaction of photons and electrons within targeted material systems opens new possibilities for generating novel electronic states, associated chemical pathways, and emergent physical phenomena. This emerging trend opens the path to the creation of novel material properties that were previously unattainable. In part, this new capability is enabled by the diversity and complexity inherent in natural sources. However, to further enhance and scale these phenomena, the deliberate design and synthesis of artificial and biomimetic systems are essential. Thus, new opportunities are emerging to tune properties from the molecular, nano-, and microscale to larger-scale substrates—enabling enhanced optoelectronics and the generation of non-classical light, while incorporating even more complex functionalities. This multifaceted tuning represents a central challenge and opportunity in the advancement of next-generation materials.

Acknowledgements

Special acknowledgment is extended to the Departement de chimie and Centre d'optique, photonique et laser (COPL), Université Laval, Québec (QC), G1V 0A6, Canada, as well as the Department of Chemistry at the University of Victoria (UVic), Vancouver Island, V8W 2Y2, British Columbia (BC), Canada, for providing postdoctoral positions and academic information related to this work. Their support has been instrumental in advancing research on the design and synthesis of materials for nanophotonics, biophotonics, dynamics, and nanomedicine. Special thanks to Professor Daniela Quinteros from the Unidad de Investigación y Desarrollo en Tecnología Farmacéutica (UNITEFA) (Unit of Research and Development in Pharmaceutical Technology), Departamento de Ciencias Farmacéuticas, Facultad de Ciencias Químicas (Dep. of Pharmaceutical Sciences, Faculty of Chemical Sci.), at UNC, and her research group, for their valuable collaboration and ongoing multidisciplinary research efforts. Finally, special thanks are extended to Professor Denis Boudreau from the Département de Chimie and Centre d'Optique, Photonique et Laser (COPL) at Université Laval, Québec, Canada, for his longstanding collaboration and support.

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