

Generation of bioimaging towards design of hybrid micro-machines and micro-swimmers

Gomez Palacios LR and Bracamonte AG*

Department of Organic Chemistry, Faculty of Chemical Sciences,
INFIQC, National University of Cordoba, Cordoba, Argentina

Corresponding author: gbracamonte@fcq.unc.edu.ar

Received on: 17/03/2022

Accepted on: 23/06/2022

Published on: 25/06/2022

ABSTRACT

Nano-labellers could show variable emission properties depending on the intrinsic matter constitution of the designed nano-particle. The composition could incorporate varied non-classical light sources. Thus, the study of metal-enhanced fluorescence (MEF), fluorescence resonance energy transfer (FRET), coupled phenomena, and other enhanced scattering light phenomena is highlighted. We discuss the deposition of nano-emitters on biostructures for targeted studies and specific applications. And in this context recently, it was reported different designs of nano-emitters for the generation of ultraluminescent biostructures, single biostructure detection, targeted light delivery through biostructures, and other applications as protection agents against antibiotics and stabilizing agents of nano-vaccines. In addition, from these studies and applications, the perspectives of these nano-biostructures as synthetic or hybrid biostructures for targeted applications within biotechnology were discussed. In these synthetic Nano-Biostructures, each component acts as a functional component to generate the final function. Moreover, it was afforded to show and discuss about Dynamics of interactions between the different components of the hybrid structure and inter-Nano-Biostructure interactions to form Nano-Bio-assemblies for multiple uses. Thus, the concept of micro-machines for nano-medicine and biotechnology was introduced. This short communication intends to show important research developments from fundamental studies towards targeted applications.

Keywords: Micro-machines, hybrid nano-biostructures, nano-bio-imaging, synthetic ultra-bio-luminescence, FRET

How to cite this article: Gomez Palacios LR and Bracamonte AG (2022). Generation of bioimaging towards design of hybrid micro-machines and micro-swimmers. *J. Chem. Res. Adv.*, 03(01): 22-27.

Introduction

The generation of bioimaging could lead to multimodal approaches and applications (Henderson, 2018). This communication was centered on the basis of bioimaging generation to achieve varied resolutions of biostructures within different scale lengths. In this perspective, it was focused on developments from the molecular level toward higher sized structures. So, varied Biostructures such as specific peptides, proteins, DNA, RNA, viruses, bacteria, and unicellular organisms (Ame, 2020), could be optically active or non-active within different energy modes. Thus, these particular properties could be used to develop bioimaging with different resolutions. However, the application of nano-biolabelling by bioconjugation techniques could lead to a more effective control of final properties (Palacios, 2021).

Accordingly, the development of new nano-emitters with stable and high emission intensity is growing in interest (Woehrstein, 2017). Hence, meta-emitters are being developed by combining varied materials and enhanced nano-emitters based on plasmonic properties, such as metal-enhanced fluorescence (MEF) (Rioux, 2017), and enhanced plasmonic phenomena (EP) (Luchowski, 2010 and Boudreau, 2019) coupled to other phenomena. Similarly, fluorescence resonance energy transfer (FRET) (Dacres, 2010) could provide alternative light pathways for targeted bio-chromophores as well as enhanced emissions by an adequate pair of donor/acceptor coupling (Salinas, 2020). By a controlled deposition of nano-emitters on biostructures, synthetic nano-biostructures with different properties in comparison to the free components are obtained (Gammoudi, 2013). Depending on the properties combined, it could be achieved different Research goals and applications.

Hence, bioimaging generation for biodetection, quantification, early diagnosis, and further analysis focused on single biostructure may lead to

Copyright: Gomez Palacios and Bracamonte. Open Access. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

functional or multi-functional nano-biostructures. For example, it could be applied, from the Nano-Bio-labelling developments, new strategies to the design of synthetic bio-machines towards higher sized micro-machines (Muiños-Landin, 2021). In these types of developments is of high importance the proper choice of each component of the hybrid structure to achieve a targeted function (Magdanz, 2020). In particular, these topics arouse interest in biotechnology, biophotonics, and nano-medicine as well as other newly emerging technology such as soft nano-robotics (Li, 2019).

In these perspectives, in the next sections it was leaded to show and discuss the most important recent reports related with many Research fields involucrated in the generation of Nano-Biostructures with applications in the design and synthesis of Nano-, Micro-Bio-machines.

Nano-biolabelling

In general, the capabilities of labelling applications using different types of small molecules with particular properties are well known. In this context, it could be mentioned coloured staining agents (Alturkistani, 2016), fluorescent dyes (Lei, 2021), radioactive nuclei (Jensen, 2021), and other spectroscopical properties (Matsumoto, 2021) applied on tissues and biostructures. The addition of an extra spectroscopical property on the targeted non-optical active biostructure generates new energy modes that permit the biodetection and bioimaging with a variable degree of resolution. However, when looking for improved performance and stable signaling, much research is being currently conducted on the design and synthesis of new nano-labellers (Soo Choi, 2010). Specifically, they focus on the confined spectroscopical properties to develop from nano-spectroscopy to tune non-classical light in the far field. Thus, it is applied to single nano-emitters capable of delivering a targeted energy mode by external optical stimulation aimed at desired biostructures to generate bioimaging and further applications. Note the importance of the specific interaction between the nano-labeller and the biostructure. This last variable mentioned could be controlled by the surface chemistry of nanoparticles according to the accessible functional sites for interaction of biostructures. For example, it could be used as a strategy, the

addition of amine groups to the nano-surface for covalent and non-covalent linking of many chemical species. Thus, as for example, it could be joined to available carboxylic groups on the biostructure by suitable bioconjugation techniques (In den Kirschen, 2021).

Nano-biolabeling is used for detection and quantification applications in bioanalytical developments. But, it could be extended to further applications such as synthetic bio-machines. Thus, it should be focused, for instance, on natural biostructures with targeted function as in gut-microbiota coupled to functional nanoarchitectures as synergistic agents. Nano-Bio-Nutraceuticals could hence be easily developed (Ostojica, 2020). Other examples could lead to the genetic engineering of biostructures and nanostructures with multifunctional properties (Golberg, 2014), including protective and stabilizing agents, bioimaging generation for tracking applications (Gontero, 2018), and drug and light delivery applications. As noticed, many approaches could be developed to be potentially applied to biology and Medicine.

Enhanced bioimaging

Enhanced bioimaging refers to the improvement of the standard characteristics of bioimages by incorporating novel nanotechnology and controlling the nano-scale. Here biostructures could lead to favorable interactions within the nano- and quantum-scale. Some physical phenomena could lead to enhanced results with the chemical control of matter in an accurate spatial distribution. For example, to increase the quantum yields of fluorophores and emission signals, metal-enhanced fluorescence (MEF) phenomena are required. This effect is based on the plasmonic interaction from the electronic oscillation of a metallic surface with fluorophores in the near field (Lakowicz, 2005 and Asselin, 2016). The phenomenon produces improvements from 2 to 100 depending on nano-structural parameters, experimental variables, and instrumental set-ups (Bondre, 2010, Golberg, 2014 and Puchkova, 2015). Major parameters include the plasmonic fluorophore coupling in the basal state to increase the higher occupied excited state levels, resulting in faster radiative emissions (Lackowicz, 2001). The increase is based on the high intensity of the electromagnetic field generated by the metallic surface in the near field where it should be placed the fluorophore. Thus;

the distance of the metallic surface-fluorophore is an important variable to control in the nanoparticle design for optimal excitations and enhancements (Geddes, 2002 and Viger, 2008). These non-classical light phenomena coupled on biostructure, could lead to enhanced bioimaging, affording faster detection, stable imaging over time, improved tracking applications, and high sensitivity used for single molecule detection (SMD) (Oi, 2020) as well.

In-flow detection and single biostructure analysis

In-flow systems such as microfluidic channels towards nanofluidics as well as other technological techniques considered standard and available in research, biochemical and clinical laboratories could incorporate nano-tools such as nano-labellers (Salinas, 2019). In addition, nano-bioimaging could be used for in-flow biodetection applications with improved performance (Cheng, 2021). Thus, these developments could be extended to further bioanalytical analysis. From these perspectives, the capability to track single biostructures linked to nano-functional-tools could allow retrieving information from inside of biostructures (Salinas, 2020) and 3D structures.

In addition, the performance of synthetic nano-biostructures with targeted functions could be evaluated or tested in vitro, for instance, within in-flow lab-on a chip (Zhao, 2019). Many studies report pharmacophore effects and efficiencies, biocompatibility test, etc.

Design of nano-bio-machines and micro-machines for targeted applications

Nano-biotechnology (Nagamune, 2017) is linked to the design of nano-enzymes (Chen, 2021), nano-vaccines (Zhao, 2014), and related nano-biostructures such as stabilizing agents in vaccines (Pelliccia, 2016). In addition, biostructures such as non-toxic bacteria genetically engineered with active flagellar are proposed as micro-swimmers (Bunea, 2020) within colloidal dispersions for targeted cargo applications. Similarly, optical active flagellar motors (Stark, 2021) were reported to be modulated with remote control by laser excitation. The use of viral vectors as cargo structures could also lead to controlled gene delivery (Hörner, 2021). Functional nanoarchitectures are being considered due to their particular properties that could be potentially joined to biostructures. Developments include: i) nano-emitters, ii) photodynamic

properties and therapies, iii) non-classical light delivery, iv) drug delivery, v) stabilizing agents, vi) targeted recognitions, vii) incorporation of multi-modal energy modes into confined nanoarchitectures, viii) nano-catalyzers, and ix) other properties such as nano-porous materials and metamaterials that could develop designs within fundamental and applied research (Fernandez-Fernandez, 2011, Agrawal, 2012, Park, 2009 and Bracamonte, 2021).

The design and synthesis of nano-biostructures and synthetic bio-machines are providing insights into micro-machines and nano-robots as well as for microswimmers (Soto, 2018). These new hybrid architectures were based on the control of molecular level and nano-chemistry within the nano-scale and beyond. Taking into account the property of the material incorporated and the new properties that could be generated, new possibilities are open up to develop new matter properties (Bracamonte, 2022 and Palacios, 2022).

Conclusions and future perspectives

In this manner, it was briefly discussed how, from the proof of concept of the formation of a simple nano-biostructure, could be proposed different research developments within life sciences. This synthetic hybrid structure occurred between nanoparticles designed for targeted nano-labelling applications and varied biostructures associated with particular biological properties. Thus, it can be underlined the importance of these approaches for the generation and biodetection of targeted bioimaging and highlight the importance of the single biostructure analysis to collect further information such as, resolution, size, internal composition, dynamics of interactions, and further interaction with external biological media. Therefore, contemplating these variables, it was introduced to enhanced physical properties by controlling nano-chemistry such as MEF, EP, FRET, and coupled phenomena, where the synthetic non-classical light could be tuned from reduced sizes within the nano-scale and beyond. It was possible to generate enhanced bioimaging, allowing bacteria and cell counting with developments of bioanalytical methods. It is to be discussed, how these designs could be applied to functional synthetic nano-biostructures in search of mimetic bio-machines and micro-machines. In these hybrid synthetic structures the point of view was modified and these approaches will afford to

smart functional or multifunctional nano-bio-materials. Numerous examples were reported, such as nano-catalyzers, nano-enzymes, and nano-vaccines, where the bioconjugation of nanomaterials showed to be particularly important. Hence, an improved performance of the targeted function, was always obtained in the presence of both components. The future perspectives in this direction are considered to be wide. While, if it is found an interesting trend of research works that could be considered as not so many were developed and reported at the moment. So, it is to be attended new developments from multidisciplinary research fields. The communication allows to open new strategies analyzing other possibilities for innovative developments based on nanophotonics and biophotonics.

Reference

- Agrawal U, Gupta M, Jadon R S, Sharma R and Vyas SP (2012). Multifunctional nano-medicines: potentials and prospects, *Drug Deliv. and Transl. Res.*, 1:1-21.
- Allturkistani HA, Tashkandi FM and Mohammedsaleh ZM (2016). Histological Stains: A Literature Review and Case Study. *Glob J Health Sci.*, 8 (3): 72-79.
- Ame M and Bracamonte AG (2020). Advances in Nano-Bio-Optics: detection from Virus towards Higher sized Biostructures. *Frontiers Drug Chemistry Clinical Res.*, 3: 1-7.
- Asselin J, Legros P, Grégoire A and Boudreau D (2016). Correlating Metal-Enhanced Fluorescence and Structural Properties in Ag@SiO₂ Core-Shell Nanoparticles, *Plasmonics*.1: 1-8.
- Bondre N, Zhang Y and Geddes CD (2010). Metal-Enhanced Fluorescence based Calcium Detection: Greater than 100-fold increase in signal/noise using Fluo-3 or Fluo-4 and Silver Nanostructures. *Sensors and Actuators B*, 152: 82-87.
- Boudreau D and Bracamonte G (2019). Ultra luminescent sub-wavelength nanoparticles base on Metal Enhanced Fluorescence and Enhanced Plasmonics. *Bitácora digital Journal*. Open call, 10^o Ed., Faculty of Chem. Sc. (UNC), 6 (10):1-32.
- Bracamonte AG (2021). *Frontiers in Nano- and Micro-device Design for Applied Nanophotonics, Biophotonics and Nanomedicine*, Book, Bentham Science Publishers, ISBN: 978-168108-857-0.
- Bracamonte AG (2022). Design of new High Energy near Field Nanophotonic materials for far Field applications, Chapter 28 (2022) Book entitled *Advances in Nanocomposite Materials for Environmental and Energy Harvesting Applications*, ISBN 9783030943189, Springer Nature, Switzerland, 859-920.
- Bunea AI and Taboryski R (2020). Recent Advances in Micro swimmers for Biomedical Applications, *Micromachines*, 11(1048):1-24.
- Chen L, Xing S, Lei Y, Chen Q, Zou Z, Quan K, Qing Z, Liu J and Yang R (2021). A Glucose-Powered Activatable Nanozyme Breaking pH and H₂O Limitations for Treating Diabetic Infections, *Angewandte Chemie International Edition*, 60 (44): 23534-23539.
- Cheng S, Fu S, Mun Kim Y, Song W, Li Y, Xue Y and Yi J (2021). Lei Tian, Single-cell cytometry via multiplexed fluorescence prediction by label-free reflectance microscopy, *Sci. Adv.*; 7 : eabe0431:1-12.
- Dacres H, Wang J, Dumancic MM and Trowell SC (2010). Experimental Determination of the Forster Distance for two commonly used Bioluminescent Resonance Energy Transfer pairs. *Anal. Chem.*, 82: 432-435.
- Fernandez-Fernandez A, Manchanda R and McGoron AJ (2011). Theranostic applications of nanomaterials in cancer: Drug delivery, image-guided therapy and multifunctional platforms, *Appl Biochem Biotechnol*; 165 (7-8): 1628-1651.
- Gammoudi I, Rokhaya Faye N, Moroté F, Moynet D, Grauby-Heywang C and Cohen-Bouhacina T (2013). Characterization of Silica Nanoparticles in Interaction with Escherichia coli Bacteria, *World Academy of Science, Engineering and Technology , International Journal of Chemical, Molecular, Nuclear, Materials and Metallurgical Engineering*, 7(7): 520-526.
- Geddes CD and Lackowicz JR (2002). Editorial: Metal-Enhanced Fluorescence, *J. Fluorescence* 12(2): 121-129.
- Golberg K, Elbaz A, McNeil R, Kushmaro A, Geddes CD and Marks RS (2014). Increased bioassay sensitivity of bioactive molecule

- discovery using metal-enhanced bioluminescence, *Nanopart Res.*, 16(2770): 1-14.
- Golberg K, Elbaz A, McNeil R, Kushmaro A, Geddes CD and Marks RS (2014). Increased Bioassay Sensitivity of Bioactive Molecule Discovery using Metal-Enhanced Bioluminescence, *J Nanopart Res*, 16, 2770: 1-14..
- Gontero D, Veglia AV, Boudreau D, Bracamonte A G (2018). Ultraluminescent gold Core@shell nanoparticles applied to individual bacterial detection based on Metal-Enhanced Fluorescence Nanoimaging, *J. of Nanophotonics. Special issue Nanoplasmonics for Biosensing, Enhanced Light-Matter Interaction, and Spectral Engineering*, 12, 1 (012505): 1-12.
- Henderson L, Neumann O, Kaffes C, Zhang R, Marangoni V, Ravoori M, Kundra K, Bankson J, Nordlander P and Halas N J (2018). Routes to Potentially Safer T1 Magnetic Resonance Imaging Contrast in a Compact Plasmonic Nanoparticle with Enhanced Fluorescence. *ACS Nano*, 12(8): 8214-8223.
- Hörner M, Jerez-Longres C, Hude A, Hook S, Sascha Yousefi O, Schamel WWA, Hörner C, Zurbriggen MD, Ye H, Wagner HJ and Weber W (2021). Spatiotemporally confined red light-controlled gene delivery at single-cell resolution using adeno-associated viral vectors. *Sci. Adv.*; 7, eabf0797: 1-12.
- In den Kirschen OW, Hutchinson W and Guillermo Bracamonte A. (2021). Conjugation Reactions of Hybrid Organosilanes for Nanoparticles and surface modifications, *J. Chem. Res. Adv. (JCRA)*, 2(1): 6-15.
- Jensen SB (2021). Radioactive Molecules 2019-2020. *Molecules*, 26 (529): 1-3.
- Lackowicz JR (2001). Radiative Decay Engineering: Biophysical and Biomedical Applications, *Anal. Biochem.* 298: 1-24.
- Lakowicz JR (2005). Radiative Energy Engineering 5: metal enhanced fluorescence and plasmon emission. *Anal. Biochem.* 337: 171-194.
- Lei Z and Zhang F (2021). Molecular Engineering of NIR-II Fluorophores for Improved Biomedical Detection. *Angewandte Chemie International Edition*, 60(30): 16294-16308.
- Li S, Bai H, Shepherd RF and Zhao H (2019). Bio-inspired design and additive manufacturing of soft materials, machines, Robots, and Haptic Interfaces. *Angew. Chem. Int. Ed.*, 58: 11182-11204.
- Luchowski R, Calander N, Shtoyko T, Apicellaa E, Borejdo J, Gryczynski Z and Gryczynski I. (2010). Plasmonic platforms of self-assembled silver nanostructures in application to fluorescence, *J Nanophotonics*; 4: 1-24.
- Magdanz V, Khalil I SM, Simmchen J, Furtado GP, Mohanty S, Gebauer J, Xu H, Klingner A, Aziz A, Medina-Sánchez M, Schmidt OG and Misra S (2020). IRONSperm: Sperm-templated soft magnetic microrobots. *Sci. Adv.*; 6 : eaba5855: 1-19.
- Matsumoto K, Mitchell JB and Krishna MC (2021). Multimodal Functional Imaging for Cancer/Tumor Microenvironments Based on MRI, EPRI, and PET. *Molecules*, 26, 1614: 1-27.
- Muiños-Landin S, Fischer A, Holubec V and Cichos F (2021). Reinforcement learning with artificial microswimmers. *Sci Robot.*, 6, eabd9285: 1-8.
- Nagamune T (2017). Biomolecular engineering for nanobio/ bionanotechnology, *Nano Convergence* , 4 (9): 1-56.
- Oi C, Gidden Z, Holyoake L, Kantelberg O, Mochrie S, Horrocks MH and Regan L (2020). LIVE-PAINT allows super-resolution microscopy inside living cells using reversible peptide-protein interactions. *Communications Biology*, 3(458): 1-10.
- Ostojica SM (2016). Mitochondria-targeted nutraceuticals in sports medicine: a new perspective, *Research in Sports Medicine*, 1: 1-10.
- Palacios LR and Bracamonte AG (2022). Development of Nano-, Microdevices for the next generation of Biotechnology, Wearables and miniaturized Instrumentation, *RSC Advances*, 12: 12806-12822
- Palacios LR, Martinez S, Tettamanti C, Quinteros D and Bracamonte AG (2021). Nanochemistry and Bio-conjugation with

- perspectives on the design of NanoImmune platforms, vaccines and new combinatorial treatments, *J Vaccines Immunol*, 7(1): 049-056.
- Park K, Lee S, Kang E, Kim K, Choi K and Chan Kwon I (2009). New Generation of Multifunctional Nanoparticles for Cancer Imaging and Therapy. *Adv. Funct. Mater*, 1: 1553-1566.
- Pelliccia M, Andreozzi P, Paulose J, D'Alicarnasso M, Cagno V, Donalio M, Civra A, Broecke R M, Haese N, Jacob Silva P, Carney RP, Marjoma V, Streblov DN, Lembo D, Stellacci F, Vitelli V and Krol S (2016). Additives for vaccine storage to improve thermal stability of adenoviruses from hours to months, *Nature Communication*, 7 (13520): 1-7.
- Puchkova A, Vietz C, Pibiri E, Wünsch B, Sanz Paz M, Acuna GP and Tinnefeld P (2015). DNA Origami Nanoantennas with over 5000-fold Fluorescence Enhancement and Single-Molecule Detection at 25 Mm. *Nano Lett.*, 15:8354–8359.
- Rioux M, Gontero D, Veglia AV, Bracamonte AG and Boudreau D (2017). Synthesis of Ultraluminiscent gold core-shell Nanoparticles as NanoImaging Platforms for Biosensing applications based on Metal enhanced fluorescence. *RSC Adv.*, 7: 10252-10258.
- Salinas C and Bracamonte AG (2019). From Microfluidics to Nanofluidics and signal Wave-guiding for Nanophotonics, Biophotonics resolution and Drug Delivery. *Frontiers in Drug, Chemistry and Clinical Research*, 2: 1-6.
- Salinas C, Amé M and Bracamonte AG (2020). Tuning silica nanophotonics based on fluorescence resonance energy transfer for targeted non-classical light delivery applications. *J. Nanophoton*, 14(4): 046007:1-19. DOI: 10.1117/1.JNP.14.046007
- Salinas C, Valeria Ame M and Bracamonte AG (2020). Synthetic non-classical luminescence generation by Enhanced Silica Nanophotonics based on Nano-Bio-FRET, *RSC Adv.*, 10: 20620-20637.
- Soo Choi H and Frangioni JV (2010). Nanoparticles for Biomedical Imaging: Fundamentals of Clinical Translation, *Mol Imaging*, 9(6): 291–310.
- Soto F and Chrostowski R (2018). Frontiers of medical micro/nanorobotics: In vivo applications and commercialization perspectives toward clinical uses. *Frontiers in Bioeng. and Biotech.*, 6 (170): 1-12.
- Stark H (2021). Artificial microswimmers get smart. *Science Robotics*, 6 (52) eabh1977:1-10.
- Viger ML, Live LS, Therrien OD and Boudreau D (2008). Reduction of Self-Quenching in Fluorescent Silica-Coated Silver Nanoparticles. *Plasmonics*, 3 (1): 33-40.
- Woehrstein JB, Strauss MT, Ong LL, Wei B, Zhang DY, Jungmann R and Yin P (2017). Sub-100 nm metafluorophores with digitally tunable optical properties self-assembled from DNA, *Sci. Adv.*; 3:e1602128:1-12
- Zhao L, Seth A, Wibowo N, Zhao CX, Mitter N, Yu C and Middelberg APJ (2014). Nanoparticle vaccines, *Vaccine*, 32: 327-337.
- Zhao Y, Kumar Kankala R, Wang SB and Zheng Chen A (2019). Multi-Organs-on-Chips: Towards Long-Term Biomedical Investigations, *Molecules*, 24: 675 1-22.
