Fluorescence waveguiding in amyloidogenic fibers

Boris Apter*, Boris Fainberg*, Amir Handelman*, Igor Lapsker*.
Antonella Accardo**, Carlo Diaferia**, Giancarlo Morelli***, Gil Rosenman***

*aFaculty of Engineering, Holon Institute of Technology, Israel
**Department of Pharmacy, Research Centre on Bioactive Peptides (CIRPeB), University of Naples “Federico II” Naples, Italy
***School of Electrical Engineering, Tel Aviv University, Israel

Abstract

Chemically synthesized biomolecules can self-assemble to bioinspired nanostructures of different morphologies such as dots, tubes, spheres, nanofibers and more. They adopt similar basic ordering as their biological counterparts either α-helical or β-sheet peptide/protein conformations. These two fundamental biomolecular architectures exhibit dissimilar physical properties. One of the most interesting physical properties found in biological and bioinspired structures is a new biophotonic phenomenon of visible fluorescence (FL). It has been observed both in neurodegenerative disease-related amyloid fibrils and in synthetic amyloidogenic biorganic di- and tri-aromatic and aliphatic peptide nanostructures. The FL effect has been also found recently in peptide nanodots and hybrid polymer/peptide thin films. All of them have been assembled to β-sheet secondary structure. In this work we report on a new development of FL optical waveguiding in elongated bioinspired fibrillar structures, self-assembled from ultrashort amyloidogenic peptides/proteins and hybrid polymer/peptides biomolecules. We show that FL propagation in these two fiber materials of different origin can be described by two completely different mechanisms. One of them is conventional FL propagation in the region of optical transparency of peptide materials in accordance with optical confinement rules. Another model is FL reabsorption mechanism where anomalous long range FL propagation has been found. We show that this intrinsic FL biophotonic waveguiding effects found in different β-sheet biomaterials is considered as a promising tool for precise biomedicine where new biocompatible visible tunable FL optical waveguides can be applied in advanced nanomedical technologies (local bioimaging, light diagnostics, therapy, optogenetics and health monitoring).

Keywords: optical waveguiding, bioinspired peptide structures, polymer-peptide compounds PEGylated hexaphenylalanine, intrinsic FL, β-sheet amyloidogenic fibers, two modes of FL propagation in amyloid-like fibers

1. INTRODUCTION

Biophotonic integrated circuits, based on optical waveguides, are the main elements of a new generation of implantable optical biochips,1,2 diverse biosensors and wearable devices.3 They are optical analogues of microelectronic chips where interconnections between miniaturized biooptical devices are provided by light transduction via optical waveguides. The emerging field of integrated bionanophotonics is applied to biomedical nanooptics towards precision optical theranostics and health monitoring.4,5

This advanced research of the biophotonic technology is inspired by nature-developed optical waveguiding nanostructures built-in in various living organisms.7 In nature visual sharpness and energy light harvesting are supported by delivering of the incident sunlight photons via optical waveguides using focusing and collecting nanosystems. Such natural facilities of light waveguiding were found both in animals and plants and also revealed in different living systems. Sclereids of the evergreen sclerophyll Phillyrea latifolia form a vertically oriented foliar light waveguiding structures that delivers photons to mesophyll.8 The plants’ roots receive light stimuli through transmission along their vascular system that serves as natural optical waveguides.9 Bioluminescent of jellyfish is

*apter@hit.ac.il
**giancarlo.morelli@unina.it
***gilr@eng.tau.ac.il
guided by fiber-like tentacles waveguides.\textsuperscript{10} Natural optical waveguides connects the lens to the light-sensitive sensory region of retinula cells in insects eyes.\textsuperscript{11}

The basic solution for studies of fundamental photonic phenomena at nanoscale and wide engineering applications in rapidly progressive field of integrated optics and communication technology is optical waveguides.\textsuperscript{12} They are made of a wide range of inorganic materials (semiconductors silicon, germanium, indium phosphide, gallium arsenide and more),\textsuperscript{14,15} dielectrics (silica glass, silicon oxide)\textsuperscript{12,13} and ferroelectrics (lithium niobate, lithium tantalate).\textsuperscript{16} The main advantage of the semiconductor light waveguiding materials is unique property to tune the region of optical transparency from ultraviolet to infrared region by the use either modulated bandgap energy technology or applying quantum confinement engineering.\textsuperscript{17} Ferroelectric materials allow combining waveguiding properties with electrooptical and nonlinear optical effects. Effective waveguiding was also found in organic polymers\textsuperscript{18,19} such as polymethylmethacrylate, polystyrene, polycarbonate, polyurethane, epoxy resin as well complex organic compounds (meso-tetratolylporphyrin molecules and more).\textsuperscript{20}

2. OPTICAL WAVEGUIDES

There are two types of light waveguides that differ in the basic physics of electromagnetic-wave propagation: passive and active waveguides. Conventional light waveguides are optically transparent elongated dielectric structures having different shapes such as slab, ridge, rod, tube, fibers, etc. Passive light waveguides are obeyed to the classical optical laws of reflection, refraction and diffraction. They guide the input light waves directly through their spectral transmission window.\textsuperscript{12,13} The waveguiding property is based on optical confinement-light trapping of the propagating electromagnetic light wave in this dielectric layer. The physical principle of this phenomenon is based on total internal reflection phenomenon when the waveguided layer have a higher refractive index that surrounds.\textsuperscript{12,13}

Another type of light waveguiding is active (FL) waveguiding where excited by input optical beam a FL (FL) signal propagates as FL wave. It was first observed both in organic nanofibers possessing strong optical absorption\textsuperscript{21} and in inorganic cadmium sulfide nanowires.\textsuperscript{22} The effect was ascribed to the propagation of exciton-polaritons, that are strongly coupled quasiparticles created between the laser-excited FL and the excitons.\textsuperscript{23,24} Micro/nanofibers fabricated of self-luminous conjugated polymers\textsuperscript{20} as well micro/nanofibers composed of nonluminous matrix polymers and doped luminescent dyes such as thiacyanine,\textsuperscript{25} rhodamine, perylene, fluorescein, etc\textsuperscript{26} opened the avenue for a new type of fluorescent waveguiding towards nanoscale innovative photonic components and optical circuits.\textsuperscript{27} Figure 1 illustrates the difference between these two mechanisms of optical waveguiding.

![Figure 1. Two types of optical waveguides. (a) Light passive waveguiding in transparent plastic plate. Passive waveguide directly guides the incoming light beam at a wavelength $\lambda_0$ from its one end to another without any spectral transformations. (b) Active FL waveguiding in a plastic rod doped by a fluorescent dye. FL waveguiding is attributed to absorption of input laser beam at wavelength $\lambda_0$ followed by excitation of broadband FL and propagation of this FL wave along the waveguide.](image-url)

The choice of the material as the light waveguiding layer or substrate for the integrated optical circuits depends on many factors. These factors include region of optical transparency, defining minimum optical absorption coefficient in the working spectral range, high refractive index contrast, and multifunctional properties such as electro-optic and nonlinear optical effects. In modern biomedical technology optical waveguides were developed for photonic diagnostic and therapy using natural and synthetic polymer materials of biological origin.\textsuperscript{5,6,17} Natural silk, produced by silkworms and spiders, is widely applied for implantable biophotonic devices\textsuperscript{28,29} due to its excellent light waveguiding properties, high strength, biocompatibility and biodegradability.\textsuperscript{30} Synthetic biopolymers are also promising candidates for integrated biophotonics. Flexible bioabsorbable photonic waveguides made of synthetic poly(L-lactic acid) polymer and poly(vinyl-alcohol) were proposed and used for light-controlled therapy, cell-based sensing and optogenetic synthesis \textit{in-vivo} in a mouse model with diabetes.\textsuperscript{1,31}
3. LIGHT PROPAGATION IN PEPTIDE FIBERS

In this work, we report on a new generation of bioinspired optical FL waveguides. Recently developed hybrid polymer-peptide PEGylated hexaphenylalanine (PEG-F6) amyloid-like fibers are studied along tri-phenylalanine (FFF)-fibers. Both have the same β-sheet peptide secondary structure and exhibit unique bio-FL. However their FL spectra are different. FFF-fibers radiate visible FL in the range 440-550 nm. FL spectrum of PEG-F6 covers the whole visible spectrum from blue to infrared. In spite of full overlapping of the FL and optical absorption spectra unexpected long distance of the FL propagation of hundreds of micrometers in these fibers has been observed. A new physical mechanism of the FL effect propagation based on photon reabsorption has been developed. In FFF-fibers with limited FL spectra passive waveguiding has been revealed. We believe that these new phenomena of FL propagation open the avenue for a new generation of biocompatible light nanoprobes and application of the found FL light transfer in ultrathin amyloid fibers and neuron circuits towards advanced precision biomedical technologies.

3.1 Waveguiding phenomena in fluorescent β-sheet tri-phenylalanine (FFF)-fibers

Fluorescent waveguiding was observed in FFF-nanofibers thermally grown from self-assembled FFF-peptide microspheres. SEM microscopic images (Figure 2,a) show native FFF-spheres with average size of about 5 μm. Heating at T ≈ 160–180 °C led to deep thermally induced modification of the native spherical shapes and their conversion to hollow nanofibers (Figure 2,b) having β-sheet peptide secondary structure. The FFF-fibers of 100-300 nm thick and 10-15 μm height were grown.

![Figure 2 Morphological transformations of triphenylalanine (FFF) nanostructures. (a) Native FFF-spheres self-assembled at room temperature in chloroform solvent; (b) Grown FFF-fibers of 100-200 nm thick and 10-15 nm height (three hours of heat treatment at 180°C).](image)

Optical FL waveguiding experimental studies and simulations conducted in FFF-fibers are displayed in Figure 3. Laser beam, (λ=405nm), focused on an individual FFF-core sphere (Figure 3, b), excites strong FL in the sphere, which is followed by the coupling of this FL light to FFF-fibers (Figure 3, c). The FL images (Figure 3,c-h) were captured through a green filter. FL waveguiding in FFF fibers is observed only when the beam impinges the FFF-sphere and the excited fluorescent radiation is coupled to the fibers. As a result, effective propagation of the fluorescent wave along a few FFF-peptide fibers grown from the same FFF-sphere was revealed (Figure 3, e, f, g). It should be noted that the fluorescent waveguiding effect is observed via FFF-fiber walls of 100-300nm thickness, which is 2-5 time less than the green FL free-space wavelength of ~500nm.

We performed Finite Difference Time Domain Method (FDTD)-based electromagnetic simulation of FL propagation in the structure, shown in SEM image (Figure 3i). The simulation setup of this structure is presented in Figure 3j. A simplified, four-level lasing material model was used to simulate FL excitation effect. This model involves all main stages of the FL process: photoexcitation, relaxation and re-radiation. Simulation results (Figure 3k,l) are consistent with the experimental observations which demonstrate excitation of FL waves by incoming light at 405 nm, FL propagation along the fiber and FL irradiating from fibers far ends. Numerical mode analysis of this structure shows that peptide nanofiber with inner and outer diameters of 500 and 800 nm, refractive index n = 1.6, placed in air environment, supports more than 10 propagating modes in the visible spectral range. For example, the intensity pattern of one of these modes was experimentally recorded at the wavelength 600 nm. It can be seen that this pattern (Figure 3o) is similar to the intensity pattern (Figure 3o, inset) of one of the calculated modes: both of them have four intensity lobes. The light propagation, observed in this experiment, most likely represents a combination of active and passive waveguiding effect, in which the initial local excitation of FL radiation is followed by its passive propagation due to the effective light confinement inside the dielectric peptide tube.

![Figure 3 Morphological transformations of triphenylalanine (FFF) nanostructures. (a) Native FFF-spheres self-assembled at room temperature in chloroform solvent; (b) Grown FFF-fibers of 100-200 nm thick and 10-15 nm height (three hours of heat treatment at 180°C).](image)
Figure 3. FL waveguiding in thermally-induced β-sheet free-standing FFF-nanofibers showing passive (conventional) FL waveguiding. (a) Sketch of the experimental setup. A laser beam ($\lambda_{\text{ex}} = 405\text{nm}$) excites visible FL in the thermally-induced FFF nanosphere. Light is coupled from the sphere to the free-standing β-sheet FFF fibers. (b) Microscope image of individual FFF-sphere and thermally grown peptide hollow FFF fibers. (c) FL image of FFF-peptide fibers exhibiting intrinsic active FL optical waveguiding. Laser spot ($\lambda_{\text{ex}} = 405\text{nm}$), focused on a single FFF sphere, excites fluorescent emission in FFF sphere and is propagated via FFF fibers as a fluorescent wave. The image was captured through a green bandpass filter with transmittance centered at 520nm, and bandwidth of 50nm. (d-h) Detailed results of exciting laser beam ($\lambda_{\text{ex}} = 405\text{nm}$), scanning from left to right over individual FFF nanosphere/nanofibers. The small circle and two crossed lines indicate the position of the nanosphere. FL waveguiding in FFF fibers is observed when the beam impinges on the sphere and is coupled only to the fibers (e, f and g). (i) SEM image of the simulated structure: a sphere with grown fibers. (j) FDTD simulation setup. (k) and (l) 3D-visualization of FDTD simulations of excitation and FL waveguiding in peptide-FFF nanofiber, thermally grown from peptide nanosphere. (m), (n) FL images of optical waveguiding captured through yellow and red color filters (excitation wavelength $\lambda_{\text{ex}} = 405\text{nm}$). (o) Experimental and simulated (inset) intensity pattern of the waveguide mode.
3.2 Long-range FL propagation in PEGylated hexaphenylalanine (PEG24-F6) amyloid-like fibers

The amyloid-like fibers, self-assembled from PEG24-F6 composition\(^\text{16}\), are formed into in-plane (Figure 4a) and out-of-plane, free-standing (Figure 4b) fibrillar configurations. They have a typical diameter about 10-20 \(\mu\)m and unusually large length which can reach 250-550 \(\mu\)m. Both fibrillar structures exhibit strong, quasi-white visible FL under local 405-nm-wavelength excitation by focused laser beam (Figure 4c) or by light, delivered through a single-mode optical fiber (Figure 4d).

Figure 4 FL propagation in PEGylated peptide amyloidogenic fibers. (a), (c) In-plane fiber. (b), (d) Free-standing, out-of-plane fiber.

To estimate FL waveguiding losses in amyloid-like fibers the focused beam of 405-nm laser was scanned along the fiber in the area, shown by dashed rectangular region-of-interest in Figure 4c. The intensity of FL radiation, out-coupled from the PEG24-F6 fiber end, was recorded as function of the distance between the excitation spot and the fiber end (Figure 5a).

Figure 5. FL and optical absorption properties of PEG24-F6 structures. (a) Broadband FL propagation in amyloid-like fibers at different positions of exciting (405 nm) light spot. (b) Decay of broadband FL radiation, propagating along the fiber. (c) Broadband, quasi-white FL of PEG24-F6 aggregate, having the same chemical composition as the fiber. (d) FL spectra of PEG24-F6 fiber and optical absorption.
Figure 5b shows FL propagation intensity vs distance from the excitation spot to the fiber end. Exponential fit of the experimental data gives attenuation coefficient, averaged across the visible spectral range, about 0.007 µm⁻¹. This attenuation coefficient for FL propagation in the fiber is much lower than that expected from directly measured optical absorption of bulky amyloid-like aggregates having the same chemical composition (Figure 5c). As can be seen from Figure 5d, the optical absorption and FL spectra measured in PEG24-F6 fiber and aggregates are totally overlapped across the entire visible range and the bulk absorption coefficient is much higher than the attenuation coefficient of FL wave, propagating along the fibers.

To emphasize the difference between the attenuation of FL and non-fluorescent waves in amyloid-like fibers, we compared the propagation distances of two waveguide modes: the green (~520 nm wavelength) fraction of broadband FL wave, excited by 405 nm-wavelength light beam (Figure 6a), and a monochromatic green (520 nm) lasers light, directly launched to the same fiber (Figure 6b). Recording the curvilinear intensity profiles of the light, scattered by the amyloid-like fiber, and fitting them to exponential intensity decays along the fiber, we got the decay characteristics, presented in Figure 6c. These decay characteristics show, that the attenuation coefficients of FL radiation are much lower than that of non-fluorescent, narrow-band laser radiation, by the factor of 6.2 in the green spectral range.

Figure 6. FL and non-fluorescent light propagation in PEG24-F6 amyloid-like fiber. (a) Excitation and propagation of green fraction (λ=520nm) of broadband FL. (b) Launching and propagation of non-fluorescent narrow-band (λ=520nm) laser radiation. (c) Attenuation characteristics of FL and non-fluorescent light propagation. (d) FL excitation and propagation at normal incidence of violet light beam in in PEG24-F6 amyloid-like fiber. (e) Normal incidence of incoming green light (λ=520nm) doesn’t result in light propagation along in PEG24-F6 amyloid-like fiber.

Such a significant difference between attenuation coefficients and propagation lengths indicates that FL and non-fluorescent (conventional, passive) light propagation in the studied amyloid-like fibers have completely different physical mechanisms. This assumption is supported by additional experimental observation in which 405 nm-wavelength light beam (Figure 6d), and a monochromatic green (520 nm) laser light beam (Figure 6e), are normally incident on amyloid-like fiber at the position, located in equal distances from both fiber’s ends. As can be seen, FL
light, excited at λ=450 nm under normal incidence, propagates in opposite directions along the fiber (Figure 6d). Unlike this, under normal illumination of the same fiber the wave guiding conditions for the convenient passive mode (λ=520 nm laser beam) are dramatically changed and the light waveguiding is not observed (Figure 6e). Figure 7a schematically shows that excitation of the FL by a laser source at frequency ω_{ex} is followed by its propagation inside the PEG24-F6 fiber at frequency ω_{FL}. In the next section we present explanation of this long-range FL propagation in highly-absorbing amyloid-like peptide fibers.

### 3.3 Mechanism of fluorescence propagation in amyloid-like fibers

In this section, we consider a new approach of FL long-range propagation in amyloid-like fibers. Bearing in mind the model of photon reabsorption used before in the description of light energy transfer in gases and molecular crystals with forming excitons, the equation for the excited electronic state population \( n_2 \) (Figure 7b) can be written as

\[
\frac{\partial n_2(z,t)}{\partial t} = \int \sigma_a(\omega) J(z,t;n,\omega) v(\omega) \eta(\omega) d\omega d\Omega - \frac{n_2(z,t)}{T_1}
\]  

where \( T_1 \) is the lifetime of the excited state; \( \sigma_a(\omega) \) is the cross section of the photon absorption at frequency \( \omega \); \( v(\omega) \) is the photon group velocity; \( \eta(\omega) \) is that part of the absorption processes of the photon of frequency \( \omega \) that leads to excited molecular generation; \( d\omega d\Omega \) refers to integration with respect to the solid angle ( \( d\Omega = sin\theta d\theta d\phi \) ); and the concentration of photons is \( J(z,t;n,\omega) \), with \( n \) being the unit vector that determines the direction of its velocity. Furthermore, we use the equation for the photon concentration \( J(z,t;n,\omega) \) and make evaluations for a large diameter of the waveguide (~16 \( \mu \)m, Figure 4c), suppose an isotropic distribution of \( J(z;n,\omega) \). In this case one can write

\[
J(z) \approx \exp[-(1-\eta)N\sigma_{a,z}]
\]

Here, \( \eta \approx 1 \) is the fitting parameter. Our experimental results, presented in Figure 6c facilitate the estimation of parameter \( \eta \). From the comparison between Eq. (2) and exponential decay fits (Figure 6c) we get \( \eta \) values of approximately 0.84 for the green (510-560 nm) fraction of FL. Equation (2) and the estimation are fully consistent with our experimental results on FL attenuation in amyloidogenic PEG24-F6 fibers (Figure 6c), where \( J(z) \approx \exp[-N\sigma_{a,z}] \) at \( \eta = 0 \) and \( N\sigma_{a,z} = \alpha_c \) describes classical absorption.

The amyloidogenic structures under study exhibit exclusive broadband, fully overlapped FL and OA spectra (Figure 5, Figure 6), which are created by the electronic structure of noncovalent hydrogen bonds responsible for visible FL in amyloid structures. FL and OA effects are detected along the entire visible spectrum in the 400-650 nm range. This effect provides the observation of any FL visible color, blue, green, yellow, red, and more. Because the reabsorption depends on the product of the equilibrium absorption and luminescence spectra, in these wide spectral regions, any optically absorbed photon can be reemitted, yielding an FL photon, and any emitted FL photon can be absorbed. Thus, there is no Stokes shift in the considered reabsorption process. The excitation of the FL by a laser source is followed by its propagation inside the PEG24-F6 fiber, owing to consecutive acts of light absorption, followed by FL photon propagation and reabsorption (Figure 7a), provided by the overlapped transitions in our system.

This process is based on the multi-well potential structure created by hydrogen bonds, which is schematically described for only one band by the simplified system (Figure 7b), showing excitation, relaxation, FL radiation, and FL photon reabsorption. This complex FL propagation process occurs along all FL centers in the amyloid-like fibers, generating a wide FL visible continuous spectrum. It should be stressed that the applied reabsorption model does not involve any scale limitations, which permits the prediction of the long-range FL propagation in diseased related amyloid nanofibers.
CONCLUSIONS

We have revealed that amyloidogenic β-sheet fibers exhibit strong visible FL effect. Two different modes of FL light waveguiding in bioinspired tri-peptides and hybrid polymer/peptide amyloidogenic fibers are observed. The first one is conventional FL light passive waveguiding based on total internal reflection phenomenon. The second mode is FL waveguiding observed in highly absorbed amyloidogenic β-sheet fibers. Despite of full overlapping of optical absorption and FL spectra the latter propagates on abnormally long distance exceeding by a few times propagation length of conventional light wave with the same wavelength. We show that the proposed mechanism of this FL non-waveguiding phenomenon is based on absorption/reabsorption photon recycling.

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5. REFERENCES

1. Choi M, Choi J.W, Kim S, Nizamoglu S, Hahn S. K, Yun S.H. "Light-guiding hydrogels for cell-based sensing and optogenetic synthesis in vivo." Nat. Photonics, 7, 987–994, (2013).
2. Nizamoglu S, Gathe M. C, Humar M., Choi M, Kim S., Kim K.S., Hahn S.K, Scarcelli G, Randolph M, Redmond R.W., Yun S.H., "Bioabsorbable polymer optical waveguides for deep-tissue photomedicine", Nat. Commun. 7, 10374-87, (2016).
3. Kendall M, Lynch I. "Long-term monitoring for nanomedicine implants and drugs". Nat. Nanotechn, 11, 206-210, (2016).
4. Humar M, Kwok S.J.J., Choi M, Cho S, Yetisen AK, Yun S.H., "Toward biomaterial-based implantable photonic devices", Nanophotonics. 5, 60-80, (2016).
5. Sykes E. A, Albanese A, Chan W.C. "Biophotonics: implantable waveguides". Nat. Photonics. 7, 940–941(2013).
6. Yun S.H, Kwok S.J.J., "Light in diagnosis, therapy and surgery", Nat. Biomed. Eng., 1, 1-33 (2017).
7. Shabahang S.S, Kim S, Yun S.H,  "Light-guiding biomaterials for biomedical applications", Adv. Funct. Mater. 1706635-17, (2018).
8. Karabourniotis G. "Light-guiding function of foliar sclereids in the evergreen sclerophyll Phillyrea latifolia: a quantitative approach", J. Experim. Botany, 49, 739–746, (1998)
9. Galen C, Rabenold JJ, Liscum E, Light-sensing in roots. Plant Signal Behav. 2(2), 106-108, (2007).
10. Zimmer M. "Glowing Genes: A Revolution in Biotechnology", Prometheus Books, Amherst, NY, USA (2005).
11. Snyder A.W., in "Comparative Physiology and Evolution of Vision in Invertebrates: A: Invertebrate Photoreceptors", Springer, Berlin 225-244, (1979).
12. Agrawal G.P, "Fiber-Optic Communications Systems", 3rd. Ed. John Wiley & Sons Ltd. England (2002)
13. Selvaraja S.K,  Sethi P, "Review on Optical Waveguides", http://dx.doi.org/10.5772/intechopen., 77150 -10, (2018)
14. Martinez A, Blasco J, Sanchis P, Galán J.V, García-Rupérez J, Jordana E, Gautier P, Lebour, Y, Hernández S, Spano R, Guider R, N. Daldosso, Garrido B, Fedeli J.M, Pavesi L, Martí J, "Ultrafast all-optical switching in a silicon-nanocrystal-based silicon slot waveguide at telecom wavelengths". Nano Lett., 2010; 10: 1506–1511.
15. Roeloffzen C.G.H., Hoekman M, Klein E.J, Wevers L.S, Timens R.B, Marchenko D, Geskus D, "Low-loss Si3N4 triPleX optical waveguides: Technology and applications overview". IEEE Journal of Selected Topics in Quantum Electronics. 24(4),1-21, (2018).
16. Weigel P.O, Savanier M, DeRose C.T, Pomerene A.T, Starbuck A.L, Lentine A.L, Stenger V, Mookherjea S, "Lightwave circuits in Lithium Niobate through hybrid waveguides with Silicon Photonics", Scientific Reports, 6:22301-8 (2016).
17. Yan R, Gargas D, Yang P. "Nanowire photonics". Nature Photonics. 3, 569–576, (2009).
18. Ma H, Jen AKY, Dalton LR. "Polymer-based optical waveguides: materials, processing, and devices". Adv. Mater. 14,1339–1365, (2002).
19. Ulrich H.P,Fischer-Hirchert, "Photonic Packaging Sourcebook", Springer-Verlag Berlin Heidelberg, (2015).
20. Chandrasekar R, "Organic photonics: prospective nano/micro scale passive optical waveguides obtained from p-conjugated ligand molecules", Phys. Chem. Chem. Phys., 16, 7173-7179, (2014).
21. Zhao Y.S., Fu H, Peng A, Ma Y, Xiao D, Yao J, "Low-dimensional nanomaterials based on small organic molecules: preparation and optoelectronic properties". Adv. Mater. 20, 2859–2876, (2008).
22. Barrelet C.J, Greytak A.B, Lieber C.M. "Nanowire Photonic Circuit Elements". Nano Lett. 4,1981-1985,(2004).
23. Takazawa K, Inoue J, Mitsuishi K., Takamasu T, "Fraction of a Millimeter Propagation of Exciton Polaritons in Photoexcited Nanofibers of Organic Dye". Phys. Rev. Lett. 105: 067401-4, (2010)
24. Ellenbogen T, Crozier K.B, "Exciton-polariton emission from organic semiconductor optical waveguides". Phys RevB, 84, 161304-8, (2011).
25. Takazawa K, Kitahama Y, Kimura Y. Kido G. "Optical waveguide self-assembled from organic dye molecules in solution", Nano Lett., 5,1293–1296, (2005).
26. Gu F.X, Yu H.K, Wang P, Yang Z.Y, Tong L.M, "Light-emitting polymer single nanofibers via waveguiding excitation". ACS Nano, 4, 5332–5338, (2010).
27. Xia H, Chen T, Hu C, Xie K. "Recent advances of the polymer micro/nanofiber fluorescence waveguide", Polymers, 10, 1086-2002, (2018).
28 Tao H, Kainerstorfer J.M, Siebert S.M, Pritchard E.M, Sassaroli A.P, Bruce J.B, Brenckle M.A, Amsden J.J, Levitt, J.F.S, Kaplan D.L, Omenetto F.G, "Implantable, multifunctional, bioresorbable optics". PNAS, 109:19584-19589, (2012).

29 Lawrence B.D, Cronin-Golomb M, Georgakoudi I, Kaplan D.L, Omenetto F.G. "Bioactive silk protein biomaterial systems for optical devices". Biomacromolecules. 9, 1214-1220, (2008).

30 Parker S.T, Domachuk P, Amsden J, Bressner J, Lewis J.A, Kaplan D.L, Omenetto F.G. "Biocompatible silk printed optical waveguides", Adv. Mater. 21, 2411–2415(2009).

31 Hoffman A.S, "Hydrogels for biomedical applications". Adv Drug Deliv Rev., 54(1), 3-12 (2002).

32 B. Apter, N. Lapshina, A. Handelman, B. D. Fainberg, G. Rosenman Peptide Nanophotonics: From Optical Waveguiding to Precise Medicine and Implantable Biochips, Invited Review, Small, 1801147-19(2018).

33 A. Handelman, N. Lapshina, B. Apter, G. Rosenman, Peptide Integrated Optics, Adv. Mater. 30, 1705776-87(2018).

34 C. Diaferia, T. Sibillano, N. Balasco, C. Giannini, V. Roviello, L. Vitagliano, G. Morelli, A. Accardo, Hierarchical Analysis of Self-Assembled PEGylated Hexaphenylalanine Photoluminescent Nanostructures Chem. Eur. J. 22, 16586-16597(2016).

35 C. Diaferia, T. Sibillano, C. Giannini, V. Roviello, L. Vitagliano, G. Morelli, A. Accardo, Photoluminescent Peptide-Based Nanostructures as FRET Donor for Fluorophore Dye, Chem. Eur J. 23, 8741-8748(2017).

36 C. Diaferia, T. Sibillano, D. Altamura, V. Roviello, L. Vitagliano, C. Giannini, G. Morelli, A. Accardo, Chem. Eur. J. 23, 14039-14048 (2017)

37 A. Handelman, N. Kuritz, A. Natan and Gil Rosenman, Reconstructive Phase Transition in Ultrashort Peptide Nanostructures and Induced Visible Fluorescence, Invited Feature Article, Langmuir, 32 (12), 2847–2862 (2016).

38 Lumerical Inc. https://www.lumerical.com/products/

39 Shih-Hui Chang and A. Taflove, "Finite-difference time-domain model of lasing action in a four-level two-electron atomic system", Optics Express, Vol. 12 Issue 16, pp. 3827-3833 (2004).

40 V. M. Agranovich, M. D. Galanin, Electronic Excitation Energy Transfer in Condensed Matter, North-Holland, Amsterdam, New York, 1983.

41 V. M. Agranovich, A. M. Ratner, M. K. Salieva, Chem. Phys. 1988, 128, 23.

42 B. D. Fainberg, J. Chem. Phys. 1998, 109, 4523.

43 B. D. Fainberg, N. N. Rosanov, N. A. Veretenov, App. Phys. Lett. 2017, 110, 203301.

44 D. Pinotsi, L. Grisanti, P. Mahou, R. Gebauer, C. F. Kaminski, A. Hassanali, G. S. Kaminski Schierle, JACS 2016, 138, 3046.