

A REVIEW ON LATEST TRENDS IN BIOPHOTONICS

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ABSTRACT

Biophotonics is an interdisciplinary field that combines biology, physics, and photonics to study and manipulate biological system using light-based technologies. it involves the interaction of light with biological materials to understand and monitor various biological processes at the cellular, molecular, and tissue levels. Biophotonics techniques such as fluorescence imaging, optical coherence tomography (OCT), raman spectroscopy, and spectroscopy are increasingly used in medical diagnostics, environmental monitoring, agricultural applications, and biotechnological research. these technologies offer non-invasive, high-resolution, and sensitive method for detecting diseases, monitoring the health of crops, and assessing environmental changes. In medical fields, biophotonics enables early detection of diseases like cancer, cardiovascular conditions, and infections through precise imaging and biomarker detection. It also

provides real-time insights into cellular activities, making it crucial for research in drug development and personalized medicine. Environmental applications of biophotonics include monitoring water quality, detecting air pollution, and tracking biodiversity. Additionally, in agriculture, biophotonic sensing helps in assessing crop health, detecting diseases, and improving yield prediction. The continuous advancements in biophotonic technology are driving innovation in diagnostics, therapy, and environmental protection, enabling a deeper understanding of living systems while reducing the need for invasive procedures. The future

of biophotonics holds significant promise for the development of more efficient, cost-effective, and portable diagnostic tools and sensors with applications across a wide range of industries.

KEYWORDS:

biophotonics

Medical therapy

Medical diagnosis

Raman spectroscopy

Multiphoton microscopy

Environment monitoring

Atmospheric pollution

INTRODUCTION

Biophotonics is not a standard word listed in a classical dictionary. The meaning of “biophotonics” is essentially the use of photonic technologies to detect and perhaps to control a biological phenomenon or event, at different levels ranging from molecules, cells, tissue, organisms, to intact animals and even human bodies. The field of biophotonics is not well defined because it is a multidisciplinary research field at the intersection of physics, biology, chemistry, medicine and engineering. As alternatives to biophotonics, the term “biomedical photonics” and “biomedical optics” have also been popularly used, with no exact distinction among them.^[47]

Biophotonics is an emerging multidisciplinary research area, embracing all light-based technologies applied to the life sciences and medicine. The expression itself is the combination of the Greek syllables ‘bios’ standing for life and ‘phos’ standing for lights.^[38] Biophotons are light waves that exist in the living cells of plants, animals, and human beings. Cells emit biophotons, which cannot be seen by the naked eye, but can be measured by special equipment. The quest for understanding the biochemical basis of human disease is the most important area in the development of modern medicine. Biochemical changes within tissue may either initiate disease or occur as a result of disease process. In physiological systems, molecular changes often precede the onset of disease. These changes, if detected and interpreted properly, could provide vital information regarding the stages of disease progression and the effect of therapy. Malignant tumor causes clinical symptoms when it is usually large enough and can be detected by various conventional methods such as X-ray,

Computerized tomography, Magnetic resonance imaging, Ultrasound, and Mammography. These techniques have their own advantages and limitations. Most of the advanced stage cancers are difficult to treat effectively, and, therefore, it is important to detect cancers at an early stage.^[44]

Biophotonics has a pervasive effect on medical methods for diagnosis and therapy. Biophotonics can be applied to the field of life science, microbiology (viral and bacterial analysis), pharmaceutical and drug analysis, medicine and clinical diagnosis. The specialty of biophotonics is that it provides a non contact, effective, rapid and painless method for diagnosing, monitoring and treating diseases.^[44]

All living systems emit electromagnetic radiation, a small number of photons of about 100 ph/sec per square centimeter of surface area, at least in the visible energy range. The scientific community calls this emission by the name of biophotons. This emission is present in all living organisms, at least in aerobic ones, and ends as soon as the organism dies.^[32]

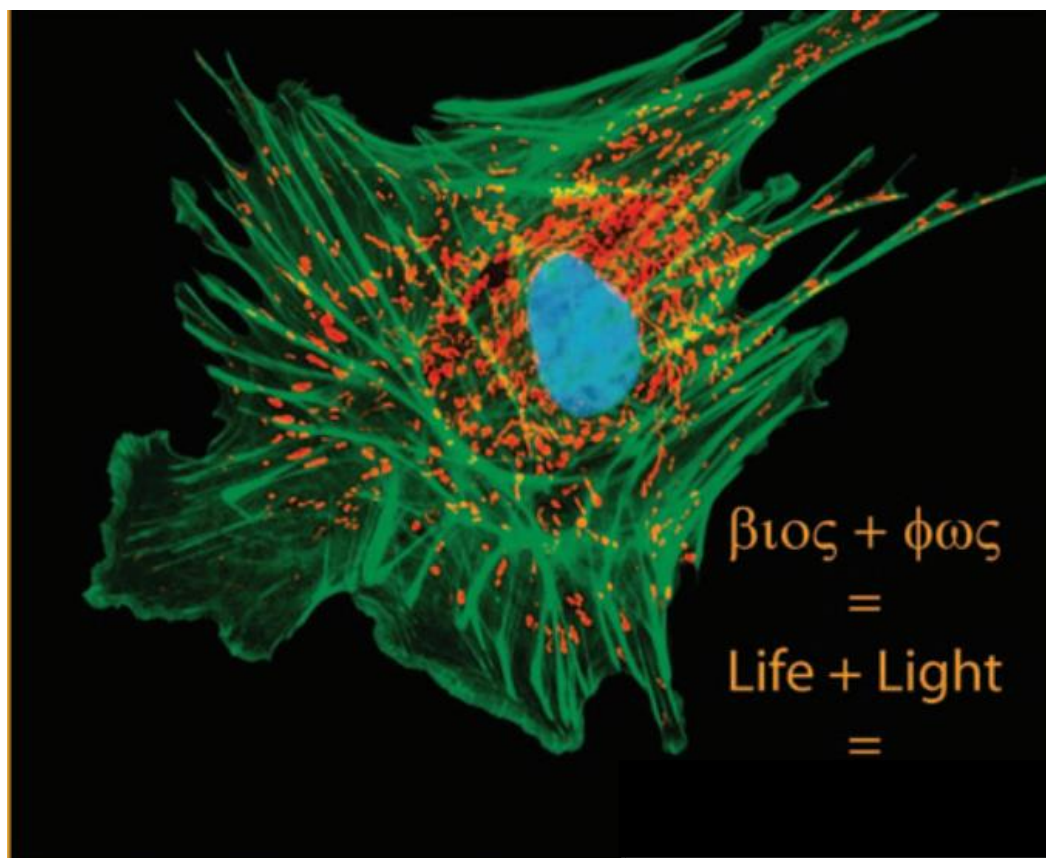


Figure 1.1 Shedding light on life: biophotonics utilizes light-based technologies for applications in medicine and the life sciences (fluorescence image: PCO AG).

Today, ultrahigh resolving microscopes enable us to observe cellular structures smaller than 20 nm across and their functions, and thus to study diseases right at their origin. We also benefit greatly from photonic technologies in medical practice – in fact both in diagnosis and in therapy of diseases. For example, laser scalpels have become routine tools which reduce the expense of many surgeries, sometimes even down to an ambulant intervention (“keyhole surgery”). Due to novel photonic technologies such as fluorescence endoscopy and photodynamic therapy (PDT), some types of cancer can be recognized much earlier and treated more gently than several years before. In ophthalmology, optical coherence tomography (OCT) has become the gold standard for detecting morphological changes in the eye by adding the third dimension, helping to obtain high-resolution 3D images of the retina and diagnose prevalent diseases such as glaucoma and macular degeneration.^[38]

Biophotonics in medical therapy involves use of light, specifically in the form of photons, to diagnose and treat medical conditions. This technology combines biology and photonics (the science of light) and has various application in healthcare.

BIOPHOTONICS APPLICATION

Biophotonics has several prominent advantages in biology, medicine, pharmaceutical science, environmental science, and agriculture. Current research trends in biophotonics are mostly categorized into the following types or any combination of them. (1) More dimensions: from 1D to 2D, from 2D to 3D, and from 3D to 4D (including time). (2) Higher spatial resolution: from microscopy to nanoscopy. (3) Higher temporal resolution: from static imaging of dead cells to functional imaging of live cells.^[29]

Biophotonic has a wide range of application in medicine, biology, and drug delivery.

Biophotonics is that the study of optical processes in biological systems, both people who occur naturally and in bioengineered materials. A particularly important aspect of this field is imaging and sensing cells and tissue. This includes injecting fluorescent markers into a biological system to trace cell dynamics and drug delivery. The term biophotonics denotes a mixture of biology and photonics, with photonics being the science and technology of generation, manipulation, and detection of photons, quantum units of light. Photonics is related to electronics and photons.^[07]

The application of biophotonics in diagnostics and therapeutics has helped patients with early detection and targeted treatments for their infections. Electron microscopy and light microscopy can detect nano-scale particles to elucidate virus morphology. Interferometric light microscopy can also differentiate viruses from other nano-scale particles with higher sensitivity to determine virus concentration.^[63]

Biophotonics is focused on translating discoveries in the sciences around lasers, light and imaging into useful medical tools. Medical imaging and in vitro diagnostics are just two of the many applications of biophotonics that already had an enormous positive impact on our lives. Besides advancing the frontiers of medical technology, biophotonics is also being applied to non-medical applications.^[38]

Photonics has contributed to the recent revolution in informatic and technology with advanced applications and physical principles. It is defined as a field that combines theoretical and optical physics to utilize the use of light. In present, not only optical fibers and telecommunication are the primary areas that photonics plays as a base role in but also medical field, visual art, agriculture, robotics, and biophotonics.^[12]

Sensitive detection of biological signals and precise observation of pathological changes are of great importance for the early diagnosis and treatment of infectious diseases, cancer, and other health disorders. However, owing to the low quantity of biochemical signals and complex microenvironment in biological systems, the detection of the targets of interest is challenging.^[59]

The previous study employed biophysical and biomaterial concepts for applications in the biomedical interface. Subsequently, the exploration and advancement of lasers have paved the way for novel avenues in biomedical applications, resulting in the wide spread incorporation of laser-based biomedical devices within clinical practices. The prior investigation focused on the exploration of selectively manipulating upconversion emission channels using tuneable biological photonic devices.^[57]

Biophotonic imaging has revolutionized the operation room by providing surgeons intraoperative image-guidance to diagnose tumors more efficiently and to resect tumors with real-time image navigation. Among many medical imaging modalities, near-infrared (NIR)

light is ideal for image-guided surgery because it penetrates relatively deeply into living tissue, while nuclear imaging provides quantitative and unlimited depth information.^[56]

In recent decades, the role of photonics in medical and biomedical applications has significantly increased, and it is as crucial as its applications in optics and optoelectronic devices. The role of photonics in medical applications, such as sensing, diagnostic imaging, therapy, drug delivery and laser surgery, is as significant as its application in optics and electronics, such as a high-quality single photon sources, semiconductor technologies and fibre optics telecommunications. In dentistry, laser and light amplification by stimulated emission of radiation (LASER) plays a crucial role in soft tissue and periodontal applications.^[17]

BIOPHOTONIC IN DRUG DELIVERY

Biophotonics in drug delivery refers to the use of light (photons) to enhance or control the delivery of drug to specific targets within the body.

The complex and uncontrollable pore structures limit its further clinical intelligent drug delivery applications. It is believed that the uniformity of pore channel arrangement and the length of pore channels in MCSs can significantly influence its photonic properties as well as their potential applications. Moreover, when materials with uniform arranged pore channels are applied as carriers for controlled drug delivery, it is widely believed that the uniformity of pore channels are strongly related with the matrix and drug interactions that determine the adsorption, mass transport and release behaviors of loaded drugs. Therefore, mesoporous materials with uniform arranged pore structures are highly demanded.^[25]

Near – Infrared(NIR) light for targeted drug delivery - nanoparticles or drug carriers can be engineered to respond to NIR light. When exposed to NIR light, these particles can release their payload at specific sites in the body. Often in tumors or diseased tissues, enhancing treatment specificity and reducing side effects.

Treatment of diseases with drug therapy has progressed greatly during the past decades. However still, while most of the diseases are limited in a precise part of the body, most drugs are dispersed throughout the whole body in high concentrations to ensure that it will reach the target.^[21]

General concepts in glass science, biomaterials, scaffolds and drug delivery systems is provided. A deeper insight to the specific areas of photonic and bioactive glasses, as well as scaffold and drug delivery system production is presented. Drug delivery systems (DDS) allow for precise control of the concentration of a drug in the organism over space and/or time. If loaded with the drugs before implantation, DDS could be engineered to release the drug under external stimulus. This stimulus could be light at 980nm which can penetrate the skin.^[20]

Biophotonics is a relatively novel, interdisciplinary science that uses light-based technology to image, detect, and characterize the interplay between light and biological materials, including cells and tissues in living organisms.^[55]

Drug delivery systems (DDS) allow for precise control of the concentration of a drug in the organism over space and/or time. If loaded with the drugs before implantation, DDS could be engineered to release the drug under external stimulus. This stimulus could be light at 980nm which can penetrate the skin. This biophotonic DDS could then fight infections locally. Such DDS need to be fabricated from bioactive glasses which react when pumped at 980nm. Such glasses are capable of firm bonding with the surrounding tissues by developing bone-like hydroxyapatite (HA) layers when reacting with physiological fluids.^[20]

BIOPHOTONIC ENDOSCOPY

Biophotonic in endoscopy refer to the use of light – based technologies to enhance the diagnostic and therapeutic capabilities of endoscopic procedures. The optical fiber is also used in medical applications to allow for minimally intrusive viewing and surgery of internal structures. An endoscope consists of a lens and a light source at the end of an optical fiber. The fiber is passed into the body and a view of the internal structure of the body is obtained. This allows a diagnosis to be made without intrusive surgery. An optical fiber can also be used to deliver high intensity laser light to an internal region in the body, for example, to remove tumors.^[44]

The integration of detection, characterization, diagnosis, and staging at the time of endoscopy is still an unmet clinical need. The advent of biophotonics in endoscopy has opened new horizons and created important new opportunities for the enhanced identification and biochemical characterization of disease.^[55]

Diagnostic endoscopy has been rolled for early detection of gastrointestinal neoplasia (1). Diagnostic accuracy can be enhanced by better training and efficient experience, however, diagnosis using conventional endoscopy is essentially limited because it is simply based on morphological changes and/or discoloration when illuminated with white-light and imaged with standard human optics. This limitation is compensated by histopathological diagnosis of biopsied specimen, which takes extra time and charge for patients and is not preferable to one taking anti-coagulants or anti-platelet medicine. There have been several attempts using novel equipments for visualization of cell morphology on the micro to nano level (4)-(6) reflection of spectroscopic characteristics.^[43]

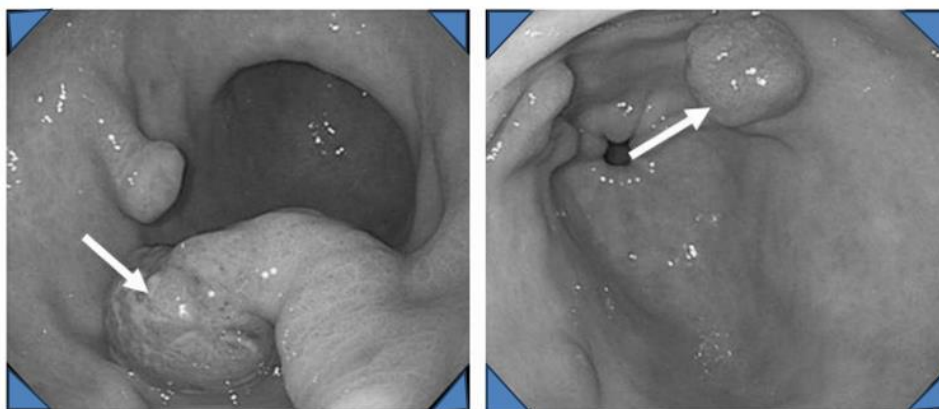


Fig. 2: Endoscopic feature with white light endoscopy.

Photoacoustic (PA) imaging is an emerging technique capable of visualizing the vasculature deep within the tissue by exploiting intrinsic molecular contrast.^[1,2] Miniaturized PA probes have many potential applications in intraoperative imaging and minimally invasive surgical guidance. These include the in situ assessment of cancerous lesions in the abdominal organs, identification of tumor margins during laparoscopic liver surgery, guidance of needle biopsies, and treatment monitoring of photocoagulation therapy. These applications often require a forward-viewing configuration to visualize the tissue directly ahead of the probe tip. However, the majority of previously reported PA endoscopic probes tend to be side viewing.^[48]

TECHNIQUE IN BIOPHOTONICS

Biophoton emission is defined as extremely weak light that is radiated from any living system due to its metabolic activities, without excitation or enhancement. We measured biophoton images of tumors transplanted in mice with a highly sensitive and ultra-low noise CCD camera system. Cell lines employed for this study were AH109A, TE4 and TE9. Biophoton images of

each tumor were measured 1 week after carcinoma cell transplantation to estimate the tumor size at week 1 and the biophoton intensity. Some were also measured at 2 and 3 weeks to compare the biophoton distribution with histological findings. We achieved sequential biophoton imaging during tumor growth for the first time. Comparison of microscopic findings and biophoton intensity suggested that the intensity of biophoton emission reflects the viability of the tumor tissue.

Cancer is a major cause of human mortality, and many diagnostic methods have been developed. Trials on ultraweak biophoton measurement of the serum or urine from cancer patients have also been performed for diagnostic applications.^[39]

It is difficult at present to classify each method according to its potential clinical use and according to what diseases it is best applied because different modalities might be used for one or all elements of diagnosis and be applied to a variety of different conditions. Although individual techniques aim to prove useful for a specific aspect of the diagnostic process.^[55]

OPTICAL COHERENCE TOMOGRAPHY (OCT)

Optical coherence tomography (OCT) is a particularly successful story of a new technology arising in the early 90s. Although based on the versatile Michelson interferometer^[1], the term “optical coherence tomography” was coined in the famous work of Huang and Fujimoto in 1991.^[2] Based on the database PubMed for biomedical literature, the number of publications with the term “optical coherence tomography” in the title increased slowly until 2002, whereas an almost linear increase in the number of publications, with a steep slope of more than 200 per year can be found since then.^[26]

Biophotonics is an exciting frontier which focuses on the interaction between light and biological matter thereby fusing photonics and biology. The use of photonics for light-activated and light-guided therapy as well as optical diagnosis promises to have major impact on fundamental biological science as well as life sciences and health care. In general, biophotonics integrates four major technology platforms: lasers, photonics, nanotechnology and biotechnology.

Optical coherence tomography (OCT) is a rapidly emerging non-invasive, imaging modality enabling in vivo cross-sectional tomographic visualization of internal microstructure in biological systems at resolution levels of a few micrometers that offers great hope for significantly improved early disease detection.^[64]

OCT performs optical ranging in biological tissue. Optical ranging has routinely been used in the telecommunications industry for locating faults or defects in optical fibers that comprise an optical communications network (Takada, Yokohama, Chida, & Noda, 1987). Faults in fiber produce a partial or complete reflection of incident optical pulses. By sending optical pulses through the optical fiber, faults can be detected by measuring the time delay between the original and reflected pulse. Analogous to optical ranging in fibers, optical ranging can be performed in biological tissue because every interface (where there is a change in the optical index of refraction) will reflect a portion of the incident optical beam.^[54]

OCT was developed in the early 1990s for the noninvasive imaging of biological tissue (Bouma&Tearney, 2001; Huang et al., 1991). The first application areas were in ophthalmology, where diagnostic imaging could be performed on the transparent structures of the anterior eye and the retina (Hee et al., 1995; Puliafito, Hee, Lin, et al., 1995; Puliafito.^[54]

PHOTODYNAMIC THERAPY (PDT)

One of the most useful applications of biophotonics in medicine is photodynamic therapy, or PDT. PDT involves three parts: a photosensitizer (a chemical compound that can be excited by a light of a particular wavelength), light, and tissue oxygen. The treatment is used for cancer, but can also be used on acne and psoriasis. In order for PDT to work, a photosensitizer must be administered to the patient.^[44]

A. Non-Malignant Diseases

1. Ophthalmic Disease
2. Ophthalmic Disease
3. Dermatological Disease
4. Urological Disease

B. Malignant Diseases

1. Brain Tumor
2. Head and Neck Cancer
3. Breast Cancer
4. Skin Premalignant and Malignant Diseases
5. Gastroenterological Cancer

SKIN CANCER

Skin cancer is a common type of cancer that emerges from the skin. It is extended due to the development of abnormal growth of cells. These cells can invade other parts of the body. More than 90% of cases occur due to the exposure of UV radiation. The UV radiation wavelength ranges from 100 nm to 400 nm. Cancer occurs due to unrepaired DNA damage to skin cells which is caused mostly due to UV radiation. In melanoma, cancer cells arise from moles on the skin which causes inflammation around the epidermal layer which in turn increases the temperature around it.^[60]

It can treat certain cancers, particularly surface – level or early-stage cancer, like skin cancer.

The development of high sensitivity noninvasive optical sensing techniques for early detection of skin tissue abnormalities, such as various skin cancer types, has been the subject of extensive academic and commercial activities during the past decade. Some optical mechanism providing it with certain ability to discriminate abnormal from healthy tissue. Example is imaging at terahertz (THz). The imaging modulation of the electromagnetic field provides sensitive to local water content in tissues. Human skin is a very complex organ both in structure and physical behavior, due to the various functions it performs as the mediator between the inner tissues and the surrounding medium.^[35]

This clinical study is a first attempt to use autofluorescence for recurrence diagnosis of skin cancer in post-operative scars. The proposed diagnostic parameter is based on a reduction in scar autofluorescence, evaluated in the green spectral channel.^[40]

CLASSIFICATION OF SKIN CANCER

Basal cell carcinoma (BCC)- this is the most common type of the it develops of basal cell, which are located in the lower part of the epidermis.

BCC appears like a flesh coloured pearl like a bump or a pinkish patch of skin. BCC is due to skin exposure especially found in the sun exposed areas such as the face, head, neck, arms, legs, and abdomen. BCC can spread over the body and grows in nerves and bones.^[60]

Squamous cell Carcinoma (SCC)–SCC occurs in the squamous cells, which are found in the outer layer of the skin.

It appears like a red firm bumps scaly patches. It is caused due to over sun exposure. It is more commonly found in people who have pale light skin.^[60]

Melanoma - Melanoma is the most aggressive and dangerous form of skin cancer. It develops in the melanocytes, the cell responsible for producing pigment (melanin) in the skin. Fair skin- people with lighter skin, hair, and eyes are more likely to develop skin cancer. A Family history of skin cancer increases your risk.

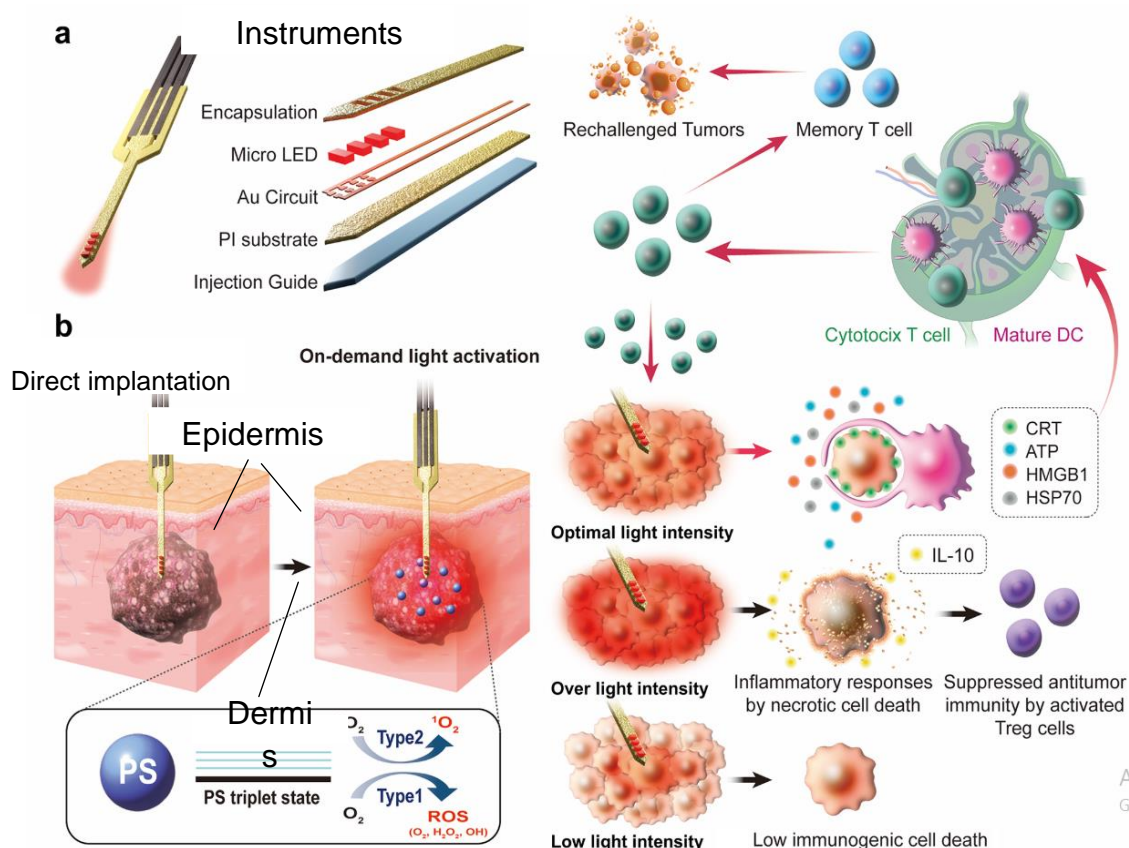


Fig. 3: Skin Cancer.

Skin cancer is a common type of cancer that arises from the skin. It spreads due to abnormal growth of cell. 90 percent of cancers are caused by exposure to UV radiation.^[19]

Fs-laser and UV irradiation

The laser beam used in this study was from a compact mode-locked Ti : Sapphire laser (Chameleon model, Coherent, California, USA) and coupled to an inverted confocal laser scanning microscope (C1, Nikon, Japan) equipped with a water immersion objective (Plan Neofluar 40X, N.A. 0.8, water). The laser was operated at 80 MHz pulse repetition frequency and produced 175 fs output pulses. A half-waveplate (Thorlabs) and a polarizing cube were used to attenuate the laser power.^[19]

Immuno-fluorescence assay for CPD

An immunofluorescence assay (IFA) is a laboratory technique used to detect specific antigens (such as proteins) within a sample using antibodies that are linked to a fluorescent dye. When the antibodies bind to their target antigen, the fluorescence emitted can be detected using a microscope or imaging system. This method is often used in research and diagnostic labs to study the presence and location of specific proteins or pathogens.^[19]

BREAST CANCER

Breast cancer is currently the most common type of cancer in women worldwide, and demographic trends indicate a continuous increase in incidence rate. According to forecasts, only in the European Union by 2020 about 394,000 new cases of breast cancer will be registered yearly together with 100,000 deaths among patients with breast cancer.^[1] Over the past decades, breast cancer treatment approaches have undergone significant progress, and current trend is the implementation of organ-preserving operations^[2–4] requiring a reliable intraoperative assessment of surgical margins.^[18]

Recently, optical express biopsy approaches for cancer diagnostics have been developed.^[5] These approaches are based on the principles of optical multispectral visualization of bioissue cellular structure and allow for retrieving information on morphological type of the tumor, the presence of malignant cells in the surgical margin during organ-preserving operations, the presence of specific molecular markers, including, those for breast cancer.^[18]

Biophotonic technologies, like optical imaging and photoacoustic imaging, can potentially detect breast cancer at an early stage. These methods often provide a non – invasive way to examine tissues and identify abnormalities that could indicate cancer.

Breast cancer accounts for nearly one in every three cancers diagnosed in Western women and, excluding skin cancers, breast cancer is the most common cancer among women. Mammography is the most common technique for detecting non-palpable and highly curable breast cancer, by quantitatively probing density changes in breast tissue. breast tissue is primarily composed of epithelial cells, an extracellular matrix and fat.^[33]

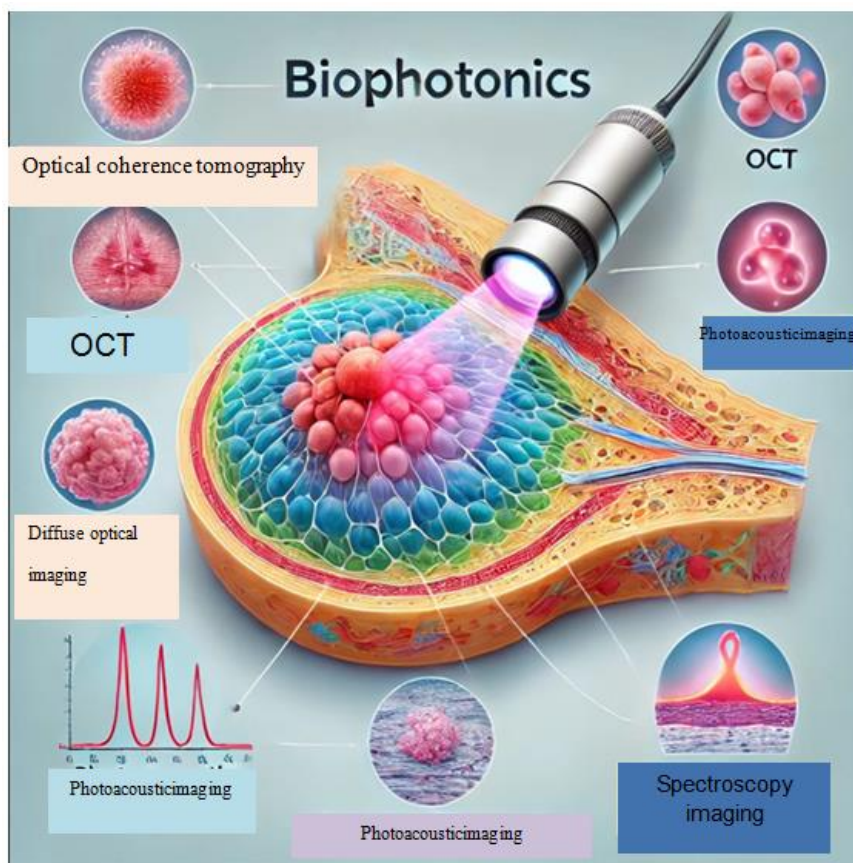


Fig.4 - Breast Cancer.

Breast tissues were obtained from patients undergoing either a lumpectomy or a mastectomy. They were harvested during surgery, and normal and tumor tissue samples were cut from the larger specimen by the pathologist.^[33]

Breast cancer is currently the most common type of cancer in women worldwide, and demographic trends indicate a continuous increase in incidence rate. According to forecasts, only in the European Union by 2020 about 394,000 new cases of breast cancer will be registered yearly together with 100,000 deaths among patients with breast cancer optical express biopsy approaches for cancer diagnostics have been developed.^[5–7] These approaches are based on the principles of optical multispectral visualization of bioissue cellular structure. Two-photon microscopy. The study involved biopsy samples of breast tissue obtained from 7 patients, diagnosed with fibroadenoma (2 cases), carcinoma in situ (1 case) and invasive carcinoma of a nonspecific type of I–II grade (4 cases) according to the results of histological examination. Biopsy material in the form of breast tissue column was obtained during a routine trephine biopsy procedure performed under ultrasound control. Within 60 min after

the biopsy, the unstained samples were imaged with a Carl Zeiss LSM 510 META laser scanning microscopy system (Germany) equipped with an inverted microscope.^[18]

Symptoms

- Lumps of thickening in the breast
- Changes in breast size, shape, or skin texture
- Nipple discharges (other than breast milk)
- Pain or tenderness in the breast area

Stage

Breast cancer is staged from 0 to 4 with stage 0 being non – invasive and stage 4 being advanced, where the cancer has spread to other parts of the body.

Breast cancer is one of the most treatable forms of cancer if it is detected and diagnosed in an early stage. Early diagnosis is also the best way to curtail the effects of the disease and improve survival². As the most commonly used screening method, mammography can often detect breast cancer in an early stage, but it is imperfect.^[65]

Biophotonics is a relatively novel interdisciplinary discipline that integrates lasers, optoelectronics, photonics and biomedical sciences. conjugated to nanoparticles producing targeted optical imaging probes for cancer detection. Nanocarriers can be served as multi-modal theranostics systems or as “Trojan Horses” In modern anti-cancer modalities, the majority approaches the delivering of new drugs which are behaving as a “Trojan horse” a nanoparticle and “decorating” its surface with a ligand that trigger the cancer cell into taking it up. Imaging can be used to trace the delivery of the drug inside the body and simultaneously to activate the release of the drug by an external stimulus such as laser light.^[15]

ORAL CANCER

AF of oral tissue shows different behavior for different conditions. NADH and FAD are complex compounds present in body and shows abatement of concentration in malignant tissues. Also, change in redox ratio in malignant tissues and healthy tissues indicates capability of AF in oral cancer screening. NADH and FAD are intracellular components and mainly participate in metabolic reactions of the cell and during amelioration of the disease, concentration of these complex compounds get changes and helps in identification of cancer

evolution. A spectral-band was observed around 430 nm- 560 nm for most of OSCC patients and AF was decreased compared to normal tissue. This spectral-band shows native fluorophores NADH, FAD and collagen crosslinks in oral tissue. Progression of OSCC from normal tissue has significant variations which assigned to altered photo physical features of native fluorophores.^[46]

The astonishing complexity and robustness of biological systems remain nature's ultimate engineering feats, perhaps best evident as the human body. Insights into its fundamental working can be most evident in human diseases, to paraphrase a human phenotype.^[53]

Cancer, responsible for more fatalities than all other major diseases combined, is projected to affect over 20 million patients by 2025, particularly in low-income countries. The detection and recognition of various cancerous cells during their early stages present significant challenges for pathologists and medical professionals.^[22]

Oral cancerous cells, originating from the tissues of the mouth or throat, are characterized by aberrant, uncontrolled cell proliferation, which can progress to malignancy. These cells may manifest in diverse regions of the oral cavity, including the lips, tongue, cheeks, and floor of the mouth. In their initial stages, oral cancer may present as persistent sores, lumps, or areas of discoloration. Laser surgery offers the advantage of a more controlled procedure, which is less invasive and can be performed under local anesthesia.^[22]

Oral squamous cell carcinoma (OSCC) is the most frequent and common malignancy (around 84%-97%) among oral cancer. Annually 77,000 people are affected by oral cancer and approximately 52,000 deaths are reported in India. Oral cancer starts from altering the epithelial cells then it turns out to hyperplasia, thereafter dysplasia and ultimately if untreated, transforms into OSCC.^[46]

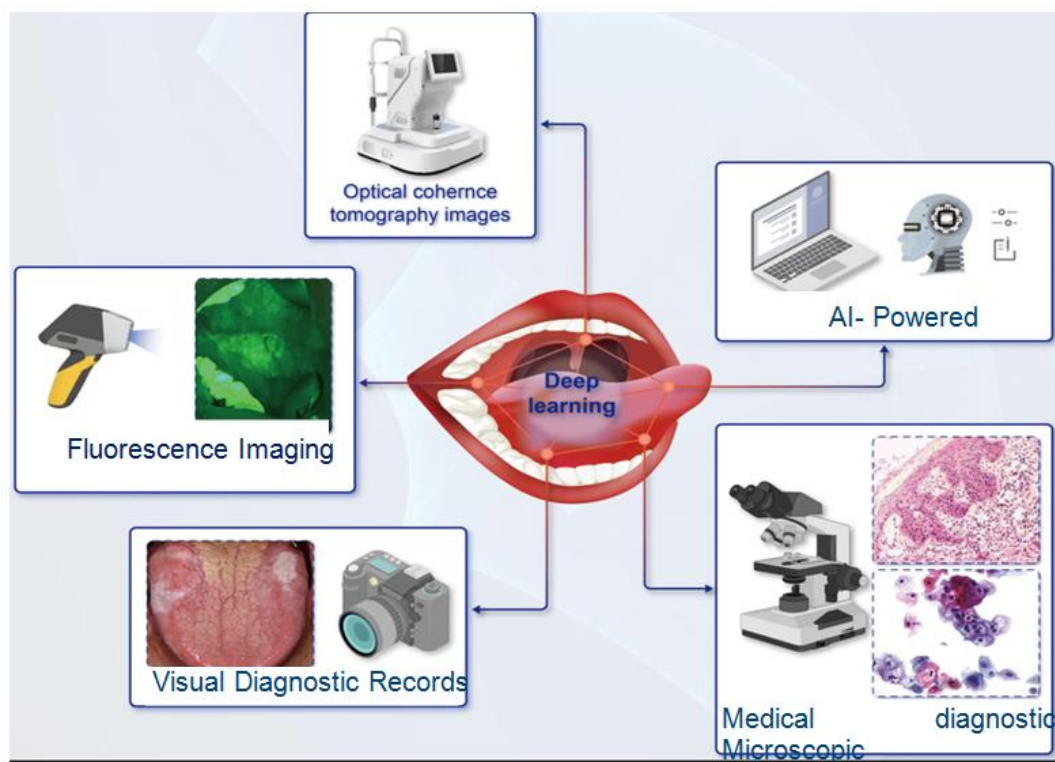


Fig.4 - Oral cancer.

A lesion in the oral cavity can start from a red (erythroplakia) or white (leukoplakic) flat patch having variable degree of dysplasia that represents the extent of the premalignancy.

This type of diagnosis has its own limitations and is subjective to sampling. Accurate diagnosis depends on many important factors such as type of biopsy, biopsy site and adequate specimen submission to the laboratory, quality of specimen and correct interpretation of biopsy. Raman spectroscopy combined with saliva analysis is an emerging biofluid spectroscopy for oral cancer diagnosis.^[50]

We report development of multi-modal autofluorescence and fluorescence imaging and spectroscopic (MAF-IS) smartphone-based systems for fast and real time oral cancer screening. Fluorescenceautofluorescence images and spectroscopic datasets shows significant change in oral cancer and normal tissue in terms of fluorescence-intensity, spectral-shape, and red-shift respectively.^[46]

COLORECTAL CANCER

Chronic alcoholism has become a global concern regarding the adverse effects it has on organs, particularly the colon. In the US, colon cancer is ranked one of the highest causes of cancer-related mortality. Studies show that alcohol is one of the significant risks of colon

cancer, affecting gut microbiota, which leads to inflammation and genetic mutations that advance adenoma to carcinoma. This cancer grows slowly, often without noticeable symptoms in its early stages, making early detection critical for better outcomes.^[23]

Type of colorectal cancer

- Colon cancer – occurs in any part of the colon (ascending, transverse, descending, or sigmoid colon)
- Rectal cancer- occurs in the rectum, the final section of the large intestine.

Colorectal cancer (CRC) remains both the third leading cause of cancer-related deaths and the third most commonly diagnosed cancer globally.^{1,2} With an estimated 1 million cases per year, the associated burden is expected to increase by 60%, approaching 2.2 million new cases and 1.1 million annual deaths by 2030.² The primary curative treatment for localized tumors is surgical resection.^[106]

The gold standard for prevention of CRC is early screening via colonoscopy, where a physician examines the colon with white light to identify precancerous polyps. Spectroscopic OCT has been used in a variety of clinical applications, including measuring hemoglobin concentration, oxime try, burn severity and others, by measuring the scattering and/or absorption spectra of tissue and then obtaining optical coefficients from that information. Faber *et al.*^[62]

Two types of genetically modified mice^[23,24] are included in this study, each representing different stages in the development of colorectal cancer.^[62]

The large mortality caused by CRC can be attributed to late-stage detection leading to poor patient prognosis. This along with the significant morbidity and cost associated with standard surgery and associated adjuvant treatment modalities has led to the widespread adoption of screening methods to detect cancer at an early stage. This is paralleled by a proliferation of minimally invasive methods such as endoscopy mucosal resection (EMR), Endoscopic submucosal dissection (ESD), Transanal Endoscopy microsurgery (TEM) and Transanal minimally Invasive surgery (TAMIS) to deal with these early lesions.^[34]

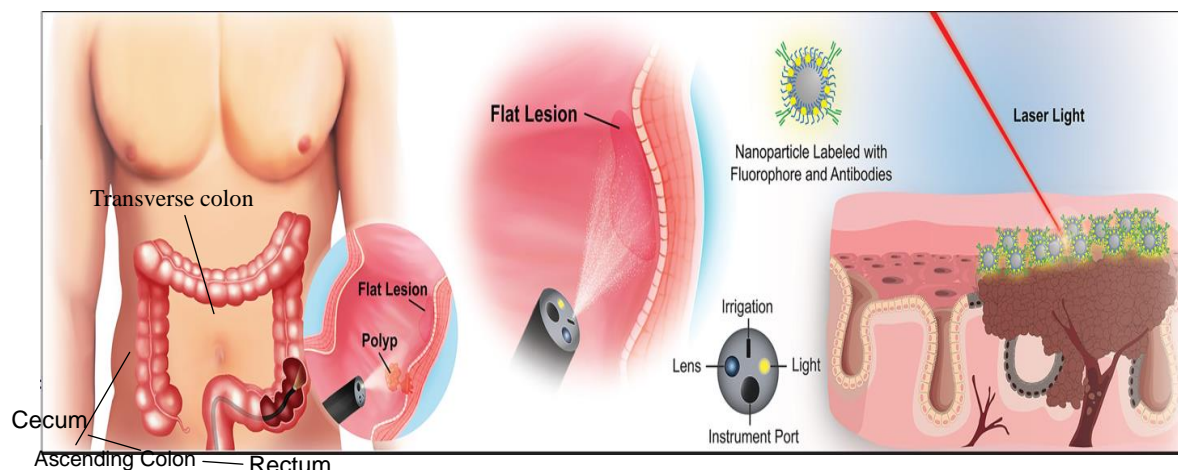


Fig.6 - Colorectal cancer.

Colorectal cancer (CRC) is largely spread worldwide. Only for 2020, it was reported 10% of new cases and 9.4% CRC related deaths among all other types of cancers were reported¹. In general, CRC diagnosis relies on endoscopic assessment of the colonic tract along with obtention of biopsies for histological characterization.^[05]

BIOPHOTONIC IN MEDICAL THERAPY

Biophotonic in medical therapy refers to the use of light and light-based technologies in the diagnosis, treatment, and monitoring of diseases. Biophotonics combines biological sciences with photonics (the science of light) to create advanced medical tools and therapies that utilize light, lasers, or other optical technologies.

The concept of cardiac stem cell therapy is to re model the ischemic myocardial tissues; a wide range of different stem cell types have been investigated for this purpose, both embryonic and adult, including skeletal myoblasts, mesenchymal stem cells and stem cells derived from bone marrow, as well as cells originating in the heart tissue itself, i.e. adult cardiac stem cells.^[10]

Low-level laser therapy (LLLT), also known as photobiomodulation (PBM), is a medical technique that stimulates cellular function, resulting in beneficial clinical effects. LLLT has two characteristics: LLLT is characterized by a biphasic dose response, namely, lower doses of light are often more beneficial than high doses, and a large number of parameters such as the wavelength, fluence, irradiance, illumination irradiation time, and timing of the applied light must be chosen for LLLT treatment.^[58]

However, when using a laser system it is hard to control the depth of the cut. Therefore it is desirable to develop closed-loop control systems that allow performing safe laser osteotomy without damaging internal and surrounding tissues.

Sensor controlled laser systems are a focus in the field of therapy. They have been already applied in experimental trials with living tissues as well as in humans. Another focus is the destruction of tumor tissue and intraluminal calculi by medical lasers. Tumors are nowadays destroyed by photodynamic therapy and by vaporization using various laser sources.^[44]

BIOPHOTONICS IN DENTAL

Biophotonic in dentistry refers to the application of light-based technologies for diagnostic, therapeutic, and treatment purposes. In contemporary dental practice, the principal priorities are early diagnosis and prevention of common oral diseases, as well as the preservation of tooth tissue as much as possible during treatment. The potential of biophotonics-based technologies to provide noninvasive highly sensitive tissue information and induce specifically localized tissue processing may therefore be of immense value. On the other hand, the ability to identify clinically relevant information much earlier than actual signs and symptoms of a disease appear indicates one of their most beneficial features, due to the possibility of performing preventive or minimally invasive treatment procedures. Different ways to classify the application of biophotonics-based techniques have been suggested, albeit very few of them in the field of dental medicine.^[14]

The application of tribology in dentistry is an important research field and it has been developed an understanding of it for successful design and selection of artificial dental materials.^[3] Likewise, stress/strain analyses is very important in dental biomechanics, because it is important for the design of implants, prostheses, and orthodontic appliances, among other.

In dental science, OCT detects qualitative and quantitative morphological changes of dental hard and soft tissues, like for early diagnosis of dental diseases, such as caries, periodontal disease, and oral cancer, because of the excellent spatial resolution ($\approx 15 \mu\text{m}$). OCT can also be used in other types of applications, such as to evaluate the microleakage of dental restorations and endodontic fillings, the dental implant status, the integrity of dental prosthesis, and the surroundings of orthodontic brackets.^[31]

Biophotonics deals with interactions between light and biological matter, integrating knowledge of physics, chemistry, engineering, biology, and medicine for solving specific biomedical or life science problems. Due to the ability to provide non-invasive, highly sensitive tissue information and inducing specific localized tissue ablation, biophotonics based technologies may be of utmost importance in improving dental healthcare.^[14]

BIOPHOTONICS AND THE CELL

Over the past decade, the nonlinear optical methods have become widely used tools for biomolecular detection, medical diagnosis in cells or tissues at the micrometer and nanometer level. Advancement of these optical methods promotes and enhances basic research in biology, pharmacy, and medicine. Compared with the optical method, radiation is usually applied for imaging modalities, including x-rays, computed tomography, plain radiography, magnetic resonance imaging, and other nuclear imaging methods. However, these techniques are costly and emit radiation. For disease detection and diagnoses and cells development process, optical imaging methods can provide molecular information on human tissues with noninvasive, real time, accurate, sensitive, and economic properties, as discussed in recent reviews.⁶ When human diseases develop, cells and tissues are used to study the genetics, drug screening, and disease control via optical imaging techniques.^[49]

Investigation of the homeostasis of red blood cells upon infection by *Plasmodium falciparum* poses complex experimental challenges. Changes in red cell shape, volume, protein, and ion balance are difficult to quantify. In this article, we review a wide range of optical techniques for quantitative measurements of critical homeostatic parameters in malaria-infected red blood cells.^[24]

Spontaneous photon or “biophoton” emission has been described as ultraweak packets of electromagnetic energy (Popp 1979). Many recent publications have reported the role these biophotons play in biological systems, looking at emission intensities from cultures of plant and animal tissues. Cultures of living cells emit biophotons.^[109]

BIOPHOTONICS AND THE DNA

DNA is the code of life, as it includes unique genetic information and is located in the nucleus of each cell in the form of chromosomes, which are a long line of DNA molecules. Each DNA molecule contains a multitude of genes responsible for building and sustaining vital activities in the human body.

Researchers David A. Jernigan and Samantha Joseph, while studying photons, discovered that they act both as waves and particles and enter the body mainly through the eyes. Electromagnetic or biophotonic energies may or may not be linked. This connection is at least partly under our control. Research has shown that a positive attitude creates a link between electromagnetic and biophoton emissions, which changes DNA and makes the body healthier.^[61]

DNA and living organisms emit biophotons, which radiation is coherent and blackbody, i.e. not thermal. DNA's biophotonic emissions provide a holographic biofield for the generation of physical structures. A seed, for instance, changes itself from a particle state into the tree's biofield for the purpose of self-reproduction. From the systems point of view a seed or genotype constitutes the phenotype tree system's input and output.

The phenomenon of ultraweak photon emission from living systems was further investigated in order to elucidate the physical properties of this radiation and its possible source. We obtained evidence that the light has a high degree of coherence because of

- (1) Its photon count statistics
- (2) Its spectral distribution
- (3) Its decay behavior after exposure to light illumination
- (4) Its transparency through optically thick materials.^[44]

RAMAN SPECTROSCOPY

Raman spectroscopy (RS) has been used in several studies on animal In recent decades, Raman spectroscopy (RS) has been used in several studies on animal cells. The method is popular among biophysicists and life science researchers. RS allows for the study of living cell in their natural conditions without any damage. Nowadays, we can see a significant increase in the use of RS in plants, and especially in algae research. RS is a well-known approach used in many of biomedical studies. Since biomolecules.^[16]

Raman spectroscopic method are used in vivo and in ex vivo to resolve various biomedical issues such as early detection of cancer, monitoring the effect of various drug on the skin, determining the structure of atherosclerotic tissue fragments and rapid identification of disease-causing sensitive tissue.^[16]

Research into SORS has also led to identifying a number of beneficial properties of transmission Raman spectroscopy to volumetric sampling of diffusely scattering samples such as tissue. Raman spectroscopy has proven to be an effective technique for analysing excised bone matrix.

Raman spectroscopy has proven to be an effective technique for analysing excised bone matrix but the difficulty in probing deep through soft tissue hampered in vivo studies. The development of deep sub-surface Raman techniques provided new opportunities for advancing this field offering promise to diagnose bone conditions, such as brittle bone disease (osteogenesis imperfecta) and osteoporosis, noninvasively. The need for developments in this field can be exemplified on osteoporosis.^[45]

Raman spectroscopy biomolecules such as DNA or proteins are highly relevant analytes in the biomedical field as they are basic components of any cell or tissue sample. Due to the chemical information concealed in the fingerprint region of the spectra, Raman spectroscopy is ideally suited for detecting changes in the DNA or protein content of a sample. More advanced and faster Raman techniques use laser line, light sheet, or wide-field illumination with dedicated signal collection schemes.^[13]

Raman spectroscopy was tested as a tool for the diagnosis and possible grading of prostate cancer. Raman spectroscopic advances were already reviewed with an emphasis on clinical translation challenges in oncology in 2016 and with a focus on cancer detection and cancer surgery guidance until 2016. The current report summarizes the translation approaches of Raman based methods and other biophotonic modalities to the clinics since 2017.^[11]

Near-infrared (NIR; 1000–2500 nm; 10,000–4000 cm^{-1}) spectroscopy might be summarized as a vibrational spectroscopy technique [1–3] that occupies a somewhat peculiar spot across the field of bioscience. On the one hand, it has earned the status of tool-of-choice in various applications concerning the qualitative and quantitative assessment of bio-related samples, e.g., in medicinal plant analysis or the issues related with the quality control of natural products. On the other hand, in several other areas it competes with better established techniques such as infrared (IR, i.e., mid infrared, MIR; 4000–400 cm^{-1} ; 2500–25,000 nm) and Raman spectroscopy. The typical key areas are e.g., bioanalytical research and biomedical diagnosis, in which NIR spectroscopy has typically been shadowed by IR and Raman techniques [4–8], and where it still has room to progress in popularity.^[27]

Raman spectroscopy is a totally non-invasive, label-free technique which excites vibrations of molecular bonds. Although infrared spectroscopy can excite these vibrational bonds, it relies on low power sources and noisy detectors.^[03]

MULTIPHOTON MICROSCOPY

Multiphoton microscopy (MPM) plays a significant role in the field of biophotonics, which involves the interaction of light with biological materials for various applications such as imaging, diagnostics, and therapy. In biophotonics, MPM is valued for its ability to provide high –resolution, non-invasive imaging of live biological samples, making it particularly useful for studying complex biological systems at cellular and subcellular levels.

Multiphoton fluorescence microscopy is a powerful, important tool in biomedical research that offers low photon toxicity and higher spatial and temporal resolution than other *in vivo* imaging modalities. The capability to collect images hundreds of micrometers into biological tissues provides an invaluable tool for studying cellular and subcellular processes in the context of tissues and organs in living animals.^[28]

Light microscopy, in particular fluorescence microscopy, has become extensively used in the study of the correlation between structure and function in modern biological sciences. Either intrinsic or extrinsic fluorescent probes are required in fluorescence microscopy using single- (Sheppard & Shotton, 1997) or two-photon (Denk et al., 1990) excitation schemes.

The most common light source for multiphoton excitation microscopy now is the femtosecond Ti: sapphire laser with an emission wavelength around 800 nm. For the purpose of SHG microscopy or 2PF microscopy, the wavelength of signals excited by a Ti: sapphire femtosecond laser will be around the blue edge (SHG) of, or inside (2PF), the visible wavelength region.^[52]

BIOPHOTONIC INFLUORESCENCE

Biophotonic in fluorescence refers to the application of light-based technologies, particularly fluorescence, to study biological samples at the molecular and cellular levels. The first applications of 2PE to fluorescence microscopy were presented at the beginning of the 1990s by Denk and colleagues (1990), who demonstrated that images with excellent optical sectioning, could be obtained without killing cells. The development of commercially available mode-locked lasers, with high peak-power femtosecond pulses and repetition rates

around 100 MHz was then the trigger for a fast uptake of the multi-photon method in biology.^[04]

FCS is at present a very powerful tool for the characterization of biomolecules in vitro and is now developing into an adjunct to microscopy in which it is possible to probe the molecular aggregation and dynamics inside cellular compartments.^[04]

Fluorescence spectroscopy serves as an ultrasensitive sophisticated tool where background noises which serve as a major impediment to the detection of the desired signals can be safely avoided for detections down to the single-molecule levels. One such way of bypassing background noise is plasmon-enhanced fluorescence (PEF), where the interactions of fluorophores at the surface of metals or plasmonic nanoparticles are probed.^[51]

DNA origami is a technique based on the molecular self assembly, which can serve as a template for the fabrication of discrete, complex nanostructures using a bottom-up approach. The complex interactions between the plasmonic nanoparticles and fluorophores can be engineered by immobilization on a 3D origami structure. The specificity of nucleic acid binding makes DNA origami an efficient tool for tuning the arrangement of plasmonicnanomaterials for enhanced emission.^[51]

The method of autofluorescence has already been shown to improve the identification of primary BCC and SCC lesions that may not be visible to the naked eye or dermoscopy.^[16,19-23] Considering the criteria for non-melanoma skin cancer identification, healthy skin has intense green autofluorescence whereas cancerous areas may appear darker.^[40]

Optical microscopy is the only means of seeing structure in living cells at submicron resolution. In recent decades, the method has gained great chemical specificity from the development of fluorescent probes.^[04]

BIOPHOTONICIN ENVIRONMENT MONITORING

Biophotonic is the study of light (photons) interaction with biological materials, and It has broad application in environmental monitoring. For decades environmental pollution, caused by heedless anthropogenic and industrial activities, has been a crucial concern and has been identified as the origin of the global climate change. Despite the concern at worldwide level and the investment in remediation actions, the slow but steady degradation of water, soil and air quality, continues. The conventional analytical techniques, based on chromatographic and

spectroscopic technologies, remain the preferred analytical methods for environmental control due to its accuracy and sensitivity.^[08]

Biophotonics is an interdisciplinary field that involves the interaction between electromagnetic radiation and biological materials, so it refers to the emission, detection, absorption, reflection and influence of photons on cells, tissues and organisms of agricultural interest. The use of artificial lighting by light-emitting diodes (LEDs) to increase the production capacity of crops in controlled environments has been considered, among the recent technologies, one of those which have great potential to optimize plant growth and make systems more efficient and sustainable.^[30]

The conventional analytical techniques, based on chromatographic and spectroscopic technologies, remain the preferred analytical methods for environmental control due to its accuracy and sensitivity. But these methods are limited to centralised laboratories, require expensive instrumentation, are time consuming and need trained personnel. To overcome the high costs and low speed of those analysis, biosensor devices emerged as a promising.^[30]

Environmental monitoring includes all procedures and actions taken to assess the state of the environment. The previous century has seen significant advancements in the field of environmental monitoring, but the on-site control of toxins remains a challenging issue. In particular, the requirement for effective early warning systems is expanding along with the number of polluting sources.^[1] The management of environmental deterioration and the preservation of the natural environment's quality for the benefit of future generations depend on real-time and on-site pollution monitoring.^[37]

BIOPHOTONIC – LIGHT OF LIFE

Biophotonics has already led to some very important medical devices and monitoring systems, not to mention the whole field of molecular imaging. Biophotonics medical devices include pulsed oxymeters, laser surgery tools etc. Some examples for new methods in this field are corneal sculpting for vision improvement, optical coherence tomography for retinal imaging to check for macular degeneration and other eye diseases. Furthermore there are lasers for cosmetic surgery, laser-activated catheter tools and many more.^[41]

We define biophotonics as the development and application of photon-based technology to the life sciences and medicine. Biomedical imaging fits within our definition of biophotonics,

but certainly only represents one topic within the field of biophotonics. We categorize biophotonics into four broad topics, bio photonics for: 1) bioimaging, 2) biosensors, 3) bioassays and 4) medical devices for monitoring, diagnosis or therapy.^[41]

The word “biophoton” has been chosen to express the fact that the phenomenon is characterized by measuring single photons, indicating that it has to be considered as a subject of quantum optics rather than of “classical” physics. Biophoton emission is a general phenomenon of living systems. Practically all organisms emit light at a steady rate from a few photons per cell per day to several 100 photons per organisms per second and square centimeter surface area, within the spectral region of at least 200 to 800 nm. Biophotons are associated to energy-matter interactions; i.e.^[42]

PHOTONIC MONITORING OF ATMOSPHERIC FAUNA

Photonic monitoring of atmospheric fauna refers to the use of light- based technologies to observe and track organisms living in the atmosphere, such as insects,birds,and even microorganisms. Flying insects are of utmost importance in ecology and for human living conditions. Certain species serve as indispensable pollinators to ensure the availability of food stuffs, while others are dangerous vectors for spreading deadly diseases, such as malaria. Agricultural pests reduce the yield of crops, and their abatement through pesticides cause many additional problems. Birds and bats are frequently carriers of diseases, which, especially for long-distance migrants, cause serious consequences.^[36]

While man inhabits the land masses of earth, and shares them with a rich fauna variety, the atmosphere and the oceans are in contrast more inaccessible to humans, but well suited for organisms of all kinds with only sporadic intrusions by humans enabled by technology. The monitoring of the atmospheric and aquatic fauna is important for many reasons. Apart from our general quest for knowledge of our environment, there are many practical reasons for a reliable assessment of conditions. The migration of birds has fascinated people for a long time.^[36]

Monitoring change in insect distribution, diversity and abundance poses a formidable challenge to entomologists. Long-term estimates of population trends among insect species are difficult to implement, they require qualified personnel to collect and identify insects captured in traps, often for years. The diversity, number, and size of insects are added difficulties making such endeavors both labor and capital intensive.^[01]

A variety of research methods have been adopted to retrieve useful information to describe the aquatic fauna in the ocean environment, e.g., sampling by trawler, sonar sounding, visual observation, or computer vision adaption. The common and traditional ways of study are laborious, time-consuming, and non-in-situ. Camera recordings can achieve high spatial resolution at short distance. Holographic cameras need more sophisticated detectors and long-time processing of the data recorded. The sonar technologies can achieve large-area monitoring at moderate spatial resolution (about 0.1 m).^[66]

BIOPHOTONICS SENSING DETECTION

Biophotonic sensing detection refers to the process of using light-based technologies to detect and analyze biological samples or biological phenomena. It leverages the interaction of light (including laser, fluorescence, and other forms) with biological systems, such as molecules, cells, tissues, or even entire organisms. This detection method is often highly sensitive, enabling precise measurements for a range of applications, from medical diagnostics to environmental monitoring.

The emergence of many diseases and health-related problems in recent years has led to the development of early detection and sensing mechanisms that enable timely diagnose of these diseases. Among the best recent technologies that have proven their worth in early sensing is the biosensor based on PC structures.^[67]

Photonic biosensors have received a large amount of attention in the analysis of different components of human blood, due to their rapid and accurate results. To carry out these investigations, the biosensors require a very small volume of blood in the sample. Thus, in this study we proposed a design for sensing and detecting the dengue virus in blood using 1D PC with a defect.^[67]

Amongst the sensors, biosensors are devices with mechanisms for measuring changes in biological systems. Researchers have used different sensors to detect the shift in hormones, enzymes, level of glucose in urine, cancerolic cells, and nucleic acids. Many new technologies use materials, such as hydrogels, nanoparticles and PCs for developing compact biosensing systems.^[02]

Optical biosensing has focused high interest during past years. These sensors allow the detection of a huge diversity of bioanalytes by measuring variations of refractive index induced by molecular binding.

CONCLUSION

In this study, we explored the principles of biophotonics and their medical application. Our findings showed that light- based techniques such as fluorescence spectroscopy and raman spectroscopy could be used in early – stage cancer detection. This has the potential to enhance diagnostic tools, which may improve patient care. However the study had some limitations, such as limited sample size and equipment constraints, which may be addressed in future studies. Future research may explore new photonic techniques and validate these methods through clinical trials. Such advancements could lead to substantial improvements in medical diagnosis and treatment. We have also observed that biophotonic methods can help in precisely controlling drug delivery systems, thereby expanding the scope of targeted medical treatment. Our finding show that light -based techniques such as laser-assisted drug delivery and photothermal therapies are effective in improving the efficiency or drug release. the use of nanomaterials enhance specific targeted drug delivery, thereby reducing side effects and increasing drug efficacy. The potential diagnostic uses of Biophotonics are numerous, with the most promising applications being in the areas of Tumor detection, Tissue imaging, Intracellular imaging, Immunohistochemistry, Infectious agent detection, Multiplexed diagnostics, and Fluoroimmunoassays. Biophotonics also have considerable potential for in vivo imaging, but there are concerns over their toxicity, both to patients and the environment.

The scope of biophotonics in India is quite broad, and b integrative this technology in medical, agriculture, environmental, and industrial application, the country's economy and healthcare system can be enhanced. Its future will play a pivotal role in bringing innovations and solutions in india.

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