

## Biophotonics: An introduction to New Laser Users

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### Abstract

**Purpose:** We aim to elucidate the scientific fundamentals behind biophotonics, to empower laser users in health care, with the basic knowledge of this fast-growing biotechnology field.

**Method:** We will present and discuss relevant aspects of biophotonics, utilizing scientific sources and publications that range from concepts of basic physics to optical properties of biological tissues.

**Discussion:** We will discuss the characteristics of laser light and the optical properties of biological tissues and matter, that governs their interaction with light, fundamental principles for achieving success and safely use this treatment modality.

**Conclusion:** The complexity of the optical properties of light and biological tissues and their interactive behavior, makes biophotonics a challenging science. A minimum understanding, however, is necessary when utilizing this biotechnology. The specific optical properties of the tissue that will be receiving the specific light, will dictate which laser parameters and treatment protocols are best for the interaction to produce the best outcome and in the safest way.

**Keywords:** Biophotonics; Laser-Tissue Interaction, Light-Matter Interaction; Optical Properties of Light; Optical Properties of Tissues; Optical Properties of Matter; Laser Parameters; Laser Characteristics; Laser Safety; Laser Types; Dental Laser; Laser; Wavelengths; Frequency; Pulse; Physics; Photonics; Diode Laser; Electromagnetic Radiation

### Introduction

The biomedical use of electromagnetic radiation (light) in health care, requires a basic foundation of all theoretical concepts involved. Biophotonics is the field of biomedical optics that deals with optical properties that govern the interaction of electromagnetic radiation with biological tissues and matter. Light-induced therapies are currently used in most fields of medicine and dentistry, including cancer treatment. The characteristics of the electromagnetic radiation and the optical properties of biological tissue and matter need to be considered, for optimizing this light-interaction and produce the best treatment outcome for the patient.

Understanding energy and some fundamental concepts of optics, sets the foundation for comprehending laser-tissue interaction. Light interacts in many ways with biological tissues, as it can be observed in the production of melanin or synthesis of vitamin D, as a result of the skin reacting to light rays. This interaction is governed by the optical properties of the tissues or matter, receiving the light energy.

The National Center for Optics and Photonics Education (NCOPE), defines Photonics as “the technology of generating and harnessing light and other forms of radiant energy whose quantum unit is the photon. Lasers and other light beams are the “preferred carriers” of energy and information for many applications. Photonics involves cutting-edge uses of lasers, optics,

fiber-optics, and electro-optical devices in numerous and diverse fields of technology - alternate energy, manufacturing, health care, telecommunication, environmental monitoring, homeland security, aerospace, solid state lighting, and many others" [1].<sup>2172</sup>

Biophotonics relates to the interaction between biological matter and photons. It is used in a wide range of science and technology, including, medical diagnostics, laser technology and therapy. The inherent characteristics of a laser have a direct influence on its interaction with the optical properties of matter, be it a biological tissue or a material.

The smallest amount of energy, that can be transported, in the form of elementary particles or waves, are called photons, and this is what is commonly referred to, as light. This energy can only be seen as light, in a small range of the visible light of the electromagnetic spectrum, however, electromagnetic radiation consists of a wide range of wavelengths and frequencies. Gamma rays, for example, have the smallest wavelengths and its photons carries the highest amount of energy. Most gamma-rays measure  $\sim 10$  picometers. Visible light is in the middle of the spectrum and measures between  $\sim 400$  to  $\sim 700$  nm. On the opposite side of the spectrum, there are low frequency radio waves, measuring up to  $\sim 100$  km in length. The longest radiation known can have a wavelength from  $\sim 10.000$  km to  $\sim 100.000$  km. Visible light has its uniqueness, in that, it is the only radiation of the electromagnetic spectrum that propagates well in water.

### Atomic particle-wave duality behavior

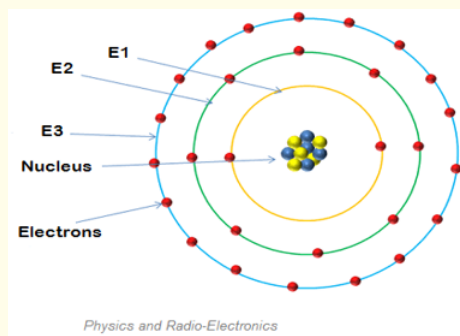
Light was initially described as particles (quantum) or corpuscles (Isaac Newton), later as a wave (Christiaan Huygens, Thomas Young, etc.) and, since the advent of quantum mechanics, light is now considered to have a duality behavior: particle-wave. In physics, all radiations and elementary particles, have the same characteristics: they all have the wave-particle duality, meaning that they can behave as particle, as wave or both and they all travel at the speed of light, but at different frequencies.

The particle behavior of light is noticed, when photons are absorbed or emitted, behaving as a stream of packets of energy (photons). The frequency they travel, is inversely proportional to their wavelengths, so, radiation with shorter wavelengths, travel at higher frequencies and carry more energy. The Wave-Particle Duality property of particles, which includes electrons and photons (particles of light), can be explained by Einstein's theory of photoelectric effect [2].

When trying to explain the phenomenon of light, Einstein stated: "It seems as though we must use sometimes one theory and sometimes the other, while at times we may use either. We are faced with a new kind of difficulty. We have two contradictory pictures of reality; separately neither of them fully explains the phenomena of light, but together they do" [3].

### Light (electromagnetic) energy production

At a microscopic level, electrons have negative charge and always revolve around the nucleus in orbits, and each orbit has a unique energy level.



**Figure 1:** Bohr model of the Atom. Source: [www.Physics-and-radio-electronics.com](http://www.Physics-and-radio-electronics.com).

The current scientific theories have evolved from the works of Max Planck, Albert Einstein, Louis de Broglie, Arthur Compton, Niels Bohr, and many others [4].

Light (electromagnetic) energy is produced, during an electron transition in the atom. In the phenomenon of electron transition, one electron absorbs the energy from one incident photon, then uses part of this energy as kinetic energy, to jump the orbit, and on the way back to its original orbital position, it releases the other part of the excess energy, as a photon. With the classical photoelectric effect, Einstein's equation (1905), a single light particle (photon), of sufficient energy, interacts with a single electron of the material. This phenomenon cannot occur if the incident photon does not contain enough energy to donate to the electron. Increasing the numbers of photons, in this case, will not make a difference, as each electron depends on the amount of energy provided by each single photon, in order to excite it enough to jump orbits. The photonic energy of the incident photon is dependent on its frequency, and this energy will be greater at higher frequencies.

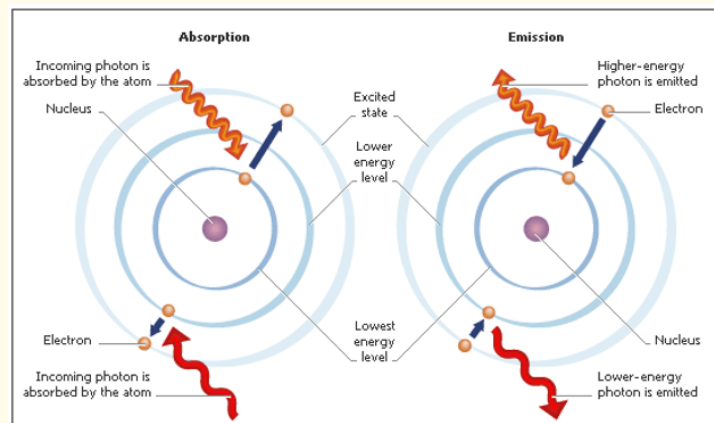


Figure 2: [http://light.physics.auth.gr/enc/wavelength\\_en.html](http://light.physics.auth.gr/enc/wavelength_en.html).

The modern Quantum field theory associate principles of quantum mechanics with those of relativity, to address the behavior of subatomic particles and their interactions. The Quantum electrodynamics (QED) theory explains the interactions of electrically charged particles, with the electromagnetic field; describes all interactions of light with matter and those of charged particles with one another. In this theory, the emission and absorption of “force-carrier particles” (photons), would lead to disturbances of electromagnetic fields. In the QED theory, the photons that carry the electromagnetic force do not radiate further photons. The QED theory, was later, explored in the Quantum chromodynamics (QCD) theory. The QCD theory, foresees the existence of gluons, as the “force-carrier particles”, a form of strong “charge”, which transmit the strong force between particles of matter that carry “color”. These interactions are explained through the emission and subsequent absorption of “particles of light” (massless photons), only possible between electrically charged particles. Here, contrary to the QED, the carrier particles of a force can themselves radiate further carrier particles (photons) [5].

These theories demonstrate that, under suitable conditions, photons may become entirely free of charged particles; becoming detectable as light and as other forms of electromagnetic radiation. Similarly, it suggests that electrons are themselves regarded as disturbances of their own quantized fields. It explains the effects of electromagnetism on electrically charged matter at all energy levels, and that the behavior of atoms and molecules is primarily electromagnetic in nature.

### Production of laser light

Photons interact with the electrons, in three ways: Absorption of radiation, Spontaneous emission (ordinary light) and Stimulated emission (laser light). In conventional light sources, the electron transition is random, and the excited electrons emit photons with different energies, frequencies and wavelengths (or “colors”), at different times and in different directions. Hence, the light of ordinary light sources has multiple wavelengths. The photons emitted by ordinary light sources are out of phase (peak with peak, trough with trough) and have a divergent focus.

In the production of laser light, which amplifies the emission of photons, the electrons must be supplied of energy, by the absorption of “force-carrier particles” (photons), in order to jump to higher orbitals, and liberate more photons on its return to the stable position (electron transition). This energy is supplied by energy from either, heat, electric field or light.

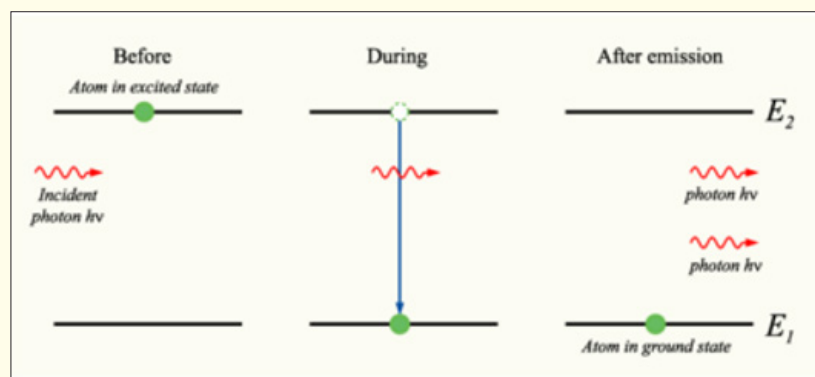


Figure 3: <https://en.wikipedia.org/wiki/Photon>.

Albert Einstein, working on Planck's radiation law, demonstrated a link between the emitted and absorbed photon's rate. The stimulated emission, predicted by Einstein in his kinetic analysis, led to the development of the laser, which inspired further developments in the quantum treatment of light. Planck's Quantum Theory states that energy is not emitted as a continuous emission of energy, but in quanta (small packets of energy) and that a quantum of energy is related to the frequency of the light emitted, by his equation  $E = h\nu$ . The energy and momentum of a photon depend only on its frequency ( $\nu$ ) or inversely, its wavelength ( $\lambda$ ). The frequency dependence of light's energy explains the ability of matter and electromagnetic radiation to be in thermal equilibrium [6]. This thermal equilibrium, determined by the radiation and interaction process, requires that the rate at which photons of any particular frequency are emitted must equal the rate at which they absorb them [2,6].

As mentioned above, electrons and the photons interact in three ways: absorption of radiation, which is the process by which electrons in the ground, low state, absorb energy from photons to jump into a higher energy level; spontaneous emission, which produces ordinary, non-coherent light, where the electron returns to the lower energy state, liberating 1 photon of energy; and the stimulated emission, in the case of a laser, where one additional photon of energy is emitted. In this process, an incoming photon of a specific wavelength interacts with an excited atomic electron, causing it to drop to the lower energy level emitting 2 photons, with the same phase, polarization, frequency, that travel in the same direction and are all identical to the photons of the incident wave. In a laser, this process is repeated, so, the emitted photons, again, interact with an excited electron, emitting another two photons, causing it to drop to the lower energy level. Population inversion occurs when there are more atoms and molecules in a higher excited energy state than in the low energy state,

disturbing the thermal equilibrium of the atom system. This is necessary for the production of laser light. By the repetition of this process, the laser amplifies the emission of photons, generating millions of photons and producing high energy light waves. This is in contrast to spontaneous emission, which occurs at random intervals without regard to the ambient of the electromagnetic field.

Laser light is produced with a single wavelength, measured in nm, as this is one of the characteristics of a laser. The electromagnetic spectrum frequencies consist of photons, which are individual quanta packets of energy. In physics, a quantum is a discrete amount of energy that is proportional to the frequency of the radiation it represents. The laser emits highly directional (polarized), amplified, intense light. Some lasers generate visible light, while others generate invisible light, and this will depend on the wavelength of the frequency (Hz) of the laser light produced.

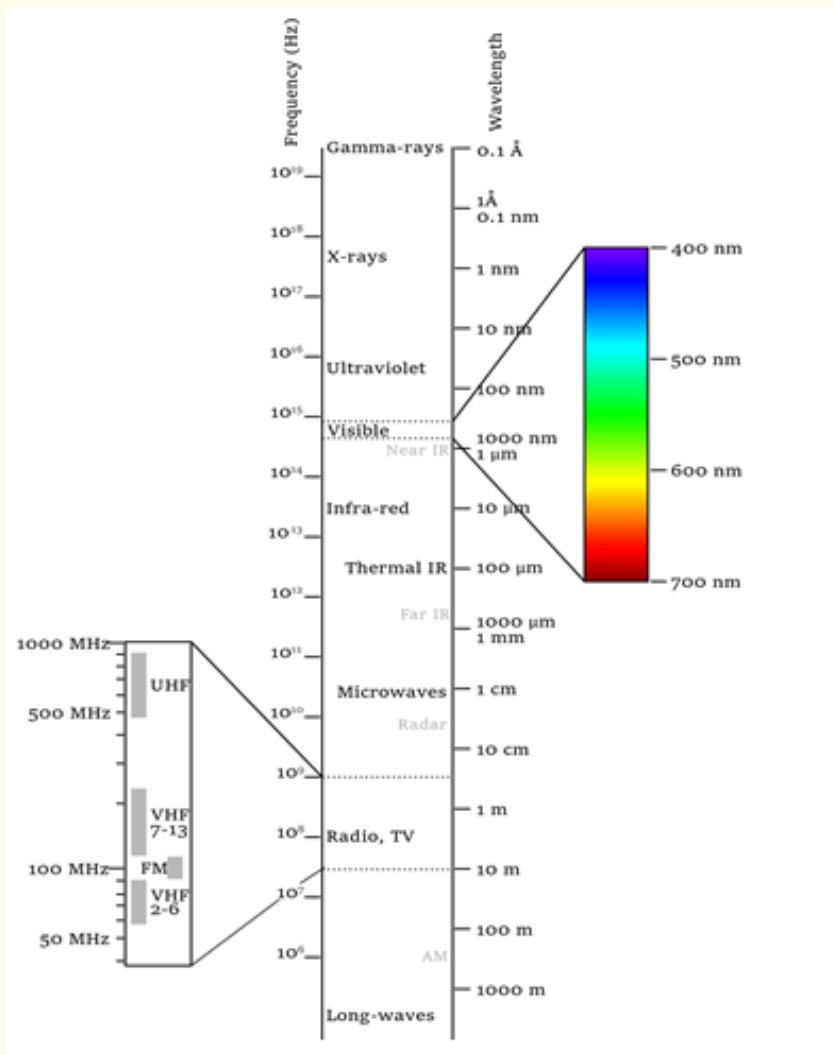
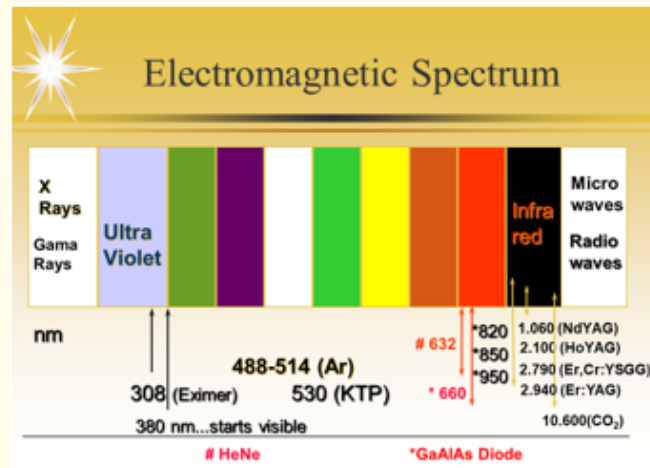


Figure 4: Electromagnetic spectrum of radiation - Source: Wikipedia.



**Figure 5:** Electromagnetic spectrum illustrating a range of most used lasers in biomedicine.

“In the weak field regime, only one photon is absorbed, but under intense field conditions more than one photon can be absorbed for a transition” [7].

“In the classical photoelectric effect process, only at very high intensities, does the multiphoton ionization occur, a process which is described in the extreme case, of highly intensive, ultra-short light flashes, such as those emitted by long-wave femtosecond lasers” [8]. Multiple photons absorption is possible in principle, but much less probable. Since the advent of high-power lasers, multiphoton ionization of atoms has become an active area of research. In multiphoton ionization, the ionization takes place, via a nonlinear optical two-photon absorption (two photons being absorbed simultaneously), creating two-photon transitions.

An excited state can absorb more energy, so multiple photons can excite an electron through multiple levels, over time, if the orbital doesn't lose its energy in the meantime. The probability for multiphoton absorption is dependent on the number of photons incident, per unit time, on the atom or molecule. The absorption of the next photon depends upon it arriving before the “de-excitation” of the atom or molecule. “Although these events are less likely than the single photon absorption, their probability scales with the intensity of the light source, so high power laser irradiation is certainly capable of producing them” [9,10].

In the extreme ultraviolet range, the behavior of interaction of high-power lasers with matter could not be explained by the standard theories developed for optical strong-field phenomena. “With extremely short wavelengths and very high intensities, light-matter interaction seems to be different than previously accepted, as with xenon, a whole light-wave packet immediately seems to knock out a huge number of internal electrons. This effect is strongly dependent on the material and not only on the characteristics of the exciting radiation, as accepted before” [8]. The exceptional behavior of light-matter interaction in the extreme ultraviolet was demonstrated in a study on the photoionization of different rare gases, when applying ion spectroscopy at the wavelength of 13.7 nm and irradiance levels of thousands of terawatts per square centimeter. It was found that the degree of nonlinear photoionization on Xenon gas, was significantly higher than those for neon, argon, and krypton. The role of giant resonances and collective effects on photoionization in the high-intensity short-wavelength regime was challenged in the particular behavior of xenon gas, demonstrating that: the inner-shell electron structure, the electron correlation and resonances, all play a significant role in explaining strong-field phenomena on photoionization in the short-wavelength regime of Einstein's photoelectric effect. It was proposed that “the collective giant 4d resonance of xenon is the driving force behind the effect that arises in this spectral range” [11].

## Light energy

Light has three important properties that are interrelated: Wavelength, speed, and amplitude. The wavelength determines the type of light, such as "color", etc. The speed is determined by the matter light will travel through, such as vacuum, water or other matter. That leaves amplitude as the variable available for determining the light intensity, independently of the type of light and/or the medium that the light is passing through.

The amplitude of the light determines how much energy the waves carry. The intensity/brightness of a monochromatic laser light is directly proportional to the number of photons. So, we can say that the amplitude of a light wave depends on the number of photons, per second, being emitted. The greater the amplitude of a certain type of light, the greater the number of photons, per second, of that type of light.

The intensity/brightness of light is proportional to the amplitude squared of the waves. If we ignore the constants, we can say that:  $I \propto A^2$ , where  $I$  = intensity and  $A$  = Amplitude. The intensity increases the number of photons, without changing the frequency or distribution of that frequency. The more photons emitted per unit time, the greater the intensity of that light.

A single photon has wavelength and speed. The energy of a photon can be calculated using Planck's equation:  $E_{\text{photon}} (\text{J}) = h\nu$ , where,  $E_{\text{photon}}$  = energy of a photon in joules (J);  $h$  = Planck's constant ( $6.626 \times 10^{-34}$  J·s);  $\nu$  = the frequency of the light in Hz.

As we can see from Planck's equation, the energy of a photon is proportional to the frequency of the light ( $\nu$ ) and the light frequency ( $\nu$ ) is inversely proportional to wavelength  $\lambda$ .  $c = \lambda\nu$ , where,  $c$  is the speed of light (constant). As the wavelength of a photon is increased, the light frequency decreases, therefore, as the wavelength of a photon increases, its energy also decreases.

## Light propagation

According to CIE (Commission Internationale de l'Eclairage) regulations, the term "wavelength" refers to "wavelength in air" unless otherwise stated. Electromagnetic waves in vacuum travel in the speed of light, whilst, in a material medium, the atoms interact with light and the phase velocity of the waves change. The velocity ( $c$ ) of this propagation depends on the nature of the wave and on the medium. A higher refractive index slows the travel velocity of the waves and reduces the wavelength (Table 1 and 2).

Optical (electromagnetic) radiation velocities in different media				
Sound	At $\lambda=434$ nm	At $\lambda=589$ nm	At $\lambda=656$ nm	
In vacuum	-	299792 km/s (n = 1)	299792 km/s (n = 1)	299792 km/s (n = 1)
In air	340 m/s	299708 km/s (n = 1.000280)	299709 km/s (n = 1.000277)	299710 km/s (n = 1.000275)
In water	1500 m/s	223725 km/s (n = 1.340)	224900 km/s (n = 1.333)	225238 km/s (n = 1.331)

**Table 1:** Velocities of sound and light in air and in water. For optical radiation, the respective index of refraction is given in parenthesis.

Source: <https://light-measurement.com/measures-of-wave/>.

A green light of 520 nm, in vacuum, for example, will have its velocity in water reduced by a factor of 1.33, therefore, the same green light will have a wavelength of only  $520/1.33 = 391$  nm. Hence, if we want to characterize a wave by its wavelength, we also have to state for which medium the actual wavelength value is given. The medium's index of refraction ( $n_{\text{Medium}}$ ) is more commonly used to specify the optical properties of a material than the velocity in the  $c_{\text{Medium}}$  [12]. A denser material has a bigger index of refraction. A non-uniform medium has different refraction indexes. When light travels from a less dense to a fender medium, at the border-line, some of the energy will reflect back to the first medium, and the remainder, transmitted to the second medium, will change direction (refraction). Also, the light passing through the first medium will be faster, that causes light to bend and change beam direction when entering and traveling through the denser second medium.

Refractive index of different materials, at specific wavelengths		
Material	Wavelength $\lambda$ (nm)	Refractive index n (-)
Air	all	$\sim 1$
Water	0.65	1.33
Al10Ga90As (AL GaAs)	885.7	3.530
Al20Ga80As (AL GaAs)	885.7	3.465
GaAs	0.88	3.6
Sapphire ( $\text{Al}_2\text{O}_3$ )	0.83	1.76

**Table 2:** Illustration of Refractive index n (-) of different materials at different wavelengths.

Source: Palik 1985, "Handbook of Optical Constant of Solids" by Edward Palik (1985)

Measurements of the reflectivity of evaporated Ag films by Hong Luo and Yun-Li Li).

### Laser-tissue interaction

The comprehension of the different characteristics between conventional light and laser light is also fundamental for understanding the production and use of laser devices.

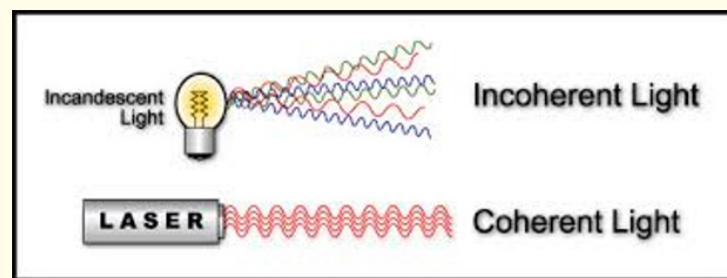
All photons emitted by a laser have the same energy, frequency, or wavelength (or "color"). The wavelengths of laser light are in phase in space and in time. Laser has the following relevant characteristics over an ordinary light source:

- **Monochromaticity:** Relates to its constant wavelength ( $\lambda$ ). Although it is impossible to achieve a perfectly monochromatic light wave, as even a monochromatic wave contains a spread of frequencies. Laser light covers a very narrow range of frequencies. Monochromaticity is a determinant factor for the interaction with biological tissues, since it needs to be absorbed in order to interact with any tissue or matter. Biological tissues have light receptors (chromophores) that are highly selective to the wavelength it absorbs. In the case of biological tissues, common chromophores include hemoglobin, oxyhemoglobin, melanin or water.
- **Polarization/directionality:** This is the other characteristic of a laser that can also affect the interaction with matter. Different polarizations of light can be absorbed to different degrees by different biological tissue or matter. In polarized light, the wave oscillates perpendicularly to the direction of propagation (peak and trough are travelling linearly, in the same plane). In most cases, the output of a laser is linearly polarized. Some modern lasers, however, do not generate a linear, polarized output, or the polarization is unstable. Mode-locked, ultra-fast fiber lasers are becoming commonplace and they depend on nonlinearity. Although, the existing market for ultrafast lasers remains dominated by solid-state lasers, primarily Titanium-sapphire lasers ( $\text{Ti:Al}_2\text{O}_3$ ), the association of optical science with applied nonlinear dynamics, allowed the increase of pulse energies by multiple orders of magnitude. These ultrafast fiber lasers have the potential to make applications of ultrashort pulses, with larger peak intensities, widespread in compact, versatile, low-cost devices [13]. The laser may be polarization dependent. i.e. some anisotropic laser crystals, (Nd: YVO4 or Nd: YLF) and some semiconductors. Laser light is polarized due to the use of a "Brewster window", which acts as a mirror and output. Optical design frequently focuses on the wavelength and intensity of light, while neglecting its polarization. Different polarizations of light, however, can be absorbed to different degrees by different matters. A study, quantifying the degree of polarization subsequent to passage through various biological tissues, found different propagation degrees for linearly and circularly polarized light. They also, identified regions that demonstrate greater likelihood of preference for polarized light, and, finally, "indicated the structural features in tissue that influence the degree of polarization and the importance of these structures on polarized light propagation". They suggested that the underlying factors for this difference in polarization within different tissues could be attributed to various scattering parameters [14]. This property, for instance, can affect the use of optical imaging, with biologic tissue, with nonionizing radiation.

- **Coherence/in phase:** Due to this property, a large amount of power can be concentrated into a narrow spot size beam. For some laser-biological tissue interactions, light coherence is not fundamental. “In recent years, non-coherent light sources such as light-emitting diodes (LEDs) and broad-band lamps have become common in biophotomodulation therapy” [15].

In weak incoherent CW light, photoinduced biological processes is induced via one photon absorption from a pulsed coherent laser source or from an incoherent thermal source of electromagnetic radiation, both, using a quantized radiation field. However, a pulsed coherent laser source has been shown to induce time evolution in the molecule, while the incoherent thermal source of electromagnetic radiation does not. Confusions in the literature regarding this issue are shown to emerge from a lack of appreciation of (a) the proper description of the absorbed photon and of (b) the role of measurement in understanding the process [16].

**Intensity (brightness):** Determined by the amplitude of the wave, as previously discussed.



**Figure 6:** Coherence of light illustration. Source: Victoria Kasamba Ngeyaabwe: <http://lightfest2.astonwordpress.co.uk/3-things-you-probably-didnt-know-about-lasers/>

**Collimation:** Non-divergent, parallel rays generate minimum beam spread as they propagate over a distance. The more collimated the light beam is, the less it becomes divergent when travelling over a distance. When collimated laser light, travels it basically maintains its beam spot size (diameter) and don't lose any significant amount of energy on the way. Laser light from gas or crystal lasers is highly collimated. Laser diode devices, on the other hand, emit less-collimated light, due to their short cavity, so they require a collimating lens, in order to achieve a higher collimation.

A laser can deposit a great amount of energy within a very small area (spot size). The diameter of the beam influence the amount of energy delivered by the laser, as light energy gets concentrated with the reduction of the beam diameter.

Ordinary light is non-collimated. As it travels, its diameter spreads out, the beam spot size increases in diameter, and the light loses energy on its way. With non-collimated light beams, it is not possible to quantify the energy dosage delivered to its target unless the beam is in direct contact with the tissue.

### Laser construction

A typical laser consists of an optical cavity, a laser medium and one mirror at each end of the cavity. when more than 50% of the atoms in the laser medium are in the excited state (population inversion), the creation of laser light is achieved.

A typical laser is constructed from three principal parts: An energy source (usually referred to as the pump or pump source), A gain medium or laser medium, and Two or more mirrors that form an optical resonator.

The pump source or energy source is the part of a laser system that provides energy to the laser medium. To get laser emission, the energy source needs to supply enough energy to create a population inversion in the active laser medium. The energy source used depends mainly on the laser medium.

Lasers can be subdivided by the type of medium:

- **Solid-state laser:** These utilize light energy as a pump source to supply energy to the medium. The medium is in a solid-state. Common solid-state laser media are sapphire ( $\text{Al}_2\text{O}_3$ ), neodymium-doped yttrium aluminum garnet (Nd: YAG), neodymium-doped glass (Nd: glass) and ytterbium-doped glass and ruby crystal laser. Dopants, such as cerium (Ce), erbium (Eu), terbium (Tb) are used to add ions as impurities, to the medium substance.
- **Gas laser:** Use electric current as the pump source. The medium is in the gaseous state and is made up of a mixture of gases, packed into a glass tube. Common gaseous state lasers mediums include carbon dioxide lasers ( $\text{CO}_2$  lasers), carbon monoxide (CO lasers) and helium-neon (He-Ne) lasers. Excimer lasers use reactive gases such as chlorine and fluorine mixed with inert gases such as xenon, krypton or argon. Excimer lasers produce light in the ultraviolet range. Carbon dioxide lasers emit energy in the far-infrared, whilst helium-neon lasers emit light in the visible red spectrum.
- **Liquid laser:** Utilize light energy as the pump source. The medium is in the liquid-state. Dye lasers use complex organic dyes in a liquid solution or suspension, as the laser medium. Common organic dyes are rhodamine B, sodium fluorescein and rhodamine 6G. They are adjustable over a broad range of wavelengths.
- **Semiconductor or diode lasers:** Electronic devices, generally small and with lower power than the above lasers. Most semiconductor diodes lasers are pumped with an electric current, in a region where the n-doped and a p-doped semiconductor material meet. There are also the optically pumped semiconductor lasers, where carriers are generated by an absorbed pump light, and the quantum cascade lasers, where intra-band transitions are utilized.

### Mode of emission of laser radiation

Laser devices can emit light energy in two main modalities:

- **Continuous wave (CW):** Emission is constant (“on all the time”), with a continuous average power.
- **Pulsed or gated-pulse mode lasers (on and off emission):** Pulsed wave lasers use pulses to interrupt the emission of the laser light at different intervals [frequency (Hz)], using different pulse durations. They emit a periodic alternation of the laser energy.

Surgical lasers tend to work with pulse, and the thermal relaxation time of biological tissues, to reduce the undesirable effects of thermal damage.

Single pulsed, also known as long pulse or normal mode lasers have varied pulse durations.

Mode-locked lasers can affect the characteristics of the output beam. It can synchronize and lock together the phases of different frequency modes, which in turn will interfere with one another to generate a “beat effect”, with regularly spaced pulses. These lasers can deliver extremely high peak powers, often in the range from  $10^{12}$  W, with extremely short pulse durations of around  $10^{-15}$  (femto) to  $10^{-12}$  (pico) sec.

Pulse duration (for how long each pulse stays on): super-pulse laser, ultra-speed, Q-Switch, picoseconds laser, etc. The pulse duration can be described in milliseconds (ms), microseconds ( $\mu\text{s}$ ), nanoseconds (ns), picoseconds (ps), femtoseconds (fs) or attoseconds (as).

Lasers with pulse duration in nanoseconds, also called “Q-switch” have high peak power, making it possible to generate pulses with durations ranging from fractions to hundreds of nanoseconds, with peak power ranging from 10 kW to 100 MW as “Giant pulses”. A

Q-switched CO<sub>2</sub> laser, for instance, can have pulse duration of about 50-100 ns, and shorter pulse durations can be achieved by mode-locking Transversely-Excited Atmospheric-Pressure (TEA)-CO<sub>2</sub> lasers. Some diode lasers have a pulse width adjustable of between 3 and 100 ns, also known as picosecond lasers.

Pulse repetition rate (PRR) or pulse repetition frequency (PRF), is the number of pulses repeated in a specific time unit, normally measured in pulses per second.

### Some reasons for pulsing lasers are:

- The inability of a particular laser to produce an emission in a continuous form;
- The ability to deliver high dosage of energy in a short time, reducing thermal damage;
- The ability to deliver high peak pulse power, to obtain nonlinear optical effects (related to the polarization dependence of some tissues).

### Laser safety - Laser hazard classification

Laser safety standards is based on the ability of a laser beam to cause biological damage to the eye or skin. The Occupational Safety and Health Administration (OSHA) and international standards classify lasers, according to their potential hazards, into four major classes. The classification is intended to establish measures and medical surveillance and to regulate the use of labels and instruction for the users. The hazards depend on the corresponding levels of accessible laser radiation [17]:

- **Class I:** Not capable of emitting hazard levels of laser radiation. Typically have a continuous wave, 0.4 μW, at visible wavelengths. Users are exempt from radiation hazard controls during operation and maintenance.
- **Class I A:** Based on a limit of a maximum 1000 second emission exposure, they are lasers "not intended for viewing" (i.e. supermarket laser scanner). They have a max power limit of 4.0 mW.
- **Class II:** Still low-power visible lasers, but the radiant power does not exceed 1 mW. Only needs limited safety controls.
- **Class III A:** The continuous wave power ranges from 1 to 5 mW. It is a hazard only to intra-beam viewing. They have only limited safety controls. The labeling requirements (caution logotype) for powers up to 2.5 mW/cm<sup>2</sup> are different than those with higher power (danger logotype) within this range.
- **Class III B:** Have moderate power on continuous wave ranging from 5 to 500 mW, pulsed at 10 J/cm<sup>2</sup> or the diffuse reflection limit, whichever is lower. It does not offer a fire hazard, nor is capable of producing a hazardous diffuse reflection. Requires specific safety controls.
- **Class IV:** These are high power lasers (continuous wave: 500 mW, pulsed at 10 J/cm<sup>2</sup> or the diffuse reflection limit). These lasers are hazardous to view, directly or diffusely scattered. They offer a potential skin and fire hazard. Significant safety controls are required for Class IV laser facilities.

There are two chief types of biomedical lasers and the major areas of laser applications in the biomedical field are in cellular research, dentistry, diagnostics, dermatology, ophthalmology and surgery.

High power lasers, also sometimes described as "hard" lasers, such as CO<sub>2</sub>; Nd: YAG; Er: YAG; Er,Cr:YSGG; Ho:YAG, Diode lasers, etc. Are used for either or both: hard and soft tissue applications.

Low power lasers, also known as low-level, "soft", "cold" or therapeutic lasers, are used for biophotomodulation and Photodynamic therapy, etc.

### Laser-tissue interaction

When planning a treatment protocol not only the knowledge of the optical properties of electromagnetic radiation is important, but also, the understanding of the optical properties of the tissue or matter which will be interacting with the specific light. When light is applied to tissues or matter, it presents different behaviors, depending on the optical properties of the recipient. Light interaction with matter will be influenced by the recipient's optical properties; light can suffer absorption, scattering, penetration (transmission) and fluorescence (reflection). Optical absorption and scattering coefficients, anisotropy, reduced scattering index, refractive index, light diffusion, reflection of multi-scattered light, are all optical properties that affects light absorption by the light receptors (chromophores) and this has been tabulated in many studies for prediction of the optical behavior of biological tissues [13]. In order for laser light to produce an effect on a tissue, it needs to be absorbed. Its wavelength has been shown to be partly responsible for the penetration depth of laser light, with visible light being more readily absorbed than infrared wavelengths [18,19].

Parameters affecting light-tissue interaction in laser therapy have been described as: Laser Variables: Laser Power, Light Delivery Protocol, Power Density Profile of the Beam, Gaussian Beam Profile, Top-Hat Beam Profile, Irradiation Spot Size, Power Density and Energy Density of a Light Source, Local Beam Angle of Incidence with the Tissue, Collimated or Diffuse Irradiation, Light wavelength, Pulse Repetition Rate, Pulse Length, Light Delivery Pulse Modulation. Tissue variables: Optical Properties of the Tissue, Tissue Index of Refraction, Surface Contour, Tissue Temperature, Thermodynamic Tissue Properties, Tissue Blood Flow and Blood Content [20].

A study demonstrating the wavelength dependence on the tissue penetration, for the application of transcranial low-level laser therapy (LLLT), compared the fluence distribution, penetration depth and the intensity of laser-tissue-interaction within brain, utilizing the Monte Carlo modeling and visible human phantom, at various wavelengths, found a better performance with 660 nm, immediately followed by 810 nm. The latter performed much better than 980, 1064 nm, with much stronger, deeper and wider photon penetration into cerebral tissue [21]. Wavelength was also shown to be partly responsible for the penetration depth of laser light, with visible light being more readily absorbed than infrared wavelengths [18,22].

The *in-vivo* optical properties variation is tissue-type dependent, and the overall trend of the absorption spectra has been described to be a function of wavelength. A main factor, which affects the accuracy of the determined fluence rates in tissue, been the heterogeneous optical properties distribution. The impact of optical properties on light fluence rate is also dependent on tissue geometries, including superficial, interstitial, and within a cavity, and the fluence rate is a function of the beam radius [23]. Refraction, reflection and back-scatter also affects laser absorption [24]. For the application of any "light" (electromagnetic radiation) therapy, the photons must penetrate the tissue and deposit its energy, via the optical absorption properties of that tissue. The varied, presence and number, of absorbing chromophores, such as blood components (Hemoglobin, Oxyhemoglobin), water, melanin, fat, yellow pigments (bilirubin, beta-carotene), in different types of tissues, and the tissue scattering properties, determine its wavelength dependence [13]. Pigment-specificity can affect penetration and absorption. Wilson and Jacques found that visible laser light, of short wavelength (between 400 nm and 700 nm) was highly absorbed by melanin, hemoglobin and myoglobin [25], whilst infrared wavelengths have little pigment-specificity and the prime absorbing media are proteins and water [26].

Laser-tissue interaction is highly complex, and laser parameters widely influence the biological tissue response. For years, studies have been demonstrating various cellular responses to different lasers, such as the increase of mast cell numbers and degranulation [18], the enhancement of procollagen production in human skin fibroblast cultures [27] and the stimulation of fibroblast proliferation and macrophage responsiveness [28]. Karu found that irradiation with monochromatic visible light in the blue, red and far red regions can enhance metabolic processes in the cell and suggested that the photobiological effects of stimulation depend on the wavelengths, dose and intensity of the light [29].

A study reporting the wavelength dependent behavior of scattering and absorption of light by various biological tissues (brain, bone, soft and fibrous tissues, skin, fat, etc.), presented “formulas for generating the optical properties of a generic tissue at any wavelength in the UV-visible-near-IR range, based on variable amounts of absorbing chromophores: blood components (Hemoglobin, Oxyhemoglobin), water, melanin, fat, yellow pigments (bilirubin, beta-carotene) and a variable balance between small-scale scatterers and large-scale scatterers in the ultrastructure of cells and tissues” [13]. According to this study, this model, would allow for the prediction of expected standard behavior of the optical properties of live tissues, based on their constitution, which yields their optical properties, at any given wavelength. Using optical absorption spectra coefficients of chromophores, optical scattering coefficients, and refraction indexes, to describe standard scattering behavior versus wavelength, he proposes that analyzing these data on three wavelengths is sufficient to predict scattering at all wavelengths in the UV, Visible and Near-IR ranges, based on variable amounts of absorbing chromophores (blood, water, melanin, fat, yellow pigments) and a variable balance between small-scale scatterers and large-scale scatterers in the ultrastructure of cells and tissues. He further suggests that these 3 parameters influence light penetration behavior and this approximate values for the optical properties of generic tissue types enables the use of light transport models to predict optical behavior.

### **Thermal properties of the biological tissues**

Bouloinois [30] classified lasers into 4 groups, according to their biological interactions:

- (1) Electro mechanical effect
- (2) Non-thermic effect (photochemical, photophysical, photo-bio-stimulating)
- (3) Photo ablative effect
- (4) Photothermal effect:
  1. Vaporization
  2. Coagulation
  3. Protein denaturation.

An important aspect of the laser-tissue interaction to be considered in biomedical studies are the thermal properties of the tissue and the thermal changes caused by the interaction of light with the tissue. The thermal properties are related to the temperature distribution in the tissue. This is well explained in the study by Ansari, *et al.* “The transportation of thermal energy in biological tissues includes different phenomenological mechanisms such as thermal conduction, convection, radiation, metabolic activities and phase change. A laser can induce multiple effects like coagulation, vaporization, carbonization or melting. These effects depend on the peak power and wavelength of the laser, as well as the thermal properties of biological tissues”. “The vaporization of water occurs at 100°C. In the vaporization, or “thermomechanical” procedure, the temperature of tissue does not alter within the vaporization phase, and gas bubbles are formed. The propagation of these bubbles, along with the alteration of their volume, causes thermal decomposition of tissue fragments. If all water molecules are vaporized, carbon atoms are released and the adjacent tissues are blackened, causing the presence of smoke. This stage is called carbonization. Finally, beyond 300°C melting might occur” [31]. This topic is well also well explored in the literature [31-34]. The distinct interaction principles of photophysical, photochemical, and photobiological mechanisms and other aspects of laser-tissue interaction is extensive and can also be easily found in the literature [35-39].

### **The Future**

Ultrafast laser pulse technology, with the exploration of nonlinearity optical engineering, recently allowed the production of lasers that operate at very high speed and support extremely high peak powers. With the innovative use of nonlinearity, it was possible to develop mode-locking technology, and ultrafast fiber lasers technology. A paper discussing the prospects for trends on future laser technology, identified three promising directions: “mode-locked oscillators that use nonlinearity to enhance performance; systems that use nonlinear

pulse propagation to achieve ultrashort pulses without a mode-locked oscillator; and multimode fiber lasers that exploit nonlinearities in space and time to obtain unparalleled control over an electric field”, They reported the increasing trend for the prospective applications of ultrafast lasers and that Mode-locked fiber lasers are becoming commonplace in chemistry, biology, and physics laboratories [40]. The increasing number of recent papers in the literature, reporting the potential benefits of the use of low power lasers for photobiomodulation and photodynamic therapy also points to an increased trend towards the use of biophotonics. This reinforces the necessity for health care professionals to seek a minimum understanding of this fast spreading biotechnology [41,42].

### Conclusion

Understanding the fundamentals of laser light, the optical properties of matter (biological tissues and dental materials) and light-tissue interaction, is essential for all health professionals wishing to work with lasers. The complexity of the optical properties of light and biological tissues and their interactive behavior, makes biophotonics a challenging science. A minimum understanding, however, is necessary when utilizing this biotechnology. The specific optical properties of the tissue that will be receiving the specific light, will dictate which laser parameters and treatment protocols are best for the interaction to produce the best outcome and in the safest way.

The recent accelerated new discoveries in the field of photonics have stimulated the rise in the interest observed in the science of biophotonics. These driving forces for the exploration of this biotechnology are constantly allowing new applications and provides great hope for newer future capabilities previously unthought of.

### Conflict of Interest

None. This work is independent and has been carried out with no financial support or commercial or monetary interest for any of the authors.

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