

# Photoacoustic Spectroscopy and Its Applications in Biology, Radiotherapy, and Imaging - A Brief Overview

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# Photoacoustic Spectroscopy and Its Applications in Biology, Radiotherapy, and Imaging - A Brief Overview

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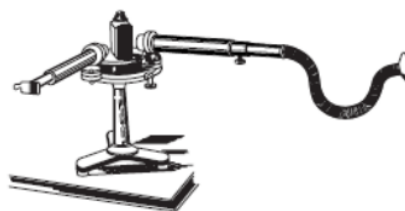
**Abstract:** The photoacoustic spectroscopy for non-destructive measurements has been developed in many attractive research areas. In this spectroscopy, high energy laser beam is used for irradiating the material. Light beam will produce a thermal expansion (increasing in heat temperature) within the material, which is then generating an acoustic wave. This review paper presents the photoacoustic spectroscopy for biology, radiotherapy, and imaging applications.

**Keywords:** photoacoustic, biology, radiotherapy, imaging

## 1. Introduction

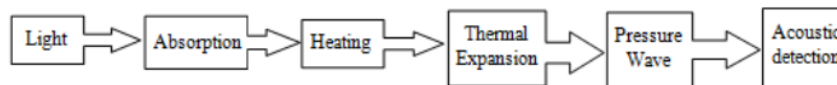
Photoacoustic phenomena were first discovered by Alexander Graham Bell, 1881, when he observed the formation of sound waves from a solid material illuminated by sunlight. The intensity of sunlight radiation is directed at a closed glass vessel containing a solid sample that absorbs infrared radiation. With a spectrophone (a kind of microphone) he can hear very weak sounds due to radiation absorption by solids. Bell used a spectrophone (as shown in Figure 1) to test the visible light absorption spectrum in the sun [1]. This instrument is wirelessly equipped.

The basic principles of photoacoustic spectroscopy can be explained as follows. In gas phase photoacoustic spectroscopy, an electromagnetic wave (e.g. laser light) as an intensity modulated radiation source is passed to a photoacoustic cell containing absorbing gas molecules. When the gas molecules absorb the energy of the photons, the gas molecules that are occupying the basic energy level will be excited to the higher energy level. Gas molecules in an excited state are unstable and will tend to return to a stable state (basic energy level) by releasing energy through the de-excitation process.



**Figure 1:** The spectrophone used for the first time for photothermal absorption analysis

The de-excitation process of molecules in this photoacoustic spectroscopy (with CO<sub>2</sub> laser radiation emitting infrared radiation at  $\lambda$  about 10  $\mu$ m) is the most dominant is non-radiation de-excitation, where in this non-radiation de-excitation a collision occurs between molecules so as to allow heating of the medium inside the cell. At constant volume heating this temperature results in a change in pressure in the cell. If the radiation source coming to the sample gas intensity is modulated periodically, then the periodic pressure changes in the cell will also be obtained which generates a sound at the same frequency as the modulated radiation frequency. The sound that is formed can be detected using a microphone, then amplified by an amplifier, then converted into an electrical signal that is displayed on the oscilloscope [2]. It can be briefly shown in Figure 2.



**Figure 2:** Basic principles of photoacoustics

This photoacoustic spectroscopy has several advantages such as simple equipment but has high (can detect gas concentrations reaching the order of ppm, parts per million) and easy calibration. Photoacoustic spectroscopy is a type of spectroscopy that utilizes its phenomena as a work basis to generate sound waves in accordance with the heat arising from radiation emission to radiation energy absorbing materials [3, 4].

## 2. Photoacoustic Applications

The photoacoustic spectroscopy is increasingly being used for various applications in non-destructive testing and has great potential in several biological/biophysics applications. Mesquita [5] studied the applications of the open photoacoustic cell (OPC) technique in studies of photosynthetic activity in plant leaves. Hu and Wang [6]

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reviewed the photoacoustic microscopy (PAM) offers unprecedented sensitivity to optical absorption for biological systems study. In terms of monitoring biophysical changes, Hys[7] has developed the functional and structural changes of tissue that form the basis of photoacoustic imaging biomarkers for early cancer treatment monitoring. Li [8] has simulated the numerical method to characterize the photoacoustic waves based on the calculation of spheroidal wave functions. Vries [9] used a photoacoustic effect to test the ripeness of fruits.

Photoacoustic laser experiments have been carried out to study the dynamic behavior of nitrogen fixation [10]. To avoid volume buffering of water, the algae *Spumigena Nodularia* type was placed on filter paper and a mixture of  $O_2$  and  $N_2$  gases with different acetylene concentrations on top of the sample. In this way the influence of parameters such as light intensity and temperature can be studied with a time resolution of 20 seconds.  $NO_2$  trace gas at pptV level is monitored by low-cost photoacoustic and the limit of detection was 33 pptV [11]. Measurements of the effects of ultraviolet (UV) radiation on human skin are presented to illustrate the possibilities of photoacoustic detection in this field. In trials skin lipid peroxidation was monitored [12]. UV radiation causes reactive oxygen species to form on the skin [13].

Photoacoustic developments in liquids or gases caused by the interaction of laser radiation are used as the assessment mechanism. The biological effects of laser radiation have been studied intensively since the inception of the use of lasers in medical research [14]. Pressure changes as the result of laser irradiation can result from either ablation or thermoelastic heating. Thermoelastic heating, has more complex pressure wave characteristics than ablation [15]. The interaction of biological tissue and photoacoustic waves has a complicated process [15, 16].

The study of the biological effects of photoacoustic waves is the combined effect of laser irradiation, heating effect, cavitation, and pressure with pulse laser energy below the ablation threshold [16, 17]. The study emphasizes the mechanical pressure waves and their physical effects on the tissue. What is known as photomechanical ablation is usually used to explain this effect. Whereas the effect of pressure changes on biological tissue is used in the approach of cell culture by using a readily absorbent material (polyimide or polystyrene) as a laser target, using a high enough pressure (several hundred bars) so that the effect of these pressure changes will be spread into cells with minimized regulation of the effects of laser radiation, heat and cavitation.

The ablation technique with laser irradiation is mainly based on three processes namely photothermal, photochemical and photomechanical decomposition [16]. Photothermal decomposition refers to the ablation of tissue by evaporation of the tissue due to irradiation at relatively high temperatures. Photochemical decomposition is caused by chemical interactions of molecules in the network with photon energy resulting in changes in chemical bonds [17].

Both of this process require a relatively high laser intensity to achieve effective ablation. On the other hand, the photomechanical ablation process requires 10 times less laser energy density than for complete evaporation [18]. This process controlled by ablation method has implications with minimal damage to tissues. The mechanism of the photochemical ablation process was described by Paltauf [15] as shown in Figure 3.

A laser pulse is used to generate thermoelastic pressure in the tissue (figure 3 (a)). The initial pressure distribution in the network is determined by the optical absorption coefficient, which is assumed to be constant. This initial pressure distribution is completely positive in the direction perpendicular to the surface. Thermoelastic pressure waves propagate in the right-hand direction at the speed of sound across the network. Due to an acoustic mismatch at the air network interface, a negative pressure (tensile stress) is created (figure 3 (b)). Since most of the materials in the network have a weaker stress than their compression, the resistance of the material will fail if the tensile stress is applied beyond its threshold. If the negative pressure (tensile stress) is at its threshold (figure 3 (c)), it is likely to cause tissue fracture or cavitation at a certain depth [19] (figure 3 (d)) followed by the release of the tissue fragments on the front surface. (Figure 3 (e). The term of "photospallation" has been used to describe this effect [15,20]. It should be noted here that not only tensile stress but heating also contributes to material ablation [15].

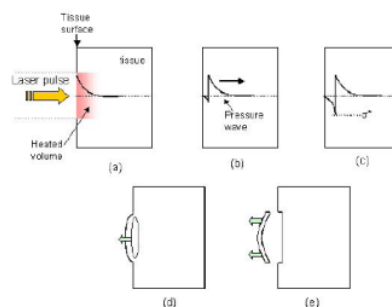


Figure 3: Mechanism of photomechanical ablation [15]

Several applications of rear detection models have been carried out including imaging of layered structures in biological tissue [21], monitoring of blood oxygenation to the brain [22, 23], and monitoring of the optical properties of blood [24]. In monitoring blood oxygenation, the Nd: YAG and Alexandrite laser systems are used to provide laser pulses at wavelengths of 1,064 and 750 nm. Blood oxygenation is a measure of oxyhemoglobin saturation, which is determined by the concentration of oxyhemoglobin and deoxyhemoglobin. Because both oxy and deoxyhemoglobin have different absorption at both laser wavelengths, optical absorption measured at both two wavelengths can provide information about blood oxygenation [23, 24].

Photoacoustic has also been developed for radiotherapy and imaging purposes. The use of a contrast agent from albumin-shelled microbubbles with encapsulated gold nanorods (AuMBs) can improve image contrast on photoacoustic

imaging used for diagnostic and therapeutic purposes [25]. Many applications of photoacoustic in radiotherapy such as gold nanorods [26], thermosensitive liposomes PLoS One [27], silver nanoparticles [28] and 3D printing of hydrogel scaffolds [29] are important development. In imaging, photoacoustic is also widely used in e.g. triggered nanodroplet vaporization [30], optically-triggered phase-transition droplets [31], thyroid cancer [32], stem cell tracking platform for ultrasound [33] and functional calcium imaging [34] are also developed.

### 3. Resume

This paper presents a brief review of the photoacoustic generation and biological effects of laser irradiation, heating effects, ablation, cavitation, and pressure. Several applications of detection models such as imaging of layered structures in tissues, monitoring of blood oxygenation to the brain, and monitoring of the optical properties of blood are explored in this paper. In the end of paper, application of photoacoustic in radiotherapy and imaging are also presented.

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