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Photoacoustics: a historical review

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We review the history of photoacoustics from the discovery in 1880 that modulated light produces acoustic waves to the current time, when the pulsed variant of the discovery is fast developing into a powerful biomedical imaging modality. We trace the meandering and fascinating passage of the effect along several conceptual and methodological trajectories to several variants of the method, each with its set of proposed applications. The differences in mechanisms between the intensity modulated effect and the pulsed version are described in detail. We also learn the several names given to the effect, and trace the modern-day divide in nomenclature.

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1. INTRODUCTION

Photoacoustic or optoacoustic imaging is arguably the most exciting biomedical imaging technique of the decade [1–4]. The method has captured the attention and imagination of applied physicists, applied mathematicians, biomedical engineers, and clinical imaging specialists, often with an affinity for biomedical optics and/or ultrasound, the two fields brought together in the method. The technique typically uses short-pulsed (or less often, rapidly modulated) electromagnetic radiation as probing energy, while detecting ultrasound generated by photon absorption and thermoelastic expansion. This is in contrast to purely optical imaging, where multiple scattering randomizes photon direction, thus deteriorating resolution and contrast when these photons are detected [5]. The particular strength of photoacoustics in relation to imaging applications arises from the fact that the detected energy is not light, but is ultrasound, which generally undergoes considerably less scattering and attenuation in tissue compared with light. The consequence is that the spatial distribution of optical absorption can be ascertained deep in tissue with better resolution and greater penetration depths than achievable with other optical imaging methods.

The primary contrast mechanism explored in biomedical photoacoustics, namely, optical absorption, possesses information regarding the presence of tissue components such as hemoglobin, oxy-hemoglobin, melanin, bilirubin, lipids, and water [6,7]. Strong optical absorption by the first two biochromes allows the visualization of blood vessels, maintaining sub-millimeter resolutions at depths of 5 cm and beyond within highly scattering living tissues [8–11]. Further, these and other biochromophores have specific spectral signatures that allow them to be distinguished from each other within an integrated absorption signal. Their relative presence carries rich information about function and/or pathological status of tissue being examined, since this presence is carefully choreographed in healthy tissue [12–14].

Photoacoustic imaging and microscopic applications have been demonstrated and envisaged in *ex vivo*, *in vitro*, and *in vivo* settings showing great potential [1–4]. Of late, medical specialists are taking note of the technique and seek to be involved in preclinical and early clinical investigations due to the myriad possibilities of the method in visualization of microvasculature with high resolution, as well as in monitoring of disease and health in the fields of dermatology [15,16], oncology [17–21], rheumatology [22–24], neurosciences [25–27], ophthalmology [28], and cardiology [29].

While several important papers have reviewed the more recent history of photoacoustics [30], its state-of-the-art implementation, and manifold applications [2,3,14], there has not yet been a detailed discussion of early work and as it has evolved into the diverse array of present-day techniques. Other than that the original physical effect was discovered by Alexander Bell, as described in introductions to papers that are intended for broad audiences, not much is presented in the literature. In this historical review, we attempt to trace the fascinating passage of photoacoustics that indeed appears to have sprung from early work by Bell along several conceptual and methodological trajectories to its major use in biomedical imaging in the present time. Along the way, we encounter a few avatars of the method, and learn of several names given to

the effect, including the term introduced by Bell, namely, "photophonic phenomenon," and the term adopted by him and others in the years following his discovery, which was "radiophony."

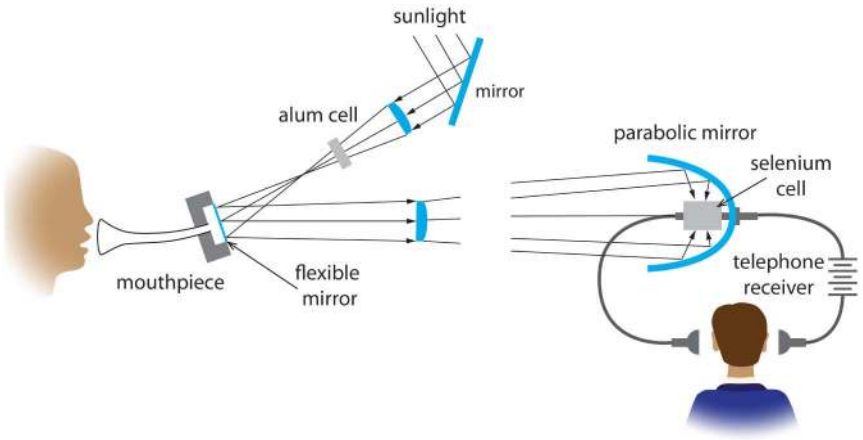
2. DISCOVERY BY BELL, THE PHOTOPHONE AND EARLY DAYS

After inventing the telephone in 1876, Bell began focusing his attention on an ingenious concept—the use of light in the transmission of speech [30]. The photosensitivity of selenium had been discovered in 1873 [31], and in 1878 Bell began experiments to adapt this property to telephone transmission. Bell himself credited A. C. Brown of London for the first demonstration of reproduction of articulate speech by the action of light upon selenium in circuit with a battery and telephone. Yet the first well-documented evidence of speech transmission by means of light belongs to Bell and his assistant Charles Sumner Tainter, who were able wirelessly transmit voice messages around 213 m in June 1880 [32–35].

On 27 August 1880, Bell delivered a lecture before the American Association for the Advancement of Science in Boston, in which he presented a functioning apparatus named the *Photophone* [32]. According to Bell, Tainter and he "devised upward of fifty forms of apparatus," but the most successful form consisted of a transmitter, which was a thin silvered glass disk mounted on a frame with a flexible rubber hose whose free end comprised the mouthpiece [32–35]. Sunlight was focused on the mirror and the associated optics so arranged that the reflected light could be collected by the remotely placed receiver—a parabolic mirror at whose focus a selenium cell incorporated into a conventional telephone circuit was arranged (Fig. 1). Speech articulated into the mouthpiece caused the mirror to vibrate, producing fluctuations in the intensity of light collected at the receiver. The voice-modulated intensity of light available at the receiver as a modulated battery current was converted into sound in the telephone circuit. The selenium-cell photophone can be considered the first practical implementation of wireless telephony or, in fact, the first optical communication device.

In addition to this innovative concept, there was a further important outcome of this investigation by Bell, and that was his serendipitous discovery that illumination of different solid substances with a rapidly interrupted beam of light energy resulted

Figure 1



Photophone designed and built by Alexander G. Bell and Charles S. Tainter is considered the first implementation of wireless telephony or, in fact, of an optical communication device [32]. The first voice telephone message was transmitted by means of light over some 213 m in Washington, D.C. in June 1880.

in the emission of acoustic energy at the same frequency as the modulation frequency. To reproduce verbatim from Ref. [32]: "… *our conclusion, that sounds can be produced by the action of a variable light from substances of all kinds*…". In a letter to his father, Alexander Melville Bell, dated 26 February 1880, Bell describes his excitement at the recent discovery [30]: *"I have heard articulate speech by sunlight! I have heard a ray of the sun laugh and cough and sing! …… I have been able to hear a shadow and I have even perceived by ear the passage of a cloud across the sun's disk."*

In a paper read to the National Academy of Arts and Sciences on 21 April 1881 [34], Bell envisaged a form of communication in which the electrical receiver employed in the selenium-cell variant of the photophone would be replaced by a lamp-black receiver, which would directly convert the light modulations into speech. In a delicately aligned system [34], "*Words and sentences spoken into the transmitter… were audibly reproduced by the lamp-black receiver*," up to a maximum distance of 40 m, an astonishing achievement at that time [34,35].

The discovery of the light-induced "sonorous" effect caused great excitement in the scientific community of the day, and in addition to Bell, many notable scientists began to conduct further experimental and theoretical investigations into the phenomenon. Lord Rayleigh concluded in 1881 [36] that the explanation for the sounds was a vibration due to an unequal heating of the diaphragms or plates when illuminated with intermittent light, which was strongly supported by Bell [34,35]. Mercadier [37,38] and Preece [39] studied the effect in a variety of materials and postulated that the cause of the sounds was not the vibration of the disk, but rather the expansion and contraction of air in contact with the intermittently heated disk. Röntgen [40] and Tyndall [41] independently also shared the view that periodic heating and cooling of air in thermal contact with the disk caused the sound production. They also showed that the phenomenon was not restricted to solid bodies, and studied the effect in absorbing gases and vapors. Röntgen studied illuminating gas (coal gas) and ammonia, while Tyndall studied a large number of gases and vapors, including those from perfumes. Tyndall predicted that one variant of the method could be used to detect extremely small quantities of inflammable gases in mines [41].

It was realized through this early research that the effect offered the possibility of eliciting spectral information from samples. To quote Bell's deduction, in his own words [34]: "… *we are warranted in concluding that the nature of the rays that produce sonorous effects in different substances depends on the nature of the substances that are exposed to the beam, and that the sounds are in every case due to those rays of the spectrum that are absorbed by the body.*" Bell, in fact, further unveiled a "spectrophone" [35], in which the absorptive properties of samples could be studied by allowing light passing through the specimen, as the spectrum was being explored, to fall in a cavity filled with nitrogen gas and whose inner walls were coated with lamp-black. The sonorous effect from the cavity could be interpreted in terms of the absorption spectrum of the sample.

Interestingly, the phenomenon was not immediately christened with a name. Bell used the title "Upon the production and reproduction of sound by light" for his pioneering 1880 paper [32], and "Production of sound by radiant energy" for his 1881 paper [34]. In the latter paper, he referred to "photophonic phenomena," and further on wrote of his preference for the term "radiophony" [34], which was, in fact, introduced by Mercadier in early 1881 [37,38] in a series of papers entitled "Notes on Radiophony." This particular name for the phenomenon was quickly adopted by the scientists actively investigating it, as a general term signifying the production of sound by any form of radiant energy, not only visible light [42].

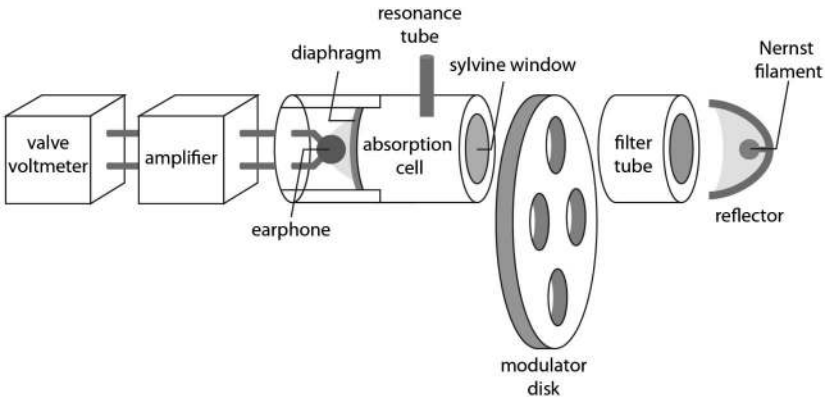
After the initial flurry of excitement and activity, the radiophonic effect faded into the footnotes of 19th century science, principally because experiments were difficult to quantify, as they depended largely on human hearing for signal detection. Bell Telephone, the company to which Bell sold his invention for a nominal fee, could not apply the photophone to practical use. During World War I, some isolated attempts to put the photophone to use for military communications were made independently by the German Navy, British Admiralty, and the U.S. Case Research Laboratories [43,44]. Transmission ranges between 8 and 11 km were variously claimed and, while impressive, were still significantly inferior to the range of Marconi's radio transmissions achieved already before the turn of the 20th century. Soon, the photophone was relegated to an object of curiosity rather than of any serious value. Nevertheless, the concept of using light to replace electrical signals as the common carrier for information exchange was destined for a great future. Today, nearly all modern high-bandwidth telecommunication systems utilize light to carry voice and video data commercially using optical fibers as the transmission medium in preference to copper wire communication. Just recently, the optical transmission record of 100 Petabit per second kilometer was broken in 2009 by scientists at Bell Labs' facility in Villarceaux, France, using 155 lasers, each carrying 100 Gigabits of data per second and operating at a different frequency [45].

3. REVIVAL AS THE OPTOACOUSTIC EFFECT AND EARLY 20TH CENTURY APPLICATIONS

The radiophonic (or photophonic) effect lay dormant for five decades before making a re-emergence with the work of Veingerov of the State Optical Institute, Leningrad [46], in a technology for infrared gas analysis. Veingerov had studied the earlier work by Röntgen and Tyndall in gases, and taken note of the latter's prediction that the method could be applied to detection of small concentrations of gases. In 1938 he published a paper [47] in the Proceedings of the USSR Academy of Sciences (Russian: Doklady Akademii Nauk SSSR) whose title literally translates as "A method of gas analysis based on the optico-acoustic Tyndall-Röntgen effect." By this, Veingerov may be credited for reviving interest in the effect. He used state-of-the-art charged capacitive microphone diaphragms and a Nernst glower as an intense blackbody infrared source, to be able to detect CO_2 concentrations in N_2 down to around 0.2 vol. % (Fig. 2).

A year later, Pfund [48] reported on a similar system in use at the Johns Hopkins Hospital for detection of CO and CO_2 gases. Instead of observing pressure changes,

Figure 2



Optico-acoustic gas analysis apparatus developed in Leningrad, USSR in 1938 by Veingerov was the first widespread application of the photophonic effect [46,47].

this system directly measured the corresponding changes of gas temperature using a thermopile shielded from direct radiation, avoiding the requirement for acoustic noise isolation. Luft introduced a commercial infrared gas analyzer based on microphone detectors, applied in the chemical industry as early as 1938 under the trade name URAS (*Ultrarotabsorptionsschreibers*—the German for infrared absorption recorder) [49]. The design described in detail in 1943 [50] was based on a double cell—one cell contained the reference gas, and the other one gas with the species of interest. Two tubes terminated in an adjoining coupled chamber separated by a membrane capacitor as a microphone. Infrared sources interrupted periodically by a rotating disk with two sectors generated the acoustic signals, which were measured as a differential signal from the microphone.

A theoretical foundation was developed for the optico-acoustic effect, and various implementations soon followed. In addition to gas concentration analysis, the method was also used in the investigation of vibrational relaxation rates and molecular energy transfer in gases [51–56]. It is interesting that the instruments were often called spectrophones in deference to Bell's early absorption spectrometer, which was developed based on the effect [57,58]. Thereafter, the use of the effect waned considerably, optico-acoustic gas analysis being superseded by the more sensitive gas chromatography, and the spectrophone replaced by the versatile infrared spectrophotometer.

With the development of the laser in 1960, there was yet another revival in gas analysis. The high powers achievable with laser technology allowed ultralow gas concentration detection and analysis. Other important advantages of the laser as light source came from the high degree of spectral purity, high stability, and reproducibility. Kerr and Atwood [59] in 1968 were the first to develop laser-illuminated absorptivity spectrophones for gas analysis, one using a pulsed ruby laser and a second using a chopped CW CO_2 laser, with acoustic detection by a capacitance microphone. Kreuzer followed up in 1971 [60] with chopped He–Ne laser excitation in a cell equipped with an electret microphone, where he showed ultra-trace gas detection at ppb levels. This work also marks arguably the first use of the term "optoacoustic" in this context.

4. PHYSICS BEHIND THE PHOTOPHONIC EFFECT: THE THERMAL PISTON MODEL

In a simple experiment, the sample is hermetically sealed in a chamber. If the sample is a solid or liquid, then it is sealed together with a coupling gas. We will further proceed with this situation. A light beam, modulated with a mechanical chopper with an intensity $I(t) = \frac{I_0}{2}(1 + e^{j\omega t})$, with $\omega = 2\pi f$ the chopping frequency, is focused on the sample. The sample absorbs the incident light and a certain fraction (η) of the energy is converted to heat through non-radiative de-excitation processes. Consequently, a periodic heat source is set up, with the form $Ae^{-\mu_a x}(1 + e^{j\omega t})$, where $A = \frac{\mu_a I_0 \eta}{2\kappa}$, with μ_a the absorption coefficient, x the depth, and κ the thermal conductivity. The heat transfer occurs by thermal diffusion, with the rate of transfer controlled by the thermal diffusivity $D = \kappa/\rho C$, where ρ is the mass density and C the specific heat capacity. The thermal diffusion phenomena are described by equations with a periodic source term, yielding time-dependent solutions equivalent to Helmholtz's equations for wave motion. These wavelike solutions are the reason that the term "thermal wave" is often used to describe this heat flow [61]. The plane thermal wave in one dimension has the form $\exp(j\omega t - \sigma x)$, where $\omega = 2\pi f$ is the chopping frequency, and $\sigma = (1 + j)\sqrt{\omega/2D}$ is a propagation vector.

Thus, the heat photothermally deposited in the material is launched as a fast-decaying thermal wave in the sample. The thermal wave is communicated across the interface to

the coupling gas, where it quickly decays, and only a thin boundary layer of the gas experiences temperature fluctuations periodic with the modulation frequency. This causes the gas layer to undergo periodic expansion and contraction, thus causing it to beat like a piston, setting up a train of compressions and rarefactions in the rest of the gas in the cell. The sound wave in the gas is picked up with a sensitive microphone that is placed flush with the inner wall of the cell.

In fact, the first theoretical and experimental foundation of thermal (or heat diffusion) waves was laid in 1861, when Ångström measured thermal diffusivity of solids by periodic heating of a rod and detecting temperature fluctuations away from the excitation point [62]. In the context of photothermally induced sound waves, the initial theoretical model was postulated by Preece in 1880 [39] and Mercadier in 1881 [37,38] but comprehensively developed by Rosencwaig and Gersho [63,64] in the mid-1970s and subsequently widely utilized in thermal wave microscopy applications [65,66] (see further Section 6). An acoustic wave in the solid can also be produced by the thermally induced expansion and contraction of the sample volume, as proposed in 1881 by Rayleigh [36] and Bell [34] (see also the composite piston model of McDonald and Wetsel [67,68]). In most cases for low modulation frequencies, the surface vibration effect that the latter creates is small compared to the effect of the thermal wave.

The original method discovered by Bell may be thus described as being a gas-microphone technique for detecting thermal waves produced in solids (liquids or gases). This is just one of several detection methods that all form the basis of the generic photothermal techniques.

Photothermal spectroscopy can be defined as the field in which the nature of matter is probed using optical excitation of the medium and then detecting the thermal energy, which results from this excitation. If this heat is detected in an appropriate manner, its measure at varying incident energies can be used to obtain spectral information about the sample. Furthermore, since heat flow is involved in the generation of the signal, the thermal properties of the sample can also be studied, and this makes it unique among spectroscopic techniques [61]. In addition to the original gas-microphone approach, there are several other detection techniques (Fig. 3) based on the measurement of

1. pressure changes causing refractive index gradients in an adjacent coupling liquid to periodically deflect a probe laser beam skimming the surface, which is monitored with a position sensitive detector, in photothermal beam deflection spectroscopy [69];
2. temperature changes using pyroelectric sensors in photopyroelectric spectroscopy [70];
3. thermal emission changes using infrared detectors, including infrared cameras, in photothermal radiometry [71]; and
4. vibrations causing acoustic waves in the specimen are picked up with piezoelectric sensors in photoacoustic spectroscopy.

The last mentioned refers to vibrations of the sample due to thermoelastic expansion. This gives us the opportunity to make the link from intensity-modulated to pulsed photoacoustics or optoacoustics.

5. PULSED EFFECT

In the photoacoustics discussed up to this point, the transfer of heat deposited locally takes place via thermal diffusion. The diffusion equation in which the source term has harmonic dependence on time, reduces to a Helmholtz-like equation for wave motion and has wave-like solutions. This is the origin for the use of the term “thermal waves” to describe heat flow in photoacoustic experiments [59]. As mentioned earlier, the

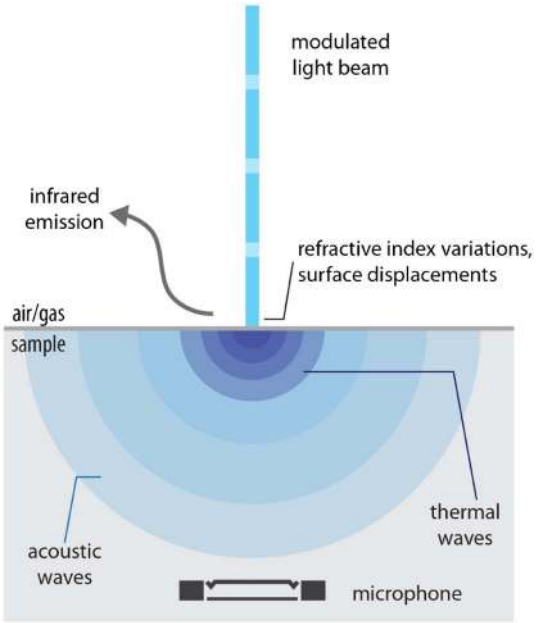
plane thermal wave in one dimension has the form $\exp(j\omega t - \sigma x)$, with propagation vector $\sigma = (1+j)\sqrt{\omega/2D}$. The imaginary part of σ is the thermal wave number, while the real part leads to rapid attenuation. The wave is damped by a factor e^{-1} in a distance called the thermal diffusion length, $\mu = \sqrt{2D/\omega}$. Thermal diffusion is thus a highly dissipative process and constitutes heavily damped transport.

There is a second transport mechanism in which there is direct coupling of the heat energy to the vibrational modes of the material. This is a thermoelastic process governed by the thermal expansion coefficient where a pressure build-up is generated, releasing a stress wave. The rate of transfer of this wave is described by the speed of sound in the material. The transfer is generally non-dissipative, except at very high frequencies, where rapid ultrasonic attenuation on a sub-millimeter scale can occur (usually in the hundreds of megahertz range for soft tissues and liquids [72]). The thermoelastic mechanism can be an efficient converter of absorbed energy into acoustic pressure waves, especially if the period of optical excitation is short (Fig. 4). For a sample exposed to a finite-duration heating pulse [73], causing a sudden temperature change at $x = 0$ from T_0 to T_1, the temperature-field solutions for the heat diffusion equation when introduced into Fourier's law yield, for heat flow,

$$q(x,t) = \frac{(T_1 - T_0)}{\sqrt{\pi t}} \exp\left(-\frac{x^2}{d_0^2}\right). \tag{1}$$

This expression describes a Gaussian spreading of the heat with a characteristic width (thermal diffusion length) of $d_0 = \sqrt{4Dt_p}$, where t_p is the pulse duration and D is thermal diffusivity of the sample.

Figure 3



A variety of techniques can be applied to probe properties of materials using intermittent light radiation, including the original Bell gas-microphone thermal wave detection method [32], measurement of refractive index gradients in an adjacent coupling liquid (beam deflection spectroscopy) [69], temperature monitoring using pyroelectric sensors (photopyroelectric spectroscopy) [70], measurement of thermal emission changes using infrared detectors (photothermal radiometry) [71], or photoacoustic spectroscopy by means of piezoelectric detection of acoustic vibrations and waves [61].

Thus, a pulse of light deposits heat in the optical absorption zone following an exponential decay of light intensity. If the thermal diffusion length satisfies $d_0 < \delta_L$, where δ_L is the resolution of the sensing system, then the heating pulse is so short that thermal diffusion is not significant during the pulse. There is, as it were, no leakage of energy out of the effective optical absorption zone, and maximal thermal energy densities can be attained. This is the thermal confinement regime of pulsed laser heating [74,75]. Considering the value of thermal diffusivity to be $D = 0.14$ mm^2/s in soft biological tissues, this condition can be readily met for typical biological imaging applications that use nanosecond-duration laser pulses [76].

Similarly, a stress confinement regime can be defined in which the laser pulse duration is smaller than the time required for the stress propagation out of the heated region defined by the effective spatial resolution, i.e., $t_p < \delta_L/v_c$, where v_c is the speed of sound in the medium [74,75]. For instance, given speed of sound of ~1500 m/s in soft tissues, the stress confinement condition would be readily fulfilled for a laser pulse duration of 10 ns and typical diffraction-limited spatial resolution of 100 μm of the imaging system (corresponding to ultrasonic detection bandwidth in the 10 MHz range).

Using pulse durations that satisfy both confinement regimes ensures that the fractional volume expansion ($\Delta V/V$) is negligible, i.e. [77],

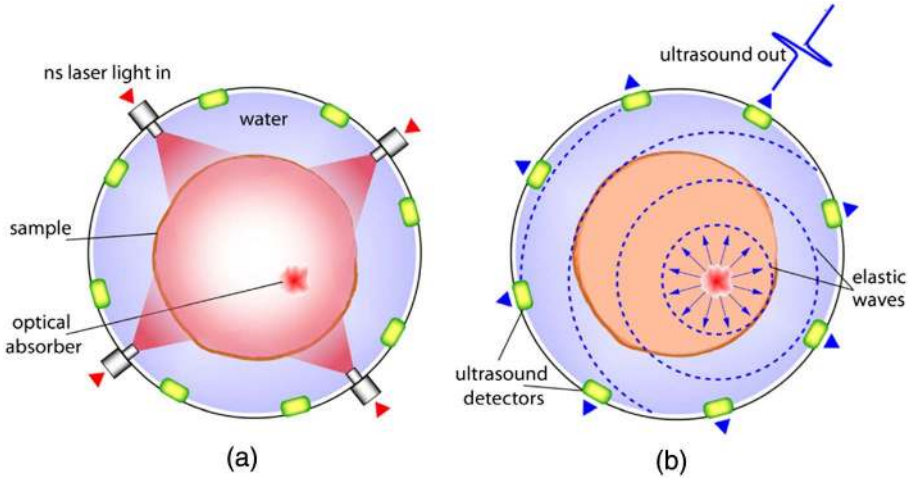
$$\frac{\Delta V}{V} = -K\Delta p + \beta\Delta T = 0, \tag{2}$$

where K is the isothermal compressibility, β the coefficient of thermal expansion, Δp the pressure change, and ΔT the temperature change. The initial pressure rise following light absorption can be written as

$$\Delta p_0 = \frac{\beta\Delta T}{K} = \frac{\beta}{K}\left\{\frac{E_a}{\rho C_v}\right\}, \tag{3}$$

with ρ the mass density, C_v the specific heat capacity at constant volume, E_a the absorbed optical energy given by the product of μ_a absorption coefficient, and I the fluence at the local absorption point. This can be written as

Figure 4



Pulsed photoacoustic effect. (a) Scattering sample containing optical absorbers is illuminated with short laser pulses. (b) Absorption of the light energy leads to thermoelastic expansion and subsequent generation of propagating elastic waves that are recorded using detector/s placed outside the sample.

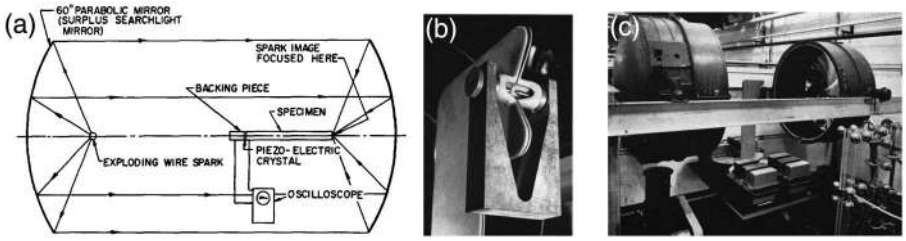
$$\Delta p_0 = \Gamma E_a, \quad \text{where } \Gamma = \frac{\beta}{K\rho C_v} = \frac{\beta v_s^2}{C_p}. \tag{4}$$

The term Γ is the Grüneisen coefficient, a parameter that lumps together the thermal expansion coefficient, the compressibility, and the speed of sound. The short excitation pulses thus satisfy both confinement regimes, ensuring that the conversion of temperature rise to a pressure buildup via the Grüneisen coefficient is maximized. This is made use of in pulsed photoacoustics, though many pulsed studies in the early days operated only in thermal confinement (see further), with stress confinement being the more restrictive of the two constants.

While the gas-microphone method is efficient in detecting low-frequency sound vibrations produced by chopped light beams, piezoelectricity has played a crucial role in development of practical technologies for detecting high-frequency ultrasound vibrations produced by short-pulsed radiation sources. The piezoelectric effect was initially discovered by Pierre and Jacques Curie in 1880 [78], around the same time that Bell was developing his photophone, with its first application for ultrasonic detection of submarines using thin quartz crystals filed as a patent by Curie's former doctoral student Paul Langévin in 1916 [79]. This was succeeded by development of transducers for industrial inspection and therapeutic applications in the 1920s and 1930s [80,81], followed by the introduction of diagnostic ultrasound in the 1940s and 1950s by Karl Dussik, George Ludwig and others [82–85].

In general, transient heating can be induced by absorption of electromagnetic radiation in various spectra, from radio frequencies and microwaves to ultraviolet, x rays, and electron beams. In fact, the first report of stress (acoustic) waves induced in solids due to pulsed radiant exposure is from Michaels [86] in 1961 (Fig. 5). Curiously enough, the studies were conducted in the context of "kill-effectiveness" of a thermo-nuclear explosion in space. The interest was in the mechanism by which stress waves are induced in a solid subjected only to a radiant heating pulse of great magnitude, where the debris of the vacuum explosion is not considered, but only the effects of electromagnetic energy transferred to an intercepting object. While earlier investigations had examined transient stresses as a result of abrupt heating of a solid surface, these were developed considering ordinary conduction and convection of heat to the surface.

Figure 5



Thermal impact experiment studying acoustic waves induced in solids due to pulsed light exposure [86]. (a) Schematic of the experimental setup. Short light pulses produced by an underwater spark were focused onto an aluminum rod. The acoustic waves produced in the rod due to absorption of the pulsed light radiation were detected by a piezoelectric detector mounted on the other side of the rod. (b) Close-up view of an underwater exploding wire spark. (c) General view of the entire thermal impact facility. Reprinted from Planet. Space Sci. **7**, J. E. Michaels, "Thermal impact—the mechanical response of solids to extreme electromagnetic radiation," 427–433 [86]. Copyright 1961, with permission from Elsevier.

Michaels studied for the first time radiant energy transfer at higher heating rates. For experiments, an underwater exploding wire spark was used to produce a light pulse (50 μs), which was focused at one end of an aluminum rod. A piezoelectric crystal was mounted at the other end and picked up strong acoustic waves.

In 1962, White [87] studied radiation-induced stress effects using a variety of sources, including a microwave pulse generator, a pulsed ruby laser, a stroboscope white lamp, and a pulsed electron beam. In this way, the acoustic waves were induced in a variety of metals, such as stainless steel and copper, and also in liquids and ordinary tap water. In 1963, White [88] developed the theory of thermoelastic wave generation in isotropic elastic bodies under several transient heating conditions.

With the arrival of the laser in 1960, investigations into the effects of pulsed light in liquids were pioneered by the inventor of the laser, Prokhorov, and his colleagues, who in 1963 observed breakdown mechanisms and formation of shock waves due to the interaction of a pulsed laser beam with water [89]. This triggered development of a new branch of investigations, in what was generically called "radiation acoustics" [90–92], which, as Lyamshev describes in his review in Ref. [88], explored the thermoelastic (thermoradiation) processes of sound excitation in liquids and solids using continuous and pulsed penetrating radiation. The radiation could take any form from laser light, x rays, and synchrotron radiation, to proton, electron, and neutral energy particle beams.

In solids or liquids, most early studies concentrated on surface heating effects, where the acoustic waves were produced by strong absorption of pulsed light and thermoelastic expansion in thin surface layers [86–94]. This launched planar acoustic waves into the solid or liquid. The spherical source arising when light is focused into a liquid was studied theoretically by Hu [95] in 1969 for long laser pulses, and later in 1978 by Sigrist and Kneubühl [96] for short pulses. In weakly absorbing liquids where the laser beam penetrates a longer distance into the medium, the acoustic source may be considered cylindrical. This situation was studied by, among others, Kasoev and Lyamshev [97], Kozyaev and Naugol'nikh [98], and Patel and Tam [99].

A substantial component of the early work in the 1960s and 1970s was conducted by Soviet researchers, and published in Russian language journals, which may remain difficult to access for English-speaking readers, although their contributions can also be learned in the reviews of Patel and Tam [99], Tam [100], and books by Zharov and Letokhov [101], and Gusev and Karabutov [77].

An additional interest in pulsed photoacoustics was raised when Ledbetter and Moulder [102] showed that laser-generated ultrasound in solids and particularly in metals produced longitudinal shear and surface ultrasound waves. More work in this area consolidated the theories and elucidated the mechanisms, which could be divided into the thermoelastic regime, and, at higher laser power densities, the plasma or ablation regime. The applications in this area had been investigated to varying degrees since White in 1963 (see, e.g., Refs. [103,104]), but reached a zenith in the 1980s [105–107]. The most applications were seen in nondestructive testing (NDT) of metals and other solids using near-infrared or visible lasers. Various types of ultrasound transducers were used, such as capacitance-based detectors [108,109], electromagnetic acoustic transducers (EMATs) [110,111], and non-contact interferometric methods [112,113]. The latter approach of detection of laser-generated ultrasound came to be called laser-ultrasonics. Various sophisticated systems were developed in the 1980s, and these, along with applications in NDT, are described in detail in Refs. [102–104]. Other related applications in the materials industry were in material characterization by determination of elastic constants and grain sizes [114];

determination of thin film thicknesses [115], and the early beginnings of acoustic microscopy [116], as outlined in the next section.

6. REDISCOVERY OF THE INTENSITY-MODULATED PHOTOPHONIC EFFECT IN SOLIDS AS THE PHOTOACOUSTIC EFFECT

Even though the effect in gases quickly saw a well-established theoretical foundation and experimental progress toward applications, it is surprising that the analogous effect in solids and liquids did not receive much attention after the nascent efforts in the late 19th century. Interestingly, in gas optoacoustic studies, the accuracy of measurements was known to be limited by the background signal due to absorption and sound production at the walls (and windows) of the cell [46]. In his review, Delany [58] refers to this background sound as being produced by the Bell effect, with solids responsible for the sound generation. Late in 1973, a paper appeared from Parker [117], who discovered in his optoacoustic experiments studying collisional deactivation of singlet molecular oxygen, which is IR active, that strong signals were also produced in gases such as nitrogen and neon, which are not IR active. Investigation revealed this to be due to light absorption in essentially transparent windows, and Parker derived the theory for acoustic signals produced from low absorbing samples.

The strong resurgence in Bell's effect in solids and liquids was mainly due to researchers at Bell Laboratories, who initiated intensive investigations of the optoacoustic effect in solids in the early 1970s, inspired by the superior sensitivity of the technique in gases previously reported by their colleague Kreuzer. Two articles appeared with work on solids in 1973, one from Rosencwaig [118], and a second from Harshbarger and Robin [119]. The latter paper had been received in February and published in October, while that of Rosencwaig was received in March, but appeared within a month in print as rapid communication. The two works used similar instrumentation with a high-pressure Xe lamp and ¼ monochromator with a chopper, and with electret foil microphones for detection. The acknowledgments in both articles indicate that the microphones were provided by Sessler and West [118–120]. While Harshberger and Robin retained Kreuzer's term "optoacoustic" in their paper, Rosencwaig introduced a new term, "photoacoustic," for the effect in solids in order to "avoid any confusion that may result between the original optoacoustic and acousto-optic"; the acousto-optic effect describing the diffraction of light by acoustic waves in a crystal. Some confusion did indeed exist between optoacoustic and acousto-optics; see, for example Refs. [61] and [94]. In the first papers, Rosencwaig showed photoacoustic spectra from various materials such as CrO_2 and Rhodamine-B [118], while Harshbarger and Robin [119] studied flower petals, carbon-black, and the dye Ultramarine Blue.

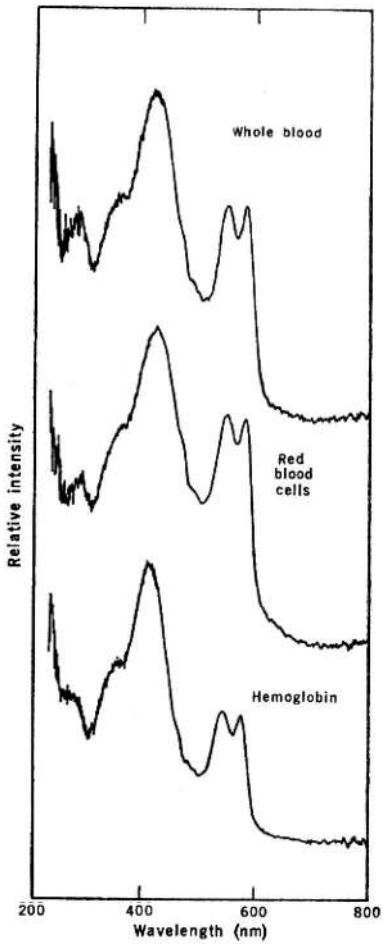
Rosencwaig proved through several experiments the exciting possibilities of the technique and the numerous promising applications [121], including for spectroscopy of biological materials such as cytochrome and hemoglobin (Fig. 6) [122]. This was soon followed by papers [63,64] on the theoretical understanding of the effect in solids. With this, the photophonic or radiophonic effect, as originally studied by Bell in solids, made a re-emergence 90 years later, initiated by researchers coincidentally at the eponymous Bell Telephone Laboratories Inc. in Murray Hill, New Jersey.

The first imaging studies were conducted on inorganic media such as semiconductors for nondestructive evaluation (NDE) of surface flaws and subsurface inhomogeneities (Fig. 7), an application that has subsequently turned into one of the considerable commercial successes of photoacoustics, along with its use in highly sensitive gas spectroscopy applications. Signal generation in low-frequency intensity modulated photoacoustics involves (A) optical absorption, (B) generation and propagation of

thermal waves, and (C) generation and propagation of elastic waves. Thus all three processes can contribute to visualization of the sample. The presence of flaws or inhomogeneities in the illuminated region affects the optical absorption coefficient. Further, the presence of cracks or voids disturbs thermal diffusion wave propagation to give rise to detectable changes in signals. Use of the first two processes, (A) and (B), was first applied by Wong *et al.* [123] using a gas-microphone photoacoustic system on silicon nitride samples with subsurface flaws. Luukkala and Penttinen [124] also used a low-frequency photoacoustic system to obtain a 5 μm resolution image of a mask structure for an interdigital acoustic-surface wave transducer on a photographic glass plate. The image formation in this case was predominantly from variations in the absorption coefficient or reflection/scattering function with position at the surface of the sample.

When the last process, (C), dominates, i.e., propagation of elastic waves, imaging of acoustic impedances becomes possible as in conventional ultrasonics. This was demonstrated by Wickramasinghe *et al.* [116] in a high-frequency acoustic microscope modified for photoacoustic studies. Light excitation was with short pulses (0.2 ns) from a mode-locked and *Q*-switched Nd:YAG laser at 1064 nm. Detection was performed using an acoustic lens and 800 MHz transducer. The sample was scanned in a

Figure 6



Photoacoustic spectra of whole blood, red blood cells, and hemoglobin measured using a Xe lamp and the gas-microphone method. From A. Rosencwaig, Science **181**, 657–658 (1973) [122]. Reprinted with permission from AAAS.

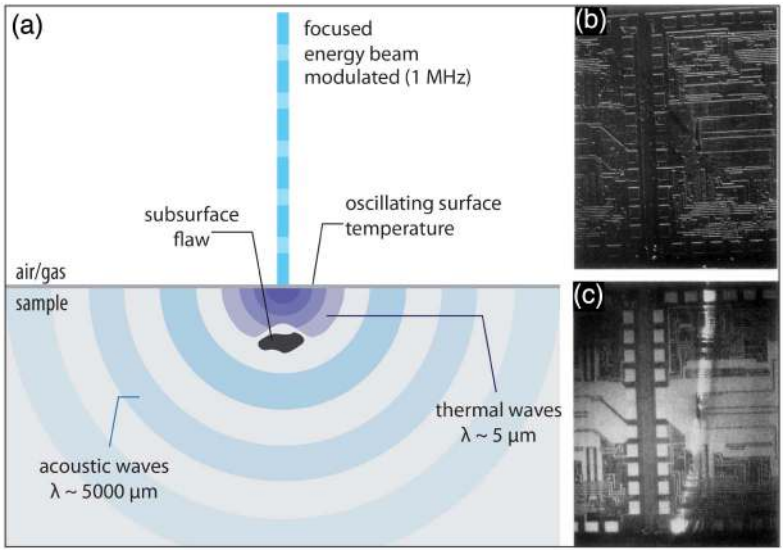
raster pattern through the confocal volume to record the photoacoustic images. Various metallic films were imaged, and in certain cases, depending on the samples, the optical absorption contrast differences and variations in the photoelastic constants also contributed to image contrast. Photoacoustic microscopy of inorganic materials has indeed played a major role in the maturation of the technique, which is reflected by a number of other important contributions from that period [125,126].

When (C) dominates, the spatial resolution of the image is in a similar range as for conventional ultrasound imaging, which is not the case when (A) and (B) dominate. The latter occurs in low-frequency modulated photoacoustics, where thermal diffusion plays an important role in signal generation. The resolution in such cases is the wavelength of the thermal waves or the thermal diffusion length, namely, $\sqrt{D/\pi/f}$. However, as mentioned earlier, thermal diffusion is a highly dissipative process and constitutes heavily damped transport, with the wave damped by a factor e^{-1} within μ. The imaging or penetration depth of the thermal waves is thus a few times the resolution dimensions. Thus, at modulation frequency of $f = 100$ Hz in biological tissue, the imaging depth is approximately 100 μm, which decreases to 1 μm when $f = 1$ MHz. This constitutes imaging with high resolution, but with low penetration depths, confining applications to the realm of microscopy. Table 1 summarizes the major differences between continuous wave and pulsed photoacoustics.

7. EVOLUTION OF BIOMEDICAL APPLICATIONS

As mentioned earlier, the regime of photoacoustics in which the thermoelastic mechanism governs signal generation results in direct coupling of the heat energy to the vibrational modes of the material with negligible thermal diffusion. This regime, where short optical excitation duration ensures negligible heat leakage and stress leakage, results in efficient conversion of the absorbed optical energy into acoustic

Figure 7



(a) Schematic representation of the physical processes that occur during thermal wave imaging. (b) Example of subsurface mechanical defect in silicon integrated circuit that is not visible in backscattered-electron images; (c) thermal-wave microscopy image of the same area reveals a subsurface microcrack. From A. Rosencwaig, Science **218**, 223–228 (1982) [66]. Reprinted with permission from AAAS.

Table 1. Differences between Continuous Wave and Pulsed Photoacoustics

	CW Modulated Photoacoustics	Short-Pulsed Photoacoustics
Nature of effect	Predominantly photothermal with flow of thermal waves setting up acoustic waves in coupling media	Thermoelastic expansion setting up acoustic waves, with minimal heat flow effects
Excitation concept	Low frequency chopping below 1 KHz[a]; high duty cycle	Short pulses (≤1 μs) in thermal confinement and often in stress confinement; low pulse repetition rates[b]
Detection concept	Indirect detection of photothermal effects using a gas-microphone configuration	Direct detection of stress waves using piezoelectric detectors often with water for inviscid coupling
Generation efficiency	Low	High
Effect of boundaries	Severe	Minor if acoustic impedance well matched
Depth of interrogation for depth-profiling or imaging application	Dependent on the wavelength of the thermal wave, and thus on chopping frequency, but generally low penetration of the order of 100 μm[a]	Depends on the optical excitation wavelength and on the available bandwidth of the ultrasound detector and is usually in the millimeter to centimeter range[c]
Main applications	Spectroscopy of solids, liquids, and gases where samples are too scattering, too absorbing, or too transparent for optical methods. Monitoring of de-excitation channels. Estimating material thermal properties. Flaw detection and microscopy in near-surface situations.	Depth profiling and determination of thin film thickness. Photoacoustic tomography and microscopy of biological tissues. Flow cytometry. Non-destructive testing of solids. Material characterization.

[a]Some modern photothermal imaging implementations use sophisticated high-frequency modulation schemes (e.g., chirped sequences [127,128]) in order to achieve higher penetration.
[b]While historically low pulse repetition rates have been used in photoacoustics, some of the recent implementations employ laser pulse repetition rates in the tens to hundreds of kilohertz range [19].
[c]The penetration depth of short-pulsed photoacoustics is usually in the range of 100–200 times the achievable spatial resolution [2], which in turn depends on the available bandwidth of the ultrasonic detector. For instance, more than 50 mm penetration depth was reported for imaging systems having spatial resolution in the 0.4 mm range [8].

pressure waves, which are generally non-dissipative, as opposed to thermal waves, which play a dominant role in the low-frequency regime of photoacoustics.

The first investigations in the biomedical field of acoustic wave generation by absorption of short light pulses appear to have been conducted in 1964 on the eyes of a living rabbit by Amar *et al.* [129]. The title of the paper translates from the French into "Detection of elastic waves (ultrasound) through the occipital bone, induced by laser pulses in the eye of a rabbit." The authors used a ruby laser running in normal mode (non-*Q*-switched mode) that produced on average 50 mJ pulses of 1 μs duration in a pulse train of 400 μs. The light was directed first into the left and then the right eye of the rabbit onto the retinas. The authors state that the energy levels used did not invoke any more than an insignificant light blinking of the eyelids. No damage to the retinas is claimed to have occurred, as ascertained post-experiment using pupil-dilation tests in response to bright lights, and using ophthalmoscopy. A disk-shaped ultrasound detector (8 mm diameter, 0.1 mm thickness) based on barium titanate was placed on the position of the left occipital lobe with skin and skull intact.

The oscillogram from the detector showed a series of acoustic transients corresponding to each of the laser pulses of the normal-mode laser output (Fig. 8). The acoustic waves produced by light absorption at the retina propagated through the brain and occipital bone to be detected. The authors were quick to point out that these pressure transients were not shock waves, but were elastic wave trains in the ultrasonic regime carrying a main frequency component around 40 KHz. The phenomena were reproducible provided that the laser beam passed clearly through the pupil, but suffered

1 order of magnitude lower amplitude when the laser beam struck the iris or sclera. No signals could be detected when parts of the face were irradiated, such as the cartilage of the nose.

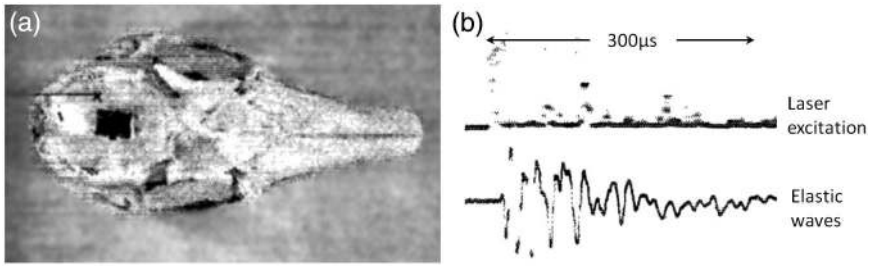
Amar *et al.* also conducted laser-induced ultrasound studies [130] on *ex vivo* human eye specimens. For the sake of completeness, we mention that they also developed a far-fetched theory to explain human vision. They postulated that when scattered light from an object entered the eye, lasing action would occur in the retina following absorption by the incoherent photons. This laser emission of coherent photons and their subsequent absorption would induce elastic waves in the retina, which would cause the sensation of sight.

Further studies of laser-induced acoustic transients in the mammalian eye were continued by others [131], mainly for investigating laser-induced damage to the retina. A theoretical analysis in Ref. [131] showed that ultrasound pulses of the same duration as Q-switched laser pulses would be produced. The theoretical predictions were confirmed using a 50 ns wide 1 J/cm^2 laser pulse from a ruby laser for excitation, and piezoelectric detection and schlieren visualization.

The observations of auditory responses to pulsed radio-frequency and microwave energies, commonly called RF (or microwave) hearing [132–134], spurned interest in the interaction of time-variant electromagnetic energy with tissue in the 1960s and 70's (see review by Elder and Chou [135]). A theory was put forward by Foster and Finch (1974) [136] in which RF (microwave) energy absorption in tissue caused heating and thermoelastic expansion, resulting in acoustic transients. They showed that pulsed 2.45 GHz radiation produced strong acoustic signals in saline that were detectable with a hydrophone. The authors proposed that RF (or microwave) hearing was due to acoustic vibrations in the head of the human, having arrived there after propagation away from the site of heating and via conduction through bone. Borth and Cain (1977) [137] performed a theoretical analysis of the induced volume and surface forces due to the thermal expansion, electrostriction, and radiation mechanisms in a one-dimensional model. Pressure and displacement waveforms in microwave-irradiated physiological saline as semi-infinite were computed. Thermal expansion was found to be considerably more effective than either electrostriction or radiation pressure in converting electromagnetic energy to acoustic energy.

In the context of studying biological samples with the original Bell method based on intensity-modulated light, Rosencwaig and others had quickly realized that the

Figure 8



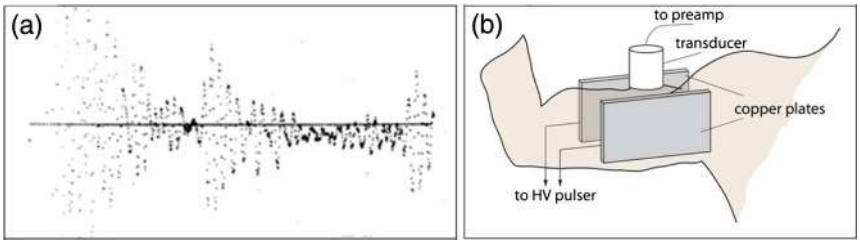
First photoacoustic traces acquired from a biological sample. (a) Photograph from the rabbit used in the experiment; (b) opto-acoustic traces obtained from a rabbit retina *in vivo* using a pulsed ruby laser and barium titanate piezo-electric detector. Reproduced with permission from Amar *et al.*, C. R. Acad. Sci. Paris **259**, 3653–3655 (1964) [129].

method was largely insensitive to scattered radiation. Photoacoustics thus permitted studies on highly light-scattering materials, such as biological specimens, not amenable to conventional study. Initial studies on biological samples were on investigating the extent of drug incorporation into skin. This was performed by measuring the photoacoustic spectra of skin to find changes in optical absorption due to presence of the drug. Reports on studies of various samples of *ex vivo* guinea pig epidermis [138] and human stratum corneum [139,140] treated with medicines such as tetracycline appeared. Photoacoustic studies on *ex vivo* human eye lenses were carried out to investigate the processes by which cataracts formed. The spectra from healthy and cataractous lenses showed differences in characteristic absorption peaks of tryptophan and tyrosine residues [139], confirming early theory on the role of these proteins in formation of cataracts.

The thermoelastic mechanism for RF/microwave hearing spurned more research into using radiation in these spectra to generate acoustic signals. Among the first studies to use these acoustic signals for characterizing tissue-like media was from Olsen and Hammer (1980) [141]. They used a radar transmitter to irradiate a muscle phantom with pulsed 5.655 GHz energy, and used a hydrophone to record the acoustic responses. The acoustic waves were found to have pulse durations corresponding to the measured penetration depth of the microwave energy.

Bowen in 1981 [142] was among the first to propose imaging of soft tissues using the method. The paper is titled "Radiation-induced thermoacoustic soft tissue imaging" and describes the phenomenon generally as originating from the deposition of heat into a finite region, using a wide range of radiation, such as RF or microwave energies, high-intensity ultrasound, or ionizing radiation. The paper presents a general solution of the thermoacoustic wave equation in a homogeneous and isotropic medium using the concept of retarded potentials, making an estimate of the signal-to-noise ratios for a point acoustic detector and a focused detector following power-law acoustic attenuation. The article concludes that a practical thermoacoustic imaging system would be possible, and that the method using non-ionizing energies would provide information complementary to conventional imaging methods, such as echography, x-ray imaging, and nuclear isotope imaging. Further, a specific application is mentioned, namely, imaging during therapeutic radiation for dosimetry and treatment planning. In the same year, Bowen *et al.* [143] showed thermoacoustic A-scans excited using electric currents with copper electrodes inserted in a two-layer phantom comprising muscle-tissue-mimicking layered samples topped with vegetable oil. Also in this paper the authors present the first *in vivo* signals from the upper arm of one of the authors (Fig. 9).

Figure 9



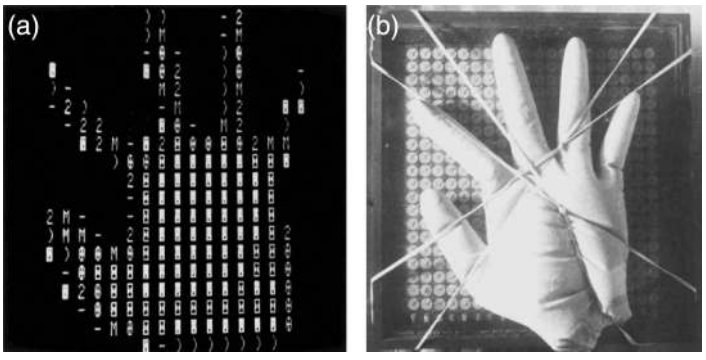
(a) Example of a thermoacoustic signal trace recorded from a human arm *in vivo*. (b) Schematics of the experiment that was used to generate thermoacoustic waves by fast discharge of a high-voltage capacitor. © 1981 IEEE. Bowen *et al.*, Proceedings 1981 Ultrasonics Symposium (IEEE, 1981), pp. 823–827 [143].

In 1984, Bowen and co-workers [144] further showed thermoacoustic A-scans excited using low-intensity pulses from a 2.45 GHz magnetron source, from interfaces of a variety of materials. These samples placed in the microwave cavity included a three-layer tissue-simulating phantom made of a lipid material, and layers simulating the microwave properties of bone and muscle.

However, the first 2D images were obtained a few years earlier in 1982 by Olsen [145], where crude projection images of simple objects were obtained by detecting the thermoacoustic waves with a 8×8 detector array following excitation of phantoms with 5.66 GHz microwave energy pulses. In 1983, Olsen and Lin [146] extended this work by using a 20×20 detector array and measured the signals from a complex human hand model, developing a projection image in which the model can be clearly identified (Fig. 10).

Returning to the use of light, researchers from Hiroshima University developed a computerized imaging analyzer for laser photoacoustic microscopy that was applied to the microanalysis of biological components in tissue slices or cell suspensions [147,148]. Cross *et al.* [149] studied the acoustic responses of human cadaver aorta subjected to short-pulse UV and visible laser radiation. The authors had interest in laser-facilitated angioplasty, the photovaporization of vessel blockages, using intraluminal optical fibers. In contrast to earlier work [150], they studied not only ablative acoustic responses, but also the subthreshold thermoelastic acoustic responses of aortas. Below the ablation threshold, acoustic signatures were observed to be consistent with thermoelastic stress wave generation mechanisms [92] with the formation of a bipolar waveform produced by rapid heating and thermal expansion of the unconstrained sample surface of the sample. Increasing fluence above the ablation threshold resulted in acoustic responses with signatures of the recoil momentum of the ablation product: the production of a predominantly compressive stress comprising the initial thermoelastic component and the ablation contribution. Attempts were made to estimate the effective absorption coefficients from the acoustic signal amplitudes and pulse profiles in this and subsequent work [151,152]. In Ref. [152], from the photoacoustically estimated absorption coefficients in the 440–500 nm spectral region, it was shown that discrimination could be made between diseased and healthy aorta tissue from human cadavers. The authors also speculated on the potential for selective tissue removal in laser angioplasty using guidance via the photoacoustic signature.

Figure 10



Thermoacoustic 2D projection image (a) from a human hand phantom (b) obtained using a short-pulsed 5.66 GHz microwave source and a 20×20 ultrasound detector array. Olsen and Lin, Bioelectromagnetics **4**, 397–400 (1983) [146]. Copyright Wiley-VCH Verlag GmbH & Co. KGaA. Reproduced with permission.

The first *in vivo* pulsed photoacoustic study appears to be from 1993, when Chen *et al.* [153] developed a probe that was used to obtain photoacoustic A-scans from a human finger. The probe comprised a concentric piezoelectric polymer detector with a 600 μm optical fiber through the central aperture coupled to a *Q*-switched Nd:YAG laser at 1064 nm producing 20 ns pulses at a 10 Hz repetition rate. This is arguably the first backward-mode or reflection-mode photoacoustic imaging device. Results were reported from the A-scans of the finger, where the surface signal is to be seen, followed by a signal from deeper within the finger corresponding to reflections of this surface signal from bone. Results at the position of the nail showed two signals whose separation corresponded to the situation when a pulse–echo ultrasound A-scan was performed in the same position. These two signals were identified to be from the top and bottom sides of the nail.

Also in 1993, Oraevsky *et al.* [154] consolidated the theory for the determination of tissue optical properties by acoustic detection of laser-induced stress waves. Referring to the method as time-resolved stress detection (TRSD), the authors performed several experiments using a lithium niobate acoustic detector and a *Q*-switched Nd:YAG laser pumping second and third harmonic crystals to give 1064, 532, and 355 nm wavelengths, respectively. Based on the acoustic signal amplitude and profile, the absorption coefficient was estimated in the reference liquid phantom. Unknown samples studied were biological tissues such as human cadaver atherosclerotic aorta, canine prostate, and bovine liver.

In 1994, Oraevsky *et al.* [155] proposed that the method could be used for the visualization of absorbed optical energy in turbid media and was applicable to layered biological tissues. In this important work the technique was referred to as the laser-based optoacoustic technique. In the same year, Kruger [156,157] showed the detection and localization of absorption contrast from an India-ink-based absorber in 0.3% Liposyn solution, as a tissue simulating medium, using ∼1 μs pulses from a xenon flashlamp. Kruger refers to the method as photoacoustic, and the ultrasound waves produced were measured using a focused large-area ultrasound detector with a resonant frequency of 0.5 MHz.

Following these seminal papers, it became quite clear that the method could develop excellent visualizations of the spatial distribution of optical absorption in tissue-like scattering media [158–171]. Figure 11 summarizes the time line of various significant events in the history of photoacoustics from 1880 toward modern times. From 2000, the method began to be investigated considerably, and excellent critical reviews may be found covering the modern work [1–5,14,20].

8. SOURCES OF THE MODERN NAMING CONVENTIONS

Through the years, a variety of names have appeared in the literature referring to the phenomenon where excitation by time-variant radiation leads to acoustic waves. As mentioned earlier, Bell referred to the effect that he discovered as the "photophonic phenomenon" [34], but elaborated that the name could mislead a reader into thinking that the authors believed the effect to arise from the action of "luminous" (visible) light only [37,38]. To avoid having labels attached to the new method depending on the nature of the excitation, such as thermophone for "thermal rays" (infrared radiation), and actinophone for "actinic rays" (ultraviolet radiation), Bell opined that a more generic name was required. He expressed preference for radiophony as introduced by Mercadier [37,38].

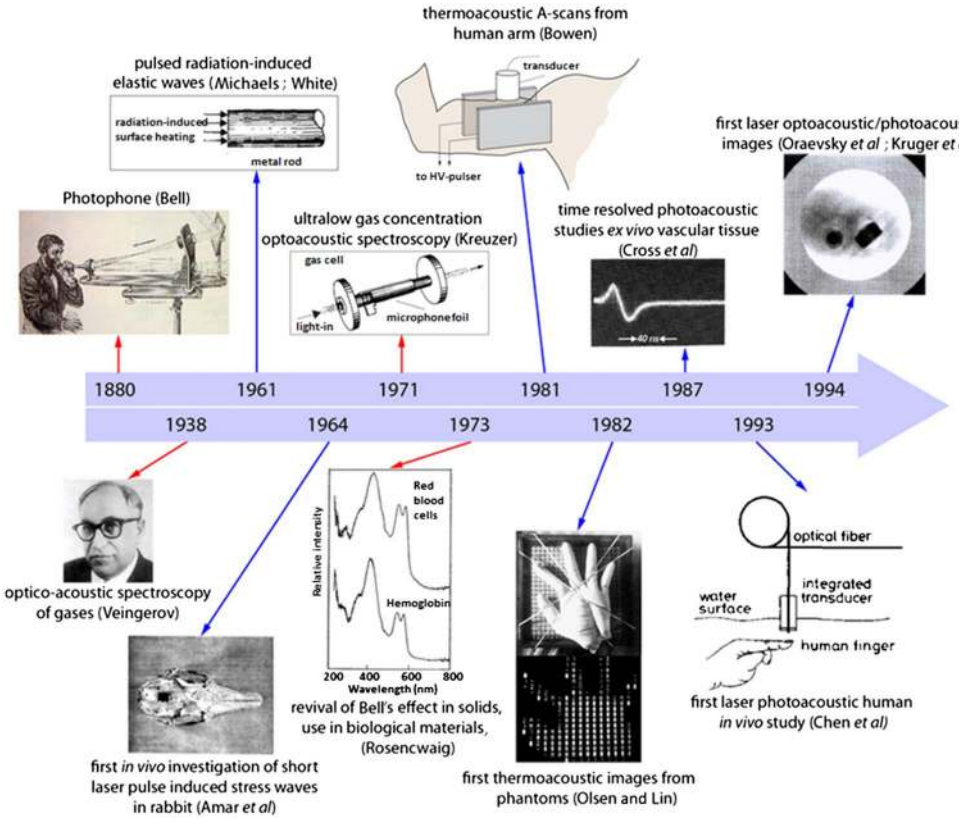
In 1938, Veingerov [46] referred to the effect in its application to gas analysis as the "Tyndall–Röntgen optico-acoustic effect." (See also Nature article from 1946 titled "An optical-acoustic method of gas analysis" [47].) Although, strictly speaking,

attaching the effect to Tyndall and Röntgen is inaccurate, it is obvious that Veingerov credits the work that the two scientists did in exploring the radiophonic effect in gases. By this, in addition to reviving the effect after a dormancy of around 50 years, he also gave the phenomenon a name that is still used today, although in a slightly different form, namely, optoacoustic.

This name held through the 1960s for gas analysis. In 1971, Kreuzer adopted the term "optoacoustic" in his work on ultra-low trace gas detection using He–Ne excitation with an electret microphone for detection [60]. In this publication, Kreuzer referred to the effect discovered by Bell, Tyndall, and Röntgen as the optoacoustic effect, which is an incorrect attribution. Nevertheless, this is arguably the first use of the term "optoacoustic" in this context. It is without doubt that Kreuzer was inspired to the term optoacoustic from the 1959 paper of Delany [58] entitled "The optic-acoustic effect in gases," which Kreuzer has cited as an "excellent survey" of early work. The term "optic-acoustic" used by Delany is itself closely similar to "optico-acoustic" introduced by Veingerov as far back as 1938 [46,47]. Delany discusses Veingerov's contribution in great detail, leading to the inescapable conclusion that he based the term "optic-acoustic" on Veingerov's "optico-acoustic."

It is interesting that while the effect in gases began to be called optoacoustic, the corresponding background signal from the optoacoustic cell walls and windows was referred to as the Bell effect by Delany [58]. Studies on solids received a boost with two articles in 1973, both from the Bell Laboratories. Rosencwaig [118], in his paper from April of that year, introduced the new term "photoacoustic" to describe the work

Figure 11



Time-line of various significant events in the history of photoacoustics from 1880 toward the modern times. Red arrows indicate the low frequency intensity modulated variant; blue arrows indicate the short pulsed variant.

on solids. Rosencwaig, in his own words as mentioned in a later publication [172], preferred the term "photoacoustic" over "optoacoustic," which was at that time being applied to the effect for the work in gases, to "avoid any confusion that may result between the original optoacoustic and acousto-optic effect." The paper of Harshberger and Robin from October that year [119], retained Kreuzer's name "optoacoustic." Interestingly, the acknowledgments of Rosencwaig are also directed toward Robin and Harshbarger for an introduction and advice on the "photoacoustic effect," which was again a non-existing term at that time.

The pulsed variant of photoacoustics may be described as direct photoacoustics, while the gas-microphone detection of photothermal effects may be described as indirect photoacoustics, or even as photothermoacoustics, which would then accentuate the role of thermal waves in the mechanism responsible for the generation of acoustic waves. The term photothermoacoustics as introduced by Sidorov *et al.* [173] is arguably the best suited to describe the phenomenon, in terms of the processes involved.

In the pulsed light variant of the technique, the emergence for biomedical use began with two groups publishing in 1994. Oraevsky *et al.* [155] referred to the method as the "laser-based optoacoustic technique," remaining perhaps faithful to the Soviet or Russian acceptance of the term. In the same year Kruger [156,157] referred to the method as "photoacoustic ultrasound." Up to this point, some semblance of difference could be observed in the basis of the nomenclature, such as applications in gases versus applications in solids leading to different names. However, the publication of these two articles in 1994, using precisely the same generic instrumentation, on the same type of media, namely, soft tissues or soft-tissue-mimicking objects, with purportedly the same arena of applications, but with different names, may be identified as the modern day origin of the divergence in names. Interestingly, in terms of their contribution to the naming conventions, it can be generally observed that the majority of researchers from Soviet or Russian origin remained faithful to the optoacoustic terminology, even after immigrating to the West.

An additional term, "thermoacoustic effect," exists and is frequently used to generally describe excitation of acoustic waves due to heat deposition in matter, although extra care should be taken to distinguish between the radiation-induced phenomena and the "singing flame" and other related phenomena discovered by Higgins [174], Sondhauss [175], and Rijke [176], which have eventually led to development of thermoacoustic heat engines and refrigerators. In general, the heat can be deposited by absorption of electromagnetic radiation in various spectra from RFs and microwaves [142] to ultraviolet and x rays [177], standing wave acoustic or ultrasonic waves [178], charged particles [179], conducting currents [180], spark discharge in air and the accompanying thunder [181], or even chemical reactions, such as explosions. In the context of radiation-induced acoustic phenomena and, in particular, modern imaging and sensing applications, the term thermoacoustic mainly emerged at the turn of 1980s, when Bowen first recorded thermoacoustic responses from a living human subject [143]. Yet, its first mention in the context of thermoacoustic power measurements of impinging microwaves is from the 1950s [182], and the initial theoretical foundation [38] was laid in early 1960s [83,84]. The term was also used to describe the effect behind microwave hearing [136]. Nowadays, particularly in the context of imaging applications, the name thermoacoustic is most frequently used in relation to generation of ultrasound by deposition of RF or microwave energy, while the terms photoacoustic and optoacoustic are equally used to describe the same phenomenon induced at optical wavelengths.

Table 2 summarizes the various names and embodiments attributed to Bell's phenomenon.

Table 2. Various Names and Embodiments over the Years

Name	Year	Author	Excitation/Detection Concept
Photophone, Spectrophone, Thermophone, Actinophone	1880	Bell [34,35]	Modulated light excitation; gas-microphone detection
Radiophony (Radiophonic)	1881	Mercadier [37,38]	Modulated light excitation; gas-microphone detection
Optico-acoustic	1938	Veingerov [46,47]	Modulated light excitation; gas-microphone detection
Thermoacoustic	1953	Vasilev and Zhabotinskii [182]	Modulated RF excitation; gas-microphone detection
	1981	Bowen [142]	Short-pulsed RF excitation; piezoelectric transducer detection
Optoacoustic	1971	Kreuzer [60]	Modulated light excitation; gas-microphone detection
Photoacoustic	1973	Rosencwaig [118]	Modulated light excitation; gas-microphone detection
Photothermoacoustic	1999	Sidorov *et al.* [173]	Modulated light excitation; gas-microphone detection

9. CONCLUDING REMARKS

Photoacoustics enables deeper insights to be gained when investigating optically turbid media as compared to other optical sensing methods. The technique is poised to revolutionize the field of bio-optical observations by transforming the conventional way of isolated surface-limited microscopy into multi-scale visualization of function of entire living systems, organs, and organisms. Yet, the lengthy history of photoacoustics to the present day, where it stands at the cusp of adoption, makes it unique among the pantheon of the physical phenomena applied to imaging. From the initial discovery of the photophonic phenomenon in 1880, through the development of gas spectroscopy and photothermal material inspection applications in the period of the 1940s to the 1980s, it was more than 120 years until the photoacoustic technology reached the level of sophistication at the turn of the 21st century where it can evolve further into a well-accepted biomedical imaging modality. Indeed, it has taken the development of suitable laser sources, sensitive and broadband ultrasound detection technology, as well as fast data acquisition and processing capacities in order to realize efficient and practical imaging devices.

The road ahead is fascinating. While some of the spectroscopic and photothermal applications have reached a mature state, many other research directions are experiencing explosive growth, in particular biomedical photoacoustics. This progress is mainly driven by a large number of unmet biological and medical needs that can be addressed by the unique contrast mechanisms and imaging performance available to the photoacoustic methods. Pre-clinical applications have rapidly developed with imaging scanners, both experimental and commercial, already found in many laboratories around the globe. The investigated areas span the entire palette of modern biology in the fields of cancer, cardiovascular diseases, neuroimaging, ophthalmology, immunology, diabetes and obesity, cell trafficking applications, and a multitude of other biological functions. The multi-disciplinary nature of photoacoustics is also evinced by the growing contribution from chemistry and nanotechnology, where innovations have taken place in areas of dedicated biomarker design, from nanoparticles and organic dyes, to targeted agents and genetically encoded markers. In parallel, development of more efficient and affordable laser technology, miniaturized and sensitive ultrasound detection approaches, and expansion of data processing limits using novel parallel computation platforms and advanced inversion models, will all continue driving photoacoustic technology into the forefront of valuable tools for biological research and into the mainstream of clinical diagnostics.

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