To build a reputation in a specialty field one should probably confine one's contributions to specialty journals, but one should be careful to choose one that is in communication (is cited) with other journals where similar papers appear. The impact factor of a journal is obviously an important determinant in journal selection.

The scientific literature contains numerous instances of 'buried treasure'; Mendel's papers are perhaps the classic example. Those who are interested in mining for undiscovered analytical ideas can see from Tables VI and VII which journals have been referenced (and thus, presumably, studied) least. The fact that physics contributes six times more information to analytical chemistry than it does to physics indicates another way of finding new methods and techniques.

Chemists in non-English speaking countries should closely examine the data concerning citations from non-English language journals. This and other similar observations hardly need further elaboration.

Finally, an admonition and caution: this study is a statistical one, and as such treats groups of journals, masses of papers, and thousands of citations. A paper, like an individual, is unique. Any author who uses these statistics to help him make a choice should always remember that he himself is not a number.

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**trends**

# Thermal lens spectrophotometry

**A thermal lens effect induced under laser irradiation is useful for the detection of very small absorptions. This forms the basis of a new technique which is becoming increasingly important as a tool for ultratrace analysis.**


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Spectrophotometry has been widely used in the determination of many inorganic and organic species because of the availability of a variety of colorimetric reagents. However, the sensitivity of conventional spectrophotometry is not sufficient for ultratrace analysis. The signal in the conventional spectrophotometer is measured indirectly as the difference between the incident and the transmitted radiation, it is therefore difficult to improve the detection sensitivity of the apparatus. If one could measure the absorbed radiant energy directly by some spectrometric method, it would be possible to detect very small absorptions simply by increasing the power of the light source, as in the case of fluorimetry.

## Historical development

In 1965 Gordon *et al.* found build-up and decay transients when a liquid cell was placed within a laser cavity of an He–Ne laser, and reported that the basic phenomenon was a lens effect produced by local heating along the laser beam[1]. As the intensity of the thermal lens effect is proportional to the absorbed radiant energy it provides a sensitive means of detecting very small absorptions when a strong exciting source is used. Most of the fundamental investigations in this field were done by physical chemists as analytical chemists showed little interest in the tech-

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nique until 1978. Several reviews are already available[2–8], consequently we would like to devote our attention to recent analytical applications.

## The fundamental principle

Fig. 1 is a schematic diagram of the dual-beam thermal lens spectrophotometric system. A stable He–Ne laser (white circle) is focused by a lens and introduced into the sample cell. Where the He–Ne laser is weak and its wavelength does not coincide with the absorption band of the sample, there is no thermal lens effect. However, when a strong $Ar^+$ laser (black circle) is introduced into the sample and is coaxially aligned with the He–Ne laser, strong light absorption takes place and the thermal lens effect occurs. In this system the sample works as a divergence lens, the heating laser ($Ar^+$) is blocked by a filter and the expansion of the probe laser (He–Ne) is measured. In a single-beam system the He–Ne laser and the filter are removed and the expansion of the heating laser is measured directly. The dual-beam system is more complex, but it has the advantage that a large signal intensity can be obtained and a small signal detected. The signal intensity under continuous wave (CW) excitation can be expressed by

$$S_c = (I_0 - I_\infty)/I_\infty \simeq -2.3(P_c/\lambda k)(\mathrm{dn/dT})A = 2.3E_cA \quad (1)$$

when absorbance is small[9]; where $I_0$ and $I_\infty$ are the probe beam intensities at beam center without and with irradiation by the heating laser, respectively; $P_c$ is the exciting power; $\lambda$ is the wavelength of the probe laser; $k$ is the heat conductivity; (dn/dT) is the variation in refractive index with temperature; $A$ is the absorbance of the sample; E is the enhancement factor (see below)[10].

The signal intensity under pulsed excitation can be expressed by

$$S_p = (I_\infty - I_0)/I_0 \simeq -3^{(3/2)} \times \frac{P_p}{\lambda_p \omega_{0p}^2} \times \frac{1}{\rho C_p}\left(\frac{\mathrm{dn}}{\mathrm{dT}}\right) \quad (2)$$

where $I_0$ and $I_\infty$ are the probe beam intensities at beam center just after and just before irradiation by the heating laser, respectively; $P_p$ is the pulse energy of the exciting laser; $\lambda$ and $\omega_{0p}$ are the wavelength and the beam radius (the distance between the beam center and the position at which the laser intensity is $1/e^2$) at the beam waist (the point where the laser beam is focused) of the pulsed exciting source; $\rho$ is the density of the sample medium; and $C_p$ is the heat capacity[11,12].

For sensitive detection of small absorptions, it is essential to use a laser source with a large output power, a medium providing a large enhancement factor, a stable probe laser, and signal processing equipment which enables the detection of the small signal buried in noise.

## Exciting source

The light source for thermal lens spectrophotometry should be tightly focused on the sample. Thus, lasers

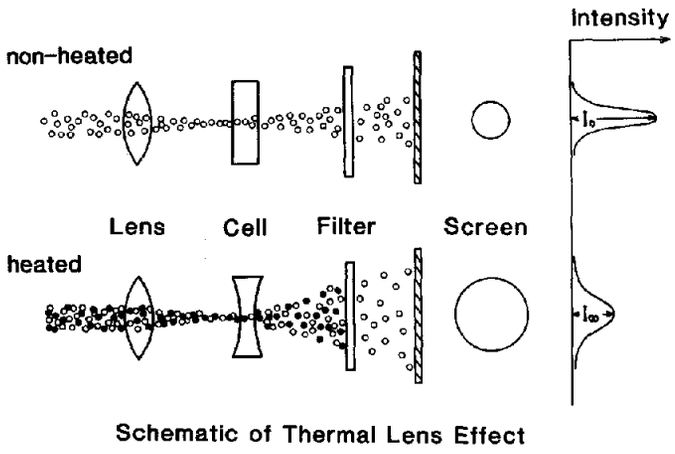


*Fig. 1. Principle of the thermal lens effect: The white circle represents a He–Ne laser (633 nm), used as a probe beam, and the black circle represents an Ar laser (515 nm) used as a heating source. Assuming that the sample has an absorption band at 515 nm, the sample absorbs the green light and the thermal lens effect takes place. The induced divergence lens in the sample expands the probe laser. In the conventional thermal lens spectrophotometer the decrease of the signal intensity at beam center is measured.*

are suitable for these investigations. However, it is possible to use solar radiation, even though it is incoherent, as long as it is tightly focused. Eqns (1) and (2) predict that the thermal lens signal is proportional to the output power of the exciting source. This has been experimentally confirmed and no saturation has been observed (at least up to 0.8 W) as long as the normalized signal intensity ($S_c$) is lower than 0.1[13]. A CW ion laser such as an Ar ion laser, which has good beam coherence and high average power, is currently used as the exciting source in thermal lens spectrophotometry. Although a pulsed dye laser, popular in fluorimetry, can also be used because of its high peak power and its wide range of tunability.

## Medium effect

The enhancement factor for a sample in the condensed phase is strongly affected by the physical parameters of the solvent in which it is dissolved. The calculated enhancement factor using a CW exciting source is shown in Table I for a number of solvents. Water is a very poor solvent for induction of the

TABLE I. Calculated enhancement factors under the exciting power of 1 W

| Solvent | E | $k$ | (d$n$/d$T$) | $\varepsilon$ |
|---|---|---|---|---|
| Heptane | 6300 | 3.00 | 5.0 | 1.924 |
| Cyclohexane | 6920 | 2.95 | 5.4 | 2.015 |
| Ethanol | 3680 | 4.00 | 3.9 | 24.30 |
| Toluene | 6650 | 3.18 | 5.6 | 2.4 |
| Nitrobenzene | 4830 | 3.60 | 4.6 | 34.82 |
| Chloroform | 8000 | 2.74 | 5.8 | 4.806 |
| Carbon tetrachloride | 8940 | 2.45 | 5.8 | 2.2 |
| Acetone | 4970 | 3.80 | 5.0 | 20.7 |
| Water | 207 | 14.6 | 0.8 | 78.54 |

E; enhancement factor
$k$; heat conductivity ($10^{-4}$ cal/s·cm·°C)
(d$n$/d$T$); variation in refractive index with temperature ($10^{-4}$ °C)
$\varepsilon$; dielectric constant

thermal lens effect, while organic solvents such as carbon tetrachloride and chloroform give large enhancement factors. The use of a solvent extraction procedure is therefore attractive for ultratrace analysis. When a 800 mW $Ar^+$ laser is used as the exciting source, the observed enhancement factors in water and chloroform are 70 and 1200, respectively[13]. In general, a solvent with a small dielectric constant has a large enhancement factor. The enhancement factors for samples in various solvents and gases have been calculated and compared under CW and pulsed excitation[12]. An enhancement factor of $\sim 10^4$ is to be expected using commercially available lasers.

## Optical configuration

The thermal lens signal is very dependent on the cell position. The signal intensity at a distance $Z$ from the focal point of the laser can be expressed by

$$(I_0-I_\infty)/I_\infty \simeq -2.3E_cA(2ZZ_c)/(Z^2+Z^2_c) \quad (3)$$

where $Z_c$ is the confocal distance, at which the beam radius is $\sqrt{2}\omega_0$ (where $\omega_0$ is the beam radius at the focal point)[5–9]. The theoretical curve of Eqn (3) is shown in Fig. 2(A). When the sample cell is placed between the focusing lens and its focal point, the laser beam is focused and the 'thermal focusing effect' is evident, but when the sample cell is placed after the focal point, the 'thermal defocusing effect' is seen. The maximum signals can be obtained at $Z = \pm Z_c$. The signs of the signals for the thermal focusing and defocusing effects are opposite but their absolute intensities are identical in a single beam experiment. Based on this phenomenon Dovichi and Harris have proposed a differential thermal lens method for background subtraction[14].

The behavior of the thermal lens signal in the dual beam is similar as long as the probe laser is completely superimposed onto the heating laser; but it should be noted that this is not always the case in the dual beam system. The exciting and probe lasers have different beam diameters and divergences so that the position of the beam waist is not identical for both lasers. In this case sensitivity for the thermal focusing and defocusing effect is different; this is shown in Fig. 2(B).

## Image detection

The formation of the thermal lens effect can be seen clearly on white paper positioned behind the sample cell. In most quantitative studies the measurement of the thermal lens signal is based on detecting the probe laser intensity at the beam center using a pin hole in front of a photodetector. The use of an image detection system makes it possible to monitor the whole intensity profile of the beam and provides a great deal of precise data. Futhermore, it removes occasional light scattering from particles in the sample. A block diagram of an on-line microcomputer-aided thermal lens spectrophotometer, with image detection by a photodiode array is shown in Fig. 3[15]. The spectrophotometer automatically controls the data collection, data processing and even the drawing of an analytical curve. The determination of the $5 \times 10^{-10}$ M Fe(II) ion is possible in an aqueous solution by using bathophenanthroline disulfonate as a colorimetric reagent and a 600 mW $Ar^+$ laser as an exciting source. In chloroform as little as $3 \times 10^{-11}$ M Fe(II)-complex can be detected.

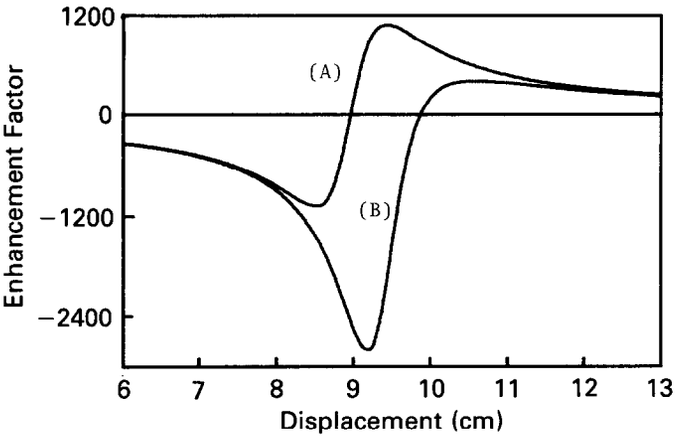


*Fig. 2. Effect of sample cell position on the enhancement factor: (A) single beam method (B) dual beam method. The separation of the beam waists for exciting and probe lasers is assumed to be 5 mm.*

## Flowing sample

Flow analysis systems such as high performance liquid chromatography (HPLC) and flow injection analysis have been developed by analytical chemists in recent years. Dovichi and Harris have applied thermal lens spectrophotometry to a flowing sample[16]. A 40-cm focal length lens focuses a 514.5 nm $Ar^+$ laser through a 70 µl or 8 µl flow cell located one confocal distance beyond the beam waist. The rate of development and decay of the thermal lens effect depends on the solvent used and the flow rate of the sample. Therefore, any fluctuation in the pumping rate induces a serious error in the determination of the trace sample and results in a poor detection limit. At a flow rate of 1.23 ml/min, a detection sensitivity of $A = 1.4 \times 10^{-4}$ has been achieved using a 160 mW Ar laser.

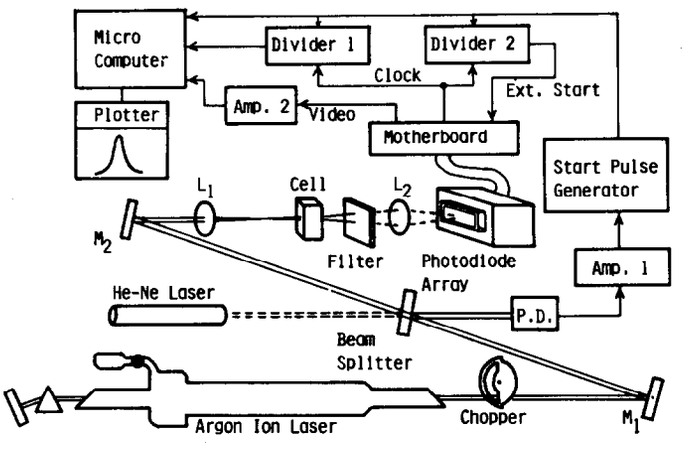


*Fig. 3. Block diagram of experimental apparatus based on image detection: The probe and heating lasers are coaxially aligned and introduced into a sample cell. The expansion of the probe beam is measured by a photodiode array, and the signal is processed by a microcomputer.*

## Applications

Thermal lens spectrophotometry has been used for colorimetric determinations of inorganic ions. Dovichi and Harris have used a 4 mW He–Ne laser for the determination of trace levels of Cu(II) ion with EDTA[10]. The minimum detectable absorbance achieved was $1.0 \times 10^{-3}$. The determination of Fe(II) ion has been reported with the colorimetric reagent bathophenanthroline disulfonate using an $Ar^+$ laser as an exciting source[17]. The determination of Fe(II) ion has been also carried out at lower concentrations using a digital phase-sensitive detection system or image detection system (the effect of solvent extraction discussed in Refs 13 and 15). Using a pulsed dye laser as the exciting source Cu(II) ion has been determined using porphyrin compounds – known to be sensitive colorimetric reagents because of their very large molar absorptivity[18]. A linear analytical curve has been obtained for Cu(II) concentrations in the region of $0–2.4 \times 10^{-6}$ M. Solvent extraction into benzene has enabled Cu(II) analysis at concentrations of as little as $0–8 \times 10^{-7}$ M. In chloroform the detection of $10^{-9}$ M porphyrin ($A = 4.7 \times 10^{-4}$) has been achieved, even when the output energy of the dye laser is as low as 20 μJ/pulse (average power, 60 μW).

Quantitative determinations of trace amounts of clinically significant substances, such as hormones, metabolites, drugs, and enzymes are of recognized diagnostic importance. For example, dopamine is a neurotransmitter and its determination is important in the study of brain function. Haushalter and Morris have used thermal lens spectrophotometry for an enzymatic determination of dopamine, which is non-fluorescent, has a broad absorption band at 475 nm, and has reaction products that are transparent in the visible region[19]. The reaction used is based on the air oxidation of dopamine, catalyzed by polyphenyloxidase. A straight analytical curve is obtained from $2.5 \times 10^{-7} \sim 20 \times 10^{-6}$ M using an $Ar^+$ laser (488 nm) as the exciting source. Fujiwara *et al.* have reported the advantages of thermal lens spectrophotometry in the determination of nitrate reductase[20]. They measured some environmental samples and reported that $4 \times 10^{-7}$ unit/ml of nitrate reductase was found in Sanshiro Pond in the University of Tokyo. The detection limit of this method was reported to be $10^{-7}$ unit/ml.

Thermal lens spectrophotometry is useful not only for samples in the condensed phase but also for samples in the gaseous phase. CW and pulsed laser sources have been used for the detection of atmospheric nitrogen dioxide. The CW laser source of an $Ar^+$ laser provides a (tentative) detection limit of 5 ppb, which is well below the upper limit of the environmental level (60 ppb)[21]. The pulsed dye laser has a detection limit of 800 ppb, because the output power of the dye laser (30 μJ/pulse, 60 μW) is much lower than that of the $Ar^+$ laser (700 mW)[12]. However, the enhancement factor for the sample in the gaseous phase is much larger under pulsed laser excitation than under CW laser excitation when the average power of the two lasers is identical. In the future a thermal lens spectrophotometer which has a pulsed laser with a large output energy may be used to detect atmospheric pollutants.

TABLE II. Comparison of the detection limit in the determination of iron

| Method | Detection limit (ng/ml) |
|---|---|
| Atomic Absorption | 4 |
| Inductively-Coupled Plasma | |
| Pneumatic Nebulization | 0.2 |
| Ultrasonic Nebulization | 0.09 |
| Thermal Lens | |
| In Water | 0.03 |
| In Chloroform | (0.002) |

## Comparison with other methods

Conventional spectrophotometry is accurate because of its ability to determine absolute absorption, but its sensitivity is relatively low. Two sensitive methods based on the direct detection of heat produced by laser irradiation have been proposed – photoacoustic and thermal lens spectrophotometry. The photoacoustic method has great advantages, since it can be used not only for transparent samples but also for opaque and solid samples, as well as gaseous samples absorbed on a solid surface. The minimum detectable absorbance achieved has been $1 \sim 2.4 \times 10^{-5}$ with an $Ar^+$ laser source[15]. However, thermal lens spectrophotometry appears to be much more sensitive than this and enables the detection of an absorbance of $6 \times 10^{-7}$. Thermal lens spectrophotometry also has one unique property. Small absorption by cell windows sometimes poses a serious problem for the detection of ultratrace samples in normal spectrophotometry. As shown in Fig. 2 the signal intensity of the thermal lens effect is very dependent on the position of the sample (light absorber). Thus, if the cell windows are placed both at the beam waist and at some distance from the beam waist, no absorption effect will be seen; the signal intensity is zero when the light absorber is placed at the focal point of the probe laser and is also negligibly small at some distance from the focal point.

One final example serves to illustrate the advantage of using thermal lens spectrophotometry as a tool for ultratrace analysis. Detection limits for iron which have been reported by using various spectrometric methods are summarized in Table II. Atomic absorption is able to detect the samples at levels of several ng/ml and inductively-coupled plasma, when combined with an ultrasonic nebulizer, gives a very low detection limit of 0.09 ng/ml. Thermal lens spectrophotometry in an aqueous solution is still more sensitive, with a detection limit of 0.03 ng/ml which is further enhanced if the iron is extracted into chloroform (and if no background problem arises). Unfortunately the selectivity of the thermal lens spectrophotometer is relatively poor, as is the case with conventional spectrophotometry. It is therefore essent-

ial to use a specific colorimetric reagent and a specific extraction procedure for the sensitive and selective determination of an ultratrace sample.

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# The determination of N-nitrosamines in foods and cosmetics


**The discovery that N-nitrosamines are carcinogenic prompted a great deal of research activity in the measurement, occurrence and significance of N-nitroso compounds. As a result, an adequate methodology has been developed for their analysis, although some problems remain to be solved.**



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**Unilever Research, Sharnbrook, U.K.**


In the last 15 years N-nitrosamines and other N-nitroso compounds have been the focus of a great deal of research. They have been found in foods, particularly those processed with nitrate or nitrite, in a variety of alcoholic drinks and are frequently present as workplace contaminants in the rubber, tanning and metal working industries. Other potential sources of exposure (albeit at the low $\mu g\ kg^{-1}$ level) include cosmetics and toiletries, tobacco and tobacco smoke, certain types of drugs, pesticides, cutting oils and other industrial chemicals.

The carcinogenicity of N-nitrosamines has been studied extensively in animals. Some N-nitrosamines induced tumours in over 20 species of animal[1] and have been shown to be very strong carcinogens. Although there is no epidemiological study which has demonstrated a direct link between N-nitrosamines and the occurrence of cancer in man, it is known that the acute toxic effects of high levels of N-nitrosodimethylamine (NDMA) and N-nitrosodiethylamine (NDEA) are the same in man as in animals. Furthermore, since N-nitrosamines are metabolized in human and animal liver cells in a similar way it is prudent to consider them carcinogenic to man.

## History

The N-nitrosamine story started in 1863 with the discovery that secondary amines reacting with nitrite or nitrous acid produced a 'nitroso amide'. However, over the next 100 years or so nobody worried greatly about the possible risks from these compounds. This lack of concern is evidenced by the fact that textbooks of practical organic chemistry quoted the reaction with nitrous acid as a means to distinguish between primary, secondary and tertiary amines and that various N-nitrosamines were patented for use as gasoline and lubricant additives, as antioxidants in the rubber industry and as nematocides.*

In 1956, Magee and Barnes[2] found that NDMA was

* Nematocide – a substance used to kill nematode worms.

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