LASER APPLICATIONS IN MEDICINE AND BIOLOGY

Volume 1

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Preface

If a basic advance in physics has any practical applications, among the first are those in biology and medicine. This is quite striking when one considers even such unlikely things as the Mössbauer effect and X rays. Within a very short period of their discovery, they had well-formulated biological and medical applications. The discovery of the laser is no exception. Although the theoretical basis for it was established in 1917 by Einstein, the techniques and materials necessary for building a laser were not then available. The laser has revitalized everything connected with optics. It has furnished the experimenter and the teacher with a pseudo-point source. It has translated many a theoretical experiment into one that can be realized practically. The highly monochromatic and coherent aspects of the light, in addition to the high power levels that can be attained, add greatly to the usefulness in this regard. The industrial applictions range from punching holes in baby bottle nipples to a surveyor's instrument of such accuracy that it can plot the position of the moon relative to the earth within a few feet.

Many years of very informal meeting on the subject of lasers in medicine and biology have been sponsored by the Gordon Research Conferences. The present book is an outgrowth of the discussions that took place at these meetings, although it is in no sense a symposium report.

In the chapters that follow, the authors endeavor to present some details of the current usage of lasers in the fields of medicine and biology. That is only part of their task. The role of Cassandra was hard, for she foretold the future but no one believed her. Nevertheless, along with the review of each subject is a discussion of what the future may hold in that particular field. As all of you certainly know, experts can make educated guesses about what will happen in the near future. After that, their guesses, frequently, are not as good as those of less well-informed persons. Thus, we can expect that the short-term predictions in this book will be excellent and the long-term predictions will be—well, we will just have to wait and see.

Certain cautions should be kept in mind. The first is that laser research has just recently emerged from the "gee whiz" era. ("Hey, mom, I pointed my laser at this bug and, gee whiz!! Look what happened!") Some "show and tell" experiments are still done, especially in the medical applications. Thus, the data obtained at the interface between the laser beam and the biological material require careful handling. Perhaps the data should be sprinkled liberally with salt before they are swallowed.

The authors represented in this book have been among the first to introduce controlled experiments and quantitative methods into this field. They have been leaders along the way from magic to science in laser applications in medicine and biology. The criteria for picking material for the book were first the quality of the author's research work and, secondarily, his ability to write. Where I have disagreed with the authors I have encouraged them to show more clearly how I was wrong, if they could. I feel that it is of more interest for students to know what the top-flight researchers consider to be their problems than how well they know the work of others. Of course, the best review for students is one that introduces them to the subject, shows them what the present situation is, and then indicates where progress will be in the future. This has been our aim.

We have tried, as far as possible, to avoid overlap and redundancy in the chapters. Of course, that has been impossible. Where it has happened, the authors have usually had different approaches to the problem and different conclusions. That is fitting in a field where certainty is still far away on many topics. This book is not exhaustive. There are many more uses and abuses of lasers in medicine and biology than are treated herein. Perhaps these other fields will be reviewed in later volumes when the knowledge in them has reached more of the status of a science than an art.

Under many conditions lasers can be dangerous. Thus, proper safety precautions are always necessary when sharing your environment with a laser. Even so, it may seem strange to some that such a large portion of the book is devoted to problems of laser safety. Probably this is related more to the background of the people who are engaged in safety research. The problem is properly one that belongs to health physics. Much, however, of the problem has been identifying exactly what mechanism causes the damage. This is particularly true in the eye, where the main hazard lies. Solar retinitis or eclipse blindness has been known since classical times as a condition that affected and degraded vision. For example, Plato described the cause: staring at the sun; and its cure or prevention: looking at the sun only as reflected in water or from a piece of crystal.† However, laser light differs in its characteristics from that emitted from the sun. It is doubtful as to whether a model of thermal injury to the retina that describes solar retinitis is also adequate to describe the similar retinal injuries received from lasers. The model is especially questionable where the pulses become very short, as in mode

† Plato, Phaedo, *in* "The Dialogues of Plato" (B. Jowett, translator) 3rd edition, 1892, pp. 159–266 (99 D), Oxford University Press, London.

locking or mode selection. In the treatment of this subject, similarities rather than differences have been sought.

I have attempted to make the subject index as detailed as possible. This will enable the reader to find whatever there is on the subject of his interest, especially if it appears in a chapter in which he would not have expected to find it.

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CHAPTER 1

Laser Characteristics that Might Be Useful in Biology

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1. INTRODUCTION

Let us start with a United Press release of October 28, 1964:

> A laser powerful enough to cut through solid steel may also be capable of destroying cancer cells. The effectiveness of the laser as an anti-cancer weapon was described at a meeting of the American College of Surgeons in San Franciso.
>
> Dr. Paul E. McGuff of the Tufts New England Medical Center in Boston and David Prushnell, project manager for Laser Systems at Raytheon's Laboratory here, delivered a paper on the subject.
>
> They reported that several hundred human cancers transplanted to hamsters have been destroyed by exposure to the beam of the laser developed by Raytheon. According to researchers, however, experiments have not yet progressed far enough for definite conclusions.

Lasers generate their force by concentrating rather than diffusing light beams.

This kind of enthusiasm, characteristic of the early stage of the game, has reached a more sober level. Extrapolations from solid steel to cancer cells do not convince any longer. The glamor of the laser has gone; to biologists the illustrious device has become a light source, a lamp with admittedly very special characteristics, but nevertheless a lamp.

In biology and medicine, light, or more generally, radiation from various regions of the electromagnetic spectrum, has always been used as an analytic and therapeutic agent. The special characteristics of the new light source will determine which of the already existing techniques can be improved and facilitated and which of the hitherto only theoretical or impractical procedures can become feasible and practical by employing a laser.

There are two ways of characterizing a light source. The "microscopic" approach describes the physical processes on an atomic level. The output of the light source is then the overall action of the internal events. The "macroscopic" approach deals from the onset only with the output as a phenomenon.

The understanding of the light amplification by stimulated emission of radiation can be gained only from the front approach. Many monographs (Lengyel, 1962; Birnbaum, 1964) have been published since 1960, when the first laser (ruby) had been successfully put to work by Maimann (1960). These books are less interesting to the biologist as a user of lasers than to the physicist and designer of lasers. A very easily readable description of the basic laser action by one of the spiritual fathers of this device, A. L. Schawlow (1962), can be found in the *American Scientist*.

In the application of a laser as a light source only the output characteristics are of importance. Therefore, for the purposes of this article we shall deal with macroscopic characteristics, an approach that also can be termed the "blackbox" approach. By this, the concept of a light source becomes sufficiently generalized so that for example, the combination of a lamp and a monochromator can be considered a single unit.

2. CHARACTERISTICS OF LASER OUTPUT

2.1. Energy

The energy output of any laser is proportional to the volume of the active laser material. Typical concentration of the participating atoms (ions) are $10^{19}/cm^3$ in solids and $3\times10^{16}/cm^3$ to $10^{18}/cm^3$ in gases. The output is not directly proportional to the input since a threshold level must be overcome before laser action sets in. Beyond this threshold a linear relationship between the input and output seems to hold (Koozekanani *et al.*, 1962).

Flash lamps used to excite solid-state lasers produce 250 J/cm³ under normal operating conditions. The spectral composition and the optical coupling to the laser determine the energy absorbed by either host or active material of the laser volume. Furthermore, only a part of the energy deposited in the active atoms is converted into actual laser energy. The final output is obtained after accounting for losses that occur during laser action. These losses are mainly dependent on the geometry of the active volume (rod). The increment in output for every increment in input, that is the differential yield, for ruby (Cr^{3+} ions in Al_2O_3 as host) at room temperature is in the order of 0.8%. At lower temperatures, the yield increases. Neodymium lasers (Nd^{3+} in glass as host) show higher yields, namely about 2%. This is independent of the temperature of the laser rod within a range of -200 to $+200$°C, as the ground level is separated from the terminal laser level by about 4 eV.

Commonly used solid-state lasers have 1–10 J (watt-sec) energy output. Combined with the proper inputs, solid-state lasers putting out a few hundreds of joules became "shelf items." Even the range of kilojoules, hitherto highly classified numbers, can be found quoted in commercial offerings. Thus, a variation in output energy by a factor 10^3 is at our disposal.

The yield of gaseous lasers is two orders of magnitude lower than that of solid-state devices. Since these lasers are operated in a continuous wave mode (CW) their output is stated as the energy delivered per unit time, that is, as power, usually in joules/sec, or watts rather than as energy. The total energy follows from the exposure time. The power scale of commercially available gas lasers varies from a few tenths of a milliwatt in He–Ne tubes up to a 75-W CO_2 laser. Five-watt argon lasers or 2-W krypton lasers are available. But note that it takes a 25-kW input to operate these giants.

If the only requirement on the radiation to be applied is a high amount of energy, the primary input may be used directly and more efficiently.

2.2. Temporal Distribution of Laser Output

Gas lasers are pumped by light sources only experimentally. The normal excitation comes from dc or ac (R.F.) power supplies that drive the laser continuously (CW). Thus, the temporal distribution of these lasers is continuous as well and does not warrant any special discussion.

Solid-state lasers are pumped by light pulses from high-intensity flash lamps, hence, the temporal laser output will depend on that of the input and on the response of the laser. Moreover, time-dependent elements (filters, optical switches) can be applied within the laser cavity to shape the output in time. According to our premises, these elements belong to the laser lamp. We shall discuss the various determinants in this order.

The minimum pulse duration of a flash lamp, say at its maximum energy output, increases with the geometry of the lamp volume. Typical values range from a few hundred to a thousand microseconds (E. G. & G., length 37.5 mm, diameter 4 mm, duration 1500 μsec). The pulse exhibits a typical maximum between a steep, almost rectilinear, ascent and an exponential decay. When the laser is pumped by such a light pulse, laser action does not start from the onset, but is delayed by the time needed to overcome the threshold (generation of population inversion). Hence, the delay depends on the pump rate. From then on, the overall time distribution of the laser follows that of the input.

To obtain a more detailed picture, we must consider the laser cavity as an oscillatory system, capable of relaxation oscillation (Tang *et al.*, 1963). If care is taken to avoid temperature effects, optical imperfections in the laser, and instabilities in the cavity, strictly periodic relaxation oscillations can be recorded. Their duration is in the order of 2 μsec, depending on the pump rate; and their envelope follows the pump light.

In a normal laser where all kinds of changes take place during firing, such as uneven thermal expansion or local change in the refractive index, the output is composed of an erratic array of sharp spikes of duration like the oscillations just mentioned, with the envelope following the pump light. The threshold is not as sharp as in the ideal situation, since, on account of absorption, the tubular columns of various radii (making up the laser rod) receive different amounts of energies and, hence, reach their thresholds at different times.

Taking half of the pump duration as a typical laser duration, we find that these values vary from 50 to 750 μsec. For high-energy lasers larger lamps are required, which in turn are slower. If we take the energy output to vary from 1 to 100 J, the power attained within these times ranges from 20 to 130 kW.

Means for controlling the output were found, should the erratic output of solid-state lasers be undesirable. These methods are advantageous also for applications for which repetitive output impulses are not imperative. They produce smooth pulses, shorter in time by two to three orders of magnitude with an increase in power by the same factor. "Giant-pulse lasers" result.

The principle of all these methods consists of inserting a switch into the cavity. This switch can be activated during the pump pulse, such that it separates the pumping proper from the lasing action. In other words, as long as the switch is closed the energy threshold is so high that the input can never overcome it; with the switch suddenly open the situation is completely changed. The deposited energy is high above the (new) lowered