8: Appendices

The Appendix includes information which is important yet not sufficiently salient to the main topic to be included in the body of the dissertation.

Section 8.1 first addresses the ethical and legal responsibilities associated with performing scientific experiments on live subjects, along with a discussion of my own personal thoughts on this issue. Datasheets for many of the optical sources, detectors, and sensors used to construct the DOT instrumentation discussed above are included in Section 8.2 as a convenience, should the reader desire more information on these components. Alternate designs for the anesthetic vaporizer and agent concentration monitor are presented in Sections 0 and 8.4 respectively.

8.1 Ethical and legal responsibilities with live subjects

8.1.1 Human Subjects

The Belmont Report (selected paragraphs):

Scientific research has produced substantial social benefits. It has also posed some troubling ethical questions. Public attention was drawn to these questions by reported abuses of human subjects in biomedical experiments, especially during the Second World War. During the Nuremberg War Crime Trials, the *Nuremberg Code* was drafted as a set of standards for judging physicians and scientists who had conducted biomedical experiments on concentration camp prisoners. This Code became the prototype of many later codes intended to assure that research involving human subjects would be carried out in an ethical manner.

The codes consist of rules, some general, others specific, that guide the investigators or the reviewers of research in their work. Such rules often are inadequate to cover complex situations; at times they come into conflict, and they are frequently difficult to interpret or apply. Broader ethical principles will provide a basis on which specific rules may be formulated, criticized and interpreted.

Three principles, or general prescriptive judgments, that are relevant to research involving human subjects are identified in this statement. Other principles may also be relevant. These three are comprehensive, however, and are stated at a level of generalization that should assist scientists, subjects, reviewers and interested citizens to understand the ethical issues inherent in research involving human subjects. These principles cannot always be applied, so as to resolve beyond dispute particular ethical problems. The objective is to provide an analytical framework that will guide the resolution of ethical problems arising from research involving human subjects.

This statement consists of a distinction between research and practice, a discussion of the three basic ethical principles, and remarks about the application of these principles.

A. Boundaries Between Practice and Research

It is important to distinguish between biomedical and behavioral research, on the one hand, and the practice of accepted therapy on the other, in order to know what activities ought to undergo review for the protection of human subjects of research. The distinction between research and practice is blurred, partly because both often occur together (as in research designed to evaluate a therapy), and partly because notable departures from standard practice are often called "experimental", when the terms "experimental" and "research" are not carefully defined.

For the most part, the term "practice" refers to interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success. The purpose of medical or behavioral practice is to provide diagnosis, preventive treatment or therapy to particular individuals. By contrast, the term "research" designates an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge (expressed, for example, in theories, principles, and statements of relationships). Research is usually described in a formal protocol that sets forth an objective and a set of procedures designed to reach that objective.

When a clinician departs in a significant way from standard or accepted practice, the innovation does not, in and of itself, constitute research. The fact that a procedure is "experimental" in the sense of new, untested or different, does not automatically place it in the category of research. Radically new procedures of this description should, however, be made the object of formal research at an early stage, in order to determine whether they are safe and effective. Thus, it is the responsibility of medical practice committees, for example, to insist that a major innovation be incorporated into a formal research project.

Research and practice may be carried on together, when research is designed to evaluate the safety and efficacy of a therapy. This need not cause any confusion regarding whether or not the activity requires review; the general rule is, that if there is any element of research in an activity, that activity should undergo review for the protection of human subjects.

B. Basic Ethical Principles

The expression "basic ethical principles" refers to those general judgments that serve as a basic justification for the many particular ethical prescriptions and evaluations of human actions. Three basic principles, among those generally accepted in our cultural tradition, are particularly relevant to the ethics of research involving human subjects: the principles of respect for persons, beneficence and justice.

Respect for Persons

Respect for persons incorporates at least two ethical convictions: first, that individuals should be treated as autonomous agents, and second, that persons with diminished autonomy are entitled to protection. The principle of respect for persons thus divides into two separate moral requirements: the requirement to acknowledge autonomy, and the requirement to protect those with diminished autonomy.

An autonomous person is an individual capable of deliberation about personal goals, and of acting under the direction of such deliberation. To respect autonomy is to give weight to autonomous persons' considered opinions and choices, while refraining from obstructing their actions, unless they are clearly detrimental to others. To show lack of respect for an autonomous agent is to repudiate that person's considered judgments, to deny an individual the freedom to act on those considered judgments, or to withhold information necessary to make a considered judgment, when there are no compelling reasons to do so.

However, not every human being is capable of self-determination. The capacity for selfdetermination matures during an individual's life, and some individuals lose this capacity wholly or in part, because of illness, mental disability, or circumstances that severely restrict liberty. Respect for the immature and the incapacitated may require protecting them as they mature or while they are incapacitated.

Some persons are in need of extensive protection, even to the point of excluding them from activities which may harm them; other persons require little protection beyond making sure they undertake activities freely and with awareness of possible adverse consequences. The extent of

protection afforded should depend upon the risk of harm, and the likelihood of benefit. The judgment that any individual lacks autonomy should be periodically reevaluated, and will vary in different situations.

In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information. In some situations, however, application of the principle is not obvious. The involvement of prisoners as subjects of research provides an instructive example. On the one hand, it would seem that the principle of respect for persons requires that prisoners not be deprived of the opportunity to volunteer for research. On the other hand, under prison conditions they may be subtly coerced or unduly influenced to engage in research activities, for which they would not otherwise volunteer. Respect for persons would then dictate that prisoners be protected. Whether to allow prisoners to "volunteer" or to "protect" them presents a dilemma. Respecting persons, in most hard cases, is often a matter of balancing competing claims urged by the principle of respect itself.

Beneficence

Persons are treated in an ethical manner, not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm; and (2) maximize possible benefits, and minimize possible harms.

The Hippocratic maxim "do no harm" has long been a fundamental principle of medical ethics. Claude Bernard extended it to the realm of research, saying that one should not injure one person, regardless of the benefits that might come to others. However, even avoiding harm requires learning what is harmful; and, in the process of obtaining this information, persons may be exposed to risk of harm. Further, the Hippocratic Oath requires physicians to benefit their patients "according to their best judgment". Learning what will in fact benefit may require exposing persons to risk. The problem posed by these imperatives is to decide when it is justifiable to seek certain benefits despite the risks involved, and when the benefits should be foregone because of the risks.

The obligations of beneficence affect both individual investigators and society at large, because they extend both to particular research projects and to the entire enterprise of research. In the case of particular projects, investigators and members of their institutions are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation. In the case of scientific research in general, members of the larger society are obliged to recognize the longer term benefits and risks that may result from the improvement of knowledge, and from the development of novel medical, psychotherapeutic, and social procedures.

The principle of beneficence often occupies a well-defined, justifying role in many areas of research involving human subjects. An example is found in research involving children. Effective ways of treating childhood diseases and fostering healthy development are benefits that serve to justify research involving children --even when individual research subjects are not direct beneficiaries. Research also makes it possible to avoid the harm that may result from the application of previously accepted routine practices that, on closer investigation, turn out to be dangerous. But the role of the principle of beneficence is not always so unambiguous. A difficult ethical problem remains, for example, about research that presents more than minimal risk, without immediate prospect of direct benefit to the children involved. Some have argued that such research is inadmissible, while others have pointed out, that this limit would rule out much research promising great benefit to children in the

future. Here again, as with all hard cases, the different claims covered by the principle of beneficence may come into conflict and force difficult choices.

Justice

Who ought to receive the benefits of research and bear its burdens? This is a question of justice, in the sense of "fairness in distribution" or "what is deserved". An injustice occurs, when some benefit to which a person is entitled is denied without good reason, or when some burden is imposed unduly. Another way of conceiving the principle of justice is that, equals ought to be treated equally. However, this statement requires explication. Who is equal and who is unequal? What considerations justify departure from equal distribution? Almost all commentators allow that distinctions based on experience, age, deprivation, competence, merit and position do sometimes constitute criteria justifying differential treatment for certain purposes. It is necessary, then, to explain in what respects people should be treated equally. There are several widely accepted formulations of just ways to distribute burdens and benefits. Each formulation mentions some relevant property, on the basis of which burdens and benefits should be distributed. These formulations are (1) to each person an equal share, (2) to each person according to individual need, (3) to each person according to individual effort, (4) to each person according to societal contribution, and (5) to each person according to merit.

Questions of justice have long been associated with social practices, such as punishment, taxation and political representation. Until recently, these questions have not generally been associated with scientific research. However, they are foreshadowed, even in the earliest reflections on the ethics of research involving human subjects. For example, during the 19th and early 20th centuries, the burdens of serving as research subjects fell largely upon poor ward patients, while the benefits of improved medical care flowed primarily to private patients. Subsequently, the exploitation of unwilling prisoners as research subjects in Nazi concentration camps was condemned as a particularly vagrant injustice. In this country, in the 1940's, the Tuskegee syphilis study used disadvantaged, rural black men to study the untreated course of a disease that is by no means confined to that population. These subjects were deprived of demonstrably effective treatment in order not to interrupt the project, long after such treatment became generally available.

Against this historical background, it can be seen how conceptions of justice are relevant to research involving human subjects. For example, the selection of research subjects needs to be scrutinized in order to determine whether some classes (*e.g.*, welfare patients, particular racial and ethnic minorities, or persons confined to institutions) are being systematically selected, simply because of their easy availability, their compromised position, or their manipulability, rather than for reasons directly related to the problem being studied. Finally, whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them, and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research.

The Institutional Review Board (IRB)

The IRB is an administrative body established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices of the institution with which it is affiliated. The IRB has the authority to approve, require modifications in, or disapprove all research activities that fall within its jurisdiction as specified by both the federal regulations and local institutional policy. Research that has been reviewed and approved by an IRB may be subject to review and disapproval by officials of the institution.

The IRB also functions independently of but in coordination with other committees. For example, an institution may have a research committee that reviews protocols to determine whether the

institution should support the proposed research. The IRB, however, makes its independent determination whether to approve or disapprove the protocol based upon whether or not human subjects are adequately protected.

The first two questions the IRB faces is whether the activity involves research, and second, whether it involves human subjects. **Research** is defined by the regulations as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge." **Human subjects** are defined by the regulations as "living individual(s) about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information." Some research that involves human subjects may be exempt from the regulations requiring IRB review. Examples include educational testing and survey procedures where no identifying information will be recorded that can link subjects to the data, and disclosure of the data could not reasonably place the subjects at risk of civil or criminal liability or be damaging to the subjects' financial standing, employability, or reputation; and research that involves the use of existing data, documents, or specimens, where no identifying information will be recorded that can link subjects to the data.

An IRB must have at least five members, with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members and the diversity of their backgrounds, including considerations of their racial and cultural heritage and their sensitivity to issues such as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. The IRB must include at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. It must also include at least one member who is not otherwise affiliated with the institution and who is not part of the immediate family of a person who is affiliated with the institution.

There are two types of IRB Review:

Full Review – Review of proposed research at a convened meeting at which a valid quorum of IRB members is present. For the research to be approved, it must receive the approval of a majority of those members present.

Expedited Review – Review of proposed research by the IRB Chair or a designated voting member rather than by the entire IRB. Expedited review is permitted for approval of minor changes to previously approved research and approval of exempt research.

Informed Consent

Informed consent is the process of communicating to the subject, the purpose, risks, benefits, and voluntary nature of a specific study. The **informed consent form** documents that such communication process took place. The consent form should be written in lay terms. If technical language cannot be avoided, the terms should be defined so that subjects can make an informed decision.

The basic required elements of the consent form must include:

- An explanation of the **purposes** of the research and the expected duration of the subject's participation
- A description of any reasonably foreseeable risks or discomforts to the subject
- A description of any **benefits** to the subjects or others which may reasonably be expected from the research
- A disclosure of appropriate **alternative procedures** or courses of treatment, if any, that might be advantageous to the subject

- A statement describing the extent to which **confidentiality** of records identifying the subject will be maintained
- For research involving more than minimal risk, or involving any invasive procedure, an explanation as to whether any **compensation for injury** and any medical treatment are available if injury occurs and, if so, what they consist of, or where further information may be obtained
- An explanation of **whom to contact** for answers to pertinent questions about the research, and whom to contact in the event of a research-related problem
- A statement that **participation is voluntary**, the subject may refuse to participate, and may discontinue participation at any time without penalty or loss of benefits to which he/she is otherwise entitled

8.1.2 Animal Experimentation

The discord concerning animal experimentation is still one of the more heated issues in society today. Many believe that any use of animals for research is fundamentally wrong, and some have even committed acts of violence against researchers and have intentionally destroyed research facilities and equipment, often resulting in the inadvertent deaths of many of the animals they set out to protect. By virtue of my direct participation in the use of animals for research, I have been forced to address this issue myself, and I feel that it is important for every researcher to, at a minimum, be cognizant of the many contrasting beliefs involved. Although this may not directly change how research is performed, it will enable researchers to act in a manner which may help mitigate much of the public ignorance and subsequent fear and loathing that surrounds the field of animal research, thus easing the tension on both sides of this contentious issue.

Information from two of the largest organizations involved in the animal rights issue is presented below. Although far from complete, this will give the reader a taste of some of the salient beliefs and concerns held by those on both sides of the issue. Readers are encouraged to search the Web, which is a valuable source of information on this topic.

People for the Ethical Treatment of Animals (PeTA):

People for the Ethical Treatment of Animals (PeTA), with more than 750,000 members, is the largest animal rights organization in the world. Founded in 1980, PeTA is dedicated to establishing and protecting the rights of all animals. PeTA operates under the simple principle that animals are not ours to eat, wear, experiment on, or use for entertainment.

PeTA focuses its attention on the four areas in which the largest numbers of animals suffer the most intensely for the longest periods of time: on factory farms, in laboratories, in the fur trade, and in the entertainment industry. We also work on a variety of other issues, including the cruel killing of beavers, birds and other "pests," and the abuse of backyard dogs.

PeTA works through public education, cruelty investigations, research, animal rescue, legislation, special events, celebrity involvement, and direct action.

The Foundation for Biomedical Research (FBR):

Animal research has played a vital role in virtually every major medical advance of the last century – for both human and animal health. From antibiotics to blood transfusions, from dialysis to organ transplantation, from vaccinations to chemotherapy, bypass surgery and joint replacement, practically every present-day protocol for the prevention, treatment, cure and control of disease, pain and suffering is based on knowledge attained through research with animals.

The anti-research element of animal rights movement frequently claims that the results of animal studies can't be applied to human health. However, physicians and researchers overwhelmingly agree that animal systems provide invaluable and irreplaceable insights into human systems because there are striking similarities between the physiological and genetic systems of animals and humans. The essential need for animal research is recognized and supported by medical societies and health agencies around the world. Concrete proof of its validity can also be found in the vast body of Nobel Prize winning work in physiology and medicine that has been based on animal studies.

Since 1900, modern medicine has boosted the average life span in the United States by almost 30 years. In 1999, infant mortality in the USA – a key indicator of the nation's health – was measured at seven deaths per 1,000 live births compared to 55 deaths per 1,000 live births in 1935.

Many diseases that once killed millions of people every year are now either preventable, treatable or have been eradicated altogether. Immunizations against polio, diphtheria, mumps, rubella and hepatitis save countless lives and the survival rates for many major diseases are at an all time high thanks to the discovery of new drugs and the design of sophisticated medical devices and surgical procedures.

Animal research has also resulted in many remarkable life-saving and life-extending treatments for cats, dogs, farm animals, wildlife and endangered species. Pacemakers, artificial joints, organ transplants and freedom from arthritic pain are just a few of the breakthroughs made in veterinary medicine thanks to animal research. Vaccinations for rabies, distemper, parvo virus, infectious hepatitis, anthrax, tetanus and feline leukemia ensure that dogs, cats, sheep, cattle, deer and foxes live longer, happier, healthier lives. New treatments for glaucoma, heart disease, cancer, hip dysplasia and traumatic injuries extend and enhance the lives of beloved companion animals.

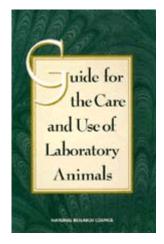
For humane, compassionate and scientific reasons, researchers are deeply concerned about the condition of the animals they study. This is not a controversial position; there is no constituency for inhumane treatment. Poor care results in unreliable research data. For results to be valid, animal subjects must be healthy. Also, pain and distress are thought to have negative impact on the immune system, so researchers are careful to protect their animals from undue stress. It is well recognized that laboratory animals have been indispensable in the cause of medical and scientific discovery. We have a moral duty to provide them the best care and treatment possible.

The USDA has set forth federal regulations governing the care and use of laboratory animals in biomedical research that are more extensive that those covering human subjects. The AWA (Animal Welfare Act) sets high standards of care for research animals with regard to their housing, feeding, cleanliness, ventilation and medical needs. It also requires the use of anesthesia or analgesic drugs for potentially painful procedures and during post-operative care. Most importantly, research institutions are required - by law - to establish an Institutional Animal Care and Use Committee (IACUC) to oversee their work with animals. IACUCs require researchers to justify their need for animals; select the most appropriate species and use the fewest number of animals possible to answer a specific question. All IACUCs include at least one veterinarian and one community representative, unaffiliated with the institution. These committees have the authority to reject any research proposal and stop any project it believes has failed to meet proper standards. The U.S. Public Health Service (PHS) Act requires that all institutions receiving research funds from the National Institutes of Health, the Food and Drug Administration or the Centers for Disease Control, adhere to the standards set out in the Guide for the Care and Use of Laboratory Animals. Under the PHS policy, institutions must follow detailed animal care recommendations and establish an IACUC to ensure that all animals are treated responsibly and humanely.

Those who work in the medical field and see the effects of disease feel no ambivalence about the value of animal research. Although research opponents portray the medical community as deeply

divided over the merits of animal research, a survey by the American Medical Association found that 99 percent of active physicians in the U.S. believed that animal research had contributed to medical progress, and 97 percent supported the continued use of animals for basic and clinical research. More recently, a survey of living Nobel Laureates for medicine found unanimous support for animal research.

The Guide for the Care and Use of Laboratory Animals



Published by The Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council, National Academy Press, Washington, D.C.

The goal of the *Guide* is to promote the humane care of animals used in biomedical and behavioral research, teaching, and testing; the basic objective is to provide information that will enhance animal well-being, the quality of biomedical research, and the advancement of biologic knowledge that is relevant to humans or animals. The use of animals as experimental subjects in the 20th century has contributed to many important advances in scientific and medical knowledge (Leader and Stark 1987). Although scientists have also developed non-animal models for research, teaching, and testing (NRC 1977; see Appendix A, "Alternatives"), these models often cannot completely mimic the complex human or animal body, and continued progress in human and animal health and well-being requires the use of living animals. Nevertheless, efforts to develop and use scientifically valid alternatives, adjuncts, and refinements to animal research should continue.

The *Guide for the Care and Use of Laboratory Animals* (the *Guide*) strongly affirms the conviction that all who care for or use animals in research, teaching, or testing must assume responsibility for their well-being. The *Guide* is applicable only after the decision is made to use animals in research, teaching, or testing. Decisions associated with the need to use animals are not within the purview of the *Guide*, but responsibility for animal well-being begins for the investigator with that decision.

The Institutional Animal Care and Use Committee (IACUC)

An Institutional Animal Care and Use Committee is established at every institution which is involved in the use of animals for research purposes. The IACUC consists of at least five members:

* One veterinarian with training or experience in laboratory animal science and medicine, who has direct or delegated authority and responsibility for activities involving animals at the institution

* One practicing scientist experienced in research with animals

* One member whose primary concerns are in a nonscientific area (e.g., ethicist, lawyer, member of the clergy), and

* One member who is not affiliated with the institution other than as a member of the IACUC Its tasks consist of the following:

Protocol Review

The IACUC oversees the specific use of animals by formally reviewing protocols, either at a convened meeting of a quorum (simple majority), or through the use of designated reviewers. **Semiannual Program Reviews and Facility Inspections**

The IACUC monitors the animal care and use program by conducting thorough reviews of the program and inspections of the animal facilities. These program review and facility inspections must occur at six-month intervals, or semiannually.

Addressing Animal Welfare Concerns

The IACUC has a mandate to evaluate concerns regarding the care and use of animals at the institution. Concerns may be raised by staff or employees of the institution, individuals in the community, or even members of the IACUC. It is a good idea for the IACUC to develop guidelines or procedures for handling allegations of mistreatment or noncompliance before such allegations are raised. The IACUC should also be cognizant of the rights of whistle blowers under the AWA, which prohibits discrimination against or reprisal for reporting violations of regulations or standards under the AWA.

Suspension of Animal Activities

The IACUC is empowered to suspend a project if it finds violations of the PHS Policy, Guide, Assurance, or Animal Welfare Regulations. Suspension may occur only after review of the matter at a convened meeting of a quorum of the IACUC, and with the suspension vote of a majority of the quorum present. Further, the IACUC must consult with the Institutional Official regarding the reasons for the suspension. The Institutional Official is required to take appropriate corrective action, and report the action and the circumstances surrounding the suspension to OLAW. Because an IACUC action to suspend a project is a serious matter, the action must be reported to OLAW promptly.

8.1.3 Certification and regulatory organizations

AAALAC

AAALAC (the Association for Assessment and Accreditation of Laboratory Animal Care) is a private nonprofit organization that promotes the humane treatment of animals in science through a voluntary accreditation program. More than 650 companies, universities, hospitals, government agencies and other research institutions have earned AAALAC accreditation, demonstrating their commitment to responsible animal care and use. These institutions *volunteer* to participate in AAALAC's program, in addition to complying with the local, state and federal laws that regulate animal research.

AAALAC certifies that an animal care program meets the standards as set forth in the latest edition of The Guide for the Care and Use of Laboratory Animals (the Guide), all federal laws and regulations, and various other universally available guidelines. On-site accreditation reviews are conducted at least every three years and include inspection of housing and research facilities, review of animal care standards, and evaluation of institutional policies as they relate to the care and use of animals in research and teaching. Compliance requirements include an annual report detailing any changes in staff, equipment, and programs and an annual usage report for all vertebrate animals.

The USDA Animal and Plant Health Inspection Service (APHIS)

The Animal and Plant Health Inspection Service (APHIS) of the United States Department of Agriculture (USDA) is the regulatory arm of the government responsible for enforcing the regulations

established by the Secretary of Agriculture under the mandate of the Animal Welfare Act (AWA). These regulations set standards for humane handling, housing, space, feeding and watering, sanitation and ventilation, adequate veterinary care, and transportation. Compliance requirements include annual reports documenting adequate veterinary care and periodic unannounced inspections by APHIS personnel.

Office of Laboratory Animal Welfare (OLAW)

OLAW is responsible for the general administration and coordination of Public Health Service policy regarding animal care and use. Federal awarding units may not make an award for a project involving animals unless the institution submitting the application or proposal is on the list of institutions that have an approved Assurance on file with OLAW, and the responsible institutional official has provided verification of approval by the IACUC.

8.1.4 My viewpoint on bioethics in animal research

Although I understand and accept the fact that my research involves the use of live animals, my working with them have given me an opportunity to become quite fond of them as well. As a consequence, my views on animal welfare concur with most of the currently accepted bioethical views towards the treatment of laboratory animals, however there are some differences. They can be simplified into the three overlapping concepts of parsimony, efficiency, and reutility:

Parsimony – Use as few animals as possible to establish your objectives. Avoid unnecessary duplication of effort unless additional knowledge and experience can be gained from each creature.

In some cases, proof-of-principle experiments can operate with much smaller control groups. Better equipment design (i.e. improved SNR, lower drift, etc.) may also reduce the need for multiple subjects.

Efficiency – Obtain as much utility as possible from each animal. Plan each experiment carefully so as to maximize the amount of knowledge gained. Fully explore the causes of every adverse outcome, and take the necessary steps to prevent similar adverse events from occurring in the future.

Experiments should be developed in such a way as to provide data of the highest possible quality. This both benefits your reputation as a researcher and minimizes the need for future researchers to replicate your work.

If an unforeseen event occurs which results in the loss of valuable data or the unnecessary or premature death of a subject, then it should be investigated carefully to be sure that all of the causes are fully understood. The procedures and/or hardware should then be modified to prevent similar events from occurring in the future.

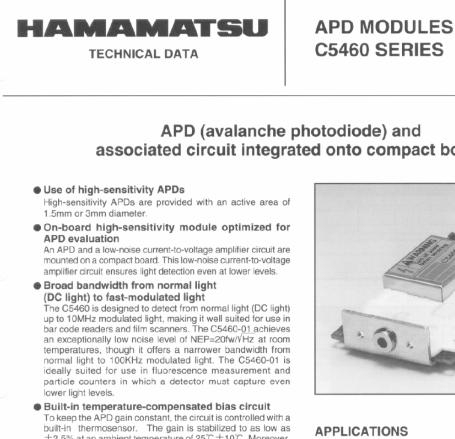
Reutility – Recycle as many creatures as possible in the form of simultaneous or consecutive experiments, as food for another creature, as fertilizer, or for some other productive use. Consider future use when developing anesthetic and drug protocols.

If one creature can serve as the subject of two or more experiments, then the life of a second animal can be spared. However this must be tempered by the degree of suffering and discomfort involved in combining multiple procedures. In many cases though, heavily anesthetized rodents used for imaging experiments and slated for euthanasia can also provide others with the opportunity to practice their surgical skills. Such use, if performed properly, does not cause any additional suffering, and in fact allows researchers to develop skills which will likely lead to both better surgical proficiency and more efficient use of rodents in the future. Many experiments involve a sizable number of control subjects. These are often quite healthy, yet are typically euthanized at the end of the experiment. It seems appropriate to allow these creatures to live out their remaining lives in relative comfort, to offer them up as pets, or to use them as food for other creatures (i.e. feeding healthy rats, mice, and rabbits to snakes, birds of prey, or predatory cats in zoos, for example). The result is a reduction in the overall number of creatures consumed.



8.2 Datasheets useful to DOT hardware designers

Hamamatsu C5460 Series APD Module



 $\pm 2.5\%$ at an ambient temperature of $25^{\circ}C \pm 10^{\circ}C$. Moreover, ripple noise inherent in high-voltage power supplies is greatly minimized.

Compact and lightweight

The board is no larger than the size of a business card.

needs. Please feel free to contact our sales office.

APD (avalanche photodiode) and associated circuit integrated onto compact board

Low cost

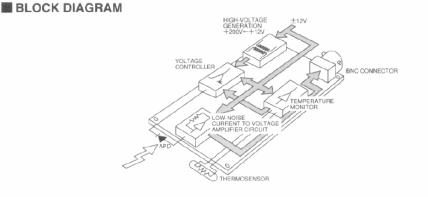
* Hamamatsu will supply customized devices with different dimensions and specifications to meet the customers'

KACCCH

APPLICATIONS

Evaluation of APD

- Fluorescence measurement
- Bar code readers
- Particle counters
- Film scanners



Information furnished by HAMAMATSU is believed to be reliable. However, no responsibility is assumed for possible inaccuracies or omission Specifications are subject to change without notice. No patent rights are granted to any of the circuits described herein. © 1995 Hamamatsu Photonics K.K.

APD MODULES C5460 SERIES

MAXIMUM RATINGS

Parameter	Value	Unit
Positive Supply Voltage	+16	V
Negative Supply Voltage	-16	V
Operating Temperature	0 to +60	°C
Storage Temperature	-30 to +70	°C

SPECIFICATIONS (Typical at Ta=25°C, Vcc=±12V, unless otherwise specified)

Photoelectric Conversion Section (APD)
--

C5460		C5460-01	Unit	
¢ 1.5		<i>ф</i> 3.0	mm	
400 to 1000				
	nm			
	0.5		A/W	
±:	2.5 Тур.	±5 Max.	%	
	¢ 1.5 400	φ 1.5 400 to 1000 800	¢ 1.5	

High-speed Amplifier Section (C5460)

Parameter		Min.	Тур.	Max.	Unit	
Cutoff Frequency	High	9	10	_	MHz	
(-3 dB)	Low	_	DC	_		
NEP (800nm)			0.2	0.4	pW/Hz1/2@10MHz	
Feedback Resistance			10		KΩ	
Photoelectric Sensitivity* (including APD, 800nm, gain=30)		1.4	1.5	1.6	10°V/W	
Maximum Input Light Intensity		5.0	6.0	_	μW	
Minimum Detection Lir	nit	_	0.8	1.6	nW	

* The gain is preset to "30" when shipping.

High-speed	Amplifier	Section	(C5460-01)
			()

Parameter		Min.	Тур.	Max.	Unit
Cut-off Frequency High		80	100	_	kHz
(-3 dB)	Low		DC		KHZ
NEP (800nm)			0.02	0.04	pW/Hz1/2@100KHz
Feedback Resistance			10		MΩ
Photoelectric Sensitivity* (including APD, 800nm, gain=30)		-1.4	-1.5	-1.6	10 ⁸ V/W
Maximum Input Light Intensity		0.05	0.06		μW
Minimum Detection Lir	nit		0.005	0.01	nW

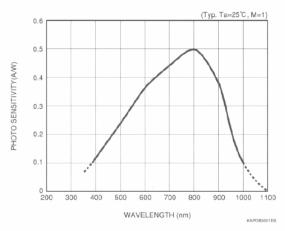
* The gain is preset to "30" when shipping.

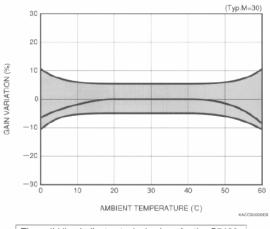
GENERAL RATINGS

Parameter			C5460			Link			
		Min.	Тур.	Max.	Min.	Тур.	Max.	Unit	
Supply Voltage	(+12V)	+11.4	+11.4 +12	+12	+12.6	+11.4	+12	+12.6	V
	(-12V)	-11.4	-12	-12.6	-11.4	-12	-12.6	v	
Current Consumption	on (+12V)	3	+30	+45		+35	+45	mA	
	(-12V)		-11	-16		-11	-16	ША	
Board Dimensions				80×	50×23			mm	
Weight				Į	52			g	

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Figure 2: Gain Variation vs. Ambient Temperature





The solid line indicates typical values for the C5460.

Figure 3: Frequency Characteristics

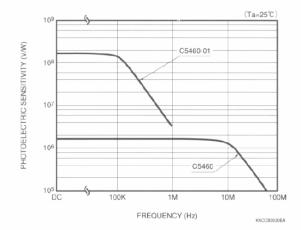


Figure 4: Response to Stepped Light Input (C5460)

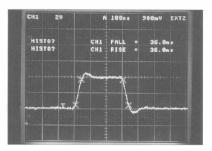


Figure 5: Response to Stepped Light Input (C5460-01)

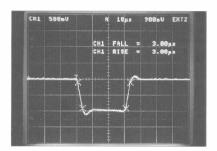
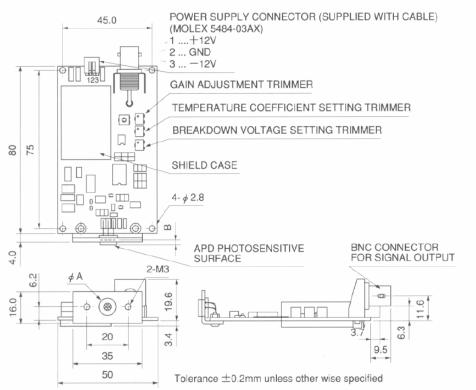


Figure 1: Spectral Response

APD MODULES C5460 SERIES

Figure 6: Dimensional Outlines (Unit: mm)



	100	

Type No.	φA	В
C5460	8.2±0.2	2.1±0.2
C5460-01	8.1±0.1	1.7±0.2

CAUTION: Do not touch adjustment trimmers other than those used for gain adjustment.

> Because a high-voltage power supply is used in this device, never remove any insulating material potted or molded onto the board.



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Cat. No. KACC1010E02 Jul. 1995 T Printed in Japan (1,000)

Metal Package PMT Photosensor Modules H5773/H5783/H6779/H6780 Series



The H5773/H5783/H6779/H6780 series are photosensor modules housing a metal package PMT and high-voltage power supply circuit. The metal package PMTs have a metallic package with the same diameter as a TO-8 package used for semiconductor photodetectors, and deliver high gain, wide dynamic range and highspeed response while maintaining small dimensions identical to those of photodiodes. The internal high-voltage power supply circuit is also compact, making the module easy to use.

Considering the mounting methods, a cable output type and a pin output type are provided, and a total of 7 types are available according to the wavelength range to be measured. A P-type is also available with selected gain and dark count ideal for photon counting under extremely low light conditions.

Product Variations

Suffix Type No.	None	-01	-02	-03	-04	-06	-20	Output Type	Features
H5773	yes	yes	yes	yes	yes	yes	yes	On-board	Low power consumption
H5783	yes	yes	yes	yes	yes	yes	yes	Cable output	
H5773P	yes	no	no	no	no	no	no	On-board	For photon counting
H5783P	yes	no	no	no	no	no	no	Cable output	Low power consumption
H6779	yes	yes	yes	yes	yes	yes	yes	On-board	Low ripple noise
H6780	yes	yes	yes	yes	yes	yes	yes	Cable output	Fast settling time

Suffix	Spectral Response
None	300 nm to 650 nm
-01	300 nm to 850 nm
-02	300 nm to 880 nm
-03	185 nm to 650 nm
-04	185 nm to 850 nm
-06	185 nm to 650 nm
-20	300 nm to 900 nm

higher sensitivity than the -03 type below 300 nm in wavelength range.

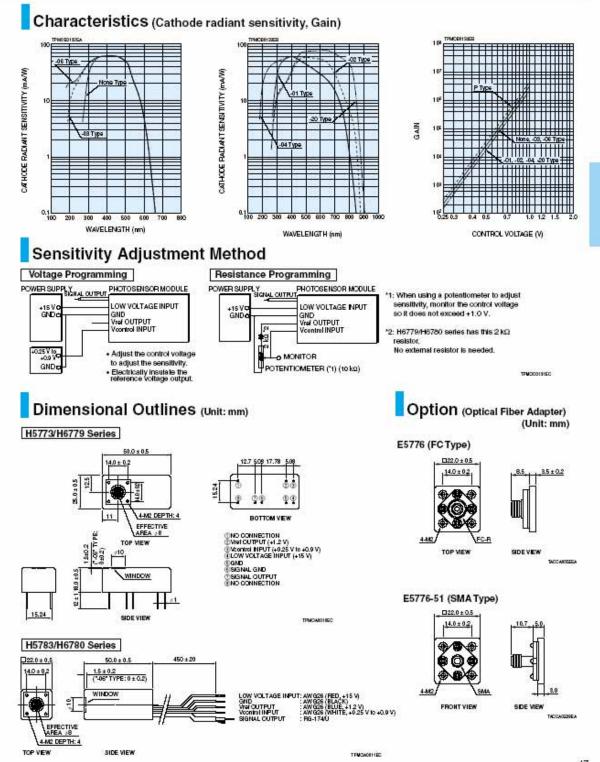
Specifications

Parameter				H5773 / H5783 / H6779 / H6780 Series						
Su	ffix	A192210510404000		None	-03, -06	-01, -04	-02	-20		
Inp	ut \	/oltage	33	+11.5 to +15.5						
Max. Input Voltage			+18							
Max. Input Current				H5773 / H5783 Series: 9 H6779 / H6780 Series: 30						
Ma	x. C	Output Signal Current				100			μA	
Ma	x. C	Control Voltage	20		+1.0 (lr	put impedance	100 kΩ)		V	
Reo	omm	ended Control Voltage Adjus	tment Range			+0.25 to +0.9	2		V	
Eff	ectiv	ve Area				¢8	к.		mm	
Sensitivity Adjustment Range				1:104			8 - s			
Peak Sensitivity Wavelength		420	420	400	500	630	nm			
	Luminous Sensitivity	Min.	40	40	80	200	350			
Cathode	Lu	Eurinious Sensitivity	Тур.	70	70	150	250	500	μA/Ir	
5	Blue Sensitivity Index (CS		5-58)	8	8				200	
Bed/White Ratio Radiant Sensitivity *1				0.2	0.25	0.45	$1 \rightarrow$			
		62	62	60	58	78	mAA			
	9 e	Luminous Sensitivity	Min.	10	10	15	25	35	A/In	
	P-		Тур.	50	50	75	125	250	5538	
	arc	Radiant Sensitivity	*1 *2	4.3 × 104	4.3 × 104	$3.0 imes 10^{4}$	2.9 × 104	3.9 × 104	AM	
	Standard	Dark Current *2 *3	Тур.	0.2	0.2	0.4	2	2		
Anode	ŝ	Dark Current	Max.	2	2	4	20	20	nA	
š	1	Gain *2	Min.	7.5×10 ⁵	3	!	. <u></u>			
-	9		Тур.	1×10 ^e			<u></u>		1.87	
	T_	Radiant Sensitivity	•1 •2	6.2×104		3			AM	
	٩	Dark Count *2 *3	Тур.	80	80 —					
		Daix Count	Max.	400	400 —					
Ris	eΤ	ime *2		AD 15.01 19		0.78			ns	
				H5773 Series	H5783 S	eries H67	79 Series	H6780 Series		
Rip	ple l	Noise *2 *4 (peak to peal	k) Max.		1.2		0.	8	mV	
		g Time *5	1740 - S		2	2	0.:	2	S	
Op	erat	ting Ambient Temper	ature	+5	to +50	1	+5 to	+45	°C	
Sto	orag	e Temperature				-20 to +50		100 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	°C	
Weight			77.	60	80		60	80	g	

*3: After 30 minute storage in darkness

*1: Measured at the peak sensitivity wavelength *2: Control voltage = +0.8 V *3: After 30 minute storage in darknes *4: Cable RG-174/U, Cable length 450 mm, Load resistance = 1 MΩ, Load capacitance = 22 pF 16 *5: The time required for the output to reach a stable level following a change in the control voltage from +1.0 V to +0.5 V.

Current Output Type Photosensor Modules



Hamamatsu H6573 Modulated PMT Module



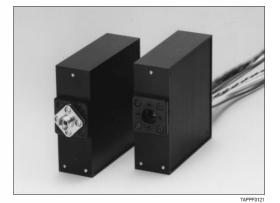
MODULATED PHOTOMULTIPLIER TUBE MODULE H6573

FEATURES

- Easy modulation
- High frequency modulation
- Fast time resolution
- Built-in high voltage power supply

APPLICATIONS

- Biochemical fluorescence decay time measurement
- LASER range finder
 - Distance measurement
 - 3-D imaging
 - Laser doppler velocimeter
- Near infrared tissue measurement



MAXIMUM RATINGS (Absolute Maximum Values)

Parameter	Value	Unit
Supply Voltage	±15.6	V
Maximum Control Voltage	+1.2	V
Maximum Anode Output Current	10	μA
Operating Temperature	0 to +50	°C
Storage Temperature	-20 to +50	C

SPECIFICATIONS (at 25 ℃)

Parameter	Value	Unit
Spectral Response	185 to 850	nm
Photocathode Minimum Effective Area	2 × 3	mm
Modulation Frequency®	1 to 400	MHz
High Voltage Settling Time (Vcont. 1.0 V to 0.5 V)	2	S
Supply Current Requirement	+12 mA / -1 mA (±15 V operation)	-

NOTE (A) :at 0.4 Modulation Factor

Subject to local technical requirements and regulations, availability of products included in this promotional material may vary. Please consult with our sales office. Information furnished by HAMAMATSU is believed to be reliable. However, no responsibility is assumed for possible inaccuracies or omissions. Specifications are subject to change without notice. No patent rights are granted to any of the circuits described herein. © 1997 Hamamatsu Photonics K.K.

MODULATED PHOTOMULTIPLIER TUBE MODULE H6573

Figure 1: Typical Spectral Response

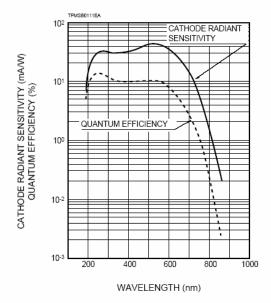


Figure 2: Typical Modulation Factor vs. Frequency

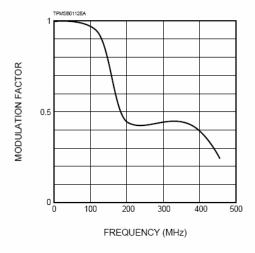


Figure 3: Typical Gain vs. Control Voltage

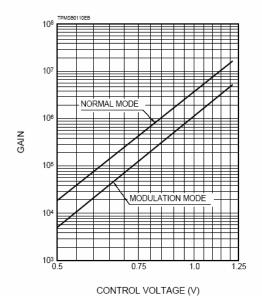


Figure 4: Block Diagram

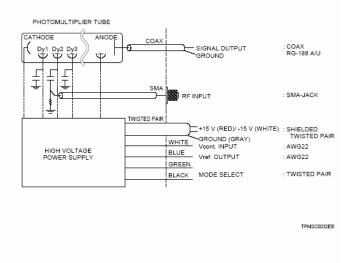
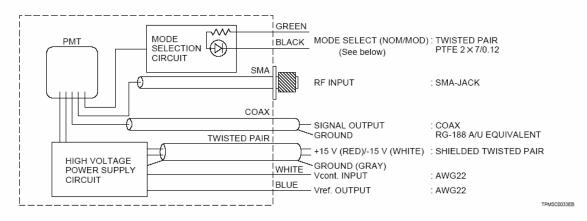


Figure 5: Module Functional Diagram

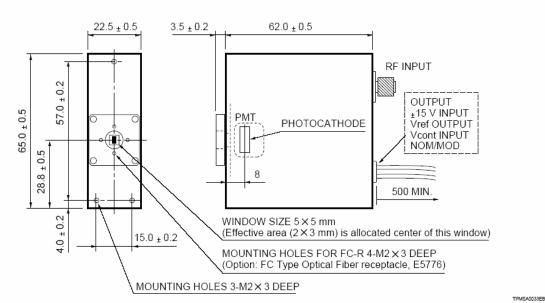


MODE

There are two operation modes in this module. They are the MODULATING(MOD) MODE and NORMAL(NOM) OPERATING MODE. The mode selection is made by the input voltage of 5 V to the NOM/MOD switch circuit.

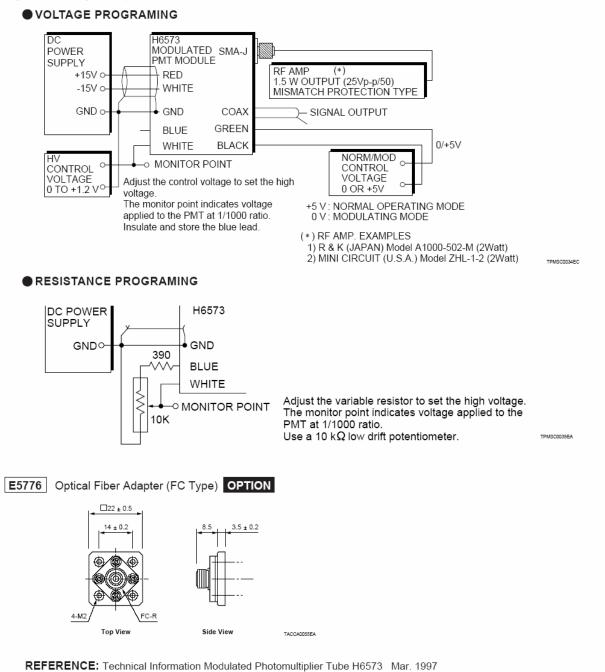
- MODULATING MODE(NOM/MOD=0 V; Either short or open circuit) The MODULATING MODE is used for PMT modulating operation. The voltage distribution to dynodes in the MODULATING MODE is different from NORMAL OPERATING MODE. Therefore, the gain is lower than NORMAL OPERATING MODE. Refer Fig. 3
- 2) NORMAL OPERATING MODE(NOM/MOD=5 V, +5 V between Green and Black cable) This is for a normal PMT operation. +5 V from an external power supply is needed to be operated at this mode.

Figure 6: Dimensional Outline (Unit: mm)



MODULATED PHOTOMULTIPLIER TUBE MODULE H6573

Figure 7: Wiring Examples

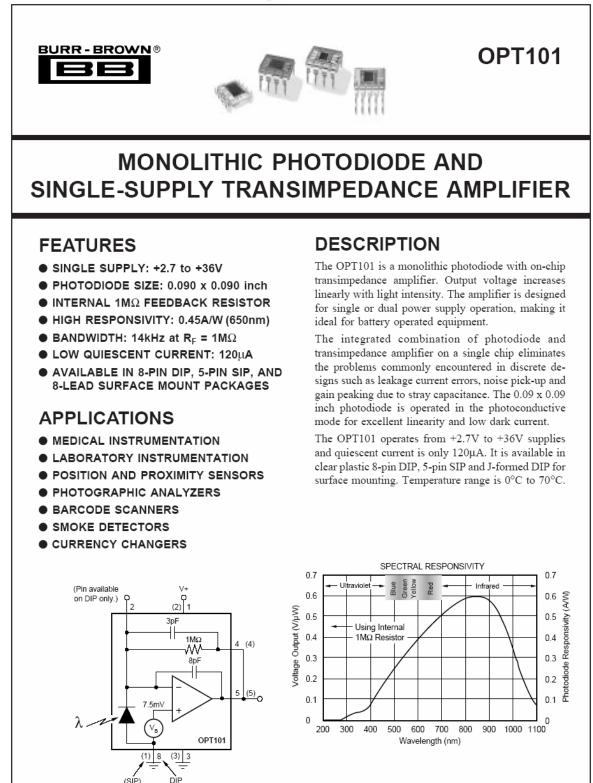


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TPMS1029E06 JUN. 1997 SI (9703) Printed in Japan



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SPECIFICATIONS

At T_A = +25°C, V_S = +2.7V to +36V, λ = 650nm, internal 1M Ω feedback resistor, and R_L = 10k Ω , unless otherwise noted.

			OPT101P, W			
PARAMETER	CONDITIONS	MIN	TYP	MAX	UNITS	
RESPONSIVITY Photodiode Current Voltage Output vs Temperature Unit to Unit Variation Nonlinearity ⁽¹⁾ Photodiode Area	650nm 650nm FS Output = 24V (0.090 x 0.090in) (2.29 x 2.29mm)		0.45 0.45 100 ±5 ±0.01 0.008 5.2		A/W V/μW ppm/°C % % of FS in ² mm ²	
DARK ERROR S , RTO ⁽²⁾ Offset Voltage, Output vs Temperature vs Power Supply Voltage Noise, Dark, f _B = 0.1Hz to 20kHz	V _S = +2.7V to +36V V _S = +15V, V _{PIN3} = -15V	+5	+7.5 ±2.5 10 300	+10 100	mV μV/°C μV/∨ μVrms	
TRANSIMPEDANCE GAIN Resistor Tolerance, P W vs Temperature			1 ±0.5 ±0.5 ±50	±2	MΩ % % ppm/°C	
FREQUENCY RESPONSE Bandwidth Rise Fall Time, 10% to 90% Settling Time, 0.05% 0.1% 1% Overload Recovery	V _{OUT} = 10Vp-p V _{OUT} = 10V Step V _{OUT} = 10V Step 100%, Return to Linear Operation		14 28 160 80 70 50		kHz µs µs µs µs	
OUTPUT Voltage Output, High Capacitive Load, Stable Operation Short-Circuit Current	V _S = 36V	(V _S) – 1.3	(V _S) – 1.15 10 15		V nF mA	
POWER SUPPLY Operating Voltage Range Quiescent Current	Dark, V _{PIN3} = 0V R _L = ∞, V _{OUT} = 10V	+2.7	120 220	+36 240	V μΑ μΑ	
TEMPERATURE RANGE Specification Operating Storage Thermal Resistance, θ _{JA}		0 0 –25	100	+70 +70 +85	သိံ ဂံ ဂံ &ဂံ ဂံ ဂံ	

NOTES: (1) Deviation in percent of full scale from best-fit straight line. (2) Referred to Output. Includes all error sources.

PHOTODIODE SPECIFICATIONS

 $T_{\rm A}$ = +25°C, $V_{\rm S}$ = +2.7V to +36V unless otherwise noted.

		Photodiode of OPT101P			
PARAMETER	CONDITIONS	MIN	TYP	MAX	UNITS
Photodiode Area	(0.090 x 0.090in) (2.29 x 2.29mm)		0.008 5.2		in ² mm ²
Current Responsivity	650nm 650nm		0.45 865		A/W μA/W/cm²
Dark Current vs Temperature	V _{DIODE} = 7.5mV		2.5 doubles every 7°C		рА
Capacitance			1200		pF

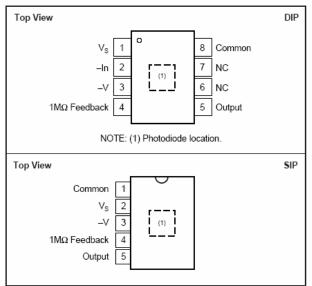
OP AMP SPECIFICATIONS

At T_A = +25°C, V_S = +2.7V to +36V, λ = 650nm, internal 1M Ω feedback resistor, and R_L = 10k Ω , unless otherwise noted.

			OPT101 Op Amp ⁽¹)	
PARAMETER	CONDITIONS	MIN	ТҮР	MAX	UNITS
INPUT Offset Voltage vs Temperature vs Power Supply Input Bias Current vs Temperature Input Impedance Differential Common-Mode Common-Mode Input Voltage Range Common-Mode Rejection	(–) Input (–) Input Linear Operation		±0.5 ±2.5 10 165 1 400 5 250 35 0 to [(V _S) – 1] 90		mV μV/°C μV/V pA pA/°C MΩ pF GΩ pF V dB
OPEN-LOOP GAIN Open-loop Voltage Gain			90		dB
FREQUENCY RESPONSE Gain-Bandwidth Product ⁽²⁾ Slew Rate Settling Time 1% 0.1% 0.05%			2 1 5.8 7.7 8.0		MHz V/μs μs μs μs
OUTPUT Voltage Output, High Short-Circuit Current	V _s = +36V	(V _s)– 1.3	(V _s) – 1.15 15		V mA
POWER SUPPLY Operating Voltage Range Quiescent Current	Dark, V _{PIN3} = 0V R _L ∞, V _{OUT} = 10V	+2.7	120 220	+36 240	ν μΑ μΑ

NOTES: (1) Op amp specifications provided for information and comparison only. (2) Stable gains ≥ 10V/V.

PIN CONFIGURATIONS



ABSOLUTE MAXIMUM RATINGS

Supply Voltage (V _S to "Common" or pin 3)	0 to +36V
Output Short-Circuit (to ground)	Continuous
Operating Temperature	–25°C to +85°C
Storage Temperature	–25°C to +85°C
Junction Temperature	+85°C
Lead Temperature (soldering, 10s)	+300°C
(Vapor-Phase Soldering Not Recommended)	

PACKAGE INFORMATION

PRODUCT	COLOR	PACKAGE	PACKAGE DRAWING NUMBER ⁽¹⁾
OPT101P	Clear	8-Pin Plastic DIP	006-1
OPT101P-J	Clear	8-Lead Surface Mount ⁽²⁾	006-4
OPT101W	Clear	5-Pin Plastic SIP	321

NOTE: (1) For detailed drawing and dimension table, please see end of data sheet, or Appendix C of Burr-Brown IC Data Book. (2) 8-pin DIP with J-formed leads for surface mounting.

ELECTROSTATIC DISCHARGE SENSITIVITY

This integrated circuit can be damaged by ESD. Burr-Brown recommends that all integrated circuits be handled with appropriate precautions. Failure to observe proper handling and installation procedures can cause damage.

ESD damage can range from subtle performance degradation to complete device failure. Precision integrated circuits may be more susceptible to damage because very small parametric changes could cause the device not to meet its published specifications.

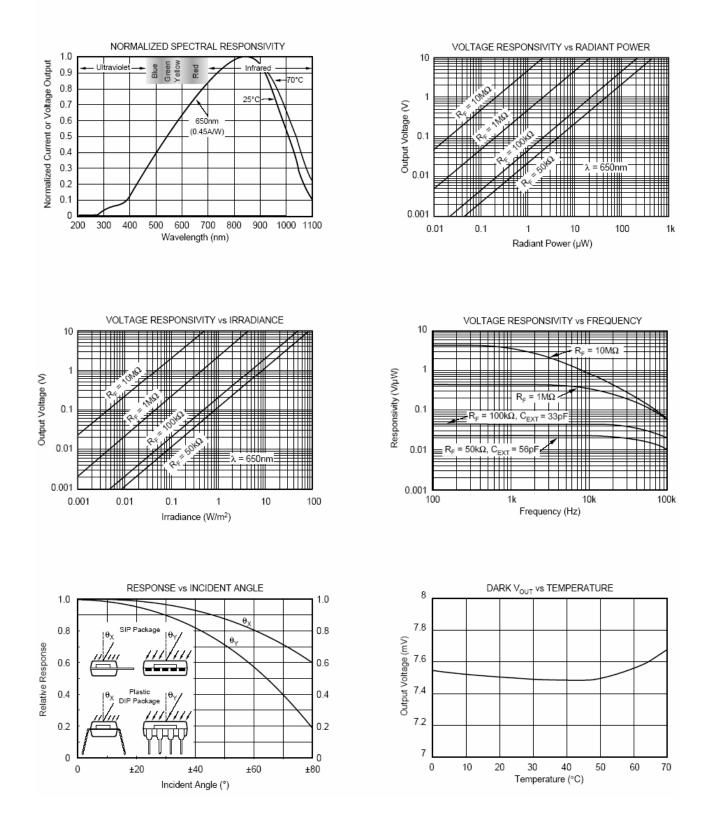
MOISTURE SENSITIVITY AND SOLDERING

Clear plastic does not contain the structural-enhancing fillers used in black plastic molding compound. As a result, clear plastic is more sensitive to environmental stress than black plastic. This can cause difficulties if devices have been stored in high humidity prior to soldering. The rapid heating during soldering can stress wire bonds and cause failures. Prior to soldering, it is recommended that plastic devices be baked-out at +85°C for 24 hours.

The fire-retardant fillers used in black plastic are not compatible with clear molding compound. The OPT101 plastic packages cannot meet flammability test, UL-94.

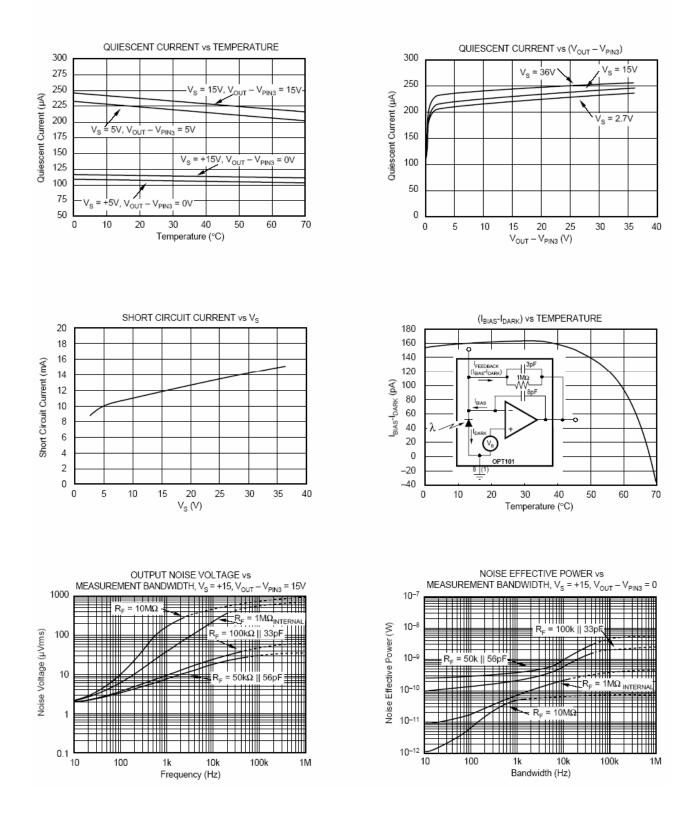
TYPICAL PERFORMANCE CURVES

At T_A = +25°C, V_S = +2.7V to +36V, λ = 650nm, internal 1M Ω feedback resistor, and R_L = 10k Ω , unless otherwise noted.



TYPICAL PERFORMANCE CURVES (CONT)

At T_A = +25°C, V_S = +2.7V to +36V, λ = 650nm, internal 1M Ω feedback resistor, and R_L = 10k Ω , unless otherwise noted.



APPLICATIONS INFORMATION

Figure 1 shows the basic connections required to operate the OPT101. Applications with high-impedance power supplies may require decoupling capacitors located close to the device pins as shown. Output is 7.5mV dc with no light and increases with increasing illumination.

Photodiode current, I_D , is proportional to the radiant power, or flux, (in watts) falling on the photodiode. At a wavelength of 650nm (visible red) the photodiode Responsivity, R_I , is approximately 0.45A/W. Responsivity at other wavelengths is shown in the typical performance curve "Responsivity vs Wavelength."

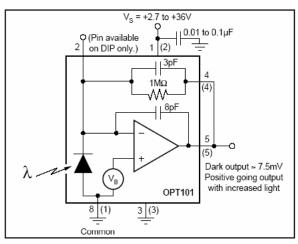


FIGURE 1. Basic Circuit Connections.

The typical performance curve "Output Voltage vs Radiant Power" shows the response throughout a wide range of radiant power. The response curve "Output Voltage vs Irradiance" is based on the photodiode area of 5.2mm².

The OPT101's voltage output is the product of the photodiode current times the feedback resistor, (I_DR_F), plus a pedestal voltage, V_B , of approximately 7.5mV introduced for single supply operation. The internal feedback resistor is laser trimmed to 1M Ω . Using this resistor, the output voltage responsivity, R_V , is approximately 0.45V/ μ W at 650nm wavelength. Figure 1 shows the basic circuit connections for the OPT101 operating with a single power supply and using the internal 1M Ω feedback resistor for a response of 0.45V/ μ W at 650nm. Pin 3 is connected to common in this configuration.

CAPACITIVE LOADING

The OPT101 is capable of driving load capacitances of 10nF without instability. However, dynamic performance with capacitive loads can be improved by applying a negative bias voltage to Pin 3 (shown in Figure 2). This negative power supply voltage allows the output to go negative in response to the reactive effect of a capacitive load. An internal JFET connected between pin 5 (output) and pin 3 allows the output to sink current. This current sink capability can also be useful when driving the capacitive inputs of some analog-to-digital converters which require the signal

source to sink currents up to approximately 100 μ A. The benefits of this current sink are shown in the typical performance curves "Small Signal Response (C_{LOAD} = 10,000pF)" which compare operation with pin 3 grounded and connected to -15V.

Due to the architecture of this output stage current sink, there is a slight increase in operating current when there is a voltage between pin 3 and the output. Depending on the magnitude of this voltage, the quiescent current will increase by approximately 100μ A as shown in the typical performance curve "Quiescent Current vs (V_{OUT} - V_{PIN3})".

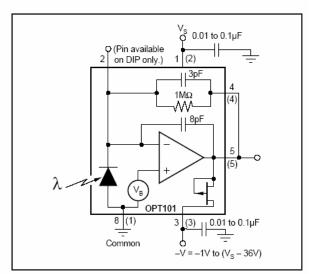


FIGURE 2. Bipolar Power Supply Circuit Connections.

NOISE PERFORMANCE

Noise performance of the OPT101 is determined by the op amp characteristics, feedback components and photodiode capacitance. The typical performance curve "Output Noise Voltage vs Measurement Bandwidth" shows how the noise varies with R_F and measured bandwidth (0.1Hz to the indicated frequency), when the output voltage minus the voltage on pin 3 is greater than approximately 50mV. Below this level, the output stage is powered down, and the effective bandwidth is decreased. This reduces the noise to approximately 1/3 the nominal noise value of 300μ Vrms, or 100μ Vrms. This enables a low level signal to be resolved.

Noise can be reduced by filtering the output with a cutoff frequency equal to the signal bandwidth. This will improve signal-to-noise ratio. Also, output noise increases in proportion to the square root of the feedback resistance, while responsivity increases linearly with feedback resistance. Best signal-to-noise ratio is achieved with large feedback resistance. This comes with the trade-off of decreased bandwidth.

The noise performance of the photodetector is sometimes characterized by *Noise Effective Power* (NEP). This is the radiant power that would produce an output signal equal to the noise level. NEP has the units of radiant power (watts), or Watts/ $\sqrt{\text{Hz}}$ to convey spectral information about the noise. The typical performance curve "Noise Effective Power" vs Measurement Bandwidth" illustrates the NEP for the OPT101. Epitex L680 Series 680nm IR LED:

epitex

Opto-Device & Custom LED

MOLD LED LAMP L680 series

L680- AU Infrared LED Lamp

This series of L680-__AU is a GaAIAs LED mounted on a lead frame and encapsulated in various types of epoxy lens which offer different design settings. On forward bias, it emits a high power radiation of typical 5mW with a peak wavelngth at 680nm.

1) Specifications

- (1) Chip material AlGaAs
- (2) Peak wavelength 680nm
- (3) Package Clear epoxy resin

Soldered

(4) Lead frame

2) Absolute Maximum Ratings

Item	Symbol	Maximum Rated Value	Unit	Ambient Temperature
Power Dissipation	PD	110	mW	Ta=25°C
Forward Current	lF	50	mA	Ta=25°C
Pulse Forward Current	I FP	200	mA	Ta=25°C
Reverse Voltage	VR	5	V	Ta=25°C
Operating Temperature	TOPR	-30 ~ +85	°C	Ta=25°C
Storage Temperature	Tstg	-30 ~ +100	°C	
Soldering Temperature	TSOL	260	°C	

3) Electro-Optical Characteristics [Ta=25°C]

Item	Symbol	Condition	Minimum	Typical	Maximum	Unit
Forward Voltage	VF	l⊧=20mA		1.9	2.3	V
Reverse Current	IR	V _R =5V			10	uA
Total Radiated Power	Po	l⊧=20mA	3.0	5.0		mW
Peak Wavelength	ΙP	l⊧=20mA		680		nm
Half Width	DI	l⊧=20mA		20		nm
Rise Time	tr	l⊧=20mA		80		ns
Fall Time	tf	l⊧=20mA		80		ns

4) Characteristics of Brightness [Ta=25°C]

	<u> </u>						
Туре	Viewing	Radiant Int	Radiant Intensity IF=20mA unit: mW/sr			Outer Dimension	
туре	Half Angle	Minimum	Typical	Maximum	Dimension	Figure	
L680-01AU	±10°		30		f5	1	
L680-02AU	±5°		45		f5	2	
L680-03AU	±15°		25		f5	3	
L680-04AU	±20°		15		f5	4	
L680-05AU	±40°		2		f5	5	
L680-06AU	±6°		40		f5	6	
L680-09AU	±25°(Long)		20	20		7	
L000-09A0	±15°(Short)		20		Oval	1	
L680-33AU	±15°		10		f3	9	
L680-36AU	±30°		5		f3	10	
t Radian	t Intensity is mea	sured by Tektro	nix J-16				

Radiant Intensity is measured by Tektronix J-16. Total Radiated Power is measured by Photodyne #500.

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epitex

Opto-Device & Custom LED

L810- AU Infrared LED Lamp

This series of L810-_ _AU is a GaAIAs LED mounted on a lead frame and encapsulated in various types of epoxy lens which offer different design settings.

On forward bias, it emits a high power radiation of typical 18W with a peak wavelngth at 810nm.

1) Specifications

- (1) Chip material AlGaAs
- (2) Peak wavelength 810nm
- (3) Package Clear epoxy resin Soldered

(4) Lead frame

2) Absolute Maximum Ratings

Item	Symbol	Maximum Rated Value	Unit	Ambient Temperature
Power Dissipation	Po	170	mW	Ta=25°C
Forward Current	lf	100	mA	Ta=25°C
Pulse Forward Current	IFP	500	mA	Ta=25°C
Reverse Voltage	Vr	5	V	Ta=25°C
Operating Temperature	Topr	-30 ~ +85	°C	Ta=25°C
Storage Temperature	Tstg	-30 ~ +100	°C	
Soldering Temperature	Tsol	260	°C	

3) Electro-Optical Characteristics [Ta=25°C]

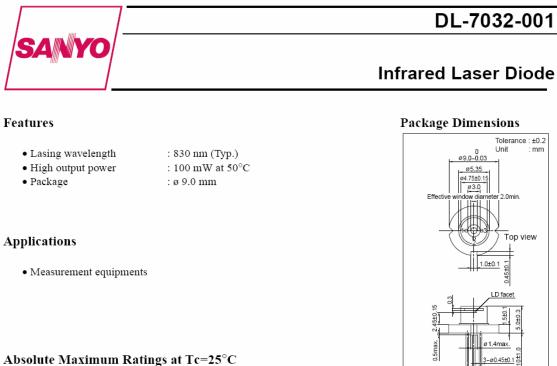
Item	Symbol	Condition	Minimum	Typical	Maximum	Unit
Forward Voltage	Vf	IF=50mA		1.60	1.8	V
Reverse Current	lr	Vr=5V			10	uA
Total Radiated Power	Po	IF=50mA	16.0	18.0		mW
Peak Wavelength	I P	IF=50mA		810		nm
Half Width	DI	IF=50mA		35		nm
Rise Time	tr	IF=50mA		60		ns
Fall Time	tf	l⊧=50mA		40		ns

4) Characteristics of Brightness [Ta=25°C]

Туре	Viewing	Radiant Inte	Outer Dimension			
	Half Angle	Minimum	Typical	Maximum	Dimension	Figure
L810-01AU	±10°		90		f5	1
L810-02AU	±5°		110		f 5	2
L810-03AU	±15°		80		f 5	3
L810-04AU	±20°		50		f5	4
L810-05AU	±40°		12		f 5	5
L810-06AU	±6°		150		f5	6
L810-09AU	±25°(Long)		60		f 5	7
	±15°(Short)		00		Oval	1
L810-33AU	±15°		45		f3	9
L810-36AU	±30°		25		f3	10
L810-36AU		sured by Tektro	25			

Radiant Intensity is measured by Tektronix J-16. Total Radiated Power is measured by Photodyne #500. ŧ

Sanyo DL-7032 780nm Laser Diode:



Parameter		Symbol	Ratings	Unit
Light Output CW		Ро	100	mW
Reverse Voltage	Laser PIN	VR	2 15	V
Operating Tempera	ature	Topr	-10 to +50	°C
Storage Temperatu	ire	Tstg	-40 to +85	°C

Parameter		Symbol	Condition	Min.	Тур.	Max.	Unit
Threshold Current		Ith	CW	-	50	70	mA
Operating Current		Iop	Po=100mW	-	140	180	mA
Operating Voltage		Vop	Po=100mW	-	1.85	2.3	V
Lasing Wavelength		λp	Po=100mW	810	830	840	nm
Beam 2)	Perpendicular	$\theta \perp$	Po=100mW	12	18	25	0
Divergence	Parallel	θ //	Po=100mW	5	7	11	0
Off Axis	Perpendicular	$\Delta \Theta \perp$	Po=100mW	-	-	±3	0
Angle	Parallel	$\Delta \theta$ //	Po=100mW	-	-	±3	0
Differential Efficiency		dPo/dIop	-	0.5	1.0	-	mW/mA
Monitoring Output Current		Im	Po=100mW	0.05	0.2	0.5	mA
Astigmatism		As	Po=100mW	-	10	-	μm

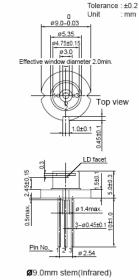
1) Initial values 2) Full angle at half maximum

Note : The above product specification are subject to change without notice.

SANYO Electric Co., Ltd. Semiconductor Company TOKYO OFFICE Tokyo Bldg., 1-10, 1 Chome, Ueno, Taito-ku, TOKYO, 110-8534 JAPAN

62503 YY IM No.7584 1/3

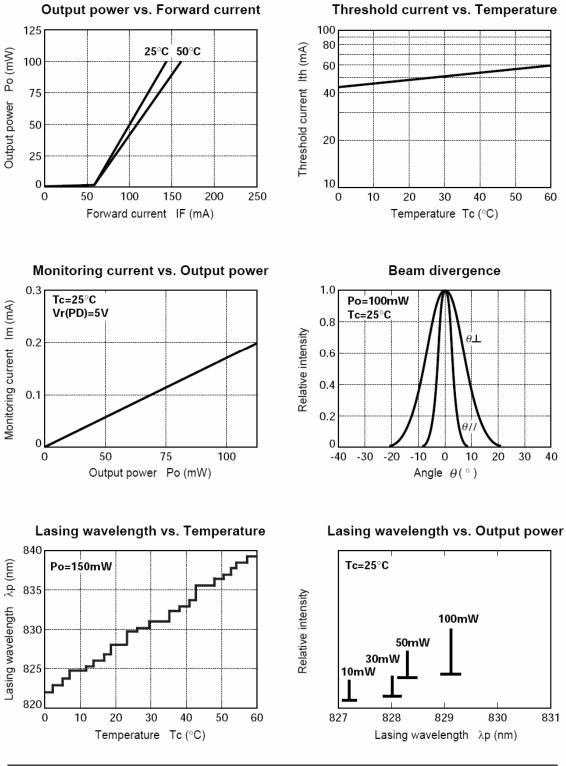
Infrared Laser Diode



Pin Connection

I D PD

Characteristics



No.7584 2/3

Laser Diodes

GH0781HA2C

Features

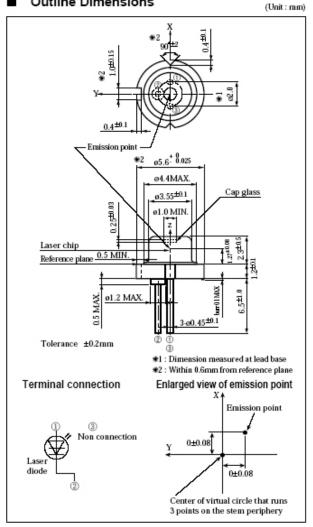
- (1) Maximum optical power output : 110mW (CW)
- (2) High power (pulse MAX. 160mW), MAX. ×24 speed writing
- (3) High coupling efficiency. The ellipticity $(\theta \perp / \theta / /)$ is close to 1.
- (4) Wavelength : TYP. 784nm
- (5) ϕ 5.6mm package

Applications

- (1) CD-R drives
- (2) CD-RW drives

High Power Laser Diode for MAX. X24 Speed CD-R Drive(784nm-110mW)

Outline Dimensions



Absolute Max	(Tc-25°C *1)			
Parame	Symbol	Rating	Unit	
*3 Optical power output	Po	110	mW	
Optical power output	Pp	160	mW	
Reverse voltage	Laser	Vrl	2	V
•1 Operating temperature	*3 CW	Tope(c)	-10 to +65	°C
Operating temperature	Pulse	Topp(c)	-10 to +70	°C
Storage temperatur	Tstg	-40 to +85	°C	
*4 Soldering temperate	TsId	300	°C	

Case temperature

*4 At the position of 1.6mm or more from

*2 Pulse width : 0.5µs, Duty : 50%

*3 CW (Continuous Wave) drive

the lead base (Within 3s)

Laser Diodes

GH0781HA2C

Electro-optical Characteristics*1							(Tc=25*C)
Parameter		Symbol	Conditions	MIN.	TYP.	MAX.	Unit
Threshold current		Ith	-	-	30	40	mA
Operating current		Iop			130	155	mA
Operating voltage		Vop	-		2.1	2.5	V
Wavelength		λ_p		780	784	787	nm
H-Rinter Street	*2*3 Parallel	θ//	Po=90mW	8	9	10	•
Half intensity angle	*2*3 Perpendicular	θ <u>⊥</u>		15	17	19	•
*4 Ripple	* Ripple			-20		+20	%
Malter	*3 Parallel	$\Delta \theta //$		-1.5		+1.5	•
Misalignment angle	* ³ Perpendicular	$\Delta \Theta \perp$		-2.5	-	+2.5	•
Differential efficiency		ηa	60mW I(90mW)-I(30mW)	0.7	0.9	1.2	mW/mA
Interference pattern intensity		α	Po=90mW			1	
*5 Kink		K-LI	P1=32mW, P2=96mW, P3=160mW			10	%
Polarization ratio		Pı	Po=3mW, NA=0.13	20			

*1 Initial value, CW (Continuous Wave) drive

*2 Angle at 50% peak intensity (full-width at half-maximum)

*3 Parallel to the junction plane (X-Z plane) Perpendicular to the junction plane (Y-Z plane)

*4 RI= $\Delta P/P \Delta P$: the maximum deviation of the far field pattern from its approximate curve P: the peak of the approximate curve

*5 Pulse drive (Pulse width : 0.5µs, Duty : 50%)

Deltran Pressure Transducer - Utah Medicaldeltran® IVOperating Pressure Range-50 tSensitivity5 μV

Non-Linearity and Hysteresis

Sensitivity Thermal Effect Zero Thermal Effect

Zero Drift With Time

Leakage Current Unbalance **Overpressure Protection Operating Temperature Excitation Voltage and Frequency** Asymmetry **Operating Life** Storage Temperature Defibrillation Withstand Natural Frequency Phase Shift **Output Impedance** Input Impedance deltran[®] I/deltran[®] II **Operating Pressure Range** Sensitivity Non-Linearity and Hysteresis Sensitivity Thermal Effect Zero Thermal Effect Zero Drift With Time Leakage Current

Unbalance Overpressure Protection Operating Temperature Excitation Voltage and Frequency Asymmetry Operating Life Storage Temperature Defibrillation Withstand Natural Frequency Phase Shift Output Impedance Input Impedance -50 to +300 mmHg $5 \,\mu V/V/mmHg$, $\pm 2\%$ (typically $<\pm 1\%$) $\pm 1\%$ of reading or ± 1 mmHg, whichever is greater in the range of -50 to 200 mmHg. Above 200 mmHg the combined linearity and sensitivity error must be less than ±3% < or equal to $\pm 0.1\%$ /degree C < or equal to $\pm 0.3\%$ mmHg/degree C < or equal to ± 1.0 mmHg/8 hours after 10 min. warm-up to operating temperature <2 µA @ 115 VAC RMS at 60 Hz ±75 mmHg -400 to +4000 mmHg 15° to 40° C 2 to 10 V DC or VAC RMS, up to 5kHz <1% >500 hours -25° C to $+70^{\circ}$ C 5 discharges/5 minutes of 400 joules into 50 ohm load >200 Hz in saline <5 degrees at 5 kHz 270 to 400 Ohms 270 to 400 Ohms -50 to +300 mmHg $5 \mu V/V/mmHg, \pm 2\%$ (typically $<\pm 1\%$) $\pm 2\%$ of reading or ± 1 mmHg, whichever is greater ±0.1%/degree C ±0.3% mmHg/degree C ± 1.0 mmHg/8 hours after 10 min. warm-up to operating temperature <2 µA @ 115 VAC RMS at 60 Hz ±75 mmHg -400 to +4000 mmHg 15° to 40° C 2 to 10 V DC or VAC RMS, up to 5kHz <1% >500 hours -25° C to +70° C 5 discharges/5 minutes of 400 joules into 50 ohm load >200 Hz in saline <5 degrees at 5 kHz < or equal to 400 Ohms 350 Ohms ±10%

8.3 Alternate designs for the anesthetic vaporizer

The following alternate vaporizer design approaches were considered for the anesthesia/ventilator system discussed in Section 5.1.2, but were not selected for the reasons discussed below.

Liquid-metered flash boiler

Drip liquid agent into a temperature-controlled or fixed-power heated metal or ceramic tube with all of the gas mix flowing through it. All of the agent flashes to vapor within the tube. Control the liquid flow rate with valve or solenoid to vary vapor concentration.

GOOD: simple in principle, precise 0% to >5% concentration control, handles any agent, room temperature-independent, no gas valving required, electronic concentration control possible using chemically-resistant (expensive) solenoid, predictable and linear vapor concentration vs. gas mix/agent flow rate (solenoid duty cycle), not fail-safe (overtemp could cook patient, generate toxic gases, and start a fire).

BAD: gas post-cooling or countercurrent heat exchanger required, need variable speed halocarboncompatible low-flow pump or pressurized agent reservoir, vapor concentration is gas flow-dependent, high power dissipation (both agent and air exit at ~60°C).

This seemed quite straightforward in principle and its flaws were readily apparent, so no prototype was constructed.

Variable-power (unpressurized) boiler with passive blending

Boil agent in an electrically heated chamber and blend pure (100%) vapor directly into gas stream. GOOD: simple in principle – no valves or solenoids required, power to boiler can be electronically controlled,

BAD: thermal safety issues, vapor concentration is gas flow-dependent and room temperaturedependent, refluxing in lines unless well insulated, vapor concentration is not linear nor predictable from boiler power due to varying thermal losses, noticeable vapor bleed into gas stream at "zero" power setting, cannot handle Desflurane, high power dissipation, not fail-safe (agent boilout could lead to overheat, generate toxic gases, and start a fire).

Since this offered the major advantage of a truly valveless design, a prototype was constructed. It revealed that:

1) Even with some insulation, the heater power dissipation was greater than 5 Watts at zero delivered agent. This meant that refluxing losses (through heat-piping) were significant.

2) Agent bleed (through turbulent mixing at the blend point) was significant, and led to either a constant agent bleed rate of $\sim 0.2\%$ (for minimum lag time), or a demand delivery lag time of > 15 seconds (for minimum bleed rate). The introduction of a baffle plate between the gas flow and the pure agent vapor reduced the bleed rate somewhat, but the additional thermal mass increased the lag time.

Although these problems could probably be addressed through proper design (low mass baffle, proper gas flow dynamics, etc.), these test results, in combination with the gas flow dependence and boilout hazards, led me to abandon this approach.

Fixed-temperature pressurized boiler with solenoid control

Boil agent in an electrically heated chamber and maintain at positive pressure. Use agent-resistant (expensive) solenoid to throttle flow of superheated vapor into gas stream.

GOOD: predictable and linear vapor concentration vs. gas mix/vapor flow ratio (solenoid duty cycle), room temperature-independent, handles any agent.

BAD: most complex design, refluxing in lines and solenoid unless well insulated, thermal safety issues, vapor concentration is gas flow-dependent, semi fail-safe (heater malfunction combined with agent boilout could lead to overheat, generate toxic gases, and start a fire).

Testing this approach would have required a significant design effort, including the construction of a well-insulated, thermostatically-controlled, overtemp-protected boiler/solenoid assembly, which would have required some rather expensive components and a lot of custom-machined hardware. (Note that this is the basis of the latest high-tech Desflurane vaporizer, which costs around \$200,000!).

Variable-bypass

Blend pure gas with saturated vapor inside vaporizer. Vapor concentration control mechanically diverts a variable portion of the gas stream through the vaporizer. Bimetallic strip compensates for vapor pressure variation due to temperature by varying the diversion ratio.

GOOD: Simple and rugged design in principle, can be room temperature-independent, gas flowindependent, true zero power dissipation, predictable and linear vapor concentration vs. blend ratio, nearly fail-safe (binding of the bimetallic strip could lead to the delivery of an incorrect anesthetic concentration, but the patient hazard is judged to be low).

BAD: Most complex to actually design and build, requires custom machined parts, electronic concentration control is impractical, cannot handle Desflurane.

This too would require significant machining in order to build a prototype. Since the benefits do not merit this level of effort, a prototype was not constructed.

8.4 Alternate anesthetic concentration monitor designs

I came up with the following conceptual approaches for monitoring the agent vapor concentration. Some of these were tested, and were later rejected for a variety of reasons, many of which are discussed below.

The mass balance approach

Coat a quartz crystal or other piezoelectric material with an organic polymer film having a high affinity for halocarbons (i.e. a large film/gas partition coefficient). Heterodyne the output with a similar crystal lacking this film. As the agent vapor diffuses into the film, its mass increases, thus slightly reducing the resonance frequency of the coated crystal. If the additional mass fraction at maximum halocarbon concentration is below 1% of the total crystal mass (which it clearly will be), the resulting beat frequency shift (measured in Hz) should be almost directly proportional (actually it will be proportional to the square root of the mass increase. since $f_r = 1/sqrt(LC)$) to halocarbon vapor concentration. Since the fractional mass change is anticipated to be in the PPM range, sensitivity should be long and film composition, film thickness, and temperature-dependent, since the diffusion rate through solid media is typically quite slow and increases with temperature. No mechanism for hysteresis is anticipated. Features include:

- Flow rate invariant
- Linear concentration response
- Very low dead volume
- Sensitivity, stability, drift probably poor
- Long settling time
- Hysteresis mechanism unknown

Since this seemed to offer the possibility of a very simple and rugged sensor, a prototype was constructed. The piezo resonator from a Sonalert-style beeper was coated with a thin layer of rubber cement. When the solvent (n-hexane) evaporated, a thin film of uncured latex remained. The piezo resonator was suspended by its leads alone (to minimize mechanical losses) and its resonances were measured using a function generator as a driver and a series-connected $100k\Omega$ resistor (to avoid electrical loading). Once these resonances were determined, the generator was frequency swept slowly through a resonance peak as halothane vapor was directed against the latex-coated surface. Unfortunately no vapor-related frequency shift was observed. A number of other piezo transducers were then examined, and a vapor concentration-dependent frequency shift was eventually noticed, but it was traced not to an adsorption effect, but rather to an acoustic cavity resonance shift due to the presence of halothane vapor within the plastic housing of that particular beeper (I chose not to remove this one from its housing, since I would have probably destroyed it in the process). Other polymers tested were: PVC pipe cement (unplasticized, low molecular weight polyvinyl chloride resin), DuPont silicone stopcock grease, and silicone RTV, but to no avail.

The absorption spectroscopy approach

Choose a narrow band somewhere in the visible or IR spectral region in which the halocarbons exhibit a strong rotational or vibrational resonance and measure the fraction of light absorbed within a gas cell. If the total optical attenuation at the maximum halocarbon concentration is less than 10% or so, then Beers Law effects can be neglected, and the relative signal decrease should be nearly linear with increasing halocarbon concentration. Features include:

- Flow rate invariant
- Linear concentration response within physiologic range
- Large dead volume or zigzag optical path
- Good temporal response
- Moderate sensitivity
- Temporal stability unknown
- Thermal stability expected to be poor
- No hysteresis expected
- Expensive and bulky optomechanics required

The AM photoacoustic spectroscopy approach

Choose the same narrow spectral band, but modulate the amplitude of the beam at an audio frequency and use a microphone mounted within a semi-sealed gas chamber (basically a Golay cell) to detect the acoustic signal generated by the slight pressure changes due to thermal expansion of the halocarbon vapor. If the single-pass absorption is below 10%, Beers Law effects can similarly be neglected, and the amplitude of the audio signal should be nearly linear with increasing halocarbon concentration. Features include:

- Flow rate invariant (at least in principle)
- Linear concentration response within physiologic range
- Small dead volume possible
- Good temporal response
- Moderate sensitivity
- Temporal stability unknown
- Thermal stability expected to be poor

- No hysteresis expected
- Expensive and bulky optomechanics required

The differential absorption, or FM photoacoustic spectroscopy approach

Modulate the wavelength of a narrowband optical source (say, by rotating a quartz etalon mounted to a galvo scanner) along the edge of (or straddling) an absorption line and use the same audiofrequency Golay cell to detect the fundamental (or second harmonic of the) acoustic signal. The straddling approach would allow for feedback stabilization to the center of the absorption line by rotating the average position of the etalon to null the fundamental, using a two-phase (I-Q) synchronous detection circuit. Features include:

- Flow rate invariant
- Linear concentration response within physiologic range
- Small dead volume possible
- Good temporal response
- Moderate sensitivity
- Temporal stability unknown
- Thermal stability expected to be poor
- No hysteresis expected
- Expensive and bulky optomechanics required

The thermal conductivity measurement approach

Measure the amount of heat which is conducted through a small gas/vapor-filled gap. The gap geometry is chosen to maintain a laminar gas flow in order to minimize convective heat transfer. Since the gas gap will, by necessity, have to be far wider than the mean free path of a halocarbon molecule at ambient pressure, the thermal conductivity decrease should be a nonlinear function of halocarbon concentration. Feedback-stabilized detection plate temperature might improve the temporal response somewhat. Features include:

- Flow rate sensitive
- Linear concentration response possible over limited range
- Very small dead volume
- Poor temporal response (from residual thermal delays)
- Unknown (probably poor) sensitivity
- Temporal stability unknown
- Thermal stability expected to be good (since thermal control will be required)
- No hysteresis expected
- Moderately expensive and bulky thermomechanics required

The partial pressure diffusion approach

Measure the slight pressure change within a small hermetically-sealed gas cell covered by a semipermeable organic membrane when the membrane is exposed to the vapor-laden gas flow. Features include:

- Flow rate insensitive
- Linear concentration response possible over limited range

- Very small dead volume
- Lousy temporal response
- Unknown sensitivity
- Temporal stability unknown
- Thermal stability expected to be poor, but predictable
- Some hysteresis expected
- Moderately expensive and bulky thermomechanics required

The corona onset voltage approach

Vary the DC voltage applied to a sharp needle to maintain a fixed corona current through the gas/vapor mixture. Since halocarbons make excellent arc-quenching agents (through free-electron capture by halide free-radicals – this is also how Halon puts out fires), the DC voltage should be linear with increasing halocarbon concentration. Features include:

- Probably flow rate sensitive
- Response linearity unknown over physiologic range
- Low dead volume possible
- Good temporal response
- Unknown sensitivity
- Poor temporal stability due to halide corrosion (halide free-radicals are nasty!)
- Thermal stability expected to be poor
- Some hysteresis expected (due to decomposition products)
- Moderately expensive and bulky HVPS required
- Probable formation of very toxic compounds (HF, HCl, HBr, PFIB, COCl₂, etc.)
- Possible fire hazard!