PHOTOMULTIPLIER TUBES

Basics and Applications

THIRD EDITION (Edition 3a)

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Introduction

Light detection technolgy is a powerful tool that provides deeper understanding of more sophisticated phenomena. Measurement using light offers unique advantages: for example, nondestructive analysis of a substance, high-speed properties and extremely high detectability. Recently, in particular, such advanced fields as scientific measurement, medical diagnosis and treatment, high energy physics, spectroscopy and biotechnology require development of photodetectors that exhibit the ultimate in various performance parameters.

Photodetectors or light sensors can be broadly divided by their operating principle into three major categories: external photoelectric effect, internal photoelectric effect and thermal types. The external photoelectric effect is a phenomenon in which when light strikes a metal or semiconductor placed in a vacuum, electrons are emitted from its surface into the vacuum. Photomultiplier tubes (often abbreviated as PMT) make use of this external photoelectric effect and are superior in response speed and sensitivity (low-light-level detection). They are widely used in medical equipment, analytical instruments and industrial measurement systems.

Light sensors utilizing the internal photoelectric effect are further divided into photoconductive types and photovoltaic types. Photoconductive cells represent the former, and PIN photodiodes the latter. Both types feature high sensitivity and miniature size, making them well suited for use as sensors in camera exposure meters, optical disk pickups and in optical communications. The thermal types, though their sensitivity is low, have no wavelength-dependence and are therefore used as temperature sensors in fire alarms, intrusion alarms, etc.

This handbook has been structured as a technical handbook for photomultiplier tubes in order to provide the reader with comprehensive information on photomultiplier tubes.

This handbook will help the user gain maximum performance from photomultiplier tubes and show how to properly operate them with higher reliability and stability. In particular, we believe that the first-time user will find this handbook beneficial as a guide to photomultiplier tubes. We also hope this handbook will be useful for engineers already experienced in photomultiplier tubes for upgrading performance characteristics.

CHAPTER 14

APPLICATIONS

Photomultiplier tubes (PMTs) are extensively used as photodetectors in fields such as chemical analysis, medical diagnosis, scientific research and industrial measurement. This chapter introduces major applications of photomultiplier tubes and describes the principle and detection methods for each application.

14.1 Spectrophotometry

14.1.1 Overview

Spectrophotometry is a study of the transmission and reflection properties of material samples as a function of wavelength, but the term commonly means chemical analysis of various substances utilizing photometry. Photometric instruments used in this field are broadly divided into two methods. One utilizes light absorption, reflection or polarization at specific wavelengths and the other uses external energy to excite a sample and measures the subsequent light emission. Photomultiplier tubes have been most widely used in this field for years. Major principles used in spectrophotometry are classified as illustrated in Figure 14-1 below.
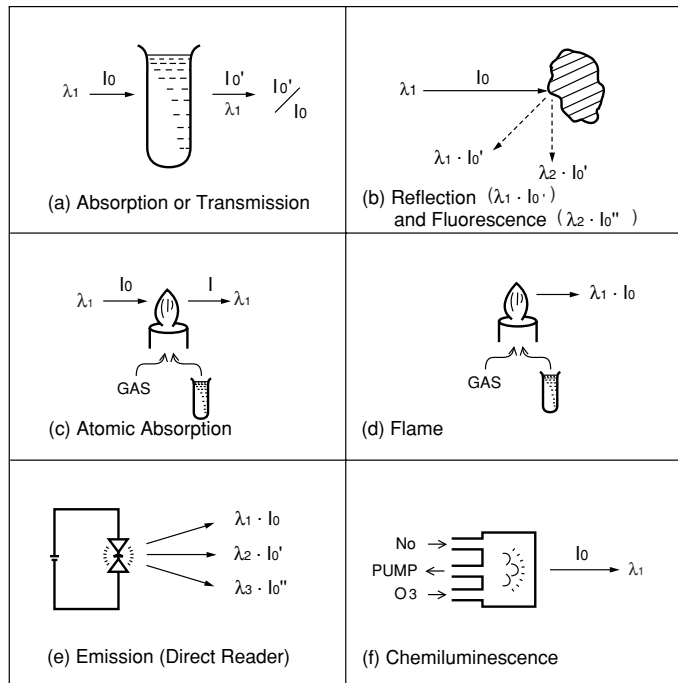
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Figure 14-1: Major principles of spectrophotometry

Specific photometric instruments currently used are:

1) Visible to UV spectrophotometers (absorption, reflection)
2) Infrared spectrophotometers (absorption, reflection)
3) Far UV spectrophotometers (absorption, reflection)
4) Emission spectrophotometers
5) Fluorescence spectrophotometers
6) Atomic absorption spectrophotometers
7) Azimuthal, circular dichroism meters
8) Raman spectrophotometers
9) Densitometers, colorimeters and color analyzers
   etc.

14.1.2 Specific applications

The following paragraphs explain specific major applications of spectrophotometers, divided into two methods utilizing absorption or emission.

(1)   UV, visible and infrared spectrophotometers

When light passes through a substance, the light energy causes changes in the electronic state of the substance (electron transition) or induces characteristic vibration of the molecules, resulting in a loss of partial energy. This is referred to as absorption, and quantitative analysis can be performed by measuring the extent of absorption.

The principle and simplified block diagram[1] of a spectrophotometer are shown in Figure 14-2.

a) Principle of absorption   **b) Block diagram of spectrophotometer**
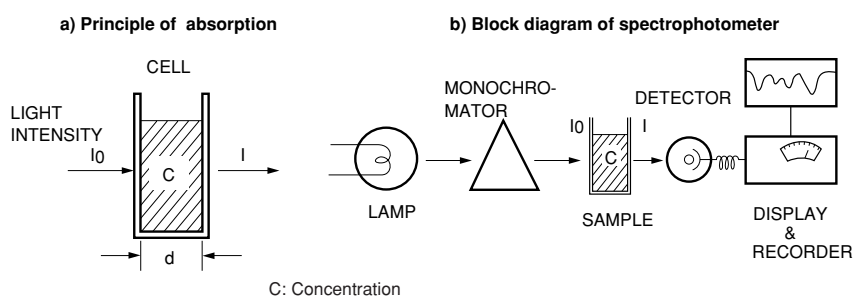
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Figure 14-2: Principle and block diagram of a spectrophotometer

There are various optical systems in use today for spectrophotometers. Figure 14-3 illustrates the optical system of a spectrophotometer using light sources that cover from the ultraviolet to visible and near infrared range.
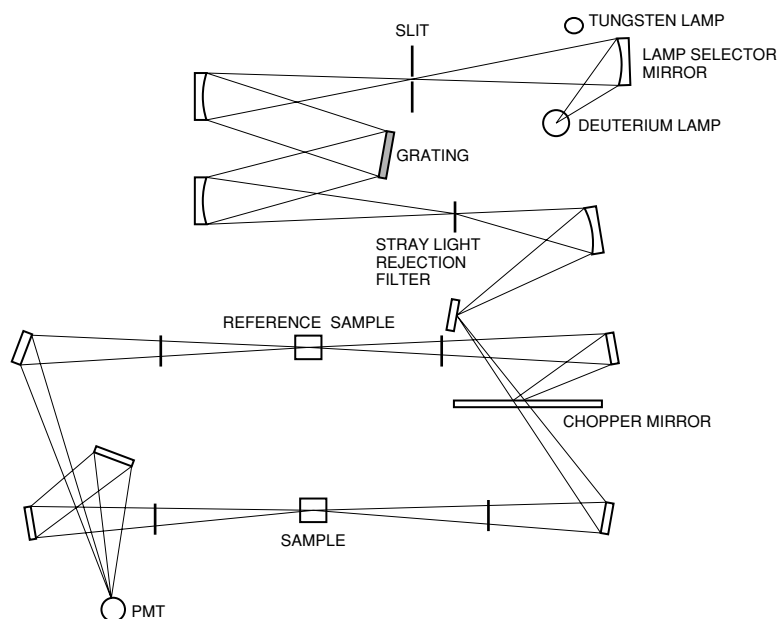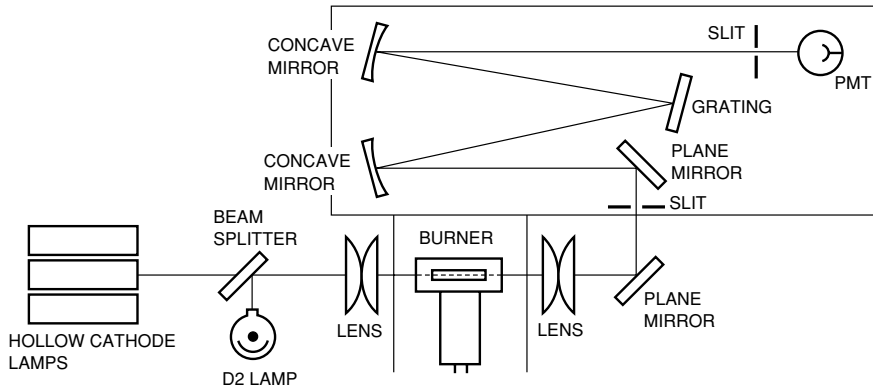

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Figure 14-3: Optical system of a UV, visible to near IR spectrophotometer

(2)   Atomic absorption spectrophotometers

The atomic absorption spectrophotometer employs special light sources (hollow cathode lamps) constructed for the particular target elements to be analyzed. A sample is dissolved in solvent and burned to atomize it, and light from a specific hollow cathode lamp is passed through the flame. The amount of light that is absorbed is proportional to the concentration of the sample material. Therefore, by comparing the extent of absorption between the sample to be analyzed and a standard sample measured in advance, it is possible to find the concentration of a specific element in the sample. A typical optical system[2] used for atomic absorption spectrophotometers is shown in Figure 14-4.

Figure 14-4: Optical system used in atomic absorption spectrophotometers

(3)   Atomic emission spectrophotometers

When external energy is applied to a sample, light is emitted from the sample. Dispersing this emission using a monochromator, into characteristic spectral lines of elements and measuring their presence and intensity simultaneously, allows rapid qualitative and quantitative analysis of the elements contained in the sample. Figure 14-5 illustrates the schematic diagram[3] of a photoelectric emission spectrophotometer in which multiple photomultiplier tubes are used.
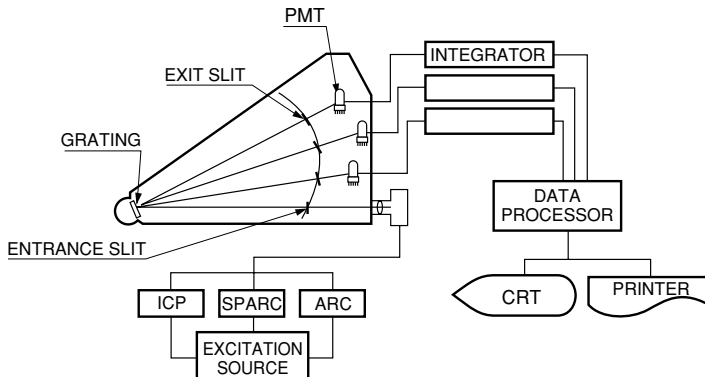
Figure 14-5: Block diagram illustrating a photoelectric emission spectrophotometer
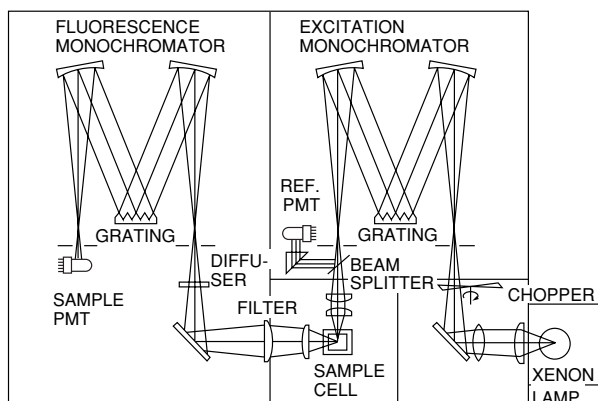
(4)   Fluorospectrophotometers

The fluorospectrophotometer is mainly used for chemical analysis in biochemistry, especially in molecular biology. When a substance is illuminated and excited by visible or ultraviolet light, it may emit light with a wavelength longer than the excitation light. This light emission is known as fluorescence and its emission process[4] is shown in Figure 14-6. Measuring the fluorescent intensity and spectra allows quantitative and qualitative analysis of the elements contained in the substance.
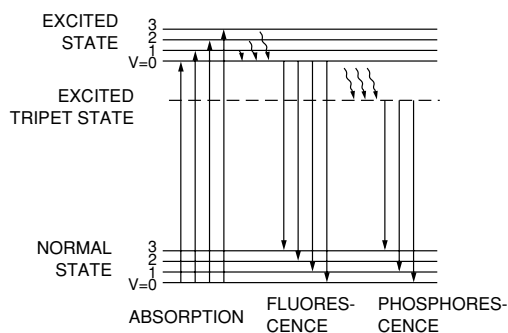
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Figure 14-6: Fluorescent molecular energy levels

Figure 14-7 shows the structure[5] of a fluorospectrophotometer using photomultiplier tubes as the detectors. This instrument roughly consists of a light source, excitation monochromator, fluorescence monochromator and fluorescence detector. A xenon lamp is commonly used as the light source because it provides a continuous spectrum output over a wide spectral range. The excitation and fluorescence monochromators use the same diffraction grating or prism as used in general-purpose monochromators.

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Figure 14-7: Fluorospectrophotometer structure

14.2 Medical Equipment

14.2.1 PET (Positron Emission Tomography)

In addition to gamma cameras and SPECT described in the next subsection, much attention has recently been focused on positron emission tomography (PET) as an application of nuclear medical diagnosis using photomultiplier tubes. This section explains specific examples of PET. The schematic diagram of a PET scanner is shown in Figure 14-8 and the external view in Figure 14-9.
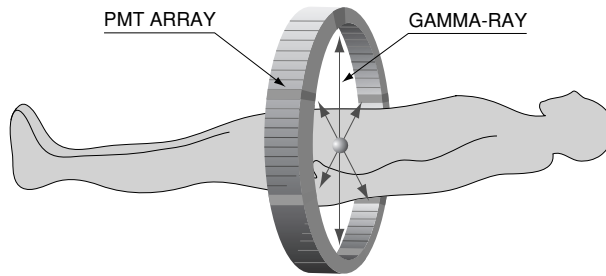

Figure 14-8: Concept view of a PET scanner

When a positron released from radioactive tracers injected into body annihilates with an electron, two gamma-ray photons of 511 keV are emitted in opposite directions. These gamma-rays are simultaneously detected by the PMT array.

Figure 14-9: [Reference example] External view of a whole-body PET scanner (Hamamatsu Photonics SHR-92000)

PET provides tomographic images of a living body in the active state and allows early diagnosis of lesions and tumors by injecting pharmaceuticals labeled with positron-emitting radioisotope into the body and measuring their concentrations. Typical positron-emitting radioisotopes used in PET are ^{11}C, ^{13}N, ^{15}O and ^{18}F.

When positrons are emitted within the body, they combine with the electrons in the neighboring tissues, releasing a pair of gamma-rays at 180 degrees opposite each other. Multiple rings of detectors surrounding the subject detect and measure these gamma rays by the coincidence technique. By arranging the acquired transaxial data at each angle, the PET scanner then creates a tomographic image by image reconstruction in the same way as X-ray computed tomography (X-ray CT).

A prime feature of PET is that quantitative measurement of physiological or biochemical information such as metabolism, blood flow and neural transmission within the body can be performed. PET has been chiefly used in research and study on brain functions and other organ mechanisms. Currently, PET is being put to active use in medical diagnosis, proving effective in diagnosing cancer.

A detector used in PET consists of a compact photomultiplier coupled to a scintillator. To efficiently detect gamma-rays of high energy (511keV) released from inside the body, scintillators with high stopping power versus gamma-rays such as BGO and LSO crystals are commonly used.

Another type of measurement technique is now being studied, which utilizes the TOF (time-of-flight) of gamma-rays generated by positron annihilation. This measurement uses high-speed photomultiplier tubes and scintillators with a short emission decay.

Scintillator	Density (g/cm^3)	Relative Emission Intensity	Emission Time (ns)	Wavelength of Peak Emission (nm)
BaF$_2$	4.89	5/26	0.8/620	220/320
BGO	7.13	20	60/300	480
LSO	7.35	72	40	420
GSO	6.71	20	60/600	430
NaI(Tl)	3.67	100	230	410

Numbers separated by a slash (/) indicate there are two emission components.

Table 14-1: Characteristics of major scintillators

PET scanners for animals are used in applications such as animal experiments for research that cannot be easily done with humans, as well as for developing new medicines and evaluating the pharmacological effects of general medicines. Small laboratory animals such as mice and rats, and monkeys or baboons are usually used with PET scanners.

Because those animals' organs are relatively small, PET scanners must provide high resolution. For this purpose, for example, the Hamamatsu Photonics model SHR-7700 PET scanner used a large number of scintillation detectors, each consisting of a position sensitive photomultiplier tube combined with 32 BGO scintillators. A total of 240 photomultiplier tubes and 7,680 BGO scintillators were used in one PET scanner.

The SHR-7700 offered an effective field of view of 330✕114 millimeters and a center resolution of 2.6 millimeters.

Figure 14-10: [Reference example] External view of Hamamatsu Photonics SHR-7700 PET scanner for animals

The detector ring and scintillation detector used in the SHR-7700 are illustrated in Figure 14-11.
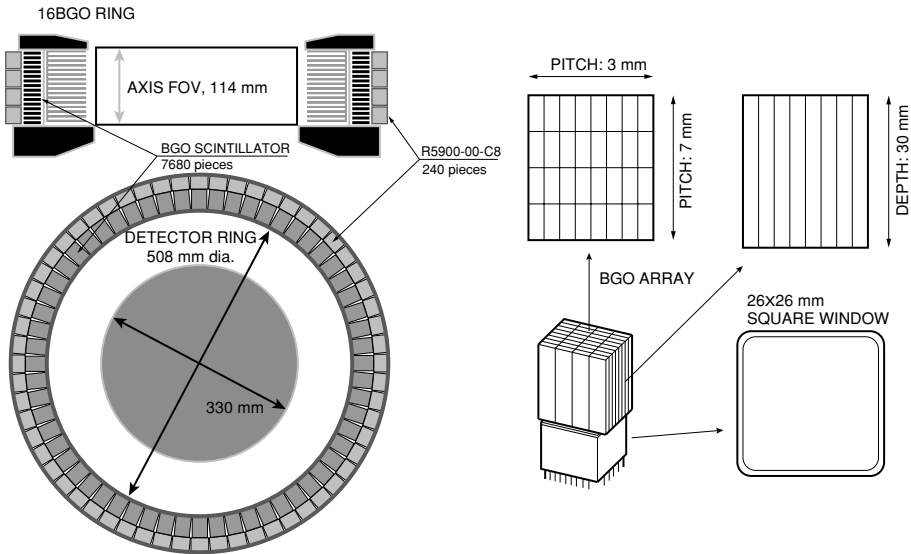
Figure 14-11: Cross section of SHR-7700 detector ring and scintillation detector

Figure 14-12 shows images of oxygen metabolic activity in a monkey brain, observed by the SHR-7700.
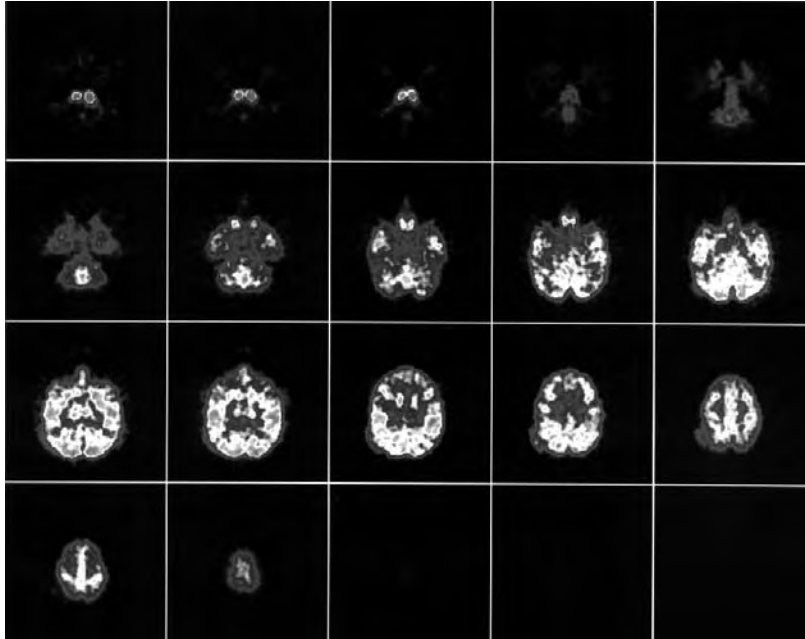

Figure 14-12: Images of oxygen metabolic activity in a monkey brain (positron imaging)
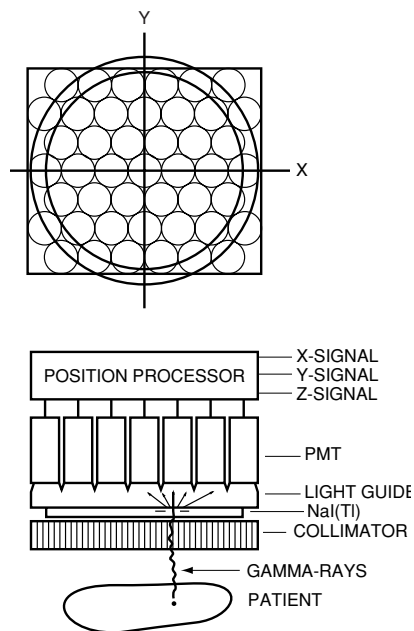
14.2.2 Gamma cameras

Imaging equipment utilizing a radioactive isotope (RI) first appeared as a scintillation scanner before undergoing successive improvements leading to the currently used gamma camera developed by Anger (U.S.A.). Recently, even more sophisticated equipment called SPECT (single photon emission computed tomography), which utilizes the principle of the gamma camera, has been developed and is now coming into wide use. An external view of a gamma camera is shown in Figure 14-13.
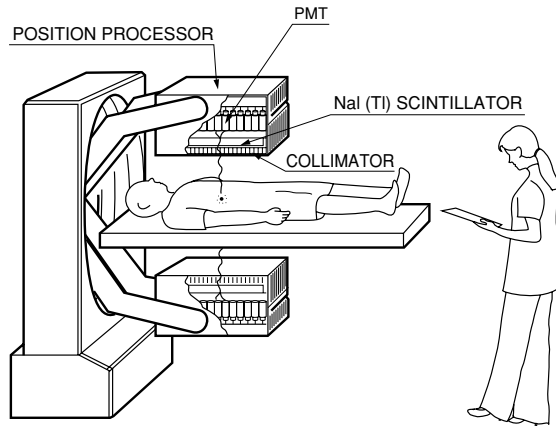
Figure 14-13: External view of a gamma camera

Figure 14-14 shows sectional views of a detector used in gamma cameras, in which dozens of photomultiplier tubes are installed in a honeycomb arrangement. Each photomultiplier tube is coupled, via a light-guide, to a large-diameter scintillator made from a thallium-activated sodium-iodide (NaI(Tl)) scintillator, serving as a gamma-ray detector.

Figure 14-14: Sectional views of a detector used in gamma cameras

To make gamma cameras more effective for medical diagnosis, a variety of gamma-ray nuclide drugs have been developed. Improvements in the position processing circuit have also achieved higher resolution, making gamma cameras more popular in medical diagnosis. Major nuclides used for nuclear medical imaging are listed in Table 14-2.

Recently, a SPECT equipped with two or three camera heads is often used to improve sensitivity.

Nuclide	Gamma-ray energy (keV)	Half-life
^{99m}Tc	141(no β)	6.01h
^{133}Xe	81(β:346)	5.243d
^{67}Ga	93(37%), 185(20%), 300(17%)	78.3h
^{201}Tl	70.8(Hg-X), 16.7(11%), 135(2.8%)	72.91h
^{131}I	364(81%)(β:606)	8.04d
^{123}I	159(83%)	13.2h
^{81m}Kr	190(67%)	13s
^{111}In	245(94%), 171(90%)	2.83d

Values in parentheses ( ) indicate stripping efficiency.

Table 14-2: Major nuclides used for nuclear medical imaging

14.2.3 Planar imaging device

A planar imaging device is designed to capture two-dimensional images using positron-emitting nuclides and a pair of radiation detectors comprised of a position sensitive photomultiplier tube coupled to a scintillator array. The pair of detector units are arranged so that they face each other and an object to be measured is placed between them. Two-dimensional images of a positron-emitting nuclide tracer injected into the subject and their changes over time can be observed.

When a living plant or a small living animal is placed between the two detector units, the activity of substances within its body can be measured as two-dimensional images at nearly real-time. Positron-emitting nuclides such as ^{11}C, ^{13}N and ^{15}O are major elements that constitute a living body and are also the basic substances used for organic synthesis. This makes it possible to use many kinds of pharmaceutical compounds labeled with positron-emitting nuclides. (Example: ^{11}CO$_2$, ^{11}C- methionine, ^{13}NH$_4$+, ^{13}NO$_3$-, ^{15}O- water, etc.)

When a positron-emitting nuclide with a short half-life period is used, for example ^{11}C (20 minutes), ^{13}N (10 minutes) or ^{15}O (2 minutes), measurements can be repeated using the same individual. This allows measurement of changes in a day or measurement under two or more different conditions while eliminating errors that may be caused by individual differences.

Since annihilation gamma-rays (511 keV) are used for imaging, self-absorption within the object being measured can be almost ignored, allowing accurate measurement of the distribution of substances in a plant or small animal. Compared to medical PET scanners, the planar imaging device can obtain images with a higher signal-to-noise ratio and spatial resolution because the image generation technique is simple.

Unlike tomographic PET images, when the object being measured is relatively thin, it is easier to visually recognize the image since the image obtained is a (pseudo-) projected image.

The block diagram and external view of a planar imaging device are shown in Figure 14-15.
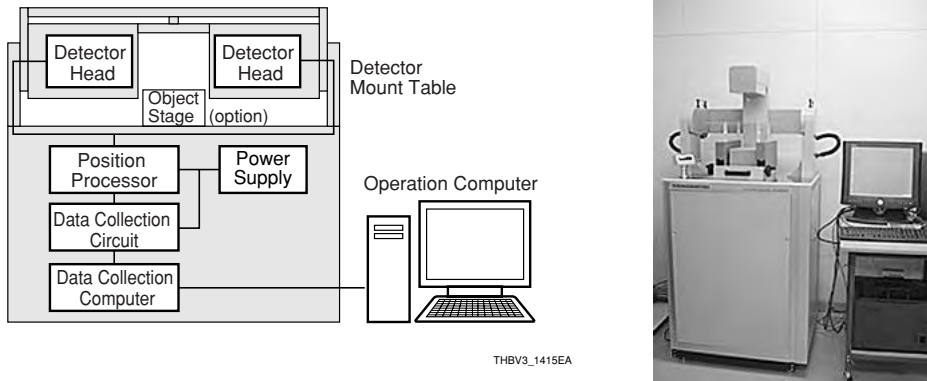
Figure 14-15: Block diagram and external view of a planar imaging device

14.2.4 X-ray image diagnostic equipment

X-ray image diagnostic equipment is used in routine examinations at many medical clinics and facilities. Photomultiplier tubes are used in many types of X-ray examination apparatus to monitor the X-ray exposure time or dose. With the recent trend toward filmless X-ray imaging systems, photomultiplier tubes have also been widely used in detectors that read out X-ray images formed on a special phosphor plate instead of X-ray films.

(1) X-ray phototimer

The X-ray phototimer automatically controls the X-ray film exposure in X-ray examinations. The X-rays transmitting through a subject are converted into visible light by a phosphor screen. A photomultiplier tube is used to detect this light and provide an electrical signal. When the accumulated electrical signal reaches a preset level, the X-ray irradiation is shut off to obtain an optimum film density.
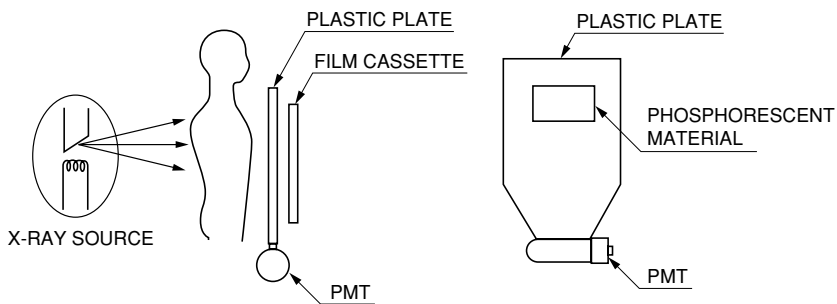
Figure 14-16: X-ray phototimer

(2) Computed radiography (CR)

X-ray image diagnosis systems also includes computed radiography equipment using a special photostimulable phosphor plate. In this equipment, an X-ray image is temporarily accumulated on the phosphor plate and a laser beam then scans (excites) the image formed on the phosphor plate, causing visible light to be emitted according to the amount of accumulated X-rays. A photomultiplier tube is then used to covert this weak visible light into electrical signals which are then digitally processed to recon-struct an image.

Computed radiography has several advantages over conventional techniques using X-ray films. It offers a short imaging time, less imaging errors, and digital image processing and data analysis that permit high-density storage and simple retrieval of image data. These useful features have led to its widespread used in the world.
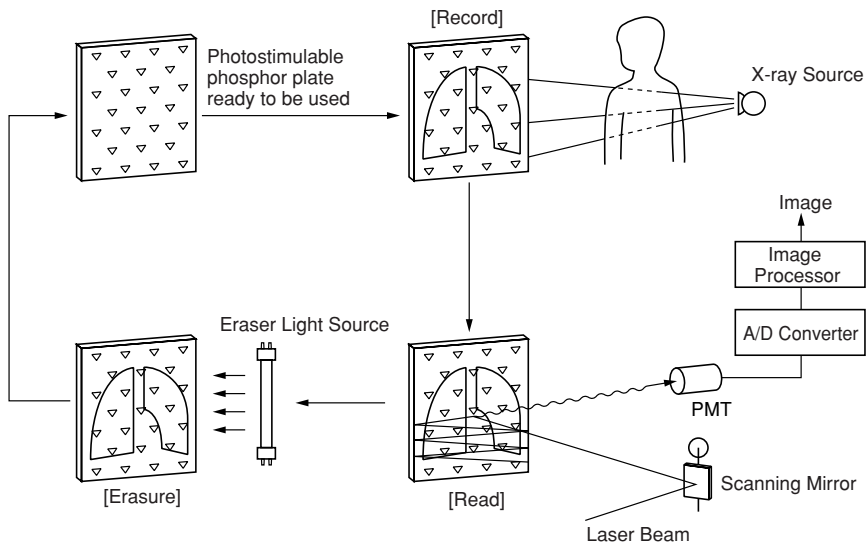
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Figure 14-17: X-ray image acquisition using photostimulable phosphor plate

14.2.5 In-vitro assay

The analysis and inspection of blood or urine samples collected out of a living body is referred to as in-vitro assay. It is used for physical checkups, diagnosis, and evaluation of drug potency. The in-vitro assay can be classified as shown in Table 14-3. Among these, the concentrations of most tumor markers, hormones, drugs and viruses classified under immunological assay are exceedingly low. Detecting these items requires extremely high-sensitivity inspection equipment that mostly must use photomultiplier tubes.

Sample Inspection ——— Biochemistry
             Enzyme, protein, sugar, lipid

             Immunology
             Tumor marker, serum protein, hormone, reagent, virus

             Hematology
             (Leukocyte, red corpuscle, hemoglobin, platelet)
              computation, classification, coagulation

             Microbiology
             Bacteria identification, susceptibility
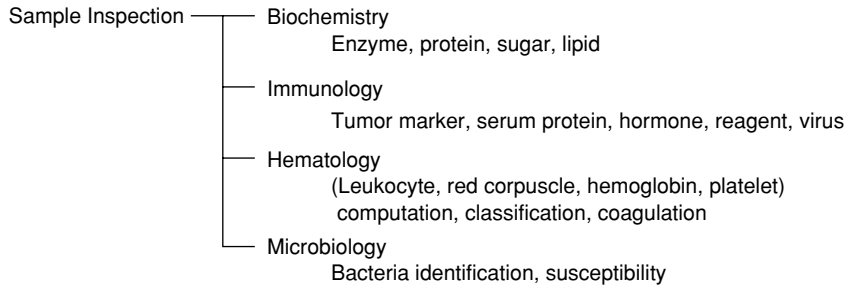
Table 14-3: Classification of in-vitro inspection

Immunoassay, a measurement technique that relies on the specificity of the antigen-antibody reaction is widely used. The principles of immunoassay[6] are illustrated in Figure 14-18 and the procedures of each method are explained in the subsequent paragraphs.

(a) Sandwich Method

(1) Solid-phase antibody+sample

OBJECT
ANTIGEN
/HORMONE
TUMOR
MARKER
REAGENT
\VIRUS, ETC.

ANTIBODY FIXED IN
VESSEL

(2) Removing liquid layer after
antigen-antibody reaction

LIQUID LAYER

ANTIGEN-
ANTIBODY
REACTION

(3) Adding labeled antibody

LABEL

/RADIO-
ISOTOPE
\ENZYME

(4) Removing upper layer after
antigen-antibody reaction

LIQUID
LAYER

SAND-
WITCHING

(5) Measuring number of labels

MEASURING NUMBER OF LABELS
Proportional to
quantity of object
antigen

(b) Competitive Method

(1) Solid-phase antibody

OBJECT
ANTIGEN

ANTIBODY FIXED IN VESSEL

(2) Introducing sample and
labeled antigen

LABELED
ANTIGEN

(3) Removing liquid layer after
antigen-antibody reaction

LIQUID LAYER

COMPETITIVE BOND
Sample antigen and labeled
antigen combine respectively
with antibody according to their
quantities

(4) Measuring number of labels

MEASURING NUMBER OF LABELS
Inversely proportional to
quantity of object antigen

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Figure 14-18: Principles of immunoassay

Figure 14-18 (a) is a technique known as the sandwich method. Step (1): Samples are introduced into a vessel in which antibodies responding to object antigens (hormones, tumor markers, etc.) are fixed (solid-phase antibody). Step (2): Antigen-antibody reaction occurs and each object antigen combines with a solid-phase antibody. This reaction has an extremely high singularity and hardly ever occurs with a different antigen. After antigen-antibody reaction, the liquid layer is removed leaving the combined antigen and antibody. Step (3): Labeled antibodies are added, which combine with object antigens. Step (4): Antigen-antibody reaction occurs again so that the object antigen is sandwiched between the antibodies. The liquid layer is then removed. Step (5): The quantity of labels is optically measured using a photomultiplier tube.

Figure 14-18 (b) shows another technique called the competitive method. Step (1): Antibodies responding to object antigens are fixed on the bottom of a vessel. Step (2): Samples are added along with the labeled object antigens. Step (3): Competitive reaction occurs in which object antigens and labeled antigens combine with labeled antibodies in proportional to their concentration, reaching a state of equilibrium. After the antigen-antibody reaction, the unnecessary upper layer is removed. Step (4): The quantity of labels is measured using a photomultiplier tube. In the sandwich method, the higher the concentration of object antigens, the larger the signal. Conversely, in the competitive method, the higher the concentration of the object antigens, the lower the signal.

Immunoassay can be further categorized according to the material used for labeling as follows

(1) Using radioactive isotopes for labeling
...... RIA (Radioimmunoassay)

(2) Using enzymes for labeling
.... EIA (Enzymeimmunoassay)

(1)   RIA (Radioimmunoassay) method

Radioactive isotope (RI) is used for the labeling as was explained above, and radiation (gamma or beta rays) emitting from the RI labels is detected by the combination of a scintillator and a photomultiplier tube, so that the object antigen can be quantitatively measured. Radioactive isotopes most frequently used for labeling are ^{3}H, ^{14}C, ^{57}Co, ^{75}Se, ^{125}I and ^{131}I. (See Table 14-4.)[7] Of these, ^{125}I offers useful characteristics for labeling and is very widely used. Because radioactive isotopes other than ^{3}H and ^{14}C emit gamma rays, sodium iodide crystals are used as a scintillator to provide a high conversion efficiency.

Radioisotope	Half-life	Energy	Detection Method
^{3}H	12.26 years	β	Liquid scintillation
^{14}C	5730 years	β	Liquid scintillation
^{57}Co	270 days	γ	Scintillation crystal
^{75}Se	120.4 days	γ	Scintillation crystal
^{125}I	60 days	γ	Scintillation crystal
^{137}I	8 days	β, γ	Scintillation crystal

Table 14-4: Radioactive isotopes used for labeling in radioimmunoassay

Recently, in in-vitro assays, the quantity of samples and the number of items to be measured are rapidly increasing. To keep pace with this trend, equipment for radioimmunoassay has been automated. A typical piece of automated equipment in use today is the well scintillation counter[8] that makes use of sodium iodide scintillators having a well-like hole to enhance the conversion efficiency of the radiation into light. Measurements are made by automatically inserting test tubes, which contain a mixture of antigens and antibodies including labels, into each hole in the scintillator. (See Figure 14-19.) Each detector section including a scintillator is covered by lead shield to block extraneous radiation.
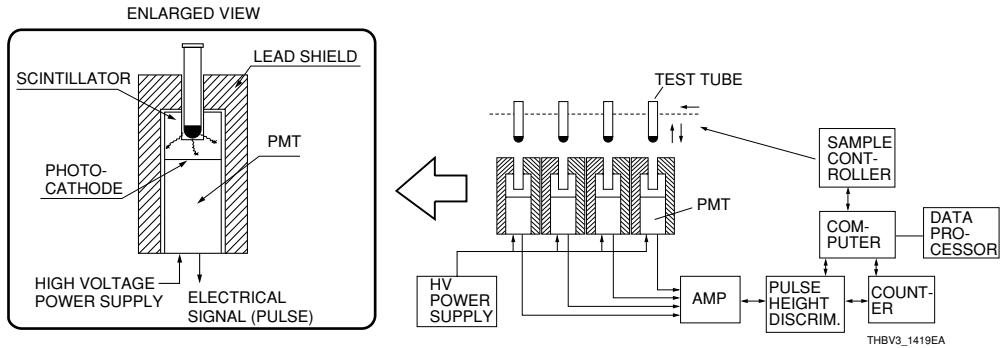
Figure 14-19: Schematic block diagram illustrating a well scintillation counter

(2) Luminescent / fluorescent immunoassay

Non radioactive immunoassay techniques called "EIA (Enzymeimmunoassay)" that do not rely on radioisotopes are currently under research and development.

One of these is fluorescent immunoassay or fluoroimmunoassay in which a fluorescent substance is used for labeling. The final remaining mixture of antigens and antibodies is irradiated by an excitation light and the resulting fluorescence is measured with regard to the intensity, wavelength shift and polarization. This technique offers slightly higher sensitivity than that of EIA. Figure 14-20 shows the schematic drawing of an immunoreaction measurement system used for fluoroimmunoassay.
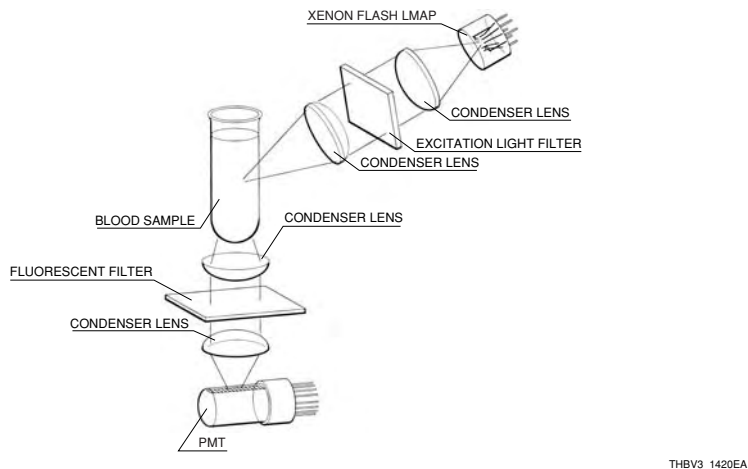
Figure 14-20: Schematic layout of a fluorescent immunoreaction measurement system

To achieve high sensitivity equal to RIA by using non-radioactive immunoassay, intensive research and development of emission-immunoassay has been carried out. This immunoassay uses a chemiluminous substance or bioluminous substance for labeling and allows the final remaining mixture of antigens and antibodies to emit light, which is detected by a photomultiplier tube. There are three types of emission-immunoassay methods, as follows:

1) Use of a chemiluminous substance such as luminol and acridinium for labeling
2) Use of chemiluminescence or bioluminescence for activation of the label enzyme used in EIA
3) Use of a catalyst for the bioluminescence reaction

Methods 2) and 3) can be thought of as variations of EIA techniques. Luminescent immunoassay has very high sensitivity equivalent to the measurable concentration ranges of RIA.

(3) Chemiluminescent immunoassay

Chemiluminescent immunoassay has several merits such as high sensitivity, wide dynamic range, and simple measurement without using detection antigens and special facilities which are usually needed by radioimmunoassay.

When enzymes are added to antibodies or antigens labeled with a luminescent reagent, a chemical reaction occurs. Light emission accompanying the reaction is detected by a photomultiplier tube.
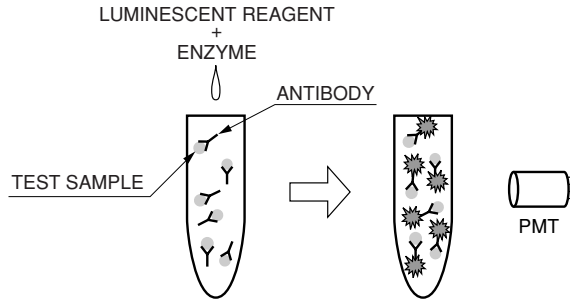
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Figure 14-21: Principle of chemiluminescent immunoassay

14.3 Biotechnology

14.3.1 Overview

In life science applications, photomultiplier tubes are mainly used for detecting fluorescence and scattered light. Major equipment used for life science includes cell sorters, fluorometers and DNA sequencers.

14.3.2 Application examples

(1) Flow cytometers

When light is irradiated onto a rapidly flowing solution which contains cells or chromosomes, a scattered light or fluorescence is released from the cells or chromosomes. By analyzing this scattered light or fluorescence, it is possible to elucidate cell properties and structures and separate the cells based on these properties. This field is known as flow cytometry. In this field, a flow cytometer like the one illustrated in Figure 14-22 is most frequently used. The flow cytometer is an instrument that selects and collects only specific cells labeled by a fluorescent substance from a mixture of cells in a solution.
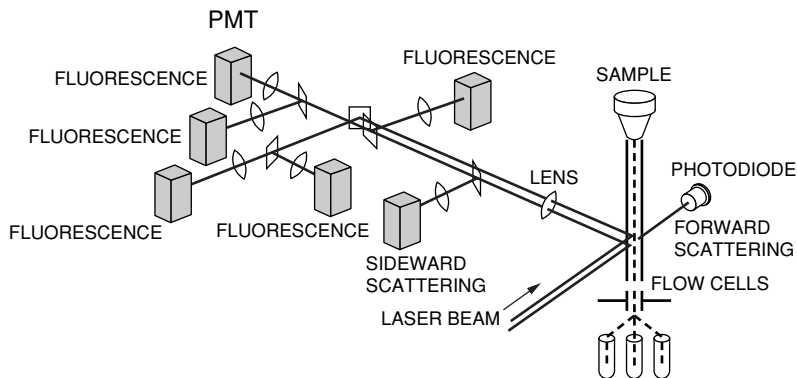
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Figure 14-22: Major components of a flow cytometer

In a cell sorter, a fluorescent probe is first attached to the cells. The cells pass through a thin tube at a fixed velocity. When each cell passes through a small area onto which an intense laser beam is focused, the fluorescence is emitted from the cell and is detected by a photomultiplier tube. The photomultiplier tube outputs an electrical signal in proportion to the number of fluorescent molecules attached to each cell. At the same time, the laser beam light is scattered forward by the cell, and detecting this scattered light yields information on the cell volume. After processing these two signals, the cell sorter creates an electrical pulse that deflects a drop of liquid, containing the desired cell into one of the collection tubes.

(2)   Confocal laser microscopes

The confocal laser microscope acquires 2 and 3-dimensional fluorescent images of a sample labeled with fluorescent dye by scanning the sample surface with a laser. The laser scans an extremely tiny spot to obtain high-resolution images by means of confocal function. (See Figure 14-23.) A biological sample stained with fluorescent dye and placed beneath the microscope is scanned by an excitation laser beam narrowed to a very small size equal to the light wavelength, and by moving the sample stage up or down, only the fluorescence from sections matching the focus point passes through the pinhole and is detected by a photomultiplier tube. The electrical signals from the photomultiplier tube are then image-processed and reconstructed into high-resolution 2D or 3D images. Confocal laser microscopes are mainly used for ob-servation of biological tissues or sections.

PMT

CONFOCAL PINHOLE

CONFOCAL PINHOLE

LASER

BEAM SPLITTER

OBJECTIVE LENS

SAMPLE

NON-CONFOCAL PLANE
FOCAL PLACE
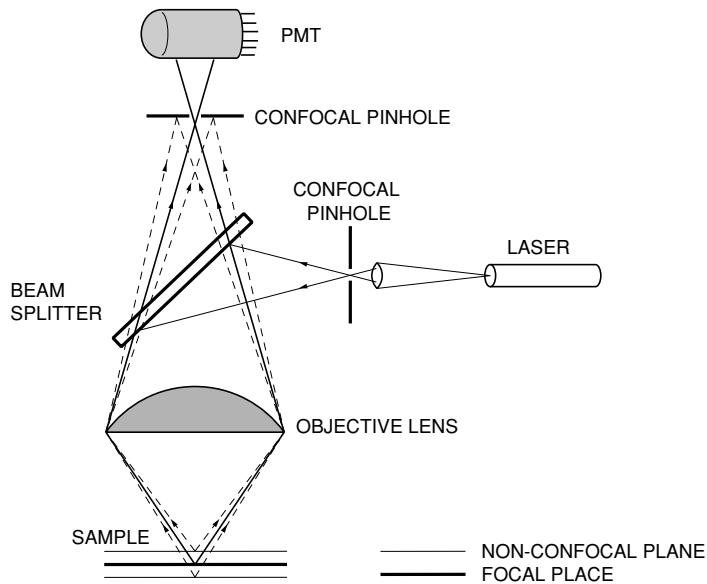
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Figure 14-23: Confocal laser microscope

(3)   DNA microarray scanners

Biochemical tools called "DNA chips" are used for analyzing vast amounts of genetic information. A DNA chip is a substrate holding large numbers of DNA probes at a high density. Some DNA chips make use of semiconductor photolithographic methods, while on others, DNA is dispensed on a slide glass using a high-precision robot mechanism. DNA probes (arrangement is known) bonded on a slide glass are hy-bridized with sample DNA segments labeled with fluorescent dye. A laser beam scans the DNA chip and the intensity of fluorescence emitted from the hybridized DNA is measured to acquire genetic information on the sample DNA.

(Hybridization is a process where single DNA strands having the same complementary base link to form a double strand.) (See Figure 14-24.)
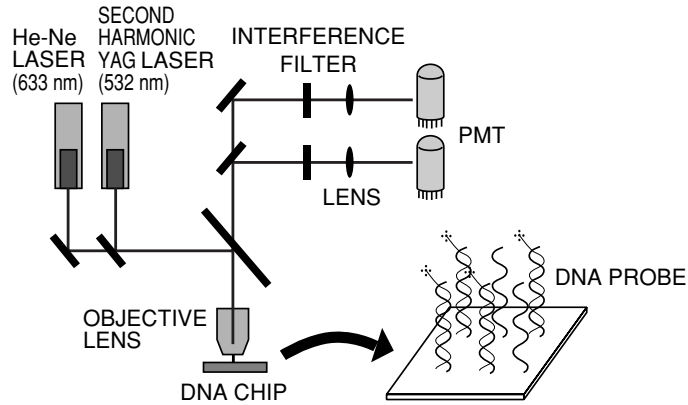
Figure 14-24: DNA microarray scanner

(4)   DNA sequencers

This is an instrument used to decode the base arrangement of DNA extracted from a cell. The principle of a DNA sequencer is shown in Figure 14-25. An extracted DNA segment is injected onto gel electro-phoresis plate or into capillary tubes along with a fluorescent label which combines with a specific base of the DNA segment. When an electric potential is applied across the gel, the DNA begins to migrate and separate based on size and charge. When the DNA segment reaches the position of the scanning line, it is excited by a laser, causing only the portion with the labeling pigment to give off fluorescence. This fluores-cent light is passed through monochromatic filters and detected by photomultiplier tubes. Computer-pro-cessing of the position at which the fluorescence has occurred gives information on where the specific bases are located. The DNA sequencer is used for the genetic study of living organisms, research into the cause and treatment of genetic diseases, tumors and adult diseases, as well as decoding of human genes.
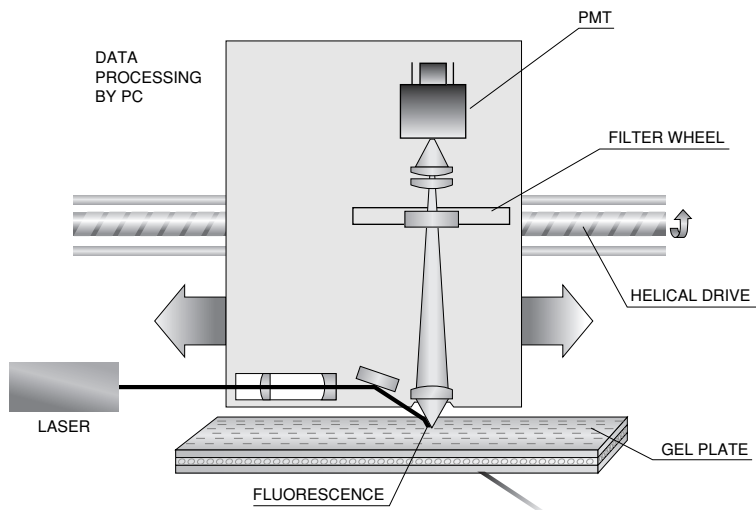
Figure 14-25: Principle of a DNA sequencer

14.4 High-Energy Physics Experiments

14.4.1 Overview

Photomultiplier tubes are widely used as detectors in high-energy physics experiments. For example, when a charged particle passes through a scintillator, a light flash is given off in accordance with the particle energy. Detecting this light flash makes it possible to measure the energy, speed and direction of the charged particle. This technique is absolutely essential in high-energy physics research which is constantly aiming for the ultimate in scientific technology.

14.4.2 Collision experiments

In collision experiments, primary particles such as electrons and protons are accelerated to high energy by an accelerator so that they collide with each other to produce secondary particles. The energy, speed and kinetic momentum of these secondary particles are detected and observed. There are several particle detection methods that use photomultiplier tubes, for example, a hodoscope, TOF counter, calorimeter and Cherenkov counter.
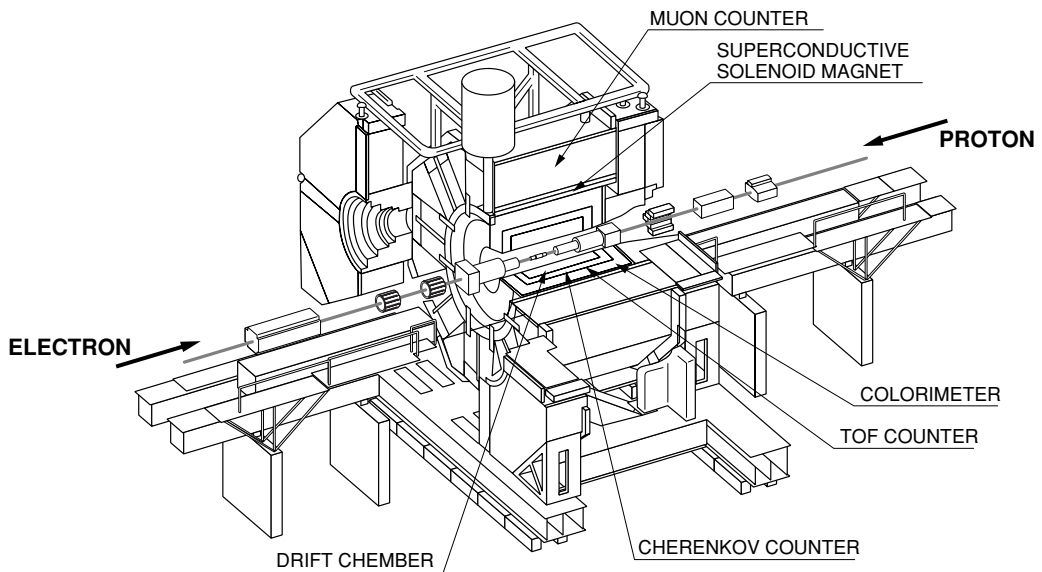
THBV3_1426EA

Figure 14-26: Example of collision experiment setup

(1) Hodoscopes

Figure 14-27 shows a simplified diagram[9] of a hodoscope. Plastic scintillators are arrayed in two orthogonal layers followed by photomultiplier tubes. The position and time at which a charged particle passes through certain scintillators are detected by the corresponding photomultiplier tubes.
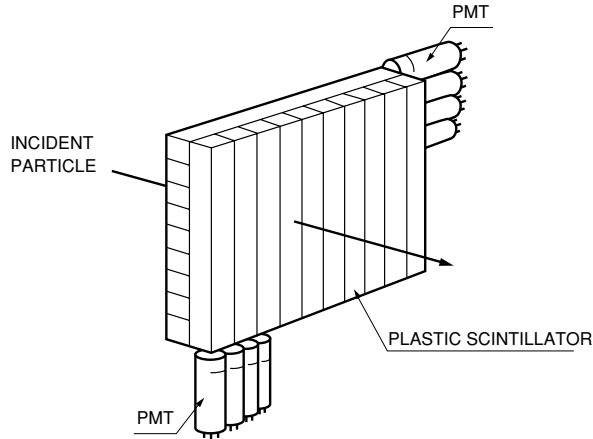
THBV3_1427EA

Figure 14-27: Simplified diagram of a hodoscope

(2) TOF counters

TOF counters measure the time of flight (TOF) of particles to identify the type of the particles. A simplified illustration of a TOF counter is shown in Figure 14-28. When primary particles collide with each other, secondary electrons are generated. The time of flight of those particles from the collision point is measured to find the velocity of the particles. A typical detector for TOF counters consists of a long plastic scintillator bar with both ends coupled to a photomultiplier tube. A large number of plastic scintillator bars are arranged cylindrically around the collision point.
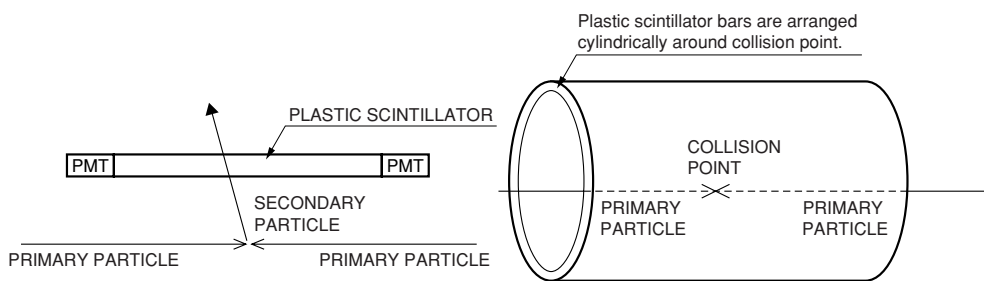
THBV3_1428EA

Figure 14-28: TOF counter setup   **Figure 14-28: Entire TOF counter**

(3) Calorimeters

Calorimeters measure the energy of secondary particles such as electrons, photons and hadrons. A simplified illustration of a calorimeter is shown in Figure 14-29. The collision point is surrounded by detectors like a TOF counter. In the case of calorimeters, the energy of particles is released into matter and converted into light or an electric charge. This is usually measured with detectors consisting of an inorganic scintillator or lead glass combined with a photomultiplier tube. Recently, sampling calorimeters are also in use, which employ a multilayer structure of plastic scintillators and heavy metals such as iron and lead instead of using inorganic scintillators.
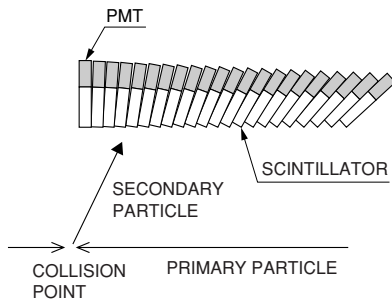
Figure 14-29: Calorimeter setup   **Figure 14-29: Entire calorimeter**
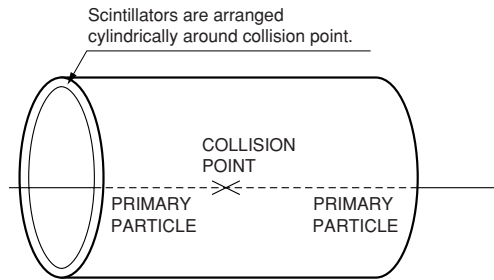
(4) Cherenkov counters

Cherenkov radiation is emitted when a charged particle passes through matter called a "radiator" (transparent medium) with a velocity or energy greater than a certain level. This Cherenkov radiation is a kind of shock wave, so it is emitted in a cone around the direction of the charged particle, forming a ring pattern. The energy and type of the particle can be identified on the basis of the size and brightness of this ring.

Figure 14-30 shows a schematic diagram of a Cherenkov counter called "RICH" (Ring Imaging Cherenkov counter). Cherenkov light is emitted when a particle passes through a radiator with energy greater than a certain level. This light reflects on a mirror and is then detected by a photodetector array installed on the opposite side. The energy and type of the particle are identified by measuring the size of the ring.
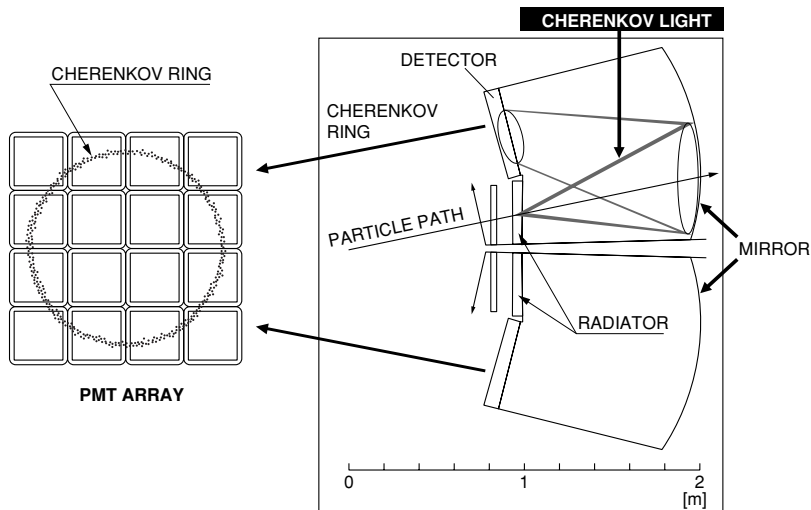
Figure 14-30: Schematic diagram of RICH

14.4.3 Proton decay, neutrino observation experiments

Proton decay observation is an experiment that attempts to capture the Cherenkov light emitted by high-energy charged particles that are supposedly produced when protons decay. Photomultiplier tubes are used to detect the Cherenkov light.

Kamiokande

In 1983, the Kamiokande (KAMIOKA Nucleon Decay Experiment) detector was installed in an underground mine in Hida City, (formerly Kamioka Town) in Gifu Prefecture, Japan, under the guidance of the Institute for Cosmic Ray Research (ICRR) and the High Energy Physics Research Laboratory, Faculty of Science, University of Tokyo. The Kamiokande detector was constructed with a huge tank filled with pure water installed 1 kilometer underground. On the side walls, bottom and roof of this tank, 1,050 photomultiplier tubes, each 20 inches in diameter making them the largest of their class in the world, were installed to wait quietly to catch the instant of photon decay. These photomultiplier tubes were manufactured to exacting specifications, for example, a large diameter glass bulb with a spherical photosensitive surface that allows catching the faint Cherenkov light traveling from a variety of angles and helps withstand the water pressure. High sensitivity, fast time response, and high photoelectron collection efficiency are also important factors.

In January 1987, besides proton decay, the Kamiokande detector was modified to allow observing solar neutrinos generated by nuclear fusion within the Sun. This modified detector catches the Cherenkov light that is rarely emitted when neutrinos flying away from the Sun pass through 3,000 tons of ultra-pure water in the tank. The 20-inch diameter photomultiplier tubes are used to detect this Cherenkov light. While waiting for the instant of proton decay, Kamiokande also detects solar neutrinos at the rate of about once every 9 days.

Since then the Kamiokande neutrino detection facility has yielded big news. At 4:35 AM on February 23rd, 1987, Kamiokande was the first facility in the world to detect neutrinos from the supernova 1987A that appeared in a corner of the Large Magellanic Cloud some 170,000 light years away. This is relatively close to the Earth and the blast from a supernova is said to occur only once every several hundred years. The last actual sighting was observed by the naked eye in 1604. A significant deficit in atmospheric neutrinos was reported from observation results with only about 46 percent of the expected number being detected.

Super-Kamiokande

In 1986, new plans for a "Super-Kamiokande" were unveiled by the University of Tokyo. Mainstream thought in the Grand Unified Theory is that proton lifetime may extend to 10^{34} years. To probe predictions in current Grand Unified Theories, plans were drawn up for a neutrino detection facility with 10 to 100 times the performance of Kamiokande. The new facility, called Super-Kamiokande, was constructed in a Kamioka mine 1 kilometer underground and about 200 meters away from Kamiokande. A huge water tank of 39.2 meters in diameter and 41.4 meters in height was constructed and filled with 50,000 tons of ultra-pure water. This is about 16 times the size of the Kamiokande tank. The 11,200 photomultiplier tubes each 20 inches in diameter are a further improvement on the Kamiokande tubes. Observation begun in April 1996 at the Super-Kamiokande.

In 1998, atmospheric neutrino oscillation was discovered indicating that neutrinos have mass. Precision testing of neutrino oscillation was made by means of artificial neutrinos and oscillation of these artificial neutrinos was also verified and observation currently continues.

KamLAND

In January 2002, experiments commenced with the "KamLAND" (Kamioka Liquid-scintillator Anti-

Neutrino Detector) operated by the Research Center for Neutrino Science, Tohoku University.

The KamLAND detector was constructed utilizing the former Kamiokande site yet is an even more sophisticated neutrino detector. Instead of pure water, KamLAND makes use of 1,000 tons of liquid scintillator to capture neutrinos. The intensity of the light emitted from the neutrinos reacting with the liquid scintillator is on a much larger scale than the Cherenkov light trapped at Kamiokande, and allows detecting neutrinos at lower energy levels. This liquid scintillator is held in a round balloon of about 13 meters in diameter made from special transparent film. The balloon itself is contained within a spherical tank of stainless steel 18 meters in diameter and having a volume of 3,000 cubic meters.

The inner wall of the tank is lined with approximately 1,900 photomultiplier tubes each 20 inches in diameter (effective area: 17 inches) that are improved versions of the Super-Kamiokande tubes. The outer wall of this spherical tank is further enclosed by a tank filled with pure water and this section is also lined with 20-inch photomultiplier tubes. At KamLAND, the time difference between two light emissions occurring from reaction with the neutrinos, and the time delay from the emission of light until the light reaches the photomultiplier tubes are measured. The location within the balloon where the neutrino reaction occurred can be determined in this way.

In 2002 it was announced that oscillation was present in neutrinos from nuclear power plants, and the mystery of solar neutrinos was determined to be due to this neutrino oscillation. Japan is a leader in the field of neutrino research and these superb devices are certainly one of the main reasons it retains this lead.

11,200 photomultiplier tuhes, each 20 inches in diameter
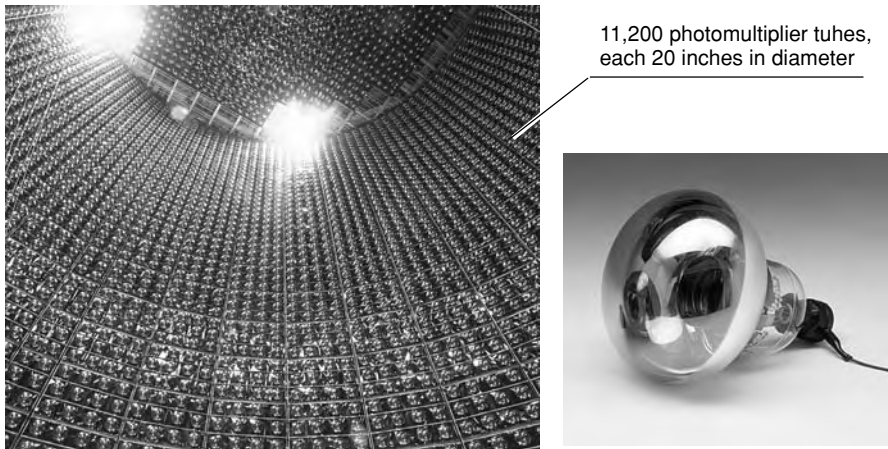
Figure 14-31: Interior of Super-Kamiokande detector tank lined with 20-inch PMT
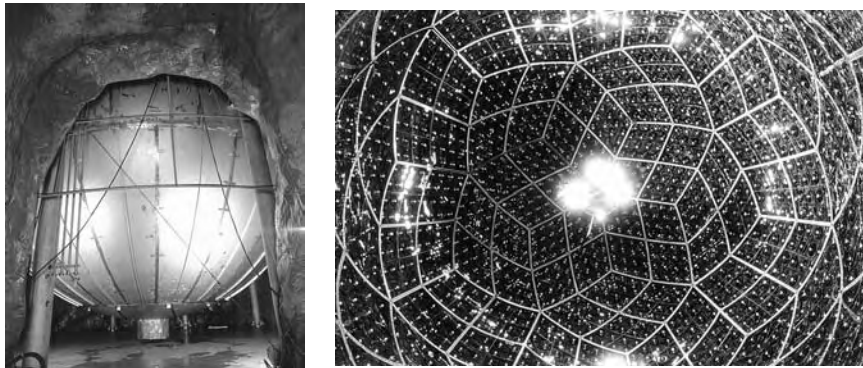
Stainless steel spherical tank   PMT installed on inner wall of spherical tank

Figure 14-32: KamLAND

14.5 Oil Well Logging

Special photomultiplier tubes have been developed that are capable of operating reliably in harsh environments including high temperature and severe vibration and shock. This section explains oil well exploration (oil well logging) as a sample application of these special tubes.

Oil well logging is used to locate an oil deposit and determine its size. This technique makes use of photomultiplier tubes as detectors for density well logging using radiation, neutron well logging and natural gamma-ray-spectrum well logging. In these well loggings. A probe containing a neutron or gamma ray source is lowered into a well as it is being drilled. The radiation or the neutrons that are scattered by the rock surrounding the well are detected by a scintillator/photomultiplier. The amount of scattered radiation detected is indicative of the density of the rock that surrounds the well. The scattered neutrons indicate the porosity of the rock which is required to ascertain if the oil can be removed. Naturally occurring gamma rays are detected to locate shale which indicates the presence of oil or gas. Figure 14-33 shows the measurement method[10] for oil well logging using radiation, and the cross sectional view of the strata layers around an oil well site.
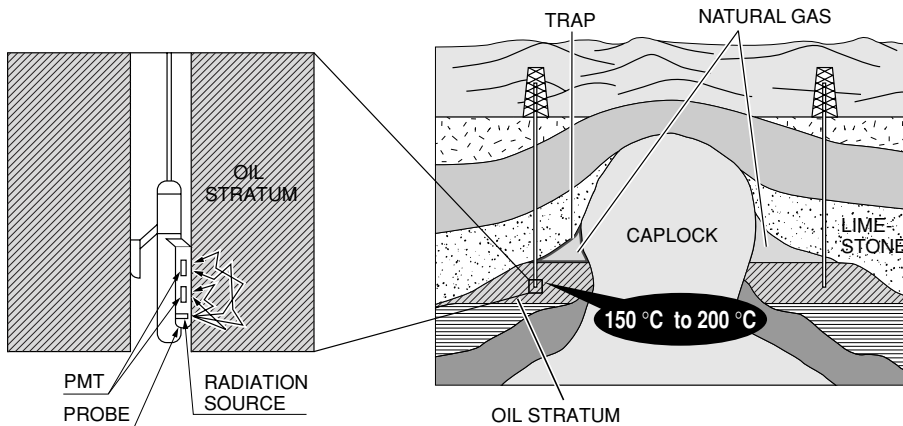
THBV3_1433EA

Figure 14-33: Oil well logging using radiation probe and cross sectional view of strata layers

The depth of a trial hole may be as deep as several thousand meters where the ambient temperature reaches as high as 150 to 200°C. In addition, shock and vibration are also applied to the photomultiplier tubes, imposing an extremely severe environment on the photomultiplier tubes. To meet these requirements, various types of ruggedized, high-temperature photomultiplier tubes have been developed which ensure adequate performance even under these severe environments. These photomultiplier tubes have a special photocathode that exhibits a minimal increase in dark current even at high temperatures and, in the multiplier section, dynode materials capable of withstanding high temperatures are employed. The electrode structures are also designed with careful consideration given to the effects of thermal expansion and vibration.

14.6   Environmental Measurement

14.6.1 Overview

Photomultiplier tubes are also used as detectors in environmental measurement equipment, for example, in dust counters used to detect dust contained in air or liquids, and radiation survey monitors used in nuclear power plants. This section explains some of these applications.

14.6.2 Application examples

(1)   Dust counters

A dust counter measures the concentration of floating dust in the atmosphere or inside a room by making use of principles such as light scattering and absorption of beta rays. Figure 14-34[11] shows the principle of a dust counter using light scattering. If dust is present in the light path, light is scattered by the dust. The quantity of this scattered light is proportional to the quantity of dust. The scattered light is detected by a photomultiplier tube and after being integrated, the output signal is converted into a pulse signal, which then corresponds to the particle concentration. This method offers an advantage that the output signal can immediately follow up on changes in the concentration, making it ideal for continuous monitor over time. However, this method has a disadvantage in that even if the mass concentration is constant, the quantity of scattered light varies with such factors as particle shape and the refractive index.
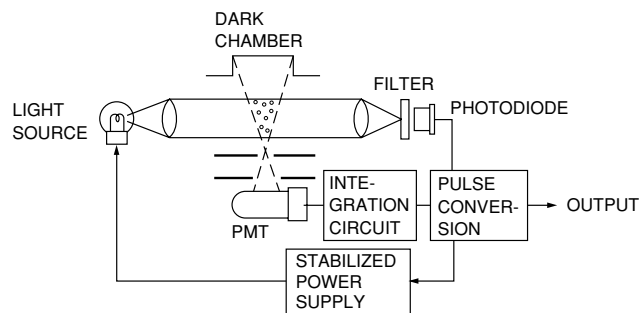
THBV3_1434EA

Figure 14-34: Block diagram of a dust counter using light scattering

Dust counters utilizing scattered light have a drawback in that the amount of scattered light varies depending on the size and refractive index of particles even if the particle concentrations are constant. Another type of dust counters make use of the absorption of beta rays which is proportional to the mass of a substance through which the beta rays are transmitted. A filter paper is used to collect the dust, and the difference in the amount of beta-ray absorption before and after collecting the dust is compared to determine the mass of the suspended particles.

(2)   Laser radar (LIDAR)[12]

Laser radar (LIDAR) transmits pulsed laser light into atmospheric space and receives the light backscattered from scatterers such as suspended matter in the atmosphere (atmospheric molecules, aerosols, clouds, etc.) and flying objects, in order to measure the distance to the scatterers as well as their concentrations, shapes and speeds. The laser transmitter and receiver are installed in the same place and the laser beam is scanned across the target area to obtain a three-dimensional spatial distribution. Optical signals detected by the receiver is converted into electrical signals, which are then converted into digital signals and processed by a computer.
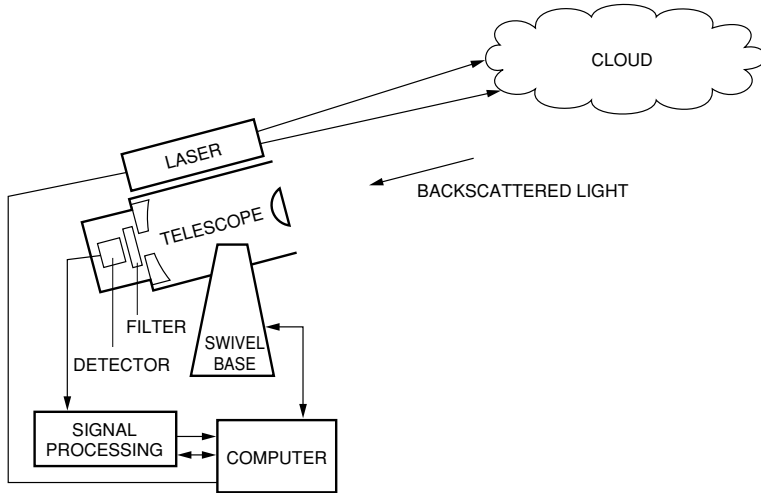
THBV3_1435EA

Figure 14-35: Schematic diagram of a laser radar for atmospheric observation

(3)   NOx analyzers

These instruments are used to measure nitrogen oxide (NOx), an air-polluting gas contained in exhaust gases from automobiles and other internal combustion engines. NOx is a general term indicating nitrogen monoxide (NO) and nitrogen dioxide (NO_2) and, in many countries, the concentration of NOx is limited by air pollution regulations so that it shall not exceed a certain level.

Figure 14-36 shows the configuration of an NOx analyzer making use of chemiluminescence.[13] When NO gas reacts with ozone (O_3) to become NO_2 gas, chemiluminescence is released. The intensity of this chemiluminescence is proportional to the concentration of NO gas. Since other gases contained in the exhaust gas do not produce such luminescence, the NO gas concentration can be selectively measured by detecting the intensity of this chemiluminescence.
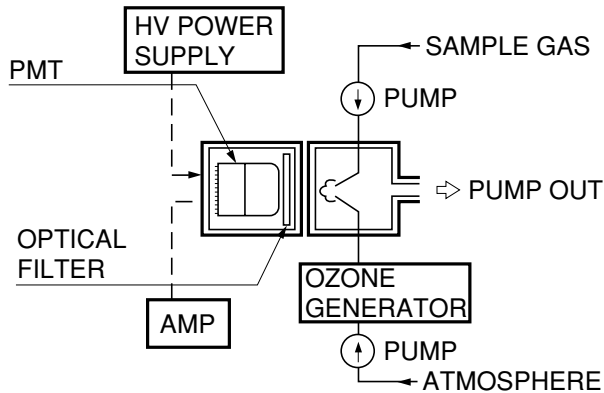
THBV3_1436EA

Figure 14-36: NOx analyzer utilizing chemiluminescence

(4) SOx analyzers

SOx analyzers are used to measure sulfur dioxide concentrations in the atmosphere. Recently, UV fluorescent sulfur dioxide analyzers are in wide use. This method irradiates the sulfur dioxide in the atmosphere with UV light to produce an excited state. The resulting fluorescence is then measured to determine the sulfur dioxide concentrations in the atmosphere. A typical setup of a UV fluorescent sulfur dioxide analyzer is shown in Figure 14-37.
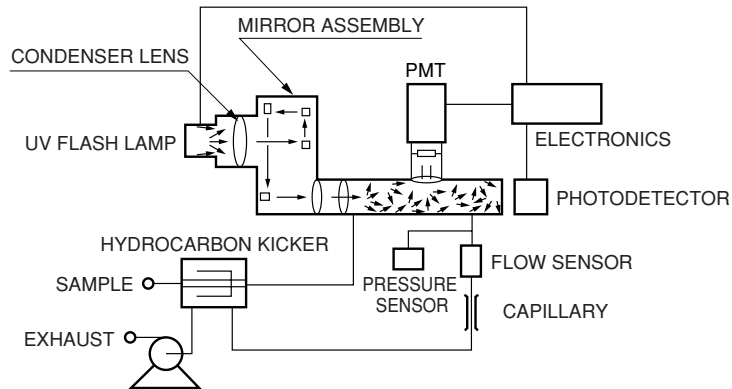
THBV3_1437EA

Figure 14-37: Typical setup of a UV fluorescent sulfur dioxide analyzer

14.7 Radiation Monitors

14.7.1 Overview

Radiation monitors have long been used at nuclear power plants and nuclear research facilities. In recent years, however, the loss or theft of nuclear materials has become a serious concern so that inspections and detection of nuclear materials has become a high priority at national borders such as harbors and airports. Photomultiplier tubes can be combined with a scintillator matching the radiation emitted from the nuclear material, to create various types of inspection devices and monitors.

14.7.2 Application examples

(1) Handheld radiation monitor (pager)

Handheld radiation monitors are designed to help customs, border guards and others keep watch for smuggled radioactive materials. A detector consisting of a photomultiplier tube coupled to a scintillator is used to detect radiation. Compact, metal package photomultiplier tubes are usually used for handheld applications. Figure 14-38 shows the internal layout and photo[14)] of a handheld radiation monitor.

THBV3_1438EA
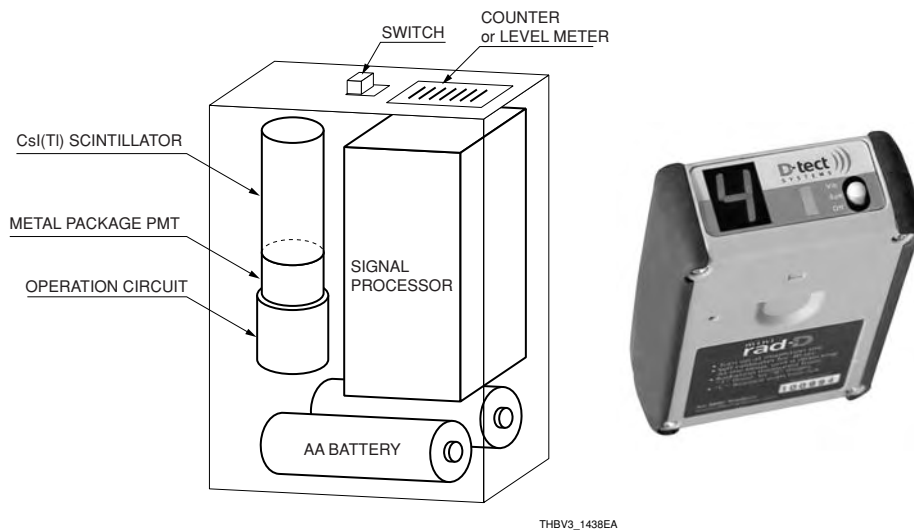
Figure 14-38: Structural view of a handheld radiation monitor

(2) Door monitors

As the name implies, the door monitor is installed near the exit door in the monitored area of a nuclear power plant in order to check the personnel going out of this area for contamination by radioactive material. A photomultiplier tube is used in conjunction with a scintillator to detect radiation released from the radioactive material. An example[15] of a door monitor is shown in Figure 14-39. The detector section consists of an array of scintillators coupled to photomultiplier tubes, enabling simultaneous measurement of the location and extent of contamination. Since the number of signals to be detected is usually very low, a coincidence counting circuit is used as in the case of scintillation counting to minimize erroneous signal counting.
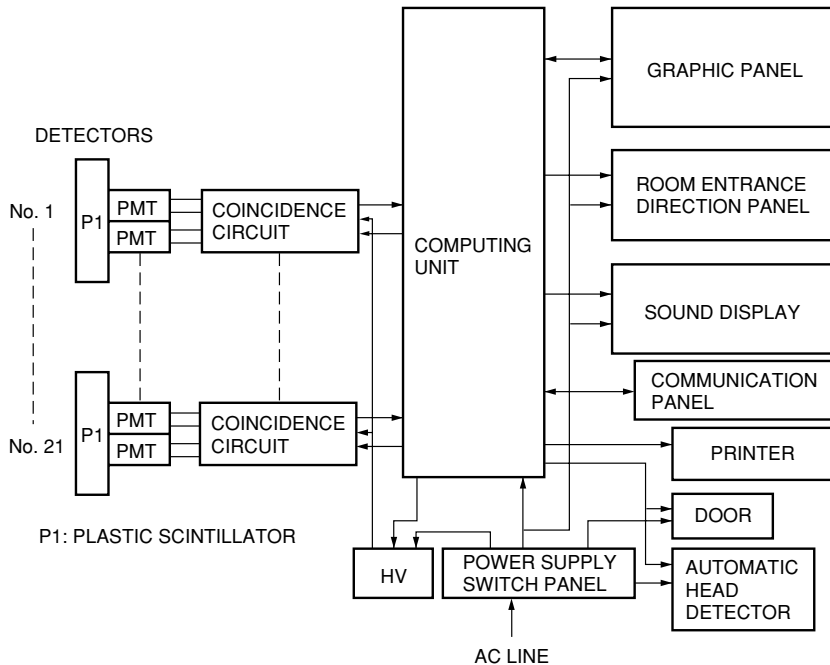
THBV3_1439EA

Figure 14-39: Block diagram of a door monitor

14.8 Industrial Measurement

14.8.1 Overview

For non-contact measurement on a production line and other industrial measurement applications where rapid measurement with a high degree of accuracy and quality is essential, extensive use is made of various devices having photomultiplier tubes as detectors. These devices include thickness gauges and laser scanners, which are briefly discussed in the following paragraphs.

14.8.2 Application examples

(1)   Thickness gauges

To measure the thickness of paper, plastics and steel plates on a production line, non-contact measurement techniques that use radiation such as beta rays, X rays or gamma rays are favored.

These techniques can be roughly divided into two methods: one measures the amount of beta or gamma rays transmitted through an object[16] (Figure 14-40) and the other measures the amount of fluorescent X-rays[17] (Figure 14-41)
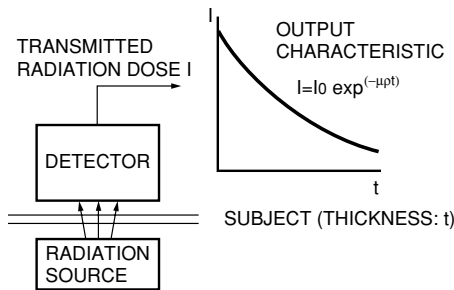
Figure 14-40: Principle of a transmission-mode thickness gauge
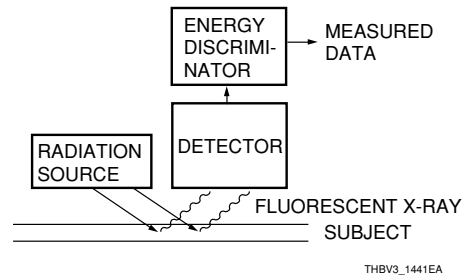
Figure 14-41: Principle of a fluorescent X-ray thickness gauge

When the intensity of radiation incident on a material is I_O, the transmitted radiation intensity I can be expressed by the following relation:

$$I = -I_0 e^{(-\mu\rho t)}$$

t : thickness (m)
ρ : density (g/m^3)
μ : mass absorption coefficient (m^2/g)

Since the transmitted radiation intensity is proportional to the count rate, the thickness of the material can be obtained by calculating the count rate. In general, beta rays are used to measure rubber, plastics and paper which have a small surface density (thickness✕density), while gamma rays are used to measure material with a large density such as metals. In addition, infrared radiation is also used for measurement of films, plastics and other similar materials.

Fluorescent X-rays are used to measure the film thickness of plating and deposition layers. Fluorescent X-rays are secondary X-rays generated when a material is excited by radiation and have characteristic energy of the material. By detecting and discriminating this energy, a quantitative measurement of the object material can be made.

There are a variety of detectors used in these applications, such as proportional counter tubes, photomultiplier tubes and semiconductor radiation detectors. Photomultiplier tubes are used in conjunction with scintillators, mainly for detection of gamma rays and X-rays.

(2) Laser scanners

Laser scanners are widely used in pattern recognition such as defect inspection and mask alignment of semiconductor wafers.

In semiconductor wafer inspection systems, a laser beam is scanned over the wafer surface or the wafer itself is scanned while a laser beam is focused onto a fixed point. In either case, photomultiplier tubes are commonly used to detect scattered light caused by dirt, stain and defects on the wafer surface. (See Figure 14-42.)
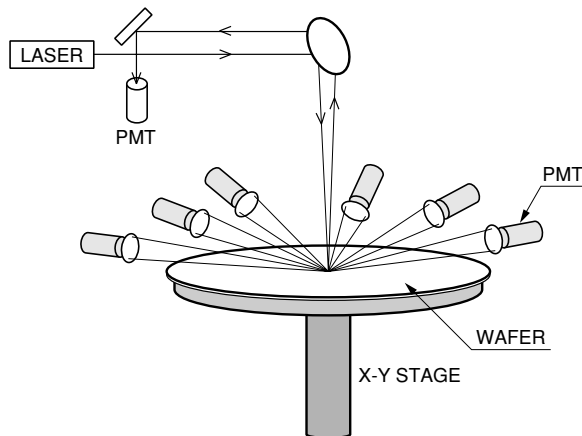
THBV3_1442EA

Figure 14-42: Optical system layout for a semiconductor wafer inspection system

14.9 Aerospace Applications

14.9.1 Overview

Photomultiplier tubes are widely used in space research applications such as detection of X-rays from outer space, planetary observation, solar observation, environmental measurement in inner or outer space and aurora observation. In addition, photomultiplier tubes are also used for spectral measurements of various radiation in the atmosphere or outer space and measurement of X-rays from supernovas.

14.9.2 Application examples

(1) X-ray astronomy

Figure 14-43 illustrates the structure of ASUKA launched and placed in its orbit in February 1993 as the fourth astronomical satellite for X-ray observation in Japan. A gas imaging spectrometer (GIS) is used as the detector, which consists of a gas-scintillation proportional counter coupled to a photomultiplier tube (Hamamatsu R2486X) as illustrated in Figure 14-44.
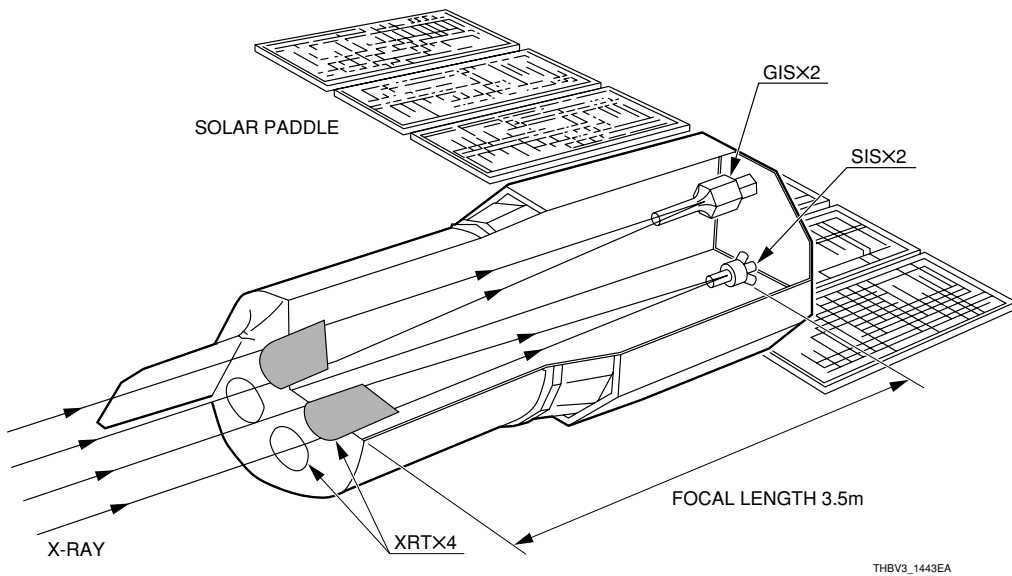
Figure 14-43: Astronomical satellite ASUKA for X-ray observation
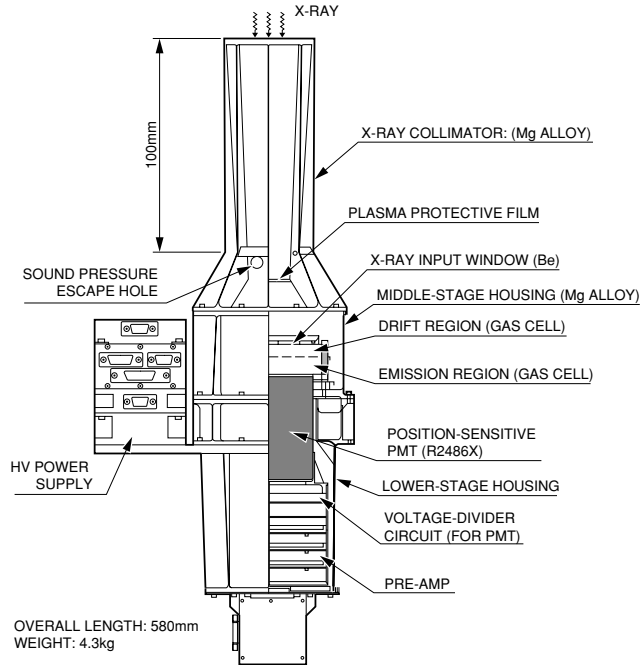
Figure 14-44: X-ray detector (GIS detector) mounted in ASUKA
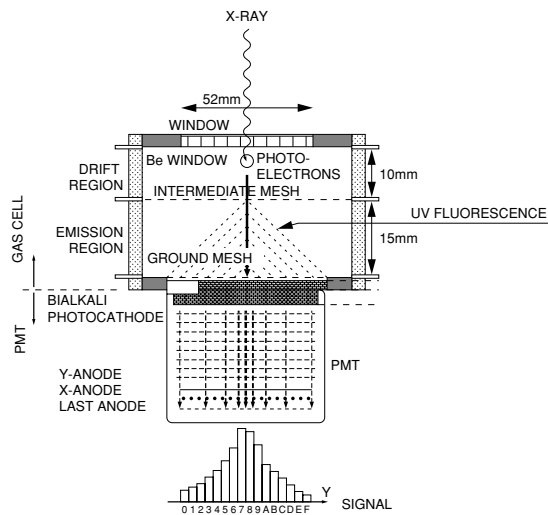
Figure 14-45: Principle of detection in GIS detector

ASUKA has succeeded in discovering various interesting facts. These include the detection of X-rays travelling from the supernova named "SN19993J", discovery of low-luminosity nucleus in the center of ordinary galaxy, and the world's first detection of inverse Compton X-rays coming from a radio galaxy. Furthermore, the ASUKA successfully revealed that the low energy spectrum of CXB (cosmic X-ray background) extends to 1 keV as single photon fingers. This discovery is expected to elucidate the CXB, which is the primary object of the ASUKA.

(2) Ozone measurement (solar backscatter radiometer)

There are vast quantities of polluted air in the Earth's atmosphere and this reacts with light from the sun to produce ozone. If this layer spreads and blocks out the sunlight, it could have drastic future effects for humanity and other life on our planet. The photo below shows a photomultiplier tube designed for an ozone detector (right in same photo) to measure ozone concentrations in the Earth's atmosphere. This was assembled in a spectrophotometer inside an artificial satellite launched from the space shuttle. It is capable of converting extremely faint amounts of light into electrical signals for ozone measurement.

Photomultiplier tubes used for outer space applications must provide high reliability, capable of withstanding strong vibrations during liftoff and operating with high stability for long periods. The ozone detector using these photomultiplier tubes was used by NASA/NOAA. It was installed in the satellite-borne SBUV/2 instrument to detect the spectrum of solar backscatter from outer space and measure ozone layer distributions.
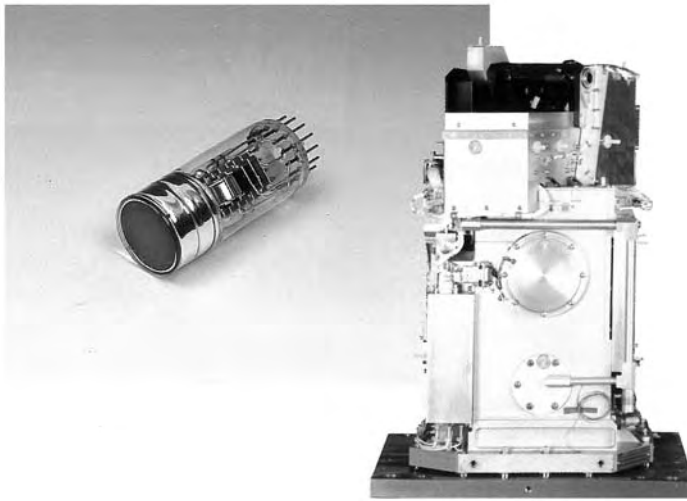
Figure 14-46: Photomultiplier tube (left) and ozone detector (right) mounted in SBUV/2

14.10 Mass Spectrometry / Solid Surface Analysis

Mass spectrometry is a technique used to identify and analyze the mass, makeup and minute quantity of a sample through the measurement of the difference in mass and movement of ions by exerting electric or magnetic energy on the sample which is ionized.

Solid state surface analysis is used to examine the surface state of a sample through the measurement of photoelectrons, secondary electrons, reflected electrons, transmitting electrons, Auger electrons or X-rays generated as a result of interactions of incident electrons with atoms composing the sample, which take place when an electron beam or X-ray irradiates the sample. Ion detectors are used as detectors in these applications.

14.10.1 Mass spectrometers[18) 19)]

Mass spectrometers are broadly classified into two groups: one using magnetic force (magnet) and one not using magnetic force. Currently used mass spectrometers fall under one of the following four types.

- Time of flight (TOF) type
- Quadrupole (Q-Pole) or ion trap type
- Magnetic field type
- Ion cyclotron (FTICR) type

Mass spectrometers are often combined with a gas chromatograph or liquid chromatograph to build a gas chromatograph mass spectrometer (GC-MS) or liquid chromatograph mass spectrometer (LC-MS). Mass spectrometers are used to identify, measure and analyze the composition of various samples such as petrochemicals, fragrance materials, medicines, biogenic components and substances causing environmental pollution. Figure 14-47 shows the schematic drawing of a quadrupole type gas chromatograph mass spectrometer.
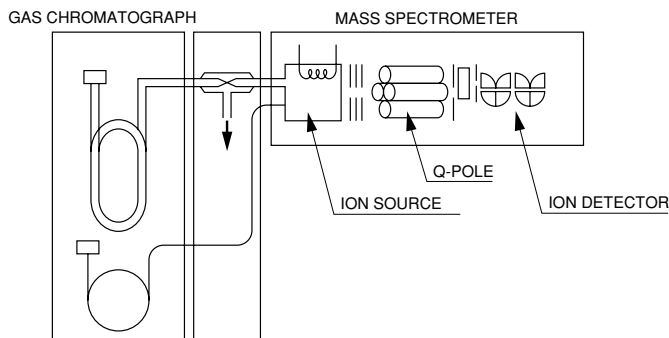
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Figure 14-47: Schematic drawing of a gas chromatograph mass spectrometer.

14.10.2 Solid surface analyzers[20)]

Solid surface analyzers are broadly divided into two groups: one using electron beams to irradiate a sample and the other using X-rays. Major solid surface analyzers presently used are as follows.

- Scanning electron microscope (SEM)

- Transmission electron microscope (TEM)

- Auger electron spectrometer (AES)

- Electron spectrometer for chemical analysis (ESCA)

Among these four types of surface analyzers, the scanning electron microscope (SEM) is the most widely used and its structure and principle are illustrated in Figure 14-48.[21)]

(1) The sample is irradiated by an electron beam to generate secondary electrons which are then collected.

(2) The sample is scanned by an electron beam, just like TV scanning.

(3) A gray level image is displayed according to the quantity of secondary electrons.

An electron beam emitted from the electron gun is narrowed into a needle-like form and focused onto the sample by the focusing lens and objective lens.

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Figure 14-48: Structure and principle of a scanning electron microscope

An electron beam emitted from the electron gun is accelerated at a voltage of 0.5 to 30 kV. This accelerated electron beam is then condensed by the electromagnetic lens action of the focusing lens and objective lens, and finally formed into a very narrow beam of 3 to 100 nm in diameter, irradiating on the surface of a sample. Secondary electrons are then produced from the surface of the sample where the electron beam landed, and are detected with a secondary electron detector. The electron beam can be scanned in the XY directions across the predetermined area on the surface of the sample by scanning the electromagnetic lens. A magnified secondary electron image can be displayed on the CRT in synchronization with the signals of the secondary electron detector. Figure 14-49 shows the structure and operation of the secondary electron detector.

(a) Secondary electron detector   (b) Secondary electron detector
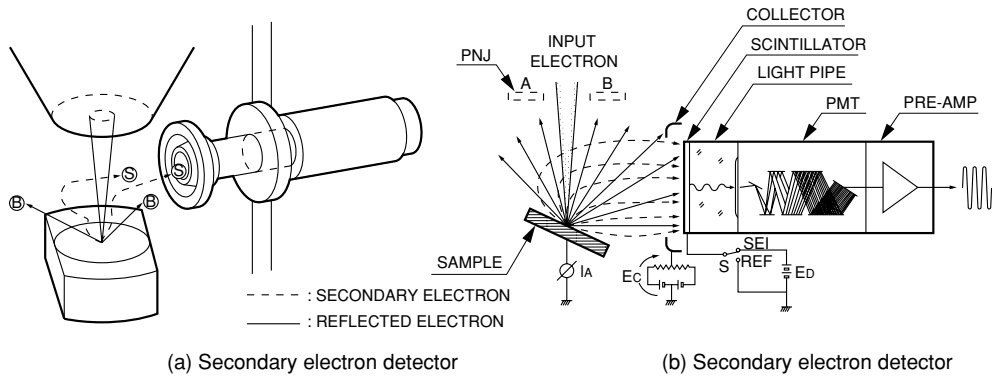
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Figure14-49: Structure and operation of a secondary electron detector

A typical secondary electron detector consists of a collector electrode, scintillator, light pipe, photomultiplier tube and preamplifier. Voltage is applied to the collector electrode and scintillator at a level required to collect secondary electrons efficiently. Most of the secondary electrons produced from the sample enter the scintillator and are converted into light. This converted light then passes through the light pipe and is detected with the photomultiplier tube.

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