Detectors for Sensitive Detection: HyD

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This article discusses detectors (more precisely: sensors), that are employed in single point, i.e. true confocal scanning microscopes. The sensors in such systems are usually photomultiplier tubes. Also, the silicon pendants of PMTs are used for particular applications, especially single-molecule measurements. A new development has led to chimeric devices called hybrid detector (HyD) which unite benefits of both technologies.

Keywords true confocal microscope, photomultiplier tube, avalanche photodiode, hybrid detector, scanning imaging, single molecule, high dynamic range

1. Photomultipliers

Photomultiplier tubes have a long history in the area of light measurement. As the name indicates, a PMT is based on vacuum tube technology, which in most areas of modern life has vanished after its peak in the 60s of the last century. Still, classical PMTs have some advantages over modern semiconductor devices, although hybrids, merging both vacuum and silicon technologies, are emerging as chimeras that cover the full scale of single point light measurement applications.

1.1 Technology

The photomultiplier tube is based on two effects that are discussed and described in length in textbooks of physics and electronics: the photoelectric effect and secondary emission. The first is the conversion of photons into an accelerated electron that is then available for electrical measurements. The photoelectric effect was first observed by Heinrich Hertz(1) in 1886 and correctly described by Albert Einstein(2), for which work he earned the Nobel prize in physics in 1921. The photoelectric effect describes the conversion of the energy of a photon into dissociation and kinetic energy of an electron after the photon has been absorbed by matter. When material interacts with a photon, the photon energy may be absorbed by the electronic system in the atoms or molecules of that matter. If the photonic energy is high enough (correlating with shorter wavelength), the electronic excitation can cause an electron to leave the matter. This dissociation requires a matter-specific minimum dissociation energy. Consequently, the wavelength of the incident light must come below a material-specific wavelength to cause a free electron.

The photocathode of a photomultiplier tube is made of materials which have sufficient low dissociation energies to measure red photons up to 800nm. As an unwanted side-effect, the lowering of the dissociation energy by selection of appropriate cathode materials also makes these systems sensitive to infrared quanta, i.e. they are prone to thermal noise. The blue or ultraviolet limit of such devices is usually controlled by the glass type that is used for the entrance window for the photons. Standard tubes are not very sensitive for photons below 350nm; quartz windows allow much shorter wavelength.

As the cathode material is obviously very critical, both concerning the spectral sensitivity and the quantum efficiency of the tube, there are a number of special cathode materials for different purposes. The quantum efficiency is the ratio of the number of incident photons and photons converted into a photo electron.

The electron that is released from the photocathode is accelerated by an electric potential and directed onto a second electrode called a dynode. At that dynode, the accelerated electron will dissipate its kinetic energy to release a couple of electrons from the dynode surface. This is the second effect used in photomultiplier tubes. The consequence is an amplification of the first (single) photoelectron into some 3 or 4 secondary electrons. These electrons can be amplified by a series of further dynodes. Current photomultiplier tubes use 6…12 dynodes. The potential difference at each dynode is some 100V at maximum and is tunable by the total voltage from the cathode to the last dynode. The PMT voltage thus typically ranges from ca 300V to ca 1200V. If the mean amplification at a given voltage is 3 per dynode, the total amplification in a 10-dynode PMT is consequently 50,000-fold.

Beyond the last dynode, the electrons will sink into an anode, where the electric current is finally measured. In analog mode, the current is integrated over a given time interval, and the brightness of the illumination can be compared by the charge collected over that time interval. The amount of charge is converted into a digital number. If the electronic circuitry is fast enough, one can measure single photons as electric pulses. This is the base for photon-counting mode, where the pulses are digitally counted. The illumination intensity can then be expressed by the number of photons in a given time interval. Also, single photon measurement requires photon-counting mode – a challenge for classical photomultiplier tubes.

1.2 Characteristics

As the photocathode is the critical point where photons are converted into an electrical signal, it is also the criterion that controls the main properties of the photomultiplier tube. Very detailed descriptions of various materials and their properties are published by Hamamatsu, one of the leading makers of photomultiplier tubes(3). For visible light applications, and therefore for confocal microscopy, the classical multi-alkali photocathode materials were the standard for a long time. These tubes show 25% quantum efficiency at blue-green light. Obviously, the quantum efficiency is a target for engineering in order to increase the sensitivity of these sensors. Three quarters of the incident light does not contribute to the signal, i.e. there is room for improvements by a factor of four, if one could increase the quantum efficiency close to 1.0.

As mentioned, the amplification in each step in the dynode cascade is somewhere between 1 and 4. At a given high voltage (which is tunable), the amplification is e.g. 3 electrons per electron. This number is but an average, as there is statistical noise in the generation of secondary electrons. The statistical noise is known as square root of the signal, in case of an average of three, the noise is 1.7 in the first amplification step, which is a high variation that also causes the final amplified signal to exceed that noise (plus some more noise). If we look at single pulses that are caused by single photons at sufficiently low photon flux (i.e. low light intensity), we will find a large variation in the peak height. Some photoelectrons will generate 3 secondary electrons at the first dynode, but many will generate only two, or even one. Others will cause 4 or 5 secondary electrons. If only 2 electrons are obtained, this corresponds to a difference of 1/3 as compared to the mean. This difference is then further distributed by the following dynodes – it does not vanish, but contributes to the noise of the output signal. A second target for improvements of light sensors is therefore to increase the initial yield in the first amplification step. This is important in integrating devices and also simplifies pulse discrimination in photon counting setups. These implications have been discussed by J. Pawley(4).

A third important parameter is the output pulse width for pulses caused by a single photon. The electronic circuitry will usually severely spread the pulse width, but the intrinsic variation of arrival times of electrons is the width at a theoretical zero spread by the circuitry. It describes the variation in the time passing from the first electron reaching the anode to the last electron reaching the anode upon a single photon initiating secondary electrons. Obviously, a narrow pulse width is desirable for fast photon counting. Also, photon counting at comparably high light intensities (i.e. short time intervals between photons striking the cathode) will require short pulse widths.

Another point of discussion is the dynamic range of the light sensor. If the dynamic range is short, the device will only operate at low intensities. A high dynamic range indicates that the device can also accept and correctly measure high light intensities. Although photomultiplier tubes are very sensitive, they are stable and give correct results for even comparably high intensities. At high intensities, the device will show saturation effects and eventually incur irreversible damage.

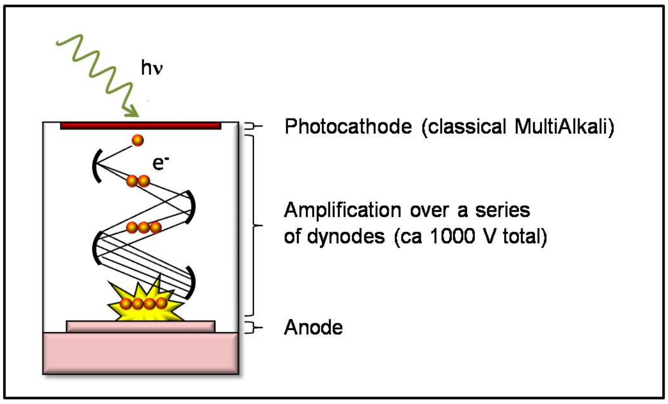

Fig. 1 Schematic drawing of a photomultiplier tube. The photon energy is converted into accelerated electrons at the photocathode. Subsequently following dynodes multiply the initial photoelectron by secondary emission. The multiplication at each step depends on the potential difference between the dynodes, which is 1/n of the total high voltage applied when the tube contains n dynodes.

2. Avalanche photodiodes

Light can also modify the electric current in semiconductor material. The simplest example is a light-dependent resistor, consisting of amorphous semiconductor material whose resistance will decrease upon illumination. Although these "LDRs" are quite sensitive, they are by far too slow for image generation. Photodiodes have a pn junction and are typically operated in reverse bias. They show a good linear behavior for quite a wide range of illumination intensity. For image generation at very low light and high temporal bandwidth, they are still not sensitive enough

2.1 Technology

Avalanche photodiodes(5) are basically modified pin diodes which have an insertion between p and n doted layers (positive-insertion-negative diode). The avalanche diode contains an additional positive doted layer. The pn region is called the "multiplication zone", because it features very high electric field strength. Photons are absorbed in the insertion layer. As described above, from the photocathode of a photomultiplier tube an electron is released upon illumination - this phenomenon is called the outer photoelectric effect. In semiconductor material (e.g. silicon), the absorption of a photon can generate an electron-hole pair (inner photoelectric effect). The applied voltage accelerates the electron towards the multiplication zone. Here, additional electrons are released from the material by impact ionization. Due to the high field strength, these are again accelerated and cause even more electrons to move to the anode. This process amplifies the initial electron by a factor of 100 up to 1000, depending on the voltage applied and assuming operation below breakdown voltage. The electron multiplication occurs in a very short time and is called avalanche effect. Obviously, the sudden increase and self-amplifying current can easily damage the device – for that reason special precautions have to be taken to avoid higher currents.

Much higher amplification in avalanche photodiodes can be reached if the applied voltage is above the breakdown limit. Here, amplifications up to 10^8 are possible. This operation scheme is called "Geiger mode". The high amplification is sufficient for direct single photon detection. Because the current would not stop after initiation by a photon, special precautions have to be added in order to interrupt it. Geiger-mode avalanche photodiodes are therefore very sensitive to damage by too many photons and inappropriate operation. The high amplification of Geiger mode APDs allows measuring the signal without additional amplification circuitry which results in very low noise.

In summary, the avalanche photodiode causes a brief and intense electric pulse upon absorption of a single photon. Consequently, the device is ideal for single photon detection and photon counting measurements. Due to its behavior, it is sometimes referred to as "silicon-pendant to photomultiplier tubes".

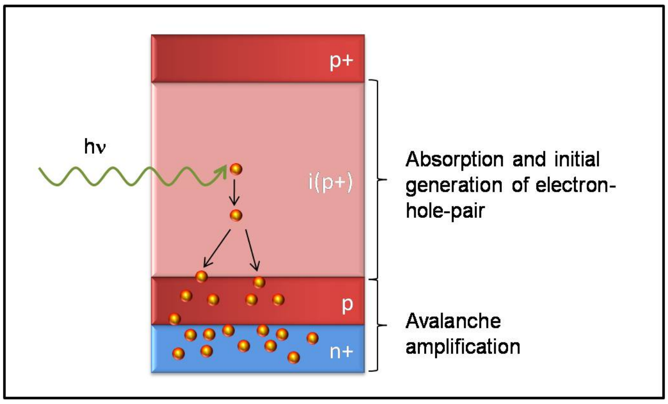

Fig. 2 Upon absorption of photons in an intrinsic (i-) layer, an electron-hole pair is generated. The avalanche is caused in a multiplication zone (pn+) by impact ionization through the arriving electrons.

2.2 Characteristics

Avalanche photodiodes have a gain of 100…1000 in non-Geiger mode, and up to 100,000,000 in Geiger mode, as mentioned above. In non-Geiger mode, the APD generates a signal which is linear to the incident light. The dynamic range is comparably small and does not allow measurement of typical signal intensities as they occur in standard confocal microscopy. Only very low intensity applications are suitable for avalanche photodiodes. This is especially true for Geiger-mode avalanche photodiodes, which are solely appropriate for single photon counting at comparably low rates (max. 10 MHz).

For visible light applications, Si-based APDs are used. The spectral sensitivity window reaches from 300nm up to 1000nm. The quantum efficiency is better than photomultiplier tubes and can reach some 45%. and even more in the red

range Due to the better sensitivity in the red range, APDs are sometimes the better option as compared to PMTs despite their low dynamic range.
Despite the sensitivity for red light, noise parameters in APDs are better than PMTs due to their small active area. Therefore, APDs are good detectors for very low intensities (where high modulations of the intensity are not expected).

3. Hybrid detectors

It seems that PMTs have their advantages, and APDs have other advantages which make them good solutions for specific applications. Nevertheless, the best solution would allow precise and fast measurements over a wide dynamic range. The solution is a combination of the two technologies, which is realized in the "hybrid detectors" (HyDs), a hybridization of vacuum-tube technology and semiconductor technology. The HyDs combine the good performances of both technologies in one single device.

3.1 Technology

The hybrid detector(6) uses a photocathode for light conversion, similar to a photomultiplier tube. The best choice of cathode material is GaAsP, which has a quantum efficiency up to 45% at 500nm (roughly double the quantum efficiency of multi-alkali cathodes). Due to the technical implementation, the device is much less likely to be damaged than photomultiplier tubes. GaAsP PMTs are routinely victims of severe light-induced damage, whereas hybrid detectors are not.

The electrons that are released upon absorption of a photon are then accelerated in a single step by a very high voltage of ca 8 kV. The acceleration energy is dissipated in a semiconductor target at once. Many secondary electron-hole pairs are generated by impact ionization in a single hit. This is possible as the efficiency of impact ionization does not saturate as quickly as the secondary-electron generation at the PMT-dynodes. Above 100V, the dynodes will not increase their amplification, but rather decrease the electron yield. In the hybrid detector, the amplification by high-voltage acceleration is ca. 1500. This compares to an amplification of ca. 3 in a single step between the dynodes of a photomultiplier tube.

The 1500 electrons are not enough to be measured without significant effort. Therefore, the hybrid detector has a built-in amplifier: the electrons, released by impact ionization by the high-energy photo electron, are accelerated towards a multiplication layer as described for the avalanche photodiodes. Here, the same avalanche effect causes an additional amplification of ca 100-fold. This combination is generating a sufficient signal for measurement. Therefore, the avalanche diode in the hybrid detector does not need to be operated in Geiger-mode. Still, the noise is very low.

The active area of a hybrid detector is much smaller than that of a PMT, but also much larger than a standard avalanche photodiode. The thermal noise that is created without photons interacting with the active area is directly related to the size of that area. Thus, a small area is advantageous. On the other hand, if the area is too small, focusing of the light beam can be a severe problem, and benefits might be lost by the need to introduce additional optical elements.

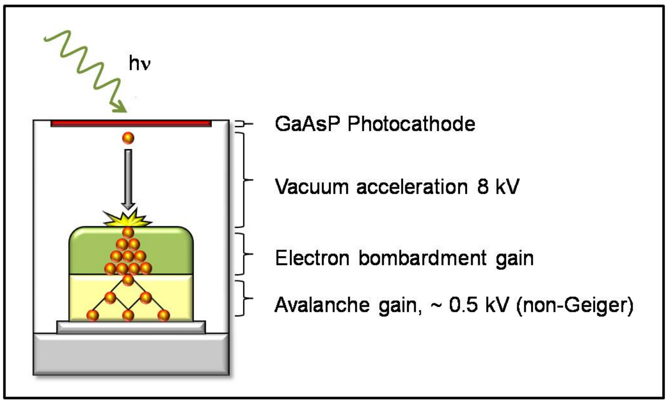

Fig. 3 Schematic drawing of a hybrid detector

3.2 Characteristics

The single-step high voltage acceleration causes a 500-times higher amplification in the first step. As mentioned in the PMT paragraph, the amplification (or more precisely: the variance of the amplification) in the first step is a significant contribution to the signal noise. If the amplification in a photomultiplier tube is 3 in the first step, there is a large probability of finding e.g. only 2 electrons or even 4 electrons at subsequent photon events. This is a variation of 33%. The signal-to-noise ratio of this parameter (peak height upon single photon) is only 1.7. The first step amplification in a hybrid detector is 1500 – there is only one step of electron acceleration in the vacuum. The signal-to-noise ratio in this case is 37 – which is a huge improvement in noise reduction in the first place.

Due to the straight movement of the accelerated photoelectron onto the semiconductor target, there is no loss of secondary electrons as is the case with photomultiplier tubes. In PMTs, the voltage between dynodes is ca 100 times less per step compared to the HyD, and the probability of losing electrons on their way from the photocathode to the anode in a PMT is comparably high. As a consequence, the photon efficiency of PMTs is some 10% less than the quantum efficiency. In hybrid detectors, the photon efficiency is very close to the quantum efficiency of the cathode.

A second benefit of a single-shot acceleration is the fact that there is no variation in the time the electrons hit the target. It is a single electron anyway. The pulse width in a PMT is very much determined by the different geometry of possible electron trajectories though the dynode cascade. Consequently, the pulse width in a hybrid detector is much shorter. This allows higher frequency photon counting – which is directly translated into higher dynamic range - and reduces the instrument time constant, a limiting factor for lifetime measurements.

Due to the comparably small detection area, hybrid detectors show a lower dark current as compared to photomultiplier tubes. The dark current causes background noise, i.e. non-zero intensity measurements in areas that have no signal and should appear black. If the signal is low – which is usually the case in biomedical fluorescence imaging – the background noise overcasts the signal. Thus, lower dark current will immediately increase signal-to-noise in critical intensity situations.

4. Comparison of the sensors

As we could see, all sensor types have their advantages and limits. In this paragraph we want to summarize the parameters that are important for image generation in a single-point imaging system. The numbers given below are just the typical numbers one would expect to see with the sensors in question. There is a wide variance, and you may well find specialized devices that differ significantly in one or the other direction. The intention here is not to compare individual brands or types, but to give an idea of the typical performance to expect. The numbers are in line with the opinion of several colleagues interviewed, but are far from being scientifically significant.

4.1 Quantum efficiency

Quantum efficiency (QE) is here referred to as the ratio of photons that impinge on the active element in the sensor and the actually released electrons or electron-hole pairs generated. Quantum efficiency depends very much on the wavelength. For simplicity, we assume blue-green photons in the range of 500nm, except the "red emission" case, which refers to 650nm. Multi-alkali cathodes in photomultiplier tubes have a comparably low quantum efficiency of some 25%, cathodes with GaAsP show an improved efficiency close to 50%. Similar efficiencies are reached with silicon absorbers in avalanche photodiodes.

4.2 Photon detection efficiency

Not all charges that are generated by the photo effect will finally reach the anode. Depending on geometry and design, path length and many other factors, charges are lost during their transit. In photomultiplier tubes, this loss is mainly due to electrons leaving the path between the dynodes. Consequently, photomultiplier tubes have a much higher risk of losses as compared to other sensor types. In PMTs, the quantum efficiency is reduced by typically 10% due to these losses. To compare the sensors, it is therefore important to measure the ratio between photons impinge on the active element in the sensor and a signal at the anode. This is referred to as photon detection efficiency PDE. Also, the spectral properties of the entrance window will modify the spectral response of the sensor and thus the apparent PDE.

4.3 First step pulse peak noise

The amplification in the first step in a photomultiplier tube (photocathode to first dynode) is in the range of 3, depending on the voltage applied. If this varies by just one electron released, the variance of the resulting signal is in the range of 30%. This is transferred through the whole sequence of dynodes to the anode signal. It contributes to the signal noise itself in analogue integration mode

In hybrid detectors, the first step amplification is some 1500, where the variation of a single charge is less than one per thousand. Pulses of homogeneous height are easier to discriminate, which is beneficial in photon counting mode.
In a Geiger-mode avalanche photodiode, the amplification is by one step anyway, which implies a very low variance, but there are other design limits that increase the peak noise.

4.4 Pulse width

Especially for photon-counting types of applications, not only the peak height of a single-photon pulse is important, but also the width of that peak. Therefore, the circuitry has to be adapted very carefully to the required signal properties.

Besides the electronic modification, there is also an intrinsic variation of arrival times of the charges at the anode which broadens the pulse. In photomultipliers, this widening is mainly caused by the high variations of different trajectories that charges can take through the sequence of the dynodes. Therefore, PMTs have a comparably wide pulse width. The pulse width has a major impact on the maximum count rate.

4.5 Dark current

To identify a signal, a sufficient contrast between signal and background is necessary. In electronic imaging, a significant contribution to background intensity and background noise is electric current occurring without illumination. This is called dark current. The false signal without photons is mainly generated by thermal release of charges from the active medium. Consequently, the size of the active area and the temperature are parameters that increase dark current. It is obvious, that increasing sensitivity in the red range also increases susceptibility for thermal noise. In many cases the sensors are cooled in order to reduce the background noise.

4.6 Active area size

APDs have very small areas, PMTs comparably large areas. Hybrid detectors range in between. As already mentioned, the area has a direct influence on the dark current. Although a small area is advantageous in that respect, areas that are too small raise the problem of focussing the light beam with sufficient long-term stability. This may cause a need for additional optical elements and then reduces the efficiency.

4.7 Maximum count rate

If PMTs are operated as mean-intensity sensors, i.e. not resolving single photons for counting, their dynamic range is very high. That is the reason for their success in confocal imaging (and in other areas). If used to count photons per unit time (which is just a different code for intensity), the very same sensors are limited to very low count rates, i.e. to very dim light. The dynamic range of a sensor therefore depends on its mode of operation. Geiger-mode APDs are excellent for rare single photon events, but also lack dynamic range, because the sensor needs recovery time after each pulse. Hybrid detectors combine good single-photon resolution for photon counting and high dynamic range, allowing them to be used in the typical emission intensity ranges of fluorescent specimens.

4.8 Afterpulsing

Due to their (different) internal effect, both photomultiplier tubes and avalanche photodiodes sometimes show a second pulse after the 'original' pulse. This is not a major problem in intensity measurements, but causes significant false measurements in fluorescence correlation spectroscopy. These types of applications therefore benefit from sensors that show little afterpulsing.

4.9 Overview

The table below shows a summary of the typical ranges of the parameters discussed above for the main types of sensors used in confocal microscopy and derivative applications:

	PMT Alkali	PMT GaAsP	APD/ SPAD	HyD
PDE (500nm) %	25	37	45	45
Pulse Noise %	60%	60%	5%	3%
Pulse width/ns	> 10	> 10	0.1 (λ)	1
Dark #/s	15000	15000	300 (❄)	2500
max M#/s	very low	very low	20	150
Area/mm²	50	50	0.05	8
Afterpulsing	high	high	medium	low

Tab 1 Overview of the various parameters that control the applicability of sensors. Keep in mind that these numbers are very coarsely integrated typical values which may be very different in a given sensor type. The snowflake indicates that the value is true for cooled devices. PDE: photon detection efficiency; Dark #/s: dark counts per second; max M#/s: maximum megacounts per second.

5. Typical applications and best fit of sensor type

What is the ideal sensor for a given application? This question is relatively easy to answer. Rather than investing large amounts of money in specialized instrumentation for each application that might be considered, the best solution is a system serving all applications, even if in some cases minor limitations would need to be accepted.

5.1 Everyday imaging

Standard samples for confocal microscopy emit in the mid-spectral range between 450nm and 600nm. Typical samples are not too dim and comparably stable concerning fluorescence bleaching. For those samples, APDs are not suitable, due to their limited dynamic range. GaAsP PMTs will not serve as the first choice either, as they are easily destroyed and not specifically necessary (there is enough light). A good solution is a standard multi-alkali PMT, which is quite "indestructible" and provides a very large dynamic range. Still, such sensors show a high background signal, which sometimes destroys the low intensity structures. Therefore, the best solution is a hybrid detector, which has an excellent low dark current, sufficient dynamic range and is robust as PMTs. As a matter of fact: experience has shown that users will not switch back to PMTs once they have worked with hybrid detectors. Only if the light intensity from the sample is very high, like in reflected mode applications, e.g. on plastic samples or semiconductor material, or in some very bright fluorescence samples, might PMTs allow a higher signal and consequently better signal-to-noise.

5.2 Sunday imaging

In applications where very high contrast is required, because the sample features very dim and strong structures at the same time, background noise is a critical parameter. Here, and for excellent imaging of any sample, the hybrid detector is clearly the sensor of choice. GaAsP PMTs may have their benefits here, but are much noisier and unstable. APDs cannot fit these requirements, and alkali PMTs will perform worst.

The same reasoning is true for short image acquisition time at low intensities, which is the standard request in physiological measurements with living material. Such samples need the lowest illumination possible to avoid phototoxic damage. Due to the low background noise, hybrid detectors allow a very dim illumination and can still produce a sufficiently contrasted signal.

5.3 NDD imaging

Two photon-excited fluorescence emission may be recorded in two different ways. One is via the classical pathway where the light is fed through the scanning system and subsequently converted. In that case, the sensor may have a small detection area, as the beam is steady due to compensation of the movement by the scanning apparatus. As two photon imaging features optical sectioning without a pinhole, one can also collect the emission light directly behind the objective lens, and omit optics and mirrors in order to increase the signal strength. In that case, the beam is not still but exhibits angular movement which translates at a given surface, e.g. the sensor, into a lateral movement. As a consequence, sensors with very small active areas are not feasible, or only with considerable optical design efforts. PMTs and hybrid detectors will be the better solution. The hybrid detector is most appropriate due to its low noise and high photon detection efficiency.

5.4 Single molecule detection (red emission)

Single molecule detection is the area for APDs. Especially for red emitting dyes, the avalanche photodiodes, both non- and Geiger mode, are the best solution, due to their high quantum efficiency, amplification and red-range sensitivity. Hybrid detectors are also useful, although their QE decays with longer wavelength. Photomultiplier tubes are not very suitable for single photon measurement; to some extent GaAsP-cathode based PMTs can do that job.

5.5 FLIM

Fluorescence lifetime imaging based on time-correlated single photon counting requires very fast sensors (narrow pulse width), with short transit time spread (the variation of pulse arrival after pulsed illumination). This is true for hybrid detectors, which are the most appropriate sensor for FLIM. Avalanche photodiodes also do a good job, although Geiger-mode devices will need long measurement times due to their low maximum count limits. Standard photomultiplier tubes are not applicable, although there are specially designed tubes that are fast enough to perform FLIM if the expected lifetime is not too short. These PMTs are also available in commercially obtainable systems and perform sufficiently well.

5.6 FCS

The main requirement for fluorescence correlation spectroscopy is high sensitivity, i.e. high photon detection efficiency. Also, very low dark count rates are beneficial for FCS. Another problem in correlation measurements is afterpulsing, which mimics photon correlation that is not from the sample. For that reason, a sensor with low afterpulsing rates is preferred – the hybrid detector is again the favourite here. Due to their high efficiency, APDs are the most frequently used sensors for FCS – so far. Photomultiplier tubes are not really good choices for correlation of single photons.

5.7 FCCS

As a specialty in correlation measurements, fluorescence cross-correlation spectroscopy is immune to afterpulsing. Here, two different dyes are observed, and the correlation is calculated between the two fluorescent species. Hence, the afterpulsing events are eliminated Avalanche photodiodes will be the most suitable choice here, although hybrid detectors will do a very good job and will be the more versatile configuration in systems that are not meant to operate for FCCS only.

5.8 Summary

The above discussion is summarized in the table below. For each type of application, each sensor type is put into a ranking which tries to fit the applicability of that given sensor for the type of experiment. Higher points mean better fit.

	PMT Alkali	PMT GaAsP	APD/ SPAD	HyD
Points	1,4	2,3	2,6	3,7
Everyday Imaging	3	2	1	4
Sunday Imaging	1	3	2	4
NDDImaging	2	3	1	4
sm Red Imaging	1	2	4	3
FLIM	1	2	3	4
FCS	1	2	3	4
FCCS	1	2	4	3

Tab 2 Hall of fame for four different types of sensors for single point detectors in scanning type microscope systems (including still FCS)

Hybrid detectors appear to outperform other sensors in most cases, indicated by the maximum of points (average of 3.7). Indeed, this sensor is suited for nearly all applications and is highly appreciated by scientists for both imaging and single molecule measurements of any kind. A PMT is only preferable in extremely bright emission situations, This is provided for in commercially available systems that include at least one PMT in multichannel systems. Standard alkali PMTs may be a solution for medium-challenging samples and are chosen for the obvious reason of having a price tag that is about 5 times lower than all other sensor solutions. Avalanche photodiodes are still good solutions for single molecule/single photon experiments, and are preferable in some cases, e.g. far red emitting fluorochromes or fluorescence cross correlation spectroscopy. Nevertheless, the hybrid detector is a similarly good choice for these types of applications, too – and can do all the other jobs better than most alternative sensor solutions.

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References

[1] H. Hertz: Ueber einen Einfluss des ultravioletten Lichtes auf die electrische Entladung. In: Annalen der Physik und Chemie. 267, Nr. 8, 1887, S. 983–1000. ISSN 00033804. doi:10.1002/andp.18872670827

[2] A. Einstein: Ueber einen die Erzeugung und Verwandlung des Lichtes betreffenden heuristischen Gesichtspunkt. In: Annalen der Physik. 322, Nr. 6, 1905, S. 132–148. ISSN 00033804. doi:10.1002/andp.19053220607

[3] Photomultiplier tubes – Basics and applications Hamamatsu Photonics K.K (2006) http://sales.hamamatsu.com/assets/applications/ETD/pmt_handbook_complete.pdf (ca 3 MB)

[4] Handbook of Biological Confocal Microscopy. Ed.: J. Pawley. 3rd edition. Springer US (2006)

[5] Hamamatsu Photonics K.K. Characteristics and use of Si APD (Avalanche Photodiode), 2004

[6] M. Suyama and M. Lares: Photomultipliers: Hybrid detector combines PMT and semiconductor-diode technologies. Laser Focus World 2008.

