

Control of Noise and Background in Scientific CMOS Technology

Introduction

Scientific CMOS (Complementary metal–oxide–semiconductor) camera technology has enabled advancement in many areas of microscopy imaging. However, this technology also poses problems that camera manufacturers need to solve to produce a device capable of accurate quantitative imaging. To achieve this, several features of CMOS sensors have to be understood and then corrected for. In this technical note, we'll briefly discuss the most important points to consider when producing a scientific CMOS camera.

The main consideration is correction of noise, which will always occur during the acquisition of an image. Noise is the uncertainty which accompanies the acquired signal and can be divided into two major groups: camera-related noise and sample-related noise. As a camera manufacturer, there's little we can do to improve the sample-related noise but our goal is to minimize all camera-related noise.

Sample-Related Noise

Photon shot noise

Photon shot noise is the inherent natural variation of the incident photon flux - there is always uncertainty associated with the process of emission of photons from a fluorescent structure upon excitation (quantum nature). Photon shot noise follows a Poisson distribution and has a square root relationship between signal and noise where:

$$\text{Photon shot noise} = \sqrt{\text{Signal}}$$

All values are displayed in electrons (e⁻).

This noise cannot be improved by advances in camera design as it is a physical phenomenon that can't be removed.

Camera-Related Noise

One of the main differences between standard CCD/EMCCD cameras and scientific CMOS cameras is the signal readout structure. A CCD/EMCCD camera converts charge (electron signal) to a voltage at the preamplifier, the voltage is then digitized by the Analogue to Digital Converter (ADC) to produce a digital signal that can be read by a computer (figure 1). CCD/EMCCDs, therefore, have a single preamplifier and ADC which digitize every single pixel one by one.

CMOS sensors, on the other hand, have a capacitor and amplifier on every pixel to convert charge into a voltage. This voltage is then digitized by an ADC at the end of every column (figure 2). This greatly increases the readout speed of the sensor but introduces other complications.

Read noise

Read noise is the noise introduced as the signal is read out i.e. passed through the preamplifier and ADC.

The architecture of CCD/EMCCD sensors (Figure 1) typically consists of a single preamplifier to convert charge into voltage. This means that every single pixel is treated the same way and so read noise will follow a Gaussian distribution. All pixels will be affected and fluctuate by a similar degree.

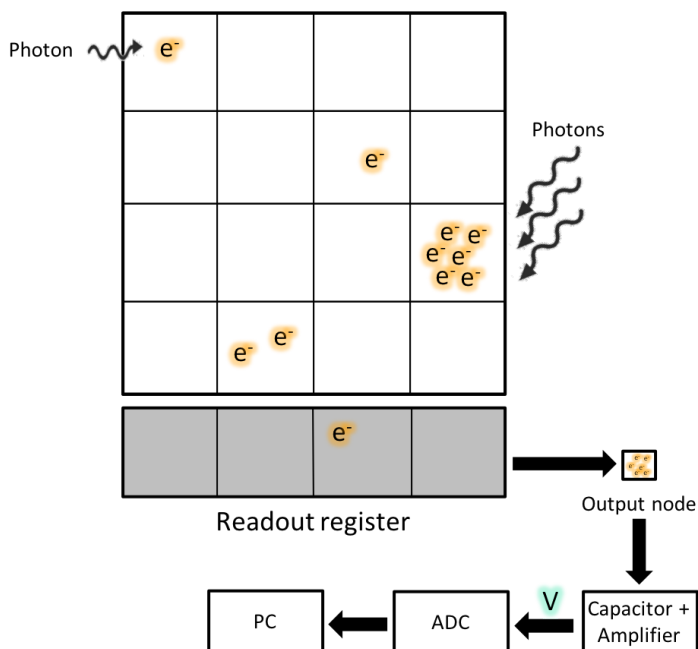


Figure 1: CCD architecture.

The number of electrons created is directly proportional to the number of photons hitting the pixel. After exposure, electrons are moved down, row by row, until they reach the readout register. The readout register shuttles the row of electrons one at a time into the output node which is connected to a capacitor and amplifier.

On CMOS sensors, each pixel has its own individual readout structure to convert charge into voltage. Furthermore, each column has its own ADC. Some scientific CMOS cameras also use a split sensor design where there are two ADCs instead, one for the top half of the chip and one for the bottom half. Although this results in a great increase in readout speed, a consequence of having multiple readout structures is that the read noise is now a distribution

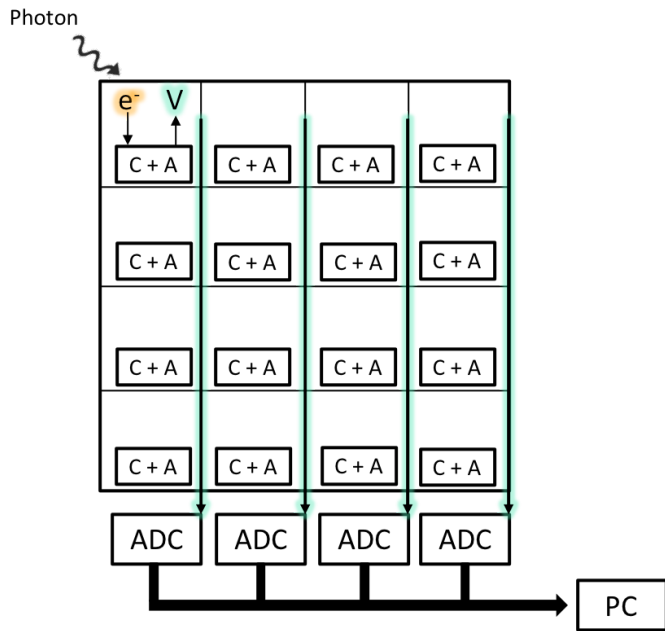


Figure 2: Scientific CMOS architecture. Photons hit the pixels and create electrons, individual capacitors and amplifiers are on every pixel. The generated voltages are sent down the whole column to the analogue to digital convertor (ADC) and the digital signal is read by a computer. This makes CMOS cameras much faster because they have one amplifier per pixel.

The true distribution of read noise which can be measured on CMOS sensors is not Gaussian but more of a skewed histogram. For this reason, read noise will be quoted on datasheets both as root mean square (RMS) and median. If a datasheet reports a median read noise of 1 electron, this means half of the pixels will report less than 1 electron read noise and half will report more. However, within this group, some pixels may report very high read noises such as 3 electrons or more. For this reason, the datasheet will also report an RMS value which is a far more meaningful description of read noise. This value will represent a true mean read noise and will, therefore, be higher than the median.

Pattern noise

Pattern noise (figure 3) is a noticeable pattern of 'hot' (bright) and 'cold' (dark) pixels in the background of the image and is produced regardless of illumination conditions. It goes hand-in-hand with CMOS read noise variation and a difference in the background offset (bias) value of individual columns, it's caused by small differences in the responsivity of individual pixels on the sensor.

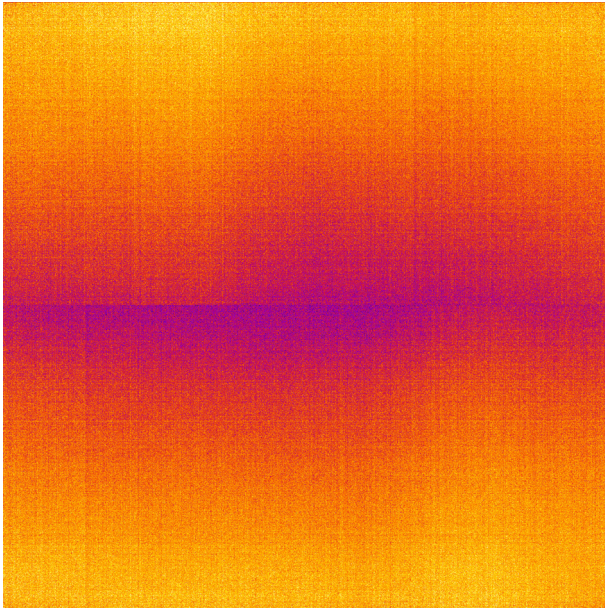


Figure 3: Fixed pattern noise.
Fixed pattern noise on a typical scientific CMOS camera with a split sensor. Variation across the background is around $6 e^-$.

Roll off

Roll off (figure 4A) is a phenomenon which can often be observed on CMOS sensors making use of split sensor technology. The roll off highlights the seam between the two sensors and displays a bias dip across it. This variation in the bias and the consequent lack of linearization makes quantitative imaging very difficult.

Newer, single-read and back-illuminated sensors such as those used in newer Teledyne Photometrics scientific CMOS cameras (Figure 4B) prevents this problem from occurring and provides a better environment for quantitative imaging.

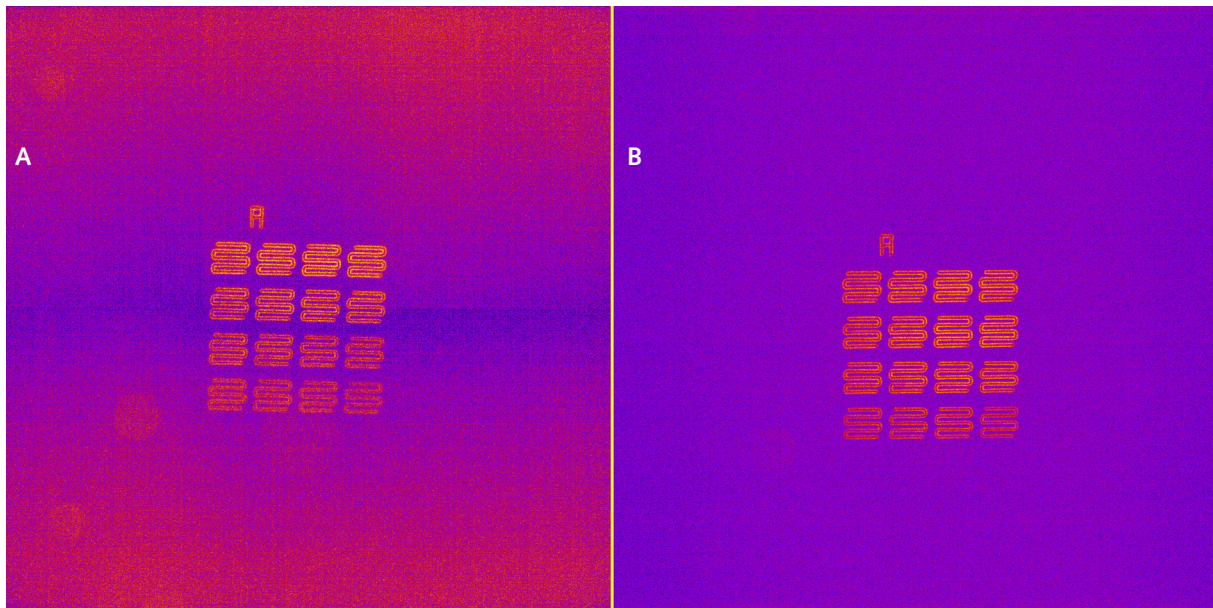


Figure 4: Roll off comparison

A) Current, standard, split sensor scientific CMOS camera and B) the GPixel GSENSE2020BSI sensor used in the Photometrics Prime BSI. Image taken using the 4x4 intensity gradient pattern on an Argolight slide

Dark current

Dark current arises from charge building up on the sensor caused by thermal energy. Crucially, this noise is light independent. Because dark current is a thermal effect, cooling (e.g. with a Peltier element) is used as a measure to counteract this problem. Typically, dark current can be halved for every 7°C of cooling.

All high-performance scientific CMOS cameras will come with a dark current specification on the data sheet. For instance, a Teledyne Photometrics Prime BSI has a dark current specification of 0.5 e⁻/p/s, resulting in 1 electron/pixel generated upon a 2 s exposure time.

Clock induced noise & random telegraph noise

It's possible to run EMCCD cameras at a very high clocking speed to achieve high frame rates but this introduces additional noise which can add up to 5 e⁻ of noise per pixel. This is called clock induced charge (CIC) and occurs when an electron is inadvertently generated without being induced by an incident photon. CIC has to be corrected for by using a spurious noise filter to identify the affected pixels and replace the measured signal by taking a mean value from its neighbours (nearest-neighbor correction).

On a CMOS sensor, the increased speed reduces the need to run the pixel clock of the chip at or over the maximum. As a result, the effect of clock induced noise is also greatly reduced.

However, CMOS sensor architecture suffers instead from random telegraph noise (RTN) or ‘salt’n’pepper’ noise (Figure 5). This noise is caused by charge moving in and out of pixel defects. The output from a single pixel thereby fluctuates between bright, average, and dark states many times over the course of an acquisition. Similar correction as that used for CIC applies to RTN and it is corrected on the sensor in engineering.

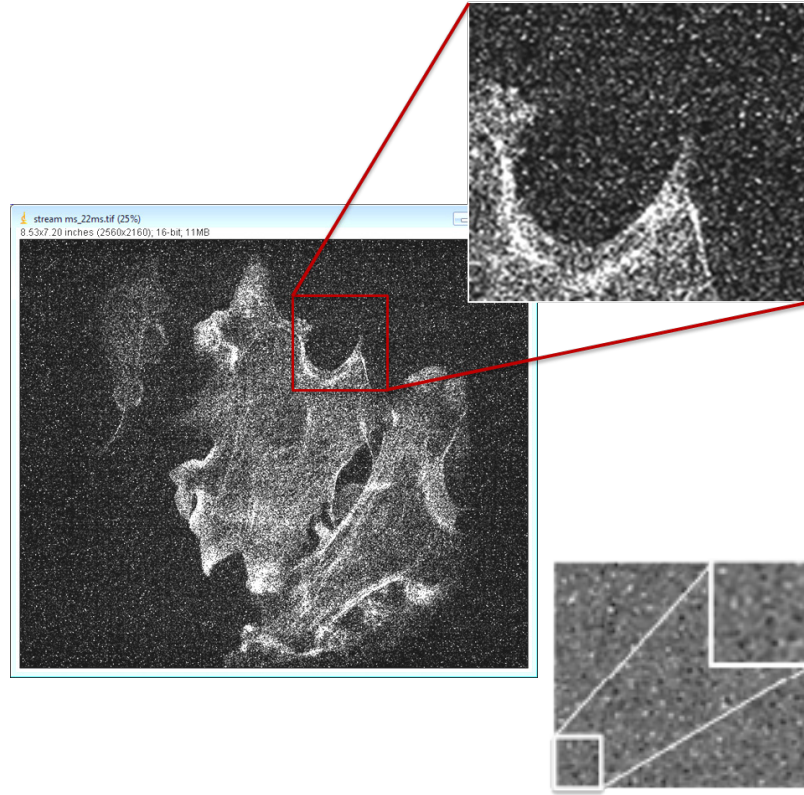


Figure 5: Random Telegraph Noise.
Example of random telegraph noise displaying the fluctuation between bright, average and dark pixel states.

Correlated noise

Correlated noise occurs due to capacitive coupling on the sensor. This is where energy is transferred between pixels by means of displacement current which causes neighboring pixels to share charge, effectively correlating the measured pixel signal. This results in an overestimation of the camera system gain which, by extension, overestimates the read noise, dark current and quantum efficiency of the camera.

This is also corrected in engineering until it is certain that all charge originates on the pixel and isn't being influenced by the charge of any surrounding pixel.

Further considerations

Binning is a common method to increase speed and sensitivity on CCD/EMCCD cameras. When binning, the signal of a 2x2 or 4x4 square of neighbouring pixels is combined. This increases the signal by summing the charge of all these pixels and as a result, fewer effective pixels require digitization which decreases the speed bottleneck at the ADC. On CCD/EMCCD cameras, summing the charge of neighboring pixels occurs before the ADC so read noise is only applied once.

In contrast, the parallelization of the read out on scientific CMOS cameras will apply read noise to each column. The combination of neighbouring pixels' signal will occur afterwards. Pixels from the same column will combine their information before read noise is applied but combining the information from pixels originating from neighbouring columns will sum their according read noise. Effectively, binning on scientific CMOS technology is partially performed in software.

As a result, binning does not have the same speed and noise benefits on scientific CMOS as it does on CCD/EMCCD cameras. Furthermore, scientific CMOS fixed pattern noise will be substantially amplified by binning. On early scientific CMOS cameras, this was a problem which couldn't be solved. However, improved correction algorithms for CMOS sensors have minimized this effect at the current state of this technology.

Teledyne Photometrics Solution for Minimizing Camera Noise

Our solution to the problems of camera noise is to carefully characterise each individual sensor and fine-tune for all eventualities. Scientific CMOS technology is in this respect very challenging as pixel-to-pixel variations, but also column-to-column variations need to be taken into consideration. Equalling bias value, linearizing the response and gain of each individual pixel across the chip is key to achieve those targets. The aim is for all columns to be perfectly balanced.

Other levers to unify the behaviour across the chip is tuning the use of facilitated correlated double sampling. Where two signals per pixel are effectively measured during acquisition: (a) bias for the offset and (b) amount of light. The difference between the two will effectively give the real signal.

Background Event Reduction Technology (BERT) enables researchers to identify the pixels that are likely to contain spurious event data and then correct the data if desired. Originally designed for EMCCD cameras, this technology has also been optimized for and applied to Photometrics scientific CMOS cameras.

BERT removes spurious events which could not have been generated via incident photons in real-time. It allows the image captured to more accurately represent what the sample is and remove artefacts.

Spuriously large pixel values which could not have come from the actual sample being imaged are replaced with a best approximation by taking the mean of the surrounding pixels and absolutely minimizes the influence of thermally-induced amplified events on acquired data.

