MICRO-428: Metrology

Week Two: Elements of Statistics

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EPFL

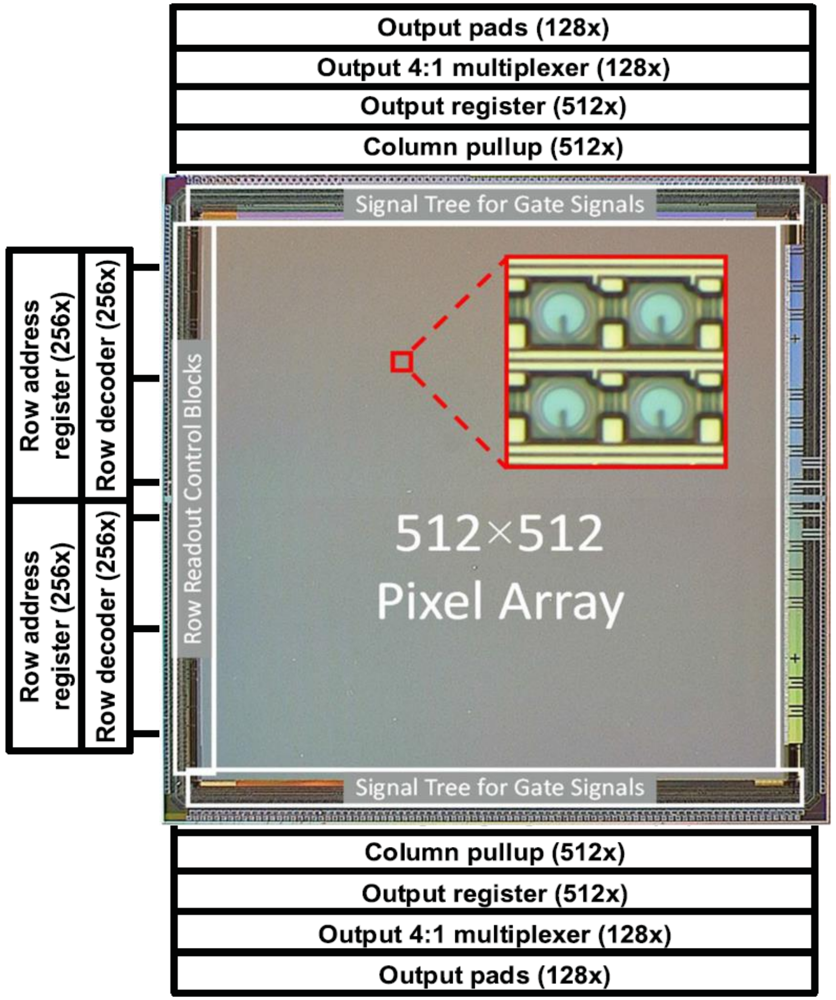
Exercise 1: Group explanation

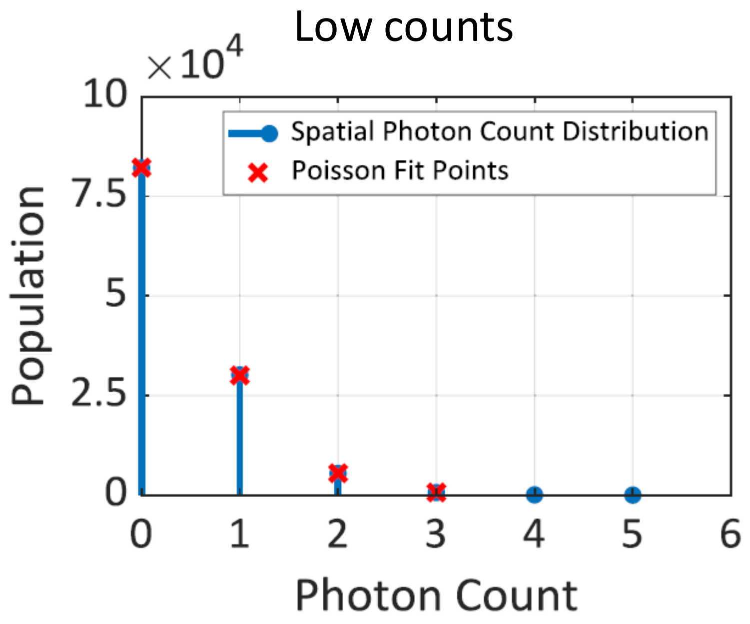
1. Divide yourself in small group (2-3 ppl).
2. Discuss the following example taken from the lecture, focusing on understanding what is happening.

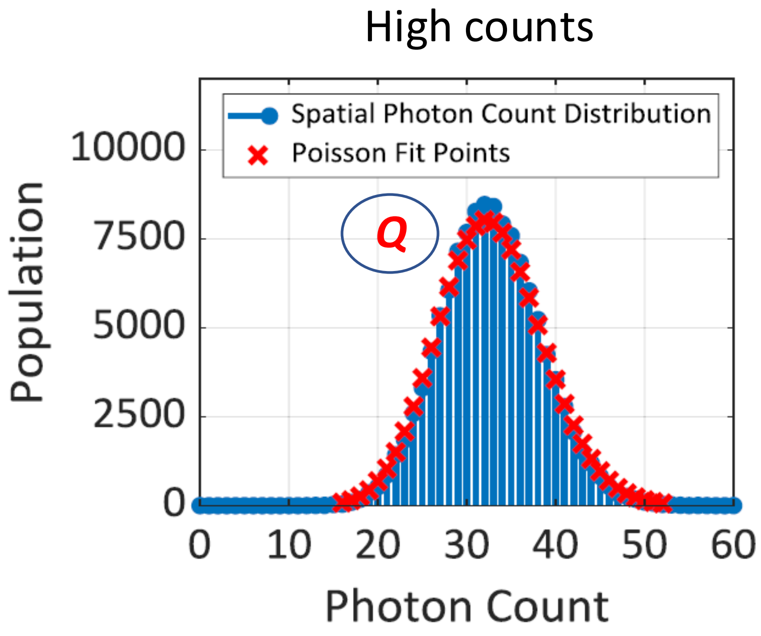
8.2.9 Example 1: Photon-flux dependent distributions

SwissSPAD2 binary SPAD imager

(intensity)

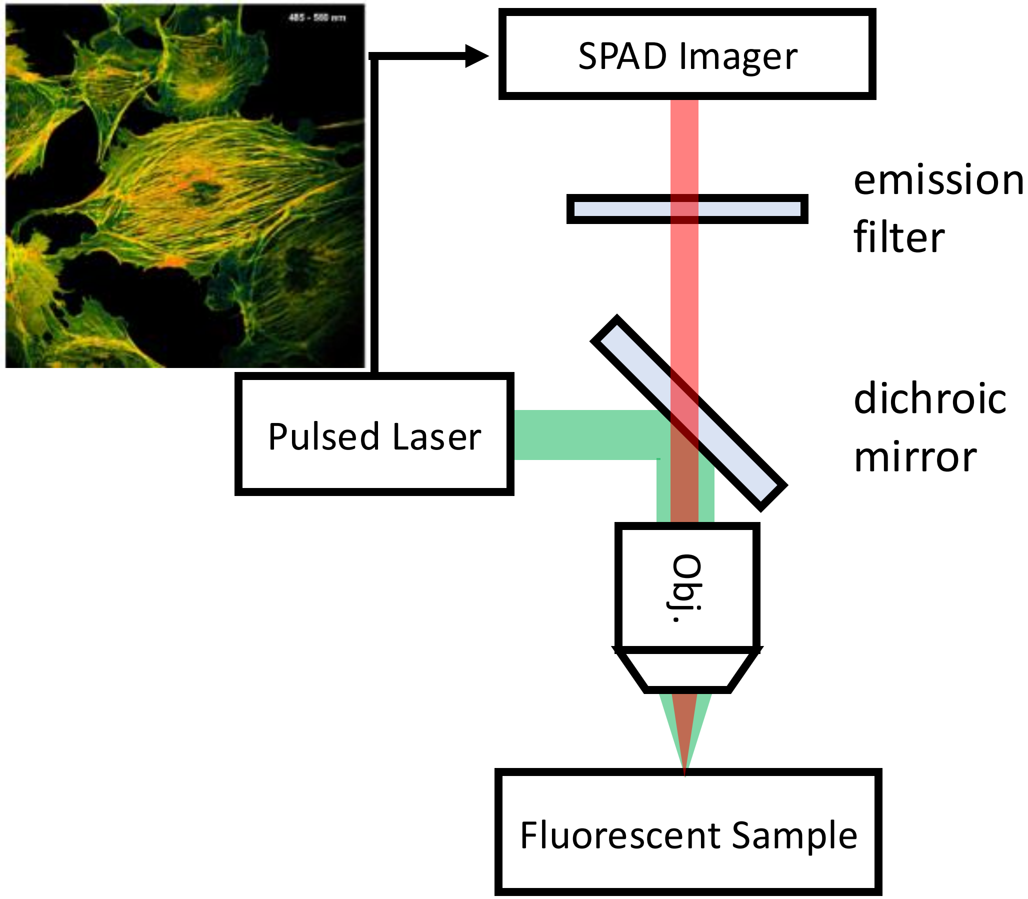


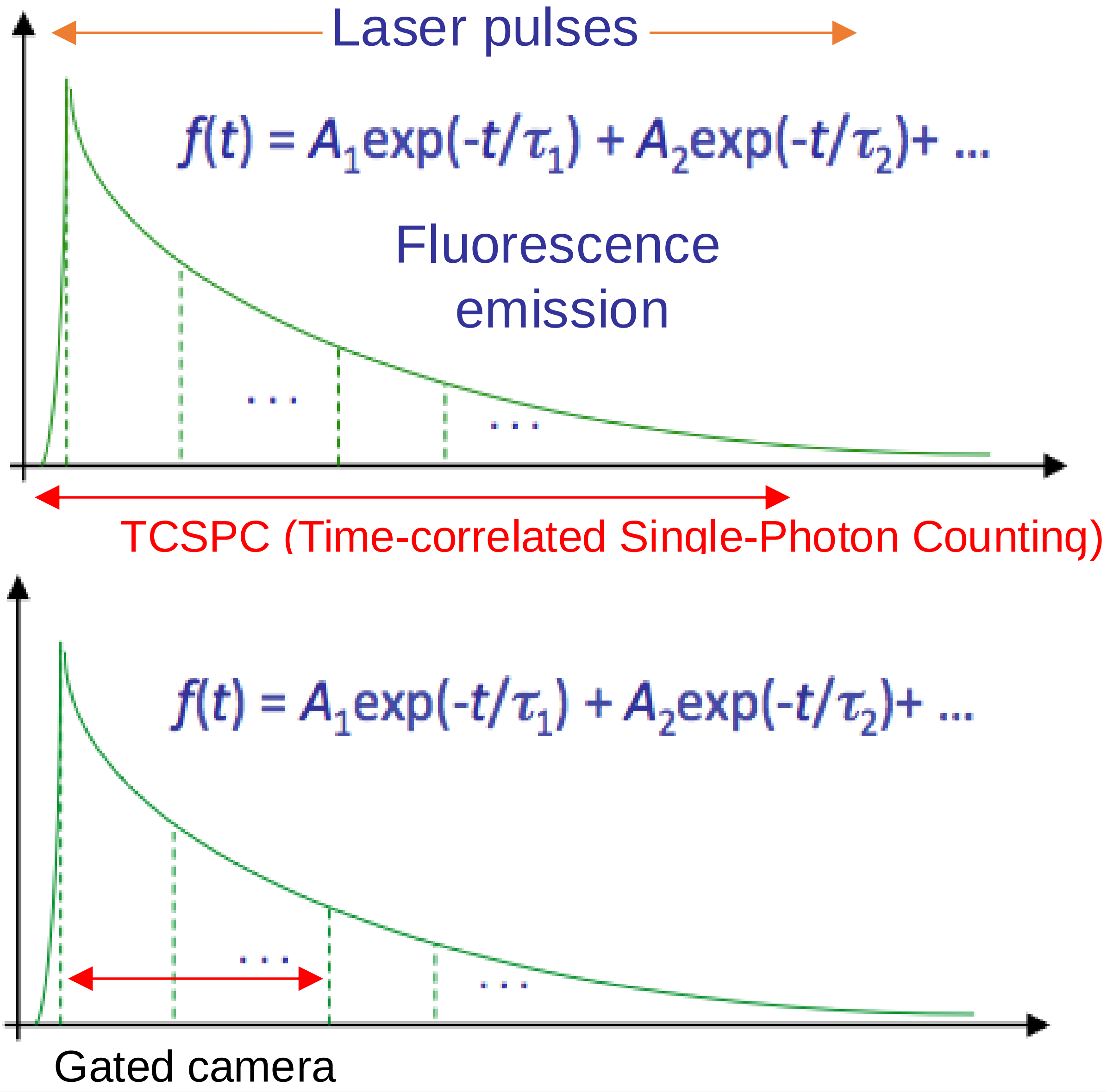




A. Ulku *et al., A 512x512 SPAD Image Sensor with Integrated Gating for Widefield FLIM.* IEEE JSTQE (2019).

8.2.9 Example 2: Fluorescence Lifetime – Time-Resolved





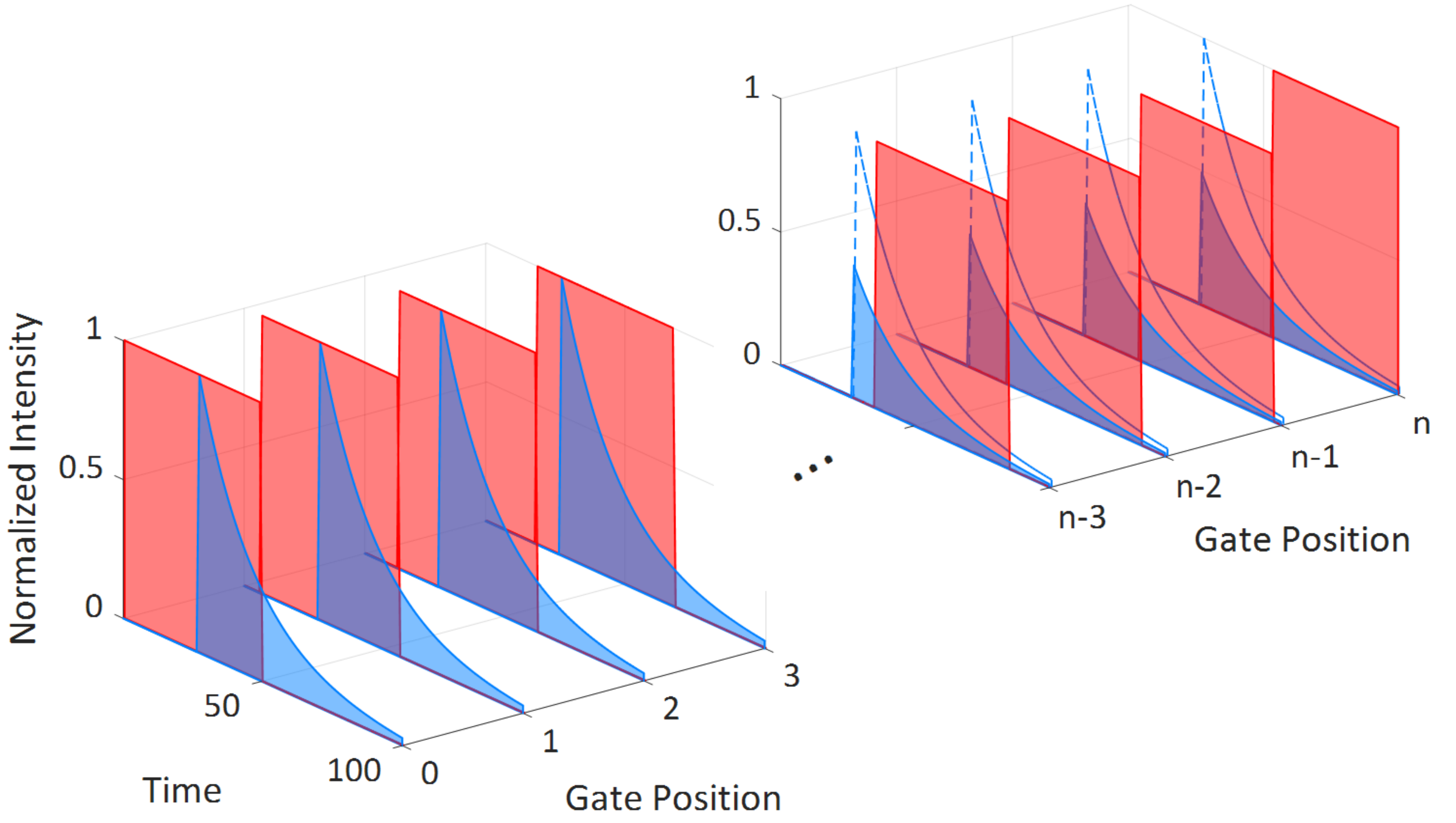
Lifetime images: the pixel time-tags all photons and calculates t_1 , t_2 , A_1

D. Li, *Strathclyde Univ.* (2016).

8.2.9 Example 2: Fluorescence Lifetime – Time-Resolved

SwissSPAD2 binary SPAD imager

(overlapping gates)



A. Ulku *et al.*, *Large-Format Time-Gated SPAD Cameras for Real-Time Phasor-Based FLIM. EPFL Thèse 8311* (2021).

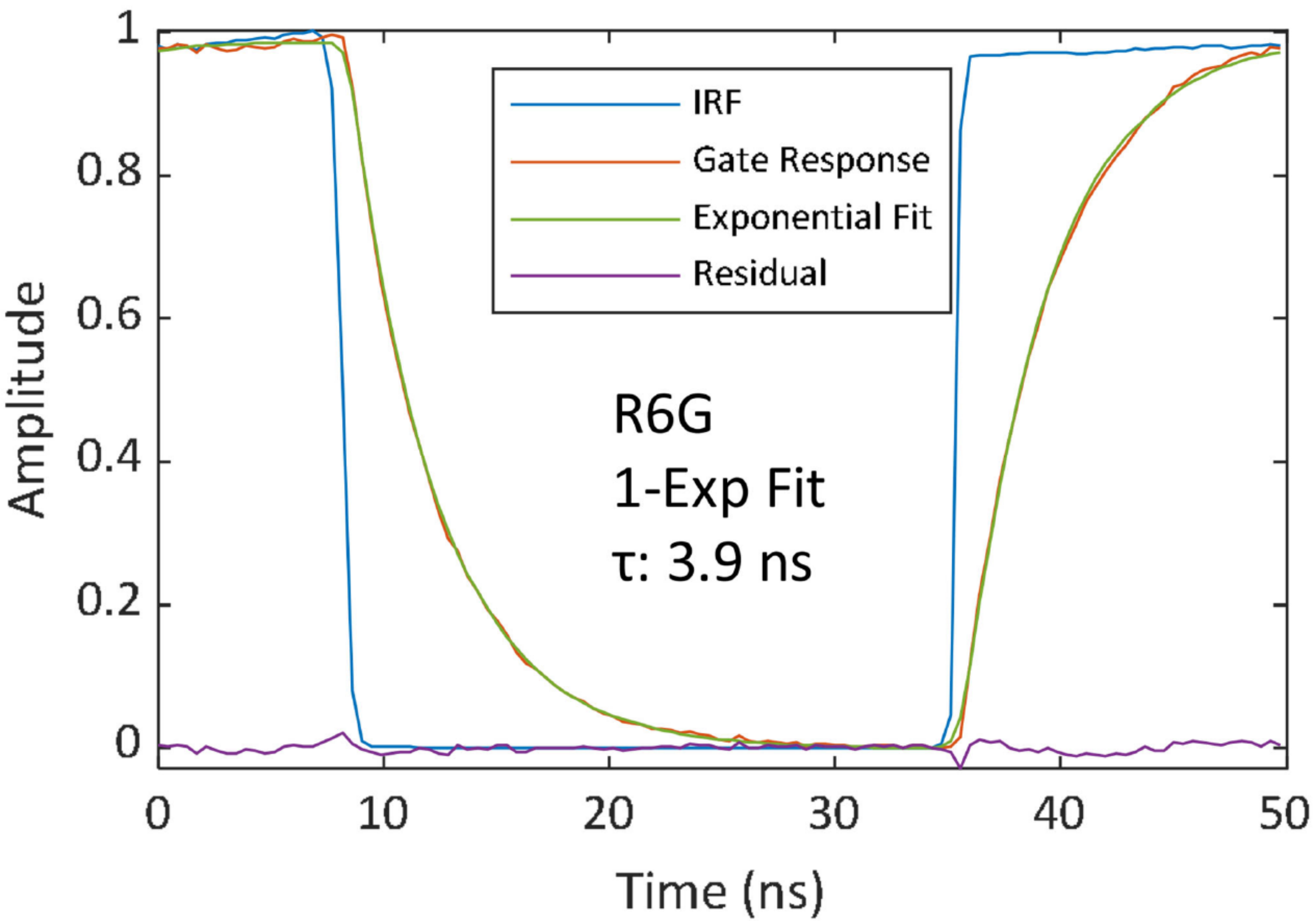
8.2.9 Example 2: Fluorescence Lifetime – Time-Resolved

SwissSPAD2 binary SPAD imager

(overlapping gates -> convolution)

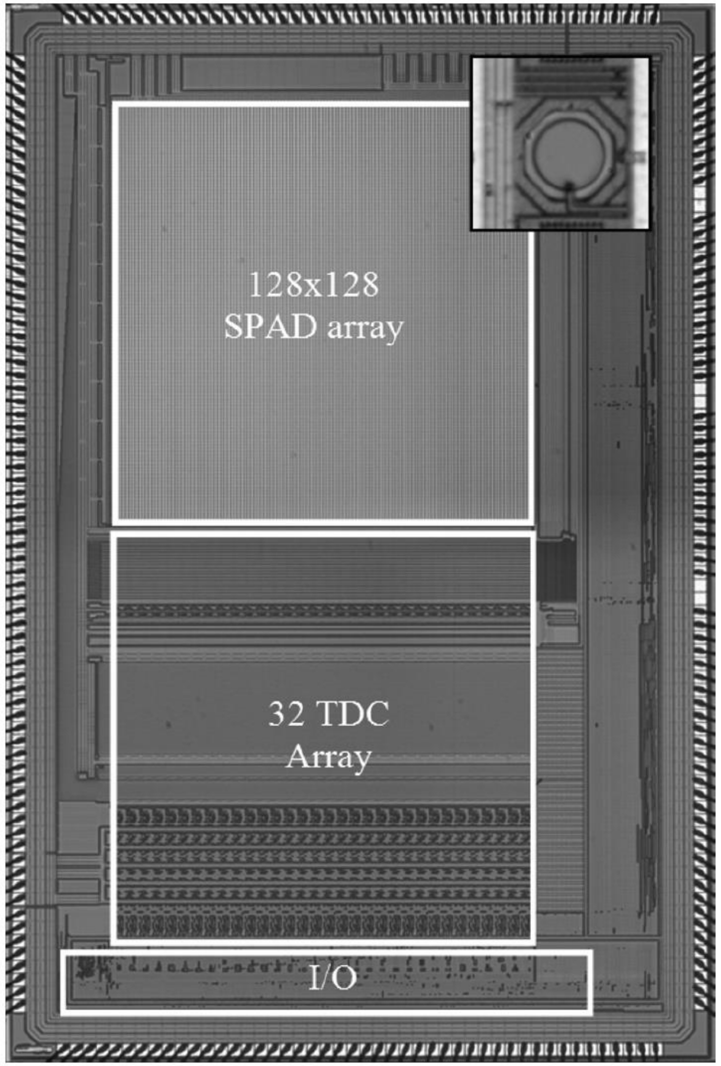
$$f(t) = g(t) * IRF(t)$$

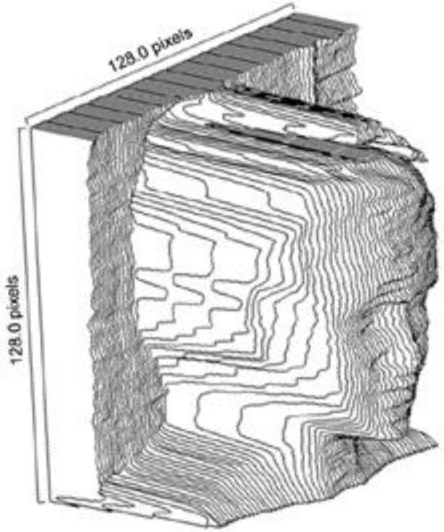
IRF: Instrument Response Function

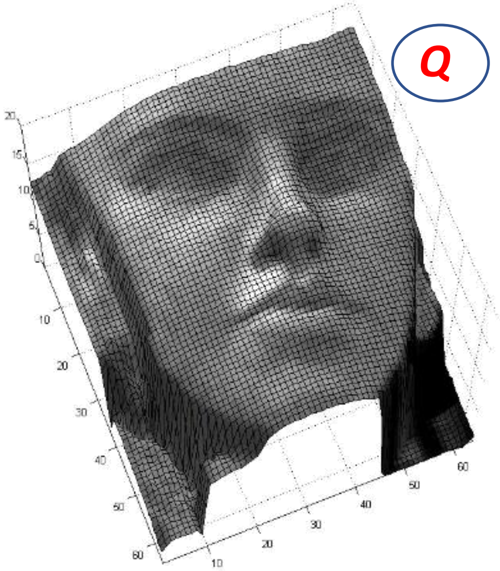


A. Ulku *et al., A 512x512 SPAD Image Sensor with Integrated Gating for Widefield FLIM.* IEEE JSTQE (2019).

8.2.9 Example 3: Real Life Truths – LIDAR & Timing Jitter in SPADs







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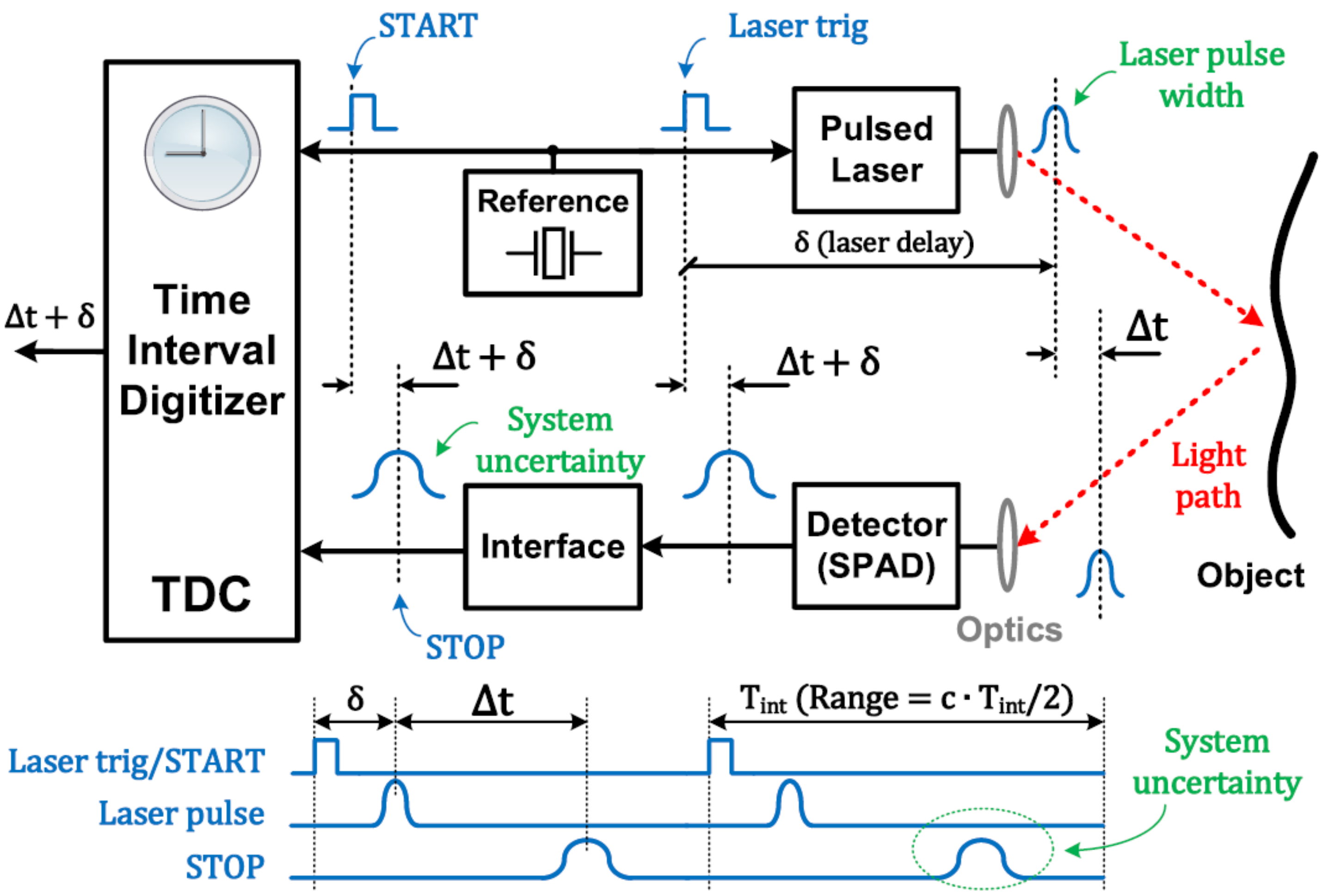
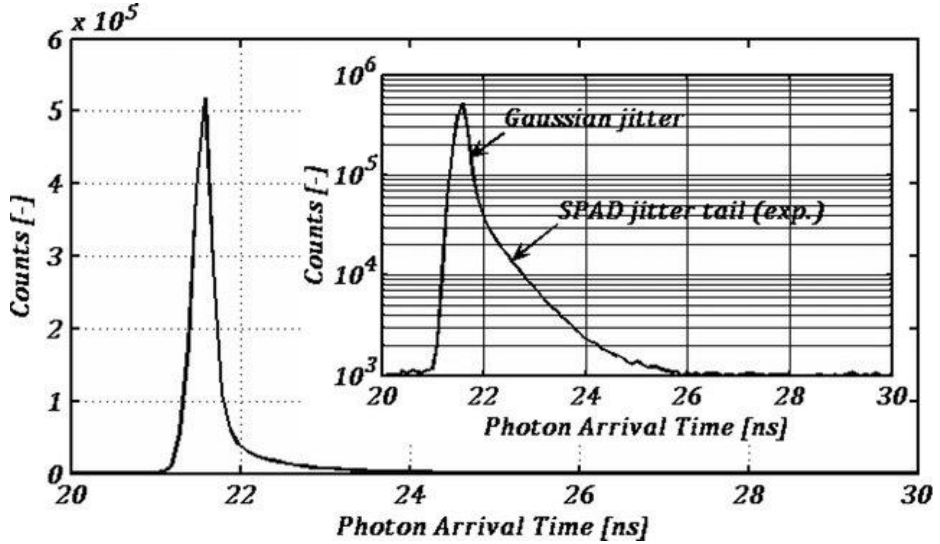
C. Niclass *et al., A 128×128 Single-Photon Image Sensor With Column-Level 10-Bit Time-to-Digital Converter Array.* IEEE JSSC 43 (2008).

8.2.9 Example 3: Real Life Truths – LIDAR & Timing Jitter in SPADs



Direct SPAD illumination -> SPAD IRF (jitter noise) ->

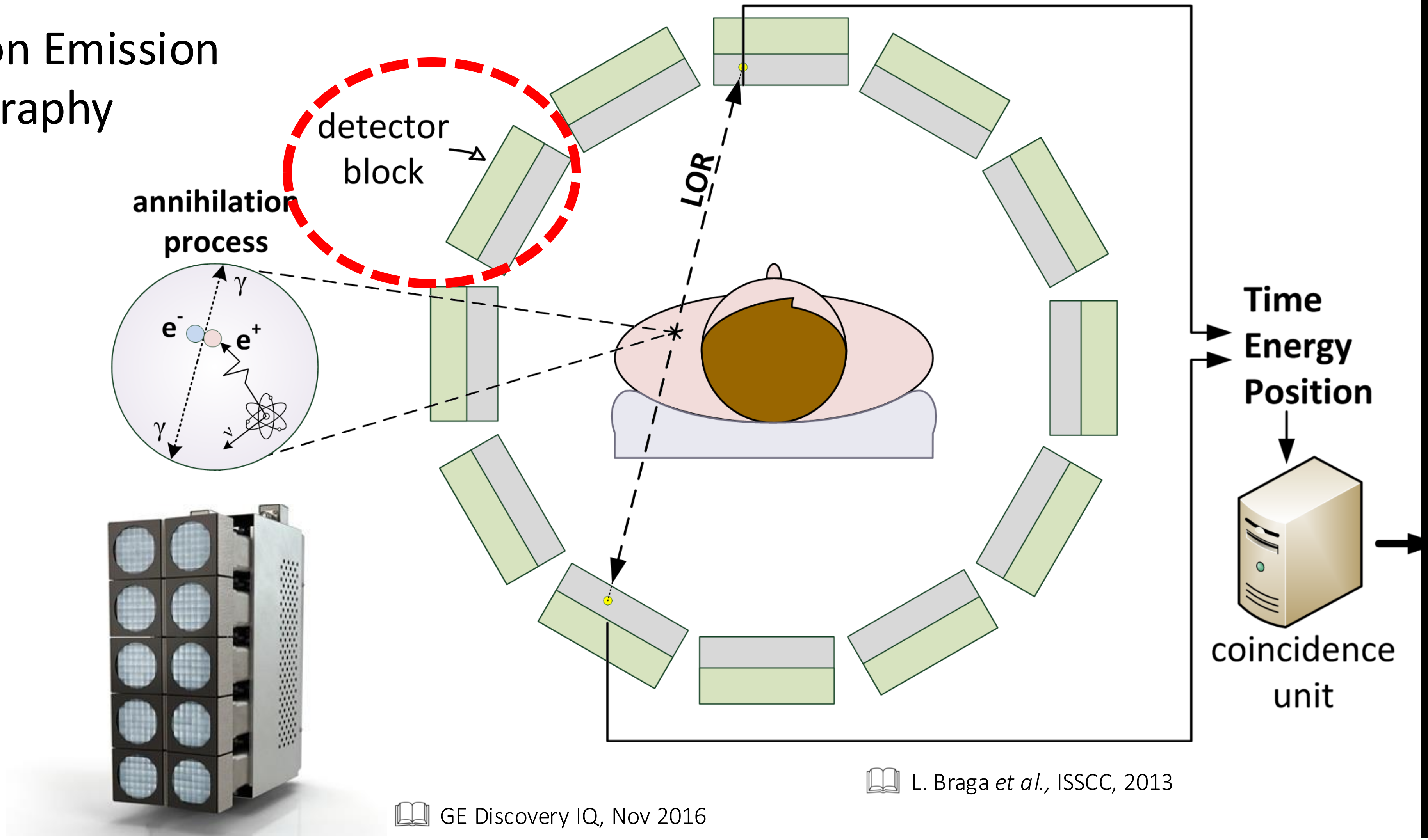
Non-Gaussian behavior of the SPADs timing uncertainty



A. R. Ximenes *et al.*, *A Modular, Direct Time-of-Flight Depth Sensor in 45/65-nm 3-D-Stacked CMOS Technology*. IEEE JSSC 54 (2019).
C. Niclass *et al.*, *A 128×128 Single-Photon Image Sensor With Column-Level 10-Bit Time-to-Digital Converter Array.* IEEE JSSC 43 (2008).

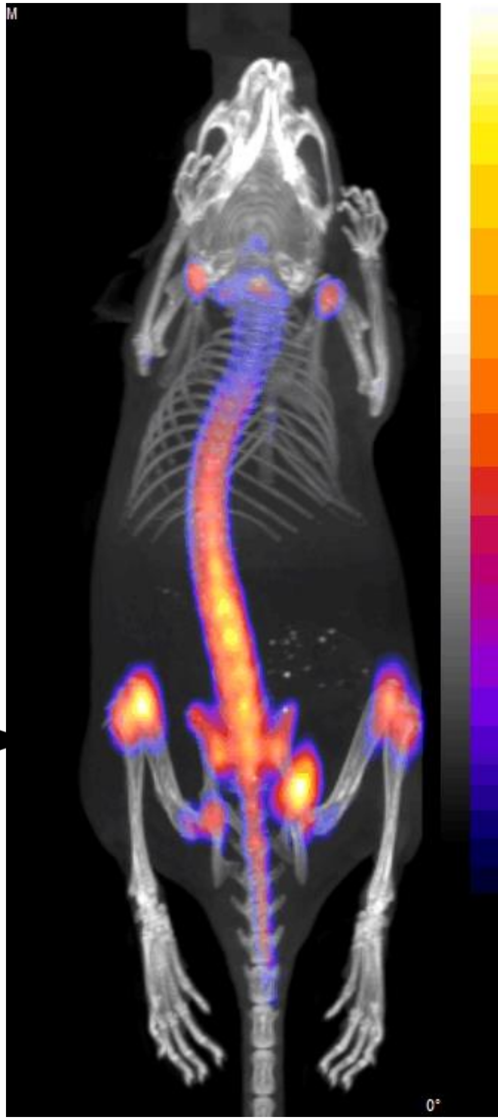
8.2.9 Example 4: Real Life Truths – Scintillation Light

Positron Emission Tomography Basics



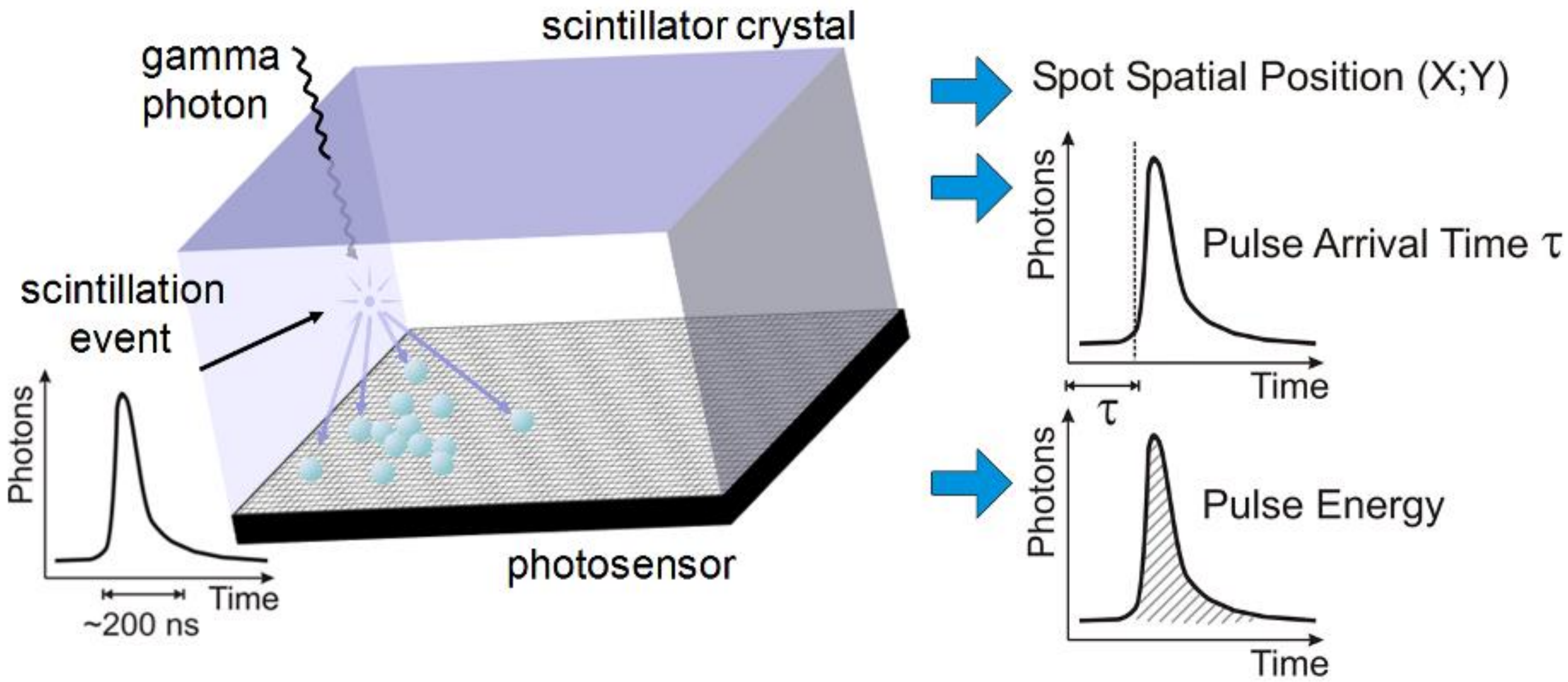
GE Discovery IQ, Nov 2016

L. Braga *et al.*, ISSCC, 2013



G. Nemeth, Mediso, Delft WS 2010

8.2.9 Example 4: Real Life Truths – Scintillation Light



R. Walker *et al.*, IISW, 2013

8.2.9 Example 4: Real Life Truths – Scintillation Light

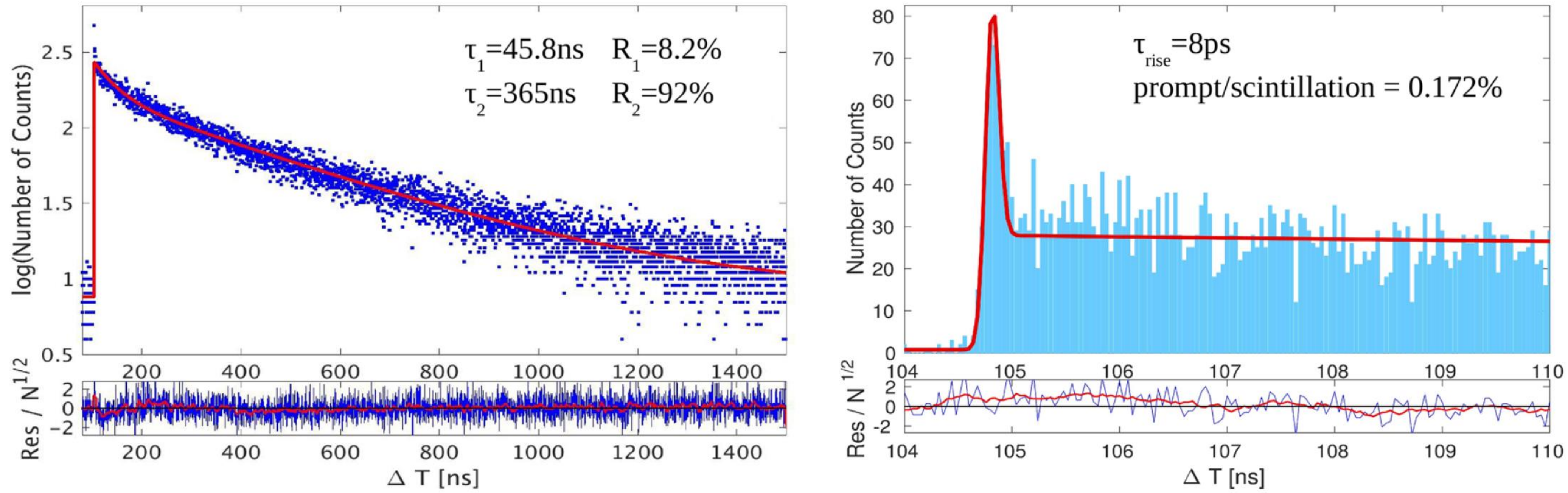


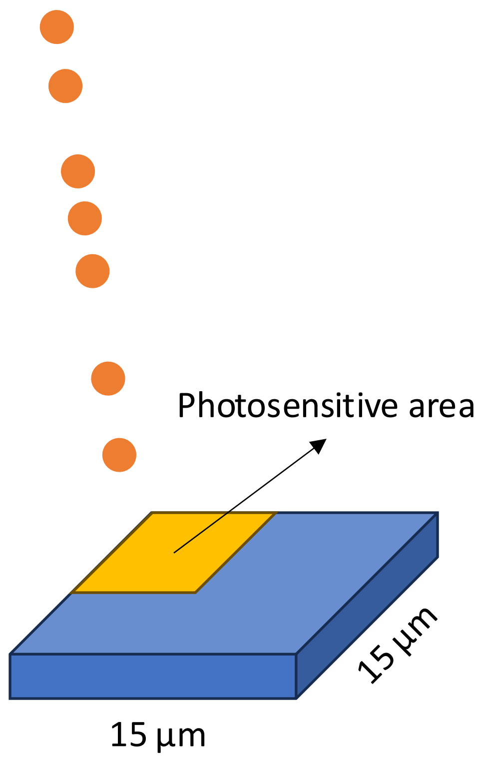
Figure 10. Scintillation decay and rise time of BGO measured with a time correlated single photon counting (TCSPC) setup using 511 keV annihilation gammas (Gundacker *et al* 2016b). The figure on the right hand side shows a pronounced Cherenkov peak at the onset of the scintillation emission with a relative abundance of 0.172% compared to the total amount of photons detected by the stop detector of the TCSPC setup.

Fast vs. "slow" scintillation photons in a heavy scintillating crystal

Gundacker S, Auffray E, Pauwels K and Lecoq P *Measurement of intrinsic rise times for various L(Y)SO and LuAG scintillators with a general study of prompt photons to achieve 10 ps in TOF-PET.* IOP Phys. Med. Biol. 61 2802–37

Exercise 2: Missed Photon Count

- A single photon detector (active area of 15x15 µm^2, fill factor of 20%) is illuminated with a continuous wave red laser (633 nm) with a uniform surface power density of 2 µW/cm^2.
- The detector has an average photon detection probability (PDP) at 633 nm of 35%.
- If the dead time of the detector (t_D, time for the detector to recover operation after clicking) is of 2 ns, what is the probability that photons are missed during detector's dead time?



Single Photon Energy:

$$E_{ph} = h\nu = h\frac{c}{\lambda}$$

Exercise 2: Missed Photon Count

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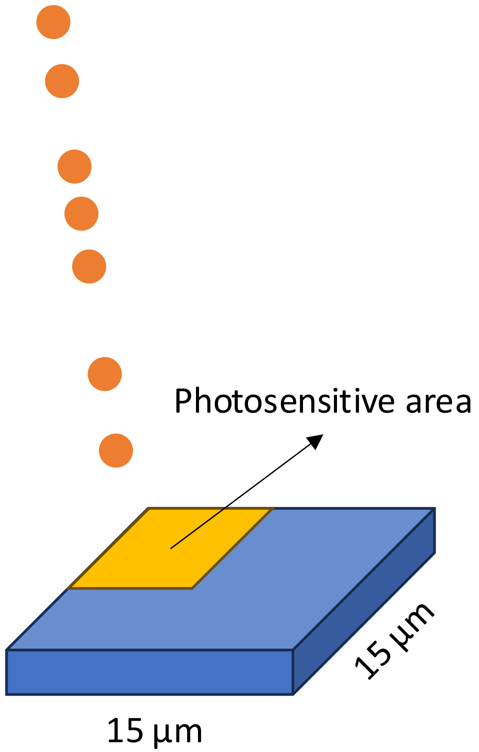
- The detector has an average photon detection probability (PDP) at 633 nm of 35%.
- If the dead time of the detector (t_D, time for the detector to recover operation after clicking) is of 2 ns, what is the probability that photons are missed during detector's dead time?
- First of all, we calculate the average number of photons striking the detector. In order to do that, we need to know the energy of a single photon and the mean optical power in the area of interest:

$$\text{Single Photon Energy:} \quad E_{ph} = h\nu = h\frac{c}{\lambda} =$$

$$= 6.62607015 \cdot 10^{-34}\, J \cdot s \times \frac{299792458\, m \cdot s^{-1}}{633 \cdot 10^{-9}\, m} = 3.138145 \cdot 10^{-19} J$$



Single Photon Energy:

$$E_{ph} = h\nu = h\frac{c}{\lambda}$$

Exercise 2: Missed Photon Count

Average Optical Power on Active Area: $\pi = P_T \, FF \, A_{active} =$

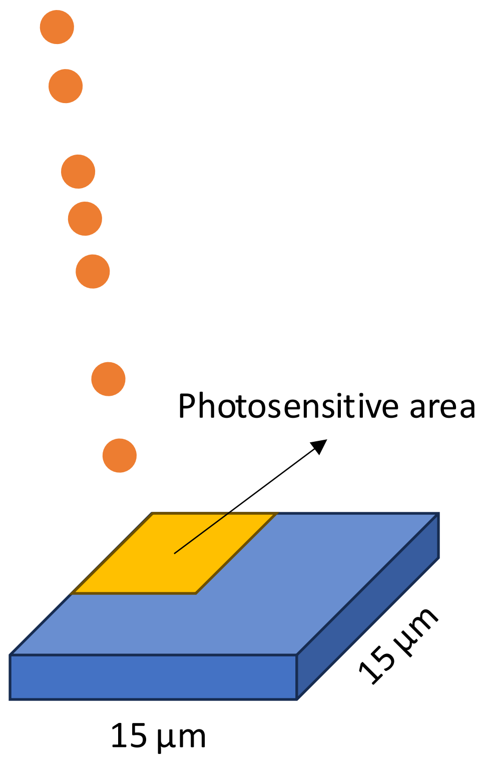
$$= 2 \cdot 10^{-6} \cdot 10^4 \frac{W}{m^2} \times 0.2 \times 225 \cdot 10^{-12} \; m^2 = 0.9 \cdot 10^{-12} \; W$$

- Now we can calculate the average number of photons seen by the detector:

Average Photon Number on Active Area: $\mu_{ph} = \frac{\pi}{E_{ph}} \, PDP =$

$$= \frac{0.9 \cdot 10^{-12} W}{3.14 \cdot 10^{-19} J} \times 0.35 = 1.003 \cdot 10^6 \text{ cps}$$

- Since we have the mean values of a time dependent random variable (time before a photon is detected by the sensor) our distribution will be an Exponential distribution. The probability for a photon to be detected is given by $X \sim \text{Expo}(\mu_{ph})$.



Single Photon Energy:

$$E_{ph} = h\nu = h\frac{c}{\lambda}$$

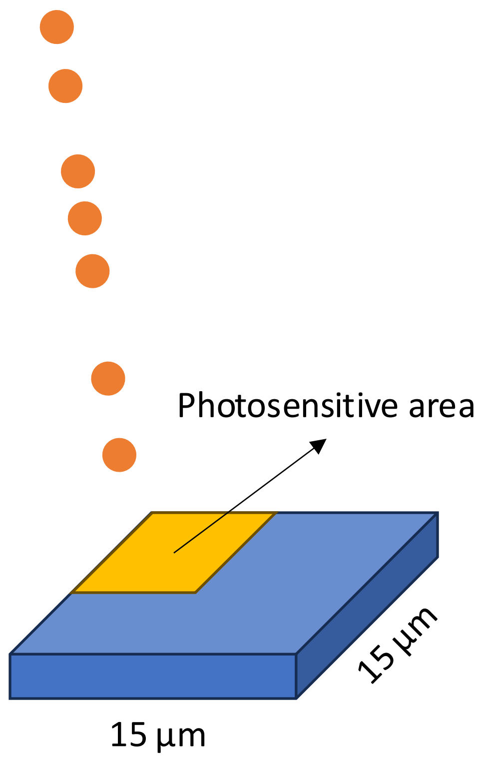
Exercise 2: Missed Photon Count

- Assuming that the first photon is absorbed at a certain time t_X, it follows that the probability that a photon is absorbed before $t_X + t_D$ is:

$$P\{X \leq t_D\} = 1 - e^{-(\mu_{ph} t_D)}$$

- However, we could have used another approach, and exploit the properties of the Poisson distribution $Y \sim \mathrm{Pois}(\lambda_{ph})$. In fact, since the average number of photons in the time t_D is given by $\mu_{ph} t_D = \lambda_{ph}$, the probability to detect at least one photon would be:

$$P\{Y > 0\} = 1 - P\{Y \leq 0\} = 1 - \sum_{y=0}^{0} \frac{(\lambda_{ph})^y}{y!} e^{-(\lambda_{ph})} = 1 - e^{-(\lambda_{ph})}$$



Single Photon Energy:

$$E_{ph} = h\nu = h\frac{c}{\lambda}$$

Exercise 3: Moment Generating Function

- Obtain the moment generating function of the normal distribution $X \sim \mathcal{N}(\mu, \sigma^2)$. Calculate the first three moments.

- The moment generating function (MGF) of a RV X is defined as:

$$\text{MGF: } \phi(t) = E\{e^{tX}\} = \begin{cases} \sum_x e^{tx} p_X(x), & \text{if } X \text{ is discrete } * \\ \int_{-\infty}^{\infty} e^{tx} f_X(x)\, dx, & \text{if } X \text{ is continuous } * \end{cases}$$

Exercise 3: Moment Generating Function

- Obtain the moment generating function of the normal distribution $X \sim \mathcal{N}(\mu, \sigma^2)$. Calculate the first three moments.

- First of all, let's find the moment generating function of the standard normal, i.e. for $Z \sim \mathcal{N}(0,1)$. It follows:

$$E\{e^{tZ}\} = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} e^{tz} e^{-z^2/2}\, dz$$

$$= \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} e^{-(z^2 - 2tz)/2}\, dz$$

$$= e^{t^2/2} \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\infty} e^{-(z-t)^2/2}\, dz$$

$$= e^{t^2/2}$$

- The moment generating function (MGF) of a RV X is defined as:

$$\text{MGF: } \phi(t) = E\{e^{tX}\} = \begin{cases} \sum_x e^{tx} p_X(x), & \text{if } X \text{ is discrete } * \\ \int_{-\infty}^{\infty} e^{tx} f_X(x)\, dx, & \text{if } X \text{ is continuous } * \end{cases}$$

Exercise 3: Moment Generating Function

- For the normal distribution, it follows that $X \sim \mathcal{N}(\mu, \sigma^2) = \sigma Z + \mu$. Therefore:

$$\phi(t) = E\{e^{tX}\} = E\left\{e^{t(\sigma Z + \mu)}\right\} =$$

$$= e^{t\mu} E\{e^{t\sigma Z}\} = \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\}$$

- By differentiating we get:

$$\phi'(t) = (\mu + t\sigma^2) \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\}$$

$$\phi''(t) = (\mu + t\sigma^2)^2 \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\} + \sigma^2 \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\}$$

- The moment generating function (MGF) of a RV X is defined as:

$$\text{MGF: } \phi(t) = E\{e^{tX}\} = \begin{cases} \sum_x e^{tx} p_X(x), & \text{if } X \text{ is discrete } * \\ \int_{-\infty}^{\infty} e^{tx} f_X(x)\, dx, & \text{if } X \text{ is continuous } * \end{cases}$$

Exercise 3: Moment Generating Function

$$\phi'''(t) = (\mu + t\sigma^2)^3 \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\} + 2\sigma^2(\mu + t\sigma^2) \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\} +$$

$$+\sigma^2(\mu + t\sigma^2) \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\}$$

- The moment generating function (MGF) of a RV X is defined as:

$$\text{MGF: } \phi(t) = E\{e^{tX}\} = \begin{cases} \sum_x e^{tx} p_X(x), & \text{if } X \text{ is discrete } * \\ \int_{-\infty}^{\infty} e^{tx} f_X(x)\, dx\,, & \text{if } X \text{ is continuous } * \end{cases}$$

- Hence it follows:

$$\phi'(0) = \mu = E\{X\}$$

$$\phi''(0) = \mu^2 + \sigma^2 = E\{X^2\}$$

$$\phi'''(0) = \mu^3 + 3\,\mu\,\sigma^2 = E\{X^3\}$$

Exercise 3: Moment Generating Function

- METHOD 2: Alternatively, we can simplify the computation by means of a Taylor-McLaurin power series expansion of the exponentials:

$$\phi(t) = \exp\left\{\frac{\sigma^2 t^2}{2} + \mu t\right\} = \exp\left\{\frac{\sigma^2 t^2}{2}\right\}\exp\{\mu t\} =$$

$$f(x) = f(0) + f'(0)\,x + \frac{f''(0)}{2!}x^2 + \frac{f^{(3)}(0)}{3!}x^3 + \ldots + \frac{f^{(n)}(0)}{n!}x^n + \ldots$$

$$e^x = 1 + x + \tfrac{1}{2}x^2 + \tfrac{1}{6}x^3 + \tfrac{1}{24}x^4 + \ldots$$

$$= \left(1 + \frac{\sigma^2 t^2}{2} + O(t^4)\right)\left(1 + \mu t + \frac{\mu^2 t^2}{2} + \frac{\mu^3 t^3}{6} + O(t^4)\right)$$

$$= 1 + \mu t + \frac{\mu^2 + \sigma^2}{2} t^2 + \left(\frac{\mu^3}{6} + \frac{\mu\sigma^2}{2}\right) t^3 + O(t^4)$$

$$= 1 + \mu t + (\mu^2 + \sigma^2)\,\frac{t^2}{2} + (\mu^3 + 3\mu\sigma^2)\frac{t^3}{6} + O(t^4)$$

which leads in an elegant and simplified way to the same moments shown on the previous slide…

J.K. Blitzstein, J. Hwang, *Introduction to Probability*, 1st ed., 2015, Chap. 6.4

Exercise 3: Moment Generating Function

… given that the MGF can indeed be expressed as a power series expansion:

$$\phi(t) = \sum_{n=0}^{\infty} \phi^{(n)}(0) \frac{t^n}{n!}$$

and

$$E\{X^n\} = \phi^{(n)}(0)$$

J.K. Blitzstein, J. Hwang, *Introduction to Probability*, 1st ed., 2015, Chap. 6.4

Homework 1: Rare disease

- A rare disease affects 1 person every 100’000. The SV researchers in EPFL are developing a new test method, which shows a sensitivity of 0.8 and a specificity of 0.9 in the 3rd phase trial. What is the probability that a patient is affected by this disease if the result is positive in the real world?
  - NB: the definition of sensitivity and specificity is given by the confusion matrix below

		Predicted Class		
		Positive	**Negative**	
Actual Class	**Positive**	True Positive (TP)	False Negative (FN) **Type II Error**	**Sensitivity** $\frac{TP}{(TP+FN)}$
	Negative	False Positive (FP) **Type I Error**	True Negative (TN)	**Specificity** $\frac{TN}{(TN+FP)}$
		Precision $\frac{TP}{(TP+FP)}$	**Negative Predictive Value** $\frac{TN}{(TN+FN)}$	**Accuracy** $\frac{TP+TN}{(TP+TN+FP+FN)}$

https://manisha-sirsat.blogspot.com/2019/04/confusion-matrix.html

Homework 2: Skew and Kurtosis

- Using the MGF, demonstrate that the skew of the normal distribution is zero.

- Then, calculate the kurtosis of the exponential.

Homework 3: (Matlab) distributions

- Reproduce with Matlab the different Random Variable distributions encountered in the Week 2 lecture.

Homework 4: Usefulness of Bayes' Theorem

- A company produces single-photon cameras with three production lines: the first one (line A) has 10% of defective devices, the second one (line B) 20% and the third one (line C) 30% (not a very reliable company…).
- Usually, these three production lines cover respectively 15%, 35% and 50% of the total production. We bought a device and we found it defective.
- What is it the probability that the defective device is from line C?