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# Derivation of the CRLB

## Potability distribution

We assume a continuous, mono-exponential probability distribution  $p$  with a constant background. The probability distribution is normalised over the range 0 to  $T$ . Therefore, the expectation value is given by  $n p$ .

The following variables are used:

$t$ : time

$\tau$ : fluorescence lifetime

$T$ : pulse repetition period/measurement window

$b$ : background fraction ( $b = 0$ , no background;  $b = 1$  only background)

$n$ : number of photons in decay

```
In[1]:= pAssumptions = { t >= 0, T > 0, tau > 0, 1 > b >= 0, n > 0, chi > 0, {t, T, tau, b, n, chi} ∈ Reals};  
p = Simplify[(1 - b) * PDF[ExponentialDistribution[1/tau], t] /  
CDF[ExponentialDistribution[1/tau], T] + b/T, pAssumptions]
```

$$\text{Out[2]= } \frac{b - b e^{-\frac{T}{\tau}} - \frac{(-1+b) e^{-\frac{T}{\tau}} T}{\tau}}{T - e^{-\frac{T}{\tau}} T}$$

Check normalization:

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In[3]:= ∫₀ᵀ p dt
```

$$\text{Out[3]= } 1$$

## CRLB for a known background

In this case only the lifetime needs to be estimated ( $\theta = \{\tau\}$ ) and the Fisher matrix  $f$  has just one entry.

```
In[4]:= fττ = Integrate[(∂τ Log[n * p])^2 * (n * p), {t, 0, T}, Assumptions → pAssumptions]
```

$$\text{Out[4]} = \frac{1}{(-1 + e^{T/\tau})^2 \tau^4} n \left( -b \tau^3 - e^{T/\tau} \tau^3 + b e^{T/\tau} \tau^3 - 2 b \tau^2 \tau + 2 b e^{T/\tau} \tau^2 \tau + \tau \tau^2 - 2 b \tau \tau^2 - 2 e^{T/\tau} \tau \tau^2 + 4 b e^{T/\tau} \tau \tau^2 + \right. \\ e^{\frac{2T}{\tau}} \tau \tau^2 - 2 b e^{\frac{2T}{\tau}} \tau \tau^2 + b \tau^2 \tau \text{Log}\left[\frac{b(-1 + e^{T/\tau}) \tau}{T - b \tau + b(-1 + e^{T/\tau}) \tau}\right] - \\ b e^{\frac{2T}{\tau}} \tau^2 \tau \text{Log}\left[\frac{b(-1 + e^{T/\tau}) \tau}{T - b \tau + b(-1 + e^{T/\tau}) \tau}\right] + 2 b \tau \tau^2 \text{Log}\left[\frac{b(-1 + e^{T/\tau}) \tau}{T - b \tau + b(-1 + e^{T/\tau}) \tau}\right] - \\ 4 b e^{T/\tau} \tau \tau^2 \text{Log}\left[\frac{b(-1 + e^{T/\tau}) \tau}{T - b \tau + b(-1 + e^{T/\tau}) \tau}\right] + 2 b e^{\frac{2T}{\tau}} \tau \tau^2 \text{Log}\left[\frac{b(-1 + e^{T/\tau}) \tau}{T - b \tau + b(-1 + e^{T/\tau}) \tau}\right] + \\ b \tau^2 \tau \text{Log}\left[e^{T/\tau} (T - b \tau + b(-1 + e^{T/\tau}) \tau)\right] + 2 b \tau \tau^2 \text{Log}\left[e^{T/\tau} (T - b \tau + b(-1 + e^{T/\tau}) \tau)\right] - \\ 2 b e^{T/\tau} \tau \tau^2 \text{Log}\left[e^{T/\tau} (T - b \tau + b(-1 + e^{T/\tau}) \tau)\right] + b \tau^3 \text{Log}\left[e^{T/\tau} (T - b \tau + b(-1 + e^{T/\tau}) \tau)\right] - \\ 2 b e^{T/\tau} \tau^3 \text{Log}\left[e^{T/\tau} (T - b \tau + b(-1 + e^{T/\tau}) \tau)\right] + b e^{\frac{2T}{\tau}} \tau^3 \text{Log}\left[e^{T/\tau} (T - b \tau + b(-1 + e^{T/\tau}) \tau)\right] - \\ b \tau^2 \tau \text{Log}\left[-b \tau + e^{T/\tau} (T - b \tau + b \tau)\right] - 2 b \tau \tau^2 \text{Log}\left[-b \tau + e^{T/\tau} (T - b \tau + b \tau)\right] + \\ 2 b e^{T/\tau} \tau \tau^2 \text{Log}\left[-b \tau + e^{T/\tau} (T - b \tau + b \tau)\right] - b \tau^3 \text{Log}\left[-b \tau + e^{T/\tau} (T - b \tau + b \tau)\right] + \\ 2 b e^{T/\tau} \tau^3 \text{Log}\left[-b \tau + e^{T/\tau} (T - b \tau + b \tau)\right] - b e^{\frac{2T}{\tau}} \tau^3 \text{Log}\left[-b \tau + e^{T/\tau} (T - b \tau + b \tau)\right] + \\ 2 b (-1 + e^{T/\tau}) \tau^2 (T + \tau - e^{T/\tau} \tau) \text{PolyLog}\left[2, \frac{(-1 + b) e^{T/\tau} T}{b(-1 + e^{T/\tau}) \tau}\right] - \\ 2 b (-1 + e^{T/\tau}) \tau^2 (e^{T/\tau} (T - \tau) + \tau) \text{PolyLog}\left[2, \frac{T - b T}{b \tau - b e^{T/\tau} \tau}\right] + \\ 2 b \tau^3 \text{PolyLog}\left[3, \frac{(-1 + b) e^{T/\tau} T}{b(-1 + e^{T/\tau}) \tau}\right] - 4 b e^{T/\tau} \tau^3 \text{PolyLog}\left[3, \frac{(-1 + b) e^{T/\tau} T}{b(-1 + e^{T/\tau}) \tau}\right] + \\ 2 b e^{\frac{2T}{\tau}} \tau^3 \text{PolyLog}\left[3, \frac{(-1 + b) e^{T/\tau} T}{b(-1 + e^{T/\tau}) \tau}\right] - 2 b \tau^3 \text{PolyLog}\left[3, \frac{T - b T}{b \tau - b e^{T/\tau} \tau}\right] + \\ 4 b e^{T/\tau} \tau^3 \text{PolyLog}\left[3, \frac{T - b T}{b \tau - b e^{T/\tau} \tau}\right] - 2 b e^{\frac{2T}{\tau}} \tau^3 \text{PolyLog}\left[3, \frac{T - b T}{b \tau - b e^{T/\tau} \tau}\right] \Big)$$

Mathematica needs some help with the simplification : We need to reduce all Log expressions and collect the  $\tau$  to enable cancelling them.

For efficient numerical evaluation, Powers are expanded again to avoid errors by to large arguments in the Log. The terms with PolyLog are grouped to minimise calls to PolyLog.

```
In[5]:= SimplifyCRLB[exprs_] := Assuming[pAssumptions,
  Simplify[
    Simplify[exprs /. {Log[a_] + Log[b_] => Log[a * b], x_ * Log[a_] => Log[a^x],
      a_ * τ + b_ * τ => (a + b) * τ}] (* Cancel τ in the log terms *)
    /. {Log[a_ * b_^x_] => Log[a] + x * Log[b],
      a_ * PolyLog[x_, c_] + b_ * PolyLog[x_, c_] => (a + b) * PolyLog[x, c]}]
    (* Optimise for numerical evaluation *)
  ]
```

We substitute the repetition period with a relative repetition period:  $\chi = T/\tau$

The CRLB ( $\sigma_\tau^2$ ) is given the inverse Fisher matrix:

In[6]:=  $\sigma\tau\text{SQ} = \text{SimplifyCRLB}[1/f_{\tau\tau} // \{T \rightarrow \chi \tau\}]$

$$\text{Out[6]} = \left( (-1 + e^{\chi})^2 \tau^2 \chi \right) / \left( n \left( \chi - 2b\chi - 2e^{\chi}\chi + 4be^{\chi}\chi + e^{2\chi}\chi - 2be^{2\chi}\chi - 2b\chi^2 + 2be^{\chi}\chi^2 - b\chi^3 - e^{\chi}\chi^3 + be^{\chi}\chi^3 - \right. \right. \\ \left. b(-1 + e^{\chi})\chi(2 + e^{\chi}(-2 + \chi) + \chi)(\text{Log}[b(-1 + e^{\chi})] - \text{Log}[b(-1 + e^{\chi} - \chi) + \chi]) + \right. \\ \left. b(1 - e^{\chi} + \chi)^2 \text{Log}\left[\frac{e^{\chi}(b(-1 + e^{\chi} - \chi) + \chi)}{-b + e^{\chi}(b + \chi - b\chi)}\right] - 2b(-1 + e^{\chi})(1 + e^{\chi}(-1 + \chi)) \right. \\ \left. \text{PolyLog}\left[2, \frac{(-1 + b)\chi}{b(-1 + e^{\chi})}\right] - 2b(-1 + e^{\chi})(-1 + e^{\chi} - \chi) \text{PolyLog}\left[2, \frac{(-1 + b)e^{\chi}\chi}{b(-1 + e^{\chi})}\right] - \right. \\ \left. 2b(-1 + e^{\chi})^2 \text{PolyLog}\left[3, \frac{(-1 + b)\chi}{b(-1 + e^{\chi})}\right] + 2b(-1 + e^{\chi})^2 \text{PolyLog}\left[3, \frac{(-1 + b)e^{\chi}\chi}{b(-1 + e^{\chi})}\right] \right)$$

Limit for zero background:

In[7]:= **Assuming[pAssumptions, FullSimplify[1/Limit[1/στSQ, b → 0, Direction → "FromAbove"]]]**  
**(\* The limits of 1/στSQ are somehow much faster to compute. \*)**

$$\text{Out[7]} = -\frac{2\tau^2(-1 + \text{Cosh}[\chi])}{n(2 + \chi^2 - 2\text{Cosh}[\chi])}$$

Limit for infinite pulse period:

In[8]:= **1/Limit[1/στSQ, χ → ∞, Assumptions → pAssumptions, Direction → "FromBelow"]**

$$\text{Out[8]} = \frac{\tau^2}{n - bn}$$

## CRLB for an unknown background

Now lifetime and background need to be estimated ( $\theta = \{\tau, b\}$ ). The Fisher matrix has the form

$$\mathbf{f} = \begin{pmatrix} f_{\tau\tau} & f_{\tau b} \\ f_{\tau b} & f_{bb} \end{pmatrix}.$$

Calculate  $f_{\tau b}$  and  $f_{bb}$ , and assemble Fisher matrix.

```
In[9]:= fcb = Integrate[(∂τ Log[n * p]) * (∂b Log[n * p]) * (n * p), {t, 0, T}, Assumptions → pAssumptions]
```

$$\text{Out[9]} = -\frac{1}{2(-1+b)(-1+e^{T/\tau})T\tau^2} n \left( 2T^2 - bT^2 + b e^{T/\tau} T^2 + 2T\tau - 2e^{T/\tau} T\tau - 2T\tau \log\left[\frac{b(-1+e^{T/\tau})\tau}{T-bT+b(-1+e^{T/\tau})\tau}\right] + \right. \\ 2bT\tau \log\left[\frac{b(-1+e^{T/\tau})\tau}{T-bT+b(-1+e^{T/\tau})\tau}\right] + 2e^{T/\tau} T\tau \log\left[\frac{b(-1+e^{T/\tau})\tau}{T-bT+b(-1+e^{T/\tau})\tau}\right] - \\ 2b e^{T/\tau} T\tau \log\left[\frac{b(-1+e^{T/\tau})\tau}{T-bT+b(-1+e^{T/\tau})\tau}\right] - 2T\tau \log\left[e^{T/\tau}(T-bT+b(-1+e^{T/\tau})\tau)\right] - \\ 2\tau^2 \log\left[e^{T/\tau}(T-bT+b(-1+e^{T/\tau})\tau)\right] + 2e^{T/\tau} \tau^2 \log\left[e^{T/\tau}(T-bT+b(-1+e^{T/\tau})\tau)\right] + \\ 2bT\tau \log\left[1 - \frac{b(-1+e^{T/\tau})\tau}{(-1+b)T}\right] - 2b e^{T/\tau} T\tau \log\left[1 - \frac{b(-1+e^{T/\tau})\tau}{(-1+b)T}\right] + \\ 2T\tau \log\left[-b\tau + e^{T/\tau}(T-bT+b\tau)\right] + 2\tau^2 \log\left[-b\tau + e^{T/\tau}(T-bT+b\tau)\right] - \\ 2e^{T/\tau} \tau^2 \log\left[-b\tau + e^{T/\tau}(T-bT+b\tau)\right] + 2(-1+b)(-1+e^{T/\tau})\tau^2 \\ \text{PolyLog}\left[2, \frac{(-1+b)e^{T/\tau}T}{b(-1+e^{T/\tau})\tau}\right] - 2b(-1+e^{T/\tau})\tau^2 \text{PolyLog}\left[2, \frac{b(-1+e^{T/\tau})\tau}{(-1+b)T}\right] - \\ 2b\tau^2 \text{PolyLog}\left[2, -\frac{b(1-e^{-T/\tau})\tau}{T-bT}\right] + 2b e^{T/\tau} \tau^2 \text{PolyLog}\left[2, -\frac{b(1-e^{-T/\tau})\tau}{T-bT}\right] - \\ 2\tau^2 \text{PolyLog}\left[2, \frac{T-bT}{b\tau-b e^{T/\tau}\tau}\right] + 2b\tau^2 \text{PolyLog}\left[2, \frac{T-bT}{b\tau-b e^{T/\tau}\tau}\right] + \\ \left. 2e^{T/\tau} \tau^2 \text{PolyLog}\left[2, \frac{T-bT}{b\tau-b e^{T/\tau}\tau}\right] - 2b e^{T/\tau} \tau^2 \text{PolyLog}\left[2, \frac{T-bT}{b\tau-b e^{T/\tau}\tau}\right] \right)$$

```
In[10]:= fbb = Integrate[(∂b Log[n * p])2 * (n * p), {t, 0, T}, Assumptions → pAssumptions]
```

$$\text{Out[10]} = -\frac{n((-1+b)T - \tau \log[T - bT + b(-1+e^{T/\tau})\tau] + \tau \log[-b\tau + e^{T/\tau}(T - bT + b\tau)])}{(-1+b)^2 b T}$$

```
In[11]:= f = {{fττ, fτb}, {fτb, fbb}};
```

The CRLB ( $\sigma_\tau^2$ ) is given the first diagonal element of the inverse Fisher matrix:

In[12]:=  $\sigma\tau\text{SQ} = \text{SimplifyCRLB}[\text{First@First@Inverse}[f /. \{T \rightarrow \chi \tau\}]]$

$$\begin{aligned} \text{Out[12]} = & \left( 4 (-1 + e^x)^2 \tau^2 \chi \left( (-1 + b) \chi - \text{Log}[b (-1 + e^x - \chi) + \chi] + \text{Log}[-b + e^x (b + \chi - b \chi)] \right) \right) / \\ & \left( n \left( b \left( 2 \chi - 2 e^x \chi + 2 \chi^2 - b \chi^2 + b e^x \chi^2 - 2 b (-1 + e^x) \chi \text{Log}\left[1 - \frac{b (-1 + e^x)}{(-1 + b) \chi}\right] - \right. \right. \right. \\ & 2 (-1 + b) (-1 + e^x) \chi \left( \text{Log}[b (-1 + e^x)] - \text{Log}[b (-1 + e^x - \chi) + \chi] \right) + 2 (-1 + e^x - \chi) \\ & \text{Log}\left[\frac{e^x (b (-1 + e^x - \chi) + \chi)}{-b + e^x (b + \chi - b \chi)}\right] - 2 b (-1 + e^x) \text{PolyLog}\left[2, \frac{b (-1 + e^x)}{(-1 + b) \chi}\right] - \\ & 2 (-1 + b) (-1 + e^x) \text{PolyLog}\left[2, \frac{(-1 + b) \chi}{b (-1 + e^x)}\right] + 2 (-1 + b) (-1 + e^x) \\ & \text{PolyLog}\left[2, \frac{(-1 + b) e^x \chi}{b (-1 + e^x)}\right] + 2 b (-1 + e^x) \text{PolyLog}\left[2, -\frac{b - b e^{-x}}{\chi - b \chi}\right] \Big)^2 + \\ & 4 \left( (-1 + b) \chi - \text{Log}[b (-1 + e^x - \chi) + \chi] + \text{Log}[-b + e^x (b + \chi - b \chi)] \right) \\ & \left( \chi - 2 b \chi - 2 e^x \chi + 4 b e^x \chi + e^{2x} \chi - 2 b e^{2x} \chi - 2 b \chi^2 + 2 b e^x \chi^2 - b \chi^3 - e^x \chi^3 + b e^x \chi^3 - \right. \\ & b (-1 + e^x) \chi (2 + e^x (-2 + \chi) + \chi) (\text{Log}[b (-1 + e^x)] - \text{Log}[b (-1 + e^x - \chi) + \chi]) + \\ & b (1 - e^x + \chi)^2 \text{Log}\left[\frac{e^x (b (-1 + e^x - \chi) + \chi)}{-b + e^x (b + \chi - b \chi)}\right] - 2 b (-1 + e^x) (1 + e^x (-1 + \chi)) \\ & \text{PolyLog}\left[2, \frac{(-1 + b) \chi}{b (-1 + e^x)}\right] - 2 b (-1 + e^x) (-1 + e^x - \chi) \text{PolyLog}\left[2, \frac{(-1 + b) e^x \chi}{b (-1 + e^x)}\right] - \\ & \left. 2 b (-1 + e^x)^2 \text{PolyLog}\left[3, \frac{(-1 + b) \chi}{b (-1 + e^x)}\right] + 2 b (-1 + e^x)^2 \text{PolyLog}\left[3, \frac{(-1 + b) e^x \chi}{b (-1 + e^x)}\right] \right) \Big) \end{aligned}$$

Limit for zero background:

In[13]:= **Assuming[pAssumptions, FullSimplify[1/Limit[1/στSQ, b → 0, Direction → "FromAbove"]]]**  
 (\* The limits of 1/στSQ are somehow much faster to compute. \*)

$$\begin{aligned} \text{Out[13]} = & \frac{4 \tau^2 (2 + \chi^2 - 2 \cosh[\chi]) \sinh\left[\frac{\chi}{2}\right]}{n \left( -4 \chi^3 \cosh\left[\frac{\chi}{2}\right] + (12 + 12 \chi^2 + \chi^4) \sinh\left[\frac{\chi}{2}\right] - 4 \sinh\left[\frac{3\chi}{2}\right] \right)} \end{aligned}$$

Limit for infinite pulse period:

In[14]:= **1/Limit[1/στSQ, χ → ∞, Assumptions → pAssumptions, Direction → "FromBelow"]**

$$\begin{aligned} \text{Out[14]} = & \frac{\tau^2}{n - b n} \end{aligned}$$

## CRLB of the background estimation

In[15]:= **obSQ = SimplifyCRLB[Last@Last@Inverse[f /. {T → χ τ}]]**

$$\begin{aligned} \text{Out[15]} = & - \left( \left( 4 (-1+b)^2 \chi \left( \chi - 2b\chi - 2e^\chi \chi + 4b e^\chi \chi + e^{2\chi} \chi - 2b e^{2\chi} \chi - 2b \chi^2 + 2b e^\chi \chi^2 - b \chi^3 - e^\chi \chi^3 + \right. \right. \right. \\ & b e^\chi \chi^3 - b (-1+e^\chi) \chi (2+e^\chi (-2+\chi) + \chi) (\text{Log}[b (-1+e^\chi)] - \text{Log}[b (-1+e^\chi - \chi) + \chi]) + \\ & b (1-e^\chi + \chi)^2 \text{Log}\left[\frac{e^\chi (b (-1+e^\chi - \chi) + \chi)}{-b + e^\chi (b + \chi - b \chi)}\right] - 2b (-1+e^\chi) (1+e^\chi (-1+\chi)) \\ & \text{PolyLog}\left[2, \frac{(-1+b) \chi}{b (-1+e^\chi)}\right] - 2b (-1+e^\chi) (-1+e^\chi - \chi) \text{PolyLog}\left[2, \frac{(-1+b) e^\chi \chi}{b (-1+e^\chi)}\right] - \\ & \left. \left. 2b (-1+e^\chi)^2 \text{PolyLog}\left[3, \frac{(-1+b) \chi}{b (-1+e^\chi)}\right] + 2b (-1+e^\chi)^2 \text{PolyLog}\left[3, \frac{(-1+b) e^\chi \chi}{b (-1+e^\chi)}\right]\right) \right) / \\ & \left( n \left( \left( 2\chi - 2e^\chi \chi + 2\chi^2 - b \chi^2 + b e^\chi \chi^2 - 2b (-1+e^\chi) \chi \text{Log}\left[1 - \frac{b (-1+e^\chi)}{(-1+b) \chi}\right] - \right. \right. \right. \\ & 2 (-1+b) (-1+e^\chi) \chi (\text{Log}[b (-1+e^\chi)] - \text{Log}[b (-1+e^\chi - \chi) + \chi]) + 2 (-1+e^\chi - \chi) \\ & \text{Log}\left[\frac{e^\chi (b (-1+e^\chi - \chi) + \chi)}{-b + e^\chi (b + \chi - b \chi)}\right] - 2b (-1+e^\chi) \text{PolyLog}\left[2, \frac{b (-1+e^\chi)}{(-1+b) \chi}\right] - \\ & 2 (-1+b) (-1+e^\chi) \text{PolyLog}\left[2, \frac{(-1+b) \chi}{b (-1+e^\chi)}\right] + 2 (-1+b) (-1+e^\chi) \\ & \text{PolyLog}\left[2, \frac{(-1+b) e^\chi \chi}{b (-1+e^\chi)}\right] + 2b (-1+e^\chi) \text{PolyLog}\left[2, -\frac{b-b e^{-\chi}}{\chi-b \chi}\right] \right)^2 + \\ & \frac{1}{b} 4 \left( (-1+b) \chi - \text{Log}[b (-1+e^\chi - \chi) + \chi] + \text{Log}[-b + e^\chi (b + \chi - b \chi)] \right) \\ & \left( \chi - 2b \chi - 2e^\chi \chi + 4b e^\chi \chi + e^{2\chi} \chi - 2b e^{2\chi} \chi - 2b \chi^2 + 2b e^\chi \chi^2 - b \chi^3 - e^\chi \chi^3 + b e^\chi \chi^3 - \right. \\ & b (-1+e^\chi) \chi (2+e^\chi (-2+\chi) + \chi) (\text{Log}[b (-1+e^\chi)] - \text{Log}[b (-1+e^\chi - \chi) + \chi]) + \\ & b (1-e^\chi + \chi)^2 \text{Log}\left[\frac{e^\chi (b (-1+e^\chi - \chi) + \chi)}{-b + e^\chi (b + \chi - b \chi)}\right] - 2b (-1+e^\chi) (1+e^\chi (-1+\chi)) \text{PolyLog}\left[ \right. \\ & \left. \left. 2, \frac{(-1+b) \chi}{b (-1+e^\chi)}\right] - 2b (-1+e^\chi) (-1+e^\chi - \chi) \text{PolyLog}\left[2, \frac{(-1+b) e^\chi \chi}{b (-1+e^\chi)}\right] - 2b \right. \\ & \left. \left. (-1+e^\chi)^2 \text{PolyLog}\left[3, \frac{(-1+b) \chi}{b (-1+e^\chi)}\right] + 2b (-1+e^\chi)^2 \text{PolyLog}\left[3, \frac{(-1+b) e^\chi \chi}{b (-1+e^\chi)}\right]\right) \right) \right) \end{aligned}$$

Limit for zero background:

In[16]:= **Assuming[pAssumptions, FullSimplify[1/Limit[1/obSQ, b → 0, Direction → "FromAbove"]]]**

$$\text{Out[16]} = - \frac{2 \chi^2 (2 + \chi^2 - 2 \text{Cosh}[\chi])}{n (12 + 12 \chi^2 + \chi^4 - (16 + 12 \chi^2 + \chi^4) \text{Cosh}[\chi] + 4 \text{Cosh}[2 \chi] + 4 \chi^3 \text{Sinh}[\chi])}$$

Limit for infinite pulse period:

In[17]:= **Limit[obSQ, {χ → ∞}, Assumptions → pAssumptions]**

$$\text{Out[17]} = - \frac{(-1+b) b}{n}$$