Supporting Material of

Video-Based Tracking of Single Molecules Exhibiting Directed In-frame Motion

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Derivatives of the log-likelihood function

In this note, we derive the first and second order derviatives of the log-likelihood function (Eq. 7 in the main article), with respect to $\mathbf{\Theta}$, which are used both in the Cramer-Rao Lower Bound computation and the iterative Maximum Likelihood algorithm.

First Order Derivatives:

A general expression for the first order partial derivative of the log-likelihood function with respect to the components of $\mathbf{\Theta}$ can be written as:

$$\frac{\partial L(\mathbf{\Theta})}{\partial \mathbf{\Theta}_i} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial \Lambda_k(T)}{\partial \mathbf{\Theta}_i}. \quad (1)$$

- Partial derivative with respect to x_0:

$$\frac{\partial L(\mathbf{\Theta})}{\partial x_0} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial \Lambda_k(T)}{\partial x_0}, \quad (2)$$

where

$$\frac{\partial \Lambda_k(T)}{\partial x_0} = \lambda_0 \int_0^T \frac{\partial p_k(\tau)}{\partial x_0} d\tau. \quad (3)$$

We can write $p_k(\tau)$ as

$$\begin{aligned} p_k(\tau) &= \int_{y_{k1}}^{y_{k2}} \int_{x_{k1}}^{x_{k2}} g(x - x_0 - v_x\tau, y - y_0 - v_y\tau) dxdy \\ &= \int_{y_{k1}-y_0-v_y\tau}^{y_{k2}-y_0-v_y\tau} \int_{x_{k1}-x_0-v_x\tau}^{x_{k2}-x_0-v_x\tau} g(x, y) dxdy. \end{aligned}$$

Therefore, the partial derivative of $p_k(\tau)$ with respect to x_0 can be written as

$$\begin{aligned}\frac{\partial p_k(\tau)}{\partial x_0} &= \int_{y_{k1}-y_0-v_y\tau}^{y_{k2}-y_0-v_y\tau} \frac{\partial}{\partial x_0}(\int_{x_{k1}-x_0-v_x\tau}^{x_{k2}-x_0-v_x\tau} g(x,y)dxdy) \\ &= \int_{y_{k1}-y_0-v_y\tau}^{y_{k2}-y_0-v_y\tau} (g(x_{k1}-x_0-v_x\tau,y) - g(x_{k2}-x_0-v_x\tau,y))dy.\end{aligned}$$

If the point spread function is Gaussian, with parameter σ, i.e.,

$$g(x,y) = \frac{1}{2\pi\sigma^2}e^{-\frac{x^2+y^2}{2\sigma^2}} = \frac{1}{\sigma^2}G(\frac{x}{\sigma})G(\frac{y}{\sigma}),$$

where $G(a) = \frac{1}{\sqrt{2\pi}}e^{-\frac{a^2}{2}}$, we can write the probability $p_k(\tau)$ as

$$p_k(\tau) = Q_{kx}(\tau)Q_{ky}(\tau), \tag{4}$$

where

$$\begin{aligned}Q_{kx}(\tau) &= \int_{\frac{x_{k1}-x_0-v_x\tau}{\sqrt{2}\sigma}}^{\frac{x_{k2}-x_0-v_x\tau}{\sqrt{2}\sigma}} \frac{e^{-x^2}}{\sqrt{\pi}}dx \\ &= \frac{1}{2}(erf(\frac{x_{k2}-x_0-v_x\tau}{\sqrt{2}\sigma}) - erf(\frac{x_{k1}-x_0-v_x\tau}{\sqrt{2}\sigma}))\end{aligned} \tag{5}$$

as

$$erf(a) = \frac{2}{\sqrt{\pi}}\int_0^a e^{-t^2}dt.$$

Similarly

$$\begin{aligned}Q_{ky}(\tau) &= \int_{\frac{y_{k1}-x_0-v_y\tau}{\sqrt{2}\sigma}}^{\frac{y_{k2}-x_0-v_y\tau}{\sqrt{2}\sigma}} \frac{e^{-y^2}}{\sqrt{\pi}}dx \\ &= \frac{1}{2}(erf(\frac{y_{k2}-x_0-v_y\tau}{\sqrt{2}\sigma}) - erf(\frac{y_{k1}-x_0-v_y\tau}{\sqrt{2}\sigma})).\end{aligned} \tag{6}$$

Thus we obtain

$$\frac{\partial p_k(\tau)}{\partial x_0} = \frac{\partial Q_{kx}(\tau)}{\partial x_0}Q_{ky}, \tag{7}$$

where

$$\begin{aligned}\frac{\partial Q_{kx}}{\partial x_0} &= \frac{1}{\sqrt{2\pi}\sigma}(e^{-\frac{(x_{k1}-x_0-v_x\tau)^2}{2\sigma^2}} - e^{-\frac{(x_{k2}-x_0-v_x\tau)^2}{2\sigma^2}}) \\ &= -\frac{1}{\sqrt{2\pi}\sigma}e^{-\frac{(x_{k1}-x_0-v_x\tau)^2}{2\sigma^2}}(e^{\frac{2\Delta_x(x_0+v_x\tau-x_{k1})-\Delta_x^2}{2\sigma^2}} - 1).\end{aligned} \tag{8}$$

- Partial derivative with respect to y_0 can be similarly obtained as:

$$\frac{\partial L(\mathbf{\Theta})}{\partial y_0} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial \Lambda_k(T)}{\partial y_0}, \tag{9}$$

where

$$\frac{\partial \Lambda_k(T)}{\partial y_0} = \lambda_0 \int_0^T \frac{\partial p_k(\tau)}{\partial y_0} d\tau, \tag{10}$$

and

$$\frac{\partial p_k(\tau)}{\partial y_0} = \int_{x_{k1}-x_0-v_x\tau}^{x_{k2}-x_0-v_x\tau} (g(x, y_{k1} - y_0 - v_y\tau) - g(x, y_{k2} - y_0 - v_y\tau))dx.$$

If the point spread function is Gaussian, with parameter σ,

$$\frac{\partial p_k(\tau)}{\partial y_0} = \frac{\partial Q_{ky}(\tau)}{\partial y_0} Q_{kx}, \tag{11}$$

where

$$\begin{aligned} \frac{\partial Q_{ky}}{\partial y_0} &= \frac{1}{\sqrt{2\pi}\sigma}(e^{-\frac{(y_{k1}-y_0-v_y\tau)^2}{2\sigma^2}} - e^{-\frac{(y_{k2}-y_0-v_y\tau)^2}{2\sigma^2}}) \\ &= -\frac{1}{\sqrt{2\pi}\sigma} e^{-\frac{(y_{k1}-y_0-v_y\tau)^2}{2\sigma^2}} (e^{\frac{2\Delta_y(y_0+v_y\tau-y_{k1})-\Delta_y^2}{2\sigma^2}} - 1). \end{aligned} \tag{12}$$

- Partial derivative with respect to v_x:

$$\frac{\partial L(\mathbf{\Theta})}{\partial v_x} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial \Lambda_k(T)}{\partial v_x}, \tag{13}$$

where

$$\frac{\partial \Lambda_k(T)}{\partial v_x} = \lambda_0 \int_0^T \frac{\partial p_k(\tau)}{\partial v_x} d\tau, \tag{14}$$

and

$$\frac{\partial p_k(\tau)}{\partial v_x} = \tau \int_{y_{k1}-y_0-v_y\tau}^{y_{k2}-y_0-v_y\tau} (g(x_{k1} - x_0 - v_x\tau, y) - g(x_{k2} - x_0 - v_x\tau, y))dy.$$

We note that

$$\frac{\partial p_k(\tau)}{\partial v_x} = \tau \frac{\partial p_k(\tau)}{\partial x_0}. \tag{15}$$

- Partial derivative with respect to v_y can be similarly obtained as:

$$\frac{\partial L(\mathbf{\Theta})}{\partial v_y} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial \Lambda_k(T)}{\partial v_y}, \tag{16}$$

where

$$\frac{\partial \Lambda_k(T)}{\partial v_y} = \lambda_0 \int_0^T \frac{\partial p_k(\tau)}{\partial v_y} d\tau, \tag{17}$$

and

$$\frac{\partial p_k(\tau)}{\partial v_y} = \tau \int_{x_{k1}-x_0-v_x\tau}^{x_{k2}-x_0-v_x\tau} (g(x, y_{k1} - y_0 - v_y\tau) - g(x, y_{k2} - y_0 - v_y\tau))dx.$$

Again, we note that

$$\frac{\partial p_k(\tau)}{\partial v_y} = \tau \frac{\partial p_k(\tau)}{\partial y_0}. \tag{18}$$

- Partial derivative with respect to λ_0:

$$\frac{\partial L(\mathbf{\Theta})}{\partial \lambda_0} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial \Lambda_k(T)}{\partial \lambda_0}, \tag{19}$$

where

$$\frac{\partial \Lambda_k(T)}{\partial \lambda_0} = \int_0^T p_k(\tau) d\tau. \tag{20}$$

Therefore,

$$\frac{\partial L(\mathbf{\Theta})}{\partial \lambda_0} = \sum_{k=1}^{N} \left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \int_0^T p_k(\tau) d\tau. \tag{21}$$

- Partial derivative with respect to λ_{bg}:

$$\frac{\partial L(\mathbf{\Theta})}{\partial \lambda_{bg}} = \sum_{k=1}^{N} (\frac{m_k}{\Lambda_k(T)} - 1) \frac{\partial \Lambda_k(T)}{\partial \lambda_{bg}}, \tag{22}$$

where

$$\frac{\partial \Lambda_k(T)}{\partial \lambda_{bg}} = T. \tag{23}$$

Therefore,

$$\frac{\partial L(\mathbf{\Theta})}{\partial \lambda_{bg}} = T \sum_{k=1}^{N} \frac{m_k}{\Lambda_k(T)} - TN. \tag{24}$$

Second Order Derivatives:

A general expression for the second order partial derivative of the log-likelihood function with respect to the components of $\mathbf{\Theta}$ can be written as:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial \mathbf{\Theta}_i \partial \mathbf{\Theta}_j} = \sum_{k=1}^{N} \left(\left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial^2 \Lambda_k(T)}{\partial \mathbf{\Theta}_i \partial \mathbf{\Theta}_j} - \frac{m_k}{\Lambda_k^2(T)} \frac{\partial \Lambda_k(T)}{\partial \mathbf{\Theta}_i} \frac{\partial \Lambda_k(T)}{\partial \mathbf{\Theta}_j} \right). \tag{25}$$

We will only consider the case $\mathbf{\Theta}_i = \mathbf{\Theta}_j$, as the algorithm will be using only the diagonal terms of the Hessian matrix.

- The second order partial derivative with respect to x_0:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial x_0^2} = \sum_{k=1}^{N} \left(\left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial^2 \Lambda_k(T)}{\partial x_0^2} - \frac{m_k}{\Lambda_k^2(T)} \left(\frac{\partial \Lambda_k(T)}{\partial x_0} \right)^2 \right), \tag{26}$$

where

$$\frac{\partial^2 \Lambda_k(T)}{\partial x_0^2} = \lambda_0 \int_0^T \frac{\partial^2 p_k(\tau)}{\partial x_0^2} d\tau. \tag{27}$$

If the point spread function is Gaussian with parameter σ, we can write

$$\frac{\partial^2 p_k(\tau)}{\partial x_0^2} = \frac{1}{\sqrt{2\pi}\sigma^3} \left((x_{k1} - x_0 - v_x\tau) e^{-\frac{(x_{k1}-x_0-v_x\tau)^2}{2\sigma^2}} \right. \\ \left. -(x_{k2} - x_0 - v_x\tau) e^{-\frac{(x_{k2}-x_0-v_x\tau)^2}{2\sigma^2}} \right) \times Q_{ky}(\tau).$$

- The second order partial derivative with respect to y_0:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial y_0^2} = \sum_{k=1}^{N} \left(\left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial^2 \Lambda_k(T)}{\partial y_0^2} - \frac{m_k}{\Lambda_k^2(T)} \left(\frac{\partial \Lambda_k(T)}{\partial y_0} \right)^2 \right), \tag{28}$$

where

$$\frac{\partial^2 \Lambda_k(T)}{\partial y_0^2} = \lambda_0 \int_0^T \frac{\partial^2 p_k(\tau)}{\partial y_0^2} d\tau. \tag{29}$$

If the point spread function is Gaussian, with parameter σ, we can write

$$\frac{\partial^2 p_k(\tau)}{\partial y_0^2} = \frac{1}{\sqrt{2\pi}\sigma^3} \left((y_{k1} - y_0 - y_x\tau) e^{-\frac{(y_{k1}-y_0-v_y\tau)^2}{2\sigma^2}} \right. \\ \left. -(y_{k2} - y_0 - y_x\tau) e^{-\frac{(y_{k2}-y_0-y_x\tau)^2}{2\sigma^2}} \right) \times Q_{kx}(\tau).$$

- The second order partial derivative with respect to v_x:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial v_x^2} = \sum_{k=1}^{N} \left(\left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial^2 \Lambda_k(T)}{\partial v_x^2} - \frac{m_k}{\Lambda_k^2(T)} \left(\frac{\partial \Lambda_k(T)}{\partial v_x} \right)^2 \right), \tag{30}$$

where

$$\frac{\partial^2 \Lambda_k(T)}{\partial v_x^2} = \lambda_0 \int_0^T \frac{\partial^2 p_k(\tau)}{\partial v_x^2} d\tau. \tag{31}$$

If the point spread function is Gaussian, with parameter σ, we can write

$$\frac{\partial^2 p_k(\tau)}{\partial v_x^2} = \tau^2 \frac{\partial^2 p_k(\tau)}{\partial x_0^2}.$$

- The second order partial derivative with respect to v_y:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial v_y^2} = \sum_{k=1}^{N} \left(\left(\frac{m_k}{\Lambda_k(T)} - 1 \right) \frac{\partial^2 \Lambda_k(T)}{\partial v_y^2} - \frac{m_k}{\Lambda_k^2(T)} \left(\frac{\partial \Lambda_k(T)}{\partial v_y} \right)^2 \right), \tag{32}$$

where

$$\frac{\partial^2 \Lambda_k(T)}{\partial v_y^2} = \lambda_0 \int_0^T \frac{\partial^2 p_k(\tau)}{\partial v_y^2} d\tau, \tag{33}$$

If the point spread function is Gaussian, with parameter σ, we can write

$$\frac{\partial^2 p_k(\tau)}{\partial v_y^2} = \tau^2 \frac{\partial^2 p_k(\tau)}{\partial y_0^2}.$$

- The second order partial derivative with respect to λ_0:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial \lambda_0^2} = -\sum_{k=1}^{N} \frac{m_k}{\Lambda_k(T)^2} \left(\frac{\partial \Lambda_k(T)}{\partial \lambda_0} \right) \tag{34}$$

- The second order partial derivative with respect to λ_{bg}:

$$\frac{\partial^2 L(\mathbf{\Theta})}{\partial \lambda_{bg}^2} = -\sum_{k=1}^{N} \frac{m_k}{\Lambda_k(T)^2} \left(\frac{\partial \Lambda_k(T)}{\partial \lambda_{bg}} \right)^2 \tag{35}$$