SUPPLEMENTARY MATERIALS: FISHER INFORMATION MATRIX FOR SINGLE MOLECULES WITH STOCHASTIC TRAJECTORIES *

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SM1. Proof of Theorem 2.2. 1. According to [SM6, SM7] and Lemma SM14.1 (see Section SM14.1), the probability \( P(D_t = \emptyset, N(t) = 0) \) is given by

\[
P(D_t = \emptyset, N(t) = 0) = P(N(t) = 0) = e^{-\int_0^t \Lambda(\tau) \, d\tau}.
\]

Also, the probability density function \( p_t \) of \( D_t \) and \( N(t) \) is given by

(SM1.1) \[
p_t(d_K) = p_{D_t|T_N}^t(\tau_1, \ldots, \tau_K|N(t)) p_{P_N|N}^t(\tau_1, \ldots, \tau_K|K) P(N(t) = K),
\]

where \( d_K \in C^t \times \mathbb{R}^t_+ \) and \( K = 1, 2, \ldots \). According to Lemma SM14.1 (see Section SM14.1),

(SM1.2) \[
P(N(t) = K) = \frac{1}{K!} e^{-\int_0^t \Lambda(\tau) \, d\tau} \left( \int_0^t \Lambda(\tau) \, d\tau \right)^K, \quad K = 0, 1, \ldots,
\]

and

(SM1.3) \[
p_{P_t|N}^t(\tau_1, \ldots, \tau_K|K) = K! \prod_{k=1}^K \Lambda(\tau_k), \quad K = 1, 2, \ldots,
\]

and using the assumption of Definition 2.1 (it is assumed that \( U_t, l = 1, \ldots, K, \) is only dependent of the previous and current time points \( T_1, \ldots, T_l \), and is independent of the future time points \( T_{l+1}, \ldots, T_K \) and the total number \( N(t) \) of the detected photons),

\[
p_{U_t|T_K, N(t)}(\tau_1, \ldots, \tau_K|\tau_1, \ldots, \tau_K, K)
\]

\[
= p_{U_K|T_K}(\tau_1, \ldots, \tau_K|\tau_1, \ldots, \tau_K)
\]

\[
= p_{U_K|T_K, \mathcal{D}_{K-1}}(\tau_K|\tau_{K-1}, d_{K-1}) p_{U_{K-1}|T_{K-1}, T_K, \mathcal{D}_{K-2}}(\tau_{K-1}|\tau_{K-2}, d_{K-2})
\]

\[
\times \cdots \times p_{U_1|T_1}(\tau_1|\tau_1, \ldots, \tau_1)
\]

\[
= p_{U_K|T_K, \mathcal{D}_{K-1}}(\tau_K|\tau_{K-1}, d_{K-1}) p_{U_{K-1}|T_{K-1}, \mathcal{D}_{K-2}}(\tau_{K-1}|\tau_{K-2}, d_{K-2})
\]

\[
\times \cdots \times p_{U_1|T_1}(\tau_1|\tau_1)
\]

(SM1.4) \[
= \prod_{l=1}^K p_{U_l|T_l, \mathcal{D}_{l-1}}(\tau_l|\tau_l, d_{l-1}).
\]

*Submitted to the editors February 2, 2019.

Funding: This work was supported in part by the National Institutes of Health (R01 GM085575).

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where \( p_{U_{i}|T_{i}, d_{i-1}}(r_{i}|\tau_{i}, d_{0}) := p_{U_{i}|T_{i}}(r_{i}|\tau_{i}) \). By substituting Eqs. (SM1.2)-(SM1.4) into Eq. (SM1.1), we have

\[
p_{[\cdot]}(d_{K}, K) = e^{-\int_{0}^{\tau_{K}} \Lambda(r) dr} \prod_{k=1}^{K} \Lambda(\tau_{k}) \left[ \prod_{l=1}^{K} p_{U_{i}|T_{i}, d_{l-1}}(r_{l}|\tau_{l}, d_{l-1}) \right].
\]

2. The probability density function \( p_{L} \) of \( D_{L} \) is given by

\[
p_{L}(d_{L}) = p_{U_{L}|T_{L}}(r_{1}, \ldots, r_{L}|T_{1}, \ldots, T_{L}) p_{T_{L}}(T_{1}, \ldots, T_{L})
\]

(SM1.5)

\[
= \left[ \prod_{l=1}^{L} p_{U_{l}|T_{l}, d_{l-1}}(r_{l}|\tau_{l}, d_{l-1}) \right] p_{T_{L}}(T_{1}, \ldots, T_{L}),
\]

where \( d_{l} \in C \times \mathbb{R}_{[0, \infty]} \) and whereby Lemma SM14.1 (see Section SM14.1),

\[
(SM1.6)
p_{T_{L}}(T_{1}, \ldots, T_{L}) = e^{-\int_{0}^{\tau_{L}} \Lambda(r) dr} \prod_{k=1}^{L} \Lambda(\tau_{k}).
\]

By substituting Eq. (SM1.6) into Eq. (SM1.5), we have

\[
p_{L}(d_{L}) = e^{-\int_{0}^{\tau_{L}} \Lambda(r) dr} \prod_{k=1}^{L} \Lambda(\tau_{k}) \left[ \prod_{l=1}^{L} p_{U_{l}|T_{l}, d_{l-1}}(r_{l}|\tau_{l}, d_{l-1}) \right],
\]

and it completes the proof.

**SM2. Proof of Corollary 2.4.** The conditional probability density function \( p_{U_{i}|T_{i}, d_{i-1}} \) in Eqs. (2.1) and (2.2) of Theorem 2.2 can be written as, for \( x := (x_{0}, y_{0}, z_{0}) \in \mathbb{R}^{3} \),

\[
p_{U_{i}|T_{i}, d_{i-1}}(r_{i}|\tau_{i}, d_{i-1})
\]

(SM2.1)

\[
= \int_{\mathbb{R}^{3}} p_{U_{i}|X(T_{i})|T_{i}, d_{i-1}}(r_{i}, x|\tau_{i}, d_{i-1}) dx
\]

\[
= \int_{\mathbb{R}^{3}} p_{U_{i}|X(T_{i})|T_{i}, d_{i-1}}(r_{i}|x, \tau_{i}, d_{i-1}) p_{X(T_{i})|T_{i}, d_{i-1}}(x|\tau_{i}, d_{i-1}) dx
\]

\[
= \int_{\mathbb{R}^{3}} f_{x}(r_{i}) p_{pr_{i}}(x|\tau_{i}, d_{i-1}) dx
\]

\[
= \frac{1}{|\text{det}(M)|} \int_{\mathbb{R}^{3}} q_{x_{0}}(M^{-1} r_{i} - (x_{0}, y_{0})) p_{pr_{i}}(x|\tau_{i}, d_{i-1}) dx,
\]

where \( d_{l} \in C \times \mathbb{R}_{[0, \infty]} \) for \( G_{[i]} \) (or \( d_{l} \in C \times \mathbb{R}_{[0, \infty]} \) for \( G_{L} \)), \( p_{pr_{i}} := p_{X(T_{i})|T_{i}, d_{i-1}}, l = 1, 2, \ldots \), denotes the distribution of the prediction of the object location, and \( p_{pr_{i}}(x|\tau_{i}, d_{0}) := p_{pr_{i}}(x|\tau_{i}) \), in which we have used the assumption of Definition 2.3.

**SM3. Proof of Theorem 3.2.** Let \( G_{[i]} \left( \left( \tilde{X}, H, \tilde{W}, Z \right), \left( U_{[i]}, T_{[i]} \right), \Phi, C, \Theta \right) \) (or \( G_{L} \left( \left( \tilde{X}, H, \tilde{W}, Z \right), \left( U_{L}, T_{L} \right), \tilde{\Phi}, C, \Theta \right) \)) be an image detection process with expanded state space \( \tilde{X} \) for a time interval \( [t_{0}, t] \) (or for a fixed number \( L \) of photons). Let \( D_{k} := (U_{k}, T_{k}), k = 0, 1, \ldots, \) and

\[
\tilde{p}_{pr_{i}}(\tilde{x}|\tau_{i}, d_{i-1}) := p_{\tilde{X}(T_{i})|T_{i}, d_{i-1}}(\tilde{x}|\tau_{i}, d_{i-1}), \quad \tilde{x} \in \mathbb{R}^{k},
\]

where \( p_{\tilde{X}(T_{i})|T_{i}, d_{i-1}}(\tilde{x}|\tau_{i}, d_{i-1}) \).
where $d_l \in C^l \times \mathbb{R}^d_0$ (or $d_l \in C^l \times \mathbb{R}^d_{[0,\infty)}$), be the distribution of the prediction of the object location, and $\tilde{p}_{pr_1}(\tilde{x} | \tau_1, d_0) := p_{pr_1}(\tilde{x} | \tau_1)$.

1. If $H = [H_{3 \times 3} \ 0_{(k-3) \times (k-3)}]$, then, for $x = H\tilde{x}, x := (x_1, x_2, x_3)^T \in \mathbb{R}^3, \tilde{x} := (\tilde{x}_1, \cdots, \tilde{x}_k)^T \in \mathbb{R}^k$, we have $\tilde{x} = (x_1, x_2, x_3, \tilde{x}_4, \cdots, \tilde{x}_k)^T$ and the probability density function $p_{pr_1} := p_{X(T_1) | T_1, D_{l-1}}$ is given by

$$p_{pr_1}(x | \tau_l, d_{l-1}) = \int_{\mathbb{R}^k} \tilde{p}_{pr_1}(\tilde{x} | \tau_l, d_{l-1}) d\tilde{x}_4 \cdots d\tilde{x}_k,$$

Next, we extend the results obtained in the previous part to more general matrices $H$. Assume that there exists non-singular matrix $H_1 \in \mathbb{R}^{3 \times 3}$ and matrix $H_2 \in \mathbb{R}^{3 \times (k-3)}$ such that $H = [H_1 \ H_2]$. Let $X(\tau) = S \tilde{X}(\tau), \tau \geq t_0$, where

$$S := \begin{bmatrix} H_1 & H_2 \\ 0_{(k-3) \times 3} & I_{(k-3) \times (k-3)} \end{bmatrix} \in \mathbb{R}^{k \times k}.$$

Hence, $S$ is a non-singular matrix with determinant $\det(S) = \det(H_1) \neq 0$ and $S^{-1}$ exists. Then, for $\dot{x} = S \tilde{x}, \dot{x} := (\dot{x}_1, \cdots, \dot{x}_k)^T \in \mathbb{R}^k, \tilde{x} := (\tilde{x}_1, \cdots, \tilde{x}_k)^T \in \mathbb{R}^k$, we have

$$\dot{x} = S \tilde{x} = (H \tilde{x}, \tilde{x}_4, \cdots, \tilde{x}_k)^T = (x_1, x_2, x_3, \tilde{x}_4, \cdots, \tilde{x}_k)^T,$$

and, according to Eq. (SM3.1),

$$p_{pr_1}(x | \tau_l, d_{l-1}) = \int_{\mathbb{R}^k} \tilde{p}_{pr_1}(\tilde{x} | \tau_l, d_{l-1}) d\tilde{x}_4 \cdots d\tilde{x}_k$$

$$= \int_{\mathbb{R}^k} \tilde{p}_{pr_1}(S^{-1} \tilde{x} | \tau_l, d_{l-1}) |H_1|^{-1} d\tilde{x}_4 \cdots d\tilde{x}_k,$$

where $\tilde{p}_{pr_1} := p_{X(T_1) | T_1, D_{l-1}}$ and $S^{-1}$ is given by

$$S^{-1} = \begin{bmatrix} H_1^{-1} & -H_1^{-1}H_2 \\ 0_{(k-3) \times 3} & I_{(k-3) \times (k-3)} \end{bmatrix}.$$

2. Then, $\tilde{p}_{pr_1}$ can be calculated through the following steps:

Step 1. For $l = 0$, Eq. (3.5) becomes

$$\tilde{X}(T_1) = \tilde{\phi}(t_0, T_1) \tilde{X}(t_0) + \tilde{W}(t_0, T_1).$$

Then, by conditioning the both sides of the above equation on $T_1 = \tau_1$, the conditional probability density function $p_{\tilde{X}(T_1) | T_1}$ is given by

$$p_{\tilde{X}(T_1) | T_1}(\tilde{x} | \tau_1) = \left( p_{\tilde{\phi}(t_0, \tau_1) \tilde{X}(t_0) * p_{\tilde{W}(t_0, \tau_1)}}^{\tilde{\phi}(t_0, \tau_1) \tilde{X}(t_0) * p_{\tilde{W}(t_0, \tau_1)}}(\tilde{x}) \right),$$

where $\tilde{x} \in \mathbb{R}^k$, and $*$ denotes the convolution operator. Then,

$$\tilde{p}_{pr_1}(\tilde{x} | \tau_1) := p_{\tilde{X}(T_1) | T_1}(\tilde{x} | \tau_1)$$

$$= \int_{\mathbb{R}^k} p_{\tilde{\phi}(t_0, \tau_1) \tilde{X}(t_0)}^{\tilde{\phi}(t_0, \tau_1) \tilde{X}(t_0)}(\tilde{x}_0) p_{\tilde{W}(t_0, \tau_1)}^{\tilde{W}(t_0, \tau_1)}(\tilde{x} - \tilde{x}_0) d\tilde{x}_0$$

$$= \frac{1}{\det(\tilde{\phi}(t_0, \tau_1))} \int_{\mathbb{R}^k} p_{\tilde{X}(t_0)}^{\tilde{X}(t_0)}(\tilde{\phi}^{-1}(t_0, \tau_1) \tilde{x}_0) p_{\tilde{W}(t_0, \tau_1)}^{\tilde{W}(t_0, \tau_1)}(\tilde{x} - \tilde{x}_0) d\tilde{x}_0.$$
Step 2l. For \( l = 1, 2, \cdots \), let \( A_l := \{ \tilde{X}(T_l) = \tilde{x} \} \), \( B_l := \{ U_l = \tau_l \} \), and \( C_l := \{ T_l = \tau_l \cap \{ D_{l-1} = d_{l-1} \} \).

Then, according to Bayes’ rule, we have the relation between the conditional probability densities of \( A_l, B_l \), and \( C_l \) as follows

\[
p(A_l|B_l, C_l) = \frac{p(B_l|A_l, C_l)p(A_l|C_l)}{p(B_l|C_l)},
\]

i.e.,

\[
p_{\tilde{X}(T_l)|B_l}(\tilde{x}|d_l) = \frac{p_{U_l|X(T_l), T_l, D_{l-1}}(r_l|\tilde{x}, \tau_l, d_{l-1})p_{\tilde{X}(T_l)|T_l, D_{l-1}}(\tilde{x}|\tau_l, d_{l-1})}{p_{U_l|T_l, D_{l-1}}(r_l|\tau_l, d_{l-1})} = \frac{p_{U_l|X(T_l), T_l, D_{l-1}}(r_l|\tilde{x}, \tau_l, d_{l-1})p_{\tilde{X}(T_l)|T_l, D_{l-1}}(\tilde{x}|\tau_l, d_{l-1})}{\int_{\mathbb{R}^k} p_{U_l|X(T_l), T_l, D_{l-1}}(r_l|\tilde{x}_o, \tau_l, d_{l-1})p_{\tilde{X}(T_l)|T_l, D_{l-1}}(\tilde{x}_o|\tau_l, d_{l-1})d\tilde{x}_o}.
\]

(SM3.2)

Since initial location of the object, observation noise, and process noise are mutually independent, according to Eq. (3.6) and Theorem 2.7 of [SM3], we have

\[
p_{U_l|X(T_l), T_l, D_{l-1}}(r_l|\tilde{x}, \tau_l, d_{l-1}) = p_{U_l|X(T_l)}(r_l|\tilde{x}) = p_{Z(H \bar{x})}(r_l), \quad \tilde{x} \in \mathbb{R}^k.
\]

Therefore, by substituting Eq. (SM3.3) into Eq. (SM3.2) (note that we calculated \( \tilde{p}_{pr_l} \) in the previous step),

\[
p_{T_l}(\tilde{x}|d_l) = p_{\tilde{X}(T_l)|D_l}(\tilde{x}|d_l) = \frac{p_{Z(H \bar{x})}(r_l)\tilde{p}_{pr_l}(\tilde{x}|\tau_l, d_{l-1})}{\int_{\mathbb{R}^k} p_{Z(H \bar{x})}(r_l)\tilde{p}_{pr_l}(\tilde{x}_o|\tau_l, d_{l-1})d\tilde{x}_o}.
\]

Step 2l + 1. By conditioning the both sides of Eq. (3.5) on \( T_{l+1} = \tau_{l+1} \) and \( D_l = d_l \), we have, for \( l = 1, 2, \cdots \),

\[
p_{\tilde{X}(T_{l+1})|T_{l+1}, D_l}(\tilde{x}|\tau_{l+1}, d_l) = p_{\tilde{\phi}(T_l, T_{l+1})\tilde{X}(T_{l+1})|T_{l+1}, D_l}(\tilde{x}|\tau_{l+1}, d_l) * p_{\tilde{W}(T_l, T_{l+1})|T_{l+1}, D_l}(\tilde{x}|\tau_{l+1}, d_l),
\]

which, according to the independence of \( \tilde{W}(T_l, T_{l+1}) \) and \( U_l, T_{l-1} \), becomes

\[
p_{\tilde{X}(T_{l+1})|T_{l+1}, D_l}(\tilde{x}|\tau_{l+1}, d_l) = p_{\tilde{\phi}(\tau_l, \tau_{l+1})\tilde{X}(T_{l+1})|D_l}(\tilde{x}|d_l) * p_{\tilde{W}(\tau_l, \tau_{l+1})}(\tilde{x}) = \int_{\mathbb{R}^k} p_{\tilde{\phi}(\tau_l, \tau_{l+1})\tilde{X}(T_{l+1})|D_l}(\tilde{x}_o|d_l) p_{\tilde{W}(\tau_l, \tau_{l+1})}(\tilde{x} - \tilde{x}_o) d\tilde{x}_o = \frac{1}{|\text{det}(\phi(\tau_l, \tau_{l+1}))|} \int_{\mathbb{R}^k} p_{\tilde{X}(T_l)|D_l}(\tilde{x}^{-1}(\tau_l, \tau_{l+1})\tilde{x}_o|d_l) p_{\tilde{W}(\tau_l, \tau_{l+1})}(\tilde{x} - \tilde{x}_o) d\tilde{x}_o,
\]
or equivalently (note that we calculated $\tilde{p}_{fi}$ in the previous step),

\[(SM3.4)\]

$$\tilde{p}_{p_{\tau_1}}(\tilde{x}|\tau_{\tau_1}, d_\tau) = \frac{1}{\det\left(\phi(\tau_{\tau_1}, \tau_{\tau_1+1})\right)} \int_{\mathbb{R}^k} \tilde{p}_{fi}\left(\tilde{\phi}^{-1}(\tau_{\tau_1}, \tau_{\tau_1+1})\tilde{x}_o|d_\tau\right)p_{R(\tau_{\tau_1}, \tau_{\tau_1+1})}(\tilde{x} - \tilde{x}_o)d\tilde{x}_o.$$

3.1. See Theorem 7.2 of [SM3].

3.2. Setting $C := M'\Sigma$, Eq. (3.7) becomes

\[(SM3.5)\]

$$U_l = Z(HX(\tau_l)) = C\tilde{X}(\tau_l) + Z_{g,l}, \quad l = 1, 2, \cdots,$$

where

$$p_{Z_{g,l}}(r) := \frac{1}{2\pi [\det(\Sigma_g)]^{1/2}} \exp\left(-\frac{1}{2}r^T\Sigma_g^{-1}r\right), \quad r \in \mathbb{C}.$$ 

Since $Z_{g,l}$ is independent of $\mathcal{D}_{l-1}$, $T_l$ and $\tilde{X}$, then, according to Eq. (SM3.5), $Z(HX(\tau_l))$ is the sum of two independent Gaussian random variables and its probability density function is given by

$$p_{U_l|T_l, \mathcal{D}_{l-1}}(r_l|\tau_l, d_{l-1}) = p_{Z(HX(\tau_l))|T_l, \mathcal{D}_{l-1}}(r_l|\tau_l, d_{l-1})$$

\[(SM3.6)\]

$$= \frac{1}{2\pi [\det(R_l)]^{1/2}} \exp\left(-\frac{1}{2}(r_l - \hat{r}_l)^TR_l^{-1}(r_l - \hat{r}_l)\right),$$

where $R_l := CP_l^{-1}C^T + \Sigma_g$ and $\hat{r}_l := C\tilde{x}_l$.

**SM4. Example of maximum likelihood estimation.** Let the 3D (or 2D) motion of an object be given by the following continuous-time stochastic differential equation

\[(SM4.1)\]

$$dX(\tau) = (V + FX(\tau))d\tau + \sqrt{2D}dB(\tau), \quad \tau \geq t_0,$$

where $V \in \mathbb{R}^3$ (or $\mathbb{R}^2$), $F \in \mathbb{R}^{3 \times 3}$ (or $\mathbb{R}^{2 \times 2}$) and $D > 0$ denote the zero order drift, first order drift and diffusion coefficients, respectively, and $\{B(\tau), \tau \geq t_0\}$ is a 3 (or 2)-vector Brownian motion process with

$$E\{dB(\tau)dB(\tau)^T\} = I_{3\times 3} (or I_{2\times 2}).$$

As an example, next, for the case that the first order drift is a diagonal matrix, i.e., $FI_{2\times 2}, F \in \mathbb{R}$, and there is no zero order drift, we derive expressions for the likelihood function and its derivative with respect to the drift and diffusion coefficients for 2D trajectories. Let $X(t_0)$ be Gaussian distributed with mean $x_0 \in \mathbb{R}^2$ and diagonal covariance matrix $P_0 := \rho_0 I_{2\times 2}, \rho_0 > 0$, which is assumed to be independent of $B(\tau)$. Assume that the photon detection rate $\Lambda$, the magnification matrix $M = mI_{2\times 2}, m > 0$, and the covariance matrix $\Sigma_g = vI_{2\times 2}, v > 0$, of the measurement noise are independent of the parameter vector $\theta \in \Theta$. Also, for the corresponding discrete system at time points $\tau_0 := t_0 \leq \tau_1 < \tau_2 < \cdots < \tau_K < \cdots$, let the transition matrix be given by $\phi(\tau_{\tau_1}, \tau_l) := \phi^s(\tau_{\tau_1}, \tau_l)I_{2\times 2}, \phi^d(\tau_{\tau_1}, \tau_l) \in \mathbb{R}$, and the process noise covariance matrix be given by $Q^p(\tau_{\tau_1}, \tau_l) := q^p(\tau_{\tau_1}, \tau_l)I_{2\times 2}, q^p(\tau_{\tau_1}, \tau_l) > 0$. Then, the covariances of the states, which can be calculated through the Kalman filter formulae recursively, are also scalar matrices, i.e., can be defined as $P_{\theta, l}^{-1} := \rho_{\theta, l}^{-1} I_{2\times 2}, \rho_{\theta, l}^{-1} > 0, l = 1, 2, \cdots$. Also, let $\tilde{x}_{\theta, l}^{-1}$ denote the means of the states.
Then, the maximum likelihood estimate $\hat{\theta}_{\text{MLE}}$ of $\theta = (\theta_1, \ldots, \theta_n)$ is the solution of the following equation, according to Eq. (SM11.6), for the acquired data denoted by $d_K \in C^K \times \mathbb{R}^K_{[\geq 1]}, K = 1, 2, \cdots$,

$$
\begin{align*}
\frac{\partial \log L(\theta) d_K}{\partial \theta_i} &= \sum_{l=1}^{K} \frac{1}{2} \text{trace} \left[ \left( \frac{m^2 d^l_{r, l}}{m^2 \rho^l_{r, l} + v} \left( I_{2 \times 2} - \frac{m z^l_{r, l}}{m^2 \rho^l_{r, l} + v} \right) \right) \right] \\
&= \sum_{l=1}^{K} \frac{1}{2} \left( \frac{m^2 d^l_{r, l}}{m^2 \rho^l_{r, l} + v} \right) \left( 2 - \frac{\|r_l - m z^l_{r, l}\|^2}{m^2 \rho^l_{r, l} + v} \right) - \frac{m d^l_{r, l}}{m^2 \rho^l_{r, l} + v} \left( r_l - m z^l_{r, l} \right) = 0,
\end{align*}
$$

where $i = 1, \ldots, n$, $\|\cdot\|$ denotes the Euclidean norm, and for $l = 1, 2, \cdots$, $\hat{X}_{\theta, l}^{(i)} := \left[ \hat{z}_{\theta, l}^{l-1, i} \ d\hat{z}_{\theta, l}^{l-1, i} \right]^T$, $\hat{d}z_{\theta, l}^{l-1, i} := \frac{\partial x_{\theta, l}^{l-1, i}}{\partial \theta_i}$, $P_{\theta, l}^{(i)} := \left[ \rho_{\theta, l}^{l-1, i} \ d\rho_{\theta, l}^{l-1, i} \right]^T$, and $d\rho_{\theta, l}^{l-1, i} := \frac{\partial \rho_{\theta, l}^{l-1, i}}{\partial \theta_i}$ can be calculated through the following recursive formulas, by combining the Kalman filtering equations (Eqs. (3.11) and (3.12)) and their derivatives, and using Lemma SM14.2 (see Section SM14.2),

$$
\begin{align*}
\hat{X}_{\theta, l+1}^{(i)} &= A_{\theta, l+1}^{(i)} \hat{X}_{\theta, l}^{(i)} + B_{\theta, l+1}^{(i)} \left( r_l - m \hat{z}_{\theta, l}^{l-1} \right), \\
P_{\theta, l+1}^{(i)} &= C_{\theta, l+1}^{(i)} P_{\theta, l}^{(i)} C_{\theta, l+1}^{(i)\ T} + \left[ \frac{q_{\theta, l}^{\left( \tau_l, \tau_{l+1} \right)}}{\partial \theta_i} \right],
\end{align*}
$$

where $\hat{A}_{\theta, l+1}^{(i)} := \left[ \frac{\partial \phi_0 \left( t_0, \tau_1 \right) x_{\theta, 0} + \phi_0 \left( t_0, \tau_1 \right) \partial \rho_{\theta, 0}}{\partial \theta_i} \right]_{2 \times 2}$, $P_{\theta, l+1}^{(i)} := \left[ \frac{\left( \phi_0^2 \left( t_0, \tau_1 \right) \right)^2 \rho_0 + q_{\theta, l}^{\left( \tau_l, \tau_{l+1} \right)}}{\partial \theta_i} \right]_{2 \times 2}$, and

$$
\begin{align*}
A_{\theta, l+1}^{(i)} &= \left[ \frac{\phi_0 \left( \tau_l, \tau_{l+1} \right)}{\partial \theta_i} \right]_{2 \times 2}, \\
B_{\theta, l+1}^{(i)} &= \left[ \frac{\phi_0 \left( \tau_l, \tau_{l+1} \right) K_{\theta, l}}{\partial \theta_i} + \left[ \frac{\phi_0 \left( \tau_l, \tau_{l+1} \right)}{\partial \theta_i} \right] \right] K_{\theta, l},
\end{align*}
$$

and

$$
\begin{align*}
C_{\theta, l+1}^{(i)} &= \left[ \left( 1 - m k_{\theta, l}^{l-1} \right) \left( \phi_0^2 \left( \tau_l, \tau_{l+1} \right) \right)^2 - m \frac{\partial k_{\theta, l}^{l-1}}{\partial \theta_i} \left( \phi_0^2 \left( \tau_l, \tau_{l+1} \right) \right)^2 \left( 1 - m k_{\theta, l}^{l-1} \right) \left( \phi_0^2 \left( \tau_l, \tau_{l+1} \right) \right)^2 \right],
\end{align*}
$$

where the Kalman gain and its derivative are given by

$$
\begin{align*}
K_{\theta, l} &= k_{\theta, l} I_{2 \times 2}, \\
k_{\theta, l}^* := \frac{m \rho_{\theta, l}^{l-1}}{m^2 \rho_{\theta, l}^{l-1} + v}, \\
\frac{\partial k_{\theta, l}^{l-1}}{\partial \theta_i} &= \frac{m v d \rho_{\theta, l}^{l-1, i}}{\left( m^2 \rho_{\theta, l}^{l-1} + v \right)^2}.
\end{align*}
$$

1. If $F \neq 0$, then, for $l = 1, 2, \cdots$,

$$
\begin{align*}
\phi^{*} \left( \tau_{l-1}, \tau_l \right) &= e^{F \left( \tau_l - \tau_{l-1} \right)}, \\
q^{*} \left( \tau_{l-1}, \tau_l \right) &= \frac{D}{F} \left( e^{2F \left( \tau_l - \tau_{l-1} \right)} - 1 \right).
\end{align*}
$$
(a) If the only unknown parameter is the first order drift coefficient $F$, i.e., $\theta = F$, then, for $\dot{\tau}_{l+1} := \tau_{l+1} - \tau_l$,

\[
A_{\theta,l+1} = \begin{bmatrix}
    e^{F\dot{\tau}_{l+1}I_{2\times 2}} & e^{F\dot{\tau}_{l+1}(I_{2\times 2} - mK_{\theta,l})}
  \end{bmatrix},
\]

\[
B_{\theta,l+1} = \begin{bmatrix}
e^{F\dot{\tau}_{l+1}K_{\theta,l}} & e^{F\dot{\tau}_{l+1}(\frac{\partial K_{\theta,l}}{\partial \theta} + \Delta \dot{\tau}_{l+1} K_{\theta,l})}
\end{bmatrix},
\]

\[
C_{\theta,l+1} = \begin{bmatrix}
(1 - mk_{\theta,l})e^{2F\Delta \tau_{l+1}} & 0
\end{bmatrix},
\]

and

\[
X_{\theta,l} = \begin{bmatrix} e^{F\Delta \tau_{l}x_0} \end{bmatrix},
\]

\[
P_{\theta,l} = \begin{bmatrix} e^{2F\Delta \tau_{l}\rho_0 + \frac{D}{2}(e^{2F\Delta \tau_{l}} - 1)} \end{bmatrix},
\]

(b) If the only unknown parameter is the diffusion coefficient $D$, i.e., $\theta = D$, then,

\[
A_{\theta,l+1} = \begin{bmatrix}
    e^{F\Delta \tau_{l}I_{2\times 2}} & 0_{2\times 2}
  \end{bmatrix},
\]

\[
B_{\theta,l+1} = \begin{bmatrix}
e^{F\Delta \tau_{l+1}K_{\theta,l}} & 0_{2\times 2}
\end{bmatrix},
\]

\[
C_{\theta,l+1} = \begin{bmatrix}
(1 - mk_{\theta,l})e^{2F\Delta \tau_{l+1}} & 0
\end{bmatrix},
\]

and

\[
X_{\theta,l} = \begin{bmatrix} e^{F\Delta \tau_{l}x_0} \end{bmatrix},
\]

\[
P_{\theta,l} = \begin{bmatrix} e^{2F\Delta \tau_{l}\rho_0 + \frac{D}{2}(e^{2F\Delta \tau_{l}} - 1)} \end{bmatrix},
\]

2. If $F = 0$, then, for $l = 1, 2, \ldots$,

\[
\phi^*(\tau_{l-1}, \tau_l) = 1, \quad q^*(\tau_{l-1}, \tau_l) = 2D(\tau_l - \tau_{l-1}).
\]

If the only unknown parameter is the diffusion coefficient $D$, i.e., $\theta = D$, then,

\[
A_{\theta,l+1} = \begin{bmatrix}
    I_{2\times 2} & 0_{2\times 2}
  \end{bmatrix},
\]

\[
B_{\theta,l+1} = \begin{bmatrix}
K_{\theta,l}
\end{bmatrix},
\]

\[
C_{\theta,l+1} = \begin{bmatrix}
1 - mk_{\theta,l} & 0
\end{bmatrix},
\]

and

\[
X_{\theta,l} = \begin{bmatrix} x_0 \end{bmatrix},
\]

\[
P_{\theta,l} = \begin{bmatrix} \rho_0 + 2D\Delta \tau_l \end{bmatrix},
\]

SM5. More estimation results for Gaussian measurements.

SM6. Sequential Monte Carlo method. Here, for the acquired data denoted by $d_l \in C^l \times \mathbb{R}_{[\infty]}$ (or $d_l \in C^l \times \mathbb{R}_{[0]}$), $l = 1, 2, \ldots$, we approximate the distribution $p_{\tau_{l+1}}(x_{l+1}|\tau_{l+1}, d_l)$ through the sequential Monte Carlo method provided in [SM5]. Note that

\[
p_{\tau_{l+1}}(x_{l+1}|\tau_{l+1}, d_l) = p_{X(\tau_{l+1})|\tau_{l+1}, d_l}
\]

\[
= \int_{\mathbb{R}^3} p_{X(\tau_{l+1}), X(\tau_{l+1})|\tau_{l+1}, d_l} (x_{l+1}, x|\tau_{l+1}, d_l) dx
\]

\[
= \int_{\mathbb{R}^3} p_{X(\tau_{l+1})|X(\tau_{l+1}), \tau_{l+1}, d_l} (x_{l+1}, x, \tau_{l+1}, d_l) p_{X(\tau_{l+1})|\tau_{l+1}, d_l} (x|\tau_{l+1}, d_l) dx
\]

(SM6.1)
where $p_{fi_l}(x|d_l) := p_{X(T_l)|D_l}(x|d_l), x \in \mathbb{R}^3$, and for the linear stochastic system with state $X(\tau) \in \mathbb{R}^3, \tau \geq t_0$, zero-mean Gaussian process noise with covariance matrix $Q_\phi(\tau, \tau+1) \in \mathbb{R}^{3 \times 3}, Q_\phi(\tau, \tau+1) > 0$, and state-transition matrix $\phi(\tau, \tau+1) \in \mathbb{R}^{3 \times 3}$, we have, for $x_l \in \mathbb{R}^3$,

$$p_{X(T_l+1)|X(T_l), T_l+1, D_l}(x_{l+1}|x_l, T_l, d_l) = p_{X(T_l+1)|X(T_l)}(x_{l+1}|x_l) = \frac{1}{(2\pi)^{3/2} |\det (Q_\phi(\tau, \tau+1))|^{1/2}} \times \exp \left( -\frac{1}{2} (x_{l+1} - \phi(\tau, \tau+1)x_l)^T Q_\phi^{-1}(\tau, \tau+1)(x_{l+1} - \phi(\tau, \tau+1)x_l) \right).$$

The distribution $p_{fi_l}$ of the filtered object location can be approximated as [SM5]

$$p_{fi_l}(x_l|d_l) \approx \sum_{i=1}^N w_i^l(\tau_l) \delta (x_l - \hat{x}_i^l),$$

where $\delta$ is the Dirac delta function, and the samples $\hat{x}_i^l$ and their corresponding weights $w_i^l(\tau_l), i = 1, \ldots, N$, are given through the following sequential Monte Carlo algorithm. Finally, by substituting Eqs. (SM6.2) and (SM6.3) into Eq. (SM6.1), the distribution $p_{pri+l}$ can be approximated as

$$p_{pri+l}(x_{l+1}|\tau_l+1, d_l) \approx \sum_{i=1}^N w_i^l(\tau_l) p_{X(T_l+1)|X(T_l)}(x_{l+1}|\hat{x}_i^l) = \sum_{i=1}^N \frac{w_i^l(\tau_l)}{(2\pi)^{3/2} |\det (Q_\phi(\tau, \tau+1))|^{1/2}} \exp \left( -\frac{1}{2} (x_{l+1} - \phi(\tau, \tau+1)\hat{x}_i^l)^T Q_\phi^{-1}(\tau, \tau+1)(x_{l+1} - \phi(\tau, \tau+1)\hat{x}_i^l) \right).$$

Sequential Monte Carlo (particle filter) algorithm: [SM5]
1. Draw initial samples \( \{ x_i^0 \}_{i=1}^N \) according to \( p_{X(t_0)}(x_0) \), i.e., \( x_i^0 \sim p_{X(t_0)}(x_0) \), \( i = 1, \ldots, N \), and set \( l = 1 \).

2. Draw independent and identically distributed samples \( \{ \dot{x}_i^l \}_{i=1}^N \) according to \( p_{X(t_l)|X(t_{l-1})}(\dot{x}_i^l| x_{i-1}^l) \), i.e., \( \dot{x}_i^l \sim p_{X(t_l)|X(t_{l-1})}(\dot{x}_i^l| x_{i-1}^l) \), \( i = 1, \ldots, N \).

3. Compute the weights sequence \( \{ w_i^l(r_l) \}_{i=1}^N \) as

\[
w_i^l(r_l) = \frac{f_{\dot{x}_i^l(r_l)}}{\sum_{i=1}^N f_{\dot{x}_i^l(r_l)}}, \quad i = 1, \ldots, N.
\]

4. Resample new particles \( x_j^l, j = 1, \ldots, N \), from the set \( \{ \dot{x}_i^l \}_{i=1}^N \) according to the importance weights \( w_i^l(r_l) \), i.e., according to

\[
P\left( x_j^l = \dot{x}_i^l \right) = w_i^l(r_l), \quad i = 1, \ldots, N,
\]

where \( P\left( x_j^l = \dot{x}_i^l \right) \) denotes the probability of \( x_j^l = \dot{x}_i^l \).

5. Increment \( l \mapsto l + 1 \) and return to step 2.

Fig. SM2. Analysis of the error of diffusion coefficient and first order drift coefficient estimates produced by the maximum likelihood estimation method for the Airy measurement model. (a) The two-dimensional single molecule trajectory simulated in Fig. 3(a). (b) Detected locations of the photons emitted from the molecule trajectory of part (a) in the image space which are simulated using Eq. (3.6) with the Airy profile (Eq. (2.4)) and \( \alpha := \frac{2\pi na}{\lambda} = 2.59 \). (c) Differences between the diffusion coefficient estimates and the true diffusion coefficient value for 100 data sets, each containing a trajectory of a molecule simulated using Eqs. (SM4.1) and (3.6) with the Airy profile, and the parameters given in parts (a) and (b). (d) Differences between the first order drift coefficient estimates and its true value for the data sets of part (c).

SM7. Estimation results for Airy measurements. Here, we analyze the error of the diffusion and first order drift coefficient estimates for simulated data sets with the Airy measurement profile, with the same standard deviation as the Born and Wolf and Gaussian data presented in Figs. 3-8, and obtain similar results (see Figs. 3-8).
We also show the differences between the means of the distributions of the prediction of the molecule locations and the true locations of the molecule in Fig. SM5 (see Section SM14.6).

**SM8. Proof of Theorem 5.2.** Let $G_{[t]} \left( (U_{[t]}, T_{[t]}), C, \Theta \right)$ and $G_{L} \left( (U_{L}, T_{L}), C, \Theta \right)$ be image detection processes for a time interval $[t_0, t]$ and for a fixed number $L$ of photons, respectively. Let $D_{[t]} := (U_{[t]}, T_{[t]}), D_{k} := (U_{k}, T_{k}), k = 0, 1, \ldots$. Assume that the conditional probability density functions $p_{U_{[t]}|T_{t}, U_{t-1}}, i = 1, 2, \ldots$, of $U_{[t]}$, given $T_{t}$ and $D_{t-1}$, satisfy the following regularity conditions, for $\theta = (\theta_1, \ldots, \theta_n) \in \Theta$,

(a) $\frac{\partial p_{U_{[t]}|T_{t}, U_{t-1}}(r_{1|\theta_l, U_{t-1}})}{\partial \theta_i}$ exists for $i = 1, \ldots, n$,

(b) $\int_{C} \left| \frac{\partial p_{U_{[t]}|T_{t}, U_{t-1}}(r_{1|\theta_l, U_{t-1}})}{\partial \theta_i} \right| dr < \infty$ for $i = 1, \ldots, n$,

where $d_t \in C^l \times \mathbb{R}_{[t]}^l$ for $G_{[t]}, d_t \in C^l \times \mathbb{R}_{[\infty]}^l$ for $G_{L}$, and $p^\theta \left( r_{1|\theta_l, d_0} \right) := p^\theta \left( r_{1|\theta_l} \right)$.  

1.1. Then, the Fisher information matrix $I_{[t]}(\theta)$ of $G_{[t]}$ is given by

$$I_{[t]}(\theta) = E \left[ \left( \frac{\partial \log L(\theta|d_K)}{\partial \theta} \right)^T \left( \frac{\partial \log L(\theta|d_K)}{\partial \theta} \right) \right],$$

where $d_K \in C^K \times \mathbb{R}_{[t]}^K$, $K = 1, 2, \ldots$, and $L$ denotes the likelihood function. By substituting the expression of the likelihood function $L_{[t]}(\theta)$ of $G_{[t]}$ (Eq. (4.1)) into Eq.
(SM8.1), according to [SM6, SM7], we have

\[
I_{\theta}(\theta) = P_{\theta}(N(t) = 0) \left( \frac{\partial \log P_{\theta}(N(t) = 0)}{\partial \theta} \right)^T \left( \frac{\partial \log P_{\theta}(N(t) = 0)}{\partial \theta} \right) \\
+ \sum_{K=1}^{\infty} \int_{t_0}^{t} \int_{t_0}^{t_2} \int_{t_0}^{t_2} \cdots \int_{t_0}^{t_K} p_{\theta}^{K}(d_K, K) \left( \frac{\partial \log p_{\theta}^{K}(d_K, K)}{\partial \theta} \right)^T \left( \frac{\partial \log p_{\theta}^{K}(d_K, K)}{\partial \theta} \right) \\
\times dr_1 \cdots dr_K d \tau_1 d \tau_2 \cdots d \tau_K
\]

\[
= \frac{1}{P_{\theta}(N(t) = 0)} \left( \frac{\partial P_{\theta}(N(t) = 0)}{\partial \theta} \right)^T \left( \frac{\partial P_{\theta}(N(t) = 0)}{\partial \theta} \right) \\
+ \sum_{K=1}^{\infty} \int_{t_0}^{t} \int_{t_0}^{t_2} \int_{t_0}^{t_2} \cdots \int_{t_0}^{t_K} \frac{1}{p_{\theta}^{K}(d_K, K)} \left( \frac{\partial p_{\theta}^{K}(d_K, K)}{\partial \theta} \right)^T \left( \frac{\partial p_{\theta}^{K}(d_K, K)}{\partial \theta} \right) \\
\times dr_1 \cdots dr_K d \tau_1 d \tau_2 \cdots d \tau_K
\]

(SM8.2)

where \( P_{\theta}(N(t) = 0) \) is the probability of \( N(t) = 0 \) and \( p_{\theta}^{K} \) denotes the probability density function of \( D_{\theta(t)} \) and \( N(t) \).

1.2. Assume that the photon detection rate \( \Lambda \) is independent of \( \theta \). By substituting Eqs. (SM1.1)-(SM1.3) into Eq. (SM8.2), we have

\[
I_{\theta}(\theta) = \sum_{K=1}^{\infty} P(N(t) = K) \int_{t_0}^{t} \int_{t_0}^{t} \cdots \int_{t_0}^{t} \left[ \int_{\mathcal{C}} \frac{1}{p_{\theta}^{K}(r_1, \cdots, r_K | \tau_1, \cdots, \tau_K)} \left( \frac{\partial p_{\theta}^{K}(r_1, \cdots, r_K | \tau_1, \cdots, \tau_K)}{\partial \theta} \right)^T \left( \frac{\partial p_{\theta}^{K}(r_1, \cdots, r_K | \tau_1, \cdots, \tau_K)}{\partial \theta} \right) dr_1 \cdots dr_K \right] \\
\times p_{\theta}^{K}(r_1, \cdots, r_K | \tau_1, \cdots, \tau_K) dr_1 dr_2 \cdots dr_K
\]

(SM8.3)

where, for \( t_0 \leq \tau_1 < \cdots < \tau_K \leq t \), \( I_{\tau_1, \cdots, \tau_K}(\theta) \) is given by

\[
I_{\tau_1, \cdots, \tau_K}(\theta) = E_{\theta K | \tau_1, K} \left\{ \left( \frac{\partial \log p_{\theta}^{K}(r_1, K | \tau_1, K)}{\partial \theta} \right)^T \left( \frac{\partial \log p_{\theta}^{K}(r_1, K | \tau_1, K)}{\partial \theta} \right) \right\} \\
= \int_{\mathcal{C}} \int_{\mathcal{C}} \frac{1}{p_{\theta}^{K}(r_1, K | \tau_1, K)} \left( \frac{\partial p_{\theta}^{K}(r_1, K | \tau_1, K)}{\partial \theta} \right)^T \left( \frac{\partial p_{\theta}^{K}(r_1, K | \tau_1, K)}{\partial \theta} \right) \\
\times dr_K \cdots dr_1
\]

(SM8.4)

where \( r_{1:K} := (r_1, \cdots, r_K), \tau_{1:K} := (\tau_1, \cdots, \tau_K), K = 1, 2, \cdots \). Since

\[
p_{\theta}^{K}(r_{1:K} | \tau_{1:K}) = \prod_{i=1}^{K} p_{\theta}^{i}(r_i | d_{i-1}) \left( r_i, d_{i-1} \right),
\]

according to Lemma 1 (chain rule
for the Fisher information matrix) of [SM8], we have

\[
I_{\tau_1, \ldots, \tau_K}(\theta) = \sum_{l=0}^{K} \int_{\tau_l}^{\tau_{l+1}} \left( \frac{\partial \log p_{\tau_l}^{\theta}(\tau_l|\tau_{l-1})}{\partial \theta} \right)^T \left( \frac{\partial \log p_{\tau_l}^{\theta}(\tau_l|\tau_{l-1})}{\partial \theta} \right)
\]

where the Fisher information matrix \( I_{\tau_1, \ldots, \tau_l}(\theta) \) of \( U_l, l = 1, \ldots, K \), calculated with respect to the conditional probability density function \( p_{\tau_l}^{\theta}(\tau_l|\tau_{l-1}) \) at fixed time points \( \tau_l = \tau_{l,l} \), is given by

\[
I_{\tau_1, \ldots, \tau_l}(\theta) = \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} p_{\tau_l}^{\theta}(\tau_l|\tau_{l-1}) \left( \frac{\partial \log p_{\tau_l}^{\theta}(\tau_l|\tau_{l-1})}{\partial \theta} \right)^T \left( \frac{\partial \log p_{\tau_l}^{\theta}(\tau_l|\tau_{l-1})}{\partial \theta} \right) d\tau_1 \cdots d\tau_l
\]  

(\text{SM}8.5)

2.1. Moreover, by substituting the expression for the likelihood function \( L(\theta) \) of \( G_L \) (Eq. (4.2)) into Eq. (SM8.1), the Fisher information matrix \( I_{L}(\theta) \) of \( G_L \) can be obtained as

\[
I_{L}(\theta) = \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} p_{L}^{\theta}(d_L) \left( \frac{\partial \log p_{L}^{\theta}(d_L)}{\partial \theta} \right)^T \left( \frac{\partial \log p_{L}^{\theta}(d_L)}{\partial \theta} \right) d\tau_1 \cdots d\tau_L
\]  

(\text{SM}8.6)

where \( d_L \in \mathcal{L} \times \mathbb{R}_{[0,\infty)} \), and \( p_{L}^{\theta} \) denotes the probability density function of \( D_L \).

2.2. Assume that the photon detection rate \( \Lambda \) is independent of \( \theta \). By substituting Eq. (2.2) into Eq. (SM8.6), we have, according to Eq. (SM1.6) and using the similar procedure used in the previous part,

\[
I_{L}(\theta) = \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} \int_{\mathcal{C}} p_{L}^{\theta}(r_{1:L}|\tau_{1:L}) \left( \frac{\partial p_{L}^{\theta}(r_{1:L}|\tau_{1:L})}{\partial \theta} \right)^T \left( \frac{\partial p_{L}^{\theta}(r_{1:L}|\tau_{1:L})}{\partial \theta} \right) d\tau_1 \cdots d\tau_L
\]

\[
= \int_{\mathcal{C}} \cdots \int_{\mathcal{C}} I_{r_1, \ldots, r_L}(\theta) e^{-\int_{\mathcal{T}_L} \Lambda(r) d\tau} \prod_{k=1}^{L} \Lambda(r_k) d\tau_1 \cdots d\tau_L.
\]

SM9. Proof of Corollary 5.4. Let \( G_{[\mathcal{L}]}(X, (U_{[\mathcal{L}]}, T_{[\mathcal{L}]}, q, \mathcal{C}, \Theta)) \) be an image detection process driven by the stochastic trajectory \( X \) and image function \( q \) for a time interval \([t_0, t]\) (or a fixed number \( L \) of photons). Assume
that the photon detection rate $\Lambda$ is independent of $\theta$. The Fisher information matrix $I_{\tau_1, \ldots, \tau_K}$ in Eq. (5.2) (or Eq. (5.6)) of Theorem 5.2 is given by

$$I_{\tau_1, \ldots, \tau_K} (\theta) = \left\{ \begin{array}{ll} \sum_{l=1}^{K} I_{U_l | \tau_l, \tau_{l-1}}^r (\theta), & \tau_1 < \cdots < \tau_K \leq t, \\ 0, & \text{otherwise,} \end{array} \right.$$ 

where, for $r_{1:l} := (r_1, \ldots, r_l), r_{1:l} := (r_1, \ldots, r_l), l = 1, \ldots, K$,

$$I_{U_l | \tau_l, \tau_{l-1}}^r (\theta) = \int_c \cdots \int_c p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_{1:l-1}|\tau_{1:l-1}) \left[ \int_c \frac{1}{p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_l|\tau_l, d_{l-1})} \times \left( \frac{\partial p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_l|\tau_l, d_{l-1})}{\partial \theta} \right) \right] \cdots dr_l \cdots dr_1,$$

and $I_{U_l | \tau_l}^r$ is given by Eq. (5.5). According to Eq. (SM2.1), we can express the conditional probability density functions $p_{U_l | \tau_l, \tau_{l-1}}^\theta$ in terms of the image profile $f_x, x \in \mathbb{R}^3$, as

$$p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_l|\tau_l, d_{l-1}) = \int_{\mathbb{R}^3} f_{x_o}^\theta (r_l) p_{pr_l}^\theta (x_o|\tau_l, d_{l-1}) dx_o,$$

where $p_{pr_l}^\theta := p_{X(\tau_l)|\tau_l, d_{l-1}}$ denotes the distribution of the prediction of the object location, $p_{pr_l}^\theta (x_o|\tau_l, d_0) := p_{pr_l}^\theta (x_o|\tau_l), l = 1, \ldots, K$, and $x_o \in \mathbb{R}^3$ denotes a running variable in the object space. By substituting Eq. (SM9.2) into Eq. (SM9.1), we have, for $dp_{pr_l}^\theta := \frac{\partial p_{pr_l}^\theta}{\partial \theta}$ and $df_x^\theta := \frac{\partial f_x^\theta}{\partial \theta}$,

$$I_{U_l | \tau_l, \tau_{l-1}}^r (\theta) = \int_c \cdots \int_c p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_{1:l-1}|\tau_{1:l-1}) \left[ \int_c \frac{1}{p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_l|\tau_l, d_{l-1})} \times \left( \frac{\partial p_{U_l | \tau_l, \tau_{l-1}}^\theta (r_l|\tau_l, d_{l-1})}{\partial \theta} \right) \right] \cdots dr_l \cdots dr_1 \times dx_{l-1}dx_{l-2}dr_l \cdots dr_1,$$
where for \( l = 1, 2, \ldots \),
\[
F_l^\theta(x, d_l) := \left( df_2^\theta(r_l) \right)^T \left( dp_{\theta r_1}(x|\tau_1, d_{l-1}) \right)^T \left( dp_{\theta \tau_1}(x|\tau_1) \right) f_\tau^\theta(r_l), \quad x \in \mathbb{R}^2,
\]
\[
p_{U_l|T_1, \mathcal{D}_{l-1}}(r_l|\tau_l, d_{l-1}) = \int_{\mathbb{R}^3} f_{x_0}^\theta(r_l) p_{\theta r_1}(x_0|\tau_l, d_{l-1}) dx_0,
\]
\[
p_{U_{l-1}|T_1}(r_{l-1}|\tau_l, d_{l-1}) = \prod_{i=1}^{l-1} \int_{\mathbb{R}^3} f_{x_0}^\theta(r_i) p_{\theta r_1}(x_0|\tau_l, d_{l-1}) dx_0,
\]
with \( I_{U_l|T_1}^\tau \) given by
\[
I_{U_l|T_1}^\tau(\theta) = \int_{\mathbb{R}^2} \int_{\mathbb{R}^3} \frac{1}{p_{U_l|T_1}^\theta(r_l|\tau_l)} \left[ \left( df_2^\theta(r) \right)^T \left( dp_{\theta r_1}(x_1|\tau_1) \right)^T \left( dp_{\theta \tau_1}(x_1) \right) \right] \times \left[ \left( dp_{\theta r_1}(x_2|\tau_1) \right)^T \left( dp_{\theta \tau_1}(x_2) \right) \right] dx_1 dx_2 dr.
\]

**SM10. Proof of Corollary 5.6.** For \( t_0 \leq \tau_1 < \cdots < \tau_K \), let \( \mathcal{G}_{\tau_1, \ldots, \tau_K}(U_K, T_K, \mathcal{C}, \Theta) \) be an image detection process at fixed time points \( \tau_1, \ldots, \tau_K \). Assume that
\[
p_{U_l|T_1, \mathcal{D}_{l-1}}(r_l|\tau_l, d_{l-1}) = p_{U_l|T_1}(r_l|\tau_l), \quad d_l \in \mathcal{C}_l \times \mathbb{R}^{l_{\infty}}, \quad l = 1, 2, \ldots.
\]

1. According to Eq. (2.8), we have, for \( r_l \in \mathbb{R}^2, l = 1, 2, \ldots, \)
\[
\text{(SM10.1)} \quad p_{U_K|T_K}(r_1, \cdots, r_K|\tau_1, \cdots, \tau_K) = \prod_{l=1}^{K} p_{U_l|T_1}^\theta(r_l|\tau_l).
\]

By substituting Eq. (SM10.1) into Eq. (5.4), we have
\[
I_{\tau_1, \cdots, \tau_K}(\theta) = \left\{ \begin{array}{ll}
\sum_{l=1}^{K} I_{U_l|T_1}^\tau(\theta), & t_0 \leq \tau_1 < \cdots < \tau_K; \\
0, & \text{otherwise},
\end{array} \right.
\]
where for \( l = 1, \ldots, K, \)
\[
I_{U_l|T_1}^\tau(\theta) = \int_{\mathbb{R}^2} \left( \int_{\mathbb{R}^3} \frac{1}{p_{U_l|T_1}^\theta(r_l|\tau_l)} \frac{\partial p_{U_l|T_1}^\theta(r_l|\tau_l)}{\partial \theta} \right) \left( \frac{\partial p_{U_l|T_1}^\theta(r_l|\tau_l)}{\partial \theta} \right) dr_l
\]
\[
\text{(SM10.2)} \quad = \int_{\mathbb{R}^2} \frac{1}{p_{U_l|T_1}^\theta(r_l|\tau_l)} \left( \frac{\partial p_{U_l|T_1}^\theta(r_l|\tau_l)}{\partial \theta} \right) \left( \frac{\partial p_{U_l|T_1}^\theta(r_l|\tau_l)}{\partial \theta} \right) dr.
\]

2. For an object with deterministic trajectory \( X_\tau(\theta) := (x_\tau(\theta), y_\tau(\theta)) \in \mathbb{R}^2, \tau \geq t_0, \) assume that there exists an image function \( q: \mathbb{R}^2 \rightarrow \mathbb{R} \), which is assumed to be independent of the parameter vector \( \theta \), such that for \( r = (x, y) \in \mathbb{R}^2, t_0 \leq \tau \leq t, \) and a magnification factor \( M > 1, \)
\[
p_{U_l|T_1}^\theta(r|\tau) = f_{X_\tau(\theta)}(r) = \frac{1}{M^2} q \left( \frac{x}{M} - x_\tau(\theta), \frac{y}{M} - y_\tau(\theta) \right).
\]
SUPPLEMENTARY MATERIALS: FISHER INFORMATION FOR MOLECULES SM15

Then, by substituting Eq. (SM10.3) into Eq. (SM10.2), \( I_{\tau_1}(\theta) := I_{U_1|U_1}^T \) is obtained as, for \( \theta = (\theta_1, \cdots, \theta_n) \in \Theta,

\[
I_{\tau_1}(\theta) = \frac{1}{M^2} \int_{\mathbb{R}^2} \left[ \frac{1}{q(x, y \circ d_{\tau_1})(\theta_1, \cdots, \theta_n)} \right] \left[ \frac{\partial q(x, y \circ d_{\tau_1})(\theta_1, \cdots, \theta_n)}{\partial \theta_1} \right]^T 
\times \left[ \frac{\partial q(x, y \circ d_{\tau_1})(\theta_1, \cdots, \theta_n)}{\partial \theta_2} \right] 
\times \left[ \frac{\partial q(x, y \circ d_{\tau_1})(\theta_1, \cdots, \theta_n)}{\partial \theta_n} \right] dxdy
\]

(SM10.4)

For each \((x, y) \in \mathbb{R}^2\), let \( h_{x, y} = (h_x, h_y) : \mathbb{R}^2 \rightarrow \mathbb{R}^2 \), such that, for \( \theta \in \Theta, (x_{\tau_1}(\theta), y_{\tau_1}(\theta)) \in \mathbb{R}^2,

\[
h_x(x_{\tau_1}(\theta), y_{\tau_1}(\theta)) = \frac{x}{M} - x_{\tau_1}(\theta), \quad h_y(x_{\tau_1}(\theta), y_{\tau_1}(\theta)) = \frac{y}{M} - y_{\tau_1}(\theta).
\]

Then, for \( d_{\tau_1} = (x_{\tau_1}, y_{\tau_1}) : \Theta \rightarrow \mathbb{R}^2 \), the composite function \((q \circ h_{x, y} \circ d_{\tau_1})(\theta)\) is given by

\[
(q \circ h_{x, y} \circ d_{\tau_1})(\theta) = q(h_{x, y}(d_{\tau_1}(\theta))) = q \left( \frac{x}{M} - x_{\tau_1}(\theta), \frac{y}{M} - y_{\tau_1}(\theta) \right),
\]

and therefore, using the formal definition of partial derivatives, we can rewrite Eq. (SM10.4) as

\[
I_{\tau_1}(\theta) = \frac{1}{M^2} \int_{\mathbb{R}^2} \left[ \frac{1}{(q \circ h_{x, y} \circ d_{\tau_1})(\theta_1, \cdots, \theta_n)} \right] \left[ \frac{(D_1 q)(h_{x, y}(d_{\tau_1}(\theta)))}{D_1 \theta} \right] 
\times \cdots 
\times \left[ \frac{(D_n q)(h_{x, y}(d_{\tau_1}(\theta)))}{D_n \theta} \right] dxdy
\]

(SM10.5)

Assume that \( d_{\tau_1} \) is continuously differentiable on all of \( \Theta \), and \( h_{x, y} \) is differentiable at \( d_{\tau_1}(\theta) \). Also, suppose that \( q \) is differentiable at \( h_{x, y}(d_{\tau_1}(\theta)) \). Then, according to Theorem SM14.3 (see Section SM14.3), for \( i = 1, \cdots, n,

\[
(D_i q)(h_{x, y}(d_{\tau_1}(\theta))) = (D_1 q)(h_{x, y}(d_{\tau_1}(\theta)))(D_1 h_{x,y})(d_{\tau_1}(\theta))(D_i x_{\tau_1}(\theta)) 
+ (D_1 q)(h_{x, y}(d_{\tau_1}(\theta)))(D_2 h_{x,y})(d_{\tau_1}(\theta))(D_i y_{\tau_1}(\theta)) 
+ (D_2 q)(h_{x, y}(d_{\tau_1}(\theta)))(D_1 h_{x,y})(d_{\tau_1}(\theta))(D_i x_{\tau_1}(\theta)) 
+ (D_2 q)(h_{x, y}(d_{\tau_1}(\theta)))(D_2 h_{x,y})(d_{\tau_1}(\theta))(D_i y_{\tau_1}(\theta))
\]

(SM10.6)

By substituting Eq. (SM10.6) into Eq. (SM10.5), we have, for \( \theta = (\theta_1, \cdots, \theta_n) \in \Theta,

\[
I_{\tau_1}(\theta) = \frac{1}{M^2} V_\mu^T(\tau_1) \left[ \int_{\mathbb{R}^2} \frac{1}{q(h_{x, y}(d_{\tau_1}(\theta)))} \left[ \frac{(D_1 q)(h_{x, y}(d_{\tau_1}(\theta))}{D_1 \theta} \right] \left[ \frac{(D_1 q)(h_{x, y}(d_{\tau_1}(\theta))}{D_2 \theta} \right] 
\times \cdots 
\times \left[ \frac{(D_n q)(h_{x, y}(d_{\tau_1}(\theta))}{D_n \theta} \right] dxdy \right] V_\mu(\tau_1)
= \frac{1}{M^2} V_\mu^T(\tau_1) \left[ \int_{\mathbb{R}^2} \frac{1}{q(h_{x, y}(d_{\tau_1}(\theta)))} \left[ \frac{(D_1 q)(h_{x, y}(d_{\tau_1}(\theta))}{D_1 \theta} \right] \left[ \frac{(D_1 q)(h_{x, y}(d_{\tau_1}(\theta))}{D_2 \theta} \right] 
\times \cdots 
\times \left[ \frac{(D_n q)(h_{x, y}(d_{\tau_1}(\theta))}{D_n \theta} \right] dxdy \right] V_\mu(\tau_1)
\]

(SM10.7)
where
\[ V_0(\tau_1) := \begin{bmatrix} (D_1x_{\tau_1})(\theta) & \cdots & (D_nx_{\tau_1})(\theta) \\ (D_1y_{\tau_1})(\theta) & \cdots & (D_ny_{\tau_1})(\theta) \end{bmatrix} \in \mathbb{R}^{2 \times n}. \]

Let \( w_1: \mathbb{R}^2 \to \mathbb{R} \), such that
\[ w_1(u, v) = \frac{1}{q(u, v)} [(D_1q)(u, v)]^2, \quad (u, v) \in \mathbb{R}^2, \]
be an integrable function. Also, let \( g_0, \tau_1 = (g_{0, \tau_1}^1, g_{0, \tau_1}^2): \mathbb{R}^2 \to \mathbb{R}^2 \), such that
\[ g_{0, \tau_1}(x, y) = (g_{0, \tau_1}^1(x, y), g_{0, \tau_1}^2(x, y)) = \left( \frac{x}{M} - x_{\tau_1}(\theta), \frac{y}{M} - y_{\tau_1}(\theta) \right) = (u, v). \]
Then, we have for the Jacobian \( J(g_{0, \tau_1}) \) of \( g_{0, \tau_1} \),
\[ J(g_{0, \tau_1}) = \begin{bmatrix} \frac{\partial g_{0, \tau_1}^1}{\partial x} & \frac{\partial g_{0, \tau_1}^1}{\partial y} \\ \frac{\partial g_{0, \tau_1}^2}{\partial x} & \frac{\partial g_{0, \tau_1}^2}{\partial y} \end{bmatrix} = \begin{bmatrix} \frac{1}{M} & 0 \\ 0 & \frac{1}{M} \end{bmatrix}, \]
and the modulus of its determinant is given by
\[ \left| \det \begin{bmatrix} \frac{1}{M} & 0 \\ 0 & \frac{1}{M} \end{bmatrix} \right| = \frac{1}{M^2}. \]

Then, according to Theorem SM14.4 (see Section SM14.4),
\[
\int_{\mathbb{R}^2} w_1(u, v) dudv = \frac{1}{M^2} \int_{\mathbb{R}^2} w_1(g_{0, \tau_1}(x, y)) dxdy \\
= \frac{1}{M^2} \int_{\mathbb{R}^2} w_1 \left( \frac{x}{M} - x_{\tau_1}(\theta), \frac{y}{M} - y_{\tau_1}(\theta) \right) dxdy.
\]

Also, let \( w_2, w_3: \mathbb{R}^2 \to \mathbb{R} \), such that
\[ w_2(u, v) = \frac{1}{q(u, v)} [(D_1q)(u, v)](D_2q)(u, v), \quad (u, v) \in \mathbb{R}^2, \]
and
\[ w_3(u, v) = \frac{1}{q(u, v)} [(D_2q)(u, v)]^2, \quad (u, v) \in \mathbb{R}^2, \]
be integrable functions. Similarly, according to Theorem SM14.4 (see Section SM14.4),
\[
\int_{\mathbb{R}^2} w_i(u, v) dudv = \frac{1}{M^2} \int_{\mathbb{R}^2} w_i \left( \frac{x}{M} - x_{\tau_1}(\theta), \frac{y}{M} - y_{\tau_1}(\theta) \right) dxdy, \quad i = 2, 3.
\]

Then, by substituting Eqs. (SM10.8) and (SM10.9) into Eq. (SM10.7),
\[
L_{\tau_1}(\theta) = V_0^T(\tau_1) \left[ \int_{\mathbb{R}^2} \frac{1}{q(u, v)} [(D_1q)(u, v)]^2 dudv \int_{\mathbb{R}^2} \frac{1}{q(u, v)} [(D_2q)(u, v)]^2 dudv \right] V_0(\tau_1) \\
= V_0^T(\tau_1) \left[ \int_{\mathbb{R}^2} \frac{1}{q(u, v)} \left( [(D_1q)(u, v)] [(D_2q)(u, v)]^T \right) dudv \right] V_0(\tau_1).
\]

2.2. The results follow by using the similar procedure used in the previous part.
**SM11. Proof of Corollary 5.7.** According to Theorem 5.2, the Fisher information matrix \( I_{\tau_1, \ldots, \tau_K}(\theta) \) in Eq. (5.2) (or Eq. (5.6)) can be calculated as
\[
I_{\tau_1, \ldots, \tau_K}(\theta) = \begin{cases} 
\sum_{l=1}^{K} I'_{U_l|\tau_l, D_{l-1}}(\theta), & t_0 \leq \tau_1 < \cdots < \tau_K \leq t, \\
0, & \text{otherwise},
\end{cases}
\]
where
\[
I'_{U_l|\tau_l, D_{l-1}}(\theta) = \int_c \cdots \int_c p_{\theta,l-1}(\tau_{l-1}) \left[ \int_c \cdots \int_c p_{\theta,l-1}(\tau_{1,l-1}) \right] \left[ \int_c \cdots \int_c p_{\theta,l-1}(\tau_{1,l-1}) \right] \partial \log p_{\theta,l-1}(\tau_{1,l-1}) \partial \theta d\tau_{1,l-1} \cdots d\tau_{l-1}.
\]
with \( d_l \in \mathbb{R}^l \) (or \( d_l \in \mathbb{R}^l \)), and \( \tau_{1,l} := (\tau_1, \ldots, \tau_l), \tau_{1,l} := (\tau_1, \ldots, \tau_l), l = 1, 2, \ldots \). Under the certain regularity conditions, for \( \theta = (\theta_1, \cdots, \theta_n) \in \Theta, i,j = 1, \cdots, n \), the \( i,j \)th entry of \( I'_{U_l|\tau_l, D_{l-1}} \) can be calculated as
\[
\left[ I'_{U_l|\tau_l, D_{l-1}}(\theta) \right]_{i,j} = \int_c \cdots \int_c p_{\theta,l-1}(\tau_{l-1})(\partial^2 \log p_{\theta,l-1}(\tau_{l-1})) d\tau_{l-1} \cdots d\tau_1.
\]
According to Eq. (SM3.6),
\[
p_{\theta,l-1}(\tau_{l-1}) = \frac{1}{2\pi \left| \det (R_{\theta,l}) \right|^{1/2}} \exp \left( -\frac{1}{2} e^T_{\theta,l} R_{\theta,l}^{-1} e_{\theta,l} \right),
\]
where \( e_{\theta,l} := \tau_l - C \hat{x}_{\theta,l}^{-1}, R_l := C P_{\theta,l}^{1/2} C^T + \Sigma_g \), and for \( l = 0, 1, \cdots \),
\[
\hat{x}_{\theta,l+1} = \hat{\phi}(\tau_l, \tau_{l+1}) \hat{x}_{\theta,l} + \hat{\delta}(\tau_l, \tau_{l+1}),
\]
and for \( l = 1, 2, \cdots \),
\[
\hat{x}_{\theta,0} = \hat{x}_{\theta,0}, P_{\theta,0} := \hat{P}_{\theta,0}. \quad \text{In order to calculate } \left[ I'_{U_l|\tau_l, D_{l-1}} \right]_{i,j}, i,j = 1, \cdots, n, \text{ in Eq. (SM11.1), we first calculate, for } \theta = (\theta_1, \cdots, \theta_n) \in \Theta \text{ and } i = 1, \cdots, n, \text{ the derivative of } \log p_{\theta,l-1} \text{ with respect to } \theta_i \text{ as below}
\]
\[
\frac{\partial \log p_{\theta,l-1}(\tau_{1,l-1})}{\partial \theta_i} = -\frac{1}{2} \text{trace} \left( R_{\theta,l} \frac{\partial R_{\theta,l}}{\partial \theta_i} \right)
\]
\[
= -\frac{1}{2} \left( \frac{\partial e^T_{\theta,l} R_{\theta,l}^{-1} e_{\theta,l}}{\partial \theta_i} \left( -e^T_{\theta,l} R_{\theta,l}^{-1} e_{\theta,l} - e^T_{\theta,l} R_{\theta,l}^{-1} e_{\theta,l} \frac{\partial R_{\theta,l}}{\partial \theta_i} R_{\theta,l}^{-1} e_{\theta,l} \right) \right).
\]
Since the covariance matrix \( R_{\theta,l} \) is symmetric, then \( \frac{\partial e^T_{\theta,l} R_{\theta,l}^{-1} e_{\theta,l}}{\partial \theta_i} = e^T_{\theta,l} R_{\theta,l}^{-1} \frac{\partial e_{\theta,l}}{\partial \theta_i} \), and therefore, according to Eq. (SM11.5), note that
\[
\frac{\partial e^T_{\theta,l} R_{\theta,l}^{-1} e_{\theta,l}}{\partial \theta_i} = e^T_{\theta,l} R_{\theta,l}^{-1} \frac{\partial e_{\theta,l}}{\partial \theta_i} = e^T_{\theta,l} R_{\theta,l}^{-1} \frac{\partial e_{\theta,l}}{\partial \theta_i} = e^T_{\theta,l} R_{\theta,l}^{-1} \frac{\partial e_{\theta,l}}{\partial \theta_i}, \text{ and therefore, according to Eq. (SM11.5), note that}
\]
Therefore, the inner integral in Eq. (SM11.1) can be calculated as

$$
\int_C p^{\theta}_{\theta_i|\tau_i, d_{i-1}} \left( r_i | \tau_i, d_{i-1} \right) \frac{\partial^2 \log p^{\theta}_{\theta_i|\tau_i, d_{i-1}}}{\partial \theta_i \partial \theta_j} \left( r_i | \tau_i, d_{i-1} \right) dr_i =
$$

$$
- \frac{1}{2} \text{trace} \left( \left( R^{-1}_{\theta_i \theta_j} \frac{\partial R_{\theta_i \theta_j}}{\partial \theta_j} \right) \left( I - R^{-1}_{\theta_i \theta_i} e_{\theta_i} e_{\theta_i}^T \right) \right)
$$

$$
- \frac{1}{2} \text{trace} \left( R^{-1}_{\theta_i \theta_i} \frac{\partial R_{\theta_i \theta_i}}{\partial \theta_j} R^{-1}_{\theta_i \theta_i} \left( \frac{\partial e_{\theta_i}}{\partial \theta_j} + e_{\theta_i} \right) \right)
$$

$$
+ \frac{1}{2} \text{trace} \left( R^{-1}_{\theta_i \theta_i} \frac{\partial R_{\theta_i \theta_i}}{\partial \theta_j} \right)
$$

$$
= \int_C p^{\theta}_{\theta_i|\tau_i, d_{i-1}} \left( r_i | \tau_i, d_{i-1} \right) \frac{\partial^2 \log p^{\theta}_{\theta_i|\tau_i, d_{i-1}}}{\partial \theta_i \partial \theta_j} \left( r_i | \tau_i, d_{i-1} \right) dr_i
$$

Therefore, the inner integral in Eq. (SM11.1) can be calculated as

$$
\frac{\partial \log p^{\theta}_{\theta_i|\tau_i, d_{i-1}}}{\partial \theta_i} \left( r_i | \tau_i, d_{i-1} \right) =
$$

$$
- \frac{1}{2} \text{trace} \left( \left( R^{-1}_{\theta_i \theta_i} \frac{\partial R_{\theta_i \theta_i}}{\partial \theta_j} \right) \left( I - R^{-1}_{\theta_i \theta_i} e_{\theta_i} e_{\theta_i}^T \right) \right)
$$

$$
- \frac{1}{2} \text{trace} \left( R^{-1}_{\theta_i \theta_i} \frac{\partial R_{\theta_i \theta_i}}{\partial \theta_j} R^{-1}_{\theta_i \theta_i} \left( \frac{\partial e_{\theta_i}}{\partial \theta_j} + e_{\theta_i} \right) \right)
$$

$$
+ \frac{1}{2} \text{trace} \left( R^{-1}_{\theta_i \theta_i} \frac{\partial R_{\theta_i \theta_i}}{\partial \theta_j} \right)
$$

where $I$ denotes the identity matrix with the corresponding size. Differentiating Eq. (SM11.6) with respect to $\theta_j$, gives [SM2]
Note that for $j = 1, \cdots, n$,

$$\int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) e_{\theta, l} \frac{\partial u_{\theta, l}}{\partial \theta_j} \frac{\partial e_{\theta, l}}{\partial \theta_j} \, dr_1$$

$$= \int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \left( r_1 - C \hat{x}_{\theta, l}^{-1} \right) \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_j} \, C^T \, dr_1$$

$$= \left[ \int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \left( r_1 - C \hat{x}_{\theta, l}^{-1} \right) \, dr_1 \right] \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_j} \, C^T$$

$$= \left[ \int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \left( r_1 - C \hat{x}_{\theta, l}^{-1} \right) \, dr_1 - C \hat{x}_{\theta, l}^{-1} \int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \, dr_1 \right] \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_j} \, C^T$$

$$= \left[ C \hat{x}_{\theta, l}^{-1} - C \hat{x}_{\theta, l}^{-1} \right] \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_j} \, C^T = 0.$$

Similarly, $\int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \frac{\partial u_{\theta, l}}{\partial \theta_j} e_{\theta, l} \, dr_1 = 0$, and therefore, Term 2, Term 3, and Term 4 in Eq. (SM11.7) are equal to zero. Then, noting that

$$\int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) e_{\theta, l} e_{\theta, l}^T \, dr_1 = R_{\theta, l},$$

we have Term 1 = 0, and Eq. (SM11.7) becomes

$$\int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \frac{\partial^2 \log p_{\theta_l}^\theta}{\partial \theta_i \partial \theta_j} \, dr_1$$

$$= -\frac{1}{2} \text{trace} \left[ R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_i} R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_j} \right]$$

$$- \left[ \int_C p_{\theta_l}^\theta \left( r_1 | \tau, d_{l-1} \right) \, dr_1 \right] \left( \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_i} \, C^T \, R_{\theta, l}^{-1} \frac{\partial \hat{x}_{\theta, l}^{-1}}{\partial \theta_j} \right)$$

By substituting the above equation in Eq. (SM11.1), we have

$$\left[ I_{\theta_l} \right]_{i, j} = \frac{1}{2} \text{trace} \left[ R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_i} R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_j} \right]$$

$$+ \int_C \cdots \int_C p_{\theta_l}^\theta \left( r_{1, l-1} | \tau_{1, l-1} \right) \left( r_{1, l-1} - C \hat{x}_{\theta, l}^{-1} \right) \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_i} \, C^T \, R_{\theta, l}^{-1} \frac{\partial \hat{x}_{\theta, l}^{-1}}{\partial \theta_j} \, dr_{1, l-1} \cdots \, dr_1$$

$$= \frac{1}{2} \text{trace} \left[ R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_i} R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_j} \right] + \text{trace} \left( R_{\theta, l}^{-1} \frac{\partial R_{\theta, l}}{\partial \theta_i} \left( \frac{\partial \left( \hat{x}_{\theta, l}^{-1} \right)^T}{\partial \theta_j} \, C^T \right) \right)$$

By Eqs. (SM11.3) and (SM11.4),

$$\hat{x}_{\theta, l+1} = \hat{x}_{\theta, l} \left( r_{l} - C \hat{x}_{\theta, l}^{-1} \right), \quad l = 1, 2, \cdots.$$
Then, according to Lemma SM14.2 (see Section SM14.2), by differentiating Eq. (SM11.10) with respect to \( \theta_i, i = 1, \ldots, n \), after some straightforward calculations, for \( X_{\theta,l}^{(i)} := \begin{bmatrix} \frac{\partial^2 x_{\theta,l}}{\partial \theta_i^2} \\ \frac{\partial^2 x_{\theta,l}}{\partial \theta_i^2} \end{bmatrix} \), we have the following recursive formulation:

\[
X_{\theta,l+1}^{(i)} = A_{\theta,l+1}^{(i)} X_{\theta,l}^{(i)} + B_{\theta,l+1}^{(i)} \theta, \quad \theta = (\theta_1, \ldots, \theta_n) \in \Theta, \quad i = 1, \ldots, n,
\]

and

\[
A_{\theta,l+1}^{(i)} := \frac{\partial \phi(\tau_1, \tau_{l+1})}{\partial \theta_i} \frac{\partial \phi(\tau_1, \tau_{l+1})}{\partial \theta_i} 0_{k \times k} + \frac{\partial \phi(\tau_1, \tau_{l+1})}{\partial \theta_i} \begin{bmatrix} I_{k \times k} - K_{\theta,l} \end{bmatrix}, \quad B_{\theta,l}^{(i)} := \begin{bmatrix} \frac{\partial \phi(\tau_1, \tau_{l+1})}{\partial \theta_i} \phi_{\theta,l} \end{bmatrix}.
\]

According to Lemma SM14.5 (see Section SM14.5) and using Eq. (SM11.11), we have, for \( l = 1, 2, \ldots, \)

\[
E \left\{ X_{\theta,l+1}^{(i)} \right\} = E \left\{ A_{\theta,l+1}^{(i)} X_{\theta,l}^{(i)} + B_{\theta,l+1}^{(i)} \theta \right\} + B_{\theta,l+1}^{(i)} E \left\{ \theta \right\} = A_{\theta,l+1}^{(i)} E \left\{ X_{\theta,l}^{(i)} \right\} + B_{\theta,l+1}^{(i)} E \left\{ \theta \right\} = A_{\theta,l+1}^{(i)} E \left\{ X_{\theta,l}^{(i)} \right\} + B_{\theta,l+1}^{(i)} E \left\{ \theta \right\} = A_{\theta,l+1}^{(i)} X_{\theta,l}^{(i)} + B_{\theta,l+1}^{(i)} \theta.
\]

Finally, by rewriting the Fisher information expression (Eq. (SM11.9)) as (let \( \tilde{C} := [0_{2 \times k} \ C] \), where \( 0_{2 \times k} \) denotes the 2 \( \times \) k zero matrix)

\[
I_{(\theta)} := \frac{1}{2} \text{tr} \left[ R_{\theta,1}^{-1} \frac{\partial R_{\theta,1}}{\partial \theta_i} R_{\theta,1}^{-1} \frac{\partial R_{\theta,1}}{\partial \theta_j} \right] + \text{tr} \left\{ R_{\theta,1}^{-1} \tilde{C} E \left\{ X_{\theta,l}^{(i)} \right\} \tilde{C}^T \right\},
\]

and substituting Eq. (SM11.12) into Eq. (SM11.13), we have

\[
I_{(\theta)} := \frac{1}{2} \text{tr} \left[ R_{\theta,1}^{-1} \frac{\partial R_{\theta,1}}{\partial \theta_i} R_{\theta,1}^{-1} \frac{\partial R_{\theta,1}}{\partial \theta_j} \right] + \text{tr} \left\{ R_{\theta,1}^{-1} \tilde{C} S_{\theta,l}^{(i)} \tilde{C}^T \right\},
\]

where \( S_{\theta,l}^{(i)} := E \left\{ X_{\theta,l}^{(i)} \right\}, i, j = 1, 2, \ldots, \) can be calculated recursively as

\[
S_{\theta,l+1}^{(i)} = A_{\theta,l+1}^{(i)} S_{\theta,l}^{(i)} + B_{\theta,l+1}^{(i)} \theta, \quad l = 1, 2, 3, \ldots
\]

and it completes the proof.
SM12. Example for Fisher information calculation. For the data model described in the example provided in Section SM4, the Fisher information matrix is given by Eqs. (5.13) and (5.14), where \( S_{\theta, l}, l = 1, 2, \cdots \), is given recursively by, for \( \theta = (\theta_1, \cdots, \theta_n) \in \Theta \) and \( i, j = 1, \cdots, n \),

\[
S_{\theta, i}^{(j)} = A_{\theta, i}^{(j)} c_{\theta, i-1}^{(j)} \left( A_{\theta, i}^{(j)} \right)^T = B_{\theta, i}^{(j)} R_{\theta, i-1} \left( B_{\theta, i}^{(j)} \right)^T, \quad l = 2, 3, \cdots,
\]

and

\[
S_{\theta, 1}^{(j)} = \left[ \frac{\partial^2 \theta(\tau_0, \tau_1) x_{\theta, 0}}{\partial \phi(\tau_0, \tau_1) x_{\theta, 0}} \right] \left[ \frac{\partial \phi(\tau_0, \tau_1) x_{\theta, 0}}{\partial \theta} \right]^T,
\]

with coefficient matrices given through Eqs. (SM4.3)-(SM4.5). In Section SM4, we calculated these coefficient matrices for the first order drift and diffusion coefficients estimation problem in different scenarios.

SM13. Computation of general Fisher information matrix. We calculate the Fisher information matrix numerically, for the case that we have one photon, through the following algorithm (here, it is assumed that \( \theta = D \), where \( D \) is the diffusion coefficient).

1. For \( a, b \in \mathbb{R}, a < b \), let \( x_i := a + ih, y_i := a + ih, i = 0, \cdots, n \), and \( h := \frac{b-a}{n} \).

   Approximate \( p_{X(\tau)} \) as

   \[
p_{X(\tau)}(x_1) = \int_{\mathbb{R}^2} p_{X(\tau)|X(t_0)}(x_1|x)p_{X(t_0)}(x) \, dx
   \approx h^2 \sum_{i=0}^{n} \sum_{j=0}^{n} p_{X(\tau)|X(t_0)}(x_1|(x_i, y_j)) p_{X(t_0)}(x_i, y_j), \quad x_1 \in \mathbb{R}^2.
   \]

2. Approximate \( dp_{X(\tau)} := \frac{dp_{X(\tau)}}{\partial D} \) as

   \[
dp_{X(\tau)}(x_1) = \int_{\mathbb{R}^2} dp_{X(\tau)|X(t_0)}(x_1|x)p_{X(t_0)}(x) \, dx
   \approx h^2 \sum_{i=0}^{n} \sum_{j=0}^{n} dp_{X(\tau)|X(t_0)}(x_1|(x_i, y_j)) p_{X(t_0)}(x_i, y_j), \quad x_1 \in \mathbb{R}^2.
   \]

3. Approximate \( p_{U_1|T_1} \) as

   \[
p_{U_1|T_1}(r|\tau_1) = \int_{\mathbb{R}^2} p_{X(\tau_1)}(x) p_{U_1|X(\tau_1)}(r|x) \, dx
   = \int_{\mathbb{R}^2} p_{X(\tau_1)}(x) f_2(r) \, dx
   = \frac{1}{|\det(M)|} \int_{\mathbb{R}^2} p_{X(\tau_1)}(x) q(M^{-1}r - x) \, dx
   \approx \frac{h^2}{|\det(M)|} \sum_{i=0}^{n} \sum_{j=0}^{n} p_{X(\tau_1)}(x_i, y_j) q(M^{-1}r - (x_i, y_j)), \quad r \in \mathbb{C}.
   \]

4. Approximate \( dp_{U_1|T_1} := \frac{dp_{U_1|T_1}}{\partial D} \) as
\[
dp_{U_1|T_1} \left( r | \tau_1 \right) = \int_{\mathbb{R}^2} dp_{X(\tau_1)}(x) f_x(r) \, dx \\
= \frac{1}{|\det(M)|} \int_{\mathbb{R}^2} dp_{X(\tau_1)}(x) q(M^{-1}r - x) \, dx \\
\approx \frac{h^2}{|\det(M)|} \sum_{i=0}^{n} \sum_{j=0}^{n} dp_{X(\tau_1)}(x_i, y_j) q(M^{-1}r - (x_i, y_j)), \quad r \in \mathbb{C}.
\]

5. Let \( r_{x_i} = M x_i, r_{y_i} = M y_i, i = 0, \ldots, n \), and \( h_r = Mh \). Approximate the Fisher information matrix \( I(D) \) of diffusion coefficient \( D \) as

\[
I(D) = \int_{C} \frac{1}{p_{U_1|T_1}(r | \tau_1)} dp_{U_1|T_1}^2 (r | \tau_1) \, dr \\
\approx h^2 \sum_{i=0}^{n} \sum_{j=0}^{n} \frac{1}{p_{U_1|T_1}(r_{x_i}, r_{y_j}) | \tau_1)} dp_{U_1|T_1}^2 \left( (r_{x_i}, r_{y_j}) | \tau_1 \right).
\]

**SM14. Appendix.**

**SM14.1. Joint probability distribution of arrival time points for a Poisson process.**

**Lemma SM14.1.** For \( t_0 \in \mathbb{R} \), let \( \{N(\tau), \tau \geq t_0\} \) be a Poisson process with intensity function \( \Lambda(\tau), \tau \geq t_0 \). Let \( T_l := (T_1, \cdots, T_l)^T, l = 1, \cdots, N(\tau), \tau \geq t_0 \), where the 1D random variable \( T_l \) describes the \( l \)th arrival time points of \( \{N(\tau), \tau \geq t_0\} \).

1. Then, \( \Lambda(D), \tau \geq t_0 \), is Poisson distributed with mean \( \int_{t_0}^{\tau} \Lambda(\psi) \, d\psi \), i.e., for \( L = 0, 1, \cdots \), the probability \( P \left( \Lambda(D) = L \right) \) is given by

\[
P(\Lambda(\tau) = L) = \frac{1}{L!} \left( \int_{t_0}^{\tau} \Lambda(\psi) \, d\psi \right)^L e^{-\int_{t_0}^{\tau} \Lambda(\psi) \, d\psi}, \quad \tau \geq t_0.
\]

2. For \( t_0 \leq \tau_1 < \cdots < \tau_L, L = 1, 2, \cdots \), the probability density function \( p_{\tau_L} \) of \( T_L \) is given by

\[
p_{\tau_L}(\tau_1, \cdots, \tau_L) = \left( \prod_{i=1}^{L} \Lambda(\tau_i) \right) e^{-\int_{t_0}^{\tau} \Lambda(\psi) \, d\psi}.
\]

3. For \( t_0 \leq \tau_1 < \cdots < \tau_L \leq t, L = 1, 2, \cdots \), the conditional probability density function \( p_{\tau_L | N(t)} \) is given by

\[
p_{\tau_L | N(t)}(\tau_1, \cdots, \tau_L | L) = \frac{L! \left( \prod_{i=1}^{L} \Lambda(\tau_i) \right)}{\left( \int_{t_0}^{t} \Lambda(\tau) \, d\tau \right)^L}.
\]

**Proof.** See Section 2 of [SM6].

**SM14.2. Derivative of state estimates.**

**Lemma SM14.2.** Let \( \Theta \) denote a parameter space that is an open subset of \( \mathbb{R}^n \), and let \( \tau_1 \in \mathbb{R} \). For \( \theta = (\theta_1, \cdots, \theta_n) \in \Theta, r_1 \in \mathbb{C}, l = 1, 2, \cdots \), and \( \tau_1 < \tau_2 < \cdots \), let

\[
\bar{x}_{\theta, l+1} = \bar{\phi}(\tau_1, \tau_{l+1}) \left( \bar{x}_{\theta, l} + K_{\theta, l}(r_1 - C \bar{x}_{\theta, l}^{l-1}) \right), \quad \bar{x}_{\theta, l+1} \in \mathbb{R}^k.
\]
where \( \hat{\phi}(\tau_1, \tau_{i+1}) \in \mathbb{R}^{k \times k}, C \in \mathbb{R}^{2 \times k}, K_{\theta,l} \in \mathbb{R}^{k \times 2}, \) and their derivatives with respect to \( \theta_i, i = 1, \cdots, n, \) exist. Let \( X_{\theta,l}^{(i)} := \left[ \frac{x_{l-1}^i}{\partial x_{l-1}^i} \right] \) and \( e_{\theta,l} := r_i - C_l K_{\theta,l}^{l-1}. \) Then,

\[
X_{\theta,l+1} = A_{\theta,l+1}^{(i)} X_{\theta,l}^{(i)} + B_{\theta,l+1}^{(i)} e_{\theta,l}, \quad l = 1, 2, \cdots,
\]

where

\[
A_{\theta,l+1}^{(i)} := \left[ \begin{array}{cc} \hat{\phi}(\tau_1, \tau_{i+1}) & 0_{k \times k} \\ \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \tau_1} & \hat{\phi}(\tau_1, \tau_{i+1}) (I_{k \times k} - K_{\theta,l} M) \end{array} \right],
\]

\[
B_{\theta,l+1}^{(i)} := \left[ \begin{array}{c} \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \tau_1} \frac{\partial K_{\theta,l}}{\partial \theta_l} + \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \theta_l} K_{\theta,l} \end{array} \right].
\]

Proof. By differentiating Eq. (SM14.1) (Kalman state estimate update formula) with respect to \( \theta_i, i = 1, \cdots, n, \) we have, for \( l = 1, 2, \cdots, \)

\[
\frac{\partial x_{l+1}^{(i)}}{\partial \theta_i} = \left[ \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \tau_1} \hat{\phi}(\tau_1, \tau_{i+1}) (I_{k \times k} - K_{\theta,l} C) \right] \frac{\partial x_{l-1}^{(i)}}{\partial \theta_i} + \left( \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \tau_1} \frac{\partial K_{\theta,l}}{\partial \theta_l} + \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \theta_l} K_{\theta,l} \right) e_{\theta,l},
\]

(SM14.2)

Then, by combining Eqs. (SM14.1) and (SM14.2), for \( X_{\theta,l}^{(i)} := \left[ \frac{x_{l}^{(i)}}{\partial x_{l}^{(i)}} \right], \) we have the following recursive formulation

\[
X_{\theta,l+1} = A_{\theta,l+1}^{(i)} X_{\theta,l}^{(i)} + B_{\theta,l+1}^{(i)} e_{\theta,l},
\]

where

\[
A_{\theta,l+1}^{(i)} := \left[ \begin{array}{cc} \hat{\phi}(\tau_1, \tau_{i+1}) & 0_{k \times k} \\ \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \tau_1} & \hat{\phi}(\tau_1, \tau_{i+1}) (I_{k \times k} - K_{\theta,l} C) \end{array} \right],
\]

\[
B_{\theta,l+1}^{(i)} := \left[ \begin{array}{c} \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \tau_1} \frac{\partial K_{\theta,l}}{\partial \theta_l} + \frac{\partial \hat{\phi}(\tau_1, \tau_{i+1})}{\partial \theta_l} K_{\theta,l} \end{array} \right].
\]

SM14.3. Chain rule.

Theorem SM14.3. Let \( S \) be an open set in \( \mathbb{R}^k \) and let \( c \) be a point of \( S. \) Let \( d := (d_1, \cdots, d_M) \) be a function mapping \( S \) into an open set \( H \) in \( \mathbb{R}^M, \) i.e., \( d: S \rightarrow H, \) that is differentiable at \( c. \) Let \( h := (h_1, \cdots, h_N) \) be a function mapping \( H \) into an open set \( Q \) in \( \mathbb{R}^N, \) i.e., \( h: H \rightarrow Q, \) that is differentiable at \( d(c). \) Let \( q \) be a real-valued function defined on \( Q \) that is differentiable at \( h(d(c)). \) Then,

\[
(D_k(q \circ h \circ d))(c) = \sum_{i=1}^{N} \sum_{j=1}^{M} (D_i q)(h(d(c)))(D_j h_i)(d(c))(D_k d_j)(c), \quad k = 1, \cdots, K.
\]

Proof. See the proof of Corollary 8.4.3 of [SM1].

SM14.4. Integral transformation theorem.

Theorem SM14.4. Let \( g := (g_1, g_2, \cdots, g_n): B \subseteq \mathbb{R}^n \rightarrow \mathbb{R}^n \) be an injective and continuously differentiable function. Let \( w: \mathbb{R}^n \rightarrow \mathbb{R} \) be an integral function and \( A \subseteq \mathbb{R}^n, \) then the integral transformation theorem is given by

\[
\int_{g(A)} w(y_1, y_2, \cdots, y_n) dy_1 dy_2 \cdots dy_n = \int_A w(g(x_1, x_2, \cdots, x_n)) \times | \det(J(g)(x_1, x_2, \cdots, x_n)) | dx_1 dx_2 \cdots dx_n,
\]
where the Jacobian matrix is given by

\[
J(g) := \begin{bmatrix}
\frac{\partial g_1(x_1, x_2, \ldots, x_n)}{\partial x_1} & \frac{\partial g_1(x_1, x_2, \ldots, x_n)}{\partial x_2} & \cdots & \frac{\partial g_1(x_1, x_2, \ldots, x_n)}{\partial x_n} \\
\frac{\partial g_2(x_1, x_2, \ldots, x_n)}{\partial x_1} & \frac{\partial g_2(x_1, x_2, \ldots, x_n)}{\partial x_2} & \cdots & \frac{\partial g_2(x_1, x_2, \ldots, x_n)}{\partial x_n} \\
\vdots & \vdots & \ddots & \vdots \\
\frac{\partial g_n(x_1, x_2, \ldots, x_n)}{\partial x_1} & \frac{\partial g_n(x_1, x_2, \ldots, x_n)}{\partial x_2} & \cdots & \frac{\partial g_n(x_1, x_2, \ldots, x_n)}{\partial x_n}
\end{bmatrix}
\]

Proof. See Section 10.3 of [SM1].

**Lemma SM14.5.** Innovation representation of the state space model.

**Lemma SM14.5.** Let \( G^o_L \left( \left( \tilde{X}, H, \tilde{W}, Z \right), \left( U_L, T_L \right), \tilde{\Phi}, M', C, \Theta \right) \) (or \( G^\circ_L \left( \left( \tilde{X}, H, \tilde{W}, Z \right), \left( U_L, T_L \right), \tilde{\Phi}, M', C, \Theta \right) \)) be an image detection process with expanded state space \( \tilde{X} \) and Gaussian process and measurement noise models for a time interval \([t_0, t]\) (or for a fixed number \( L \) of photons). Let \( C := M' H \). Assume that \( C \) and \( Z \) are independent of the parameter vector \( \theta \in \Theta \). For \( \theta = (\theta_1, \ldots, \theta_n) \) and \( \tilde{x}_{\theta, t}^{L-1} := E \left[ \tilde{X}_\theta(\tau) | r_1, \ldots, r_L \right] \), let \( X_{\theta, t}^{(i)} := \left[ \frac{x_{\theta, t}^{L-1}}{\partial \tilde{x}_{\theta, t}^{L-1}} \right] \), \( i = 1, \cdots, n \), be the extended state vector and \( e_{\theta, t} := r_t - C \tilde{x}_{\theta, t}^{L-1} \) be the prediction error. Then, \( E \left[ e_{\theta, t} X_{\theta, t}^{(i)} \right] = 0, i = 1, \cdots, n \).

Proof. Since the measurement noise \( Z \), the process noise \( \tilde{W} \), and the initial condition of the state vector \( \tilde{X} \) are independent, the prediction error \( e_{\theta, t} \) and the extended state vector \( X_{\theta, t}^{(i)}, i = 1, \cdots, n \), are independent (see the proof of Theorem 5 of [SM4]), and we have

\[
E \left[ X_{\theta, t}^{(i)} e_{\theta, t} \right] = E \left[ X_{\theta, t}^{(i)} \right] E \left[ e_{\theta, t} \right]
= E \left[ X_{\theta, t}^{(i)} \right] E \left[ C (\tilde{X}_\theta(\tau) - \tilde{x}_{\theta, t}^{L-1}) + Z \right]
= E \left[ X_{\theta, t}^{(i)} \right] \left\{ C \left( E \left[ \tilde{X}_\theta(\tau) \right] - E \left[ X_{\theta, t}^{L-1} \right] \right) + E \left[ Z \right] \right\}.
\]

According to the law of total expectation, \( E \left[ E \left[ X_{\theta, t}^{L-1} | r_1, \cdots, r_L \right] \right] = E \left[ X_{\theta, t}^{L-1} \right] \), and therefore, we have

\[
E \left[ X_{\theta, t}^{(i)} e_{\theta, t} \right] = E \left[ X_{\theta, t}^{(i)} \right] \left\{ C \left( E \left[ \tilde{X}_\theta(\tau) \right] - E \left[ X_{\theta, t}^{L-1} \right] \right) \right\} + 0 = 0.
\]

**SM14.6.** Analysis of the error of the predicted locations of the molecule.

In this section, the errors between the means of the distributions of the prediction of the molecule locations and the true locations of the molecule for Born and Wolf, Airy and Gaussian measurements are shown in Figs. SM4, SM5 and SM6, respectively.

**REFERENCES**


**SUPPLEMENTARY MATERIALS: FISHER INFORMATION FOR MOLECULES**

**Fig. SM4.** Analysis of the error of the predicted locations of the molecule for the Born and Wolf measurement model. Shown in the left and right plots are the differences between the means of the distributions of the prediction of the molecule x-locations and the true x-values, and the means of the distributions of the prediction of the molecule y-locations and the true y-values, respectively, for the data sets of Fig. 5.

**Fig. SM5.** Analysis of the error of the predicted locations of the molecule for the Airy measurement model. Shown in the left and right plots are the differences between the means of the distributions of the prediction of the molecule x-locations and the true x-values, and the means of the distributions of the prediction of the molecule y-locations and the true y-values, respectively, for the data sets of Fig. SM3.


Fig. SM6. Analysis of the error of the predicted locations of the molecule for the Gaussian measurement noise case. Shown in the left and right plots are the differences between the means of the distributions of the prediction of the molecule $x$-locations and the true $x$-values, and the means of the distributions of the prediction of the molecule $y$-locations and the true $y$-values, respectively, for the data sets of Fig. 8.