Supplementary Information for

Autocorrelation analysis for cryo-EM with sparsity constraints: Improved sample complexity and projection-based algorithms

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Supplementary text
Legend for Movie S1
SI References

Other supplementary materials for this manuscript include the following:

Movie S1
1. Proofs of auxiliary results for Theorems 1 and 2

A. Proof of Lemma 8. Note that $S_{ij}$ is connected and compact, since $S_{ij} = \theta_{ij}(\text{SO}(3))$ and $\text{SO}(3)$ is compact and connected, while $\theta_{ij}$ is continuous. It also is semialgebraic, as $\text{SO}(3)$ is a real algebraic variety and $\theta_{ij}$ is a polynomial map (see the Tarski-Seidenberg theorem (1)).

Define $T_{ij} \subseteq \mathbb{R}^2 \times \mathbb{R}^2$ as the set cut out by the three constraints in Eq. (14). Assume $((x_1, y_1), (x_2, y_2)) \in S_{ij}$. By definition of $S_{ij}$, there exist $R \in \text{SO}(3)$ and $z_1, z_2 \in \mathbb{R}$ such that $Ra_i = (x_1, y_1, z_1)\top$ and $Ra_j = (x_2, y_2, z_2)\top$. Then

$$\|a_i\|^2 - x_1^2 - y_1^2 = \|Ra_i\|^2 - x_1^2 - y_1^2 = z_1^2,$$

likewise $\|a_j\|^2 - x_2^2 - y_2^2 = z_2^2$, and

$$(a_i, a_j) - x_1x_2 - y_1y_2)^2 = (Ra_i, Ra_j) - x_1x_2 - y_1y_2)^2
= (z_1z_2)^2.$$

Also, $x_1^2 + y_1^2 \leq \|Ra_i\|^2 = \|a_i\|^2$, and similarly $x_2^2 + y_2^2 \leq \|a_j\|^2$. These show that $((x_1, y_1), (x_2, y_2)) \in T_{ij}$, whence $S_{ij} \subseteq T_{ij}$.

For the converse, take $((x_1, y_1), (x_2, y_2)) \in T_{ij}$. Let

$$z_1 = \sqrt{\|a_i\|^2 - x_1^2 - y_1^2} \quad \text{and} \quad z_2 = \varepsilon \sqrt{\|a_j\|^2 - x_2^2 - y_2^2},$$

where $\varepsilon = \text{sign}((a_i, a_j) - x_1x_2 - y_1y_2)$. Put $b_i = (x_1, y_1, z_1)^\top$ and $b_j = (x_2, y_2, z_2)^\top$ in $\mathbb{R}^3$. By the choice of $z_1$ and $z_2$,

$$\|b_i\| = \|a_i\| \quad \text{and} \quad \|b_j\| = \|a_j\|.$$

[1]

Also, from the equality constraint in Eq. (14), it holds $z_1^2z_2^2 = ((a_i, a_j) - x_1x_2 - y_1y_2)^2$. This with the choice of $\varepsilon$ implies

$$\langle b_i, b_i \rangle = \langle a_i, a_i \rangle.$$

[2]

From Eq. (1) and (2), there exists $R \in \text{SO}(3)$ such $b_i = Ra_i$ and $b_j = Ra_j$. Hence $((x_1, y_1), (x_2, y_2)) \in S_{ij}$, whence $T_{ij} \subseteq S_{ij}$.

We conclude $T_{ij} = S_{ij}$.

The dimension of $S_{ij}$ as a semialgebraic set is the maximal dimension of a cell in any cylindrical algebraic decomposition of it (1, Cor. 2.8.9). This agrees with the maximal rank attained by the differential of $\theta_{ij}$:

$$\text{dim}(S_{ij}) = \max \text{rank}(D\theta_{ij} : T_R(\text{SO}(3)) \to T_{\theta_{ij}(R)}(\mathbb{R}^2 \times \mathbb{R}^2)),$$

where $T$ denotes tangent space. We recall that the tangent space to rotation matrices is parameterized by skew-symmetric matrices. Specifically, $T_R(\text{SO}(3)) = \{[s] \times s : s \in \mathbb{R}^3\}$, where

$$[s] \times := \begin{pmatrix} 0 & s_3 & -s_2 \\ -s_3 & 0 & s_1 \\ s_2 & -s_1 & 0 \end{pmatrix}.$$

Then, $D\theta_{ij}([s] \times R) = (\pi[s] \times Ra_i, \pi[s] \times Ra_j) \in \mathbb{R}^2 \times \mathbb{R}^2 = T_{\theta_{ij}(R)}(\mathbb{R}^2 \times \mathbb{R}^2)$. Putting $(x_1, y_1, z_1)^\top := Ra_i$ and $(x_2, y_2, z_2)^\top := Ra_j$, we rewrite

$$D\theta_{ij}([s] \times R) = W(R)s, \quad \text{where} \quad W(R) := \begin{pmatrix} 0 & -z_1 & y_1 \\ z_1 & 0 & -x_1 \\ y_2 & z_2 & 0 \end{pmatrix}.$$

Thus, $\text{dim}(S_{ij}) = 3$, unless $W(R)$ is rank-deficient for all $R \in \text{SO}(3)$. We claim it is rank-deficient for specific $R$ if and only if $(x_1, y_1, z_1)$ and $(x_2, y_2, z_2)$ are linearly dependent or $z_1 = z_2 = 0$. This is proven using a computer algebra system, e.g. (2).

Indeed, if $I$ is ideal in the ring $\mathbb{Q}[x_1, y_1, z_1, x_2, y_2, z_2]$ generated by the $3 \times 3$ minors of $W(R)$, the claim follows from calculating the primary decomposition (3):

$$I = (z_1y_2 - y_1z_2, z_1x_2 - x_1z_2, y_1x_2 - x_1y_2) \cap (z_2^2, z_1z_2, z_2^2).$$

Given the claim, $\text{rank}(W(R)) < 3$ for all $R \in \text{SO}(3)$ if and only if $a_i$ and $a_j$ are linearly dependent. In other words, $S_{ij}$ has dimension 3 if and only if $a_i$ and $a_j$ are linearly independent. The proof of Lemma 8 is complete.

B. Proof of Lemma 9. As mentioned in the main text, this is immediate from Definitions 6 and 7 and Eq. (10).
C. Proof of Lemma 10. If \( X \) is a subset of a real Euclidean space \( \mathbb{R}^k \), we write \( \overline{X} \) for the Zariski closure in \( \mathbb{R}^k \), and \( \mathcal{I}(X) \) for the real radical ideal of \( \overline{X} \).

First, note that \( \overline{S} \) is irreducible. This is because \( S_i = \theta_i/(\text{SO}(3)) \), \( \theta_i \) is polynomial and \( \text{SO}(3) \) is an irreducible algebraic variety. So, \( \mathcal{I}(\overline{S}) \) is prime (1, Thm. 2.8.3(ii)). Also, \( S_i \) has dimension 3 as an algebraic variety. This is by (1, Prop. 2.8.2), and Lemma 8 which states \( S_i \) has dimension 3 as a semialgebraic set. So, \( \mathcal{I}(\overline{S}) \) has height 1 (1, Def. 2.8.1). Here, every prime ideal with height 1 is principal, as \( \mathbb{R}[x_1, y_1, x_2, y_2] \) is a unique factorization domain. It follows that
\[
\mathcal{I}(\overline{S}) = \langle f \rangle, \tag{3}
\]
for some irreducible polynomial \( f \in \mathbb{R}[x_1, y_1, x_2, y_2] \), where angle brackets indicate ideal generation.

By Lemma 8, we know \( S_i \subseteq \mathcal{Z}(q_i) \), where \( \mathcal{Z} \) denotes the zero set in \( \mathbb{R}^2 \times \mathbb{R}^2 \). Taking closures, \( \overline{S_i} \subseteq \mathcal{Z}(q_i) \). Equivalently, \( q_i \in \mathcal{I}(\overline{S_i}) \). By Eq. (3), this means \( f \) evenly divides \( q_i \), say,
\[
q_i = fg, \tag{4}
\]
for some \( g \in \mathbb{R}[x_1, y_1, x_2, y_2] \). To conclude the proof, it suffices to prove that \( g \) is a nonzero scalar. Then \( \langle q_i \rangle = \langle f \rangle = \mathcal{I}(\overline{S_i}) \), and \( q_i \) is irreducible because \( f \) is.

For a contradiction, assume that \( f \) has positive degree. Then, Eq. (4) implies
\[
\langle q_i \rangle_{\text{top}} = f_{\text{top}}g_{\text{top}}, \tag{5}
\]
where the subscript indicates the top total degree part of the polynomial. Here,
\[
q_i = (\|a_i\|^2 - \langle a_i, a_j \rangle)^2 - 2\|a_i\|^2\|a_j\|^2 - 2\|a_i\|^2\|a_j\|^2 - 2\|a_i\|^2\|a_j\|^2 - 2\|a_i\|^2\|a_j\|^2 + 2(a_i, a_j)x_1x_2 + 2(a_i, a_j)y_1y_2 + 2x_1^2y_2 + 2y_1^2x_2 - 2x_1y_1x_2y_2. \tag{6}
\]
Thus,
\[
\langle q_i \rangle_{\text{top}} = x_1^2y_2^2 + y_1^2x_2^2 - 2x_1y_1x_2y_2 = (x_1y_2 - y_1x_2)^2.
\]
From Eq. (5), the assumption that \( f \) has positive degree and unique factorization, we deduce that (possibly after multiplying by nonzero scalars)
\[
f_{\text{top}} = g_{\text{top}} = x_1y_2 - y_1x_2.
\]
Therefore,
\[
f = x_1y_2 - y_1x_2 + \alpha x_1 + \beta y_1 + \gamma x_2 + \delta y_2 + \varepsilon,
\]
\[
g = x_1y_2 - y_1x_2 + \zeta x_1 + \eta y_1 + \theta x_2 + \iota y_2 + \kappa, \tag{7}
\]
for some \( \alpha, \beta, \gamma, \delta, \varepsilon, \zeta, \eta, \theta, \iota, \kappa \in \mathbb{R} \). Now we insert Eq. (7) and Eq. (6) into Eq. (4). Equating the constants and the coefficients of \( x_1^2, y_1^2, x_2^2, y_2^2 \) gives
\[
\begin{align*}
\|a_i\|^2 - \langle a_i, a_j \rangle - \|a_j\|^2 &= \varepsilon \kappa \\
-\|a_i\|^2 &= \alpha \zeta \\
-\|a_j\|^2 &= \beta \eta \\
-\|a_j\|^2 &= \gamma \theta \\
-\|a_i\|^2 &= \delta \iota,
\end{align*} \tag{8}
\]
whence the 4 \times 2 matrix has rank 1. So all its 2 \times 2 minors vanish, in particular
\[
\alpha \eta - \beta \zeta = 0. \tag{9}
\]
Finally, we equate the coefficients of \( x_1y_1 \) in Eq. (4):
\[
0 = \alpha \eta + \beta \zeta. \tag{10}
\]
Eq. (9) and (10) imply
\[
\alpha \eta = \beta \zeta = 0. \tag{11}
\]
But this contradicts the earlier finding that \( \alpha, \ldots, \kappa \) are all nonzero. So the assumption that \( f \) has positive degree is false, and \( f \) is a nonzero scalar. This proves Lemma 10. \( \square \)
D. Proof of Corollary 11. By Lemma 9, the support of \( M_2 \) is \( \cup_{i,j=1}^{p} S_{ij} \). This has Zariski closure \( \cup_{i,j=1}^{p} \overline{S_{ij}} \). We claim its irredundant irreducible decomposition is

\[
\{(x_1, x_2) : x_1 = x_2 \} \cup \bigcup_{i \neq j} \overline{S_{ij}}. \tag{12}
\]

The claim follows from several facts. First, for all \( i \neq j \), \( \overline{S_{ij}} \) is irreducible. It has dimension 3 and defining equation \( q_{ij} \) (6), by A1 and Lemma 10. When \( i \neq j \), \( i' \neq j' \) and \( (i,j) \neq (i',j') \), then \( q_{ij} \) and \( q_{ij'} \) are not scalar multiples of each other by A2 (cf. their coefficients on \( x_i^2 x_j x_{i'}^2 x_j' \)). Hence \( \overline{S_{ij}} \neq \overline{S_{ij'}} \). Next, \( \overline{S_{ii}} = \{(x_1, x_2) : x_1 = x_2 \} \) (all \( i \)). Further, \( \{(x_1, x_2) : x_1 = x_2 \} \not\subseteq \overline{S_{ij}} \) for all \( i \neq j \), because when we substitute \( x_1 = x_2 \) and \( y_1 = y_2 \) into Eq. (6) we get a nonzero result as the constant term does not vanish. All together, (12) is the claimed irredundant irreducible decomposition as wanted. □

E. Proof of Lemma 13. This follows from \( \mathcal{I} (\overline{S_{ij}}) = \langle q_{ij} \rangle \) (Lemma 10), the expression (6) for \( q_{ij} \), and the proof of (4, Thm. 3). □

F. Proof of Lemma 14. From Eq. (15), we have

\[
M_2 (S_{ij}) = \sum_{i'j'=1} w_{ij} e^{\sqrt{2\pi R} a_{ij}} \mu (\theta_{ij}^{-1} (S_{ij})).
\]

Here \( \mu (\theta_{ij}^{-1} (S_{ij})) = \mu (\text{SO}(3)) = 1 \) by definition of \( S_{ij} \). On the other hand, for all \( i', j' = 1, \ldots, p \) with \( (i', j') \neq (i, j) \), \( S_{ij} \cap S_{ij'} \) is a semialgebraic set with positive codimension in \( S_{i'j'} \) by the fact that (12) is an irredundant irreducible decomposition. Then \( \theta_{ij}^{-1} (S_{ij}) = \theta_{ij'}^{-1} (S_{ij}) \cap S_{ij'} \) is a semialgebraic set with positive codimension in \( \text{SO}(3) \). Since \( \mu \) is absolutely continuous, it implies \( \mu (\theta_{ij}^{-1} (S_{ij})) = 0 \). Eq. (25) follows. □

2. Proof of Theorem 3

We show how to reduce the proof to an application of Theorem 1. We have

\[
R \cdot \Phi (x) = \sum_{i=1}^{p} w_i e^{-\frac{|x - R a_i|^2}{2\pi \kappa^2}} = \sum_{i=1}^{p} w_i e^{-\frac{|x - R T_{\kappa} a_i|^2}{2\pi \kappa^2}}. \tag{13}
\]

Writing \( x = (x, y, z) \) gives the following expression for the projection images

\[
I_R (x, y) = \sum_{i=1}^{p} w_i e^{\frac{-(x - R^T a_i)^2}{2\pi \kappa^2}} \int_{-\infty}^{\infty} e^{-(z - R^T a_i)^2} dz = \sum_{i=1}^{p} \sqrt{2\pi \kappa} w_i e^{\frac{-(x - R^T a_i)^2}{2\pi \kappa^2}}, \tag{14}
\]

where \( \pi_z (a_1, a_2, a_3) := a_3 \) is the projection operator onto the last coordinate. The second moment \( M_2^G \) can then be written as

\[
M_2^G ((x_1, y_1), (x_2, y_2)) = \sum_{i,j=1}^{p} 2\pi \kappa^2 w_i w_j \int_{\text{SO}(3)} e^{-\frac{((x_1, y_1) - R a_i)^2 + ((x_2, y_2) - R a_j)^2}{2\pi \kappa^2}} d\mu (R) \tag{15}
\]

where the second equality used the fact that the Haar measure on \( \text{SO}(3) \) is invariant to transpositions (5, Theorem 4.36), and \( M_2 \) is the second moment in the model of Theorem 1. Since \( k \) has non-vanishing Fourier-transform, this equation can be deconvolved to obtain \( M_2 \). By Theorem 1, \( M_2 \) determines the weights and atomic positions \( (w_i, a_i) \) up to a joint rotation and reflection, which concludes the proof. □

3. Sample complexity: Proofs of Theorems 4 and Corollary 5

A. Proof of Theorem 4. The proof is divided into several steps.

Step 0: We state a general fact about real analytic functions that we will use: Let \( H (y, z) : \mathbb{R}^n \times \mathbb{R}^n \to \mathbb{R} \) be real analytic jointly in \( (y, z) \). Let \( \nu \) be a compactly supported and absolutely continuous measure on \( \mathbb{R}^n \). Then \( \int H (y, z) d\nu (z) \) is real-analytic in \( y \). This can be justified by appropriately differentiating under the integral sign, see (6).

Step 1: We introduce notation.

First, define

\[
X = (B (0, r) \times [w_-, w_+])^{\times p} \subseteq \mathbb{R}^{4p}, \tag{16}
\]

where \( B (0, r) \) is the \( \ell^2 \)-ball of radius \( r \) in \( \mathbb{R}^3 \) centered at 0. \( X \) is the space of possible molecules.

Next, slightly modifying the notation in the main text, write

\[
M_2^{[m]} : X \to \mathbb{R}^{2m} \times 2^m \otimes \mathbb{R}^{2m} \times 2^m
\]
for the map associating a molecule to its pixelated second moment (Eq. (13)) when $2^m \times 2^m$ pixels are used. Explicitly,

$$M_2^{[m]}(\{(a_i, w_i)\}) = \left\{ \int_{\mathcal{S}} \int_{\mathcal{S}} \int_{\mathcal{S}} \int_{\mathcal{S}} \sum_{j_i=1}^p w_{i,j} \delta_{e} \mathcal{R}_{a_i}(x_1, y_1) \delta_{e} \mathcal{R}_{a_j}(x_2, y_2) (k(x_1, y_1)k(x_2, y_2))d\mu(R)dx_1dy_1dx_2dy_2 \right\}$$

for $j_1, j_2, j_3, j_4 \in \{-2^{m-1}, \ldots, 2^{m-1} - 1\}$. Then, $M_2^{[m]}$ is a real analytic function by Step 0. Indeed, the Gaussian kernel $k(x, y)$ is real analytic, so the above integrand is real analytic in all variables. (Also, integration over $SO(3)$ is replaced by integration against a compactly supported absolutely continuous measure on $\mathbb{R}^3$ if we parameterize $SO(3)$ with Euler angles.)

Thirdly, we put

$$L^{[m]}: \mathbb{R}^{2^m+1} \times \mathbb{R}^{2^m+1} \rightarrow \mathbb{R}^{2^m} \otimes \mathbb{R}^{2^m}$$

for the obvious linear map which lowers the resolution of the second moment by a factor of two, i.e. $L^{[m]}(t) = s$ where

$$s_{j_1,j_2,j_3,j_4} = \sum_{\gamma_4 \in \{0,1\}} \sum_{\gamma_3 \in \{0,1\}} \sum_{\gamma_2 \in \{0,1\}} \sum_{\gamma_1 \in \{0,1\}} (j_1, j_2, j_3, j_4 + \gamma_1 + \gamma_2 + \gamma_3 + \gamma_4)$$

for $j_1, j_2, j_3, j_4 \in \{-2^{m-1}, \ldots, 2^{m-1} - 1\}$. For all $m$, it holds

$$M_2^{[m]} = L^{[m]} \circ M_2^{[m+1]}.$$  \[17\]

**Step 2:** We prove that a certain stabilization occurs as $m \to \infty$.

Consider $X \times X = (B(0, r) \times [w_-, w_+])^{\otimes p} \times (B(0, r) \times [w_-, w_+])^{\otimes p} \subseteq \mathbb{R}^{8p}$, where the variables on $\mathbb{R}^{8p}$ are $\{(a_i, w_i)\}$, $\{(b_i, v_i)\}$.

Regard $X \times X$ as a semianalytic set (i.e., a subset of Euclidean space locally defined by real analytic equations and inequalities). Let $\mathcal{O}(X \times X)$ denote the ring of real analytic functions on $X$. Then $\mathcal{O}(X \times X)$ is a Noetherian ring, because $X$ is compact (7, Théorème 1.9). (Note that $X \times X$ automatically satisfies the Stein hypothesis in loc. cit. since we are in the real case, see (8).)

We define

$$T^{[m]} = \text{ideal in } \mathcal{O}(X \times X) \text{ generated by the } 2^{4m} \text{ coordinate functions of } M_2^{[m]}(\{(a_i, w_i)\}) - M_2^{[m]}(\{(b_i, v_i)\}) .$$

For all $m$, we have

$$T^{[m+1]} \supseteq T^{[m]}$$

by Eq. (17). From Noetherianity, there exists $m' = m'(p, r, w_+, w_-)$ such that

$$T^{[m]} = T^{[m']} \quad \forall m \geq m'.$$

Thus the corresponding zero sets in $X \times X$ stabilize too:

$$\left\{ \{(a_i, w_i)\}, \{(b_i, v_i)\} : M_2^{[m]}(\{(a_i, w_i)\}) = M_2^{[m]}(\{(b_i, v_i)\}) \right\} \subseteq X \times X $$

is constant in $m$ if $m \geq m'$.  \[18\]

Equivalently, for all $\{(a_i, w_i)\} \in X$ we have:

the fiber $(M_2^{[m]})^{-1}(M_2^{[m]}(\{(a_i, w_i)\})) \subseteq X$ is constant in $m$ if $m \geq m'$.  \[18\]

**Step 3:** We deduce an equality in which there is no pixelation.

Specifically, fix $\{(a_i, w_i)\}, \{(b_i, v_i)\} \in X$ such that $\{(a_i, w_i)\}$ satisfies A1-A2 in the main text and

$$M_2^{[m']}(\{(a_i, w_i)\}) = M_2^{[m']}(\{(b_i, v_i)\})$$

holds. We claim there is an equality between unpixelated (but still blurred) second moments:

$$M_2(\{(a_i, w_i)\}) \ast (k \otimes k) = M_2(\{(b_i, v_i)\}) \ast (k \otimes k).$$  \[20\]

To see this, note by Step 0 that both sides of Eq. (20) are real-valued real analytic functions on $\mathbb{R}^2 \times \mathbb{R}^2$. From continuity, if they differ on $[-1,1]^2$ there must exist a product of sufficiently small pixels where their integrals differ, i.e. $m \geq m'$ and $j_1, j_2, j_3, j_4 \in \{-2^{m-1}, \ldots, 2^{m-1} - 1\}$ such that

$$M_2^{[m]}((\{(a_i, w_i)\}((j_1, j_2), (j_3, j_4)) \neq M_2^{[m]}((\{(b_i, v_i)\}((j_1, j_2), (j_3, j_4)).$$  \[21\]

However, Eq. (21) contradicts Eq. (19) and (18). Thus, Eq. (20) holds on $[-1,1]^2 \times [-1,1]^2$. By real analyticity, Eq. (20) then holds on all of $\mathbb{R}^2 \times \mathbb{R}^2$ as wanted.

**Step 4:** We undo the Gaussian blurring.
Continue with Eq. (20). Because $M_2(\cdot)$ is compactly supported, it identifies with a tempered distribution. The Fourier transform is thus applicable to Eq. (20). By the convolution theorem (9, Thm. 7.1.15), it gives

$$\hat{M}_2^i(\{a_i, w_i\}) \hat{k} \otimes \hat{k} = \hat{M}_2^i(\{b_i, v_i\}) \hat{k} \otimes \hat{k}.$$ \[22\]

Note that the Paley-Wiener theorem (9, Thm. 7.1.14) implies $\hat{M}_2(\cdot)$ is a function rather just a distribution (moreover it is extendable to an entire function). Also, $\hat{k} \otimes \hat{k}$ is a Gaussian function. Therefore, Eq. (22) can be regarded as an equality of functions rather than just distributions. Since $\hat{k} \otimes \hat{k} \neq 0$ everywhere, it implies

$$\hat{M}_2^i(\{a_i, w_i\}) = \hat{M}_2^i(\{b_i, v_i\}),$$

whence

$$M_2^i(\{a_i, w_i\}) = M_2^i(\{b_i, v_i\}),$$ \[23\]

using the fact that the Fourier transform is an automorphism on tempered distributions.

**Step 5:** We use Theorem 2 to conclude.

The above steps have shown: there exists $m' = m'(p, r, w_+, w_-)$ such that if $m \geq m'$ then $\{a_i, w_i\}, \{b_i, v_i\} \in X$ and $M_2^{[m]}(\{a_i, w_i\}) = M_2^{[m]}(\{b_i, v_i\})$ imply $M_2(\{a_i, w_i\}) = M_2(\{b_i, v_i\})$. However by Theorem 2, $M_2(\{a_i, w_i\}) = M_2(\{b_i, v_i\})$ implies $\{a_i, w_i\}$ and $\{b_i, v_i\}$ are equal up to a rotation/reflection in $\mathbb{R}^3$, provided $\{a_i, w_i\}$ satisfies A1-A2.

The proof of Theorem 4 is complete.

**B. Proof of Corollary 5.** This now follows immediately from (10, Sec. 3) or (11, Sec. 2), because by Theorem 4 the second moment $M_2^{[m]}(\{a_i, w_i\})$ uniquely determines the signal $\{a_i, w_i\}$ up to the group action of $O(3)$, provided $\{a_i, w_i\}$ satisfies the Zariski-open conditions A1-A2.

**4. Normalized Bessel functions and the Nyquist criterion**

The spherical Bessel basis defined in the main text uses the normalized spherical Bessel functions $j_{\ell s}(k)$ defined by

$$j_{\ell s}(k) = \frac{1}{c \sqrt{\pi} j_{\ell+1}(Rc)} j_{\ell}(Rc/s),$$ \[24\]

where $j_{\ell}$ is the $\ell$th spherical Bessel function of the first kind (12, Eq. 10.2.1), $c$ the bandlimit of the projection images and $R_{\ell,s}$ the $s$th positive solution to $j_{\ell} = 0$. The Nyquist criterion determines the maximally allowable value of the truncation parameter $S_\ell$ by defining $S_\ell$ as the largest integer $s$ satisfying,

$$R_{\ell,s+1} \leq 2\pi c R,$$ \[25\]

assuming the projection images are supported on a disk of radius $R$ (13). Our numerical experiments used $c = 0.5$ and a radius $R$ of 32 voxels.

**Movie S1.** The movie shows a 3D view of the reconstructed molecule as a function of the iteration number.

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