Denoiser-based projections for 2-D super-resolution multi-reference alignment

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Abstract—We study the 2-D super-resolution multi-reference alignment (SR-MRA) problem: estimating an image from its down-sampled, circularly-translated, and noisy copies. The SR-MRA problem serves as a mathematical abstraction of the structure determination problem for biological molecules. Since the SR-MRA problem is ill-posed without prior knowledge, accurate image estimation relies on designing priors that well-describe the statistics of the images of interest. In this work, we build on recent advances in image processing, and harness the power of denoisers as priors of images. In particular, we suggest to use denoisers as projections, and design two computational frameworks to estimate the image: projected expectation-maximization and projected method of moments. We provide an efficient GPU implementation, and demonstrate the effectiveness of these algorithms by extensive numerical experiments on a wide range of parameters and images.

I. INTRODUCTION

The 2-D super-resolution multi-reference alignment (SR-MRA) problem entails estimating an image \( x \in \mathbb{R}^{L_{\text{high}} \times L_{\text{high}}} \) from its \( N \) circularly-translated, down-sampled, noisy copies:

\[
y_i = PR_y x + \varepsilon_i, \quad i = 1, \ldots, N, \tag{I.1}
\]

where \( R_y \) denotes a 2-D circular translation, \( P \) denotes a down-sampling operator that collects \( L_{\text{low}} \times L_{\text{low}} \) equally-spaced samples of \( R_y x \), and \( \varepsilon_i \in \mathbb{R}^{L_{\text{low}} \times L_{\text{low}}} \) is a noise matrix whose entries are drawn i.i.d. from \( \mathcal{N}(0, \sigma^2) \). To ease exposition, we consider only square images, but the model can be easily extended to non-square images as well. The 2-D translation \( s \) is composed of a horizontal translation \( s_1 \) and a vertical translation \( s_2 \), which are drawn i.i.d. from unknown distributions, \( \rho_1 \) and \( \rho_2 \), respectively. Explicitly, each observation \( y_i \in \mathbb{R}^{L_{\text{low}} \times L_{\text{low}}} \) takes the form

\[
y_i[n_1, n_2] = \left( x \left[ ((n_1 K - s_1^i) \mod L_{\text{high}}, (n_2 K - s_2^i) \mod L_{\text{high}}) \right] + \varepsilon_i[n_1, n_2], \right),
\]

where \( n_1, n_2 = 0, \ldots, L_{\text{low}} - 1 \), and \( K := \frac{L_{\text{high}}}{L_{\text{low}}} \) is assumed to be an integer. Our goal is to estimate \( x \) (the high resolution image) from \( N \) low-resolution observations \( y_1, \ldots, y_N \), when the translations \( s_1, \ldots, s_N \) are unknown. Figure 1 shows a few examples of observations generated according to (I.1) at different noise levels.

The SR-MRA model, first studied for 1-D signals [2], is a special case of the multi-reference alignment (MRA) model: the problem of estimating a signal from its noisy copies, each acted upon by a random element of some group, see for example [3], [4], [5], [6], [7], [8]. The MRA model is mainly motivated by the single-particle cryo-electron microscopy (cryo-EM) technology: an increasingly popular technique to constitute 3-D molecular structures [9]. In Section V we introduce the mathematical model of cryo-EM in detail and discuss how the techniques proposed in this paper have the potential to make a significant impact on the molecular reconstruction problem of cryo-EM. The MRA model is also motivated by a variety of additional applications in biology [10], [11], robotics [12], radar [13], [14], and image processing [15], [16].

Previous works on MRA mostly focused on two computational frameworks: the method of moments and expectation-maximization (EM); see for example [5], [6]. They are currently considered the leading techniques for solving MRA problems. The method of moments is a classical parameter estimation technique, aiming to recover the parameters of interest (e.g., signal, image, 3-D molecular structure) from the moments of the observed data. The method of moments requires a single pass over the observations, making it an efficient technique for massive data sets (large \( N \)). Yet, the method of moments is not statistically efficient. The EM algorithm aims
to maximize the likelihood function (or the posterior distribution in a Bayesian framework) \cite{17}. While each EM step does not decrease the likelihood function, it is not guaranteed to achieve the maximum of the likelihood function of \((I.1)\) due to its non-convexity. Section \(\text{II}\) provides the necessary background for this paper, including an introduction to both methods.

As we prove in Section \(\text{II-A}\), it is impossible to uniquely identify the image \(x\) only from the SR-MRA observations \((I.1)\), regardless of the specific estimation algorithm, as there are many different images that result in the same likelihood function. Thus, to accurately estimate the image, it is necessary to incorporate a prior on the image. Incorporating a prior into the method of moments and EM, and its application to SR-MRA, is the main interest of this paper.

In this work, we harness a recent line of works that use denoisers as priors. Utilizing existing state-of-the-art denoisers has been originally proposed as part of the Plug-and-Play technique \cite{18}. The Plug-and-Play method and its variants have been proven highly effective for many imaging inverse problems, see for example \cite{19}, \cite{20}, \cite{21}, \cite{22}, \cite{23}, \cite{24}, \cite{25}, \cite{26}, \cite{27}, \cite{28}, \cite{29}, \cite{30}, \cite{31}, \cite{32}, \cite{33}. Essentially, the underlying idea is exploiting the impressive capabilities of existing denoising algorithms in order to replace explicit, traditional, priors. Indeed, these techniques are especially useful for natural images, whose statistics is too complicated to be described explicitly, but for which excellent denoisers were devised.
Our proposed computational framework, presented in Section [III], uses denoisers as projection operators. Specifically, every few iterations of either the method of moments or EM, we apply a denoiser to the current estimate. This stage can be interpreted as projecting the image estimate onto the implicit space spanned by the denoiser. In contrast to Plug-and-Play, our technique requires a minor modification to existing algorithms. Moreover, we found that this strategy leads to better results than Plug-and-Play in the SR-MRA setting. Section [IV] demonstrates the effectiveness of the method by extensive numerical experiments on natural and cryo-EM images. Section V concludes the paper by discussing how our framework can be modified to other statistical models, and in particular to recover molecular structures using cryo-EM.

II. BACKGROUND

Before introducing our proposed framework, we elaborate on the four pillars of this work: the non-uniqueness of the SR-MRA model (I.1), the method of moments, EM, and denoiser-based priors. Hereafter, we let \( \rho := [\rho_1, \rho_2]^T \), and define the set of sought parameters as \( \theta := (x, \rho) = (x, \rho_1, \rho_2) \). With a slight abuse of notation, we treat the image \( x \) and a measurement \( y_t \) as vectors in \( \mathbb{R}^{L_{\text{high}}} \) and \( \mathbb{R}^{L_{\text{low}}} \), respectively. We also define \( \Theta = \mathbb{R}^{L_{\text{high}}} \times \Delta_{L_{\text{high}}} \times \Delta_{L_{\text{low}}} \), where \( \Delta_{L_{\text{high}}} \) is the \( L_{\text{high}} \)-dimensional simplex, so that \( \theta \in \Theta \).

A. SR-MRA observations do not identify the image \( x \) uniquely

The following theorem states that the likelihood function of (I.1) does not determine the image \( x \) uniquely. This in turn implies that a prior is necessary for accurate estimation of the sought image.

**Theorem 1.** The likelihood function \( p(y_1, \ldots, y_N|x, \rho) \) does not determine uniquely the sought parameters \( x \) and \( \rho \).

**Proof.** The proof follows the guidelines of the proof of [2] Theorem 3.1. Recall that \( y = PR_x x + \varepsilon \), and that \( K := \frac{L_{\text{high}}}{L_{\text{low}}} \) is an integer. Let us define a set of \( K^2 \) sub-images, indexed by \( n_1, n_2 = 0, \ldots, K - 1 \):

\[
x_{n_1, n_2}[\ell_1, \ell_2] := x[n_1 + \ell_1 K, n_2 + \ell_2 K],
\]

for \( \ell_1, \ell_2 = 0, \ldots, L_{\text{low}} - 1 \). Then, the SR-MRA model can be equivalently written as

\[
y = R_{\ell} x_{n_1, n_2} + \varepsilon,
\]

where \( R_{\ell} \) is a translation over the low-resolution grid of size \( L_{\text{low}} \times L_{\text{low}} \). We denote the distribution of choosing the sub-image \( x_{n_1, n_2} \) and translating it by \( t \) as \( \rho[n_1, n_2, t] \). Thus, the likelihood function of (I.1) for a single observation \( y \), can be written, up to a constant, as

\[
p(y; x, \rho) = \sum_{n_1, n_2 = 0}^{K-1} \sum_{t} \rho[n_1, n_2, t] e^{-\frac{1}{2\sigma^2} \|y - R_{\ell} x_{n_1, n_2}\|^2}. \tag{II.2}
\]

It is readily seen that the likelihood function is invariant under any permutation of the sub-images (over all \( K^2 \) permutations), and under any translation of each one of them (overall \( (L_{\text{low}}^2)K^2 \) possible translations). This implies that there are \( K^2!(L_{\text{low}}^2)^{K^2} \) different images with the same likelihood function.

Figure 2 compares recoveries of the images presented in Figure 1 using the projected method of moments and the projected EM, which are our proposed algorithms and are discussed in Section III. Specifically, the first and third rows show recoveries using Algorithm 1 and Algorithm 2, respectively, while the second and fourth rows show the outputs of standard method of moments and EM, with no prior. Evidently, in light of Theorem 1, the latter results are of low quality.

B. The method of moments

The method of moments aims to estimate the parameters of interest (in our case, the image \( x \) and the distribution \( \rho \)) from the observable moments. Recall that the \( d \)th observable moment is given by

\[
\hat{M}_d := \frac{1}{N} \sum_{i=1}^{N} y_i^\otimes d, \tag{II.3}
\]

where \( y^\otimes d \) is a tensor with \( (L_{\text{low}}^2)^d \) entries. Computing the observable moments requires a single pass over the data and results in a concise summary of the data. By the law of large numbers, for sufficiently large \( N \), we have

\[
\hat{M}_d \approx \mathbb{E} y^\otimes d := M_d(\theta), \tag{II.4}
\]

where the expectation is taken against the distribution of the translations and the noise. Finding the optimal parameters \( \theta \) that fit the observable moments is usually performed by minimizing a least squares objective as a function of the parameters \( \theta \):

\[
\min_{\theta \in \Theta} \sum_{d=1}^{D} \lambda_d \|M_d - M_d(\theta)\|^2, \tag{II.5}
\]

for some predefined weights \( \lambda_1, \ldots, \lambda_D \).


observations for the EM was conducted on images of size $N \times L$ was vital for accurate recovery. The experiment indicated, the projection (or alternative prior information) is available. EM has been proven effective in many practical scenarios, including for processing cryo-EM experimental datasets.

Model (I.1) was studied in [6] when $P$ is identity (no down-sampling). In particular, it was shown that if the discrete Fourier transform of the signal is non-vanishing, and $\rho$ is almost any non-uniform distribution, then the signal and distribution are determined uniquely, up to an unavoidable translation symmetry, from the second moment of the observations. While this is not necessarily true when $P$ is a down-sampling operator, we keep using the first two moments in this work (namely, $D = 2$).

Specifically, the first two moments of the SR-MRA model (I.1) are given by [34]:

$$M_1 = PC_x \rho,$$

$$M_2 = PC_x D_{\rho} C_x^T P^T + \sigma^2 PP^T,$$

where $C_x \in \mathbb{R}^{L_{\text{high}}^2 \times L_{\text{high}}^2}$ is a block circulant with circulant blocks (BCCB) matrix of the form:

$$C_x = \begin{pmatrix}
c_0 & c_{L_{\text{high}}-1} & \cdots & c_1 \\
c_1 & c_0 & c_{L_{\text{high}}-1} & \cdots & c_2 \\
\vdots & \vdots & \ddots & \vdots & \vdots \\
\cdots & \cdots & \cdots & c_{L_{\text{high}}-1} & c_1 \\
c_{L_{\text{high}}-1} & c_{L_{\text{high}}-2} & \cdots & c_1 & c_0
\end{pmatrix}, \quad (\text{II.8})$$

where the block $c_i \in \mathbb{R}^{L_{\text{high}} \times L_{\text{high}}}$ represents a circulant matrix of the $i$th column of the image $x$ (as an image, not as a vector). Each column of $C_x$ contains a copy of the image after 2-D translation and vectorization. The matrix $D_\rho \in \mathbb{R}^{L_{\text{high}}^2 \times L_{\text{high}}^2}$ is a diagonal matrix, whose diagonal is a vectorization of the matrix $\rho_1 \rho_2^T$. Therefore, the least squares objective (II.5) can be explicitly written as

$$\min_{\theta \in \Theta} ||PC_x D_\rho C_x^T P^T + \sigma^2 PP^T - \hat{M}_2||_F^2 + \lambda||PC_{\rho} x - \hat{M}_1||_2^2.$$ 

In this paper, we set $\lambda = \frac{1}{L_{\text{high}}^2(1+\sigma^2)}$, as suggested in [6]. We note that while the maximum likelihood estimator is asymptotically efficient (under mild conditions), the method of moments is not an efficient estimator. In addition, the objective function (II.9) consists of polynomials of degree 4 (in $x$) and thus is non-convex. Therefore, we are not guaranteed to find its global minimizer. Nevertheless, our numerical experiments in Section IV reveal that, when using denoiser-based projections, minimizing (II.9) using a standard gradient-based algorithm leads to accurate recoveries.

C. Expectation-maximization (EM)

The log-likelihood of (I.1) is given, up to a constant, by

$$\log p(y_1, \ldots, y_n; \theta) = \sum_{i=1}^{N} \log \sum_{s^1, s^2=1}^{L_{\text{high}}} \rho[s] e^{-\frac{1}{2\sigma^2} ||y_i - PR_s x||_2^2},$$

where we remind that $s = [s^1, s^2]^T$. We note that this is a special case of the Gaussian mixture model, where all centers are connected through the group action (i.e., a translation). A popular way to maximize the likelihood function is using the EM algorithm [17]. EM can be also used to maximize the posterior distribution (rather than the likelihood function) when an analytical prior is available. EM has been proven effective in many practical scenarios, including for processing cryo-EM experimental datasets [35], [36].

EM is an iterative algorithm, where each iteration consists of two steps. In the first step, called the E-step, we compute the expected value of the log-likelihood function with respect to the translations, given the current

\[1\text{The results of [6] concern 1-D signals, but they can be readily extended to 2-D.}\]
estimate of $\theta := (x, \rho)$. In the $(t+1)$-th iteration, it reads

$$Q(x, \rho|x_t, \rho_t) = \sum_{i=1}^N \sum_{s,s'=1}^{L_{\text{high}}} w_{t}^{i,s} \left( \log \rho[s] - \frac{1}{2\sigma^2} ||y_i - P R_s x||^2_F \right),$$

where

$$w_{t}^{i,s} = C_t^i \rho_t[s] e^{-\frac{1}{\sigma^2} ||y_i - PR_s x||^2},$$

and $C_t^i$ is a normalization factor so that $\sum_s w_{t}^{i,s} = 1$. The next step, called the M-step, maximizes (II.10) with respect to $x$ and $\rho$:

$$(x_{t+1}, \rho_{t+1}) = \arg\max_{x,\rho} Q(x, \rho|x_t, \rho_t).$$

In our case, the maximum is attained by solving the linear system of equations:

$$Ax_{t+1} = b,$$

where

$$A = \sum_{i=1}^N \sum_s w_{t}^{i,s} R_s^{-1} P^{-1} P R_s,$$

$$b = \sum_{i=1}^N \sum_s w_{t}^{i,s} R_s^{-1} P^{-1} y_i,$$

and

$$\rho_{t+1}[s] = \frac{\sum_{i=1}^N w_{t}^{i,s}}{\sum_{i=1}^N \sum_{s'} w_{t}^{i,s'}}.$$  

(D. Plug-and-Play and denoiser-based priors)

Using denoisers as priors was first proposed as part of the Plug-and-Play approach [18]. The Plug-and-Play method aims to maximize a posterior distribution $p(\theta|y_1, \ldots, y_n)$, which is equivalent to the optimization problem:

$$\arg\min_{\theta\in\Theta} l(\theta) + s(\theta),$$

where $l(\theta) := -\log p(y_1, \ldots, y_n|\theta)$, $s(\theta) := -\log p(\theta)$, $p(\theta)$ is a prior on $\theta$, and recall that $\theta = (x, \rho)$. This work only considers a prior on the image $x$, but a prior on the distribution might be learned as well using the technique proposed in [37]. The Plug-and-Play method proceeds by variable splitting

$$\arg\min_{\theta, v \in \Theta} l(x) + \beta s(v) \quad \text{subject to} \quad \theta = v,$$

where $\beta$ is a Lagrangian multiplier, which in practice can be tuned. This minimization problem can be then solved using ADMM by iteratively applying the following three steps:

$$\theta^{k+1} = \arg\min_{\theta \in \Theta} l(\theta) + \frac{\lambda}{2} ||\theta - (v^k - u^k)||^2_2,$$

$$v^{k+1} = \arg\min_{v \in \Theta} \frac{\lambda}{2} ||\theta^{k+1} + u^k - v||^2_2 + s(v),$$

$$u^{k+1} = u^k + (\theta^{k+1} - v^{k+1}).$$

The main insight here is that the second step aims to solve a Gaussian denoising problem, with a prior $s(v)$ and noise level (standard deviation) of $\sqrt{\frac{\beta}{\lambda}}$. Instead of solving this problem with respect to an analytical explicit prior, it was suggested in [18] to apply empirical denoisers that have been developed over the years, such as BM3D or data-driven neural networks.

While the Plug-and-Play provides impressive results in many image processing tasks, it requires to tune the hyper parameters $\lambda, \beta$ and the number of iterations for the first step; these parameters have a significant impact on its performance. In particular, for our setup, we did not find a set of parameters that yields accurate estimates for the SR-MRA problem in a wide range of scenarios.

As an alternative, in the next section we describe how denoisers can be used as projectors for EM and the method of moments.

(III. Denoiser-based projected algorithms)

This section introduces the main contribution of this work: incorporating a projection-based denoiser into the method of moments and EM, and their implementation to SR-MRA. Importantly, there is no agreed way of
including a prior into the method of moments, and there is no standard way of incorporating natural images prior to EM. The projected method of moments algorithm is presented in Algorithm 1, and the projected EM is presented in Algorithm 2. The numerical experiments are deferred to Section IV.

The main idea of our approach is rather simple: every few iterations of either the method of moments or EM, we apply a predefined denoiser that acts on the current estimate of the image. Specifically, for the method of moments, we apply the denoiser every few steps of BFGS (with line-search) that minimizes the least squares objective (II.9); BFGS can be replaced by alternative gradient-based algorithms. For EM, we apply the denoiser every few EM steps.

As a denoiser, we chose to work with the celebrated BM3D denoiser [38] because of its simplicity and effectiveness for denoising natural images. However, replacing BM3D with alternative denoisers is straightforward. This might be especially important when dealing with specific applications, where a data-driven deep neural net may take the role of the denoiser. In Section V, we discuss such potential applications to cryo-EM data processing.

Our algorithm requires tuning only two parameters. The first parameter is the noise level of the denoiser, denoted hereafter by $\sigma_{BM3D}$. Low noise level increases the weight of the data (either likelihood or observed moments), while increasing the noise level strengthens the effect of the denoiser. In particular, we found that starting from a high noise level and gradually decreasing it with the iterations leads to consistent and accurate estimations. Specifically, in the numerical experiments of Section IV, we set the noise level to be

$$\sigma_{BM3D}^t = 2^{-1/10} \sigma_{BM3D}^{t-1}, \quad \sigma_{BM3D}^1 = 1,$$

where $\sigma_{BM3D}^t$ is the noise level of the $t$th application of the BM3D denoiser.

The second parameter, which we denote by $F$, determines the number of EM iterations or BFGS iterations (or other gradient-based algorithm) for the method of moments between consecutive applications of the denoiser. Small or large $F$ may put too much or too little weight on the prior (rather than on the data). Empirically, the projected method of moments is quite sensitive to this parameter and requires carefully tuning $F$, as presented in Section IV-E, whereas EM is less sensitive. In contrast to Plug-and-Play (see II-D), we found it to be quite easy to tune these two parameters and get consistent results for a wide range of images and parameters. The simplicity of the parameter tuning, perhaps, stems from the fact that each parameter affects only one term ($F$ the fidelity, and $\sigma_{BM3D}^t$ the prior), whereas tuning the $\lambda$ parameter in the Plug-and-Play approach (II.17) affects both terms.

### Algorithm 1: Projected method of moments

**Input:** Measurements $y_1, \ldots, y_N$, denoiser $D$, and the parameter $F$

**Output:** An estimate of $\theta := (x, \rho)$ of the image and the distribution

1) Compute the empirical moments $\hat{M}_1, \hat{M}_2$ according to (II.3)

2) Until a stopping criterion is met:
   a) Run $F$ BFGS (or alternative gradient-based algorithm) steps to minimize (II.9)
   b) Apply the denoiser $x \leftarrow D(x, \sigma_{BM3D})$
   c) Update $\sigma_{BM3D}^t$ according to (III.1)

### Algorithm 2: Projected EM

**Input:** Measurements $y_1, \ldots, y_N$, denoiser $D$, and the parameter $F$

**Output:** An estimate of $\theta := (x, \rho)$ of the image and the distribution

Until a stopping criterion is met:

1) Run $F$ EM steps according to (II.11), (II.13), and (II.14).
2) Apply the denoiser $x \leftarrow D(x, \sigma_{BM3D})$
3) Update $\sigma_{BM3D}^t$ according to (III.1)

### IV. Numerical experiments

We turn to examine the numerical performance of the proposed algorithms. For all experiments, we used the BM3D denoiser [38], where the noise level decays as in (III.1). Unless specified otherwise, we set $F = 5$ for both algorithms. For the method of moments, we minimized the least squares objective (II.5) using the BFGS algorithm with line-search. The distributions $\rho_1, \rho_2$ and their initial guesses were drawn from a uniform distribution on $[0, 1]$, and normalized so that $\rho_1, \rho_2 \in \Delta_{L_{\text{sup}}}$. The pixel values of all images are in $[0, 1]$. Each pixel in the initialization of the image estimate, for both algorithms, was drawn i.i.d. from a uniform distribution on $[0, 1]$, which was then normalized to include the entire $[0, 1]$ range.

Despite the non-convexity of the EM and the method of moments, we observed that a single random initial guess provides consistent results, which are not significantly improved when adding more initial guesses.
To account for the shift-invariance of \((I.1)\), we measure the error by:

\[
\text{error}(\hat{x}) = \min_{s} \frac{||R_s\hat{x} - x||_F}{||x||_F}, \tag{IV.1}
\]

where \(\hat{x}\) is the estimated image, and \(R_s\) denotes a 2-D translation. We define SNR as

\[
\text{SNR} = \frac{||x||_F^2}{L_{\text{high}}^2 \sigma^2}. \tag{IV.2}
\]

Our algorithms were implemented in Torch. The recovery of a high-dimensional signal requires an efficient implementation of the algorithms over GPU. Actually, without this implementation, we were unable to recover images of size \(L_{\text{high}} \geq 32\) within a reasonable running time, where reducing the resolution beyond that adversely affects denoising performance. The code to reproduce all experiments is available at [https://github.com/JonathanShani/Denoiser_projection](https://github.com/JonathanShani/Denoiser_projection)

### A. Performance comparison

This section compares the performance of the projected method of moments of Algorithm (1) and the projected EM of Algorithm (2). We applied the algorithms to the 68 "natural" images of the CBSD-68 dataset and to a cryo-EM image of the E. coli 70S ribosome, available at the Electron Microscopy Data Bank [1]. We set \(L_{\text{high}} = 128\), and the images were down-sampled to \(L_{\text{low}} = 64, 32, 16, 8\) (namely, down-sampling factors of \(K = 2, 4, 6, 8\), respectively).

1) **Visual examples:** Figure 3 presents a collection of visual recoveries from the CBSD-68 dataset using both algorithms, with a down-sampling factor of \(K = 2\). For the projected method of moments, we assumed to have access to the population (perfect) moments (which is the case when \(N \gg \sigma^4\)), and the projected EM used \(N = 10^4\) observations with noise level of \(\sigma = 1/8\) (corresponding to SNR\(\approx15\)). Clearly, the projected EM provides more accurate recoveries, although the method of moments uses perfect moments. However, as we show next, the computational load of the projected EM is much heavier.

2) **Comprehensive comparison:** We conducted a systematic comparison between the projected EM algorithm and the projected method of moments in terms of estimation error and running time. While the reported running times should be taken with a grain of salt as they depend on the implementation and hardware, our goal here is to show the general behavior of the algorithms.

Table 1 presents the error and running time, averaged over 20 trials. We used the Lena image of size \(L_{\text{high}} = 128\) with down-sampling factors of \(K = 4, 8\), and of size \(L_{\text{high}} = 64\) with \(K = 2\); the number of observations was set to \(N = 10^2, 10^4\), and the noise level to \(\sigma = 0.125, 0.25, 0.5\) (corresponding to SNR\(\approx17, 4, 1\), respectively). Both algorithms were limited to 100 iterations per trial. For each trial, we drew a fresh set of observations based on a new distribution and initial guesses. The projected EM shows a clear advantage for almost all values of \(N\) and \(\sigma\) in terms of estimation error (besides some cases when \(\sigma\) is large and \(N\) is small). However, the computational burden of EM is much heavier; there are cases (e.g., \(L_{\text{high}} = 128, N = 10^4, \sigma = 0.25\)) where the running time of the projected EM algorithm is 30 times longer than the running time of the projected method of moments. The reason is that EM iterates over all observations, whereas the method of moments requires only a single pass over the observations [39], while the dimension of the variables in the least squares objective (II.9) is proportional to the dimension of the image.

3) **Error as a function of the iterations:** We next examined the behavior of the algorithms as a function of their iterations, averaged over all images in the CBSD-68 dataset of size \(L_{\text{high}} = 128\). The projected method of moments used perfect moments, and the projected EM used \(N = 10^4\) observations and noise level of \(\sigma = 1/8\).

The results, for a variety of sampling factors, are presented in Figure 4. As can be seen, the algorithms with projections significantly outperform the unprojected versions for all down-sampling factors. Notably, the projected algorithms provide non-trivial estimates even for \(K = 16\) (when each measurement is down-sampled from \(128 \times 128\) to \(8 \times 8\)). We note that the denoiser leads to locally non-monotonic error curves.

The following section presents more visual results of the projected EM algorithm. The experiments in Sections IV-C, IV-D, and IV-E study the influence of different parameters on performance. These experiments require averaging over multiple trials, which makes it virtually impossible to produce results for EM in a reasonable running time. For that reason, these experiments were only conducted for the method of moments. In addition, we also tested the Plug-and-Play approach as described in Section II-D, where the minimization function \(f(\theta)\) is based on moment matching. However, we were unable to find any pair of parameters \((\lambda, \beta)\) that provided satisfactory results across a variety of images.

### B. Visual examples of the projected EM algorithm

Figure 5 presents recoveries of the images presented in Figure 1, using the projected EM algorithm with sampling factors of \(K = 2, 4, 8, N = 10^4\) observations
Fig. 3. A gallery of 6 examples from the CBSD-68 dataset, and the corresponding recoveries using projected EM in a high-SNR regime ($\sigma = 1/8$) and projected method of moments with perfect moments ($N \gg \sigma^2$); the images were down-sampled by a factor of $K = 2$. It can readily seen that the projected EM outperforms the projected method of moments. However, as we show in Table I, the computational load of the projected EM algorithm is much heavier.

and noise level of $\sigma = 1/8$. It is quite remarkable that the projected EM provides accurate estimates with $K = 8$, namely, when the number of pixels is reduced from $128^2$ to $16^2$: a factor of 64.

C. The performance of the projected method of moments as a function of SNR

Figure 6 shows the average recovery error of the projected method of moments algorithm as a function of the SNR. All experiments were conducted with the Lena image of size $L_{\text{high}} = 32$, with a sampling factor of $K = 2$, and noise level of $1/8$, corresponding to SNR $\approx 17$. Figure 7 presents the average error, over 100 trials, as a function of $N$. For each trial, we drew a fresh distribution. The error indeed decreases with $N$, as expected, but the slope is smaller than $-1/2$ (in logarithmic scale), as the law of large numbers predicts. This is due to the effect of the prior (manifested as a denoiser in our case), which does not depend on the observations (namely, on the data).

D. The performance of the projected method of moments as a function of the number of measurements

By the law of large numbers and according to (11.4), for any fixed SNR, the empirical moments almost surely converge to the analytic moments. To assess the impact of the number of observations on the estimation error, we used the image of Lena of size $L_{\text{high}} = 32$, down-sampling factor of $K = 2$, and noise level of $1/8$, corresponding to SNR $\approx 17$.

E. How frequently should we apply the denoiser?

An important parameter of the proposed algorithms, denoted by $F$, determines after how many gradient steps (or EM iterations for the projected EM algorithm) we apply the denoiser. For example, $F = 1$ means that we apply the denoiser after each gradient step, whereas $F = 100$ means that we run 100 gradient steps before applying the denoiser. This is especially important since the computational complexity of a single gradient step is significantly heavier than a BM3D application. To study the effect of this parameter for the projected method of moments, we used the image of Lena of size $L_{\text{high}} = 128$, down-sampling factor of $K = 2$. 


and assumed to have access to the population (perfect) moments.

Figure 8 shows the average error (over 10 trials) of the method of moments for different values of $F$; each trial was conducted with a fresh distribution. Plainly, the impact of $F$ on the performance is significant. The optimal value seems to be around $F = 10$ in this case; larger and smaller values of $F$ lead to sub-optimal results.

V. POTENTIAL IMPLICATIONS FOR CRYO-EM

Single-particle cryo-EM is an increasingly popular technology for high resolution structure determination of biological molecules, and in particular proteins [9]. The cryo-EM reconstruction problem is to estimate a 3-D structure (the electric potential map of the molecule of interest) from multiple observations of the form

$$y = TR_\omega X + \varepsilon,$$  \hspace{1cm} (V.1)

where $X$ is the 3-D structure to be recovered, $R_\omega$ represents an unknown 3-D rotation by some angle $\omega \in SO(3)$, and $T$ is a fixed, linear tomographic projection. The noise level is typically very high. The SR-MRA problem (1.1) can be interpreted as a toy model of the cryo-EM problem, where the image plays the role of the 3-D structure, and the 2-D translations and the sampling operator $P$ replace, respectively, the unknown 3-D rotations and the tomographic projection.

The standard reconstruction algorithms in cryo-EM are based on EM [36], [35], aiming to maximize the posterior distribution based on analytical, explicit priors. Recently, techniques based on the method of moments were also designed for quick ab initio modeling [40], [41]. The techniques proposed in this paper can be readily integrated into these schemes, which may lead to improved accuracy and acceleration. A similar idea was recently suggested by [42], who used the regularization by denoising technique [19], and showed recoveries of moderate resolution with simulated data.

Current cryo-EM technology cannot be used to reconstruct small molecular structure (below ~ 40 kDa); this is one of its main drawbacks, see for example [43]. A recent paper suggested to overcome this barrier using a variation of the method of moments [44]. However, the moment matching problem of [44] is ill-conditioned, and therefore the resolution of the recovered structures is poor. We hope that a version of Algorithm [1], where the denoiser is replaced with a data-driven projection operator, can be used to increase the resolution of the reconstructions, and thus will allow to elucidate multiple new structures of small biological molecules.

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Fig. 4. Error as a function of the iteration (averaged over all images in the CBSD-68 dataset, each of size $L_{\text{high}} = 128$), for different sampling factors. The upper panel presents the projected method of moments and the unprojected method of moments, based on the perfect moments (corresponding to $N \to \infty$). The lower panel presents the projected and unprojected EM, with $N = 10^4$ observations and noise level of $\sigma = 1/8$.

Fig. 5. Recoveries using the projected EM algorithm of the images presented in Figure 1 with noise level of $\sigma = 1/8$ and $N = 10^4$ observations. The down-sampling factors are $K = 2$ (top row), $K = 4$ (middle row), and $K = 8$ (bottom row).

Fig. 6. Mean error of the projected method of moments as a function of the SNR with $N = 10^5$ observations. The experiments were conducted on an image of size $L_{\text{high}} = 32$ with a down-sampling factor of $K = 2$. Remarkably, the slope of the curve increases as the SNR decreases, hinting that the sample complexity of the problem increases in the low SNR regime.

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Fig. 7. Mean error of the projected method of moments as a function of the number of observations $N$. The experiments were conducted on an image of size $L_{\text{high}} = 32$ with a down-sampling factor of $K = 2$ and noise level of $\sigma = 1/8$.

Fig. 8. Mean error of the projected method of moments as a function of the iteration, for different values of $F$ (number of gradient steps between consecutive denoising operations). The experiments were conducted on an image of size $L_{\text{high}} = 128$, assuming to have access to the population moments, and with a down-sampling factor of $K = 2$. The optimal value seems to be around $F = 10$; larger and smaller values of $F$ lead to sub-optimal results.

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