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GSURE criterion for unsupervised regularized reconstruction in Tomographic Diffractive Microscopy

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We propose an unsupervised regularized inversion method for the reconstruction of the 3D refractive index map of a sample in Tomographic Diffractive Microscopy (TDM). It is based on the minimization of the Generalized Stein's Unbiased Risk Estimator (GSURE) to automatically estimate optimal values for the hyperparameters of one or several regularization terms (sparsity, edge-preserving smoothness, Total Variation). We evaluate the performance of our approach on simulated and experimental limited-view data. Our results show that GSURE is an efficient criterion to find suitable regularization weights, that is a critical task, particularly in the context of reducing the amount of required data to allow faster yet efficient acquisitions and reconstructions. © 2021 Optical Society of America

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1. INTRODUCTION

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Optical microscopy techniques constitute the reference tools for 5 the study of biological phenomena, thanks to their capability 6 of imaging living specimens. Among them, three dimensional 7 (3D) imaging techniques are of great interest because they allow 8 the observed specimens to keep their natural 3D structure and 9 properties. In this context, advanced fluorescence nanoscopy 10 methods (STED [1], PALM/STORM [2–4]) are able to achieve 11 high resolved 3D images above ten times beyond the diffraction 12 limit. However, they require long acquisition times which can 13 be incompatible with live imaging. Moreover, the required la-14 belling of the sample is a complex and invasive technique that 15 can degrade the specimen. In this case, label-free imaging tech-16 niques are preferred but must be adapted to observe transparent 17 samples. Optical diffraction tomography (ODT) or Tomographic 18 Diffractive Microscopy (TDM) is an emergent technique, which 19 permits to image transparent specimens in 3D [5], without prepa-20 ration or staining. TDM brings a morphological information 21 about the observed objects. It is less specific and less resolved 22 than fluorescence-based nanoscopy techniques which focus on 23 precise metabolic targets (kernels, mitochondria, etc.). However, 24

this information is complementary as it can allow to register anatomical (TDM) and functional (fluorescence) phenomenons. Moreover, TDM allows for the imaging of a wider field-of-view at a resolution up to twice larger than the diffraction limit, and possibly at a very fast acquisition range. It is almost similar to Structured Illumination Microscopy (SIM) that also performs a kind of synthesis aperture of the object's spectral content, and can go further than twice the diffraction limit.

TDM is an interferometric imaging technique based on digital holographic measurements in tomographic mode, *i.e.* for multiple illuminations and/or sample orientations. Thus, acquisitions are performed by either a specimen rotation or an illumination scanning (one projection orientation per hologram). It gives access, by image reconstruction, to the 3D refractive index (RI) map of a specimen.

Several reconstruction methods from TDM measurements have been proposed in the last decades. The first Born or Rytov approximation allows for a direct 3D mapping of the object in the Fourier space, combining each view's 2D Fourier spectrum. Thus, an isotropic exploration of the object, for example by combination of illumination orientations and sample rotations, leads to a fully-3D mapping of the object's spectrum and allows to reach an isotropic resolution in the 100nm range [6, 7]. However, this reconstruction quality requires a huge number of holograms with almost isotropic exploration. Moreover, the Born or Rytov inversion is limited to weakly scattering samples. To overcome limitations involved in classical inversion, one has to turn to more sophisticated approaches. The Gerchberg-Papoulis algorithm [8] proposes an iterative framework based on the alternating projections principle - similar to the so-called Fienup Error Reduction algorithm in 2D digital holography [9] with the imposition of a positivity (or negativity) constraint on the RI difference map. This algorithm is a representative of what we call inverse problems approaches [8, 10, 11]. These last are mostly based on the minimization of a global penalty criterion constructed as a combination of two components: a so-called data-fidelity term measuring the error between the data and an image formation model, and one or several priors taking the form of regularization terms or bound constraints. Inverse approaches are more flexible because they allow for the use of more accurate models, e.g. multiple-scattering based approaches

[12–15]. Thanks to this gain of accuracy, the data information is 66 127 better exploited. Therefore, the useful amount of measurements 67 can be drastically reduced if an appropriate trade-off is found 68 between the relative influences given on both the data-fidelity 69 130 70 and the *a priori* information on the targeted object. This trade-off 71 is most of the time achieved by weighting properly the regu-132 72 larization penalty terms in the global criterion. These scalar 133 weights are called hyperparameters, and their tuning is critical 73 to ensure the consistency of the inverse problem and thus its 74 solution 75

The optimal hand tuning of the hyperparameters is a too 76 fastidious task, so finding unsupervised tuning approaches is 135 77 of great interest in image reconstruction. If the ground truth 78 was known, the optimal hyperparameters' values would be 79 those that minimize an error between the reconstruction and the 80 ground truth (e.g. the estimation Mean Square Error). Obviously 81 in practice, such a ground truth being unknown, unsupervised 82 tuning approaches consist in using a "blind" criterion to find 83 optimal values for the hyperparameters. Popular methods in 84 this context are the generalized cross-validation (GCV:[16]), the 85 143 *L*-curve [17], hierarchical Bayesian strategies [18] and the Gener-86 144 alized Stein unbiased Risk Estimator (GSURE: [19, 20]). Lately, 87 145 some hyperparameters-free methods have exploited neural net-88 works for learning appropriate regularizers [21, 22]. 89

147 In this work, we discuss the performance of GSURE for the 90 1/18 unsupervised tuning of the regularization hyperparameters in 91 149 the context of TDM reconstruction. The application of GSURE 92 150 in such a context constitutes the main contribution of this work. 93 151 Our paper is organized as follows. In Section 2 we introduce the TDM principle with some mathematical notations, and present 95 the forward model used in our experiments. In Section 3, we 96 present a regularized inverse approach for TDM reconstruc-152 97 tion that involves popular regularization terms (sparsity, edge- 153 98 preserving, Total Variation), which we "plug" in a minimization 99 procedure of the GSURE criterion to estimate optimal regular-100 ization hyperparameters. Finally, in Section 4, we evaluate the 101 155 performance of our unsupervised reconstruction approach using 102 156 103 GSURE, on both simulated and real data. Our datasets consist in realistic simulations of TDM acquisitions of a single transparent 157 104 bead (5 and 10 µm diameter), using a Lorenz-Mie scattering 158 105 model [23], and experimental TDM acquisitions of a Jerusalem 106 artichoke pollen grain ($\sim 30 \ \mu m$ diameter). We perform the 107 reconstructions from very limited TDM views to show how the 108 optimal trade-off between the data-fidelity and the regulariza-109 tion is helpful in this context. Our results tend to demonstrate 110 this claim. 111

2. TDM DATA ACQUISITION PRINCIPLE AND FORWARD 112 MODEL 113

A. Object and data models 114

We consider a single object (e.g. a bead as in Fig. 1), or a distribu-115 tion of objects, immersed in a medium of RI n_0 . In the following, 116 the object in the medium is sampled and considered as the three 117 dimensional (3D) array $\mathbf{n} \in \mathbb{C}^{K}$, where *K* is the total number of 118 voxels. Each voxel value \mathbf{n}_k , for $k \in \{1, \dots, K\}$, is the complex 119 RI difference of the object with the medium in this voxel. Hence 120 each \mathbf{n}_k can be decomposed into two components $\mathfrak{Re}(\mathbf{n}_k)$ and 121 $\mathfrak{Im}(\mathbf{n}_k)$, defining its respective real and imaginary parts such 122 that $\mathbf{n}_k = \Re \mathfrak{e}(\mathbf{n}_k) + j \Im \mathfrak{m}(\mathbf{n}_k)$. Moreover, $\mathbf{n}_k = 0$ means that the 123 voxel $k \in \{1, \dots, K\}$ contains only the medium. 124

A TDM dataset consists in the recording, on a digital sensor of M 125 pixels, of L complex holograms obtained by the diffraction and 126

propagation into the sample of L respective coherent illumination plane waves $\underline{u}_{\ell}^{(inc)}$ that are tilted with respect to the sensor plane (see Fig. 1). We denote $\mathbf{d}_{\ell} * \in \mathbb{C}^M$ the ℓ^{th} sampled complex hologram corresponding to a unique tilted view of parameter ϕ_{ℓ} .

The model of the respective noisy data acquired by the camera is given as:

$$\mathbf{d}_{\ell} = \mathbf{d}_{\ell}^* + \boldsymbol{\eta}_{\boldsymbol{\ell}} \tag{1}$$

where η_{ℓ} corresponds to a vector of *M* noise values.

B. The hologram formation model

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In practice, the true complex holograms $\mathbf{d}_{\ell} * \in \mathbb{C}^{M}$ are unknown. Several methods exist [14] to calculate an approximation of these projections as the first Born or Rytov approximation [5, 24-26], the beam propagation method (BPM) and similar strategies such the wave propagation method (WPM) [10, 27], the Lippmann-Schwinger model [28], etc. We denote by $u_{\ell}(\mathbf{n})$ the hologram formation model. In this work, we focus on BPM that performs a cascading propagation of the diffracted wave through the sample - from the "top" to the "bottom" - decomposed in several slices, each one interacting successively with the upper wave (multiplication of the wave with the transmittance slice). This model is adapted to simulate multiple scattering (in the propagation direction) into a dense volume. However, the unsupervised method proposed in this paper can be applied using another hologram formation model. The forward-model, approximating the true data formation process, is thus the following:

$$\mathbf{d}_{\ell} \approx u_{\ell}(\mathbf{n}) + \boldsymbol{\eta}_{\ell}$$
 (2)

Note that this model is now an approximation of the true data formation process in Eq. (1) because of the additional modeling errors.

3. PROPOSED METHOD

A. Regularized inverse approach

We aim at retrieving $\mathbf{n} \in \mathbb{C}^{K}$ from the complex dataset $(\mathbf{d}_{\ell})_{\ell \in \{1,...,L\}}$. The classical inverse approach is to find **n** mini-



Fig. 1. Scheme of the TDM principle for the ℓ -th hologram acquisition \mathbf{d}_{ℓ}^* of a sample (here a bead). The hologram is acquired for an orientation of illumination wave $\underline{u}_{\ell}^{(inc)}$, parametrized by the angles ψ_{ℓ} in the (z, x) plane and ϕ_{ℓ} in the (x, y) plane, at a distance z_d from the center of the object. 59 mizing the following cost function:

$$f(\mathbf{n}) = \sum_{\ell=1}^{L} \frac{1}{2} \| \mathbf{d}_{\ell} - u_{\ell}(\mathbf{n}) \|_{\mathbf{C}}^{2}.$$
 (3)

¹⁶⁰ It is equivalent to the co-log-likelihood minimization under the

assumption that $\forall \ell \in \{1, ..., L\}$, $\mathbf{d}_{\ell} \sim \mathcal{N}(u_{\ell}(\mathbf{n}), \sigma^2 \mathbf{Id}_M)$ (*i.e.* the additive noise η_{ℓ} follows a centered multidimensional Gaus-

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¹⁶⁹ To palliate this issue, a prior term g^{ρ} is added to the problem ¹⁷⁰ Eq. 3, that can be a composition of one or several regularizers, ¹⁷¹ and parametrized by a set of hyperparameters ρ . This set is ¹⁷² composed of at least one hyperparameter per regularization ¹⁷³ term to weight their contribution. The reconstruction problem ¹⁷⁴ of the 3D RI map **n** becomes:

$$\widehat{\mathbf{n}} \in \underset{\mathbf{n} \in \Omega}{\arg\min} \left\{ f(\mathbf{n}) + g^{\boldsymbol{\rho}}(\mathbf{n}) \right\}$$
(4)

where $\Omega \subset \mathbb{C}^{K}$ is a set of separable bound constraints applied ²¹⁷ on the real and imaginary part of each element of **n**. ²¹⁸

In this work we compare two regularizations: $g^{\text{EP}+\ell_1}$ that is the combination of an Edge Preserving smoothing prior [29] and the ℓ_1 -norm sparsity constraint (EP + ℓ_1) applied separately on the real part $\Re(\mathbf{n})$ and imaginary part $\Im(\mathbf{n})$ of \mathbf{n} , and g^{TV} the Total Variation (TV) [30]. On one hand, the EP+ ℓ_1 regularization, given by:

$$g^{\mathrm{EP}+\ell_{1}}(\mathbf{n}) = \lambda^{\mathrm{EP}} \sum_{n=1}^{N} \left(\sqrt{\|\mathbf{D}_{n}\mathbf{n}\|^{2} + \mu^{2}} - \mu \right)$$
$$+ \lambda^{\ell_{1}} \sum_{n=1}^{N} \left(|\mathfrak{Re}(\mathbf{n}_{n})| + |\mathfrak{Im}(\mathbf{n}_{n})| \right)$$
(5) 226

has the advantage of being differential (thanks to the relaxing 177 228 parameter $\mu > 0$) when all the voxels of **n** are constrained to 178 have the same sign. D_n is a finite difference operator at each 179 voxel *n*, giving a vector of six components: three gradient com-180 ponents for both the real part $\mathfrak{Re}(\mathbf{n})$ and imaginary part $\mathfrak{Im}(\mathbf{n})$ 181 of **n**. Thus the squared norm $\|\mathbf{D}_n\mathbf{n}\|^2$ applied to this gradient 182 230 vector is the sum of its six squared components. When μ tends to 183 231 184 zero, the Edge Preserving Smoothing tends to TV. The ℓ_1 sparsity 232 prior applied on **n** is there to ensure zero values outside of the 185 233 object, thus it acts as a support constraint. In such a case of regu-186 234 larization, the set of hyperparameters is $\rho = (\lambda^{\text{EP}}, \mu, \lambda^{\ell_1})$. The 187 whole criterion in Eq. 4 is differentiable (smooth), so we achieve 188 236 the minimization using the VMLM-B algorithm [31], which is a 189 237 limited memory quasi-newton method with line search. 190 238

¹⁹¹ On the other hand, the Total Variation, given by:

$$g^{\mathrm{TV}}(\mathbf{n}) = \lambda^{\mathrm{TV}} \sum_{n=1}^{N} \sqrt{\|\mathbf{D}_n \mathbf{n}\|^2}.$$
 (6)

requires only one hyperparameter, thus $\rho = \lambda^{\text{TV}}$. This regularization is not differentiable and the criterion in Eq. 4 is then a 241 sum of a smooth (*f*) and a non-smooth (g^{TV}) terms. This leads 242 to the use of proximal algorithms for the minimization of the 243 cost function. In this work, we use the primal-dual Condat-Vũ 244 algorithm with backtracking [32–34]. 245

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B. GSURE for unsupervised reconstruction

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An appropriate tuning of the regularization hyperparameters is essential to achieve a good reconstruction of the object. An under-regularized reconstruction will lead to a wrong estimation of the 3D map n. For example, the "missing cone" effect, a classical problem in TDM due to the limited angular coverage, will be exhibited by the defective closure of the object in the axial (z) direction. On the contrary, an over-regularized reconstruction can yield over-smoothing, i.e. a loss of details. The tuning of the hyperparameters can be achieved by finding the set ρ for which the reconstruction optimizes a given quality criterion, for example: the estimation Mean Square Error (MSE), the absolute error, or the prediction Mean Square Error (pMSE). These three quality criterions require the knowledge of the ground truth, unknown in practice, but the pMSE can be estimated using the Generalized Stein's Unbiased Risk Estimator [19, 20] which requires only the knowledge of the data \mathbf{d}_{ℓ} .

We denote $\hat{\mathbf{n}}_{\rho}$ the reconstruction obtained for a given set of hyperparameters ρ . The pMSE is defined as follows:

$$pMSE(\widehat{\mathbf{n}}_{\boldsymbol{\rho}}) = \sum_{\ell=1}^{L} \mathbb{E}\Big[\|\mathbf{d}_{\ell}^* - u_{\ell}(\widehat{\mathbf{n}}_{\boldsymbol{\rho}})\|_{C}^2 \Big].$$
(7)

where **E** stands for the expectation. Note that the use of such a criterion to find ρ for which the reconstructions is minimizing the pMSE requires an accurate image formation model. In fact, this criterion only "sees" the data and the modeling approximations. If it is not accurate enough, the pMSE minimization will lead to a reconstruction minimizing these modeling errors at the expense of its accordance to the ground truth object.

The GSURE criterion is given by:

$$\text{GSURE}(\widehat{\mathbf{n}}_{\rho}) = \sum_{\ell=1}^{L} \left[\frac{1}{2\sigma^2} \left\| \mathbf{d}_{\ell} - u_{\ell}(\widehat{\mathbf{n}}_{\rho}) \right\|_{\text{C}}^2 + 2\text{tr}\left(\frac{\partial u_{\ell}(\widehat{\mathbf{n}}_{\rho})}{\partial \mathbf{d}_{\ell}}\right) - M \right]$$
(8)

where σ^2 is the variance of the noise in the data, tr stands for the trace (sum of the diagonal elements) of a matrix, and *M* the number of pixel in each hologram. Since GSURE is an estimator of the pMSE, then

$$\mathbb{E}[\text{GSURE}(\widehat{\mathbf{n}}_{\rho})] = \text{pMSE}(\widehat{\mathbf{n}}_{\rho})$$
(9)

and both criterion, as a function of ρ , achieve their minimum for the same argument. Hence, we can find the optimal hyperparameter set $\hat{\rho}$ minimizing the pMSE, by minimizing GSURE.

The trace term tr $(\partial u_{\ell}(\hat{\mathbf{n}}_{\rho})/\partial \mathbf{d}_{\ell})$ is equal to div $u_{\ell}(\hat{\mathbf{n}}_{\rho})$ and is obtained with the Monte-Carlo method presented in [35]. Its principle is to generate a perturbed dataset $\mathbf{d}_{\ell}^{\delta}$ by adding a random deviation on the data $(\mathbf{d}_{\ell})_{\ell \in \{1,...,L\}}$, with a centered Gaussian noise of standard deviation ε . Then a reconstruction from $\mathbf{d}_{\ell}^{\delta}$ is performed to obtain a map $\hat{\mathbf{n}}_{\rho}^{\delta}$. From this reconstruction, the computation of the trace is performed from the following formula:

$$\operatorname{tr}\left(\frac{\partial u_{\ell}(\widehat{\mathbf{n}}_{\rho})}{\partial \mathbf{d}_{\ell}}\right) = \frac{\left\langle \mathbf{d}_{\ell}^{\delta} - \mathbf{d}_{\ell}, u_{\ell}(\widehat{\mathbf{n}}_{\rho}^{\delta}) - u_{\ell}(\widehat{\mathbf{n}}_{\rho})\right\rangle}{\varepsilon^{2}}.$$
 (10)

A good choice of ε is critical to ensure GSURE is a good estimate of the pMSE. If chosen too small or too large, the trace will be underestimated or overestimated, leading to a wrong GSURE criterion. In this work we compute ε as the tenth of the median of the real part of the data, which gives a good GSURE criterion in practice.

To achieve the minimization of GSURE, the most intuitive 288 246 method is to create a mapping of different hyperparameters 247 289 set ρ_{1} to proceed to the reconstruction on both datasets and 290 248 perturbed datasets to compute GSURE for each ρ , and finally 291 249 find on the mapping the set $\hat{\rho}$ that gives the minimum of the 250 obtained discretized GSURE map. However, such a method can 251 252 become computationally intractable when the set ρ is composed with two or more hyperparameters. Hence, an optimization of 253 the GSURE criterion is performed using a Powell method [36], 254 which does not require the computation of the gradient for the 255 search of the minimum. 256

257 4. RESULTS

In this section, we observe and discuss the performance of our
 GSURE based unsupervised method on reconstructions from
 simulated and experimental data.

First, we consider simulated TDM measurements of a perfect 261 sphere of diameter Δ , using the realistic Lorenz-Mie scattering 262 model [23], that simulates the diffracted field from this kind 263 of object almost perfectly. For the reconstruction, we choose 264 the BPM model that fits at best the simulated one and over-265 comes the classical Born or Rytov model, particularly when the 266 267 size of the object of interest or the RI gradient grows. Moreover, the simplicity of the object of interest (a homogeneous 268 sphere with sharp edges) corresponds exactly to the chosen 269 Edge-Preserving and TV regularizers (promoting piecewise con-270 stant images) as its characteristics validate precisely such prior 271 assumptions. Hence, our choices lead to a really good toy model 272 and an "inverse crime"-less reconstruction, allowing the valida-273 tion of our method. We aim to prove that we can find optimal 274 values of the hyperparameters in the sense of the prediction 275 Mean Square Error (pMSE), under such controlled conditions. 276

Second, we consider experimental TDM acquisitions of a
Jerusalem artichoke pollen grain. We aim to validate the conclusion obtained on simulated data.

280 A. Results on a simulated bead

We aim at reconstructing independently three non-centered spherical beads of different diameters Δ (see Table. 1), with a RI n_{bead} = 1.45 and immersed in a medium of RI n_0 = 1.519 - mimicking a silica bead in immersion oil. For each bead, our datasets consist in *L* on-focus holograms \mathbf{d}_{ℓ}^* (i.e. $z_d = 0 \, \mu m$), simulated from an implementation of the Lorenz-Mie model [23]. The incident wave orientations are displayed on Fig. 2



Fig. 2. Scheme of the *L* projections parametrized by the angles $\psi_{\ell} \in \{0^{\circ}, 45^{\circ}, 45^{\circ}, 45^{\circ}\}$ and $\phi_{\ell} \in \{0^{\circ}, 0^{\circ}, 120^{\circ}, 240^{\circ}\}$.

and the size of the holograms are given in Table. 1. Finally, we compute the data following Eq. 1, where each element η_k of the additive noise vector η is randomly generated using a stationary complex normal law $CN(0, 2\sigma^2)$ with $\sigma^2 = 0.1$. Table. 1 summa-



Fig. 3. Moduli and phases of the true holograms d_{ℓ}^* and of the related data d_{ℓ} , for $\ell \in \{1, \ldots, 4\}$, simulated with the Lorenz-Mie model for the parameters summarized in Table. **1**.

| case | Δ | $(x_{\text{bead}}, y_{\text{bead}}, z_{\text{bead}})$ | ψ_L | L | М | N | $oldsymbol{ ho}^{\mathrm{EP}+\ell_1}$ | $ ho^{\mathrm{TV}}$ |
|------|------|---|--------------|---|---------------|-----------------------------|---------------------------------------|---------------------|
| (a) | 5µm | $(-2.3467\mu m, -2.3467\mu m, 0\mu)$ | 45° | 4 | 64 	imes 64 | 64 	imes 64 	imes 64 | $(10^{0.38}, 10^{-0.27}, 10^{-0.99})$ | $10^{-0.67}$ |
| (b) | 10µm | $(-2.3467\mu m, -2.3467\mu m, 0\mu)$ | 45° | 4 | 128 	imes 128 | $128 \times 128 \times 128$ | $(10^{1.53}, 10^{0.44}, 10^{-1.4})$ | 10 ^{0.49} |

Table 1. Summary of the beads and data properties, and list of the regularization hyperparameters obtained with the Powell minimization of the GSURE criterion.

rizes the simulations parameters. The modulus and the phase of
 the Lorenze-Mie simulations for all the incidences are displayed
 on Fig. 3 along with the modulus and the phase of the data.

Since the difference between the Lorenze-Mie model and 312 295 BPM is growing with the RI difference and with the size, the 313 296 case (a) in Table 1 is an intermediate case and the case (b) is 314 29 the harder case. We only consider L = 4 projections. More 315 298 projections could make the task easier but we make the choice 316 290 to show configurations where the tuning of regularizations is 317 300 critical to get the best trade-off with the accordance to the data 318 30 model. 302 319

Fig. 4 presents the maps (respectively curves), of pMSE values and GSURE, for the EP+ ℓ_1 regularization (respectively TV). First are close. In the case of EP+ ℓ_1 , the μ hyperparameter is fixed to the best hyperparameter obtained with the Powell method. For this regularization GSURE seems to be less sensitive to the ℓ_1

norm, which can be problematic since the sparsity constraint is important to have a good support of the object, *i.e.* to have zero values outside of the object.

Fig. 5 shows the 3D reconstructions of the bead compared to the ground truth in the different configurations. For each case and each regularization, the bead is well reconstructed. The reconstructions with the EP + ℓ_1 regularization seems noisier than with the TV regularization and the edges of the object are smoother. Such an observation is coherent with the assertion that for EP + ℓ_1 the GSURE criterion is less sensitive to the ℓ_1 norm. In fact, since the reconstruction is under-regularized for the sparsity-promoting part, the values outside the support of the object are not sufficiently constrained to zero. Moreover, it leads to a smoothing of the edges along the *z*-axis. On the opposite, the edges in the reconstructions with TV are sharp, and the medium is uniform and noiseless. The reconstruction with TV is thus satisfying and seems really close to the ground



Fig. 4. Maps of pMSE and GSURE values for both regularizations and for each case presented in Table 1. For EP+ ℓ_1 , the values of μ are fixed to those estimated (see Table. 1). The minimum of the pMSE (respectively GSURE) values are marked with a blue (respectively red) circle.

truths.

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An overview of under-regularized and over-regularized re- 338 327 constructions, in the case of the TV regularization, is presented 339 328 in Fig. 6. For the under-regularized case, the object is not well 340 329 defined. The edges and the inner region are lost. This highlights 341 330 the fact that the amount of data, in this simulation configuration 342 331 and with such hyperparameters, is not sufficient to reconstruct 343 332 the bead correctly, evidencing the need of appropriately tuned 344 333 regularizations. For the over-regularized case, the bead is well 345 334 defined but some artifacts are appearing. 346 335 Overall, the GSURE criterion seems to be an effective tool to 347

select automatically a good set of hyperparameters for the reconstruction as it manages to capture a set of optimal regularization weights ensuring a satisfactory solution that fits at best the data model and the prior constraint.

To compare which regularization term, for the best set of hyperparameters estimated by GSURE, gives the best performances, we perform a quantitative study of the RI difference distribution in the reconstructed bead in Fig.7. In case (a) and (b), the median with EP+ ℓ_1 is closer to the true RI than with TV. However, the interquartile range is smaller with TV than with $EP+\ell_1$. In the end, with $EP+\ell_1$, since the bead is less compact

Edge Preserving Smoothing + ℓ_1 Ground Truth **Total Variation** (a) 5µm (b) 10µm Fig. 5. 3D segmented views of the ground truth and reconstructed beads obtained with optimal regularization weights minimizing GSURE, for both regularization terms EP + ℓ_1 and TV, and each case presented in Table 1. Side views displays the *xy*, *xz* and *yz* orthogonal slices through the object's center.

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Fig. 6. Reconstructions of the bead (b) with the TV regularization for several choices of hyperparameters and with the optimal parameter obtained with the minimization of the GSURE criterion. Case (i) and (ii) are under-regularized reconstructions, case (iii) is the reconstruction minimizing the GSURE criterion and case (iv) is over-regularized.

due to an under-regularization, the precision on the RI difference
is worse than with TV. Yet, with TV, the average RI difference
obtained in the bead is smaller than the ground truth. Note that
a loss of intensity is common with TV.

To conclude, in these simulations GSURE is effective to tune 370 352 353 automatically the hyperparameters leading to reconstruction 371 354 with a satisfying quality, a difficult task due to the low amount 372 of data in this context. The reconstruction with TV gives better 373 355 results than with EP+ ℓ_1 because GSURE is less sensitive to the 374 356 sparsity-promoting constraint. However, it suffers from a bias in 375 357 the reconstructed RI difference in the bead. Note that this object 376 358 has a piecewise constant gradient, thus the TV regularization is 377 359 at ease in this context. With a more detailed object such a prior 378 360 can be too strong and lead to the flattening of some structures. 379 36 This is why in the following we still apply both regularizers. 362 380

B. Results on a pollen grain sample

We used the GSURE criterion to reconstruct the 3D index map ³⁸³ of a Jerusalem artichoke pollen grain. These data are given ³⁸⁴



Fig. 7. Distribution of the RI difference value of the reconstructed beads giving the best GSURE for both regularization and each case presented in Table 1. Each blue boxes corresponds to the interquartile range and the red line is the median. The red crosses represent the outliers.

with the courtesy of the IRIMAS laboratory, Mulhouse, France. A detailed description of the TDM setup that performed the measurements can be found in [7]. It is based on holographic measurements in off-axis configuration. In our reconstructions, the considered dataset is the measured complex diffracted waves on the sensor plane (focal plane of the setup), extracted from the raw off-axis measurements.

To estimate the noise in the data, we suppose it is an homogeneous Gaussian noise and estimate its variance on a patch containing only background. We proceed to the GSURE optimization for the reconstruction with $EP+\ell_1$ and TV regularizations respectively, using only L = 20 projections. These projections are chosen by the following method. First we sort the entire set of 600 projections by their angles ϕ_{ℓ} and group them in 20 subsets. Thus, we ensure that the 20 subsets are covering the entire circle on which ϕ_{ℓ} evolves. Then, one projection is randomly chosen in each subset to create the dataset. Since problem Eq.4 is non-convex due to the BPM approximation, to avoid the convergence to a local minimum [12], we initiate the reconstruction obtained with an unregularized inversion using the first Born approximation [5, 24–26]. We made the hypothesis that the object has no absorption (*i.e* $\mathfrak{Im}(\mathbf{n}_k) = 0$ for all $k \in \{1, ..., N\}$) and that the object's absolute RI values are larger than the medium RI value n_0 (the RI difference is greater or equal to 0), leading to the following separable bound constraints set:

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$$\Omega = \left\{ \mathbf{n} \in \mathbb{R}^N \mid \forall k \in \{1, \dots, N\}, \ \mathbf{n}_k \ge 0 \right\}.$$
(11)

Figure 8 presents different views of the object reconstructed with a direct inversion using Rytov approximation for L = 600without any constraint or regularization (courtesy from IRIMAS team), with the Gerchberg-Papoulis (GP [8]) method including a non-negativity constraint for L = 600 and L = 20, and with the presented method for both regularization terms. The set of hyperparameters obtained for the reconstructions are $\rho^{\text{EP}+\ell_1} = (10^{0.61}, 10^{-3.53}, 10^{0.84})$ and $\rho^{\text{TV}} = 10^{-0.26}$. First, comparing Rytov and GP reconstructions for L = 600, we see that the constraint on the sign of the RI difference improves clearly the contrast and, as in [8], alleviate the underestimation of RI values. Thus, the reconstruction with GP seems better, and this is why we consider it as our "ground truth" for our comparisons with L = 20.

For both reconstructions using our method, the object is well reconstructed and the contrast is enhanced compared with GP for L = 20. On the TV reconstruction, even if the apparent resolution is lower than for the Rytov and GP reconstructions (for L = 600), we can observe the same structured features inside the object. For example, in Fig. 8: (a)-(c) and (e), we highlighted some dense regions with red arrows and kind of porosities with purple arrows. These features are better reconstructed with our methods than with GP for L = 20. However, the reconstruction with EP+ ℓ_1 is a little smoother than the reconstruction with TV, leading to the loss of these small features. Finally, our methods deal better with the zero values outside the object (support estimation). It is mainly visible in the 3D views in rows (e) and (g) and for the central frame (*i.e.* z = 256) shown on row (b). Furthermore, we can see on row (f) that our methods deal also better with the missing cone effect.

Fig. 9 presents wrongly tuned reconstructions of the pollen grain with the TV regularization. We can see that in the underregularized case, the contrast is slightly lighter, and some porosities are lost in case (a) and (b). However, the reconstruction is close to the reconstruction obtained with GSURE even though



Fig. 8. Views of the Jerusalem artichoke pollen grain for the Rytov inversion and with the GP method for L = 600 projections, and the reconstructions with the GP method and giving the best GSURE values for the EP+ ℓ_1 and TV regularizations for L = 20 projections. Rows (a)-(d) represents the (x, y) slices for $z \in \{231, 256, 282, 303\}$ and are highlighted on the (x, z, y) 3D view on row (e) with the same colored frames. Row (f) is the (x, z) view for y = 256 and is highlighted on the (x, z, y) 3D view on row (g) with the same colored frame.

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the hyperparameter is a lot smaller. In the over-regularized case,
 all the details are lost. The reconstruction is really different from
 the reconstruction obtained with GSURE even though the hyperparameter is not far from the optimal one (in the sense of the
 pMSE).

449 In conclusion, in this experimental case, when using the 431 450 TV regularization, the optimization of the GSURE criterion 432 451 is effective to achieve a satisfying reconstruction. In the case 433 434 of EP+ ℓ_1 , some further hand tuning could help lower the regularization and recover the features inside the object. Thus, 435 454 it only gives a starting set. Overall, an important point in 436 455 these experiments is the demonstration that an appropriate 437 456 tuning of the regularization hyperparameters can favor a better 438 457 exploitation of the data by the model, opening the way to 439 drastically reduce the amount of useful TDM projections (from 440 459 an order of magnitude in this experiment) while preserving a 44 460 442 satisfying reconstruction in terms of contrast and resolution. 461 443 462



Fig. 9. Comparison of reconstructions of the pollen grain, on the slices Fig.8-(a) to (c), (e), and (f), with the TV regularization for different hyperparameters. From the left to the right : an under-regularized reconstruction, the reconstruction giving the best GSSURE value and an over-regularized reconstruction.

5. CONCLUSION

In this work, we propose an unsupervised method for automatically tune the hyperparameters of a regularized 3D reconstruction method from TDM measurements using GSURE. We applied it with both differentiable and non-differentiable regularization terms. We prove its capability to find a good tuning of the regularization hyperparameters on both simulated and experimental data. This work show how an appropriate tuning of the hyperparameters helps to exploit at best the data information, which is particularly critical when the amount of measurements is or has to be reduced, for example for experiment or setup optimization purposes.

However, this work only presents a brief application of GSURE and raises several perspectives. First, it would be interesting to study how GSURE behaves with other models (e.g. the first Born Approximation). Second, an empirical study of how the GSURE minimal argument varies with the number of projections used for the reconstruction could be useful to see if it is predictable. Such a case would allow us to tune the hyperparameters only on a few holograms (the minimum required) and then perform a reconstruction with all the data (or a sufficient amount to have the best quality). Third, an optimization of the computational time could be done. In fact, it takes two reconstructions to compute one iteration of GSURE and several iterations are needed to converge to its minimum. Depending on the complexity of the hologram formation model (Born or BPM), it can take several hours to several days. Finally, a comparison with other autotunning method should be performed.

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78 8. DISCLOSURES

79 The authors declare no conflict of interest.

• 9. DATA AVAILABILITY

Data underlying the results presented in this paper are not publicly available at this time but may be obtained from the authors upon reasonable request.

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