Source location from fluorescence lifetime in disordered media

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We show that the source location problem can be solved in a scattering medium using the fluorescence lifetime and realistic *a priori* information. The intrinsic ill-posedness of the problem is reduced when the level of scattering increases. This work is a proof of principle demonstrating the high potential of quantitative lifetime imaging in complex media.
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In a structured material, the excited-state lifetime of a fluorescent emitter depends on its position [1]. In a disordered scattering medium, the spontaneous decay rate (inverse of lifetime) fluctuates due to changes of the local environment [2–7]. The amplitude of the fluctuations substantially increases in the multiple scattering regime [5,8] and/or in the presence of near-field interactions [7,9]. Since the decay rate depends on the location of the emitter, one can wonder whether the inverse source problem could be solved using the lifetime as data in a given configuration of a disordered medium. The purpose of this Letter is to address this question based on numerical simulations in a simple geometry. We show that the source location problem can be solved in two steps, using first a coarse-grain location of the fluorophore (e.g., from a standard microscope fluorescence intensity image) defining a domain of interest (DOI), and then using the lifetime to reconstruct the source location in the DOI. Interestingly, the ill-posedness of this peculiar inverse problem is reduced when the level of scattering increases. This proof of principle might pave the way toward novel approaches for lifetime imaging in complex media [10]. In the active field of inverse problems in scattering media, it also shows that reconstructions can be improved by the use of signals that are very sensitive to the local environment, e.g., due to near-field interactions [11] or the quantum nature of the emitters [12].

In the weak coupling regime, the spontaneous decay rate of a fluorescent source located at position $\mathbf{r}_0$ is given by $\Gamma(\mathbf{r}_0,\omega) = \Gamma_0 + (2\mu_0\omega^2/\hbar)|\mathbf{p}_{\rm eg}|^2\,\mathrm{Im}[\mathbf{u}\cdot\mathbf{G}_s(\mathbf{r}_0,\mathbf{r}_0,\omega)\mathbf{u}]$ [13], where Γ_0 is the decay rate in free space, ω is the emission frequency, $\mathbf{p}_{\rm eg}$ is the transition dipole between excited and ground states, and $\mathbf{u} = \mathbf{p}_{\rm eg}/|\mathbf{p}_{\rm eg}|$. In this expression, the electrodynamic response of the environment is described by the scattered part of the Green function $\mathbf{G}_s$, that connects a classical electric dipole source $\mathbf{p}$ at $\mathbf{r}_0$ to the scattered field at position $\mathbf{r}$ through the relation $\mathbf{E}_s(\mathbf{r},\omega) = \mu_0\omega^2\mathbf{G}_s(\mathbf{r},\mathbf{r}_0,\omega)\mathbf{p}$. In this work, we give a proof of principle in a simple two-dimensional (2D) geometry under TE illumination (the source dipole and the electric field are parallel to the invariance axis) so that we are left with a scalar problem. The relative change in the decay rate reads

$$\frac{\Gamma(\mathbf{r}_0,\omega)-\Gamma_0}{\Gamma_0} = \frac{2\mu_0\omega^2|\mathbf{p}_{\rm eg}|^2}{\hbar\Gamma_0}\mathrm{Im}[G_s(\mathbf{r}_0,\mathbf{r}_0,\omega)]. \quad (1)$$

This quantity encodes the source position $\mathbf{r}_0 = (x_0, y_0)$ through the imaginary part of the scattered Green function G_s, or, equivalently, through the imaginary part of the scattered field $E_s(\mathbf{r}_0,\omega)$ [14].

To model a disordered scattering medium, we consider M pointlike scatterers with polarizability $\alpha(\omega)$ randomly located at positions $\mathbf{r}_j$. Wave propagation and multiple scattering in such a medium can be formulated in terms of the so-called Foldy–Lax equations [15,16]:

$$E_s(\mathbf{r},\omega) = k^2\sum_j G_0(\mathbf{r},\mathbf{r}_j,\omega)\alpha(\omega)E_{\rm exc}(\mathbf{r}_j,\omega), \quad (2)$$

$$E_{\rm exc}(\mathbf{r}_j,\omega) = E_{\rm inc}(\mathbf{r}_j,\omega) + k^2\sum_{m\neq j} G_0(\mathbf{r}_j,\mathbf{r}_m,\omega)\alpha(\omega)E_{\rm exc}(\mathbf{r}_m,\omega), \quad (3)$$

where G_0 is the scalar free-space Green function, and $k = \omega/c$, with c the speed of light in vacuum. The summations are extended over the discrete set of scatterers. Equation (2) gives the scattered field $E_s(\mathbf{r},\omega)$ at point $\mathbf{r}$ in terms of the exciting fields $E_{\rm exc}(\mathbf{r}_j,\omega)$ at each scatterer position. Both the scattered and the exciting fields depend on the position $\mathbf{r}_0$ of the fluorescent source and the frequency ω (the dependence on $\mathbf{r}_0$ is not explicitly shown for brevity). The self-consistent Eq. (3) gives the exciting fields at each scatterer position, where $E_{\rm inc}(\mathbf{r}_j,\omega)$ is the incident field radiated by the dipole source placed at $\mathbf{r}_0$.

The 2D scatterers are described by a resonant polarizability $\alpha(\omega) = -(2\gamma/k^2)(\omega-\omega_0+i\gamma/2)^{-1}$, where ω_0 is the resonance frequency and γ is the linewidth. Different multiple scattering regimes can be explored by adjusting the detuning $\delta = \omega-\omega_0$, with $\delta \ll \omega_0$. As a measure of the scattering strength, we use $1/(k\ell_s)$, where $\ell_s = [\rho\sigma_s(\omega)]^{-1}$ is the scattering mean free path, ρ is the density of scatterers, and $\sigma_s(\omega) = \omega^3/(4c^3)|\alpha(\omega)|^2$ is the scattering cross section. In this work, we have chosen $\omega_0 = 2\cdot 10^6$ GHz ($\lambda_0 = 0.94$ μm), $\gamma = 1$ GHz, and $\delta = 1.0 - 2.3$ GHz in order to explore regimes corresponding to $1/(k\ell_s) = 0.06 - 0.28$.

For a fluorescent point source placed at $\mathbf{r}_0$ inside the scattering medium, the direct problem consists of solving the $M \times M$ linear system [Eq. (3)] for the exciting fields, computing the scattered field at $\mathbf{r}_0$ using Eq. (2), and deducing the change in the fluorescent decay rate (or, equivalently, $\mathrm{Im}[E_s(\mathbf{r}_0, \omega)]$) from Eq. (1). In Fig. 1, we show maps of $\mathrm{Im}[E_s(\mathbf{r}_0, \omega)]$ in one realization of the disordered medium, for different scattering strengths [from left to right, $1/(k\ell_s) = 0.28, 0.15$, and 0.06]. The size of the domain is $2\,\mu\mathrm{m} \times 2\,\mu\mathrm{m}$. The bottom row shows cross sections at $x = 1.7\ \mu\mathrm{m}$. The variation of $\mathrm{Im}[E_s(\mathbf{r}_0, \omega)]$ is larger for larger scattering strengths. Furthermore, the variation is smoother, leading to a simpler resolution of the inverse problem. Note that the oscillatory behavior of $\mathrm{Im}[E_s(\mathbf{r}_0, \omega)]$ for smaller scattering strength increases the ill-posedness of the inverse problem.

The inverse problem consists of finding the position of the source $\mathbf{r}_0$ from the knowledge of its decay rate $d(\omega) = \Gamma(\mathbf{r}_0, \omega)$, at different frequencies. In the inverse source problem using $d(\omega)$ as data, we seek values of the coordinates (x, y) that satisfy the nonlinear equations

$$\Gamma(x, y, \omega_i) = d(\omega_i) \quad i = 1, 2, \ldots. \tag{4}$$

To solve this nonlinear problem with two unknowns, we need data for at least two frequencies. Note that different frequencies lead to different scattering strengths, and thus correspond to different regimes of interaction between the fluorescent source and its environment. The choice of a set of frequencies, for which the solution of Eq. (4) gives the correct source location in a robust way, is a key point. Without noise, two frequencies may be sufficient if the spatial variation of Γ is large and smooth enough. In the presence of noise, and/or in a situation for which Γ is weakly dependent on position (weak disorder), multifrequency data are needed. To solve Eq. (4), different numerical approaches are available. Here we use an iterative gradient-based method. Since this is a local method, convergence to the correct solution is guaranteed only for a close enough initial guess. The initial guess can be constrained by *a priori* information. In the examples shown below, we define a domain of interest (DOI) of size $1\,\mu\mathrm{m} \times 1\,\mu\mathrm{m}$ around the source. In the case of a dilute sample with statistically less than one emitter per $\mu\mathrm{m}^2$, this DOI could be defined from a diffraction-limited microscope image. Other methods having global convergence could be used, as, for example, statistical search methods. Optimizing the inverse method is not the goal of the present work, which is devoted to a proof of principle. In particular, the sensitivity of the inverse problem regarding the prior knowledge of the number of scatterers will be examined in a future work.

To demonstrate the feasibility of the inverse problem, we have carried out numerical experiments. In Fig. 2, we show reconstructions of the source position in the same $2\,\mu\mathrm{m} \times 2\,\mu\mathrm{m}$ disordered medium as in Fig. 1, and in different scattering regimes (the scattering strength decreases from left to right). The top row shows the position of the scatterers (dots), and the real (star) and reconstructed (circle) source positions. The bottom row shows the corresponding residuals $\sum_i |\Gamma(x_0, y, \omega_i) - d(\omega_i)|^2$ plotted along the y direction. We have used data with two frequencies, corrupted by an additive 8% Gaussian noise [the two values of $1/(k\ell_s)$ indicated in each case correspond to the two frequencies used in the data]. For strong scattering (left panel), the global minimum of the residual is well defined. It is efficiently reached by the local gradient method, and is also weakly dependent on noise. As a consequence, the source location is found with precision. For weaker scattering (center panel), the minimum of the residual is less well defined and, therefore, the solution of the inverse problem gives rise to a less precise source location. The situation is worse when the scattering strength decreases even more. In the right panel, we observe that the oscillations of the residual lead to several local minima of the residual that prevent a correct source location.

Although not shown for brevity, increasing the number of data (using more frequencies) improves the reconstruction (with six frequencies, the localization is successful in the three situations in Fig. 2). We stress that the reconstruction is performed with a resolution that

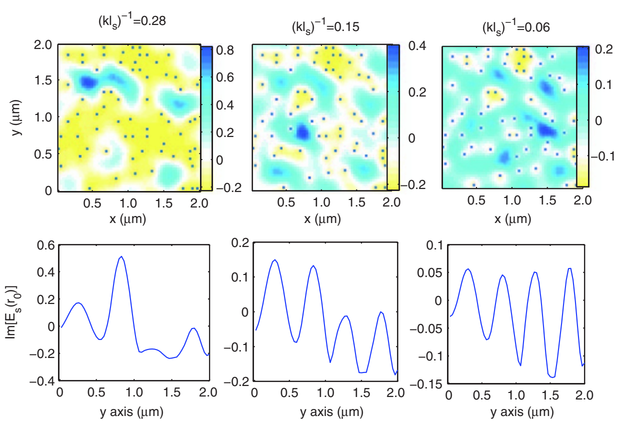

Fig. 1. (Color online) Top row: maps of $\mathrm{Im}[E_s(\mathbf{r}_0, \omega)]$ in one realization of the disordered medium with 63 scatterers indicated by dots. From left to right: $1/(k\ell_s) = 0.28$, 0.15, and 0.06 ($\ell_s = 0.5$, 1, and 2.4 μm). Bottom row: cross sections at $x = 1.7\ \mu$m. Size of domain: $2\,\mu\mathrm{m} \times 2\,\mu\mathrm{m}$.

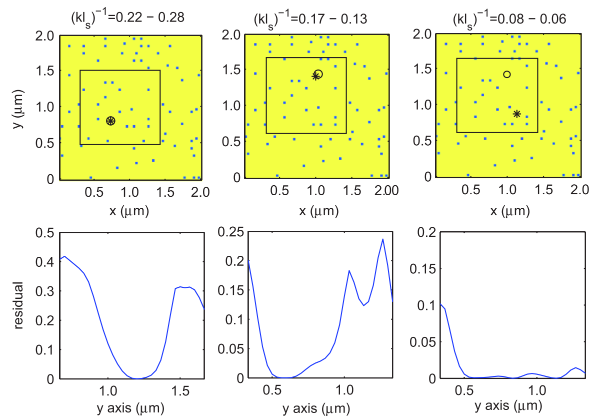

Fig. 2. (Color online) Top row: reconstructions inside a $1\,\mu\mathrm{m} \times 1\,\mu\mathrm{m}$ DOI (black square) in the same disordered medium as in Fig. 1, for three scattering strength regimes. Left: $(k\ell_s)^{-1} = 0.22 - 0.28$, $(k\ell_s)^{-1} = 0.13 - 0.17$, and $(k\ell_s)^{-1} = 0.06 - 0.08$. Two-frequency data are used for the reconstruction. Bottom row: residuals along the y directions.

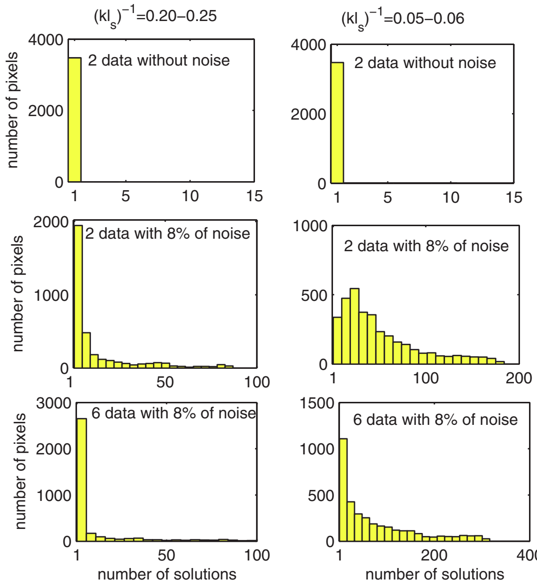

Fig. 3. (Color online) Number of solutions with the same decay rate as $\mathbf{r}_0$ scans the medium. Left column: $(k\ell_s)^{-1} = 0.20 - 0.25$. Right column: $(k\ell_s)^{-1} = 0.05 - 0.06$. Top row: two-frequency data without noise. Middle row: two-frequency data with 8% noise. Bottom row: six-frequency data with 8% noise.

is not diffraction limited. Changes in the decay rate encode the source location on a scale limited by the spatial variation of the local environment [4] (interparticle distance or spatial correlation length in a continuous disorder), offering the possibility of superresolution in a medium structured at subwavelength scale.

The numerical results suggest that an increased scattering strength $1/(k\ell_s)$ should improve the feasibility of the inverse source reconstruction. Indeed, as shown qualitatively in Fig. 1, the probability of getting two different source positions generating identical values of the decay rate Γ decreases for large $1/(k\ell_s)$ (the broadening of the statistical distribution of Γ in the presence of strong scattering has been demonstrated previously [5–8]). It is useful to investigate which values of $1/(k\ell_s)$ lead to a better robustness of the inversion procedure. To analyze this issue quantitatively, we plot in Fig. 3 the statistics of the number of solutions (ill-posedness) when $\mathbf{r}_0$ scans the medium. We use data with two or more frequencies within two ranges of scattering strength parameters $(k\ell_s)^{-1} = 0.20 - 0.25$ (left panel) and $(k\ell_s)^{-1} = 0.05 - 0.06$ (right panel). In the absence of noise, one unique solution exists and the reconstruction is perfectly robust with two-frequency data, whatever the scattering strength (top row in Fig. 3). With 8% of noise (middle row in Fig. 3), the histograms show two or more solutions for some source positions, and the problem is substantially ill-posed. By using more frequencies (bottom row in Fig. 3), we can get a much narrower distribution with almost a unique solution, the result being always better for a larger scattering strength.

In summary, we have shown that it is possible to solve the source location problem for a fluorescent emitter in a disordered scattering medium, using the fluorescence lifetime as data and realistic *a priori* information. The ill-posedness of the inverse problem is reduced in the presence of strong scattering, in agreement with known results on fluorescence lifetime statistics in multiple scattering media. To the best of our knowledge, this is the first proof of principle of an inverse source reconstruction from lifetime measurements that takes advantage of disorder and multiple scattering.

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References and Notes

1. R. R. Chance, A. Prock, and R. Sylbey, Adv. Chem. Phys. **37**, 1 (1978).
2. E. A. Donley and T. Plakhotnik, J. Chem. Phys. **114**, 9993 (2001).
3. R. A. L. Vallée, N. Tomczak, L. Kuipers, G. J. Vancso, and N. F. van Hulst, Phys. Rev. Lett. **91**, 038301 (2003).
4. L. S. Froufe-Pérez, R. Carminati, and J. J. Sáenz, Phys. Rev. A **76**, 013835 (2007).
5. M. D. Birowosuto, S. E. Skipetrov, W. L. Vos, and A. P. Mosk, Phys. Rev. Lett. **105**, 013904 (2010).
6. V. Krachmalnicoff, E. Castanié, Y. De Wilde, and R. Carminati, Phys. Rev. Lett. **105**, 183901 (2010).
7. R. Sapienza, P. Bondareff, R. Pierrat, B. Habert, R. Carminati, and N. F. van Hulst, Phys. Rev. Lett. **106**, 163902 (2011).
8. R. Pierrat and R. Carminati, Phys. Rev. A **81**, 063802 (2010).
9. A. Cazé, R. Pierrat, and R. Carminati, Phys. Rev. A **82**, 043823 (2010).
10. K. Suhling, P. W. French, and D. Philipps, Photochem. Photobiol. Sci. **4**, 13 (2005).
11. P. S. Carney, V. A. Markel, and J. C. Schotland, Phys. Rev. Lett. **86**, 5874 (2001).
12. J. C. Schotland, Opt. Lett. **35**, 3309 (2010).
13. J. M. Wylie and J. E. Sipe, Phys. Rev. A **30**, 1185 (1984).
14. Since Γ_0 is proportional to $|\mathbf{p}_{eg}|^2$, the prefactor in Eq. (1) is independent on $\mathbf{p}_{eg}$. The knowledge of the transition dipole is not required to solve the inverse problem.
15. L. L. Foldy, Phys. Rev. **67**, 107 (1945).
16. M. Lax, Rev. Mod. Phys. **23**, 287 (1951).