Self-prior strategy for organ reconstruction in fluorescence molecular tomography

YUAN ZHOU,1 MAOMAO CHEN,1 HAN SU,1 AND JIANWEN LUO1,2,*

1Tsinghua University, School of Medicine, Department of Biomedical Engineering, Beijing 100084, China
2Tsinghua University, Center for Biomedical Imaging Research, Beijing 100084, China
*luo_jianwen@tsinghua.edu.cn

Abstract: The purpose of this study is to propose a strategy for organ reconstruction in fluorescence molecular tomography (FMT) without prior information from other imaging modalities, and to overcome the high cost and ionizing radiation caused by the traditional structural prior strategy. The proposed strategy is designed as an iterative architecture to solve the inverse problem of FMT. In each iteration, a short time Fourier transform (STFT) based algorithm is used to extract the self-prior information in the space-frequency energy spectrum with the assumption that the regions with higher fluorescence concentration have larger energy intensity, then the cost function of the inverse problem is modified by the self-prior information, and lastly an iterative Laplacian regularization algorithm is conducted to solve the updated inverse problem and obtains the reconstruction results. Simulations and in vivo experiments on liver reconstruction are carried out to test the performance of the self-prior strategy on organ reconstruction. The organ reconstruction results obtained by the proposed self-prior strategy are closer to the ground truth than those obtained by the iterative Tikhonov regularization (ITKR) method (traditional non-prior strategy). Significant improvements are shown in the evaluation indexes of relative locational error (RLE), relative error (RE) and contrast-to-noise ratio (CNR). The self-prior strategy improves the organ reconstruction results compared with the non-prior strategy and also overcomes the shortcomings of the traditional structural prior strategy. Various applications such as metabolic imaging and pharmacokinetic study can be aided by this strategy.

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OCIS codes: (260.2510) Fluorescence; (170.6960) Tomography; (170.3010) Image reconstruction techniques.

References and links

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1. Introduction

Fluorescence molecular tomography (FMT) visualizes the physiological and pathological process in biological tissues at cellular and molecular levels, through noninvasively monitoring the three-dimensional (3-D) distribution of fluorescent probes in the tissues in vivo. Fluorescent probes are emitted by an excitation source and the fluorescence signals are detected in multiple angles. Spatial and quantitative distribution of fluorescent probes in the tissues can be obtained by tomographic reconstruction.

Tumor detection and organic functional imaging are two typical applications of FMT [1–5]. In the studies of tumor detection, early-stage tumors are generally selected as the studied targets and labeled with specific fluorescent probes. In this situation the imaged targets are usually much smaller than the background in the image domain. The reconstruction task can be treated as a sparse problem. A series of L1-based reconstruction algorithms such as greedy reconstruction, restarted nonlinear conjugate gradient based L1 regularization, adaptive support driven reweighted L1-minimization and discrete cosine transform-based regularization are proposed to solve this problem [6–10].

In the situations of organ functional imaging, the assumption of sparsity of the imaging targets becomes invalid, due to the large-scale accumulation of fluorescent probes in the organ. The non-sparse and complex distribution of fluorescent probes also introduce the mixture of fluorescent signals from the observed organ with signals from non-targeted regions and/or noises. The reconstruction quality suffers from the above issues, and therefore the accuracy and visibility of the observed organ are decreased. Generally, structural priors obtained from other imaging modalities are applied to constrain the reconstruction of the investigated organs. Structural prior information from magnetic resonance imaging (MRI) or X-ray computed tomography (XCT) has been used to constrain the reconstruction of organ or tumor [11, 12] and to assist the localization of the metabolic region in small animals [4].
Various multi-modality imaging systems such as computed tomography (CT)/FMT system, MRI/FMT system and positron emission computed tomography (PET)/FMT system, can provide different kinds of prior information for FMT reconstruction [13–15]. Although the structural prior strategy is currently the mainstream solution and can provide the fluorescence reconstruction results with significantly higher quality than other reconstruction methods, the introduction of other imaging modalities increases the complexity and cost of the imaging system. More noise interference and ionizing radiation also decrease the stability and safety of FMT.

In this study, a self-prior reconstruction strategy is proposed to realize the reconstruction of organ in FMT. Unlike the structural prior methods, this strategy only uses the data collected by FMT. The proposed strategy is designed as an iterative architecture and in each iteration, the self-prior information is extracted from the reconstruction results obtained at the previous iteration. The reconstructed distribution of fluorescent probes in the observed organ is improved significantly by updating the self-prior information and cost function of the inverse problem. Therefore, the self-prior strategy can be applied to the reconstruction of organ in the functional imaging, and also metabolic analysis such as dynamic fluorescence molecular tomography (DFMT).

The paper is organized as follows. Section 2 describes the details of the proposed strategy. Sections 3 and 4 describe the setups of simulations and in vivo experiments. Section 5 shows the reconstruction results and quantitative analysis. The discussion and conclusion are presented in Section 6.

2. Methods

2.1 Forward model

In FMT, within the near-infrared spectral window, the photon migration through highly scattering media can be modeled using the coupled diffusion equations (DE), which are known as the low-order approximation of the radiative transfer equation (RTE), as follows [16]

\[
\begin{align*}
-\nabla \left[ D_e (r) \nabla \Phi_e (r) \right] + \mu_e (r) \Phi_e (r) &= S(r) \\
-\nabla \left[ D_m (r) \nabla \Phi_m (r) \right] + \mu_m (r) \Phi_m (r) &= \Phi_e (r) \eta \mu_e (r)
\end{align*}
\]

Here the subscripts \(e\) and \(m\) denote the excitation and emission, respectively. \(D\) is the diffusion coefficient given by \(D = 1/(3(\mu_a + \mu_s'))\), where \(\mu_a\) is the absorption coefficient and \(\mu_s'\) is the reduced scattering coefficient. \(\Phi\) is the optical flux density and \(S(r)\) is the excitation source term. \(\eta\) and \(\mu_{e}(r)\) are the quantum yield and absorption coefficient of the fluorescent probe. The product of the two variables is the fluorescence yield \(x(r)\) which reflects the distribution of fluorescent probes in the media.

If the optical properties are known, the fluorescence measurement \(\Phi(r_s, r_d)\) can be obtained according to the first-order Born-type approximation [17].

\[
\Phi(r_s, r_d) = \Theta \int_V G_m (r_s, r) x(r) G_e (r_d, r) d^3 r
\]

where \(V\) is the image domain, \(G_e (r, r_d)\) and \(G_m (r_s, r)\) denote the functions describing the photon propagation from the source position to an arbitrary position and from the arbitrary position to the detector position, respectively. \(\Theta\) is a calibration parameter depending on the system characteristics.
The finite element method is used to solve $G_e(r, r_f)$ and $G_m(r, r_f)$ [18]. After discretization the forward model can be formulated as a linear matrix equation:

$$\Phi_m = WX$$

where $W_{(M \times N)}$ is a weight matrix and each element represents the contribution of each voxel in the discrete volume of interest to the fluorescence measurement $\Phi_{m(M \times N)}$. Vector $x_{(N \times 1)}$ is the fluorescence yield to be reconstructed, which represents the fluorescence distribution. $M$ and $N$ stand for the numbers of discrete voxels in the detector domain and image domain, respectively.

### 2.2 Tikhonov regularization

The goal of the inverse problem of FMT is to obtain the fluorescence yield $x_{(N \times 1)}$ by solving Eq. (3). To overcome the ill-posed nature of the inverse problem, Eq. (3) can be modified by employing the Tikhonov regularization method, which is a reconstruction strategy without any prior information. The problem is transferred into an optimization problem presented as [19, 20]

$$x = \arg\min_{x} \{ || \Phi_m - WX ||^2 + \lambda || x ||^2 \}$$

where $\lambda$ is the regularization parameter ($\lambda > 0$). The iterative Tikhonov regularization (ITKR) algorithm can be adopted to solve Eq. (4). The solution $x_{k_{-itr}}$ and residual item $r_{k_{-itr}}$ are updated as [20]

$$\begin{align*}
    x_{k_{-itr}} &= x_{k_{-itr-1}} + (W^H W + \lambda I)^{-1} W^H r_{k_{-itr-1}}, \quad k_{-itr} = 1, 2, \ldots \\
    r_{k_{-itr}} &= \Phi_m - WX_{k_{-itr}}
\end{align*}$$

where $k_{-itr}$ denotes the index of iteration and $W^H_{(N \times M)}$ is the conjugate transpose matrix of $W_{(M \times N)}$.

### 2.3 Self-prior strategy and Laplacian regularization

The self-prior strategy aims at extracting the locational information of fluorescence yield from the initial reconstruction results as a self-prior information, and then modifying the inverse problem of the FMT. The strategy is designed as an iterative architecture and each iteration includes three steps: extraction of the self-prior information, modification of the cost function of the inverse problem and reconstruction of the distribution of fluorescence yield. The fluorescence distribution $x_{0(N \times 1)}$ reconstructed by the ITKR algorithm is used as the initial input of the iterative architecture. Figure 1 shows the flowchart of the iterative architecture of the self-prior strategy.

#### 2.3.1 Extraction

The self-prior spatial information is extracted from the reconstructed fluorescence distribution $x_{0(N \times 1)}$ ($t$ stands for the index of iteration in the self-prior strategy; for the first iteration, the fluorescence distribution is $x_0$). In general, the spatial distribution of fluorescence tends to have large variations, leading to the difficulties in extracting the self-prior information directly from the spatial domain with threshold based methods. Because the self-prior information is more pronounced and easier to clarify in the spatial-frequency domain than in...
the spatial domain due to the energy accumulation phenomenon, the self-prior information will be extracted in the spatial-frequency domain in this study, in order to obtain the positions of self-prior information in both the spatial and frequency domains. In detail, a short time Fourier transform (STFT) is performed on the one-dimensional (1-D) spatial sequence $x_t$ to obtain the space-frequency spectrum,

$$S_{\omega}(n, \omega_k) = \sum_{m=0}^{N-1} x_m(n) g(mT) e^{-j \frac{2\pi}{H} m k}, \quad k = 0,\ldots, H-1$$

where $\omega_k$ is the circular frequency, $g$ is a time-shifted window function and $H$ stands for the width of the window function. $H$ can influence both the spatial and frequency resolutions. In order to extract relatively accurate information from the frequency domain, the value of $H$ is set to be $N/1000$ after multiple tests with different widths of window function, where $N$ denotes the length of the 1-D spatial sequence $x_t$. The space-frequency energy spectrum $F_{\omega}(n, \omega_k)$ of $x_t$ can be presented as

$$F_{\omega}(n, \omega_k) = \sum_{m=0}^{N-1} x_m(n) g(mT) e^{-j \frac{2\pi}{H} m k}^2, \quad k = 0,\ldots, H-1$$

By assuming that the regions with fluorescence distribution contain higher energy than the background regions, the self-prior information can be extracted in the space-frequency energy domain by selecting the spectral components with relatively high energy. An energy threshold $T_F$ is selected and the components higher than this threshold are chosen to be the self-prior information of fluorescence distribution, and the regions corresponding to these components are defined as the self-prior regions. The discrete voxels within the self-prior regions are located in the space-frequency energy spectrum, corresponding to the 1-D spatial sequence.
self-prior vector $K_{t(Nx1)}$ corresponding to the current reconstructed $x_t$ is then formed as follows:

$$K_{t,i} = \begin{cases} 1, & \text{if } \exists F_t(i, \omega_k) > T_k, k = 0,1,...,M - 1 \\ 0, & \text{else} \end{cases}, \quad i = 0,1,...,N - 1$$  \hspace{1cm} (8)

The self-prior vector $K_{t(Nx1)}$ is a binary vector, where entries of 1 stand for the voxels within the self-prior region and entries of 0 stand for the voxels outside the region. Therefore, this vector contains the extracted spatial self-prior information.

2.3.2 Modification

The cost function of the inverse problem is modified using the self-prior information obtained from the previous iteration. In detail, a Laplacian-type constraint matrix $L_{t(NxN)}$ is generated based on the 1-D self-prior vector $K_{t(Nx1)}$:

$$L_{t,ij} = \begin{cases} 1, & \text{if } i = j \\ -\frac{1}{N_n}, & \text{if } K_{t,i} = K_{t,j} = 1, \quad i, j = 0,1,...,N - 1 \\ 0, & \text{else} \end{cases} \quad (9)$$

where $N_n$ denotes the number of elements that satisfy $K_{t,i} = K_{t,j} = 1$, namely the number of voxels within the self-prior region [11].

The cost function of the inverse problem is updated by replacing the identity matrix with $L_{t(NxN)}$ in the penalty item and the new reconstructed fluorescence distribution $x_{t+1}$ can be updated by solving:

$$x_{t+1} = \arg \min_x \left\{ \| \Phi_m - Wx \|^2 + \lambda \| L_{t,x} \|^2 \right\}$$  \hspace{1cm} (10)

The Laplacian-type matrix relaxes the smoothness constraint at the tissue boundary and enhances the smoothness inside the tissues, which is appropriate for the non-sparse reconstruction in FMT. Since the cost function is updated in each iteration, the optimal regularization parameter $\lambda$ will change among different iterations. A U-curve method based automatic selection algorithm is used in this strategy [21] to update the regularization parameter $\lambda$ along with the modification of the cost function. Obviously, the initial regularization parameter in the self-prior strategy is the same as that in the ITKR method.

2.3.3 Reconstruction

After the modification of the inverse problem, the updated cost function can be optimized by the iterative algorithm as follows:

$$\begin{align*} x_{t+1, k, self} &= x_{t+1, k, self}^{-1} + \left( W^H W + \lambda L_{t}^H L_{t} \right)^{-1} W^H r_{k, self}^{-1} \\
W r_{k, self} &= \Phi_m - W x_{t+1, k, self} \\
k_{self} &= 1,2,... 
\end{align*}$$  \hspace{1cm} (11)
where $k_{self}$ denotes the index of iteration in the optimization process. The reconstructed fluorescence distribution $x_{k_{self}}$ is updated by the solution of Eq. (11) after $k_{self}$ iterations and will be imported into the next iteration until the iterative process is terminated.

3. Simulations

Numerical simulations are performed to evaluate the performance of the proposed strategy. Digimouse, a 3-D mouse atlas, is used to construct a 3-D biological simulation model [22]. Figure 2(a) shows the anatomic structure of the atlas, and four kinds of organs including the heart, lungs, liver and kidneys are contained in this model. As shown in Table 1, different optical properties are assigned to these organs to constitute a heterogeneous model.

Indocyanine green (ICG) is chosen as the fluorescent probe. The metabolism of ICG in realistic environment is a dynamic process and different organs have different metabolic characteristics. Figure 2(b) shows the ICG concentration curves which simulate the metabolic process of ICG in different organs. In the simulations, the distribution of ICG concentration is uniform in a single organ at a specific time point. The ICG is injected at the time of 0 minute. The liver is selected to be the investigated organ and the distribution of ICG at the time of 9th minute is chosen to generate the fluorescent signal used for reconstruction because it reaches the peak value at this time point, according to Fig. 2(b). The detailed ICG concentrations of each organ at this time point are also listed in Table 2.

Table 1. Optical Properties of Different Regions

| Regions  | Absorption Coefficient (cm$^{-1}$) | Reduced Scattering Coefficient (cm$^{-1}$) |
|----------|-----------------------------------|-------------------------------------------|
| Heart    | 0.350                             | 23                                        |
| Liver    | 0.500                             | 13                                        |
| Lungs    | 0.250                             | 30                                        |
| Kidneys  | 0.175                             | 20                                        |
| Background | 0.300                           | 10                                        |

Fig. 2. Setup of simulations. (a) 3-D geometry of the Digimouse model used in the simulations with a length of 3.2 cm from the neck to the base of the abdomen. The anatomical information of different organs is depicted with different colors. (b) ICG concentration (with arbitrary unit, a.u.) curves simulating the metabolic process of ICG in different organs. The red circle indicates the data chosen to generate the fluorescent signal used for reconstruction.

The mouse torso from the neck to the base of the abdomen is chosen as the image domain, with a length of 3.2 cm. 24 fluorescence projections are generated equidistantly in a full view of 360° with an angular increment of 15°. The rotation axis of the mouse is defined as the z
axis with the bottom plane set as $z = 0.0$ cm. In the reconstruction, the image domain is discretized into $70 \times 42 \times 32$ mesh voxels using COMSOL Multiphysics 3.5 (COMSOL Inc., Stockholm, Sweden) is used for the discretization process. Since the structural information is not obtainable for the reconstruction process, the discretization of the image domain is homogeneous and not constrained by any prior information such as tissue boundary.

Three sets of simulations are conducted to test the influence of three different factors, i.e., the energy threshold, number of iterations and noise level, on the proposed strategy. The studies on the influence of the energy threshold and number of iterations, which are two important parameters in the self-prior reconstruction process, provide a set of reference values for the studies on the influence of different noise levels.

| Regions   | ICG Concentration (a.u.) |
|-----------|--------------------------|
| Heart     | 1.2949                   |
| Liver     | 0.9013                   |
| Lungs     | 0.5856                   |
| Kidneys   | 0.9678                   |
| Background| 0.4050                   |

4. **In vivo experiments**

In vivo animal experiments are conducted to further test the performance of the proposed strategy, under realistic physiological environment. In the in vivo experiments, the liver is selected as the objective organ to be reconstructed, which is consistent with the simulations. The data acquisition is based on a hybrid FMT/XCT system previously developed by our laboratory [13]. A Xenon lamp (300 W, MAX-302, Asahi Spectra, Torrance, CA, USA) is employed as the excitation source. A fiber is attached to the lamp to generate a line-shaped excitation source with a length of 4 cm. A $780 \pm 6$ nm band-pass filter (XBPA780, Asahi Spectra, Torrance, CA, USA) is used to select the excitation light from the fiber. The emitted fluorescence is filtered by an $840 \pm 6$ nm band-pass filter (FF01-840/12-25, Semrock, Rochester, NY, USA) and detected by a $512 \times 512$ pixel, $-70^\circ C$ cooled charge coupled device (CCD) (iXon DU-897, Andor Technologies, Belfast, Northern Ireland, UK). The XCT module is used for acquiring the XCT images to make a comparison with the FMT reconstruction results.

All animal studies are conducted under the protocol approved by the Ethical Committee of Tsinghua University. A female nude mouse (BALB/c, 8 weeks old) is used in the experiments. A bolus of ICG (0.1 mL, 50 μg/mL) is injected via the tail vain. With similar setups to the simulations, the mouse is fixed on the rotation stage, and the fluorescence image frames are collected by the CCD with an angular increment of $15^\circ$. The fluorescence data collection lasts for 20 minutes and every 24 frames are arranged as a single data set, corresponding to a full view of $360^\circ$. Similar to the simulation, the data set at the time point when the corresponding fluorescent signal of the liver reaches the highest intensity, is extracted for reconstruction. After the fluorescence data acquisition, the XCT signals are collected by a complementary metal oxide semiconductor flat-panel detector (C7921-02, Hamamatsu, Japan).

A set of $62 \times 62 \times 26$ mesh voxels are generated to discretize the image domain, without any constraint of structural prior information. All the parameters of the self-prior reconstruction strategy are set to be the same as those in the simulations. Figure 3 shows the white light image of the nude mouse fixed on the rotation stage and its meshed volume of the image domain.

5. **Results**

In this section, the reconstruction results of the simulations and in vivo experiments are presented. In order to compare different reconstruction methods and evaluate the performance
of the proposed strategy, the results of the non-prior strategy (i.e., the ITKR method) and structural prior strategy are also presented.

5.1 Evaluation indices

![Image](attachment:fig3.png)

Fig. 3. Setup of in vivo experiments. (a) The white light image of the nude mouse fixed on the rotation stage. The red line indicates the top and bottom of the image domain. (b) The meshed volume of the image domain.

The RLE demonstrates the reconstruction accuracy of spatial structure (or locational accuracy). The normalized reconstruction result \( x_{\text{recon}} \) is binarized to obtain the locational reconstruction result \( x_{\text{loc-recon}} \), as follows,

\[
x_{\text{loc-recon},i} = \begin{cases} 1, & \text{if } x_{\text{recon},i} > 0 \\ 0, & \text{if } x_{\text{recon},i} < 0 \\ \end{cases}
\]  

(12)

where the subscript \( i \) stands for the \( i \)th element of \( x_{\text{loc-recon}} \). The true locational result \( x_{\text{loc-true}} \) of the objective region \( R_{\text{obj}} \) can be described as

\[
x_{\text{loc-true},i} = \begin{cases} 1, & \text{if node } i \in R_{\text{obj}} \\ 0, & \text{if node } i \notin R_{\text{obj}} \\ \end{cases}
\]  

(13)

Then the RLE can be defined as follows,

\[
RLE = \left\| x_{\text{loc-recon}} - x_{\text{loc-true}} \right\|^2 
\]  

(14)

The RE evaluates the reconstruction accuracy of the fluorescence yields. It is defined as the relative difference between the normalized reconstruction result \( x_{\text{recon}} \) and the true distribution of the fluorescence yields \( x_{\text{true}} \), as follows,

\[
RE = \frac{\left\| x_{\text{recon}} - x_{\text{true}} \right\|^2}{\left\| x_{\text{true}} \right\|^2}
\]  

(15)

The CNR describes how much the reconstructed fluorescence distribution is recovered in the objective region or lost in the background, and it is defined as

\[
CNR = \frac{\mu_{\text{VOL}} - \mu_{\text{BG}}}{\left( \omega_{\text{VOL}} \sigma_{\text{VOL}}^2 + \omega_{\text{BG}} \sigma_{\text{BG}}^2 \right)^{1/2}}
\]  

(16)
where $\mu_{\text{VOI}}$ is the mean value of the reconstructed fluorescence yields within the volume of interest (VOI) where the fluorescent probes are located; $\mu_{\text{BG}}$ is the mean value of the reconstructed fluorescence yields over the background (BG). $\omega_{\text{VOI}} = S_{\text{VOI}} / (S_{\text{VOI}} + S_{\text{BG}})$ and $\omega_{\text{BG}} = S_{\text{BG}} / (S_{\text{VOI}} + S_{\text{BG}})$ are the weights of the VOI and BG, where $S_{\text{VOI}}$ and $S_{\text{BG}}$ are the volumes of the VOI and BG, respectively. $\sigma^2_{\text{VOI}}$ and $\sigma^2_{\text{BG}}$ are the variances of the reconstructed fluorescence yields in the VOI and BG, respectively. In this work, the region which contains the main distribution of the fluorescent yields is selected as the volume of interest, and then the rest of the image domain is set as the background.

### 5.2 Results of simulations

#### 5.2.1 Influence of energy threshold

The energy thresholds are set to be 25%, 45%, 65% and 85% of the maximum value in the space-frequency energy spectrum of the reconstruction results in each iteration, respectively. To eliminate the influence of other factors, the number of iterations is set to be 5 and zero-mean Gaussian noise with the signal-to-noise ratio (SNR) of 26 dB is added to the fluorescence data.

Figure 4 shows the reconstruction results at different energy thresholds in the simulations. The energy threshold significantly influences the reconstruction results. A higher energy threshold (i.e., 65% and 85%) will generate a relatively smaller self-prior region and may lead to the insufficient reconstruction results. On the contrary, a lower threshold (i.e., 25%) results in more non-target or background information in the self-prior region and the reconstruction results are more likely to contain the true distribution of fluorescent probes in the liver. Table 3 shows the results of REs. The energy threshold of 45% obtains the best reconstruction accuracy with the minimum RE, which is in agreement of the qualitative results in Fig. 4.

| Energy Threshold | RE   |
|------------------|------|
| 25%              | 0.164|
| 45%              | 0.093|
| 65%              | 0.158|
| 85%              | 0.369|

#### 5.2.2 Influence of number of iterations

The number of iterations is set to vary from 1 to 10 for a single reconstruction task, with an SNR of 26 dB and an energy threshold of 45% of the maximum energy in each iteration.

Figure 5 presents the variations of REs and CNRs along with the number of iterations. The REs decrease dramatically after the second iteration and then reach a plateau afterwards. The CNRs show an opposite tendency of variation. This phenomenon demonstrates that the second iteration shrinks the reconstruction region and the following iterations search for the final results gradually in this region. Because no self-prior information can be used in the first iteration (i.e. the ITKR method), insufficient performance is obtained, with high RE and low CNR. After the self-prior information is extracted iteratively, the reconstruction results turn to be much closer to the ground truth.

#### 5.2.3 Influence of noise level

Three sets of simulations with additive zero-mean Gaussian noise are conducted, with an SNR of 26 dB, 20 dB and 14 dB, respectively. According to the reference values provided by the previous studies in 1) and 2), in the self-prior reconstruction strategy, the number of iterations is configured to be 5. In each iteration, the energy threshold in the extraction step is set to be 45% of the maximum value in the space-frequency energy spectrum, and 100 iterations are executed in the optimization process.
Figure 6 shows the reconstruction results at different noise levels in the simulations. Figure 6(a) shows the true distribution of ICG in the liver in the 3-D and transverse views. It can be seen that the distribution of ICG is uniform in the liver. Figure 6(b) shows the space-frequency energy spectrum of the reconstruction result of the non-prior strategy with an SNR of 26 dB. Figures 6(c)-6(k) display the reconstruction results by the non-prior, self-prior and structural prior strategies at different noise levels, respectively. The reconstruction quality of the self-prior strategy is observed to be better than that of the non-prior strategy at all noise levels and is closer to that of the structural prior strategy on the aspects of the size, shape and location of the reconstructed region, by comparing the reconstruction results with the liver in Fig. 6(a). As the noise level increases, the self-prior strategy also shows greater noise resistance than the non-prior strategy.

![Figure 4](image)

**Fig. 4.** Influence of energy threshold on simulation results. (a) (left) 3-D and (right) transverse views of the true distribution of ICG in the liver. The red solid curve indicates the slice of the tomographic images selected. (b)-(e) The transverse view of the reconstruction results with the energy threshold being set as 25%, 45%, 65% and 85% of the maximum value in each space-frequency energy spectrum, respectively.

![Figure 5](image)

**Fig. 5.** REs and CNRs varied with the number of iterations.
Quantitative evaluation of different reconstruction strategies is shown in Table 4. Compared with the non-prior strategy at SNR levels of 26 dB, 20 dB and 14 dB, the self-prior strategy reduces the RLEs by 70.9%, 70.0% and 78.4%, reduces the REs by 67.6%, 72.8% and 67.8%, and increases the CNRs by 322.0%, 416.1% and 479.1%, respectively. This means that the proposed strategy obtains higher reconstruction accuracy and improves the detectability of the fluorescent probes. The RLEs and REs of the self-prior strategy maintain lower value than the non-prior strategy when the SNR decreases from 26 dB to 14 dB, which indicates that the self-prior strategy obtains higher reconstruction accuracy without sacrificing the stability when the noise level increases. Additionally, the locational accuracies (calculated by the RLEs) of the self-prior strategy reach 92.6%, 89.4% and 88.0% of those of the structural prior strategy with SNRs of 26 dB, 20 dB and 14 dB, respectively. In contrast, the RLEs of the non-prior strategy are 74.3%, 63.7% and 42.0% of those of the structural prior strategy, respectively. Similar results are found for the REs and CNRs. These results indicate that the performance of the self-prior strategy is much better than that of the non-prior strategy and it approaches the performance of the structural prior strategy in the simulations.

5.3 Results of in vivo experiments

Figure 7 presents the tomographic reconstruction results of different methods in the in vivo experiments. Figure 7(g) shows the XCT image in the coronal view and Figs. 7(a)-7(f) shows the tomographic images of different methods in the transverse view at the position indicated by the red dotted line shown in Fig. 7(g). The FMT result of the self-prior strategy has higher quality and more uniform distribution of fluorescence yield than the non-prior strategy, as can be seen in Figs. 7(a) and 7(d). The FMT images are merged with XCT images to present the locational performance of each method. Figs. (c) and (f) show the merged images of FMT/XCT reconstructed by the non-prior strategy and the self-prior strategy, respectively. The regions of the liver are covered by the reconstructed fluorescent signals in both images, which means that the accumulation of ICG in the liver is detected and located by both
methods. However, the self-prior strategy shows higher locational quality of the liver in the merged images according to the coverage of the FMT results and XCT results.

| Evaluation Index | Method          | SNR 26dB | SNR 20dB | SNR 14dB |
|------------------|-----------------|----------|----------|----------|
|                  | Non-prior       | 0.258    | 0.366    | 0.583    |
|                  | Self-prior      | 0.075    | 0.110    | 0.126    |
|                  | Structural prior| 0.001    | 0.005    | 0.007    |
|                  | Non-prior       | 0.287    | 0.459    | 0.677    |
|                  | Self-prior      | 0.093    | 0.125    | 0.218    |
|                  | Structural prior| 0.002    | 0.008    | 0.010    |
|                  | Non-prior       | 8.36     | 5.42     | 3.25     |
|                  | Self-prior      | 35.28    | 27.97    | 18.82    |
|                  | Structural prior| 42.31    | 35.28    | 25.62    |

Figure 7. Reconstruction results of in vivo experiments. (a) and (d) Reconstructed FMT images in the transverse view by the non-prior strategy and self-prior strategy, respectively. (b) and (e) XCT images in the transverse view. (c) and (f) Merged images of FMT/XCT in the transverse view. (g) XCT image in the coronal view. The red dotted line in (g) indicates the location of the tomographic images in (a)-(f).

Figure 8 shows the reconstruction results of the in vivo experiments in the 3-D view. Figures 8(a) and 8(c) shows the FMT results in the 3-D view. Then they are merged with XCT results in the 3-D view to exhibit the relative relation between reconstructed fluorescent signals and anatomic structures, as shown in Figs. 8(b) and 8(d). Figs. 8(e) and 8(f) are the XCT image as the reference for location in the transverse and 3-D views, respectively. The self-prior strategy obtains higher accuracy in locating the liver and higher smoothness of the fluorescence yield within the liver than the non-prior strategy, as shown in Fig. 8. Quantitative evaluation indexes of the RLE and CNR are demonstrated in Table 5. The REs are not calculated because the true distribution of fluorescence yield in the mouse cannot be obtained. The XCT results are set to be the ground truth in the calculation of the RLEs. Compared with the non-prior strategy, the self-prior strategy reduces the RLE by 81.1% and increases the CNR by 952.6%.
Fig. 8. Reconstruction results of in vivo experiments in the 3-D view. (a) and (c) Reconstructed FMT images in the 3-D view by the non-prior strategy and self-prior strategy, respectively. (b) and (d) Merged images of FMT and XCT image in the 3-D view. (e) and (f) XCT reconstructed image of the liver and merged image of the liver and skeleton in the 3-D view, respectively.

Table 5. Reconstruction Results by Different Methods in the in vivo experiments

| Method    | RLE   | CNR   |
|-----------|-------|-------|
| Non-prior | 0.657 | 3.21  |
| Self-prior| 0.124 | 33.79 |

6. Discussion and conclusion

Organ reconstruction is an intractable task when applying FMT to organ functional imaging and metabolic research. The large-scale accumulation of fluorescent probes in the organ makes the problem non-sparse and complex. Structural prior strategies based reconstruction methods have been developed, but the introduction of the anatomical imaging modalities increase the cost and system complexity. Since the structural prior strategies considerably rely on the information provided by the introduced anatomical imaging modalities, its performance would directly influence the accuracy and stability of the reconstruction results. Additionally, the ionizing radiation from the anatomical imaging modalities may decrease the safety of FMT.

In this study, a self-prior reconstruction strategy is proposed to realize the organ reconstruction in FMT. The strategy is designed as an iterative architecture and the self-prior information is extracted to constrain the inverse problem solving. In the simulations conducted on the Digimouse model, the distribution of fluorescent probes in the liver is reconstructed by the proposed strategy. The effects of three influence factors (i.e., the energy threshold, number of iterations and noise levels) on the performance of the proposed strategy
are investigated. The energy threshold mainly influences the locational accuracy of the reconstruction, because a small or large threshold leads to insufficient or excessive self-prior region. The number of iterations influences both the locational accuracy and CNR of the reconstruction results. The lack of the self-prior information causes significant deviations in the first iteration and the reconstruction results approach the ground truth gradually as the number of iterations increases.

To investigate the influence of the noise level, comparison is conducted among the non-prior strategy, self-prior strategy and structural prior strategy. The results show that the self-prior strategy reduces the REs by 70.0-78.4%, reduces the RLEs by 67.6%-72.8% and increases the CNRs by 322.0-479.1% compared with the non-prior strategy. Additionally, the self-prior strategy can reach 88.0-92.6% of the locational accuracy evaluated by the RLE, 79.0-90.9% of the reconstruction accuracy of fluorescence yield evaluated by the RE and 73.5-85.9% of the CNR of the structural prior strategy. However, the corresponding values are 42.0-74.3% (RLE), 32.6-71.4% (RE) and 12.7%-19.8% (CNR) for the non-prior strategy. In vivo experiments are also conducted to further test the performance of the methods. Similar results are found that the self-prior strategy achieves higher performance than the traditional non-prior strategy in the liver reconstruction of a nude mouse. By using the self-prior strategy, the RLE is reduced by 81.1% while the CNR is increased by 952.6%, compared with the non-prior strategy. The proposed strategy is demonstrated to significantly improve the reconstruction performance without the need of the prior information provided by other imaging modalities. By using the proposed strategy, the size, shape and location of the reconstructed organ is observed to approach the ground truth. However, the reconstruction results also show some disparities between the proposed strategy and the structural prior strategy, especially at high level of noise.

The extracted self-prior regions are affected significantly by the energy threshold. Selection of this parameter is a non-trivial task. In this study, the energy threshold is determined empirically. In addition, a single threshold used for the whole domain may also affect the accuracy of the reconstruction results. In the situation of multiple reconstruction targets, it will be difficult to classify all the targets using a single threshold. In the future, an adaptive method will be studied to select the energy threshold automatically.

In the reconstruction step of the self-prior iterative architecture, only the regularized item (i.e., $\lambda \|x\|_1$) is updated by reassembling the Laplacian matrix according to the self-prior information, while the forward model remains the same in each iteration. In fact, the biological tissue is assumed to be homogeneous in the construction of the forward model, leading to an inaccurate cost function of the inverse problem. In order to solve this issue, a heterogeneous forward model can be constructed by modifying the optical properties of the updated self-prior regions in the iterative process.

From the methodological aspect, more reliable algorithms will be developed for accurate and stable self-prior information extraction. For biomedical applications, the proposed strategy can be combined with DFMT and multispectral FMT [5, 23, 24] to achieve dynamic and real-time metabolic imaging of organs in vivo. In the present study, only liver has been selected as the objective organ to be reconstructed, which has limited utility in terms of biological applications. To generalize this method into more scenarios of organ imaging, tests on different organs should be conducted in the future. The technique of FMT can also be used in pharmacokinetic study and drug development, without the need of other imaging modalities.

**Funding**

This work is supported by the National Natural Science Foundation of China under Grant Nos. 81227901, 81271617, 61322101, and 61361160418 and the National Major Scientific Instrument and Equipment Development Project under Grant No. 2011YQ030114.
Acknowledgments

The authors would like to thank Dr. Fei Liu in their lab for her help on experiments. The authors declare that there are no conflicts of interest related to this article.

Disclosures

The authors declare that there are no conflicts of interest related to this article.