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A fast imaging method of scanning ion conductance microscopy

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ABSTRACT

Scanning ion conductance microscopy (SICM) has attracted considerable attention in the biological field as a noninvasive, high-resolution and non-force contact imaging technology. However, the development of improvement to the SICM imaging rate remains a great challenge for applications of rapid or dynamic imaging. In this paper, a fast SICM imaging method is proposed to improve the imaging efficiency via the design of a compressive sampling strategy and a reduction in the reconstruction time of sparse signals using the 2D normalized iterative hard thresholding (2D-NIHT) algorithm. The imaging performance of the method is validated by the simulation of recovery of a random synthetic image, and the superiority of the 2D-NIHT algorithm is also demonstrated by comparison of its reconstruction performance with that of other typical algorithms. The actual imaging performance of the method in SICM is also validated by the imaging of two biological samples, a virus and a living cell, and the results show that the method can duplicate the sample surface topography with high-definition and shorter imaging time. Our study offers a general imaging method for the applications of scanning probe microscopies to realize faster and higher-resolution imaging of biological samples.

1. Introduction

Scanning ion conductance microscopy (SICM) is a scanning probe microscopy technique that uses an electrode inserted in a micropipette as the probe tip to detect the surface topography of micro-/nano-samples in aqueous media conduction electrolytes in a non-contact manner. The SICM technique was invented by Hansma and colleagues in 1989 (Hansma et al., 1989) and was improved by Korchev and colleagues for application to high-resolution imaging of living biological cells (Korchev et al., 1997a, b). The SICM technique has been rapidly developing and is currently applied in many fields, including biological (Shevchuk et al., 2011), chemical (Ji et al., 2011) and material (Laslau et al., 2012) science, due to its unique advantages over other scanning probe microscopies (e.g., atomic force microcopy), such as high-resolution imaging, simple probe preparation and absence of damage to the sample surface (Liu et al., 2013). However, acquisition of a high-resolution image by SICM requires a few minutes to dozens of minutes, which restricts its applications in rapid or dynamic imaging, for example, monitoring the dynamic changes of living cells.

Progress in improving the imaging speed of SICM has been emerged in recent reports. For example, L. Liu and colleagues proposed amplitude modulation mode of SICM by employing an AC voltage to enhance the stability and improve the scanning speed (Li et al., 2015c). P. R. Unwin and colleagues presented a method that generates a feedback signal to control the distance between the end of a nanopipette and a surface by applying an oscillating bias between a quasi-reference counter electrode (QRCE) in the SICM nanopipette probe and a second QRCE in the bulk solution, and the method opens up the prospect of faster SICM imaging (McKelvey et al., 2014). L. Liu and colleagues reported a phase modulation model that modulates the current through the resistance path via the tip-sample distance to reduce the electronic and DC drift but maintains high scanning speed (Li et al., 2014b), and also proposed an in-phase bias modulation mode with a capacitance compensation method to increase the signal-to-noise ratio of SICM and improve the scanning speed (Li et al., 2015b). In a word, these methods can efficiently enhance the stability and imaging speed of SICM, but a portion of the hardware of SICM must also be improved. In addition, another type of strategy was also proposed to enhance the scanning speed. G. Li and colleagues reported a method of compressive sampling that can acquire a high-resolution image with smaller samples than that of the Shannon sampling rate based on compressive sensing theory (Li et al., 2014a). A similar method was also applied to atomic force microcopy imaging and tremendously improved the observation rate (Andersson and Pao, 2012; Li et al., 2015a). The strategy enhances the imaging speed of SICM by designing the movement trajectory of the probe to acquire the compressive samples within a shorter scanning time. However, another challenge that compressive imaging faces is that the reconstruction time of the compressive samples is much too

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In this paper, we propose a fast SICM imaging method designed to improve the imaging speed of SICM. The method tremendously reduces the time needed to collect samples via the design of a compressive sampling strategy and reduces the reconstruction time of sparse signals by recovering the reconstruction image directly in matrix domain using 2D normalized iterative hard thresholding (2D-NIHT) algorithm. The 2D compressive sampling strategy can be applied as general method in actual applications of 2D compressive sensing. The experiments on recovery of random synthetic images and imaging for two biological samples using SICM validate the performance for improved the SICM imaging efficiency.

2. Method

2.1. 2D compressive sensing model

The compressive sensing theory is formulated as follows. For a k-sparse signal $x \in R^N$, which contains no more than k nonzero elements, a measurement matrix $\Phi \in R^{M\times N}$ $(M < N)$ and an observation vector $y \in R^N$, then the core problem of compressive sensing can be described as reconstruction of the sparse signal x from the measurement matrix Φ and the observation vector y using the following linear equation:

$$y = \Phi x. \tag{1}$$

Eq. (1) is under-determined in that the unique candidate signals $\bar{x}$ cannot be acquired for $\Phi\bar{x} = y$. However, many reports demonstrate that the signal $\bar{x}$ can still be recovered from Φ and y if the signal x is sufficiently sparse ($k \ll N$) and the measurement matrix Φ satisfies the restricted isometry property (RIP) condition (Baraniuk, 2007; Candes, 2008).

2D compressive sensing is extended from the above compressive sensing theory and is formulated as follows. For a 2D K -sparse signal $X \in R^{N_1\times N_2}$, where the sparsity K of the 2D signal X is defined as $Spa(X) = \sum_{i=1}^{N_2} ||x_i||_0 < K$ (x_i denotes the ith column vector of the matrix X), a measurement matrix pair $A \in R^{M_1\times N_1}$ and $B \in R^{M_2\times N_2}$, and an observation matrix $Y \in R^{M_1\times M_1}$, the problem of 2D compressive sensing consists of recovery of the 2D sparse signal X using the following equation:

$$Y = AXB^T, \tag{2}$$

where B^T is the transpose of B, $M_1, M_2 < N_1, N_2$, and $K < M_1 \times M_2$ (Li et al., 2017). In addition, many natural signals are not sparse and they need be expressed in a convenient basis to transform the signals as sparse representations. For example, suppose all the image pixels of the image matrix X have nonzero values, a wavelet transform or a Fourier transform is used to sparsely represent the X by the equation $X = \Psi S$, where Ψ is the transform basis and S is the corresponding transform coefficients. The coefficients offer a concise summary: most coefficients are small and the relatively few large coefficients capture most of the information.

The 1D compressive sensing model can be treated as a special form of the 2D compressive sensing in the case for which $N_2 = M_2 = 1$. Moreover, the 2D compressive sensing model is also equivalent to the 1D compressive sensing model by the following operations:

$$\Phi = B \otimes A,\ y = vct(Y),\ x = vct(X), \tag{3}$$

where '$\otimes$' is the operation of the Kronecker product, and $vct(\bullet)$ denotes the vectorization of a matrix by stacking the columns of the matrix into a single column vector. Thus, we obtain the following:

$$Y = AXB^T \Leftrightarrow y = vct(Y) = (B \otimes A) \times vct(X) = \Phi x. \tag{4}$$

2.2. Compressive sampling strategy of SICM

To apply the 2D compressive sensing theory in SICM imaging, an effective measurement matrix should be first designed to reduce the length of the observation signals. In fact, the measurement matrix must satisfy the RIP condition, and some matrices, such as the Fourier matrix and Gaussian matrix (Candes and Tao, 2006; Rudelson and Vershynin, 2006), have been proven to satisfy the RIP condition. Specifically, for the measurement matrix used in compressive sampling of the SICM, any element of the measurement matrix is either 1 or 0 because for any pixel of the image acquired by SICM, only two states exist: sampled or un-sampled. Therefore, the measurement matrix pair of the 2D compressive sensing used in SICM imaging is designed by the following procedures (Li et al., 2017) :

- Set a matrix $D \in R^{N_2\times N_1}$, where each entry d_{ij} is either 1 ($i = j$) or 0 ($i \neq j$);
- Randomly select M_1 rows of the D to produce the measurement matrix A ;
- Randomly select M_2 columns of the D to produce the measurement matrix B^T.

The measurement matrix pair A and B compress the row and column of the 2D sparse signal X, respectively, and reduce the number of samples from the $N_1 \times N_2$ dimensions to $M_1 \times M_2$ dimensions. To clearly describe the 2D compressive sampling process, a simple example is given, as shown in Fig. 1. The Fig.1 shows that the observation matrix Y can be treated as the set of $M_1 \times M_2$ elements collected from the original 2D sparse signal X at the rows and columns, which are determined by the row position of "1" of A and the column position of "1" of B^T.

With the designed measurement matrix pair, the compressive sampling rate and the location of samples that are collected can be determined. The second problem in compressive imaging of SICM is collection of all samples in the shortest time. In order to achieve this goal, the scanning strategy should be designed to further decrease the imaging time by optimizing the movement path of the probe over the shortest distance. Indeed, the design of the scanning strategy is similar to that of solving a typical traveling salesman problem, in which, given a list of coordinate points, the scanning strategy must ensure that the probe visits each point without repetition and using the shortest possible route. In this study, the ant colony optimization algorithm is used to solve the optimal route and design the scanning strategy.

2.3. 2D-NIHT algorithm

The 2D-NIHT algorithm is used to efficiently reduce the reconstruction time by recovering the images directly in the matrix domain. The purpose of the design of the 2D-NIHT algorithm is to recover the 2D sparse signal X based on a 2D compressive sensing model (Eq. (2)), and the problem can be transformed to solve the following optimization problem:

$$X^* = \arg \min_{Spa(X)\le K} ||Y - AXB^T||_F^2 + \lambda \times Spa(X), \tag{5}$$

where $||\bullet||_F$ denotes the Frobenius norm of a matrix, that is, $||X||_F = \sqrt{\sum_{i=1}^{N_1}\sum_{j=1}^{N_2} x_{ij}^2}$, and λ is the penalty factor. After simplify the Eq. (5), the optimization problem must solve the following iterative procedures:

$$X^{n+1} = H_K[X^n + \mu^n A^T(Y - AX^nB^T)B], \tag{6}$$

where $H_K[X]$ is a nonlinear operation that sets all elements of the matrix X to zero except for the maximum K elements of X in absolute terms.

Let $T^n = supp(X^n) = \{\tau_{ij}^n\}$ denote the support matrix of X^n in which $\tau_{ij}^n = \mathrm{sgn}(abs(x_{ij}^n))$ and x_{ij}^n are the entries of the matrices T^n and X^n at ith row and jth column, respectively, and $\mathrm{sgn}(\bullet)$ is the signum function. $G^n = \{g_{ij}^n\} = A^T(Y - AXB^T)B$ is the negative gradient matrix of $||Y - AXB^T||_F^2$ evaluated at X^n at the nth iteration; G_{T^n} denotes the