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Tutorial 3: Continuous domain sparse recovery of biomedical imaging data using structured low-rank approaches

JONG CHUL YE, KAIST MATHEWS JACOB, UNIV. OF IOWA

CBIG, Univ. Iowa

- 1. Dr. Gregory Ongie
- 2. Dr. Merry Mani
- 3. Mr. Arvind Balachandrasekaran
- 4. Ms. Ipshita Bhattacharya
- 5. Ms. Sampurna Biswas

<u>KAIST</u>

- 1. Dr. Kyong Hwan Jin
- 2. Mr. Juyoung Lee
- 3. Dongwook Lee

1. Introduction

- 2. Review of Compressive Sensing
- 3. FRI extrapolation from uniform samples
- 4. Structured low-rank interpolation for non-uniform samples
- 5. Fast implementations
- 6. Biomedical applications

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Motivation: MRI reconstruction



Main Problem:

Reconstruct image from Fourier domain samples

Related: Computed Tomography, Florescence Microscopy

Motivation: MRI Reconstruction



Fourier Series Coefficients

Types of "Compressive" Fourier Domain Sampling

low-pass





Fourier Extrapolation Fourier Interpolation "Compressed Sensing" recovery

Extrapolation: super-resolution microscopy

The Nobel Prize in Chemistry 2014



Photo: Matt Staley/HHMI Eric Betzig Prize share: 1/3



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Stefan W. Hell

Prize share: 1/3



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William E. Moerner

Prize share: 1/3





S. Hell et al, Science 2007.

Interpolation: accelerated MRI



25% Random Fourier samples (variable density) Rel. Error = 5%

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Compressed Sensing (CS)

- Incoherent projection
- Underdetermined system
- Sparse unknown vector



Courtesy of Dr. Dror Baron

Sparse-Low Rank Recovery in Nutshell



Application to biomedical imaging



 $\xrightarrow{\mathcal{F}}$



Full sampling is costly!

Randomly undersample

Application to biomedical imaging



Analysis formulation of Compressed Sensing



Example: Assume discrete gradient of image is sparse

Piecewise constant model





Recovery by Total Variation (TV) minimization

TV semi-norm:
$$\|\mathbf{g}\|_{\mathsf{TV}} = \sum_{i,j} \sqrt{|\mathbf{g}_{i+1,j} - \mathbf{g}_{i,j}|^2 + |\mathbf{g}_{i,j+1} - \mathbf{g}_{i,j}|^2}$$

i,

i.e., L1-norm of discrete gradient magnitude

Recovery by Total Variation (TV) minimizationTV semi-norm: $\|\mathbf{g}\|_{\mathsf{TV}} = \sum_{\mathbf{i},\mathbf{j}} \sqrt{|\mathbf{g}_{\mathbf{i}+1,\mathbf{j}} - \mathbf{g}_{\mathbf{i},\mathbf{j}}|^2 + |\mathbf{g}_{\mathbf{i},\mathbf{j}+1} - \mathbf{g}_{\mathbf{i},\mathbf{j}}|^2}$ *i.e., L1-norm of discrete gradient magnitude* $\sum_{\mathbf{i},\mathbf{j}} |\mathbf{i}|_{\mathbf{i},\mathbf{j}} |\mathbf{i}|_{\mathbf{i},\mathbf{j}}$

 $\min_{g \in \mathbb{C}^{N \times N}} \|g\|_{\mathsf{TV}} \text{ subject to } F_{\Omega}g = F_{\Omega}f \quad (\mathsf{TV}\text{-min})$

Recovery by Total Variation (TV) minimization

TV semi-norm:
$$\|\mathbf{g}\|_{\mathsf{TV}} = \sum_{i,j} \sqrt{|\mathbf{g}_{i+1,j} - \mathbf{g}_{i,j}|^2 + |\mathbf{g}_{i,j+1} - \mathbf{g}_{i,j}|^2}$$

i.e., L1-norm of discrete gradient magnitude



Recovery by Total Variation (TV) minimization

TV semi-norm:
$$\|\mathbf{g}\|_{\mathsf{TV}} = \sum_{i,j} \sqrt{|\mathbf{g}_{i+1,j} - \mathbf{g}_{i,j}|^2 + |\mathbf{g}_{i,j+1} - \mathbf{g}_{i,j}|^2}$$

i.e., L1-norm of discrete gradient magnitude

Sample locations

FISTA, Primal-Dual, etc.

Recovery using zero filled IFFT



25% Random Fourier samples (variable density) Rel. Error = 30%

Recovery using TV minimization



25% Random Fourier samples (variable density) Rel. Error = 5%

Limitations of CS



- Discrete domain theory
- Explicit form of sensing matrix
- RIP issue → no direct interpolation





Beautiful analytic reconstruction results from fully sampled data

(a) MR Imaging



(b) Time-reversal of a scattered wave



 $\mathcal{I}_1(x) = \int_{\Omega} f(z) \int_0^T \int_{\partial \Omega} \frac{\partial G(x, y, T, t)}{\partial \nu_y} \frac{\partial \Gamma}{\partial t}(z, y, 0, T - t) d\sigma(y) dt \, dz.$

<u>Project Goal:</u> Unification of CS and analytic reconstruction for biomedical imaging using a 2-layer approach



"True" measurement model:



F



Continuous

"True" measurement model:







Continuous

Continuous

Approximated measurement model:

 \approx







DISCRETE

DISCRETE

DFT Reconstruction



Continuous

 ${\cal F}$



Continuous



DFT Reconstruction



Continuous





Continuous



DISCRETE

DFT Reconstruction



Continuous



Continuous



Exact Derivative







Super-resolution setting: ringing artifacts !!



(a) Fully sampled

(b) IFFT, SNR=10.8dB

(c) TV, SNR=16.6dB
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Classical Off-the-Grid Method: Prony (1795)



• Robust variants:

Pisarenko (1973), MUSIC (1986), ESPRIT (1989), Matrix pencil (1990) . . . Atomic norm (2011)

Main inspiration: Finite-Rate-of-Innovation (FRI) [Vetterli et al., 2002]



• Recent extension to 2-D images:

Pan, Blu, & Dragotti (2014), "Sampling Curves with FRI".



Stage 2: solve linear system for amplitudes





Similar 1-D FRI idea by [Liang & Hacke 1989]

IEEE TRANSACTIONS ON ACOUSTICS, SPEECH, AND SIGNAL PROCESSING, VOL. 37, NO. 4, APRIL 1989

Superresolution Reconstruction Through Object Modeling and Parameter Estimation

E. MARK HAACKE, ZHI-PEI LIANG, AND STEVEN H. IZEN

Abstract—Fourier transform reconstruction with limited data is often encountered in tomographic imaging problems. Conventional techniques, such as FFT-based methods, the spatial-support-limited extrapolation method, and the maximum entropy method, have not been optimal in terms of both Gibbs ringing reduction and resolution enhancement. In this correspondence, a new method based on object modeling and parameter estimation is proposed to achieve superreso-!ution reconstruction.







Fig. 2. (a) Fourier reconstruction of a phantom from real magnetic resonance data using 256 data points in the vertical direction and 64 points in the horizontal direction. (b) Same as (a), but vertical direction is reconstructed using the proposed method. An example profile through the phantom shows the improvement in image behavior.

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Extension to higher dims: Singularities not isolated



Extension to higher dims: Singularities not isolated



2-D PWC functions satisfy an annihilation relation



Zero-set of a 2-D trigonometric polynomial [Pan et al., 2014]



 $\mu(\mathbf{x},\mathbf{y}) = \sum_{(\mathbf{k},\mathbf{l})\in\mathbf{\Lambda}} \mathbf{c}_{\mathbf{k},\mathbf{l}} \, \mathbf{e}^{\mathbf{j}2\pi(\mathbf{k}\mathbf{x}+\mathbf{l}\mathbf{y})}$,

"FRI Curve"



Piecewise analytic model [Pan et al., 2014]

• Signal model: piecewise analytic signal

$$f(z) = \sum_{i=1}^{N} g_i(z) \cdot \mathbf{1}_{\Omega_i}(z)$$

s.t. g: analytic in Ω_i

- Not suitable for natural images
- 2-D only
- Recovery is ill-posed: Infinite DoF





Piecewise polynomial model [O. & Jacob, SampTA 2015]

• Proposed model: piecewise smooth signals

$$f(x) = \sum_{i=1}^{N} g_i(x) \cdot \mathbf{1}_{\Omega_i}(x)$$

s.t. g_i smooth in Ω_i

- Extends easily to n-D
- Provable sampling guarantees
- Fewer samples necessary for recovery





Annhilation relation for PWC signals

Prop: If *f* is PWC with edge set $\mathbf{E} \subseteq \{\mu = \mathbf{0}\}$ for μ bandlimited to Λ then

$$\sum_{\mathbf{k}\in\Lambda}\widehat{\mu}[\mathbf{k}]\widehat{\partial \mathbf{f}}[\ell-\mathbf{k}] = \mathbf{0}, \quad \forall \ell \in \mathbb{Z}^{\mathsf{n}}$$

any 1st order partial derivative



Annhilation relation for PW linear signals

Prop: If **f** is PW linear, with edge set $\mathbf{E} \subseteq \{\mu = \mathbf{0}\}$ and μ bandlimited to Λ then

$$\sum_{\mathsf{k}\in 2\Lambda}\widehat{\mu^2}[\mathsf{k}]\widehat{\partial^2 \mathsf{f}}[\ell-\mathsf{k}] = \mathsf{0}, \ \forall \ell \in \mathbb{Z}^{\mathsf{n}}$$

any 2nd order partial derivative



Wide class of images: Annihilation relations

$$\begin{split} f(x) &= \sum_{i=1}^{N} g_i(x) \cdot \mathbf{1}_{\Omega_i}(x) \\ \text{s.t.} \quad Dg_i &= 0 \text{ in } \Omega_i \end{split}$$



Signal Model: PW Constant PW Analytic* PW Harmonic PW Linear PW Polynomial Choice of Diff. Op.: $D = \nabla$ $D = \partial_{x} + j\partial_{y}$ $D = \Delta$ $D = \{\partial_{xx}, \partial_{xy}, \partial_{yy}\}$ $D = \{\partial^{\alpha}\}_{|\alpha|=n}$ $n^{\text{th} \text{ order}}$ 1-D FRI Sampling Theorem [Vetterli et al., 2002]:A continuous-time PWC signal with K jumps can be uniquely recovered from 2K+1 uniform Fourier samples.

Proof (a la Prony's Method):

Form Toeplitz matrix T from samples, use uniqueness of Vandermonde decomposition: $\mathbf{T} = \mathbf{V}\mathbf{D}\mathbf{V}^{\mathsf{H}}$

"Caratheodory Parametrization"

Challenges proving uniqueness, cont.

Extends to *n*-D if singularities isolated [Sidiropoulos, 2001]

Not true when singularities supported on curves:

$$\xrightarrow{\mathcal{F}} \widehat{\nabla f}[k] = \oint_{\partial \Omega} e^{-j2\pi k \cdot x} n \, ds$$

 $\stackrel{\mathcal{F}}{\longrightarrow} \quad \widehat{\mathbf{f}}[\mathbf{k}] = \sum_{i} a_{i} \mathrm{e}^{-\mathrm{j} 2\pi \mathrm{k} \cdot \mathbf{x}_{i}}$

Requires new techniques:

- Spatial domain interpretation of annihilation relation
- Algebraic geometry of trigonometric polynomials

Theorem: If **f** is PWC* with edge set $\mathbf{E} = \{\mu = \mathbf{0}\}$ with μ minimal and bandlimited to Λ then $\mathbf{c} = \widehat{\mu}$ is the unique solution to $\sum_{\mathbf{k} \in \Lambda} \mathbf{c}[\mathbf{k}] \widehat{\nabla} \mathbf{f}[\ell - \mathbf{k}] = \mathbf{0}$ for all $\ell \in 2\Lambda$

*Some geometric restrictions apply



 $\subseteq \mathbb{Z}^2$ Requires samples of $\hat{\mathbf{f}}$ in 3Λ to build equations 2. Uniqueness of signal (given edge set)

Theorem: If f is PWC* with edge set $\mathbf{E} = \{\mu = \mathbf{0}\}$ with μ minimal and bandlimited to then $\mathbf{g} = \mathbf{f}$ is the unique solution to $\mu \cdot \nabla \mathbf{g} = \mathbf{0}$ s.t. $\widehat{\mathbf{f}}[\mathbf{k}] = \widehat{\mathbf{g}}[\mathbf{k}], \mathbf{k} \in \mathbf{\Gamma}$ when the sampling set $\Gamma \supset 3\Lambda$ *Some geometric restrictions apply

Ongie & Jacob, SIAM J Imag. Science, in press

2. Uniqueness of signal (given edge set)

Theorem: If f is PWC* with edge set $\mathbf{E} = \{\mu = \mathbf{0}\}$ with μ minimal and bandlimited to Λ then $\mathbf{g} = \mathbf{f}$ is the unique solution to $\mu \cdot \nabla \mathbf{g} = \mathbf{0}$ s.t. $\widehat{\mathbf{f}}[\mathbf{k}] = \widehat{\mathbf{g}}[\mathbf{k}], \mathbf{k} \in \mathbf{\Gamma}$ when the sampling set $\Gamma \supset 3\Lambda$ *Some geometric restrictions apply

Equivalently,

$$\mathbf{f} = \arg\min_{\mathbf{g}} \| \boldsymbol{\mu} \cdot \nabla \mathbf{g} \|$$
 s.t. $\widehat{\mathbf{f}}[\mathbf{k}] = \widehat{\mathbf{g}}[\mathbf{k}], \mathbf{k} \in \mathbf{\Gamma}$

Ongie & Jacob, SIAM J Imag. Science, in press

Super-resolution MRI [O. & Jacob, ISBI 2015]



Super-resolution of MRI Medical Phantoms



Ongie & Jacob, SIAM J Imag. Science, in press

Can we generalize to non-uniform setting ??



Improve recovery using non-uniform sampling

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Sampling vs low-rank interpolation



* FRI Sampling theory



<u>* Jin KH et al. IEEE TCI (to appear)</u>

* Ye JC et al. IEEE TIT, 2016

* Jin KH et al.,IEEE TIP, 2015

* ALOHA : Annihilating filter based LOw rank Hankel matrix Approach



 κ : # of annihilating filter coef.





Sparsity in spatial domain \Leftrightarrow **low rankness** in k-space

Low-Rank Hankel matrix minimization

$$\operatorname{Rank}\mathcal{H}\left(\widehat{f}\right) = k$$

<u>* Jin KH et al IEEE TCI, 2016</u> <u>* Jin KH et al.,IEEE TIP, 2015</u> <u>* Ye JC et al., IEEE TIT, 2016</u>

Missing elements can be found by low rank Hankel structured matrix completion

$$\min_{\mathbf{m}} \|\mathcal{H}(\mathbf{m})\|_{*}$$
subject to $P_{\Omega}(\mathbf{M}) = P_{\Omega}(\hat{f})$

$$\|\cdot\|_{*} \text{ Nuclear norm } P_{\Omega} \text{ Projection on sampling positions}$$

General TV Signals

$$Lf(x) = \sum_{j=0}^{k-1} a_j \delta(x - x_j), \quad x_j \in [0, \tau].$$

$$L := a_K D^K + a_{K-1} D^{K-1} + \ldots + a_1 D + a_0$$
cewise smooth Weighted Fourier data

Piec Splines, polynomials

$$\mathcal{F}{Lf(x)} = \hat{l}(\omega)\hat{f}(\omega) = \sum_{j=0}^{k-1} a_j e^{-i\omega x_j}$$
$$\hat{l}(\omega) = a_K(i\omega)^K + a_{K-1}(i\omega)^{K-1} + \ldots + a_1(i\omega) + a_0$$

Annihilating filter for weighted Fourier data

$$\hat{h}(\omega) * \left(\hat{l}(\omega)\hat{f}(\omega)\right) = 0$$

General Low-Rank Hankel Matrix Completion

(P) $\min_{\mathbf{m}\in\mathbb{C}^n} \operatorname{RANK}\mathscr{H}(\mathbf{m})$ subject to $P_{\Omega}(\mathbf{m}) = P_{\Omega}(\hat{\mathbf{l}}\odot\hat{\mathbf{f}})$,

Extension to general signal models



<u>* Ye JC et al.,IEEE TIT 2016</u>

Exact Recovery

$$\begin{array}{l} \min_{\mathbf{m}} \|\mathcal{H}(\mathbf{m})\|_{*} \\ \text{subject to } P_{\Omega}(\mathbf{m}) = P_{\Omega}(\hat{\mathbf{f}}) \\ m \geq c_{1}\mu c_{s}k \log^{\alpha} n \\ \end{array}$$

$$\alpha = \begin{cases} 2, \text{ on grid} \\ 4, \text{ off grid} \\ \end{cases}$$
Stable Recovery

$$\begin{array}{l} \min_{\mathbf{m}} \|\mathcal{H}(\mathbf{m})\|_{*} \\ \text{subject to } \|P_{\Omega}(\mathbf{m}) - P_{\Omega}(\hat{\mathbf{f}})\| \leq \delta \\ \|\mathcal{H}(\mathbf{m}) - \mathcal{H}(\hat{\mathbf{f}})\|_{F} \leq c_{2}n^{2}\delta \\ \end{aligned}$$

* Ye JC et al., IEEE TIT 2016

$$\mu \leq \max\left\{\frac{\zeta_{n-d+1}}{\sigma_{\min}\left(\mathcal{V}_{n-d+1}^{*}\mathcal{V}_{n-d+1}\right)}, \frac{\zeta_{d}}{\sigma_{\min}\left(\mathcal{V}_{d}^{*}\mathcal{V}_{d}\right)}\right\}$$
Confluent Vandermonde matrix
$$\mathcal{H}(\hat{\mathbf{x}}) \neq \mathcal{V}_{n-d+1} \mathcal{B} \mathcal{V}_{d}^{T}, \qquad \zeta_{N} = N\left[\frac{(N-1)!}{(N-(\max)!)!}\right]^{2}$$
Multiplicity of roots

$$\mu \le \frac{n/2}{n/2 - 1/\Delta - 1}$$

Using extreme function for bounding singular value See Moitra (2015)

* Ye JC et al., IEEE TIT 2016

Relation to Super-resolution: Minimum separation



 $\Delta > \frac{2}{n}$

Same as Candes et al (2013) Tang et al (2015)

Using extreme function for bounding singular value See Moitra (2015)

* Ye JC et al., IEEE TIT 2016
<u>* Ye JC et al.,IEEE TIT 2016</u>

On grid model using cardinal setup

• Unknown singularities are located on integer grid

$$\mathcal{L}x(t) = \sum_{l \in \mathbb{Z}} a[l]\delta(t-l)$$

• Discrete whiting filter with uniform sampling accounts for the sparsity



* Ye JC et al., IEEE TIT 2016

Hankel Matrix: off-grid $\hat{y}[1] \quad \cdots \quad \hat{y}[d-1]$ $\hat{y}[0]$ $\hat{y}[2]$... $\hat{y}[d]$ $\hat{y}[1]$ $\hat{y}[n-d] \quad \hat{y}[n-d+1] \quad \cdots \quad \hat{y}[n-1]$ Periodic repetition $m \ge c_1 \mu c_s k \log^{\alpha} n$ $\alpha = \begin{cases} 2, & \text{on grid} \\ 4, & \text{off grid} \end{cases}$



Regularized Weighting → *more stable*



* Ye JC et al., IEEE TIT 2016

Phase transition: piecewise constant signals



Compressed sensing

Proposed method





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2-D PWC functions satisfy an annihilation relation



Matrix representation of annihilation

 $\mathcal{T}(\widehat{f})\boldsymbol{c}=0$

2-D convolution matrix (block Toeplitz)

vector of filter coefficients



Basis of algorithms: Annihilation matrix is low-rank

Prop: If the level-set function is bandlimited to
$$\Lambda$$

and the assumed filter support $\Lambda' \supset \Lambda$ then
 $\operatorname{rank}[\mathcal{T}(\widehat{f})] \leq |\Lambda'| - (\# \operatorname{shifts} \Lambda \operatorname{in} \Lambda')$



Spatial domain

 $\mu(\mathbf{x},\mathbf{y}) \longrightarrow e^{j2\pi(\mathbf{k}\mathbf{x}+\mathbf{l}\mathbf{y})}\mu(\mathbf{x},\mathbf{y})$

Prop: If the level-set function is bandlimited to
$$\Lambda$$

and the assumed filter support $\Lambda' \supset \Lambda$ then
 $\operatorname{rank}[\mathcal{T}(\widehat{f})] \leq |\Lambda'| - (\#\operatorname{shifts} \Lambda \operatorname{in} \Lambda')$









Assumed filter: 33x25 Samples: 65x49

Rank ≈ 300

Jointly estimate edge set and amplitudes



Accommodate random samples

$\min_{\widehat{f}} \quad \mathrm{rank}[\mathcal{T}(\widehat{f})] \quad \text{s.t.} \quad \widehat{f}[k] = \widehat{b}[k], k \in \Gamma$

$\label{eq:rank_formula} \min_{\widehat{f}} \ \mathrm{rank}[\mathcal{T}(\widehat{f})] \ \text{s.t.} \ \widehat{f}[k] = \widehat{b}[k], k \in \Gamma$

1-D Example:



$\label{eq:rank_formula} \min_{\widehat{f}} \ \mathrm{rank}[\mathcal{T}(\widehat{f})] \ \text{s.t.} \ \widehat{f}[k] = \widehat{b}[k], k \in \Gamma$

1-D Example:

Complete matrix





$\label{eq:rank_formula} \min_{\widehat{f}} \ \mathrm{rank}[\mathcal{T}(\widehat{f})] \ \text{s.t.} \ \widehat{f}[k] = \widehat{b}[k], k \in \Gamma$

1-D Example:



$\label{eq:relation} \min_{\widehat{f}} \ \mathrm{rank}[\mathcal{T}(\widehat{f})] \ \text{s.t.} \ \widehat{f}[k] = \widehat{b}[k], k \in \Gamma$

NP-Hard!

$$\min_{\widehat{\mathbf{f}}} \operatorname{rank}[\mathcal{T}(\widehat{\mathbf{f}})] \text{ s.t. } \widehat{\mathbf{f}}[\mathbf{k}] = \widehat{\mathbf{b}}[\mathbf{k}], \mathbf{k} \in \mathbf{\Gamma}$$

$$\int_{Convex Relaxation} Convex Relaxation$$

$$\min_{\widehat{\mathbf{f}}} \|\mathcal{T}(\widehat{\mathbf{f}})\|_{*} \text{ s.t. } \widehat{\mathbf{f}}[\mathbf{k}] = \widehat{\mathbf{b}}[\mathbf{k}], \mathbf{k} \in \mathbf{\Gamma}$$

$$Nuclear norm - sum of singular values$$

Recovery from 20-fold random undersampled data



Fully sampled

TV regularized recovery

Structured low-rank recovery

Ongie & Jacob, SAMPTA 15 https://arxiv.org/abs/1609.07429

Fully sampled

TV (SNR=17.8dB)

GIRAF (SNR=19.0)



<u>Ongie & Jacob, SAMPTA 15</u> <u>https://arxiv.org/abs/1609.07429</u>

Performance guarantee

Theorem: Let **f** be PWC with edge-set according to our model, sampled uniformly at random at **m** locations on a Fourier domain grid of size $\mathbf{n} = \mathbf{n}_1 \times \mathbf{n}_2$. Then there exists a universal constant **c** such that $\hat{\mathbf{f}}$ is the unique solution to the SLRMC problem with high probability provided

 $\mathsf{m}>\mathsf{c}\,\kappa\,
ho_1\,\mathsf{r}\,\mathsf{c}_{\mathsf{s}}\,\log^4\mathsf{n}$

- $\kappa = ext{condition number of } \mathcal{T}(\widehat{\mathbf{f}})$
- $ho_1=$ incoherence measure of edge-set
 - $\mathbf{r} = \operatorname{rank} \operatorname{of} \mathcal{T}(\widehat{\mathbf{f}})$
- $c_s =$ ratio of grid size to filter size <u>Ongie & Jacob, ICIP16,</u> https://arxiv.org/abs/1703.01405

Incoherency measure ρ_1

Intuition: minimum separation distance when packing r points on the edge-set curve, where $\mathbf{r} = \operatorname{rank} \mathcal{T}(\hat{\mathbf{f}})$



Small regions: high incoherence & more measurements

Complex boundaries: high rank/bandwidth

Phase transitions



Magnetic Resonance in Medicine 64:457–471 (2010)

SPIRiT: Iterative Self-consistent Parallel Imaging Reconstruction From Arbitrary *k***-Space**

Michael Lustig 1,2* and John M. Pauly 2

Discrete formulation exploiting multichannel acquisition

IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 33, NO. 3, MARCH 2014

Low-Rank Modeling of Local *k*-Space Neighborhoods (LORAKS) for Constrained MRI

Justin P. Haldar, Member, IEEE

Discrete formulation exploiting sparsity, smoothly varying phase, and multichannel acquisition

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$$\min_{\widehat{f}} \|A\widehat{f} - b\|^2 + \lambda \|X\|_* \text{ s.t. } X = \mathcal{T}(\widehat{f})$$

ADMM = Singular value thresholding (SVT)

Singular value thresholding step

 compute *full SVD* of X!

2. Solve linear least squares problem-analytic solution or CG solve

Alternating projections ["SAKE," Shin 14], ["LORAKS," Haldar, 14]

Alternating projection algorithm (Cadzow)

1. Project onto space of rank r matrices

-Compute truncated SVD: $\mathbf{X}^{\star} = \mathbf{U} \mathbf{\Sigma}_{\mathbf{r}} \mathbf{V}^{\mathsf{H}}$

- 2. Project onto space of structured matrices
 - -Average along "diagonals"



U, V factorization [O.& Jacob, SampTA 15, Jin et al., ISBI 15]

$$\min_{\widehat{\mathbf{f}}} \|\mathbf{A}\widehat{\mathbf{f}} - \mathbf{b}\|^2 + \lambda \|\mathbf{X}\|_* \text{ s.t. } \mathbf{X} = \mathcal{T}(\widehat{\mathbf{f}})$$

"U,V factorization trick"



U, V factorization [O.& Jacob, SampTA 15, Jin et al., ISBI 15]

$$\begin{split} \min_{\widehat{f}, U, V} \|\mathbf{A}\widehat{f} - \mathbf{b}\|^2 + \frac{\lambda}{2} \left(\|\mathbf{U}\|_{\mathsf{F}}^2 + \|\mathbf{V}\|_{\mathsf{F}}^2 \right) \\ \text{s.t. } \mathbf{U}\mathbf{V}^{\mathsf{H}} = \mathcal{T}(\widehat{f}) \end{split}$$

UV factorization approach

1. Singular value thresholding step

-compute *full SVD* of X!

SVD-free \rightarrow fast matrix inversion steps

Solve linear least squares problem
 -analytic solution or CG solve

Main challenge : Computational complexity & memory



Exploit convolutional structure of the matrix



Fast evaluation using FFT

Direct computation of small Gram matrix: avoid storage

IRLS algorithm along with structure exploitation

• Original IRLS: To recover low-rank matrix X, iterate $W \leftarrow (X^H X + \epsilon I)^{-\frac{1}{2}}$ $X \leftarrow \arg \min_{X} ||XW^{\frac{1}{2}}||_F^2 + \lambda ||AX - B||_F^2$

IRLS

• Original IRLS: To recover low-rank matrix X, iterate $| \mathsf{W} \leftarrow (\mathsf{X}^{\mathsf{H}}\mathsf{X} + \epsilon \mathsf{I})^{-\frac{1}{2}} \\ \mathsf{X} \leftarrow \arg\min_{\mathsf{X}} \|\mathsf{X}\mathsf{W}^{\frac{1}{2}}\|_{\mathsf{F}}^{2} + \lambda \|\mathsf{A}\mathsf{X} - \mathsf{B}\|_{\mathsf{F}}^{2}$

• We adapt to structured case: $\mathbf{X} = \mathcal{T}(\widehat{f})$ $| \mathbf{W} \leftarrow (\mathcal{T}(\widehat{f})^{\mathsf{H}} \mathcal{T}(\widehat{f}) + \epsilon \mathbf{I})^{-\frac{1}{2}}$ $\widehat{\mathbf{f}} \leftarrow \arg\min_{\widehat{f}} \|\mathcal{T}(\widehat{f})\mathbf{W}^{\frac{1}{2}}\|_{\mathsf{F}}^{2} + \lambda \|\mathbf{A}\widehat{f} - \mathbf{b}\|^{2}$ • Original IRLS: To recover low-rank matrix X, iterate $W \leftarrow (X^{H}X + \epsilon I)^{-\frac{1}{2}}$ $X \leftarrow \arg \min_{X} ||XW^{\frac{1}{2}}||_{F}^{2} + \lambda ||AX - B||_{F}^{2}$

• We adapt to structured case:
$$\mathbf{X} = \mathcal{T}(\widehat{f})$$

 $\mathbf{W} \leftarrow (\mathcal{T}(\widehat{f})^{\mathsf{H}} \mathcal{T}(\widehat{f}) + \epsilon \mathbf{I})^{-\frac{1}{2}}$
 $\widehat{\mathbf{f}} \leftarrow \arg\min_{\widehat{f}} \|\mathcal{T}(\widehat{f}) \mathbf{W}^{\frac{1}{2}}\|_{\mathsf{F}}^{2} + \lambda \|\mathbf{A}\widehat{\mathbf{f}} - \mathbf{b}\|^{2}$

Without modification, this approach is still slow!

Ongie & Jacob, ISBI16 https://arxiv.org/abs/1609.07429

Idea 1: Embed Toeplitz lifting in circulant matrix



<u>Ongie & Jacob, ISBI16</u> <u>https://arxiv.org/abs/1609.07429</u>

Idea 2: Approximate matrix lifting



Ongie & Jacob, ISBI16 https://arxiv.org/abs/1609.07429

GIRAF: fast [O. & Jacob, 2016 (arXiv)]

Complexity similar to IRLS for TV minimization










	15×15 filter		31×31 filter	
Algorithm	# iter	total	# iter	total
SVT GIRAF	7 6	110s 20s	11 7	790 s 44 s
Onun	U	200	,	115

Table: iterations/CPU time to reach convergence tolerance of NMSE < 10⁻⁴

> <u>Ongie & Jacob, ISBI16</u> <u>https://arxiv.org/abs/1609.07429</u>

Convergence speed of GIRAF



AP-PROXSVT+UVGIRAF-0NMSE = 4.9e-3NMSE = 11.6e-3NMSE = 1.8e-3Runtime: 1000 sRuntime: 1090 sRuntime: 49 s

1. Introduction

- 2. Review of Compressive Sensing
- 3. FRI extrapolation from uniform samples
- 4. Structured low-rank interpolation for non-uniform samples
- 5. Fast implementations
- 6. Biomedical applications
 - a. Applications to MRI
 - b. Other applications





k-t dynamic sparse signal cases



k-t dynamic sparse signal cases



Single coil static MRI



$$\mathcal{Y}_h = \left[\mathscr{H}_c(\hat{\mathbf{l}} \odot \hat{\mathbf{g}}_1) \quad \cdots \quad \mathscr{H}_c(\hat{\mathbf{l}} \odot \hat{\mathbf{g}}_{N_c}) \right]$$

$\operatorname{RANK}\mathcal{Y}_h \leq \operatorname{RANK}\mathscr{H}_c(\hat{\mathbf{w}}) + \operatorname{RANK}\mathscr{H}_c(\hat{\mathbf{f}}_{tr})$

Sparsity of common image In transform domain Sparsity of sensitivity map In Fourier domain

Jin et al, IEEE TCI, 2016



Parallel MRI





MR Parameter Mapping

What is MR parameter mapping?



Result : in vivo acceleration study (ME-SE, T2)



Reconstruction of x12.8 accelerated scan – ME-SE (4th echo)

Lee et al, MRM, 2015

Result : in vivo acceleration study (ME-SE, T2)



Mapping from the reconstruction of x12.8 accelerated scan – T2 mapping

Lee et al, MRM, 2015

Result : Signal intensity curves (SE-IR, T1)



Lee et al, MRM, 2015

Summary of Results

• Goal : Acceleration of MR Parameter mapping by undersampling and reconstruction



Extension to 3-D applications using GIRAF



3D applications: dynamic MRI



Fast 3-D implementation using GIRAF



Cardiac CINE MRI



Balachandrasekaran & Jacob, ICIP 16

Exponential signals with spatially smooth parameters



MR parameter mapping

Exponential signals with spatially smooth parameters



1-D signal satisfies an annihilation relation!



Spatially smooth parameters



Convolution as multidimensional Toeplitz matrix relation



Multidimensional Toeplitz matrix is low-rank



Number of filters satisfying $\mathcal{T}(\hat{\rho}) \mathbf{d} = \mathbf{0} \geq |\Lambda : \Theta|$

$$\implies$$

$$\operatorname{Rank}(\mathcal{T}(\hat{
ho})) \leq |\Lambda| - |\Lambda:\Theta|$$

Balachandrasekaran & Jacob, ISBI 17, Wed AM

Fast algorithm using an extension of GIRAF



Proposed method \approx 7.5 times faster than IRLS (direct) method

Balachandrasekaran & Jacob, ISBI 17, Wed AM

Spatially bandlimited filters provide better reconstruction

Effect of filter size on SNR of T_2 weighted images.

filter size	SNR
128x128x10	28.05
122x122x10	30.30
114x114x10	31.00
108x108x10	31.12
102x102x10	31.21
100x100x10	31.20

(a) Varying spatial dimension

filter size	SNR (dB)
102x102x11	30.80
102x102x10	31.21
102x102x7	31.13
102x102x4	30.96
102x102x2	30.78
102x102x1	29.88

(b) Varying temporal dimensions

Parameter mapping in MRI

mask



Balachandrasekaran & Jacob, ISBI17

Parameter mapping in MRI



Balachandrasekaran & Jacob, ISBI17

Parameter mapping in MRI



Balachandrasekaran & Jacob, ISBI17

Motion-induced inter-shot phase errors



Self calibration methods: Image domain

 $I_{2}(\mathbf{r}) = I(\mathbf{r})\theta_{2}(\mathbf{r})$ θ_{2} θ_{1} θ_{2} θ_{1} θ_{2} θ_{1} θ_{2} θ_{2} θ_{3} θ_{3} θ_{4} θ_{5} θ

Image domain annihilation relation [Morrisson, Do & Jacob 2007]

$$I_2(\mathbf{r})\cdot \mathbf{ heta}_1(\mathbf{r}) - \hat{I}_1(\mathbf{r})\cdot \hat{\mathbf{ heta}}_2(\mathbf{r}) = 0$$

Model sensitivities as polynomials: EVD

Better than SOS estimates

Self calibration methods: Fourier domain



Fourier domain relation [Lustig 2012, Haldar 2014]

 $\hat{I}_2[\mathbf{k}] * \hat{\theta}_1[\mathbf{k}] - \hat{I}_1[\mathbf{k}] * \hat{\theta}_2[\mathbf{k}] = 0$

Phase: linear combination of exponentials FIR filter

Self calibration methods: matrix form

Fourier domain relation

$$(\hat{I}_2[\mathbf{k}] * \hat{\theta}_1[\mathbf{k}] - \hat{I}_1[\mathbf{k}] * \hat{\theta}_2[\mathbf{k}] = 0$$

Convolution: matrix multiplication


Fourier domain relation

$$\hat{I}_2[\mathbf{k}] * \hat{\theta}_1[\mathbf{k}] - \hat{I}_1[\mathbf{k}] * \hat{\theta}_2[\mathbf{k}] = 0$$

Compact matrix representation

$$\underbrace{\left[\mathbf{H}\left(\hat{I}_{2}[\mathbf{k}]\right),\mathbf{H}\left(\hat{I}_{1}[\mathbf{k}]\right)\right]}_{\mathbf{Q}(I_{1},I_{2})}\begin{bmatrix}\hat{\theta}_{1}[\mathbf{k}]\\-\hat{\theta}_{2}[\mathbf{k}]\end{bmatrix}=0$$
N shots: $\binom{N}{2}$ null space vectors

Q is low-rank & structured



Smoothness regularized multishot MRI

Multi-shot recovery

Smoothness regularization

Combine the matrix liftings

Structured low-rank recovery

 $\|\mathcal{A}(\boldsymbol{I_1},\boldsymbol{I_2}) - \mathbf{b}\|^2 + \lambda \|\mathcal{G}(\boldsymbol{I_1},\boldsymbol{I_2})\|_*$

 $\mathbf{H}\left(\hat{I}_{2}[\mathbf{k}]\right)$ $\mathbf{H}\left(\hat{I}_{1}[\mathbf{k}]\right)$ $\mathbf{k}_{x}\hat{\mathbf{f}}[\mathbf{k}]$





Mani & Jacob, Magnetic Resonance Medicine, in press

Structured low-rank recovery: MUSSELS

Can also account for partial Fourier





0.8 x 0.8 x 2mm; 3 avgs; 25 directions; b=700

Mani & Jacob, Magnetic Resonance Medicine, in press, EMBC 2016

Comparison with MUSE (state of the art)



Mani & Jacob, Magnetic Resonance Medicine, in press

MUSE

 \mathbf{VS}

MUSSELS

Radial trajectory correction



MUSSELS

Radial trajectory correction

NUFFT using nominal trajectory



NUFFT using nominal trajectory



TrACR trajectory corrected



TrACR trajectory corrected



MUSSELS

MUSSELS



Mani & Jacob, ISMRM 17

• What is <u>MR artifacts</u>?

Spike noise

During acquisition, external interruptions (ex. fluctuation power supply of gradient, motion of object, etc.) distort signals.



Respiratory motion

M. Graves, et. al., JMRI (2013)

Motivation



Motivations: MR artifacts as sparse outliers

✓ Herringbone (spikes 2-D k-space)



$$\widetilde{M}(k_x, k_y) = \widehat{M}(k_x, k_y) + \underbrace{\sum_{j=1}^{S} \epsilon_j \delta[k_x - k_{x_j}, k_y - k_{y_j}]}_{\text{sparse outliers}},$$

 \sim

Motivations: MR artifacts as sparse outliers

✓ Motion artifact (spikes 1-D k-space parallel to readout)



$$= \begin{cases} \widehat{M}(x,k_y) \exp(j2\pi k_y d(k_y)), & \text{when } k_y \in \{k_{y_1}, \cdots, k_{y_S}\} \\ \widehat{M}(x,k_y), & \text{otherwise} \end{cases}$$

$$= \widehat{M}(x,k_y) + \sum_{j=1}^{S} \widehat{M}(x,k_y) (\exp(j2\pi k_y d(k_y)) - 1) \delta[k_y - k_{y_j}] \\ \text{sparse outliers} \end{cases}$$

$$Motion artifact \\ k_y \\ Motion \end{cases}$$

Motivations: MR artifacts as sparse outliers

Zipper artifact (spikes 1-D k-space perpendicular to readout)





* Sparse outlier is still sparse in weighted Hankel matrix



ALOHA: Annihilating filter based LOw rank Hankel matrix Approach



 ✓ Extension of ALOHA for decomposition of sparse outliers (E) out of mixed signal*
 ✓ Can be addressed ADMM[†]

✓ K-space weighting

* E. Candes, et. al, JACM (2011), R. Otazo, et. al, MRM (2015)

[†]S. Boyd, et. al., Foundations and Trends in Machine Learning (2011)

[‡]Z. Wan, et. al., Mathematical Programming Computation (2012)

Algorithm Flowchart



Retrospective results



Low intensity

Spike noise with down sampling (x5)

In Vivo Motion artifact



sudden motion (3 times)

Cardiac Motion artifact



Artifact component

Spectrum of artifact



Zipper artifact



Low-rank component



2-D herringbone (in-vivo)

before



after



2-D herringbone (in-vivo)



In EPI, Gradient is distorted by eddy currents and this causes phase shift



Conventional correction





EPI model



where $A = m(x, y) \exp (j2\pi [\Delta f(x, y) ((TE + (n - N/2)ESP))])$

The ghost generating phase term can be changed into a sine term

$$S_{n,\Delta}(k_x, k_y) = S_{n,+}(k_x, k_y) - S_{n,-}(k_x, k_y)$$

$$= \int \int A(x, y) \left(e^{j2\pi\Delta f(x, y)\frac{k_x}{\sqrt{G_x}}} - e^{-j2\pi\Delta f(x, y)\frac{k_x}{\sqrt{G_x}}} \right) e^{j2\pi(k_x x + k_y y)} dxdy$$

$$= \int \int A(x, y) 2j\sin\left(2\pi\Delta f(x, y)\frac{k_x}{\sqrt{G_x}}\right) e^{j2\pi(k_x x + k_y y)} dxdy$$

$$\sin\left(2\pi\Delta f(x, y)\frac{k_x}{\sqrt{G_x}}\right) \simeq 2\pi\Delta f(x, y)\frac{k_x}{\sqrt{G_x}}$$

$$S_{n,\Delta}(k_x, k_y) \simeq j2\pi k_x \int \int \frac{2}{\sqrt{G_x}} A(x, y)\Delta f(x, y) e^{j2\pi(k_x x + k_y y)} dxdy$$

$$= \frac{2}{\sqrt{G_x}} \mathcal{F} \underbrace{\frac{\partial A(x, y)\Delta f(x, y)}{\partial x}}_{\partial x} \text{ Sparse}$$

How can we use this sparsity?

 $S_{n,\Delta}(k_x, k_y) = \mathcal{F}(Sparse signal)$

Hankel structure matrix constructed by $S_{n,\Delta}(k_x, k_y)$ is low-ranked

Reconstruction flow

• SE-EPI in-vivo data, 128x128 matrix size, 6/8 partial Fourier



Result : GRE-EPI in-vivo



Result : fMRI analysis



Applications to Image Processing

Inpainting & Impulse noise removal



ig. 2. (Color online) 3D SD-OCT image reconstruction a







Spectral Domain Sparsity



2-D Hankel matrix





Hankel Matrix construction



Why patch processing ?

- Spectrum changes for each patch
- Need to adapt the local Image statistics



Rotation invariant sparsity



Experimental results (x5)

Barbara	Missing (80%)	Mesh	Kernel
	PSNR 6.54	PSNR 23.09	PSNR 22.91
	SSIM 0.06374	SSIM 0.8042	SSIM 0.7551
Kernel (Steering)	K-SVD	C-SALSA	Proposed
PSNR 23.08	PSNR 24.27	PSNR 23.38	PSNR 31.34
SSIM 0.7491	SSIM 0.8075	SSIM 0.7918	SSIM 0.9547

18. APK. 2015.

Experimental results (x5)



Text inlayed image reconstruction ORIG

Missing(15.3%)



PatchMatch

IPPO

Proposed


Line scratches

Missing(12.7%)



PatchMatch

IPPO

Proposed



Object removal ORIG

Missing(7.99%)

Mesh



PatchMatch

IPPO

Proposed





*K.H. Jin, et. al, IEEE TIP (2015)

Impulse Noise Removal







 $S = \mathcal{H}{E}$



Low-rank Hankel matrix

Sparse outliers





TVL1 PSNR : 28.68





Application to B-mode US Imaging



Sub-sampled Dynamic Aperture B-mode Imaging



Low-Rankness of B-mode US Data

Temporal slices of Pre-beamformed RF data





Similar & Sparse spectral support

Exploiting Temporal Redundancy

 \rightarrow inter-temporal annihilating filter

$$\min_{\boldsymbol{\mathcal{X}}} \quad \|\boldsymbol{\mathcal{Z}}\{\boldsymbol{\mathcal{X}}\}\|_{*}$$

subject to
$$\boldsymbol{\mathcal{Z}}\{\boldsymbol{\mathcal{X}}\} = [\mathscr{H}\{\mathbf{X}_{1}\} \cdots \mathscr{H}\{\mathbf{X}_{F}\}].$$
$$X_{i}(j,k) = M_{i}(j,k),$$



Reordered *subsampled pre-beamformed* data



Reconstructed slices

Low-Rankness of B-mode US Data



In-vivo Acquisition



- Verasonics system with a Linear type probe (L7-4)
- Center freq:5MHz
- Sampling:20 MHz.
- 128 scanlines (SC) x 128 RX channels
- RX element
 - Width:133um
 - space between RX

elements: 158um

Snapshot image from dynamic scan



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Beam forming





ALOHA





Beam forming



Dynamic reconstruction (x8)

Full Sampling



ALOHA





Beam forming



Dynamic reconstruction (x12)

Full Sampling



ALOHA



Localization microscopy

- Nanoscopy based on localization
 - Localization precision is not diffraction limited
 - Sparsely activated probes + localization => super-



- However, sparse activation scheme has too slow temporal resolution for live imaging
 - Tens of seconds or several minutes
- High-density imaging for fast live imaging
 - Require a robust localization algorithm and system



Existing high density algorithm

Greedy approach

We first i

CORRESPONDENCE

DAOSTORM: an algorithm for highdensity super-resolution microscopy

To the Editor: Astronomy and biology have more in common than you might expect. Here we show that methods originally used to study crowded stellar fields can improve the performance of localizationoscopies (stochastic optical reconstruc sed super-resolution mi tion microscopy (STORM)1, photoactivated localization microscopy and others), which currently have slow imaging rates (typically < 0.01 image s⁻¹), limiting their utility in studies of live-cell dynamics. These techniques, which use stochastic photoswitching to resolve

closely spaced fluorophores and thus reconstruct super-resolved images, require that the specimen has a low density of active fluoro-phores (hereafter called 'imaging density'; <1 molecule µm*²), limiting maging speed and spatial resolution (Supplementary Discussion) A major cause of this issue is that current super-resolution localization algorithms work by fitting images of fluorescent molecules asing only a single model point spread function (PSF; the diffraction imited image of a fluorophore). We observed that astronomy software, DAOPHOT II (refs. 3.4), can simultaneously fit overlapping molec ular PSFs (hereafter called 'molecules') with multiple model PSFs instead of just one, facilitating analysis at high imaging density (up to 10 molecules µm⁻²). We developed DAOSTORM (Supplementary Software and Supplementary Note), which adapts DAOPHOT II for super-resolution imaging by increasing its aut ation and robustness (Supplementary Fig. 1 and Supplementary Methods).

ompared DAOSTORM to two common localization algorithms. Sparse algorithm 11 (SA1)1 fits candidate molecules with a single Gaussian ization errors even at low imaging density (>0.1 molecules um⁻²). In PSF of variable size and ellipticity. Localizations arising from overlapping molecules are rejected if the fitted PSF appears too elliptical (shape-based filtering), too large or too small (size-based filtering). 'Sparse algorithm 2' (SA2)⁵ fits candidate molecules with a single Gaussian PSF of fixed shape and size, without shape- or size-based filtering

(a) A single image of fluor ubules was analyze using SA1, SA2 and DAOSTORM Crosses represent localizations for each algorithm (b,c) Recall (b) and localization error (c) of th algorithms used in a measur for simulated images of rand distributed surface-immobil nolecules. Error bars, s.d. (n = 10 (d) Super-resolved mic images from a 2,000-frame data series. (e) Line plots of cross section indicated by dashed in d. Scale bars, 1 u

for images of Alexa Huor 647-immunolabeled microtubules in fixed COS-7 cells. We recorded data at high imaging density using total internal reflection fluorescence microscopy and direct (d)STORM photoswitching conditions5 (100 ms integration time, ~4,000 photons fluorophore⁻¹ frame⁻¹). We plotted localizations on raw images, illus trating the characteristic performance of each algorithm (Fig. 1a) SA1 only localized isolated molecules, which were fitted with small localized tion error. SA2 localized a larger fraction of the molecules but vielded large localization errors for overlapping molecules. DAOSTORM out performed both sparse algorithms, identifying almost all molecules with small localization erro We quantified the performance of each algorithm by analyzing sim

tigated the qualitative performance of each alg

ulations of randomly distributed surface-immobilized fluorophores6, We compared observed localizations to simulated positions, calc the recall⁵ and localization error at different imaging densities. Recal is the percentage of simulated fluorophores detected. Localization error is the root-mean-square distance between a localization and the simulated position. We also measured the precision5 and redundancy (Supplementary Methods), which did not vary substantially, DAOSTORM substantially outperformed the sparse algorithms in simulations at high signal-to-noise ratio typical of STORM data (bright organic fluorophores, 5,000 photons molecule⁻¹ frame⁻¹; Fig 1b-c). SA1 showed poor recall at high density, with imaging den sity at half-maximum recall, ρ_{HM} of 1.2 molecule μm^{-2} . However, SA1 yielded small localization errors even at high imaging density because most overlapping molecules were rejected. SA2 had bette recall performance ($\rho_{HM} = 3.4$ molecules μm^{-2}) but gave large localcontrast, DAOSTORM gave small localization errors similar to the other 'precise' algorithm, SA1, together with a sixfold improvement in recall performance ($\rho_{HM} = 7.5$ molecules μm^{-2}). For simulations at low signal-to-noise ratio typical of photoactivated localization microscopy data (fluorescent proteins, 200 photons molecule⁻¹ frame⁻¹

Faster STORM using compressed sensing

Lei Zhu¹, Wei Zhang², Daniel Elnatan³ & Bo Huang²⁻⁴

-resolution microscopy methods based on singl molecule switching, the rate of accumulating single-molecul activation events often limits the time resolution. Here we developed a sparse-signal recovery technique using compressed sensing to analyze images with highly overlapping fluorescent spots. This method allows an activated fluorophore density an order of magnitude higher than what conventional single molecule fitting methods can handle. Using this method we demonstrated imaging microtubule dynamics in living cells with a time resolution of 3 s

pite many achievements in the field of super-resolution micro copy in the past few years1.2, live cell imaging remains a challenge because of the need for high temporal resolution. Using the sam optical system and detector as in conventional light microscopy, super-resolution microscopy naturally requires longer acquisition time to obtain more spatial information, leading to a trade-off sum of the absolute value of each element) between its spatial and temporal resolution. In super-resolution microscopy methods based on single-molecule stochastic switching, also known as stochastic optical reconstruction microscopy ORM) or (fluorescence) photoactivated localization micros

copy ((F)PALM)3-5, each camera image samples a random subset of probe molecules in the sample. The temporal resolution is mostly determined by the time required to accumulate enough single-molecule switching events so that adjacent localization points can be closer than one-half of the desired spatial resolution (Nyquist criterion)⁶. Achieving a 50- to 70-nm spatial resolu-tion usually requires several thousand frames, or tens of seconds. Increasing the switching rates using stronger excitation can improve the time resolution7, but such high excitation intensity can increase photodamage. Moreover, in the case of fluorescent proteins, which are often the best labels for live samples, attempt-

ing a fast switching rate can cause signal degradation7. An alternative approach is to increase the density of activated fluorophores so that each camera frame samples more molecules. However, this high density of fluorescent spots causes them to overlap, invalidating the widely used single-molecule localiza-

the single fluorophore signals overlap. These methods are based on fitting clusters of overlapped spots with a variable number of point-spread functions (PSFs) with either maximum likelihood estimation^{8,9} (for example, using the DAOSTORM algorithm⁸) or Bayesian statistics¹⁰. The Bayesian method has also been applied the whole image set11. Here we present another appro based on global optimization using compressed sensing, which does not involve estimating or assuming the number of mole-cules in the image. We show that compressed sensing can work with much higher molecule densities compared to DAOSTORM and demonstrate live cell imaging of fluorescent protein-labeled microtubules with 3-s temporal resolution. Compressed sensing has shown great success in many different

BRIEF COMMUNICATIONS

fields of signal processing^{12,13}. If the original signal is sparse (that is, mostly zeros) or can be made sparse after a given tran tion, compressed sensing can precisely recover signal from highly noisy or corrupted measurements. Compressed sensing class deals with a linear measurement b of the original signal x

```
b = Ax
```

minimize $\|x\|_1$ subject to b = Ax

where the matrix A is a known measurement function. If x is Correspondence and sparse, it can be exactly recovered by minimizing its L1 norm (the requests for materials should be addressed to M.U. (michael.unser@ (2)

These author

this work.

(1)

even when b has far fewer elements than x has In STORM, the camera image has a linear and shift-invariant relationship with the true molecule distribution to be recovered To model this relationship as in equation (1), we introduce a discrete grid to describe the molecule positions instead of using a list of molecule coordinates as is typically done to represent super resolution images. The grid spacing is kept much smaller than the camera pixel size (for example, one-eighth the pixel size) to ensure sufficient accuracy. In this representation, both the molecule distribution in each camera frame, x, and the final superresolution image summed from all frames are pixelated image (Supplementary Fig. 1). In each camera frame, every grid poin in x represents the brightness of a molecule located at this point Grid points with no molecules fluorescing will have a value of 0 We then model the camera image as the convolution of the fluore phore distribution, x, with the PSF, in a matrix form, as shown in equation (1). In this case, b corresponds to the camera image tion method. Recently, a number of methods have been reported that can efficiently retrieve single-molecule positions even when

³Nachara nd Bahihgiqia Engineering and Madical Physics Programs. The George W Woodruff School of Mochanical Engineering: Georgia Institute of Fachonology. Mattas, Georgia, Eds. "Doperations of Phranecoscial Chemistry University of California, Star Paracico, Salfarina, USA" Predit Galakare Program. University of California, Sun Francisco, California, USA: "Opputtene of Biochemistry and Biophysics, University of California, Sun Francisco, San Francisco, Salfarin, USA: "Opputtene of Phranece and Data Physics and Data Physics, San Francisco, San Francisco, California, USA: Compositionet and Data Physics and Data D. Z. (Ethiophysica), edited physics, Editor, San Francisco, San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysica), editor, BL, OSA: Datagenet of Human Physics, Paracella, San Francisco, San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysics, Data), editor, BL, Osa, Datagenet and San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysics, Data), editor, BL, Osa, Datagenet and San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysics, Data), editor, BL, Osa, Datagenet and San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysics, Data), editor, BL, Osa, Datagenet Andrea, San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysics, Data), editor, BL, Osa, Datagenet Andrea, San Francisco, California, USA: Compositionet and Data Physics and D. Z. (Ethiophysics, Data), editor, BL, Osa, Datagenet and Data Physics an RECEIVED 4 OCTOBER 2011: ACCEPTED 28 FEBRUARY 2012: PUBLISHED ONLINE 22 APRIL 2012: DOI:10.1038/NMETH.1978

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SCIENTIFIC REPORTS 1 4: 4577 1 DOI: 10.1038/sree04577

Min, J.et al, Sci. Rep, 2014

Better Localization Performance

Sparsity based approach

SCIENTIFIC

REPORTS

FALCON: fast and unbiased OPEN reconstruction of high-density SUBJECT AREAS: MATHEMATICS AND COMPUTING super-resolution microscopy data

NANOSCIENCE AND TECHNOLOGY Junhong Min¹, Cédric Vonesch²⁺, Hagai Kirshner²⁺, Lina Carlini³⁺, Nicolas Olivier^{3,4}, Seamus Holden³, Suliana Manley³, Jong Chul Ye¹ & Michael Unser³ MOLECULAR BIOLOGY

¹Department of Bio and Brain Engineering, KAIST, Daejeon, Republic of Korea, ²Institute of Microengineering, EPFL, Switzerland ³Institute of the Physics of Biological Systems, EPFL, Switzerland, ⁴Department of Physics, King's Callege Landon, UK. 14 August 2013

Super resolution microscopy such as STORM and (F)PALM is now a well known method for biological 18 March 2014 Super resolution microscopy use A sTORM and (PPAMA is now a well known method for biological addes at the maconerism of the strength and the strength of the strength of the strength of the photo-which hade functional the strength and the strength of the PSF. Our algorithm is designed to provide unbiased houldaristics on continuous space and high read reads high-density algorithms. We vialisated our algorithm on both simulated and experimental data, and demonstrated live-strength image with imagent production of providing and E & pomanica-tion strength of the strength and the strength of the strengt 3 April 2014

S ingle-molecule localization microscopy methods, such as STORM' and (F)PALM'', utilize sparse activa-tion of photo-switchable fluorescent probes in both temporal and spatial domains. Each activated probe can be assimilated to an ideal point sources of hut the acquired images consist of solitated replicates of the point epfl.ch) spread function of the microscope (PSF). This allows one to achieve sub-pixel assume repleased or or goant period function of the microscope (PSF). This allows one to achieve sub-pixel accuracy on the order of tens of nanometers for the estimated location of each probe²⁴. In general, reconstruction of sub-cellular structures relies on numerous localized probes, and the required acquisition time of them entholds is therefore relatively long, i.e. contributed equally to

on numerous localized probes, and the required acquisition time of these methods is therefore relatively long, Le. on the order of minarios this is a acrino limitation while strength lipecal dynamics. One possible approach for evercoming this limitation is high-density imaging. ⁴ Jonczening the density of activated probes, short acquisition times for a single super-ostication image as the Advect However this complicates the localization task due to overlapping FSR-DASTORAT. For example, fits multiple everlapping FSR-1 and textures more by analyzing predicates in the seriosia image. The positions of the probes are determined by maintaining a lacat-squares criterion. CSINGNM "(Compressed sensing STIORA) and constructional dynamics and the parabolic sensitivity of the probes are determined by maintaining a lacat-squares criterion. CSINGNM "(Compressed sensing STIORA) and constructional dynamics and the strength sensitivity and the advectional of probes (in CSINGNM "Compression in CSINGNM"). aleorithm, the localization task is formulated as a convex optimization problem and solved by means of linea vgramming, while deconSTORM uses a modified Lucy-Richardson deconvolution algorithm by exploitin ion of activated probes. In general, these sparsity promoting methods provide in tempeta corretato o nazvese protes, in guerra, tote spinny promong mensos proves messas trais mets compared to multi-muiter fining a the expense of higher compational competitivi, in a different approach, super resolution optical fluctuations imaging (SOT)¹⁰ and 38 analysis¹⁰ utilize stockastic photon-ensisons processes and a photo-Beaching and binking to resourch tigh-fluctuations (and for example, 33) analysis based on realistic models of photo-Beaching and binking processor reconstruct high-fluctuation (and for the stockastic) and the stockastic processor from the high-fluctuation (and for the stockastic) and the stockastic processor reconstruct high density of the stockastic processor reconstruct high-fluctuating and binking processor reconstruct high-fluctuating and guera stockastic) and the stockastic processor reconstruct high-fluctuating and the stockastic processor reconstructuation and the stock

but it can be made faster by using a computationally efficient Bayesian algorithm or parallel computing " In addition, all of these sparsity-promoting methods are based on similar discrete formulations. They recons Struct a high resolution image on a pre-defined usb-prived prive day. What has pixel size CO nm. Such formulations however, have three inherent limitations. First, discrete-domain formulations can account for only pre-defined Investors, are titles units contained and a series are constructed in the series and a series of the probe locations. Second, using a finer sub-pixel grid increases the computational load, especially with the linear

Zhu, L.et al, Nat Methods, 2012

Figure 1 | Comparison of TORM to existing sup



Holden, S.et al, Nat Methods, 2011

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ALOHA for localization microscopy



PSF estimation

- HD localization algorithms usually assume that PSF is <u>known and fixed</u>
 - Requiring additional training low-density data set
 - In live experiment, PSF is varying in time and space both.

Key idea: <u>Optimal PSF h* => minimum rank of Hankel matrix</u>

$$\frac{1}{\hat{h}^{*}} \cong \prod_{i=1}^{\hat{f}} \bigoplus_{i=1}^{Minimum} Rank\left(\mathcal{H}\left\{\widehat{g} \odot \widehat{h}^{-1}\right\}\right)$$

• Under symmetric Gaussian PSF model, its width (σ) is estimated by minimizing Schatten norm

$$\sigma^* = \min_{\sigma} \left\| \left(\mathcal{H} \left\{ \widehat{\boldsymbol{g}} \odot \widehat{\boldsymbol{h}_{\sigma}}^{-1} \right\} \right) \right\|_{P(p<1)}$$

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Grid-free localization

- Now, we have entire Fourier spectrum \hat{f}
- <u>Localization is nothing but spectral estimation problem!</u> $\hat{f}(m,n) = \sum_{i} c_{i} e^{-j2\pi (\frac{mx_{i}}{M} + \frac{ny_{i}}{N})} = \sum_{i} c_{i} p_{i}^{m} q_{i}^{n}$
- We used ACMP (algebraically coupled matrix pencils) algorithm (Vanpoucke et al, 1994)
- Data matrix $Z^{M \times N}$ of rank k, having no shared harmonics of p_i , q_i

$$\mathbf{Z}^{M \times N} = P^{M \times k} \ C^{k \times k} \ Q^{\prime N \times k}$$

- In Matrix form: $Z^{M \times N} = P^{M \times k} C^{k \times k} Q'^{N \times k}$
- <u>P,Q</u> are Vandermonde matrix, C is diagonal

Algorithm procedure



PSF variation along time



Reconstruction



Localization bias



Infrared spectroscopy



1D IR spectroscopy





Accelerated imaging using GIRAF

Humston et al, Journal of Physical Chemistry Bhattacharya et al, Optics Letters, submitted

- Off-the-grid = Continuous domain representation
- *Compressive* off-the-grid *imaging*:

Exploit continuous domain modeling to improve image recovery from few measurements

- Two realizations: extrapolation, interpolation
 - Extrapolation: FRI theory
 - Interpolation: Structured low-rank matrix completion
- Performance guarantee for structured low-rank approach
 - 1D, 2D theory \rightarrow near optimal performance guarantee

Conclusions (cont.)

- Extensive applications
 - MRI
 - Compressed sensing MRI, parallel MRI
 - Super-resolution MRI
 - MR artifact removal
 - Image processing: inpainting, impulse noise denoising
 - Other imaging applications
 - US imaging
 - Optics
- A missing link between analytic recon and CS ?

CBIG, Univ. Iowa

- 1. Dr. Gregory Ongie
- 2. Dr. Merry Mani
- 3. Mr. Arvind Balachandrasekaran
- 4. Ms. Ipshita Bhattacharya
- 5. Ms. Sampurna Biswas

<u>KAIST</u>

- 1. Dr. Kyong Hwan Jin
- 2. Mr. Juyoung Lee
- 3. Dongwook Lee

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