MIRST: Mid-Infrared Spectroscopic Tomography

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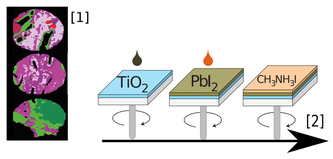
Chemically Specific, Spatially Resolved, Non-invasive Imaging

Goals

- **What** chemicals are present and **where** are they?
- Non-invasive$\Longrightarrow$3D spatial imaging! Can't assume thin object.
- Intrinsic contrast: no dyes, stains, or fluorescent labeling
- Require economical data collection and efficient image reconstruction

Applications

- Tissue classification
- Disease diagnosis
- Drug diffusion
- Manufacturing



Limitations of existing modalities

- Optical Coherence Tomography (OCT) / Interferometric Synthetic Aperture Microscopy (ISAM)
  - Limited chemical specificity
  - Tradeoff: spatial/spectral resolution, spectral accuracy
- Fourier Transform Infrared Spectroscopy (FTIR)
  - Bulk: No spatial resolution
  - Microscopy: requires thinly sectioned object
- Fluorescence microscopy
  - Must label area of interest; phototoxicity

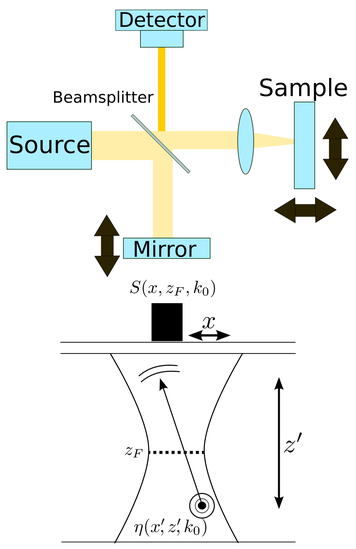
Overview of approach

- New imaging modality combining OCT & mid-infrared spectroscopy.
  - Contrast comes from scattering and absorption in mid-infrared "fingerprint" region
- Model object by its complex refractive index: $n(x, y, z, k_0)$
  - Real part: dispersion — Imaginary part: absorption
- Low-dimensional, physically justified model for $n(x, y, z, k_0)$ $\Longrightarrow$ reduced data collection and efficient image reconstruction

Data Acquisition and Forward Model

- Illuminate with broadband source or tunable laser focused to a plane z_F within the object
- Asymmetric interferomeric microscope acquires magnitude & phase of backscattered field
- Under the first Born approximation, we acquire linear measurements of complex susceptibility $\eta = n^2 - 1$:

$$S(x, k_0; z_F) = \int A(x - x', z_F - z', k_0)\eta(x', z', k_0)\, dx'dz'$$
$$\Updownarrow \text{ (Fourier transform along } x\text{)}$$
$$\tilde{S}(q_x, k_0; z_F) = \int \tilde{A}(q_x, z_F - z', k_0)\eta(q_x, z', k_0)\, dz'$$



- We could obtain enough data to reconstruct η by scanning spatial dimensions (x, y, z) and wavelength k_0, but requires lengthy acquisition, massive storage, and expensive reconstruction

Question

Can we recovery η from a small number of foci?

Hyperspectral Tomography

- Asymptotic approximation to forward model at one focal plane:

$$\tilde{S}(q_x, k_0; z_F) = \int \tilde{A}(q_x, z_F - z', k_0)\eta(q_x, z', k_0)\, dz'$$
$$\approx H(q_x, k_0) \cdot \mathcal{F}_{z\to q_z}\left\{W(\cdot - z_F, k_0) \cdot \eta(q_x, \cdot, k_0)\right\}\Big|_{q_z=-2\sqrt{k_0^2-\frac{q_x^2}{4}}}$$

- $H(q_x, q_y, k_0)$: Bandpass filter: limiting aperture, diffraction limit
- $W(z - z_F, k_0)$: Decay of illumination away from focus
- Measurements are proportional to bandlimited Fourier transform of $\eta \cdot W$ along a trajectory controlled by q_x, q_y, and k_0.
  - 3D slice of a 4D object!

Observable locations of $\mathcal{F}\{W \cdot \eta\}(q_x, q_z, k_0)$

Low-Rank Object Model

- Assume object comprises N_s distinct chemical species

$$\eta(x, y, z, k_0) = \sum_{j=1}^{N_s} \underbrace{p_j(x, y, z)}_{\text{spatial density}} \cdot \overbrace{f_j(k_0)}^{\text{spectral signature}}$$

- Measurements are linear in p_j if the f_j are fixed:

$$\tilde{S}(q_x, z_F, k_0) = \sum_{j=1}^{N_s} f_j(k_0) \underbrace{\int \tilde{A}(q_x, z_F - z', k_0)p_j(q_x, z')\, dz'}_{\text{ISAM}}$$
$$\Updownarrow \text{ Discretization (sampling } q_x, k_0 \text{ for fixed } z_F\text{)}$$
$$\tilde{\mathbf{s}}_{z_F} = \sum_{j=1}^{N_s} \underbrace{\text{diag}\left\{f_j\right\}}_{\triangleq \mathbf{D}_j} \mathbf{A}_{z_F}\mathbf{p}_j$$

Comparison to FTIR/OCT

Existing imaging modalities reconstruct η under severe restrictions on the structure of the sample. Our low-rank constraint is a compromise between these restrictions and arbitrary samples.

Method	Object	Degrees of Freedom
Scanning	$\eta(x, y, z, k_0)$	$N_xN_yN_zN_{k_0}$
OCT	$p(x, y, z)f(k_0)$	$N_{k_0} + N_xN_yN_z$
FTIR (Bulk)	$f(k_0)$	N_{k_0}
FTIR (Thin)	$p(x, y)f(k_0)$	$N_{k_0} + N_xN_y$
Proposed	$\sum_{j=1}^{N_s} p_j(x, y, z)f(k_0)$	$N_s(N_{k_0} + N_xN_yN_z) - N_s^2$

Block Matrix Form

$$\begin{bmatrix} \tilde{\mathbf{s}}_{z_{F1}} \\ \tilde{\mathbf{s}}_{z_{F2}} \\ \vdots \\ \tilde{\mathbf{s}}_{z_{FN_F}} \end{bmatrix} = \begin{bmatrix} \mathbf{D}_1\mathbf{A}_{z_{F1}} & \mathbf{D}_2\mathbf{A}_{z_{F1}} & \dots & \mathbf{D}_{N_s}\mathbf{A}_{z_{F1}} \\ \mathbf{D}_1\mathbf{A}_{z_{F2}} & \mathbf{D}_2\mathbf{A}_{z_{F2}} & \dots & \mathbf{D}_{N_s}\mathbf{A}_{z_{F2}} \\ \vdots & \vdots & \ddots & \vdots \\ \mathbf{D}_1\mathbf{A}_{z_{FN_F}} & \mathbf{D}_2\mathbf{A}_{z_{FN_F}} & \dots & \mathbf{D}_{N_s}\mathbf{A}_{z_{FN_F}} \end{bmatrix} \begin{bmatrix} \mathbf{p}_1 \\ \mathbf{p}_2 \\ \vdots \\ \mathbf{p}_{N_s} \end{bmatrix}$$

Spatial densities $\mathbf{p}_j$ recoverable (within optical passband) when spectra are known, linearly independent and $N_F \geq N_S$

Reconstruction: Dictionary of Species

- Suppose $s < N_s$ active species from a set of candidate species ("materials dictionary"): $\{f_j(k_0)\}_{j=1}^{N_s}$
- $\phi(\mathbf{P}) = \sum_{j=1}^{N_s}\|\mathbf{p}_j\|_2 \Longrightarrow$ reconstruction with few active species
- Conjecture: recovery possible for $N_F = C \cdot s \leq N_s$

Reconstruction: Known Species

Penalized Weighted Least Squares

$$\arg\min_{\mathbf{P}} \sum_{z_F} \frac{1}{2}\|\tilde{\mathbf{s}}_{z_F} - \sum_{j=1}^{N_s} \mathbf{D}_j\mathbf{A}_{z_F}\mathbf{p}_j\|_2^2 + \lambda \underbrace{\phi(\mathbf{P})}_{\text{regularizer}}$$

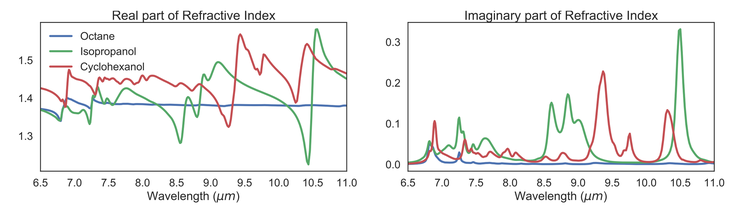
- Regularization is necessary to overcome null space of imaging system and to incorporate prior information on structure of $\mathbf{P} = [\mathbf{p}_1, \mathbf{p}_2, \dots \mathbf{p}_{N_s}]^T$
  - $\phi(\mathbf{P}) = \sum_{j=1}^{N_s}\|\mathbf{p}_j\|_2^2$ (minimum-norm solution)
  - $\phi(\mathbf{P}) = \sum_{j=1}^{N_s}\|\Psi\mathbf{p}_j\|_1$ (sparsity in a basis)
- Solve using your favorite algorithm
  - Tikhinov regularization: Conjugate Gradient
  - Otherwise: Alternating Direction Method of Multipliers

Simulation: Point Scatterers

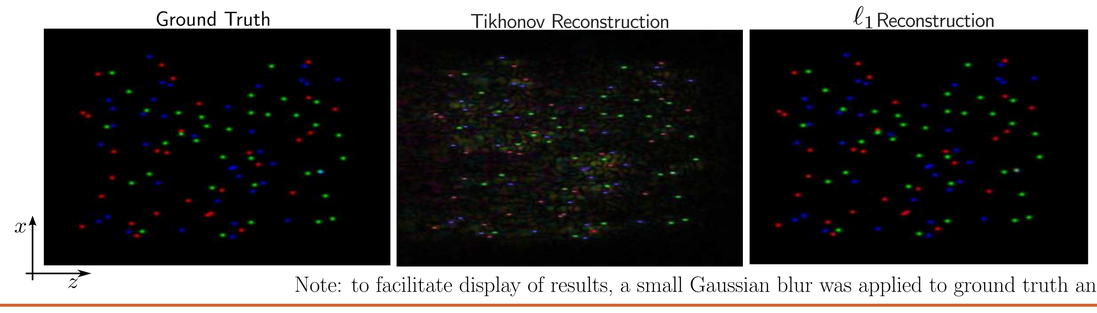
Setup

- Synthetic measurements from point scatterers (Foldy-Lax)
- Chemical spectra: FTIR measurements of bulk samples
- 3 focal planes distributed evenly in 512×512µm volume
- 256 wavelength samples between 6 to 11µm; NA = 0.5

Spectra $f_j(k_0)$



Reconstructions



Note: to facilitate display of results, a small Gaussian blur was applied to ground truth and ℓ_1

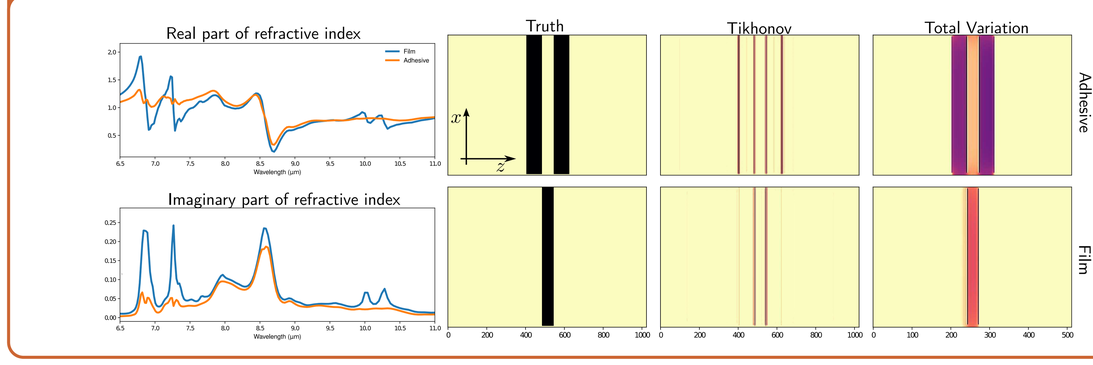
- Tikhinov recon: ringing/multiple scattering artifacts present; some leakage between species, but correct species largely identified
  - Tradeoff: large $\lambda \to$ fewer artifacts, but more leakage between species (smoothing)
- ℓ_1 recon: Negligible leakage, fewer artifacts. Natural choice for point scatterers!

Simulation: Tape

Setup

- 40µm film sandwiched between 50µm layers of adhesive
- Chemical spectra: FTIR of film+adhesive & film only.
- 256 wavelength samples between 6 to 11µm; NA = 0.5
- 3 focal planes in 256×1024µm volume

Reconstructions



- Tikhinov regularization $\Longrightarrow$ linear inversion; can't recover low spatial frequencies. Only edges are visible.
- Total variation: natural choice for piecewise constant objects; reasonable success at support identification.

References

[1] Fernandez, et al. "Infrared spectroscopic imaging for histopathologic recognition." Nature biotechnology, 2005.
[2] Im, et al. "Growth of CH3NH3PbI3 cuboids with controlled size for high-efficiency perovskite solar cells." Nature nanotech, 2014.
[3] Deutsch, et al. "Compositional prior information in computed infrared spectroscopic imaging." JOSA A, 2015.

Acknowledgments

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