Research Statement

My research activities are primarily focused on the signal processing and machine learning tool development for high-resolution high-sensitivity image reconstruction from real-world bio-medical imaging systems. One of the most important and challenging issues in this regard is overcoming the fundamental limitations of resolution and sensitivity with minimal invasiveness. Such problems pose interesting challenges that often lead to investigations of fundamental problems in various branches of physics, mathematics, signal processing, biology, and medicine.

While most of the biomedical imaging researchers are interested in addressing this problem using off-the-self tools from signal processing, machine learning, statistics, and optimization and combining their domain-specific knowledge: my approaches to biomedical imaging problems are unique in the sense that I believe that actual bio-medical imaging applications are a source of endless inspiration for new mathematical theories and I am eager to solve both specific applications and application-inspired fundamental theoretical problems. Specifically, I see that the imaging system and algorithm design problem is indeed a signal sampling problem under physical and biological constraints, so the resolution and sensitivity benefits can be maximized rigorously under given measurement samples. Thus, the primary issue is what rigor we should choose; and I am keen to determine this. This perspective has provided me with many rewarding experiences and a unique academic status as summarized below:

- **Academic Innovations:** *World-first demonstrations* of high resolution compressed sensing dynamic MRI *(k-t FOCUSS [1, 2]), self-reference quantitative phase microscopy [3], sparse dictionary learning for fMRI connectivity analysis [4, 5]*, deep learning for

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![Figure 1: Past and current research scopes.](image-url)
low-dose CT reconstruction \cite{6}, and non-iterative exact inverse scattering methods for diffuse optical tomography \cite{7, 8}, electric impedance tomography \cite{9}, and elastic wave imaging \cite{10}; world-first mathematical discoveries \cite{11} of the link between array signal processing and multiple measurement vector problems (Compressive-MUSIC \cite{11}), the link between Bedrosian identity and interior tomography problem \cite{12, 13}, the link between structured matrix completion and the sampling theory of finite rate of innovation (ALOHA \cite{14, 15}), and the link between deep learning and convolutional framelets (Deep Convolutional Framelets \cite{16}); the development of very popular toolboxes \cite{17} for functional near-infrared spectroscopy (NIRS-SPM \cite{17}) and super resolution microscopy (FALCON \cite{18, 19}).

• Broad and In-depth Research Scope: My research covers extensive arrays of medical imaging modalities such as MRI, x-ray CT, PET, ultrasound, optics, and neuro-imaging based on strong physics, biology and mathematical background; I have produced the world-leading results by winning several international challenges and producing high impact papers (see Fig. 1).

• Truly Interdisciplinary Research: My research spans neuroscience/biology, optics experiments, physics, computational algorithms, and fundamental mathematical theory; I have collaborated extensively with medical doctors, biologists, physicists, mathematicians, and engineers, and supervised the research of bioengineers, electrical engineers, medical doctors, and mathematicians.

• Application-driven Mathematical Theory: Unlike the most mathematicians and signal processors, all my theoretical works are inspired by real-world biomedical imaging applications. Examples: Inverse scattering application-inspired fundamental theory of joint sparse recovery \cite{11}, accelerated MRI-inspired fundamental theory of compressive sampling using low-rank interpolation \cite{14}, and deep learning-inspired deep convolutional framelets theory \cite{16}

• Extensive Technology Transfer: Successful IP licensing of imaging technology to domestic vendors (about $400,000 USD)

1 Significant Scientific Contributions

I have summarized a few of my contributions to biomedical imaging problems below.

1.1 Magnetic Resonance Imaging (MRI)

**k-t FOCUSS**

Imaging time-varying objects such as beating hearts or brain hemodynamics using an MRI requires significantly reducing the data acquisition time. Such aggressive acceleration would result in aliasing artifacts in classical MR imaging approaches. In a series of papers \cite{1, 2, 20, 21, 22, 23} with over 1,000 total citations, we identified the classical k-t BLAST as a sub-optimal approximation of
our compressed sensing dynamic MRI algorithm called k-t FOCUSS, which is optimal from a compressed sensing perspective (See Figure 2). Since the publication of k-t FOCUSS, a flurry of papers have been published by independent research teams all over the world comparing their algorithms with k-t FOCUSS. In a 2009 International Society for Magnetic Resonance in Medicine (ISMRM) Workshop in Sedona, the effectiveness of k-t FOCUSS was recognized by radiologists from various leading hospitals and I was awarded 1st Place at the Reconstruction Challenge of the ISMRM Workshop on Data Sampling and Image Reconstruction. In addition, intellectual properties related to k-t FOCUSS have been successfully transferred to industries.

**ALOHA: Annihilating filter-based low-rank Hankel matrix approach**

Standard compressed sensing approaches require alternative processing in k-space and the image domain, so using existing analytic recovery algorithms is difficult. To address this issue, we proposed an annihilating filter based low-rank Hankel matrix approach (ALOHA) as a general framework for a sparsity-driven k-space interpolation method that unifies pMRI and CS-MRI [14, 15, 24, 25, 26]. Specifically, our framework is based on the novel observation that the transform domain sparsity in the primary space implies the low-rankness of the weighted Hankel matrix in the reciprocal space. This converts pMRI and CS-MRI to a k-space interpolation problem using a structured matrix completion, as shown in Fig. 3.

![Figure 3: ALOHA implementation using pyramidal decomposition. Construction of Hankel matrices from (a) $k_x - k_y$ data by assuming that 2-D dyadic wavelet transform of images is sparse, and (b) $k_t$ subsampled data by assuming that dynamic images can be sparsified using spatial wavelet and temporal Fourier transform. Note that for the case of dynamic MRI, one dimensional weighting is required along the phase encoding direction, whereas 2-D weighting is necessary for the case of static imaging. The color coding in the Hankel structure matrix indicates the values of weighting.](image-url)

The ALOHA concept is so general that it can extend to MR artifact correction problems [25, 26]. For example, MR measurements from an EPI sequence produce Nyquist ghost artifacts that originate from inconsistencies between odd and even echoes. Several reconstruc-
tion algorithms have been proposed to reduce such artifacts, but most such methods require additional reference scans, parallel acquisition, or multi-pass acquisition. In [25], after converting a ghost correction problem into separate k-space data interpolation problems for even and odd phase encoding, our algorithm exploits an observation that the differential k-space data between even and odd echoes is a Fourier transform of an underlying sparse image. Accordingly, we can construct a rank-deficient Hankel structured matrix whose missing data can be recovered using an annihilating filter-based low rank Hankel structured matrix completion approach (ALOHA) as shown in Fig. 4.

![Figure 4: ALOHA-based EPI ghost correction algorithm flow for SE-EPI in vivo data with partial Fourier encoding.](image)

Other important MRI artifacts originate from various sources including MR system instability, patient motion, and inhomogeneities in gradient fields: such MRI artifacts are usually considered irreversible, so additional artifact-free scans or navigator scans are necessary. We proposed a novel robust ALOHA approach in [26] for the removal of various MRI artifacts to overcome these limitations. Specially, because MR artifacts usually appear as sparse k-space components, the low-rank Hankel matrix from underlying artifact-free k-space data can be exploited to decompose sparse outliers, and a the sparse + low-rank decomposition framework using a Hankel matrix can be used to remove MRI artifacts. Experimental results demonstrated that the proposed algorithm can correct MR artifacts including herringbone (crisscross) patterns, motion (see Fig. 5), and zipper artifacts without distorting the image [26].

1.2 Functional Near-Infrared Spectroscopy (fNIRS)

Another interesting and rewarding moment in my neuroimaging research was the development of one of the most popular statistical analysis toolboxes for functional near-infrared spectroscopy (fNIRS) [17, 27, 28, 29, 30]. Previously existing approaches found quantifying the
statistical significance of activation detection in fNIRS difficult. I realized that such statistical significance could be addressed as the excursion probability of an inhomogeneous random field.

Based on this idea, I provided the first rigorous formulation of $p$-value calculation in fNIRS analysis and published a public domain statistical analysis toolbox called NIRS-SPM that incorporates this idea. Since the web release of NIRS-SPM (http://bisp.kaist.ac.kr/NIRS_SPM), it has been downloaded more than 5,000 times by numerous institutions and it has been employed by various fNIRS systems vendors across the world. For example, Shimadzu Co. of Japan graciously invited me to Tokyo to open the first NIRS-SPM short course for their Shimadzu fNIRS system users working with NIRS-SPM. Furthermore, I am proud that NIRS-SPM is the only Korean neuroimaging toolbox registered at the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC), the NITRC being funded by the National Institutes of Health Blueprint for Neuroscience Research (http://www.nitrc.org/projects/nirsspm/). My contributions to the fNIRS community garnered me an invitation to write a review article on the statistical analysis of fNIRS in the 2014 special issue of NeuroImage to celebrate 20 years of functional near-infrared spectroscopy [31].

1.3 Sparse SPM for Functional Connectivity MRI (fc-MRI)

Recent studies of functional connectivity MR imaging have revealed that default-mode network activity is disrupted in diseases such as Alzheimer’s disease (AD). However, there is currently no consensus on the preferred method for resting-state analysis. As the brain reportedly has complex interconnected networks according to graph theoretical analysis, the independency assumption in the popular independent component analysis (ICA) approach often does not hold. In [4, 5], instead of using the independency assumption, we presented a new statistical parameter mapping (SPM)-type analysis method based on a sparse graph model in which the temporal dynamics at each voxel position were described as a sparse combi-
nation of global brain dynamics. If we further assume that local network structures within a group are similar, we have demonstrated for the first time that the estimation problem of global and local dynamics can be solved using sparse dictionary learning, as shown in Fig. 7 where the global dictionary updates and global seed-based clustering are alternatively applied. Moreover, under the homoscedasticity variance assumption across subjects and groups that is often used in SPM analysis, the aforementioned individual and group analyses using sparse dictionary learning can be accurately modeled using a mixed-effect model, which also facilitates a standard SPM-type group-level inference using summary statistics. We used an extensive resting fMRI data set obtained from normal, mild cognitive impairment (MCI), and Alzheimer's disease patient groups to demonstrate that the subnetwork structure can be easily identified - as shown in Fig. 8 - and the changes in the default mode network extracted by the proposed method are more closely correlated with the progression of Alzheimer's disease [5].

![Figure 8: All networks extracted by SSPM.](image)

### 1.4 Optics for Biological Imaging

Optical bioimaging is another of my favorite research topics. In the course of developing image reconstruction algorithms, I was interested in applying mathematical insight to real system development. Thus, I started to building optical benches to invent new optical imaging systems based on the mathematical principle. These efforts resulted in various achievements including the hardware implementation of the world-first self-reference quantitative phase microscopy [3], ultra-fast terahertz imaging systems [32, 33, 34, 35, 36], and speckle-based super-resolution microscopy [37]; and software tools for deconvolution microscopy [38], super-resolution microscopy [18, 19], and diffuse optical tomography [7, 39].

For example, structured illumination microscopy (SIM) breaks the optical diffraction limit by illuminating a sample with a series of line-patterned lights, but the illumination patterns have strin-
Research Statement

Jong Chul Ye, Ph.D.

Research Statement

gent associated conditions.

In [37], we presented a novel speckle illumination microscopy technique that overcomes the diffraction limit by exploiting the minimal requirement that all existing super-resolution microscopy have in common, i.e., that the fluorophore locations do not vary during the acquisition time (see Fig. [9]). Our proposed method succeeds for standard fluorescence probes and experimental protocols, thus it can be applied in routine biological experiments.

On the other hand, super-resolution microscopy systems such as STORM and (F)PALM are now well-known methods for nanometer-scale biological studies. However, conventional imaging schemes based on the sparse activation of photo-switchable fluorescent probes have inherently slow temporal resolutions, which is a serious limitation when investigating live-cell dynamics. In [18, 19], we presented the fast and unbiased reconstruction of high-density super-resolution microscopy data (FALCON), which combined a sparsity-promoting formulation with the Taylor series approximation of the PSF. We validated our algorithm for both simulated and experimental data and demonstrated live-cell imaging with a 2.5 s temporal resolution by recovering fast ER dynamics (see Fig. [10]).

One major limitation of existing sparsity-driven approaches for super-resolution microscopy is the need for a fine sampling grid or for Taylor series approximation, which may result in a degree of localization bias towards the grid. Furthermore, they require prior knowledge of the point-spread function (PSF). We sought to address these drawbacks: in [40], we proposed a true grid-free localization algorithm with adaptive PSF estimation. Specifically, the proposed method converts source localization problems into Fourier-domain signal processing problems based on the observation that sparsity in the spatial domain implies a low rank in the Fourier domain, so that a true grid-free localization was possible. We verified the performance of the newly proposed method with several numerical simulations and a live-cell imaging experiment as shown in Fig. [11].
1.5 X-ray Computed Tomography (CT)

Due to the potential risk of inducing cancer, reducing the radiation does is one of x-ray CT’s most important research topics, so the interior tomography has been extensively studied as a possible alternative. In addressing the classic interior tomography problem in which projections at each view only extend to the shadow of a circular region that is completely interior to the subject being scanned, we showed that the exact recovery of 2D and 3D piecewise smooth images is guaranteed using a 1D generalized total variation semi-norm penalty that permits much faster reconstruction [13]. We proposed a novel multiscale reconstruction method that

![Figure 12: Reconstructed images by the truncated circular cone-beam simulation of the 3D XCAT phantom. For the simulation, the $K$ of the $L$ is 1, and the iteration number of the POCS is 30. The $l$ and $v$ are 0 and 0.0309, respectively, and the $\lambda$ is 0.02, and $N$ is 20. The depth of the multiscale implementation is 2. From the first to third column, each column shows the slice image when the slice number is (a) 50, (b) 105, and (c) 180 when the mid-plane is the 160th slice, and each row is for the ideal phantom, FDK, BPF, 3D TV, and proposed method. The last column shows the cut views indicated by the white line on the images. The number written at the corner of the reconstructed image shows the RMSE and NRMSE in the HU scale.](image-url)
exploits the Bedrosian identity of the Hilbert transform in [12] to further accelerate the algorithm up to a level for clinical use.

Specifically, we showed that the high frequency parts of 1D signals can be quickly recovered analytically with a Hilbert transform because of the Bedrosian identity: this implies that computationally expensive iterative reconstruction only needs to be applied to low resolution images in the downsampled domain, which significantly reduces the computational burden. Moreover, we demonstrated that the proposed multiscale interior tomography approach can be combined with a novel spectral blending method to mitigate cone-beam artifacts from missing frequency regions, even for incomplete trajectories such as circular cone-beam geometry (see Fig. 12). We showed the efficacy of the proposed multiscale algorithm using circular fan-beam, helical cone-beam data, and circular cone-beam geometry. We demonstrate that the speed of the algorithm could be significantly accelerated with a graphics processing unit (GPU) implementation to a suitable level for clinical use in various acquisition geometries [12].

1.6 Non-iterative Exact Inverse Scattering

Inverse scattering problems arise from various bio-medical imaging applications that use electromagnetic, diffuse photon density, elastic wave propagation, etc. However, the inverse problem of the quantitative evaluation of constitutive parameters from scattered waves is notorious for its complexity and ill-posed characteristics. Many dedicated mathematical and computational algorithms for the reconstruction of location and the parameters of anomalies of different geometrical natures have been proposed over the past few decades. Most classical techniques are based on either linearizations with respect to the leading order of the scale factor of inclusions, or variations in the constitutive parameters. Born, Rytov and Foldy-Lax-type approximations are also adopted. These simplifications are not always valid and are too strong to allow for accurate reconstruction, which results in a dramatic loss of image resolution and quality. The algorithms that avoid such assumptions usually require iterative updates and there are only a handful of direct reconstruction algorithms in the literature. Specifically, these techniques are computationally very expensive and are highly prone to instabilities, as they require the computation of numerous forward solutions for iterative updates and suffer from problems’ intrinsic ill-posedness. In a nutshell, the existing results found in the literature are clearly unsatisfactory in practice.

In a series of papers on diffuse optical tomography [7, 8], electric impedance tomography [9] and elastic imaging problems [10], we proposed an accurate novel imaging algorithm for

![Figure 13: 3D reconstruction of tumors embedded in the mouse phantom with (a) conventional MUSIC, (b) generalized MUSIC criterion, and linearized reconstruction approaches using (c) Tikhonov regularization, and (d) l1-penalty regularization. The scattered flux is corrupted by additive Gaussian noise of SNR 40dB.](image)
the reconstruction of multiple inclusions that are present in a bounded isotropic homogeneous formation. One of the proposed algorithm's most important features is that it does not require linearization or iterative updates of Green's function, yet it felicitously furnishes the spatial support of inclusions and their material parameters very accurately. This breakthrough comes from a novel interpretation of the Lippmann-Schwinger type integral representation of the displacement field derived in terms of unknown densities having jointly sparse spatial support for the location of inclusions. Therefore, the support identification problem can be recast as a joint sparse recovery problem for the unknown densities, given that the support set of inclusions is itself sparse. This allows the invoking of various compressed sensing signal recovery algorithms. Consequently, when using any one of such algorithms, a solution can be obtained to the joint sparse recovery problem that yields both the spatial support of inclusions and renders unknown densities. For example, as shown in Fig. 13, the new algorithm outperforms existing algorithms and reliably reconstructs optical inhomogeneities in diffuse optical tomography problems. This clearly indicates that the proposed formulation may be so general that it can provide a unified reconstruction framework for assorted inverse scattering problems.

1.7 Application-inspired Mathematical Theory

Compressive MUSIC

While applying compressed sensing for biomedical imaging such as super-resolution microscopy and inverse scattering problems, I quickly became interested in the theoretical aspect of the so-called multiple measurement vector (MMV) problem, in which jointly sparse signals of unknown value are measured through the same imaging sensors. As MMV problems are found in many medical imaging applications such as Electroencephalography (EEG), Magnetoencephalography (MEG), and diffuse optical tomography, many researchers have investigated this problem using either compressed sensing or classical array signal processing. However, I thought it strange that the apparent dichotomy between the probabilistic compressed sensing and deterministic sensor array signal processing approaches had not been fully explored. As set forth in a paper published in IEEE Transactions on Information Theory [11], I discovered the fundamental geometry in MMV problems that lends itself to the natural hybridization of compressed sensing and array signal processing. The new algorithm, called Compressive MUSIC (CS-MUSIC), identifies partial support using compressed sensing, after which the remaining supports are estimated using a novel generalized MUSIC criterion. More specifically, in rank deficiency measurement vectors, the true support vector \( a_j \) is not orthogonal to the standard noise subspace from the multiple signal classification (MUSIC) algorithm \( R(Q) \) as shown in Fig. 14. However, if we augment partial support \( A_{1:k-r} \) and calculate its orthogonal complement \( R(P_{R(Q)} - P_{R(\text{gg})} A_{1:k-r}) \), the true support \( a_j \) is now orthogonal to the new subspace. We used a large system MMV model to show that our compressive MUSIC requires fewer sensor elements to achieve accurate support recovery than the existing CS methods and that it could approach the optimal sampling rate with a finite number of snapshots, even in cases where the signals were linearly dependent.
Compressive Sampling using Low-rank Interpolation

While compressed sensing theory provides the opportunity to overcome the Nyquist limit in various biomedical imaging problems, a solution approach typically takes the form of an inverse problem for an unknown signal, which is crucially dependent on specific signal representation. In another IEEE Trans. on Information Theory paper [14], we proposed a drastically different two-step Fourier compressive sampling framework in a continuous domain that could be implemented via measurement domain interpolation, after which signal reconstruction can be performed through classical analytic reconstruction methods. The main idea originates from the fundamental duality between the sparsity in the primary space and the low-rankness of a structured matrix in the spectral domain, which show that a low-rank interpolator in the spectral domain can enjoy all the benefits of sparse recovery with performance guarantees. Most notably, the proposed low-rank interpolation approach can be regarded as a generalization of recent spectral compressed sensing to recover large classes of finite rate of innovations (FRI) signals at a near-optimal sampling rate. Moreover, in the instance of cardinal representation, we can show that the proposed low-rank interpolation scheme benefits from inherent regularization and the optimal incoherence parameter. We used a powerful dual certificate and the golfing scheme to show that the new framework could still achieve a near-optimal sampling rate for a general class of FRI signal recovery, while the sampling rate could be further reduced for a class of cardinal splines [14]. Numerical results using various types of FRI signals confirmed that the proposed low-rank interpolation approach offered significantly better phase transitions than conventional CS approaches.

2 Current Work and Research Goals

Ever since our group demonstrated the world-first deep learning algorithm for low-dose CT reconstruction and won second prize at the 2016 American Association of Physicists in Medicine (AAPM) X-ray CT Low-dose Grand Challenge [6], the new field of machine learning-based image reconstruction has grown exponentially and deep learning approaches with various network architectures have achieved significant performance improvements over existing iterative reconstruction methods for various imaging problems. Thanks to our pioneering work, I was invited to be a guest editor for the IEEE Trans. Medical Imaging special issue on machine learning for image reconstruction. Due to its stellar performance with minimal run-time complexity, I believe that the machine learning-based biomedical image reconstruction is a revolutionary technology in biomedical imaging area and I am fully dedicated to this new exciting research area in the future. Let me briefly elaborate on the preliminary developments from our group that are related to these concepts, which will be a starting
2.1 Deep Convolutional Framelets for Inverse Problems in Biology and Medicine

While deep learning approaches with various network architectures have achieved significant performance improvements over existing iterative reconstruction methods, it remained unclear why these deep learning architectures work for specific inverse problems. Moreover, unlike the usual evolution of signal processing theory around classical theories, the link between deep learning and classical signal processing approaches such as wavelets, non-local processing, and compressed sensing remains poorly understood.

We have sought to address this issue in our recent work [16] by showing that the long-sought-for missing link is convolutional framelets that represents a signal by convolving local and non-local bases. Convolutional framelets were originally developed by Yin et al. [41] to generalize the theory of low-rank Hankel matrix approaches for inverse problems, and we significantly extended the idea to derive a deep neural network using multi-layer convolutional framelets with perfect reconstruction (PR) under rectified linear unit (ReLU) nonlinearity. Our analysis also shows that popular deep network components such as residual blocks, redundant filter channels, and concatenated ReLU (CReLU) indeed help achieve the PR, while pooling and unpooling layers should be augmented with multi-resolution convolutional framelets to achieve PR condition. This discovery suggests that deep learning’s success is not from the magical power of a black-box, but instead from the power of a novel signal representation using a non-local basis combined with data-driven local basis, which is indeed a natural extension of classical signal processing theory.

More specifically, let $\Phi \in \mathbb{R}^{n \times m}$ (resp. $\Psi \in \mathbb{R}^{d \times q}$) be the frame and its dual frame, respectively, that satisfy the frame condition:

$$\tilde{\Phi} \Phi^\top = I_{n \times n}, \quad \Psi \tilde{\Psi}^\top = I_{d \times d}. \quad (1)$$

We refer to $\Psi$ and $\Phi$ as the local and non-local bases, respectively. Here, the column of the local basis $\Psi$ and $\tilde{\Psi}$ are referred to as local filters and its dual filters. In addition, the columns of $\Phi$ denote non-local filters. Then, for any $n$-dimensional vector $f \in \mathbb{R}^n$, Yin et al. [41] showed the following convolutional framelet expansion:

$$f = \frac{1}{d} \sum_{i=1}^{m} \sum_{j=1}^{q} \langle f, \phi_i \odot \psi_j \rangle \tilde{\phi}_i \odot \tilde{\psi}_j \quad (2)$$
where $\circledast$ denotes the circular convolution, and $\phi_i$ and $\psi_i$ denote the $i$-th column of $\Phi$ and $\Psi$, respectively; $\{\phi_i \circledast \psi_j\}$ and $\{\phi_j \circledast \psi_i\}$ then constitute the frame bases and its dual, respectively. Furthermore, they showed that for a fixed non-local bases $\Phi$ and $\Phi$, the local bases $\Psi$ and $\Psi$ can be optimally learned from the data such that the framelet coefficients $\langle f, \phi_i \circledast \psi_j \rangle$ can be sparsified. This allows for image denoising by retraining a small set of framelet coefficients using the shrinkage operation.

One of the most important discoveries made in our pioneering work [16] is the demonstration that (2) can be equivalently represented by two convolution operations: the decoder-part convolution is given by

$$f = \left(\tilde{\Phi} C\right) \circledast \tau(\tilde{\Psi}) \quad (3)$$

where $C$ is the framelet coefficient matrix obtained from the encoder-part convolution:

$$C = \Phi^T (f \circledast \Psi) \quad (4)$$

Here the local filters for the encoder and decoder part convolutions are given by

$$\Psi := \begin{bmatrix} \psi_1 & \cdots & \psi_q \end{bmatrix} \in \mathbb{R}^{d \times q}, \quad \tau(\tilde{\Psi}) := \frac{1}{d} \begin{bmatrix} \tilde{\psi}_1 \\ \vdots \\ \tilde{\psi}_q \end{bmatrix} \in \mathbb{R}^{dq}.$$  

The convolution in (4) is the single-input multi-output (SIMO) convolution, whereas the convolution in (3) corresponds to the multi-input single-output (MISO) convolution [16]. This implies that an interesting CNN structure emerges from the convolutional framelets. More specifically, if $\Phi = I$, then the structure in (3) and (4) is in fact equivalent to one layer of the encoder-decoder network [42], as shown in Fig. 16(a). Obtaining a multi-layered CNN structure requires that the convolutional framelet expansion is extended for multiple inputs, because a SIMO convolution generates multiple outputs. More specifically, for a given matrix input $Z \in \mathbb{R}^{n \times p}$, we have the following convolutional framelet expansion [16]:

$$Z = (\Phi C) \circledast \tau(\tilde{\Psi}) \quad (5)$$

where the framelet coefficients $C$ is given by

$$C = \Phi^T (Z \circledast \Psi) \quad (6)$$

Here, the encoder and decoder filters are defined by

$$\Psi := \begin{bmatrix} \psi_1^1 & \cdots & \psi_q^1 \\ \vdots & \ddots & \vdots \\ \psi_1^p & \cdots & \psi_q^p \end{bmatrix} \in \mathbb{R}^{dp \times q}, \quad \tau(\tilde{\Psi}) := \frac{1}{d} \begin{bmatrix} \tilde{\psi}_1^1 \\ \vdots \\ \tilde{\psi}_q^1 \\ \vdots \\ \tilde{\psi}_1^p \\ \vdots \\ \tilde{\psi}_q^p \end{bmatrix} \in \mathbb{R}^{dq \times p} \quad (7)$$

and the convolution in (5) and (6) correspond to the multi-input multi-output (MIMO) convolution [16]. The simple convolutional framelet expansion using (3), (5), (4) and (6) is so powerful that the deep CNN architecture can emerge from them. Specifically, by inserting the pair of (6) and (5) between the pair of (4) and (3), a deep CNN structure as shown in Fig. 16(b) can be interpreted as the multi-layered convolutional framelet expansion.
2.2 Machine Learning for Biomedical Image Reconstruction

Inspired by the theoretical findings of deep convolutional framelets, I have been investigating various extensions and biomedical imaging applications. In fact, the designing problems are 1) how to determine the optimal combination of the non-local basis from physics principles, and 2) what types of cost functions should be used for valid training without over-fitting. In the following, I show a few examples of the successful real-world biomedical imaging applications of our theoretical findings, but I am dedicated to explore further applications that are associated with important biology and clinical needs.

X-ray CT

We addressed the low-dose CT reconstruction problem by proposing the world’s first deep convolutional neural network (CNN) for low-dose X-ray CT and won second place at the 2016 AAPM Low-Dose CT Grand Challenge [6]. However, some of the texture was not fully recovered. We sought to cope with this problem in [43] by proposing a deep residual learning approach in directional wavelet domain. The proposed method is motivated by the observation that a deep convolutional neural network can be interpreted as a multilayer convolutional framelets expansion using a non-local basis that is convolved with a data-driven local basis. We further extended the idea to derive a deep convolutional framelet expansion by combining global redundant transforms and signal boosts from multiple signal representations. Extensive experimental results confirmed that the proposed network’s performance was significantly improved performance and the detailed texture of the original images was preserved (see Fig. 18).

Although X-ray computed tomography (CT) using sparse projection views was often used to reduce the radiation dose, the insufficiency of the projection views means that a reconstruction approach using a filtered back projection (FBP) produced severe streaking artifacts. Recently, deep learning approaches using large receptive field neural networks such as U-net have demonstrated impressive performance for sparse view CT reconstruction. However, the theoretical justification is still lacking. In [44], we developed a mathematical theory and discussed how to improve these algorithms. Moreover, inspired by the recent theory of deep convolutional framelets, we showed that the U-net for image recovery relies on a sub-optimal non-local bases that places too much emphasis on low frequency components. This discovery leads to dual frame and tight frame U-net architectures for the effective recovery of directional image components.

Figure 17: The proposed WavResNet architecture for low-dose X-ray CT reconstruction.
MRI

Accelerated MR acquisition with compressed sensing and parallel imaging algorithms is a powerful method of reducing the scan time in MR imaging. However, many reconstruction algorithms have high associated computational costs. Moreover, most algorithms require k-space data, which is unavailable in many routine experiments. We addressed this by investigating deep residual learning networks in the image domain that directly remove the aliasing artifacts from the artifact-corrupted images [45]. Specifically, our deep residual learning networks are composed of magnitude and phase networks, so the magnitude network could be used without access to k-space data. Furthermore, we provided a mathematical theory for proposed residual networks using the recent theory of deep convolution framelets. We used extensive comparative studies using 3T and 7T data to show that the deep residual networks provide good reconstruction results and the computational time is orders of magnitude faster than existing CS methods from single and multi-coil data (see Fig. 19).

In another application [46], a transfer-learning based algorithm was developed for accelerated projection reconstruction MRI. The proposed deep network estimated the streaking artifacts from insufficient k-space radial spokes. Once the streaking artifacts were estimated, an artifact-free image could then be obtained by subtracting the estimated streaking artifacts from the distorted image. We addressed the situation given the limited available data in [46] by proposing a domain adaptation scheme that employs a pre-trained network using a large number of x-ray computed tomography (CT) data sets, which was then fine-tuned with only a few MR data sets. The proposed deep learning method surpassed the existing compressed sensing algorithms in terms of both image quality and computation time. In addition, we
were the first to demonstrate the possibility of a domain-adaptation approach from CT to MRI when only limited amount of MR data was available.

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**Figure 19:** Reconstruction results of magnitude images using proposed network for 7T MR images.

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**Publications**


Research Statement

Jong Chul Ye, Ph.D.


