A generalized reconstruction framework for unconventional PET systems

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(Received 12 November 2014; revised 25 May 2015; accepted for publication 16 June 2015;
published 13 July 2015)

Purpose: Quantitative estimation of the radionuclide activity concentration in positron emission tomography (PET) requires precise modeling of PET physics. The authors are focused on designing unconventional PET geometries for specific applications. This work reports the creation of a generalized reconstruction framework, capable of reconstructing tomographic PET data for systems that use right cuboidal detector elements positioned at arbitrary geometry using a regular Cartesian grid of image voxels.

Methods: The authors report on a variety of design choices and optimization for the creation of the generalized framework. The image reconstruction algorithm is maximum likelihood-expectation-maximization. System geometry can be specified using a simple script. Given the geometry, a symmetry seeking algorithm finds existing symmetry in the geometry with respect to the image grid to improve the memory usage/speed. Normalization is approached from a geometry independent perspective. The system matrix is computed using the Siddon's algorithm and subcrystal approach. The program is parallelized through open multiprocessing and message passing interface libraries. A wide variety of systems can be modeled using the framework. This is made possible by modeling the underlying physics and data correction, while generalizing the geometry dependent features.

Results: Application of the framework for three novel PET systems, each designed for a specific application, is presented to demonstrate the robustness of the framework in modeling PET systems of unconventional geometry. Three PET systems of unconventional geometry are studied. (1) Virtual-pinhole half-ring insert integrated into Biograph-40: although the insert device improves image quality over conventional whole-body scanner, the image quality varies depending on the position of the insert and the object. (2) Virtual-pinhole flat-panel insert integrated into Biograph-40: preliminary results from an investigation into a modular flat-panel insert are presented. (3) Plant PET system: a reconfigurable PET system for imaging plants, with resolution of greater than 3.3 mm, is shown. Using the automated symmetry seeking algorithm, the authors achieved a compression ratio of the storage and memory requirement by a factor of approximately 50 for the half-ring and flat-panel systems. For plant PET system, the compression ratio is approximately five. The ratio depends on the level of symmetry that exists in different geometries.

Conclusions: This work brings the field closer to arbitrary geometry reconstruction. A generalized reconstruction framework can be used to validate multiple hypotheses and the effort required to investigate each system is reduced. Memory usage/speed can be improved with certain optimizations.

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Key words: positron emission tomography (PET), image reconstruction, arbitrary geometry, symmetry, unconventional PET systems

1. INTRODUCTION AND BACKGROUND

Positron emission tomography (PET)¹ has become a major clinical imaging modality for the study of functional processes. For whole-body imaging capability across a wide patient population and increased sensitivity, the majority of these systems have used a ring geometry. The last two decade

has seen research into customized geometries that trade global utility for application specific performance (breast,^{2–6} small animals,^{7–10} and imaging probes^{11–14}). A variety of individual reconstruction codes have been developed by investigators for specific systems. The commonly used algorithm used for estimation of PET images is the expectation-maximization (EM) algorithm¹⁵ or a variation, such as ordered subsets

expectation–maximization, generalized expectation–maximization, maximum *a posteriori* with one-step-late, maximum *a posteriori* with line search, rescaled block iterative expectation–maximization, or convergent ordered subsets expectation–maximization.¹⁶ Differences arise due to the data model used.

A reconstruction framework for arbitrary geometry was proposed by Hu *et al.*¹⁷ for prostate imaging. Achieving this goal requires further investigation such as the optimization of the framework, particularly the automatic computation of symmetries, choice of subsets, and normalization components. These choices are vital for the framework to be adaptable to a large subset of PET geometries, while simultaneously being able to reconstruct in an efficient manner.

We have been involved in developing novel PET imaging systems with unconventional geometries. Reconstruction for these challenging geometries requires a precise data model, comprising of a random and scatter model, normalization approach, and system matrix.¹⁸ Custom reconstructions for individual systems are time consuming and require repetitive effort. The goal of this work is to develop a general-purpose image reconstruction framework that provides a consistent postproduction reconstruction across different geometries to save developmental effort. By general purpose, we specifically mean that the framework can reconstruct images under different spatial arrangements of the cuboidal detector blocks of different sizes and materials. This unified framework may substantially contribute to the development and optimization of novel unconventional PET designs. Furthermore, the algorithms developed for such a framework may also benefit all reconstruction methods that require a forward and backward operator for PET.

Generalizing a design specific reconstruction program requires the rethinking of traditional design choices. We have also reworked a variety of data representation and manipulation routines existing in traditional PET reconstruction codes such that the advantage they offered is maintained in the general-purpose framework. For instance, the concept of sinogram, which requires thinking in terms of ring systems, is no longer applicable. Although sinograms helped in visualization of the data space before reconstruction, as well as compression in the data space through sinogram binning, they are not necessarily the most generic representation of data. In the proposed platform, the geometry of the PET system is specified in a simple MATLAB script which records the translation/rotation of each detector and its corresponding dimensions.

Traditional PET image reconstruction codes have taken advantage of the inherent symmetry in detector arrangement to reduce the processing time. Significant speedup of algorithm and lower storage requirement can be realized by estimating system matrix uniquely for detector pairs symmetrical to each other.¹⁹ To utilize symmetry in a general PET reconstruction, the framework automatically computes the symmetry in the system. For 3D PET reconstruction, Scheins *et al.*¹⁹ have previously proposed a method to exploit symmetries. Unlike ring or pseudoring geometries considered by their group, this work focuses on a more general class of PET geometries.

Acquiring and reconstructing data at different points in time helps visualize dynamic and complex molecular process. We have adjusted the framework to reconstruct sets of data jointly. Therefore, the framework is capable of reconstructing a single 3D image and multiple frames of independent 3D images. The framework is optimized through parallelization techniques using the open multiprocessing [OpenMP (Ref. 20)] and message passing interface [MPI (Ref. 21)] libraries.

The wide types of systems that the framework can reconstruct are shown through the application to each system. Each system to which we apply the framework investigates a different application, with PET as the underlying imaging modality. We show that treating lines of response (LORs) having different qualitative properties is unnecessary given that they are quantitatively modeled. For some of the systems presented, a large number of lines of response pass through detector crystals. Unlike prior implementations,^{18,22,23} we do not group and process the data differently.

2. METHODS

Reconstruction in PET is the task of estimating radionuclide activity concentration from detected coincidence events of 511 keV gamma rays. We denote the radioactivity concentration across the image space by a lexicographically ordered vector, $X = \{x_0, x_1, x_2, \dots, x_{N-1}\}$, where x_i is the rate of radioactive decay at the i th voxel.

Let the detected counts across the data space be represented by another random vector, $Y = \{y_0, y_1, y_2, \dots, y_{M-1}\}$, where y_j is the counts detected in j th detector pair and M is the number of detector pairs. The system matrix $H(j, i)$ is a function of the solid angle coverage of the image voxel by the detector pair and the interaction physics of gamma rays through the medium between the voxel and the detector. The expected counts at the detector pair, j , are the sum of $H(j, i)$ weighted radioactivity concentration from every image voxel.

The solution that we seek in this paper is the maximum likelihood estimate given by

$$x = \operatorname{argmax}_x \sum_j y_j \log \left(\sum_i H(j, i) \times x_i \right) - \sum_i H(j, i) \times x_i. \quad (1)$$

We have implemented the EM algorithm.²⁴ For k th iteration, the algorithm is compactly written as

$$x_i^{k+1} = \frac{x_i^k}{\sum_j H(j, i)} \times \left[\sum_j H(j, i) \times \frac{y_j}{\sum_i H(j, i) \times x_i^k} \right]. \quad (2)$$

Accurate estimation of the spatial distribution of radioactivity concentration requires correction of physical effects, by modeling them in the forward model. The forward model includes the emission system matrix, attenuation, and normalization that approximates the PET physics. The forward model used in this generalized platform is the same as that used in the work by Keesing *et al.*¹⁸

The attenuation image is computed by obtaining a CT image (when available), registering, and scaling it to 511 keV attenuation. This is forward projected through the system matrix weights, negated, and exponentiated to obtain attenuation

along a line of response. Alternatively, if the shape and composition of the object are known or can be estimated, attenuation coefficients can be calculated.^{26,27}

The proposed image reconstruction framework is broken down into several functional blocks as shown in Fig. 1. The geometry specific routines are only the specify geometry block and mapping block. The rest of the framework are written generally so as to be able to process any geometry given the specification files from the first block. The programs in the center block are the main routines for image reconstruction, normalization, projection, and sorting. The blocks on the right side are common routines used in the center blocks.

2.A. Specify geometry

The system geometry is specified using a MATLAB script. Each system consists of a collection of detector-units. Each detector-unit is a combination of detector crystals. Pairs of detector-units are termed detector-unit-pairs. For instance, the detector-units could potentially be defined as detector blocks. When symmetry of detector-unit-pairs is computed, the symmetry is computed only between detector-units and not within crystals belonging to a detector-unit. Defining detector-units as individual crystals enable the program to obtain the maximum symmetry. In this case, a detector-unit-pair is the same as a LOR. However, this slows the symmetry computation and leads to integer overflow for complex PET systems. Therefore, in all the PET systems that are discussed in this paper, we group individual crystal elements into detector-units that are smaller than a detector block.

Each detector-unit is treated as a MATLAB struct variable, having a box struct inside it to specify the position and orientation of the unit. It is assumed that the detector-unit is cuboid. The orientation of the detector-unit is specified by storing the eight vertices of the cuboid as well as three face normal vectors. The detector-unit struct variable records the number of crystals along each dimension of the detector-unit. The detector-unit is assumed to be uniformly cut in each of

the dimensions by the number of crystals. The subcrystal approach²⁸ of computing the system matrix requires further subdivision of the crystals into subcrystals. Three variables denoting the number of subcrystal cuts in each crystal along each dimension are also stored in the struct variable. The system designer can position detector-units using a series of translations and rotations.

The output is a plain text file which records contents of all the detector-units such as the center, vertices, face normals of the detector-unit box, as well as number of crystal elements and subcrystal cuts along each detector-unit dimension. A visualization of the geometry is generated automatically. This generated visualization is shown in Sec. 3 as an illustration for each system.

2.B. Compute symmetry

The compute symmetry block finds those detector-unit-pairs that are symmetrical to each other on a regular rectangular grid. This information is used later to compute the system matrix only on a representative detector-unit-pair of each symmetrical set. This reduces the system matrix size as well as increases the speed of system matrix computation.

The methodology undertaken is to find a set of parameters that define each nonsymmetrical pair of detector-units uniquely but have the same value for all detector-unit pairs within a symmetrical group. The symmetry property arises from the interplay between the location of detector-units and the image grid.

For completeness, we introduce the following notation. We operate on a regular Cartesian grid of image voxels. Let the global coordinate system be indexed by (x, y, z) .

Assuming that all detector-units are right cuboids, the rigid body rotation of a detector-unit with respect to a reference orientation can be represented by a set of three Euler rotational angles. All detector-units in the geometry are defined as a rotated, translated version of a reference detector-unit orientation. The reference detector-unit has a fixed frame axes

FIG. 1. Reconstruction framework block diagram.

(X,Y,Z) . Each detector-unit, p , has a position, $\vec{C} = [C_x, C_y, C_z]^T$, on the global coordinate system.

Let each detector-unit in geometry be indexed and (p,q) define a detector-unit-pair whose first detector-unit has index p and second detector-unit has index q . Since (p,q) pair is same as (q,p) , and $p \neq q$, we consider only (p,q) where $p < q$.

From this minimalistic set definition, we can uniquely encode all detector-unit-pairs using a 12 element parameter vector, comprising of position of first detector-unit, position of second detector-unit, Euler rotational angles of first detector-unit, and Euler rotational angles of second detector-unit.

2.B.1. Property of symmetry

Symmetry is invariance under a transformation. For instance, mirror symmetry implies that the features of object remain the same during a mirroring operation. From our previous definition of encoding the state of a detector-unit-pair based on a unique parameter vector, we see that an operation such as mirroring or rotation changes the values of each of the parameters. Therefore, symmetry cannot be inferred from the above parameter vector as it exists. The solution is to convert the original parameter vector into a feature vector, where symmetrical detector-unit-pairs have same feature vector. In effect, the transformation that maps the original parameter vector to the feature vector is an invariant operation of symmetry.

The two properties that must be satisfied by the invariant operation, $\mathcal{T}$, are

1. property A: $\mathcal{T}(x_1) = \mathcal{T}(x_2) \Rightarrow x_1, x_2 \in \mathcal{S}_i$ and
2. property B: $x_1 \in \mathcal{S}_i, x_2 \in \mathcal{S}_j, i \neq j \Rightarrow \mathcal{T}(x_1) \neq \mathcal{T}(x_2)$,

where x is an original parameter vector and $\mathcal{T}(x)$ is a feature vector. $\mathcal{S}_i$ is a single set of symmetrical detector-unit-pairs.

2.B.2. Types of symmetry

There are six types of symmetrical arrangements that we consider, as shown in Fig. 2:

1. translational symmetry;
2. reflection symmetry;
3. rotational symmetry;
4. interchangeability of detector-units forming a detector-unit-pair;
5. interchangeability of a normal face vector of a detector-unit and its reverse;
6. detector-units having equal sides.

To find the invariant operation, we could potentially examine candidate functions whose inclusion into the feature vector would maintain property A. The process is stopped once sufficient candidate functions are included in the feature vector such that no detector-unit-pairs falling in different symmetrical sets have the same feature vector. That is, until property B is satisfied.

Assuming a choice for the first detector-unit, p , and second detector-unit, q , forming the detector-unit-pair, we discuss

FIG. 2. Different types of symmetry.

FIG. 3. Drawing of the line of response between two detectors, p , and q , illustrating the vectors used.

the candidate functions below. Figure 3 illustrates the vectors involved.

1. *Cartesian distance, $L_{p,q}$.* The Cartesian distance is the $\mathcal{L}_2$ norm distance between centers of two detector-units, $\vec{C}_p$ and $\vec{C}_q$. Any two detector-units, separated by same distance, fall within the same space with this function.
2. *Unit direction vector between detectors, p and q , $\vec{w}_{pq}$.* The unit direction vector is with respect to the global coordinate system, that is, $\vec{w}_{pq} = [w_x \ w_y \ w_z]^T$.
3. *Orthogonal face vectors for p and q detectors.* Although there are six face vectors for each detector-unit, along $-X$, $+X$, $-Y$, $+Y$, $-Z$, and $+Z$, only three of these (say, $+X$, $+Y$, and $+Z$) are necessary to uniquely identify the detector-unit orientation. Each of these vectors have three elements, giving the x , y , and z components in the global coordinate system. Let us denote these as ${}^a N_c^b$, where a is an element of $\{p, q\}$, b is an element of $\{+X, +Y, +Z\}$, and c is an element of $\{x, y, z\}$.

It is clear that given a detector-unit pair (p, q) ,

$$\{\vec{C}_p, L_{p,q}, W, \text{detPairType}\}$$

$$\text{with } W = \begin{bmatrix} w_x & {}^p N_x^X & {}^p N_x^Y & {}^p N_x^Z & {}^q N_x^X & {}^q N_x^Y & {}^q N_x^Z \\ w_y & {}^p N_y^X & {}^p N_y^Y & {}^p N_y^Z & {}^q N_y^X & {}^q N_y^Y & {}^q N_y^Z \\ w_z & {}^p N_z^X & {}^p N_z^Y & {}^p N_z^Z & {}^q N_z^X & {}^q N_z^Y & {}^q N_z^Z \end{bmatrix} \text{ and}$$

detPairType encoding the type of detector-unit-pair, such as those joining detector-units of different crystal sizes, completely describes the geometry of the detector-unit-pair. Let us call this a feature of the detector-unit-pair, $\mathbf{F}_1$.

2.B.3. Group operations

We consider each form of symmetry and its effect on the above formulation.

1. *Translational symmetry [Fig. 2(b)].* Given a detector-unit-pair (p, q) , the only component that depends on translation is the center of the first detector-unit, $\vec{C}_p$. The system matrix for the LOR varies as a function of the vector displacement between the center of the first detector-unit and the image voxel it is located in, along each global axis. The system matrix for the LOR is a copy if this distance is the same as the reference LOR.

If Δ is the absolute displacement of $\vec{C}_p$ from the bounding voxel, the Hadamard product of Δ with $\text{sign}(\vec{w}_{pq})$ indicates the displacement invariance to LOR rotation. All LORs having the different $\Delta \circ \text{sign}(\vec{w}_{pq})$ fall in different symmetry sets.

Therefore, we replace $\mathbf{F}_1$ by

$$\{\Delta \circ \text{sign}(\vec{w}_{pq}), L_{p,q}, W\}.$$

Since the effect of $\Delta \circ \text{sign}(\vec{w}_{pq})$ is small if the image voxel is small compared with the length of the LOR, we did not consider this offset in the implementation. However, this is easily added. Without considering the offset, the new feature is $\mathbf{F}_2 = \{L_{i,j}, W\}$.

All LORs having the same $\mathbf{F}_2$ feature vectors are translated versions of each other.

2. *Interchangeability of detector-units forming a detector-unit-pair [Fig. 2(e)].* For any detector-unit-pair (p, q) , the response function remains unchanged if the detector-unit-pair is ordered as (q, p) . The effect of interchanging the two detector-units in the feature is that columns 2–4 are replaced with columns 5–7. Switching the two indices in the feature, $\mathbf{F}_2$, would have had the effect of negating the sign of the direction vector such that $\vec{w}_{qp} = -\vec{w}_{pq}$. We can model this by a matrix multiplication with a matrix R , chosen from a set

$$\{L_{p,q}, W \times R\},$$

$$R_{+1} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix},$$

$$R_{-1} = \begin{bmatrix} -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \end{bmatrix}.$$

3. *Detector-units having equal sides.* There are additional degrees of freedom associated with a square cuboid with at least two faces being equal. This is modeled similarly to detector-unit interchange symmetry, where R is allowed to take on additional values in the set. For instance, if the first detector-unit is square cuboid with normals 2 and 3 interchangeable, additional R that should be introduced is

$$R_{+2} = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix},$$

$$R_{-2} = \begin{bmatrix} -1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}.$$

4. *Reflection symmetry* [Fig. 2(c)]. Reflection symmetry is the invariance of the detector-unit-pair to reflection along the axes plane of the global coordinate system. To model this invariance, we examine the effect reflection on yz plane on feature $\mathbf{F}_2$.

A reflection operation for a particular detector-unit-pair having this feature vector along yz plane ($x = 0$) uniformly multiplies all the x components in $\mathbf{F}_2$ by -1 . Therefore, the operation can be modeled by introducing a variable, say, g , which multiplies all the x components by ± 1 . Similarly, let us introduce variables h and i to model reflection along xz and xy planes, respectively.

This changes the feature into $\mathbf{F}_3 = \{L_{p,q}, T \times W \times R\}$, where $T = \begin{bmatrix} g & 0 & 0 \\ 0 & h & 0 \\ 0 & 0 & i \end{bmatrix}$ and $g, h, i \in \{-1, +1\}$.

5. *Interchangeability of a normal face vector of a detector-unit and its reverse* [Fig. 2(f)]. We consider the interchangeability of a normal face vector and its reverse. This property is due to the cuboidal nature of the detector-units. For example, the detector-unit-pair response function is unchanged if a normal face vector $[^p N_x^X \ ^p N_y^X \ ^p N_z^X]^T$ is multiplied by -1 . We model this effect by the multiplication of a, b, c, d, e, f , such that the new feature vector is

$$\{L_{p,q}, T \times W \times U \times R\},$$

$$\text{where } U = \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & a & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & b & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & c & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & d & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & e & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & f \end{bmatrix}$$

and $a, b, c, d, e, f \in \{-1, +1\}$.

6. *Rotational symmetry* [Fig. 2(d)]. Here, we are rotating with respect to the regular rectilinear grid. Hence, there are only finite rotations available. Rotation interchanges all components in $\mathbf{F}_3$ belonging to one axis with another one and negates those components along some or all the axis. Row negation is already modeled in the reflection symmetry. Therefore, in this section, we only consider the interchanging of coordinate components. We need to make the feature invariant of the ordering of x, y, z components of the direction vector and face normals. We model this symmetry property as premultiplication by a

matrix, $S, \{L_{p,q}, S \times T \times W \times U \times R\}$,

$$S_1 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}, S_2 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 0 & 1 \\ 0 & 1 & 0 \end{bmatrix}, S_3 = \begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix},$$

$$S_4 = \begin{bmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ 1 & 0 & 0 \end{bmatrix}, S_5 = \begin{bmatrix} 0 & 0 & 1 \\ 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix}, S_6 = \begin{bmatrix} 0 & 0 & 1 \\ 0 & 1 & 0 \\ 1 & 0 & 0 \end{bmatrix},$$

$$S \in \{S_1, S_2, S_3, S_4, S_5, S_6\}.$$

Hence, all the group operations are modeled as

$$\{L_{p,q}, S \times T \times W \times U \times R\}.$$

From the above formulation, it is clear that apart from translational symmetry and detector-units having equal sides, the number of potential members of any one group can be as high as $6 \times 2^9 \times 2 = 6144$. Given any member of a group, we wish to replace by unique element of the group representing that group.

2.B.4. Algorithm for symmetry computation

In this algorithm, we attempt to replace the parameter vector of each detector-unit-pair with a representative feature vector of the symmetry group it belongs to.

Symmetry is computed by considering every combination of group operations (S, T, U, R) that model symmetry for every detector-unit-pair (p, q). We compute $W_{\text{temp}} = S \times T \times W \times U \times R$ for each group operation and assemble the feature vector given by $\{L_{p,q}, W_{\text{temp}}, \text{detPairType}\}$. A unique symmetry invariant feature vector is found by finding the minimum across all group operations after reordering the elements of the feature vector into a single row.

The array consisting of symmetry invariant feature vectors for each detector-unit-pair is sorted, and unique rows are found. These unique rows form the *canonical elements* of the symmetry table. The mapping between different detector-unit-pairs and the canonical element is stored in binary files.

A 2D array, *lorOrder*, which is a three element row for every detector-unit-pair is also stored. The variable tracks the detector-unit-pair through rotation and reflection symmetry and enables quick computation of voxel location for a symmetrical detector-unit-pair in relation to its canonical detector-unit-pair.

Details on the exact implementation of the algorithm can be found in Ref. 29.

2.C. Create symmetry encoded data cluster (SEDC) groups

To make the code easy to parallelize, it is advantageous to bin the canonical elements found during the symmetry operation into groups. For easy description, we introduce a new name for these groups called SEDCs. During a projection operation, each SEDC is processed using a single core at a time. The number of SEDCs is large enough such that each SEDC has only a few canonical elements, enabling us to control the memory footprint of each core at any instant.

The number of SEDCs is on the order of thousands, where the cores on a system are on the order of tens. A set of SEDC are distributed to each core in a dynamic fashion, until all the SEDCs are processed.

After the symmetry computation, the canonical elements are ordered by the first variable of the feature vector, which is the length of the detector-unit-pair. Since computational complexity is roughly proportional to the length, we interleave the detector-unit-pairs across SEDCs so as to balance the computational load. Although taking into account the varying number of detector-unit-pairs that are mapped into each canonical element estimates the computational load more precisely, we do not currently take that into account.

The allocation of canonical elements to SEDCs and the set of all detector-unit-pairs mapped to each canonical element are calculated and stored in binary files.

2.D. Look-up table generation

Running the framework with an offline system matrix requires precomputation of the look-up table. The look-up table generation code computes the system matrix for each SEDC and stores it as a separate file. We use a factorized system matrix which separates the full matrix into a diagonal normalization matrix, a diagonal attenuation matrix, and emission system matrix,¹⁸

$$H = H_{\text{atten}} \cdot H_{\text{norm}} \cdot H_{\text{emission system matrix}}.$$

The diagonal elements of the normalization matrix and diagonal elements of the attenuation matrix are multiplicative elements in the data space. The emission system matrix encodes the detection probability of back to back gamma between a voxel and LOR.

The attenuation system matrix is computed using Siddon's algorithm³⁰ and subcrystal approach. The routine generates the system matrix for each SEDC at a time and only for the canonical elements. In each line of response within the canonical element from the symmetry computation, the two contributing crystals are subdivided into subcrystals. Lines joining the subcrystals are termed sub-LORs and the Siddon's algorithm is used to compute the length of intersection of sub-LORs with voxels of the image space. The values are averaged across sub-LORs to obtain weight linking each voxel and LOR, and this forms the attenuation system matrix. These weights can either be stored on disk or computed on-the-fly. When stored on disk, they are split up based on SEDC ordering into multiple files.

The attenuation of photons along each LOR through the image space is computed by forward projection of attenuation coefficients in the image space through the attenuation system matrix. For certain unconventional PET systems presented in Sec. 3, such as the virtual-pinhole PET (VP-PET) half-ring system and flat-panel system, the attenuation caused by addition of detectors in the field-of-view is corrected by generating a map of attenuation coefficients in the image space that is added to attenuation image by the object.¹⁸ For the plant PET

system presented, the field-of-view and LORs were chosen such that there are no LORs passing through the detectors.

To equalize the LORs that join detectors of different materials and sizes, it is necessary to model a multiplicative factor to the computed weights. This is taken care of by normalization, where LORs joining crystals of different sizes and materials are grouped separately. The estimation of normalization weights is explained in detail in Sec. 2.F.

To get the emission system matrix that models the detection probability of back to back gamma between a voxel and LOR, the weights of the attenuation system matrix are divided by the square of length of LOR during the projection operation. This division accounts for square distance loss, which is the loss of coincidence flux, due to the distance between the detectors.

2.E. Forward/backward projection

The projection routines project the sorted data space into the image space or vice versa. Projection operation in both directions is implemented together, using a data driven methodology. The projection routine processes a subset of the SEDCs, at a given time. Different subsets are scheduled on different nodes through the MPI parallelization library. The routine is further parallelized using OpenMP such that each core on a node processes a separate SEDC, with dynamic scheduling. The routine may either read the system matrix or compute it on-the-fly.

The program iterates through each *canonical element* in the SEDC and then through every LOR within the canonical element denoted here as *canonical LOR*. Within each *canonical LOR*, each symmetrical detector-unit-pair mapped to the *canonical element* is iterated. Within each symmetrical detector-unit-pair, the program moves through image space voxels computed from the system matrix, converts them to correct locations for the symmetrical LOR, and updates the value in either the data space or image space depending on the projection direction.

During the system matrix generation, we consider each canonical detector-unit-pair and compute the tube of response of its component LORs. The tube of responses can either be stored on disk or computed on-the-fly.

The computed response function across voxels for each unique LOR has to be remapped to correct coordinates for the symmetrical LORs. To perform this, we first subtract each voxel with the center of the first detector-unit in the canonical detector-unit-pair. The *lorOrder* variable stored during symmetry calculation is used to reorient the tube of response. The center of the first detector-unit of the current detector-unit-pair is then added.

2.F. Normalization

Unmodeled factors in the system matrix causes artifacts in the reconstructed image. These factors are unmodeled either due to gaps in our understanding of the physics model or day-to-day variations in a real system, such as detectors fluctuating in efficiency or failing. The estimation of these unmodeled factors by comparing data collected from a known

phantom with the expected data from a digital representation of the phantom projected through the system matrix is called normalization.

We have implemented the model-based normalization approach.³¹ There are a few requirements for successful normalization. The activity distribution of the normalization phantom must be known. Furthermore, the normalization acquisition must have sufficient statistics to estimate all the normalization parameters.

The normalization framework is applied to crystals of different sizes and materials. LORs joining crystals of different types must have different normalization components. Instead of modeling these effects in the emission system matrix, they are modeled as the components of the normalization matrix and estimated experimentally.

Current framework uses the L-BFGS optimization library.³² The L-BFGS library is a limited-memory quasi-Newton algorithm implementation and requires only the computation of the gradient. We have a non-negativity constraint on each of the components. The constraint is modeled by estimating the square root of the component values, which makes the problem unconstrained.

Each component is a collection of individual multiplicative variables known as efficiency factors. Each variable multiplies the system matrix weights of certain set of LORs. For instance, the crystal efficiency component has multiplicative variables equal to the number of crystals. Each variable multiplies all LORs containing the corresponding crystal.

Additionally, a LOR might be multiplied by more than one variable of a component. An example is the crystal efficiency component, where the weights of each LOR are multiplied by the multiplicative factors associated with two crystals.

To make the framework general, we estimate a common table of efficiency terms termed the efficiency_matrix. The first dimension of the efficiency_matrix is the component, and the second dimension indexes the multiplicative factors in the component.

We define membership of multiplicative variables to each LOR using a table known as efficiency_index_matrix. Improving the estimated normalization matrix by addition of new components or removing components can be done by changing the table instead of the code. The table is 3D. The

first dimension of efficiency_index_matrix is the index of the LOR, and the second dimension indexes the component. The third dimension indexes the different multiplicative variables belonging to a component that contribute to the LOR. The number of symbols in the third dimension is variable depending on the component it belongs to. The values stored inside the efficiency_index_matrix are indices of the efficiency_matrix for each component. The concept is illustrated in Fig. 4.

The Poisson log-likelihood equation is used to estimate the unknown efficiencies. The main difference is that in this problem, the activity distribution in image space is known, and the maximization is over the multiplicative factors to be estimated,

$$L = \sum_j y_j \log \left(\left[\prod_{k \in S(j)} \eta_k^2 \right] \left[\sum_i H(j,i) \times x_i \right] \right) - \left(\left[\prod_{k \in S(j)} \eta_k^2 \right] \left[\sum_i H(j,i) \times x_i \right] \right), \quad (3)$$

where y_j is the acquired normalization coincidence data for j th LOR, $H(j,i)$ is the system matrix values for j th LOR and i th voxel in image space, and X_i is the known image. η_k is the square root of the efficiency values stored in the k th location of the efficiency_matrix. The set $S(j)$ maps the index of each LOR to a set of efficiency_matrix values through the efficiency_index_matrix.

The gradient of the likelihood equation is

$$\frac{\partial L}{\partial \eta_{k'}} = \sum_{j: S(j) \ni k'} 2\eta_{k'} \left[\prod_{\substack{k \in S(j) \\ k \neq k'}} \eta_k^2 \right] \left[\sum_i H(j,i) \times x_i \right] \times \left[\frac{y_j}{\left[\prod_k \eta_k^2 \right] \left[\sum_i H(j,i) \times x_i \right]} - 1 \right]. \quad (4)$$

The computation of the gradient is programmed into a routine that is called by the L-BFGS optimization library with different values of $\eta_{k'}$ within its iteration loop.

FIG. 4. Diagram illustrating the data structures used in normalization.

FIG. 5. Half-ring system concentric with Siemens Biograph-40. (a) 3D view of Half-ring insert integrated into a Siemens Biograph 40 scanner; (b) front view; (c) top view.

During the course of our investigation, we have encountered problems where normalization succeeds in the immediate region of the image space covered by the normalization phantom but has improper normalization further away from the phantom. For instance, the boundary of the normalization phantom might divide the normalization parameters.

This is true especially when the phantom used for normalization is small and does not cover enough LORs to normalize them. Therefore, we have a multiposition normalization procedure, where the normalization phantom is placed in multiple locations in the imaging field of view. Assuming that each acquisition is independent, we estimate the component efficiencies through a joint objective function which comprises of the sum of the likelihood function at different positions. The gradient of total likelihood is the sum of the gradients at each location with respect to the unknown multiplicative factors.

Our normalization procedure is a two stage process. In the first stage, the forward projection of known activity distribution at each N location is computed, with corresponding known attenuation, and forms $\sum_i H(j,i) \times x_i$. In the second stage, the l-BFGS routine is run, with gradients of the likelihood function computed as mentioned above. The second stage of the code is parallelized using OpenMP over the data space, in the computation of the gradient.

Currently, two types of components are modeled for all the geometries, one which separates coincidence data between different types of detectors and another separating crystals. The components are computed in sequence, rather than jointly. Joint estimation requires the addition of further constraints to the estimated variables.

3. APPLICATION AND RESULTS

Three novel PET systems are modeled as applications of the framework. Data for each system are simulated using Monte Carlo tools or collected experimentally. The result of reconstructing the data is presented. The candidate PET systems presented are not meant to encompass the gamut of applicable PET systems of unconventional design.

Table I lists the configuration of each system presented. The size of the voxel and image size were chosen to get best performance for the system. If symmetry computation was not used, the iteration time, system matrix size, and total memory used would increase by the factor given in the symmetry saving column.

For the three PET systems, the main difference is in the geometry specification and data sorting routines. Limitation

TABLE I. Specification of each system.

PET system	Voxel size (mm)	Image size	Number of detector-units	Number of detector-unit-pairs	Selected detector-unit-pairs	Canonical detector-unit-pairs	Symmetry savings
Half-ring center	1.0×1.0×2.0	600×600×83	2236	2 498 730	1 269 334	25 229	50.31
Half-ring offset	1.0×1.0×2.0	600×600×83	2236	2 498 730	1 269 334	27 166	46.73
Flat-panel	1.0×1.0×2.0	600×600×120	2944	4 332 096	2 494 704	50 654	49.25
Plant PET	0.8×0.8×0.8	400×400×160	1312	860 016	661 280	12 867	5.14

in the coincidence processing electronics such as a fan-angle limitation would cause some LORs to be not measured. Failure to model this effect would introduce artifacts into the reconstructed images. Within the sorted detector matrices, these data points would be zero. Artifacts are introduced through the sensitivity image [denominator term in Eq. (2)]. Furthermore, there might be locations in the imaging field of view where no activity is located. The LORs that pass only through this region is excluded. The LORs that are to be masked out are either specified in the symmetry routines or using masks in the data domain.

Components for normalization must be specified separately depending on system configuration through the `efficiency_index_matrix`. The voxel size for reconstruction and image size are specified through configuration text files. The rest of the framework is independent of geometry and can be computed and modeled automatically.

For each reconstruction, the iterations are run for 50 iterations. The log-likelihood as a function of iterations shows satisfactory convergence properties. Currently, the framework does not include an automatic stopping criterion.

Table II lists the system matrix size and machine specification that was used to process the data, with metrics such as iteration time and RAM used. The reported values are after utilizing the symmetry computation.

3.A. Virtual-Pinhole PET half-ring system

We are focused on new PET geometries, particularly, the VP-PET technology³³ enhanced devices. The particular technology calls for the addition of smaller sized detectors close to a region of interest in a regular PET scanner.

Our recent work involves the investigation of a device, half-ring VP-PET insert, in a clinical PET scanner to improve its imaging quality for head and neck cancers.³⁴ The function-

ally complex region within the head and neck region with multiple lymph nodes could potentially benefit from the high resolution capability provided by the insert system. From the PET system designer's perspective, resolution and contrast recovery are the main metrics that need to be optimized, due to the complex structural anatomy of the region. The higher resolution imaging capacity could also potentially help study neurodegenerative diseases like Alzheimer's and Parkinson's diseases.

As illustrated in Fig. 5, the insert device is a half-ring of 28 LSO detector modules in two half-rings with radius of 124 mm. Each module comprises of 13×13 LSO crystals of $2 \times 2 \times 5$ mm³ size. The insert device is integrated into a Siemens Biograph-40, having 192 detector modules arranged in four rings of radius 438 mm. To connect the insert device, we disabled one of the four rings of the Biograph-40 and connected the insert electronics to the coincidence processor.

We have previously shown the design of the half-ring system,³⁴ data modeling and reconstruction framework,¹⁸ and scatter estimation.^{25,35} We have also shown that such a system could improve local image resolution, but still maintain the scanner field of view for imaging whole body.³⁶ However, the earlier version of the reconstruction program had hard coded symmetry and was only applicable when the system was at the center of the field of view.

Here, we have reimplemented the geometry within the current framework. Each detector-unit consists of 13 crystals in the same z plane within a detector block. Pairs of detector-units with length lower than a threshold were not used. This corresponds to sinogram trimming by the scanner hardware. Additionally, those detector-unit pairs with unit direction vector greater than 0.2 mm in the z component were also not used. This corresponds to a maximum ring difference of 22.

TABLE II. Computational resources utilized for each system.

PET system	System matrix size (GB)	Machine specification (computers × cores)	Iteration time (s)	Total RAM memory used (GB)
Half-ring center	73	2×64	3732	113
Half-ring offset	85	2×64	3477	100
Flat-panel	102	16×8	3403	374
Plant PET	345	2×64	1191	379

FIG. 6. Half-ring system concentric with Siemens Biograph-40 reconstructed axial, coronal, and sagittal views of an experimental study consisting of glass spheres of 3.3, 4.3, 6, 8, 9.6, and 11.4 mm diameter, arranged in a Derenzo-like pattern in a cylindrical phantom. The phantom was filled with ^{64}Cu at 11.16:1 tumor-to-background ratio and scanned for 30 min.

3.A.1. Results

To investigate the reconstruction performance with the VP-PET half-ring insert, and to show the versatility of the reconstruction framework, we scanned a cylindrical phantom. The images were acquired with the half-ring insert concentric to the Siemens Biograph 40 and with the half-ring insert moved down 76.20 mm. Moving the half-ring insert down increases the imaging field of view of the system.

For both the configurations, we scanned a cylinder phantom having 5.6 mCi (207.2 MBq) of ^{64}Cu with a Derenzo-like pattern of spherical hollow glass spheres. The glass spheres are 3.3, 4.3, 6, 8, 9.6, and 11.4 mm in diameter. The glass spheres were filled with activity with 11.16:1 tumor-to-background ratio. The reconstructed images and line profiles drawn through the tumor plane are presented in Fig. 6 for the half-ring concentric to the Biograph-40 and in Fig. 7 for the half-ring moved down. There is a minor artifact at the bottom of the phantom

FIG. 7. Half-ring system moved 76.20 mm to bottom with Siemens Biograph-40 reconstructed axial, coronal, and sagittal views of an experimental study consisting of glass spheres mimicking tumors of 3.3, 4.3, 6, 8, 9.6, and 11.4 mm diameter, arranged in a Derenzo-like pattern in a cylindrical phantom. The phantom was filled with ^{64}Cu at 11.16:1 tumor-to-background ratio and scanned for 30 min.

when the half-ring insert is at the center. The artifact is possibly due to imprecise modeling of PET physics very close to the detector crystals.

The line profiles indicate that there is a slight loss in resolution and contrast recovery when the half-ring insert is moved

to the bottom. This is counterintuitive considering the larger magnification effect from the VP-PET geometry when the half-ring insert is located at the bottom of the scanner. The reduction of image resolution is believed to be attributed to increased parallax error when the object is moved away from

the center of the scanner. Additional investigation is needed in order to characterize the net effect between these two factors (geometric magnification from VP-PET and parallax error from the scanner detectors). However, this is beyond the scope of this work and is left for future work.

With the half-ring insert at the center of the PET scanner, it has been difficult to image parts of the head-and-neck region of patients of various body shapes and sizes. The freedom to move the insert down increases the variety of patients that can benefit from the system.

3.B. Flat-panel system

Extending the concept of VP-PET to study other organs of interest requires development of a modular and flexible PET insert. We are currently developing a flat-panel VP-PET insert device.³⁷ The flexible positioning capability of the insert device allows for patient specific PET geometries. An initial study investigated the potential application of the technology to breast cancer using the half-ring VP-PET insert and showed improved image resolution without losing whole-body imaging capability.³⁶ Positron emission mammography, a competing technology, also improves image resolution² but has difficulty resolving tumors or secondary lymph node involvement near the chest wall and in mediastinum.

The insert device (see Fig. 8) has 28 detector modules in a 7×4 panel, with 16×16 LSO crystals per module. Each crystal is $1 \times 1 \times 3$ mm³. The scanner is the Siemens Biograph 40 with 192 detector modules in four rings. Each detector module has 13×13 crystals of $4 \times 4 \times 20$ mm³ crystals.

Crystals within a detector block with the same z coordinate were grouped together into detector units. For the flat-panel system, all coincidences between detector-units of the flat-panel were not used, as well as detector units separated by less than 641.7 mm between scanner detector units. We also did not use detector-unit pairs with z component of their direction greater than 0.2, similar to the half-ring system.

3.B.1. Results

The reconstructed results of a Monte Carlo study of the new flat-panel design with 7×4 detector modules of 16×16 crystals each are shown in Fig. 9. The phantom that was simulated is a model breast cancer patient with background in the body (box) and breast (sphere). A Derenzo pattern of spherical tumor sources was embedded in the breast region, with 2, 3, 4, 6, 8, and 12 mm diameter spherical tumors. The tumor to background ratio is 10:1 or the contrast ratio is 9. For a typical 70 kg patient with water density of 1 gm cm^{-3} and 10 mCi (370 MBq) of ^{18}F -FDG injected dose, the background activity

FIG. 8. Flat-panel system concentric with Siemens Biograph-40. (a) 3D view of the flat-panel insert integrated into a Siemens Biograph 40; (b) front view; (c) top view.

FIG. 9. Flat-panel system concentric with Siemens Biograph-40 reconstructed axial, coronal, and sagittal views of a Monte Carlo study consisting of spheres mimicking tumors of 2, 3, 4, 6, 8, and 12 mm diameter, arranged in a Derenzo-like pattern in a cylindrical phantom. The data are equivalent to 6.78 min of a typical ^{18}F -FDG acquisition with 10:1 tumor to background ratio.

concentration within body is $0.143 \mu\text{Ci}/\text{cm}^3$ ($5291 \text{ Bq}/\text{cm}^3$). The background activity concentration simulated is $0.064598 \mu\text{Ci}/\text{cm}^3$ ($2390 \text{ Bq}/\text{cm}^3$) of ^{18}F -FDG for 15 min. Therefore, the simulation presented is 6.78 min of a typical patient scan.

The reconstructed figures may be compared with results presented by Mathews *et al.*³⁶ Tumors of 4 mm diameter are resolvable with 6.78 min with the flat-panel insert. However, due to the approximations within the Monte Carlo simulation, we do not claim a particular resolution or contrast by

FIG. 10. Plant PET imaging system. (a) 3D view of the plant imager geometry; (b) top view of the plant imager; (c) side view of the plant imager.

this particular system under investigation. We are currently revising the design of the flat-panel insert and construction is only partially complete. Therefore, we do not present any experimental results.

3.C. Plant PET system

We are investigating a novel PET system dedicated to plant imaging.³⁸ The plant imaging system enables plant biologists to study the response of plants under various environmental conditions.

The plant PET imager (see Fig. 10) is integrated into a plant growth chamber and with horizontal PET detector rings. The system is built of two half-rings, having MicroPET R4 modules on one side and Inveon modules on the other. The bigger half-ring comprises of MicroPET R4 modules having 84 detector modules in 4 rings. Each module has 8×8 LSO crystals with $2.4 \times 2.4 \times 10$ mm³ crystals. Inveon modules form the smaller half-ring and have 32 detector modules in four rings, with 20×20 LSO crystals per module. Each crystal is $1.59 \times 1.59 \times 10$ mm³.

The plant is placed in between, and the two half-rings of the imager are able to move up and down, providing vertical imaging capability of whole plants. The plant imaging system has a reconfigurable geometry that can be adapted for plants of different widths and heights and at different stages of growth.

We grouped together crystals having the same z coordinate and within the same detector block as a detector-unit. Detector-unit pairs with z component of their unit direction vector greater than 0.8 mm were ignored. Additionally, there are Inveon-R4 pairs of detector-units that pass through the Inveon module that was also ignored.

3.C.1. Results

We conducted an experimental study of a cylindrical phantom of 10 cm diameter with glass spherical spheres. The spheres were filled with ⁶⁴Cu with sphere-to-background ratio of 11.16:1. The total activity in the phantom at imaging time was 4.6 mCi (170.20 MBq). Coincidence data were acquired for 30 min. The plant imaging system does not have a mechanism to measure attenuation. We reconstructed PET

images from the plant imaging system using attenuation maps obtained from the CT scan of the phantom and subsequently scaled to 511 keV attenuation. The attenuation map was registered to images reconstructed without attenuation. The reconstructed images and line profiles through the glass spheres are shown in Fig. 11. The plant PET system is capable of resolving glass spheres of 3.3 mm diameter.

In Fig. 12, we present the change in radionuclide uptake of a maize plant over time to showcase the parallel reconstruction capability of the framework. When run on a supercomputing cluster with a precomputed system matrix loaded in RAM, joint reconstruction of multiple frames is much faster than reconstructing each frame sequentially. The maize plant was grown in a 28 cm long glass jar. The plant was labeled with ¹¹C-CO₂, by pumping the gas into the chamber. After a short uptake period, the glass chamber was flushed. Some positrons escape from the leaves and annihilate when they hit the glass wall, as seen in the images. The quantitative accuracy of PET images of thin objects such as leaves requires further investigation and is beyond the scope of this work. The plant was imaged at three bed positions, and the images were stitched together to get the whole plant. Eight time spots are presented. In total, 24 frames of data are reconstructed together to obtain this set of images. The carbon absorbed by the plant during photosynthesis is transported to different parts of the plant. The growing tips of the plant root have increased carbon uptake.

4. DISCUSSION AND FUTURE WORK

In this work, we have created a reconstruction framework to reconstruct multiple images from PET systems of unconventional design. The work is progression toward an arbitrary geometry reconstruction framework.

Although current systems are field specific or application specific, the next generation systems are potentially patient specific,³⁹ where prior knowledge of the region of interest or desired image quality dynamically shapes the imaging system design. This investigation is a component of the overarching theme of designing application specific PET imaging devices, adaptable to the imaging target, and is a precursor to optimizing the design of PET systems.

FIG. 11. Plant PET imaging system reconstructed axial, coronal, and sagittal views of an experimental study consisting of glass spheres of 3.3, 4.3, 6, 8, 9.6, and 11.4 mm diameter, arranged in a Derenzo-like pattern in a cylindrical phantom. The phantom was filled with ^{64}Cu at 11.16:1 tumor-to-background ratio and scanned for 30 min. The image was reconstructed with attenuation correction. The outer edge of the images was streaky due to the slanted edge between the MicroPET R4 and Inveon modules. The edges of the field of view are cropped to remove artifacts at edges due to incomplete sampling.

The reported framework can model a large variety of PET systems with different crystal sizes, positions, and geometries. For each system, different types of symmetry are activated depending on their applicability. The symmetry computation

was initially written for voxels of the same length on each side. For voxels of nonuniform length, a column, $\vec{\Delta v}$, which denotes the voxel size in each dimension, could be appended to W ,

FIG. 12. Plant PET imaging system. Maximum intensity projection of radionuclide uptake in a maize plant, grown in a 28 cm long glass jar, over time. Each image was obtained by stitching three bed positions. The image was reconstructed without attenuation correction. The image is shown with a red color look-up table for clarity.

$$W = \begin{bmatrix} w_x & \Delta v_x & pN_x^X & pN_x^Y & pN_x^Z & qN_x^X & qN_x^Y & qN_x^Z \\ w_y & \Delta v_y & pN_y^X & pN_y^Y & pN_y^Z & qN_y^X & qN_y^Y & qN_y^Z \\ w_z & \Delta v_z & pN_z^X & pN_z^Y & pN_z^Z & qN_z^X & qN_z^Y & qN_z^Z \end{bmatrix}.$$

Presently, the framework does not account for time of flight PET or depth of interaction (DOI) detectors. Furthermore, more accurate system matrices could potentially provide better quantitation accuracy. In this regard, we have not modeled positron range correction or Point Spread Function (PSF) deblurring. Exotic detector crystal shapes such as tapered LSO arrays are also not addressed in this work. Such features may be included in an expanded version of the framework.

Since 4D PET reconstruction requires further investigation of the information shared between frames or dynamic geometries, we do not claim the capability to perform 4D reconstruction.

The current framework can handle very large system matrices. Memory usage and computational time are high for accurate image reconstruction. There is scope for further research for geometry independent memory/speed optimization. Other groups have shown progress in these areas, which can be potentially included in our framework. For instance, our approach of reducing the memory requirement is an extension of the existing approach of manual symmetry computation. This is a loss-less form of compression. More gains in memory can be made designing a lossy compression scheme, capable of trading of accuracy for memory usage.⁴⁰ With respect to computational speed, range-domain decomposition methods⁴¹ and optimization transfer⁴² could be potentially explored.

In developing this framework, we have learned that the expectation-maximization algorithm¹⁵ is robust in its ability

to reconstruct artifact free images under various geometrical arrangements of detectors of varying sizes, provided that there is complete sampling of the basis functions in the image. In the absence of complete sampling, artifacts are introduced. Since these artifacts must be addressed through an external signal or prior understanding that is dependent of system geometry on a case by case basis, we have not attempted to correct for such artifacts. Nonuniform sampling leads to nonuniform recovery metrics in the reconstructed images and are also not investigated.

5. CONCLUSION

We have developed an image reconstruction framework for reconstructing PET coincidence data from multiple frames, acquired from unconventional positron emission tomography systems. The reconstruction framework helps to accelerate the development of novel PET application using systems of unconventional geometry.

Traditional data ordering using sinograms is not pursued in this work due to its inapplicability for unconventional PET systems. We have generalized some of the traditional concepts in PET reconstruction to model systems of arbitrary geometry, with crystals of different sizes and materials. Lines of response between different types of crystals which were treated differently in our previous works are approached through the same mechanism. Modeling of unknown components that are to be estimated using the normalization procedure can be implemented easily given an understanding of the unknown variables and the lines of response that they affect.

ACKNOWLEDGMENTS

The code for the framework was developed as a continuation of codes developed by Dan Keesing, Debashish Pal, and David Politte. This work is supported in part by the National Cancer Institute of the National Institutes of Health (Grant No. R01 CA136554), National Science Foundation (DBI-1040498), and the Department of Energy (DE-SC0005157). The authors would also like to thank the Fashion Footwear Charitable Foundation, Inc. and the Alvin J. Siteman Cancer Center at Washington University School of Medicine and Barnes-Jewish Hospital in St. Louis, MO for their support. The Siteman Cancer Center is supported in part by a NCI Comprehensive Cancer Center Support Grant (No. P30 CA91842). Computations were performed using the facilities of the Washington University Center for High Performance Computing, which were partially provided through Grant No. NCR11S10RR022984-01A1.

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- ¹M. E. Phelps, E. J. Hoffman, N. A. Mullani, and M. M. Ter-pogossian, "Application of annihilation coincidence detection to transaxial reconstruction tomography," *J. Nucl. Med.* **16**, 210–224 (1974).
- ²C. Thompson, K. Murthy, Y. Picard, I. Weinberg, and R. Mako, "Positron emission mammography (PEM): A promising technique for detecting breast cancer," *IEEE Trans. Nucl. Sci.* **42**, 1012–1017 (1995).
- ³R. Freifelder and J. S. Karp, "Dedicated PET scanners for breast imaging," *Phys. Med. Biol.* **42**, 2463–2480 (1997).
- ⁴A. I. Santos, P. Almeida, M. V. Martins, N. Matela, N. Oliveira, N. C. Ferreira, J. a. D. Aguiar, F. G. Almeida, F. Lopes, J. Sampaio, P. Bento, F. Gonçalves, C. Leong, P. Lousã, L. Silva, I. C. Teixeira, J. a. P. Teixeira, M. C. Abreu, B. Carriço, P. R. Mendes, R. Pereira, P. Sousa, M. Ferreira, R. Moura, C. Ortigão, L. Peralta, R. Ribeiro, P. Rodrigues, J. C. Silva, A. Trindade, and J. a. Varela, "Design and evaluation of the clear-PEM detector for positron emission mammography," in *IEEE Nuclear Science Symposium Conference Record* (IEEE, Piscataway, New Jersey, 2004), pp. 3805–3809.
- ⁵L. MacDonald, J. Edwards, T. Lewellen, D. Haseley, J. Rogers, and P. E. Kinahan, "Clinical imaging characteristics of the positron emission mammography camera: PEM Flex Solo II," *J. Nucl. Med.* **50**, 1666–1675 (2009).
- ⁶B. Ravindranath, S. S. Junnarkar, M. L. Purschke, S. H. Maramraju, X. Hong, D. Tomasi, D. Bennett, K. Cheng, S. S. Southeikal, S. P. Stoll, J.-F. Pratte, P. Vaska, C. L. Woody, and D. J. Schlyer, "Results from prototype II of the BNL simultaneous PET-MRI dedicated breast scanner," in *IEEE Nuclear Science Symposium Conference Record* (IEEE, Piscataway, New Jersey, 2009), pp. 3315–3317.
- ⁷S. R. Cherry, Y. Shao, and R. Silverman, "MicroPET: A high resolution PET scanner for imaging small animals," *IEEE Trans. Nucl. Sci.* **44**, 1161–1166 (1997).
- ⁸N. K. Doshi, R. W. Silverman, Y. Shao, and S. R. Cherry, "maxPET, a dedicated mammary and axillary region PET imaging system for breast cancer," *IEEE Trans. Nucl. Sci.* **48**, 811–815 (2001).
- ⁹P. Vaska, C. L. Woody, D. J. Schlyer, S. Shokouhi, S. P. Stoll, J.-F. Pratte, P. O. Connor, S. S. Junnarkar, S. Rescia, B. Yu, M. L. Purschke, A. Kandasamy, A. Villanueva, A. Kriplani, V. Radeka, N. Volkow, R. Lecomte, and R. Fontaine, "RatCAP: Miniaturized head-mounted PET for conscious rodent brain imaging," *IEEE Trans. Nucl. Sci.* **51**, 2718–2722 (2004).
- ¹⁰S.-J. Park, W. L. Rogers, and N. H. Clinthorne, "Design of a very high-resolution small animal PET scanner using a silicon scatter detector insert," *Phys. Med. Biol.* **52**(15), 4653–4677 (2007).
- ¹¹S. S. Huh, W. L. Rogers, and N. H. Clinthorne, "Real time image reconstruction using GPUs for a surgical PET imaging probe system," in *2009 IEEE Nuclear Science Symposium Conference Record (NSS/MIC)* (IEEE, Piscataway, New Jersey, 2009), pp. 4148–4153.
- ¹²K. Brzezinski, J. F. Oliver, J. Gillam, and M. Rafecas, "Study of a high-resolution PET system using a Silicon detector probe," *Phys. Med. Biol.* **59**(20), 6117–6140 (2014).
- ¹³J. S. Huber, Q. Peng, W. W. Moses, B. W. Reutter, J. Pouliot, and I. C. Hsu, "Development of a PET-transrectal ultrasound prostate imaging system," *IEEE Trans. Nucl. Sci.* **58**(3), 674–681 (2011).
- ¹⁴T. C. Meyer, "Endo-TOFPET-US: A multimodal ultrasonic probe featuring time of flight {PET} in diagnostic and therapeutic endoscopy," *Nucl. Instrum. Methods Phys. Res., Sect. A* **718**, 121–125 (2013).
- ¹⁵A. P. Dempster, N. M. Laird, and D. B. Rubin, "Maximum likelihood from incomplete data via the EM algorithm," *J. R. Stat. Soc.* **39**, 1–38 (1977); available at <http://www.jstor.org/stable/2984875>.
- ¹⁶J. Qi and R. M. Leahy, "Iterative reconstruction techniques in emission computed tomography," *Phys. Med. Biol.* **51**, R541–R578 (2006).
- ¹⁷J. Hu, J. Qi, J. S. Huber, W. W. Moses, and R. H. Huesman, "MAP image reconstruction for arbitrary geometry PET systems with application to a prostate-specific scanner," in *The Eighth International Meeting on Fully Three-Dimensional Image Reconstruction in Radiology and Nuclear Medicine*, July (Utah Center for Advanced Imaging Research, Salt Lake City, 2005), pp. 416–420.
- ¹⁸D. B. Keesing, A. J. Mathews, S. A. Komarov, H. Wu, T. Y. Song, J. A. O'Sullivan, and Y.-C. Tai, "Image reconstruction and system modeling techniques for virtual-pinhole PET insert systems," *Phys. Med. Biol.* **57**, 2517–2538 (2012).
- ¹⁹J. J. Scheins, H. Herzog, and N. J. Shah, "Fully-3D PET image reconstruction using scanner-independent, adaptive projection data and highly rotation-symmetric voxel assemblies," *IEEE Trans. Med. Imaging* **30**(3), 879–892 (2011).
- ²⁰OpenMP Architecture Review Board, "OpenMP Application Program Interface Version 4.0," July 2013, <http://openmp.org/wp/openmp-specifications/>.
- ²¹E. Gabriel, G. E. Fagg, G. Bosilca, T. Angskun, J. J. Dongarra, J. M. Squyres, V. Sahay, P. Kambadur, B. Barrett, A. Lumsdaine, R. H. Castain, D. J. Daniel, R. L. Graham, and T. S. Woodall, "Open MPI: Goals, concept, and design of a next generation {MPI} implementation," in *Proceedings, 11th European PVM/MPI Users' Group Meeting, Budapest, Hungary* (Springer, Berlin, Heidelberg, 2004), pp. 97–104.
- ²²D. Pal, J. A. O'Sullivan, H. Wu, M. Janecsek, and Y.-C. Tai, "2D linear and iterative reconstruction algorithms for a PET-insert scanner," *Phys. Med. Biol.* **52**, 4293–4310 (2007).
- ²³J. Zhou and J. Qi, "Theoretical analysis and simulation study of a high-resolution zoom-in PET system," *Phys. Med. Biol.* **54**, 5193–5208 (2009).
- ²⁴H. Hudson and R. Larkin, "Accelerated image reconstruction using ordered subsets of projection data," *IEEE Trans. Med. Imaging* **13**, 601–609 (1994).
- ²⁵C. C. Watson, D. F. Newport, and M. E. Casey, "A single scatter simulation technique for scatter correction in 3D PET," in *Three-Dimensional Image Reconstruction in Radiology and Nuclear Medicine* (Springer, Netherlands, 1996), pp. 255–268.
- ²⁶S. Siegel and M. Dahlbom, "Implementation and evaluation of a calculated attenuation correction for PET," *IEEE Trans. Nucl. Sci.* **39**, 1117–1121 (1992).
- ²⁷H. Zaidi and B. Hasegawa, "Determination of the attenuation map in emission tomography," *J. Nucl. Med.* **44**, 291–315 (2003).
- ²⁸R. H. Huesman, G. J. Klein, W. W. Moses, J. Qi, B. W. Reutter, and P. R. G. Virador, "List-mode maximum-likelihood reconstruction applied to positron emission mammography (PEM) with irregular sampling," *IEEE Trans. Med. Imaging* **19**, 532–537 (2000).
- ²⁹A. J. Mathews, "A four-dimensional image reconstruction framework for PET under arbitrary geometries," Ph.D. thesis, Washington University in St. Louis, 2014, <http://dx.doi.org/10.7936/K7BG2M3Q>.
- ³⁰R. L. Siddon, "Fast calculation of the exact radiological path for a three-dimensional CT array," *Med. Phys.* **12**, 252–255 (1985).
- ³¹B. Bai, Q. Li, C. H. Holdsworth, E. Asma, Y.-C. Tai, A. F. Chatzioannou, and R. M. Leahy, "Model-based normalization for iterative 3D PET image reconstruction," *Phys. Med. Biol.* **47**, 2773–2784 (2002).
- ³²D. Liu and J. Nocedal, "On the limited memory BFGS method for large scale optimization," *Math. Program.* **45**, 503–528 (1989).
- ³³Y.-C. Tai, H. Wu, D. Pal, and J. A. O'Sullivan, "Virtual-pinhole PET," *J. Nucl. Med.* **49**, 471–479 (2008).
- ³⁴H. Wu, T. Y. Song, D. Pal, D. B. Keesing, S. A. Komarov, J. A. O'Sullivan, and Y.-C. Tai, "A high resolution PET insert system for clinical PET/CT scanners," in *Nuclear Science Symposium Conference Record* (IEEE, Piscataway, New Jersey, 2008), pp. 5442–5444.
- ³⁵S. A. Komarov, H. Wu, D. B. Keesing, J. A. O'Sullivan, and Y.-C. Tai, "Compton scattering in clinical PET/CT with high resolution half ring PET insert device," *IEEE Trans. Nucl. Sci.* **57**, 1045–1051 (2010).

- ³⁶A. J. Mathews, S. Komarov, H. Wu, J. A. O'Sullivan, and Y.-C. Tai, "Improving PET imaging for breast cancer using virtual pinhole PET half-ring insert," *Phys. Med. Biol.* **58**, 6407–6427 (2013).
- ³⁷B. Ravindranath, J. Wen, A. J. Mathews, S. A. Komarov, H. Wu, F. Dehdashti, J. A. O'Sullivan, and Y.-C. Tai, "A flat panel virtual-pinhole PET insert for axillary and internal mammary lymph node imaging in breast cancer patients," *J. Nucl. Med.* **53**(Suppl. 1), Abstract No. 432 (2012).
- ³⁸Q. Wang, A. J. Mathews, K. Li, J. Wen, J. A. O'Sullivan, and Y.-C. Tai, "A dedicated high-resolution PET imager for plant sciences," *Phys. Med. Biol.* **59**, 5613–5629 (2014).
- ³⁹J. Zhou and J. Qi, "Adaptive imaging for lesion detection using a zoom-in PET system," *IEEE Trans. Med. Imaging* **30**, 119–130 (2011).
- ⁴⁰J. Zhou and J. Qi, "Fast and efficient fully 3D PET image reconstruction using sparse system matrix factorization with GPU acceleration," *Phys. Med. Biol.* **56**, 6739–6757 (2011).
- ⁴¹S. Oh, C. A. Bouman, and K. J. Webb, "Multigrid tomographic inversion with variable resolution data and image spaces," *IEEE Trans. Image Process.* **15**, 2805–2819 (2006).
- ⁴²K. Lange, D. R. Hunter, and I. Yang, "Optimization transfer using surrogate objective functions," *J. Comput. Graphical Stat.* **9**, 1–20 (2000).