

# Contribution of Mathematical Models in Biomedical Sciences – An Overview

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## ARTICLE INFO

Received 16 Jan. 2016  
Received in revised form 08 Feb. 2016  
Accepted 12 Feb. 2016

**Keywords:** Medical imaging,  
Fourier transform,  
Radon transform

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## ABSTRACT

Over the past several decades advanced mathematics has implied itself into many facets of our day-to-day life. Mathematics is at the heart of all technologies. Arguably no technology has had a more positive and profound effect on our lives than medical imaging, and in no technology is the role of mathematics more pronounced or less appreciated. Biomedical imaging is very important for life sciences and health care. Many of the innovations in biomedical imaging are fundamentally related to the mathematical sciences. There are various imaging techniques which have simply transformed the practise of medicine and enabled a non-invasive diagnosis and surgical planning to guide surgery, biopsy and radiation therapy.

This paper presents an overview on the development of various mathematical models, algorithms which are beneficial in imaging techniques such as Ultrasound, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). A number of reconstruction algorithms have been studied with the help of various numerical techniques to serve the purpose. The paper presents an insightful observation into the emerging topics in this important inter-disciplinary field.

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## INTRODUCTION

Biomedical imaging is very important for life sciences and health care. Many of the innovations in biomedical imaging are fundamentally related to the mathematical sciences (Jain, 2013). All algorithms developed for imaging techniques are based on rigorous mathematical formulations, methods and models. Mathematical analysis guarantees that the constructed algorithm serves the purpose.

Software based on these techniques support the effective guidance for several image procedures such as biopsy, non-invasive surgery planning and radiation therapy. Researchers in image processing are regularly developing new tools in order to improve these techniques to make them more accurate so as to reduce the cost and negative health effect. In their study, Shepp & Kruskal (1978) compared different

reconstruction algorithms in imaging techniques with the use of 'mathematical phantom' which involves simulating a body section that can be mathematically described by a function. Smith (1985) derived new results on derivation of reconstruction formulas in his study. Further, Natterer (1999) studied the filtered back-projection algorithm, Fourier reconstruction and found these as useful tools in image reconstruction. Even, Tabbone & Wendling (2002) developed a new utilization of the Radon transform and given other algorithm which differs from previous applications of 2D Radon transforms.

In today's era, medical science is incomplete without these imaging techniques. Biomedical imaging techniques help a physician to detect damaged tissues or growth of tumour in any part of the body non-invasively. This paper attempts to study the development of various mathematical models, algorithms which are beneficial in imaging techniques such as Ultrasound, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). Broadly, the paper consists of two parts. The first part consists of brief history of different imaging techniques and the second part poses a survey of relevant methods and research efforts made in these imaging techniques. This paper is not only a study, but a detailed look into mathematics behind the various imaging techniques.

## ANTECEDENTS OF BIOMEDICAL IMAGING TECHNIQUES

Imaging techniques are based on different physical principles and these techniques suit more or less to the particular organ of species under study. X-ray imaging, ultrasonography, Computed Tomography (CT), Magnetic Resonance Imaging (MRI), Single Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET) are some of the widely used imaging techniques now-a-days. Angenent et al. (2006) explained these techniques separately as detailed below:

### X-Ray Imaging

X-ray imaging relies on the principle that an object will absorb or scatter X-rays of a particular energy quantified by attenuation coefficient ( $\mu$ ). The intensity changes because of the attenuation coefficient of the object. This depends on the electron density of the substance.

### Ultrasonography

In this technique sound waves with high frequency are sent into the body with transmitter and they produce distinct echoes for different tissues and organs. These echoes are received by a receiver and sent to the computer which converts them into an image on a screen. Ultrasound supports to differentiate among soft and fluid filled tissues and is mainly useful in imaging the abdomen.

### Computed Tomography (CT)

It is based on transmission of X-ray photons that are recorded on a computer by rotation from different angles around the body of the patient. This technique is boom to the imaging techniques. CT provides a picture of single thin slice through the body and it becomes possible with the help of Radon transform which re-constructs 3-D image from 2-D projections. It is beneficial in contrast among soft tissues and bones to augment the good quality image. Initially CT was developed for parallel beam, afterwards fan beam came into existence. Later on the cone beam CT was introduced. In this technique detector is placed on a complete circular ring and x-ray source is rotated around the object. Most of the time, spiral or helical CT technology is used by the medical professionals.

### Magnetic Resonance Imaging (MRI)

Earlier, name of this technique was Nuclear Magnetic Resonance (NMR). It is beneficial for discovery of neural activities and it measures the flow of water molecules as white matter in the brain. In MRI soft tissue contrast is much better than X-ray. It is useful especially in Brain and spinal cord scanning.

### Positron Emission Tomography (PET)

Now-a-days PET scanner is also used for diagnosing the abnormality in the patient. This technique supports in attaining the radioisotopes with different rates of intake for different tissues as compared to MRI and CT and is also helpful in better soft tissue contrast such as change of blood flow in the body.

### Single Photon Emission Computed Tomography (SPECT)

It is a nuclear medicine tomographic imaging technique using Gamma rays. It is also useful to present across sectional slices through the patient and provide 2-D view of a 3-D structure. Besides these techniques, Multi- model imaging scanners such as PET-CT, PET-MR, or SPECT-CT are also used for reconstruction of better quality imaging.

## MATHEMATICAL MODELS IN IMAGING TECHNIQUES

Mathematical models/methods are base for the construction of all imaging techniques. In CT and MRI imaging, Radon transform helps in reconstruction of function in the plane from its line integral or plane integral. Reconstruction algorithm such as Filtered Back Projection (FBP) is a technique based on Fourier slice theorem. It is a method for reconstruction from projection and is used in CT, PET and SPECT. In addition, Exponential radon transform is helpful in SPECT. Statistical techniques and algorithm such as maximum likelihood estimator are widely used in PET, SPECT and in X-ray CT.

### The Radon transform

J. Radon, an Austrian mathematician introduced the theory of transform and integral operator. The Radon transform is widely applicable to tomography. In CT one deals with the problem of finding a function  $f(x)$  i.e. the tissue density at the internal point  $x$  is denoted by  $f(x)$  that provides a picture (tomogram) with which the physician can look the internal structure of the patient. The approximation of

the measurement of internal structure of an object is called 2-dimensional. The Radon transform takes the function on the plane and is obtained by integral over all lines  $L$  is given by:

$$[f] \rightarrow Rf(L) = \int_L f(x,y) dl$$

one can determine line integral of the attenuation coefficient  $\mu$  through the object by calculating level of its density. After making these calculations for the full rotation, it is possible to reconstruct the 2D slice of the object and compilation of multiple slices which allows 3D reconstruction of the object (Toft, 1996; Freeman, 2010).

In the circular geometry of CT scans, it is suitable to parameterize lines  $ax+by=c$  in  $R^2$  to a set of oriented lines with radical parameters  $l_{t,\theta}$  in  $R^2$ .

Let the vector  $w = \langle \cos \theta, \sin \theta \rangle$  perpendicular to the line  $ax+by=c$  and the vector  $\hat{w} = \langle -\sin \theta, \cos \theta \rangle$  be parallel to this line. We get a vector equation in terms of  $t$  and  $\theta$  for the line  $l_{t,\theta} = tw + s \hat{w} = \langle t \cos \theta, t \sin \theta \rangle + s \langle -\sin \theta, \cos \theta \rangle$

The line is same as  $ax+by=c$  with the parameters  $t$  and  $\theta$ .

Definition: Let  $f$  be some function in  $R^2$ , parameterized over the lines  $l_{t,\theta}$ . The Radon transform  $Rf(t,\theta)$  is defined as:

$$Rf(t,\theta) = \int_L f ds = \int_{-\infty}^{+\infty} f(t \cos \theta - s \sin \theta, t \sin \theta + s \cos \theta) ds$$

This definition describes the Radon transform for an angle  $\theta$ . It accurately models the data acquired from the cross-sectional scans of an object from a large set of angles, as in CT scanning its inverse can be used to reconstruct an object from CT data. The 3D Radon Transform based on Grangeat's inversion formula is favourable for Cone beam CT (Clack & Defrise, 1994; Hiriyannaiah, 1997; Natterer & Ritman, 2002; Katsevich, 2003; Quinto, 2006).

### Unfiltered back-projection

Let  $f$  be some function in  $R^2$ ,

parameterized over the lines  $l_{t,\theta}$ . The unfiltered back-projection  $B[f(t,\theta)]$  is defined as

$$B[f(t,\theta)] = \frac{1}{2\pi} \int_0^{2\pi} \int_{-\infty}^{\infty} Rf(t,\theta) dt d\theta$$

Unfiltered back-projection is a simple and logical computation, but is not a faithful representation of  $f$ . Unfiltered back-projection is not much effective for medical imaging applications because it portrays a blurry image. For inverting the Radon Transform, other method known as filtered back-projection is greatly applicable in medical imaging (Epstein, 2008).

Fourier transform

The Radon transform is closely related to the Fourier transform, a method for which inverse is well-described by the Central Slice Theorem. In order to work in two-dimensional CT geometry, it is useful to include an extension of the Fourier transform into two dimensions (Natterer,1999).

Definition: Let  $f(x; y)$  be an absolutely integrable function. Then the two-dimensional Fourier transform is defined as:

$$\hat{f}(r,w) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} f(x,y) e^{-i(w_x x + w_y y)} dx dy$$

The Central Slice Theorem

According to Epstein(2008), this theorem connects both of the two transforms i.e. Radon and Fourier.

Theorem: Let  $f$  be an absolutely integrable function in this domain. For any real number  $r$  and unit vector  $w=(\cos\theta, \sin\theta)$

we have the identity

$$\hat{f}(r,w) = \int_{-\infty}^{\infty} Rf(t,\theta) e^{-i r t} dt$$

From this theorem, we can see that the 2-dimensional Fourier transform  $\hat{f}(r,w)$  is equivalent to 1-dimensional Fourier transform of Radon transform  $Rf(t,\theta)$ .

Filtered back-projection

It is a technique of inversion of Radon

transform and is most useful reconstruction algorithm used in CT. In this technique, X-Ray tube runs on a circle of radius  $r$  and is called fan beam scanning. This technique avoids the blurring artifact and lack of clarity as compared to unfiltered back-projections. Mathematically, this method can be used to reduce the level of radiation exposure required to achieve the same level of diagnostic accuracy (Natterer and Ritman, 2002).

There are several methods for inverting the Radon transform, some of which use Fourier transforms, the Central Slice Theorem, and functional analysis (Nievergelt, 1986).

Circular Radon Transform

This technique is used in two dimensional cases with unit circle (Ambartsoumian and Kuchment, 2005)

The circular Radon transform of a function  $f$  is defined as:

$$Rf(p,\rho) = \int_{|y-p|=\rho} f(y) d\sigma(y)$$

where  $d\sigma(y)$  is the surface area on the sphere  $|y - p| = \rho$  centered at  $p \in R^d$ .

Exponential Radon Transform

This technique is very much helpful in SPECT (Kuchment & Lvin, 2013) and is defined as:

$$R_{\mu} f(\omega, s) = g(\omega, s) = \int_{-\infty}^{\infty} f(s\omega + t\omega^{\perp}) e^{\mu t} dt$$

Here  $\mu > 0$  is the attenuation coefficient.

Radon Inversion from Plane Integral

It is a measure of reconstruction from its plane integral and mainly useful in NMR (Shepp, 1980). The formulae to approximate plane integral of density  $f(x,y,z)$  of hydrogen nuclli at each point of an object is given by

$$f(x,y,z) = -\frac{1}{2\pi} \left( \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2} + \frac{\partial^2}{\partial z^2} \right) F(x,y,z)$$

Where  $F(x,y,z) = F(Q)$

$$= \frac{1}{4\pi} \iint_{u \in S} P(t(Q), u) dS(u)$$

And  $u \in S$  means that  $u$  runs over the unit sphere  $S$  of unit vector with  $dS(u)$  the local element of area on  $S$  and  $t(Q)$  being the value of  $t$  for which  $P(t, u)$  is the 2 Dimensional projection of  $f$  contains the point  $Q=(x, y, z)$ .

Further, Shepp (1980) proved that reconstruction from plane integral is as appropriate and accurate as reconstruction from line integral.

### Attenuated Radon Transform $(R_a)$

According to Natterer (2001); Boman & Stromberg (2004), it is very beneficial reconstruction algorithm of FBP for SPECT and is defined as:

$$(R_a f)(\theta, s) = \int_{x \cdot \theta = s} e^{-D(x) \cdot \theta^\perp} f(x) dx$$

Where  $dx$  stands for the restriction of lebesgue measure in  $R^2$  to  $x \cdot \theta = s$  and

$$\theta = (\cos\theta, \sin\theta) \text{ And } \theta^\perp = (-\sin\theta, \cos\theta)$$

$$\text{Also } Da(x, \theta) = \int_0^\infty a(x + l\theta) dl$$

Where  $x \in R^2$

### Expectation Maximization (EM) Algorithm

This algorithm is having a decent application in emission tomography and is based on Maximum Likelihood Estimators. This technique is useful in displaying physical difference between transmission and emission techniques. It provides a better quality of reconstruction. Lange & Corsan (1984); Hudson & Larkin (1994) has described this algorithm for SPECT. They examined that the sequential processing of ordered subsets is very natural in SPECT, as projection data is collected separately for each projection angle (as camera rotates around the patient in SPECT) counts a single projection. As photon recordings on gamma cameras are discarded to provide counts  $y_t$  on

detectors indexed by  $t$  and the expected number of photon emission from pixel  $j$  is denoted by  $x_j$ , where the image is defined by  $x = \{x_j : j = 1 \dots j\}$  then detector counts are poisson distributed with expected values  $\mu = Ey = Ax$ . Where,  $A$  is the projection matrix with elements  $a_{ij}$  represents the probability that an emission from pixel  $j$  is recoded at  $t$ . The poisson likelihood function for all counts data following sub-iteration  $i$  is given by:

$$L(y, x^{i+1}) = L(y, x^i) + \sum_{t \in S_i} \{y_t \log \mu_t^{i+1} - \mu_t^{i+1}\} - \sum_{t \in S_i} \{y_t \log \mu_t^i - \mu_t^i\}$$

The final two terms of the right hand side provide the increase in likelihood function of the data subset  $\{y_t, t \in S_i\}$  resulting from sub-iteration  $i+1$ .

### Statistical Image Reconstruction Algorithm

In multi model imaging system such as PET-MR, PET-CT or SPECT-CT this algorithm of reconstruction gives better quality images. Chun et.al, (2012) described this technique for improved quality of image in SPECT. He used poisson log likelihood function for this purpose. The SPECT image  $x$  can be reconstructed iteratively from

$$\hat{x} \triangleq \underset{x \geq 0}{\operatorname{argmin}} L(y/x)$$

where  $y$  is a measured sinogram data and  $L$  denotes the negative poisson log-likelihood function:

$$L(y/x) = \sum_i \bar{y}_i(x) - y_i \log \bar{y}_i(x)$$

Where  $y_i$  is the  $i^{\text{th}}$  element of the measurement  $y$  such that  $\bar{y}_i(x) \triangleq [Ax]_i + s_i$  and  $A$

denotes the system model and  $s_i$  is the scatter component for the  $i^{\text{th}}$  measurement. Further, Elbakri & Fessler (2002) introduced statistical iterative reconstruction algorithm for X-ray attenuation to establish its effectiveness for bone and soft tissue objects.

Wang & Qi (2015) proposed kernel based image model in which coefficient are estimated by Maximum Likelihood (ML) or penalized likelihood image reconstruction and they proved that the kernel method is easier to implement and provides better image quality for low-count data in PET image reconstruction as

compared with other methods. PET projection data  $y$  is well modeled as independent poisson random variable with log likelihood function:

$$L(y/x) = \sum_{i=1}^M y_i \log \bar{y}_i - \bar{y}_i - \log y_i!$$

Where  $M$  is the total no. of lines of response and the expectation  $\bar{y}$  is related to the unknown

emission image  $x$  through  $\bar{y} = Px + r$  with  $P$  being the detection probability matrix and  $r$  the expectation of random and scattered event.

The Maximum Likelihood (ML) estimate of the image  $x$  is found by maximizing the Poisson log

likelihood is given by 
$$\hat{x} = \underset{x \geq 0}{\operatorname{argmax}} L(y/x)$$

### Markov Random Field

Bai and Leahy (2013) have given a model which is useful in combined PET and MR technologies and shown that the method has produced significant improvement in reconstructed image quality as compared to the FBP. This is a probabilistic image model with property of joint distribution in terms of local ‘potential’ that describes the interaction between neighbor groups of voxels. The joint density is the form of a Gibbs distribution:

$$P(\lambda) = \frac{1}{Z} e^{-\beta U(\lambda)}$$

Where,  $Z$  is the normalizing constant  $\beta$  is the parameter that determines the degree of smoothness of the image and  $U(\lambda)$  is the Gibbs energy function of the form:

$$U(\lambda) = \sum_{c \in C} V_c(\lambda)$$

Where  $V_c(\lambda)$  are a set of potential function defined on a clique  $c \in C$  (set of all clique) consisting of one or more voxels all of which are mutual neighbors of each other.

### CONCLUSION

It is evident from above discussion that all the methods are having a significant impact on biomedical imaging and it has been felt that new algorithms developed from time to time has

transformed medical imaging. From the above discussion, it is quite notable that EM algorithm offered improvement in imaging techniques for SPECT and has provided a more quantitative image reconstruction for emission and transmission tomography. Statistical techniques addressed the shortcoming of FBP and can model such phenomena leading to more accuracy in imaging. Fourier based inversion formulas are used for reconstruction of a function from its line integral as this method is having an ability to reconstruct only a portion of the field of view whereas all other algorithm techniques reconstruct the entire field.

All mathematical algorithms discussed above are beneficial from different aspects. The list is necessarily incomplete, new imaging modalities are frequently coming up. These novel techniques present interesting and new perspectives on the medical imaging problems. The goal of this study is not to determine the overall best method but to present a study of some mathematical models and techniques used in improving biomedical imaging. I hope this paper may support mediation between the mathematical models and medical imaging reconstruction.

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