Chapter 1

Introduction

1.1 Nuclear Medicine

Nuclear medicine is a medical specialty that aids diagnosis as well as treatment planning and monitoring by producing noninvasive, diagnostic images using radiopharmaceuticals. Radiopharmaceuticals are radioactive pharmaceutical agents or drugs labeled with one or more unstable atoms (radionuclides) in their molecular structures. Nuclear medicine can also be used in the study the dynamic processes of physiological and biochemical functions of living organisms [117]. If an agent is administrated into a patient’s body by targeting an organ or tissue, the biodistribution process undergoes absorption, distribution, metabolism, and excretion. In biodistribution, the radioactive agent localizes in the organ or tissue of interest through the biochemical nature of the radiopharmaceutical. While the radiopharmaceutical resides in the organ, it is emitting gamma rays in all directions. The amount of radiopharmaceutical absorbed depends on the physiological function of the organ or tissue [28]. Through the use of appropriate detection device, one can record and compute the spatial distribution of radionuclide in the organ of interest. Compared to a known normal biodistribution, any irregular concentration may indicate the presence of disease. Thus, a medical diagnosis can be made through the investigation of the recorded
data.

However, the recorded data from the detecting device is not a recognizable image and must be transformed through some mathematical operation into an image recognizable by a radiologist, which is the final diagnostic image of a cross-sectional biodistribution. Such a mathematical operation is called reconstruction.

Nuclear medicine is a powerful tool of visualizing physiological functions or function metabolism unlike other imaging methods that instead show anatomical structure, such as magnetic resonance imaging (MRI) [17] or X-ray computed tomography (CT) [24]. Figure 1.1(a) illustrates the anatomy of a two dimensional slice of human brain from a T1-weighted MR scan [17] while (b) shows a slice of a functional brain image of blood flow reconstructed from a nuclear medicine scan. The anatomical scan in Fig. 1.1(a) has better resolution, but cannot show function.

![Figure 1.1](image_url)

Figure 1.1: (a) One slice of an MR image shows anatomical brain structure, and (b) a slice from a single-photon emission computed tomography (SPECT) image shows function.
1.2 Emission Computed Tomography (ECT)

1.2.1 Nature of the Acquired Data

The signal one would like to detect in a nuclear medicine scan is the three dimensional (3-D) radionuclide distribution, which depends on the physiological functions of tissues within organs of interest. However, the camera in effect is a two-dimensional (2-D) detector which records a projection of the 3-D radioactivity distribution into collapsed 2-D view. Figure 1.2 illustrates the 2-D image that results in a projection of a 3-D object. This is the idea of a conventional planar imaging system [28]. Notice that in Fig. 1.2 the 1-D projection in the planar view comes from one 2-D cross-sectional image out of the 3-D object. Later, it will be explained how a collection of such 1-D projections is useful to reconstruct the 2-D image.

Planar imaging is in wide clinical use and can be found in virtually every nuclear medicine facility in the world [24]. For example, it can be used for bone studies [28], planar scintimammography for breast cancer studies [125], and for evaluating pulmonary deposition of inhaled aerosols [88]. However, the 3D structures in a 2D planar image are superposed, and thus making diagnosis difficult. It would be useful if one could obtain the spatial distribution of the 3-D biochemical functions within the body.

Rather than planar imaging, tomographic data acquired by rotating the detectors around the patient’s body can be used for reconstructing the 3-D image. When applied to nuclear medicine, this idea results in a type of imaging called emission computed tomography (ECT). Consider the problem of reconstructing a single 2-D “slice” of the 3-D data. A transaxial slice of brain is indicated in Fig. 1.2. For example, if we are only interested in the photons coming out of the slice, a 1-D projection array can be collected shown on the planar view in Fig. 1.2. If one further collects the 1-D
Figure 1.2: Planar imaging is acquired with only a single 3-D projection array into a 2-D array. For each cross-sectional image, there is a corresponding 1-D projection (dark line).

projection array from many angles, over 360°, a 2-D array of 1-D projections can be obtained [24, 11]. As shown in Fig. 1.3(b), the 2-D array is called a “sinogram”, which is collected by stacking the line at each projection angle displayed in Fig. 1.3(a). By applying a reconstruction method on the sinogram, one can recover the 2-D source distribution. A 3-D radiotracer concentration can be built by simply stacking the many 2-D reconstructed images.

It can be shown that detected data can be roughly approximated by the line integral of the spatial distribution along the line that detected gamma rays travel [54, 11], and thus the collection of all these line integrals is the “projection” data. Typically, the set of lines at a given angle are parallel to one another and perpendicular to the camera face. This line-integral model is the basis of reconstructing the image from the projection data [54] and will be discussed later in Chapter 2.
Figure 1.3: (a) By collecting each 1-D projection at each angle around the patient’s body (here, a 2-D slice of brain), a sinogram (b) is obtained. Ideally, one can recover the 2-D image by “reconstructing” it from the sinogram. Note that in (a), only eight projection views with angle step size of 45-degree are shown for clarity, but in practice, there are usually many more projection views collected, where some parts of projection positions overlap as shown.

1.2.2 SPECT vs. PET

From the physical mechanism point of view, there are two different imaging systems in emission tomography, single-photon emission computed tomography (SPECT) and positron emission tomography (PET). SPECT and PET differ in the radiation source, the physiological aspects, and instrumentation.

The radiotracers used in SPECT, such as $^{99m}$Tc-labeled, $^{123}$I-labeled, $^{201}$Tl-labeled radiotracers [99, 110], involve a nuclear decay with emission of a single-photon as illustrated in Fig. 1.4(a). The photon energies in SPECT range from roughly 75 to 400 KeV. As for PET, the radionuclides such as $^{15}$O – oxygen, $^{11}$C – glucose, and $^{18}$F – FDG (fluorodeoxyglucose) [144] produce a positron ($\beta^+$) that travels a distance ($\approx$ 1 to 3 mm) followed by annihilation with an ordinary electron ($e^-$), followed further by the emission of two 511 KeV photons going in opposite directions (180°) as shown in Fig. 1.4(b). Since the positron-emitting isotopes of carbon, nitrogen,
oxygen, and fluorine are the major components of the molecules in many compounds of biological interest, PET isotopes can be readily incorporated into a wide variety of useful radiopharmaceuticals [109]. Therefore, PET can be used to study the metabolic processes in human physiology. For example, FDG (fluorodeoxyglucose) is a chemical analog of glucose in which a hydrogen atom is replaced by the positron emitter $^{18}$F, and is used to study the function of glucose metabolism in the organ of interest [110]. However, in SPECT, the relatively heavy isotopes used such as $^{201}$Tl, and $^{99m}$Tc, do not occur naturally in biologically active molecules. Nevertheless, the radiotracers in SPECT are useful in measuring various physiological quantities including blood flow. For instance, $^{99m}$Tc sestamibi can be used to detect both myocardial perfusion and viability [110].

![Diagram of gamma emission and positron emission](image)

Figure 1.4: (a) A single $\gamma$-ray photon emission results from a nuclear decay from SPECT radiotracers such as $^{99m}$Tc, $^{123}$I, or $^{201}$Tl. (b) A positron ($\beta^+$) is produced from positron emitters. It collides with an electron, resulting in a matter-antimatter decay into two gamma rays traveling in opposite directions as shown.

1.2.3 SPECT Camera

For SPECT, the basic structure of a detecting device, called an Anger camera [4] or gamma camera, is depicted in Fig. 1.5. A collimator typically made of lead or a
similar high atomic number substance attached to the area detector allows only those photons traveling approximately normal to the detector face to hit the detector. The detector head consists of a large diameter (roughly 40 cm) scintillation NaI(Tl) crystal, and therefore an incoming photon causes a localized light flash [24]. An array of photomultiplier tubes (PMTs) is optically coupled to the back of the scintillation crystal [63]. When a photon hits the crystal, the light from the scintillation is recorded by the PMTs [141]. The signals coming out of PMTs are evaluated by electronic circuitry that combines the PMT signals from the flash to compute the 2-D position and energy level of the photon, and sends the digitized version of this information to a computer system. Note that the purpose of the collimator is to mechanically confine the direction of incident photons, and thereby to relate positions of detected photons on the crystal to those of incident directions of the photons coming from the object [5]. The collimator illustrated here is a parallel-hole collimator with parallel
apertures. Other forms of collimators, for instance, converging- or diverging-hole collimators [141, 24], are used for different applications, but the principle is the same. Figure 1.6 is a triple-head SPECT camera with three detectors as shown in Fig. 1.5. The three-head SPECT configuration is popular because of its efficiency and versatile geometric position settings [99].

![SPECT Detector](image)

Figure 1.6: Picture illustrates the acquisition geometry of a triple-head SPECT camera. Note that physical collimators are shown in each head of the SPECT camera. The three heads rotate around the emitting object in order to collect the data at all angles. One head needs rotate 120°.

### 1.2.4 PET Camera

For PET, rather than one photon being detected, there are a pair of 511KeV photons generated by a coincidence “event”. Therefore, in order to detect the coincidence, two photons produced after an annihilation event and going in opposite directions must be recorded nearly simultaneously (within a short time, i.e., $10^{-8}$ sec or less) [117, 24]. The right side of Fig 1.7 illustrates a typical PET geometry, an array of discrete detectors arranged in a ring and coupled to a timing circuit, rather than a single large area detector as in SPECT. A ring or multiple rings in PET cameras allow dynamic, simultaneous acquisition of a complete data set without rotating the system [82].
A coincidence detector pair posed exactly in opposite sides is shown in the left of Fig 1.7. The coincidence is triggered by a coincidence detection circuit. Thus, due to the coincidence detection, a positron event is collimated "electronically" rather than mechanically as in SPECT. This leads to high sensitivity for PET relative to SPECT. In SPECT, the 2-D position of the scintillation and the collimator geometry determines the direction, or ray, along which the photon traveled. In PET, the line connecting the two detectors involved in a coincidence event determines the ray along which the photon traveled.

![Diagram of coincidence detection in PET and SPECT](image)

Figure 1.7: As shown in the right, a PET camera is usually a ring of detectors made up of an array of discrete detectors rather than a single large area detector as in SPECT, while at left, shown is a pair of opposing PET detectors, which detects coincident photon pairs through a timing circuit.

### 1.2.5 2-D Reconstruction Models for ECT

For SPECT, the number of counts recorded by a given detector is determined mainly by the physical collimator. Since a collimator restricts counts to come from a given direction, the total counts are determined approximately as the line integral...
of the activity distribution along a line typically perpendicular to the collimator. For PET, the total number of coincidence events recorded by a given pair of detectors is also equivalent to a measure of the line-integral projection data along the strip connecting the two detectors [24]. Thus, the same reconstruction methods can be applied to both SPECT and PET since both share the same line-integral data formation. Further differences in SPECT and PET physical models will be discussed later in chapter 2. Again, the line integral model is very approximate, and deviations from this formulation will be discussed.

The process of 2-D image reconstruction in ECT is an inverse problem which produces an image of a two-dimensional distribution (object) from the projection data. Thus, the formulation of the inverse problem needs a model that relates object to data. That is, a mathematical model of the physical process of detecting photons from a radioactive emission is needed. In Chapter 2, a mathematical model will be described, but here, only a qualitative summary of the various physical effects that must be included in the model is given.

First, as mentioned previously, the basic process of the projection can be modeled as collection of many “ray sums” of activities along a given ray path [24, 130]. Moreover, the various sources of degradation from the physical effects [141, 150, 109], including detector blur, photon scatter, and attenuation, and instrumentation limitations such as detector efficiency, must be accounted for in order to solve the problem more accurately. Detector blur leads to, in SPECT, a resolution distance that increases (gets worse) with distance from the source to the collimator. Photon scatter leads to a change of emitting direction and hence an incorrect photon ray, while attenuated photons are totally absorbed by the tissue or not detected by the system. Therefore, the image reconstruction is concerned not only with inverting the
line-integral of projection data, but is also concerned with the corrections for effects of physical blurring by detector blur, and signal loss due to scattering, and attenuation by tissue as well. (This aspect of reconstruction is often called “compensation”.) Among all, attenuation is a major limiting effect [148].

1.2.6 Attenuation

Although attenuation is but one of several image degradations, it affects image quality severely and hence it receives much attention [74]. Attenuation is defined as the reduction of the number of detected gamma rays due to photoelectric absorption and Compton scatter [141]. Given a narrow beam of intensity $I_0$, the intensity drops as $I(x) = I_0 e^{-\int_0^x \mu(x') dx'}$ where the attenuation coefficient $\mu(x)$ (cm$^{-1}$) is characteristic of the medium as well as the energy of the beam [141]. The attenuation coefficient depends on a number of factors including photon energy, scattering cross-section of the material, and electron density. The effects of attenuation for photons emitted from inside the body can be quite significant, as only 20% to 25% of photons survive to reach the detector at 140KeV [150]. Also its value varies with location. Therefore, attenuation correction (AC) is very important in that it can improve quantitation accuracy, as well as avoid image artifacts in emission reconstruction, especially in the bodily areas with non-uniform attenuation such as thorax.

1.3 Transmission Computed Tomography

Attenuation correction needs an attenuation map, i.e. an image of attenuation coefficients in the patient body. How can one get an attenuation map? It turns out that obtaining an attenuation map is itself a separate imaging and reconstruction problem. In transmission computed tomography one acquires the transmission data,
and uses this to reconstruct the attenuation map. The map is then used for the compensation of photon attenuation in ECT. Figure 1.8 illustrates an attenuation map derived from transmission reconstruction of physically acquired PET data for a thorax phantom [59].

![Image of attenuation map](image1.png)

Figure 1.8: A noisy image of attenuation coefficients (attenuation map) reconstructed from physically acquired PET data for a thorax phantom.

The use of transmission computed tomography is a new development in nuclear medicine. *Its purpose is to help ECT (emission computed tomography) by providing an attenuation map useful in restoring the emission image.* Transmission tomography (TT) is similar to X-ray computed tomography (CT) where, by using an external X-ray tube, attenuated X rays passing through a body are collected to reconstruct the attenuation coefficients. However, instead of an X-ray tube, in nuclear medicine an external radioactive source is used in transmission computed tomography. One might ask: Why not use a CT scan instead of a transmission reconstruction? There are couple of problems associated with the use of an X-ray attenuation image in ECT. First, the reconstructed images in CT are attenuation maps calculated from photon data with a broader energy spectrum from 40 KeV to 140 KeV [3], but attenuation of monochromatic energy spectra such as 140 KeV in SPECT and 511 KeV in PET is more appropriate for emission tomography. Moreover, there are problems associated
with the extra registration procedure needed to superpose the ECT scan and a CT image, the increased expense due to a separate CT scan, and the high radiation dose of CT. For these reasons, the external radioactive source is used in TT. But because dose is limited, very few counts are detected in TT, and the data are quite noisy.

1.3.1 Instrumentation

![Diagram](image)

Figure 1.9: Camera geometries for transmission tomography of (a) a single-headed SPECT camera with a scanning line transmission source and parallel hole collimator, (b) a single-headed SPECT camera with fan-beam collimation and a fixed line transmission source at the focal distance, and (c) PET camera using a rotating rod source.

Since transmission data is acquired in TT for AC (attenuation correction) in an ECT reconstruction, it requires that the patient be positioned in the very same SPECT or PET scanner during ECT acquisition in order to reduce registration error. One might then first perform a transmission scan, then an emission scan. However, in addition to the registration problem, the sequential acquisition of transmission data before emission data increases the total scan time, and thus reduces the overall patient throughput. Thus for both PET and SPECT, transmission data are often acquired after the patient has been injected with radiopharmaceutical. This leads to both transmitted and emitted photons hitting the detector, which causes crosstalk
problems to be discussed later.

Some common transmission configurations for SPECT and PET (ref [8] has a good overview for PET) are shown in Fig 1.9, where (a) a single-head camera using a scanning line source and parallel hole collimator [142], and (b) a single-headed camera with a fan-beam collimator and a stationary line source fixed at the collimator’s focus [151]. The disadvantages of geometry in Fig. 1.9(a) are the need of a more complex mechanical design, and reduced sensitivity. However, the “crosstalk” for a simultaneous emission and transmission acquisition caused by the contamination between the emission and transmission is sufficiently low, due to the employment of electronic windowing of the detector. The system in Fig. 1.9(b) has higher sensitivity, and is found on several existing commercial SPECT systems. As for PET, the most popular geometry, as shown in Fig.1.9(c), is to use rotating rod sources which are continuously rotated around the patient [8]. The benefit of using rotating rod sources is the ability to window the transmission data so that only two photons detected collinearly with the known location of a rod source are recorded as an event. Such a windowing scheme can reduce scatter in the transmission data, and also reduce the crosstalk in a simultaneous acquisition of both ECT and TT data [8].

1.3.2 Problems in Transmission Reconstruction

Several factors make the reconstruction of transmission data difficult. First, the necessities of a short-time scan and low dosage usage lead to noisy data as the result of low counts. The noise introduced by short-time scan is the most serious problem for transmission reconstruction. Secondly, simultaneous transmission/emission scans (called STEP for SPECT [9] and post-injection [97] scans in PET), necessary to reduce the problem of registration, can create crosstalk artifacts by interfering counts.
between ECT and TT (transmission tomography). Physical effects such as scatter or accidental coincidences (only for PET), which contaminate the image quality in both SPECT or PET, are other major degrading factors for transmission reconstruction. In addition, the geometry of fan beam collimators with line sources for transmission tomography in SPECT can cause data truncation [20]. Other problems, including patient or organ movement, degrade the image quality as well. In sum, TT is a challenging reconstruction problem requiring a sophisticated mathematical approach.

1.4 Overview

We have described the nature of nuclear medicine in this chapter, as well as a brief overview of instrumentation, properties, and problems of emission computed tomography and transmission tomography. The main focus of this thesis is to study the transmission tomography reconstruction problem as applied to both PET and SPECT. For this thesis, we focus on the use of Bayesian methods on the reconstruction of emission and transmission tomography. Thus the following chapters are organized as follows:

In chapter 2, we will discuss the process of projection formation in ECT and TT including models for physical effects as well as statistical models of the noise process. Two types of reconstruction methods, deterministic and statistical, are reviewed in chapter 3. First, we will discuss the taxonomy of reconstruction methods and further use this as a roadmap to classify all reconstruction methods. For deterministic approaches, the popular filtered backprojection (FBP) method is mentioned briefly, as well as some algebraic ones. Maximum likelihood (ML) reconstruction is formulated and also the expectation maximization (EM) algorithm used for ML calculation is mentioned. A conventional numerical optimization method, preconditioned conjugate
gradient (PCG) algorithm, is introduced as an alternative to the EM algorithm.
Maximum a posteriori (MAP) reconstruction is a way of stabilizing the ML method and capable of incorporating extra prior information about the object. We will discuss MAP methods and introduce two types of priors, pointwise and smoothing object models for MAP reconstruction methods. It turns out that pointwise priors lead to problems and which can be solved by the introduction of a so-called mixture model for the object. This is discussed in chapter 4. The mixture decomposition is carried out by an EM (expectation maximization) algorithm. An intriguing alternate interpretation of EM algorithm for mixture decomposition will also be introduced.

In chapter 5, we will apply the MAP reconstruction method with a gamma mixture model to transmission tomographic reconstruction and emission reconstruction. We propose a joint-MAP scheme with two MAP steps per iteration including transmission reconstruction and mixture model decomposition. The PCG algorithm applied to the MAP reconstruction in TT is derived.

Anecdotal reconstructions using the proposed method for transmission tomography are shown in chapter 6. Since transmission tomography is used mainly for attenuation correction in emission tomography, we also present results of performance testing of various AC methods upon a tumor detection task in the emission reconstructions, using attenuation correction from the transmission reconstructions. For emission, the poor performance of applying the mixture model is presented, and the inclusion of more information into the emission reconstruction, possible from anatomy, is discussed.

In chapter 7 we discuss the future work and directions resulting from this thesis, and summarize contributions.