

AN NONNEGATIVELY CONSTRAINED ITERATIVE METHOD FOR POSITRON EMISSION TOMOGRAPHY

JOHNATHAN M. BARDSLEY

Department of Mathematical Sciences
University of Montana
Missoula, Montana 59812, USA

ABSTRACT. In positron emission tomography (PET), data is collected via the detection of photons emitted by a radioactive tracer within the subject. The noise in PET data is Poisson, and hence, it is typical to reconstruct the tracer density distribution via the computation of an approximate minimizer of the negative-log Poisson likelihood function. In this paper, we present an iterative method for the solution of the PET inverse problem. A weighted least squares approximation of the negative-log Poisson likelihood is used. The method is nonnegatively constrained and, due to the ill-conditioned nature of the PET inverse problem, requires a stopping rule for its iterations. We present a statistically motivated stopping rule based on the χ^2 -test. The approach is implemented on a synthetically generated example, and is shown to be effective.

1. INTRODUCTION

Positron emission tomography (PET) is a medical imaging modality often used in cancer diagnostics. In PET, a radioactive tracer element is injected into a subject. After the tracer has been allowed to diffuse throughout the subject's body, the internal tracer density is reconstructed from measurements of emitted photons. For some examples of PET images, see [15].

The most common tracer element used in PET imaging is fluorodeoxyglucose (FDG) [15], a radioactive form of glucose. Knowledge of the FDG density distribution within an injected subject gives information about regional glucose uptake, which is in turn an indicator of metabolic activity. The presence of a cancerous tumor, for example, in a specific region will result in increased glucose uptake, and hence a higher concentration of FDG. This explains the usefulness of PET in diagnosing cancer.

After injection into the subject, the tracer exhibits radioactive decay, emitting positrons, which annihilate with electrons, producing a pair of annihilation photons moving in diametrically opposite directions. If two photons reach the detector ring at the same time (i.e. within a few nanoseconds of each other), an event is registered along the line connecting the corresponding detector pair. This line is known as the line of response (LOR). The collection of all such events from a particular experiment corresponds to a PET data set. From such data, the task is to reconstruct the tracer density distribution within the subject. In this paper, we present a method for this problem.

2000 *Mathematics Subject Classification*: 65J22, 65K10, 65F22.

Key words and phrases: positron emission tomography, iterative methods, regularization, statistical methods.

Email: bardsleyj@mso.umt.edu.

PET data is typically much more noisy than data obtained in more traditional medical imaging modalities (e.g. computed tomography) and also in image processing applications in which a CCD camera is used (e.g. astronomical imaging). Because of this, it is very important to accurately model PET noise statistics. We follow [4], and use the statistical model

$$(1) \quad \mathbf{z} = \text{Pois}(\mathbf{A}\mathbf{u}_e + \boldsymbol{\gamma}),$$

where \mathbf{u}_e is the true tracer density; \mathbf{A} is a discretization of the forward model (positron emission-to-event) matrix; $\boldsymbol{\gamma}$ is a background density vector (see [4] for details); and $\text{Pois}(\boldsymbol{\lambda})$ denotes a Poisson random vector with Poisson parameter vector $\boldsymbol{\lambda}$.

The probability density function for \mathbf{z} then has the form

$$(2) \quad p_{\mathbf{z}}(\mathbf{z}; \mathbf{u}) := \prod_{i=1}^n \frac{([\mathbf{A}\mathbf{u}]_i + \gamma_i)^{z_i} \exp[-([\mathbf{A}\mathbf{u}]_i + \gamma_i)]}{z_i!}.$$

Given image data \mathbf{z} arising from model (1), the maximum likelihood estimate of \mathbf{u}_e is obtained by minimizing $-\ln p_{\mathbf{z}}(\mathbf{z}; \mathbf{u})$ subject to the constraint $\mathbf{u} \geq \mathbf{0}$ (i.e. $u_i \geq 0$ for $i = 1, 2, \dots, n$); that is, by solving

$$(3) \quad \mathbf{u}_{\text{ML}} = \arg \min_{\mathbf{u} \geq \mathbf{0}} T(\mathbf{u}; \mathbf{z}),$$

where

$$(4) \quad T(\mathbf{u}; \mathbf{z}) \stackrel{\text{def}}{=} \sum_{i=1}^n \{([\mathbf{A}\mathbf{u}]_i + \gamma_i) - z_i \ln([\mathbf{A}\mathbf{u}]_i + \gamma_i)\}.$$

As is the case for least squares estimation, solutions of (3) tend to be noise-corrupted due both to random errors in \mathbf{z} as well as to the structure of \mathbf{A} . Thus some form of regularization is needed. One way that this can be accomplished is by truncating an iterative method applied to (3) [5]. When this approach is taken, the choice of stopping iteration becomes extremely important and is akin to the choice of regularization parameter in the standard Tikhonov approach to regularization [5, 14].

In the context of PET imaging, the Richardson-Lucy algorithm—an iterative method for solving (3) [8, 12]—is widely used, and stopping rules for its iterations have been given [7, 10, 11]. In this paper, we apply the iterative method and stopping rules of [1, 3]—developed in the context of astronomical imaging—to the PET imaging problem.

The paper is organized as follows. We begin in Section 2 with a brief description of the discrete forward model for PET image formation. Then in Section 3, we present the iterative method and stopping rule that we will use for the image reconstruction step. Finally, we perform a numerical experiment showing the effectiveness of the method and stopping rule in Section 4 and end with conclusions in Section 5.

2. THE PET DISCRETE MATHEMATICAL MODEL

In this section, we provide a summary of the derivation of the PET mathematical model found in [2].

PET data consists of counts of coincident photon pairs emitted in opposite direction by a radioactive tracer from a location within the subject (see [4] for details on the physics of PET). If two photons are sensed at the same time by the i th detector

pair, an event is registered along the connecting line L_i . For the discussion that follows, we parameterize L_i by length s ; that is, $L_i = \{x(s) \mid 0 \leq s \leq S\}$, where $x(0)$ and $x(S)$ correspond to the positions of the two detectors. We will use M to denote the number of detector pairs.

We focus on two-dimensional images and assume that the image domain Ω is the unit square. For practical purposes, Ω is divided into an $n \times n$ uniform grid. The tracer density u is then approximated on the grid by an $n \times n$ array, which yields, via column-stacking, the tracer density vector $\mathbf{u} = (u_1, \dots, u_{n^2})$. The intensity z_i measured via the number of incidents along L_i by detector pair i is then modeled by

$$z_i = \int_0^S g_i(t)u(t)dt \approx \sum_{k=1}^{n^2} b_{ik}g_{ik}u_k, \quad i = 1, \dots, M,$$

which can be written in matrix-vector form as

$$(5) \quad \mathbf{z} = \mathbf{A}\mathbf{u}, \quad \mathbf{A} = \mathbf{B} \odot \mathbf{G},$$

where “ \odot ” denotes Hadamard (component-wise) multiplication; $[\mathbf{B}]_{ik} = b_{ik}$ is the standard discrete Radon transform matrix (i.e. b_{ik} is the length of the intersection of L_i and the k th pixel); and $[\mathbf{G}]_{ik} = g_{ik}$, with g_{ik} the value of the instrument response function g_i (for connecting line L_i) at the k th pixel.

A model for the instrument response functions g_i , for $i = 1, \dots, M$, remains to be defined. The value of $g_i(x(r))$ corresponds to the measured intensity from an emitting δ -function source located at the point $x(r)$ on L_i . We make the standard assumption that the change in intensity dI along the line segment ds of L_i satisfies

$$dI(x(s)) = -\mu(x(s))I(x(s))ds,$$

where $\mu(x(s))$ is the mass absorption of the subject at the point $x(s)$. Then if $I(x(r)) = 1$, the intensities measured at $x(0)$ and $x(S)$ are given, respectively, by

$$I(x(0)) = \exp\left(-\int_0^r \mu(s)ds\right), \quad I(x(S)) = \exp\left(-\int_r^S \mu(s)dx\right).$$

Now, in practice, if the detector $x(0)$ (resp. $x(S)$) registers a photon, while one is not registered at $x(S)$ (resp. $x(0)$), no event is recorded. Thus we have

$$(6) \quad g_i(r) = \min\left\{\exp\left(-\int_0^r \mu(s)ds\right), \exp\left(-\int_r^S \mu(s)dx\right)\right\}.$$

Passing to the discrete setting, suppose μ_j is the value of the absorption density at pixel j , and g_{ik} is the value of the instrument response for L_i at pixel k . Then from (6) we have

$$(7) \quad g_{ik} \approx \min\left\{\exp\left(-\sum_{j \leq k} b_{ij}\mu_j\right), \exp\left(-\sum_{j \geq k} b_{ij}\mu_j\right)\right\}.$$

Defining $[\mathbf{G}]_{ik} = g_{ik}$ completes model (5). Since the absorption density within the subject is unknown, it much also be estimated via the solution of a computed tomography (CT) problem. In fact, modern PET machines often contain integrated PET/CT scanners [15] for this very reason.

Finally, since in practice \mathbf{z} is measured via the counting of photons and contains random noise, in place of (5), we use statistical model (1), with $\mathbf{A} = \mathbf{B} \odot \mathbf{G}$.

3. AN ITERATIVE METHOD AND STOPPING RULE

With the mathematical model in hand, it is now time to present our numerical method for approximately solving (3). In [1], a Taylor series argument is used to motivate the following quadratic approximation of T :

$$(8) \quad T(\mathbf{u}; \mathbf{z}) \approx T(\mathbf{u}_e; \mathbf{z}) + T^{\text{wls}}(\mathbf{u}; \mathbf{z}),$$

where

$$(9) \quad T^{\text{wls}}(\mathbf{u}; \mathbf{z}) \stackrel{\text{def}}{=} \frac{1}{2} \|\mathbf{C}^{-1/2}(\mathbf{A}\mathbf{u} - (\mathbf{z} - \boldsymbol{\gamma}))\|^2, \quad \mathbf{C} = \text{diag}(\mathbf{z}).$$

Here we assume that $\mathbf{z} > \mathbf{0}$. This leads to the following approximation of (3):

$$(10) \quad \mathbf{u}_{\text{WLS}} = \arg \min_{\mathbf{u} \geq \mathbf{0}} T_{\text{wls}}(\mathbf{u}; \mathbf{z}).$$

The algorithm of [3] for the numerical solution of (10) has the form

$$(11) \quad \mathbf{u}_{k+1} = \mathbf{u}_k - \tau_k \mathbf{u}_k \odot \mathbf{A}^T \mathbf{C}^{-1}(\mathbf{A}\mathbf{u}_k - (\mathbf{z} - \boldsymbol{\gamma})),$$

where “ \odot ” denotes Hadamard (component-wise) multiplication, and the line search parameter τ_k in (11) is given by

$$\tau_k = \min\{\tau_{\text{uc}}, \tau_{\text{bd}}\}.$$

Here, if $\mathbf{v}_k = \mathbf{u}_k \odot \nabla T_{\text{WLS}}(\mathbf{u}_k)$,

$$(12) \quad \tau_{\text{uc}} = \frac{\langle \mathbf{v}_k, \nabla T_{\text{WLS}}(\mathbf{u}_k) \rangle_2}{\langle \mathbf{v}_k, \mathbf{A}^T \mathbf{C}^{-1} \mathbf{A} \mathbf{v}_k \rangle_2},$$

and

$$\tau_{\text{bd}} = \min \{ [\mathbf{u}_k]_i / [\mathbf{v}_k]_i \mid [\mathbf{v}_k]_i > 0, [\mathbf{u}_k]_i \neq 0 \}.$$

This method has been shown to be effective on several astronomical imaging examples [1, 3].

Next, we develop a stopping rule for (11). From (8) we have

$$E(T(\mathbf{u}_e; \mathbf{z})) \approx T(\mathbf{u}_e; \mathbf{z}_e) + E(T_{\text{wls}}(\mathbf{u}_e; \mathbf{z})),$$

where E is the expected value function. Thus it is reasonable to say that acceptable iterates \mathbf{u}_k will be those for which

$$T_{\text{wls}}(\mathbf{u}_k; \mathbf{z}) \approx E(T_{\text{wls}}(\mathbf{u}_e; \mathbf{z})).$$

In order to obtain an estimate of $E(T_{\text{wls}}(\mathbf{u}_e; \mathbf{z}))$ we first approximate (1) as is often done in practice (see [3]):

$$(13) \quad \mathbf{z} - \boldsymbol{\gamma} = \mathbf{A}\mathbf{u}_e + \mathbf{e},$$

where \mathbf{e} is distributed as a zero-mean Gaussian random vector with covariance matrix \mathbf{C} defined in (9); that is, $\mathbf{e} \sim N(\mathbf{0}, \mathbf{C})$, where “ \sim ” means “is distributed as”. This in turn implies

$$(14) \quad \mathbf{r}(\mathbf{u}_e) \sim N(\mathbf{0}, \mathbf{I}_n),$$

where

$$(15) \quad \mathbf{r}(\mathbf{u}) \stackrel{\text{def}}{=} \mathbf{C}^{-1/2}(\mathbf{A}\mathbf{u} - (\mathbf{z} - \boldsymbol{\gamma})).$$

A standard statistical result then tells us that given (14),

$$(16) \quad \|\mathbf{r}(\mathbf{u}_e)\|_2^2 \sim \chi^2(n),$$

where $\chi^2(n)$ denotes the chi-squared distribution with n degrees of freedom, and hence

$$E(T_{\text{wls}}(\mathbf{u}_e)) \approx \frac{1}{2}E(\chi^2(n)) = \frac{n}{2}.$$

Since in early iterations $\frac{2}{n}T_{\text{wls}}(\mathbf{u}_k)$ is typically much larger than 1, a stopping rule of the form

$$(17) \quad \frac{2}{n}T_{\text{wls}}(\mathbf{u}_k; \mathbf{z}) \leq 1 + \epsilon_n$$

is therefore reasonable. We note that $\epsilon_n = 0$ corresponds to Morozov's discrepancy principle [9, 14], and we recommend its use unless (17) won't be satisfied in a feasible number of iterations. Otherwise, ϵ_n can be taken to be, for example, $\sqrt{2n}/n$, or $2\sqrt{2n}/n$, i.e. one, or two times the standard deviation of $\chi^2(n)$.

Stopping rule (17) for (11) was originally presented in [1], where stopping rules motivated by the generalized cross validation and unbiased predictive risk estimation methods were also introduced. We focus on the discrepancy principle (DP) stopping rule here because of its simplicity, as well as its effectiveness in the PET setting.

4. NUMERICAL RESULTS

We now demonstrate the effectiveness of our method on a synthetically generated example. The location of the emitting source is marked in dots on the left in Figure 1. The remaining regions of this image correspond to the absorption density array $\boldsymbol{\mu}$, which is needed in the definition of \mathbf{g} in (7). The forward model matrix \mathbf{A} is then defined as in (5). Data is generated following the approach of [2, 6] – in which a Monte Carlo method is used to simulate photon emission and detection – together with statistical model (1). The resulting noisy sinogram data is given on the right in Figure 1.

The inverse problem is to obtain the source location given the sinogram data \mathbf{z} and the forward model matrix \mathbf{A} . We do this using the iterative method and stopping rule presented in Section 3. With an initial guess of $\mathbf{u}_0 = \mathbf{1}$, stopping rule (17) with $\epsilon_n = 0$ was satisfied in the fifth iteration. The corresponding reconstructed source is given in Figure 2. Computations were done in MATLAB.

5. CONCLUSIONS

We have presented a statistically motivated iterative method and stopping rule for solving problems of the form (9), in the context of positron emission tomography (PET). A quadratic approximation of the negative-log Poisson likelihood function is needed in order to motivate the use of (9) in the PET setting. The Gaussian approximation (13) of the Poisson statistical model (1), on the other hand, is used to motivate our stopping rule. This rule is based on the χ^2 -test and is closely related to the classical discrepancy principle. In order to show that our method can be effectively used on PET data, we apply it to a synthetically generated data set with good results. Worth noting (for this example, anyway) is the lack of a need to choose any tuning (e.g. regularization) parameters. The method is also simple and efficient. On the other hand, the resolution of the reconstructed source location is not as high as was obtained with the more sophisticated method of [2].

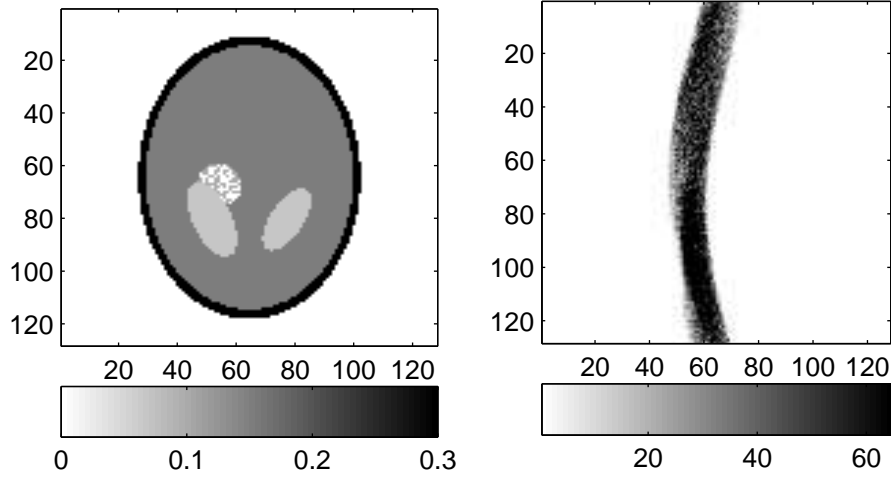


FIGURE 1. The absorption density μ is pictured on the left with the emission area marked with dots. The Monte Carlo simulation of the emission data \mathbf{z} (with Poisson noise) is pictured on the right.

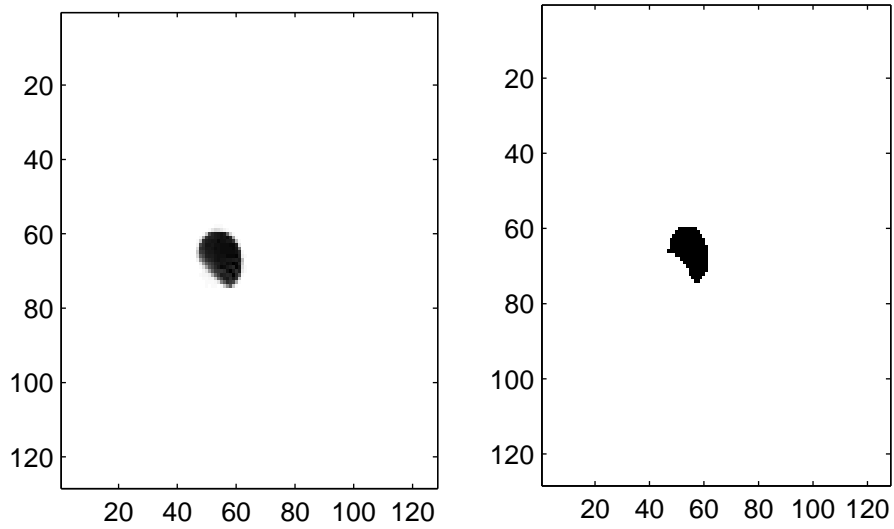


FIGURE 2. On the left is the tracer source location as estimated by the CPMRNSD iteration with DP stopping rule. On the right is the true source location.

ACKNOWLEDGEMENTS

The author would like to thank Daniela Calvetti and Erkki Somersalo for the permission to use their emission data generation codes for the numerical experiments.

REFERENCES

- [1] Johnathan M. Bardsley, *Stopping Rules for a Nonnegatively Constrained Iterative Method for Ill-Posed Poisson Imaging Problems*, BIT Numerical Mathematics, Volume 48, Number 4, December, 2008, pp. 651-664.
- [2] Johnathan M. Bardsley, Daniela Calvetti, and Erkki Somersalo, *Hierarchical regularization for edge-preserving reconstruction of PET images*, submitted, University of Montana, Department of Mathematical Sciences Tech. Report #1 2009.
- [3] Johnathan M. Bardsley and James G. Nagy, *Covariance-Preconditioned Iterative Methods for Nonnegatively Constrained Image Reconstruction*, SIAM Journal on Matrix Analysis and Applications, 27 (4), 2006, pp. 1184-1198.
- [4] John M. Ollinger and Jeffrey A. Fessler, *Positron-Emission Tomography*, IEEE Signal Processing Magazine, January 1997, pp. 43-55.
- [5] P. C. Hansen, *Rank-Deficient and Discrete Ill-Posed Problems*, SIAM, Philadelphia, 1997.
- [6] J. Heiskala, I. Nissilä, T. Neuvonen, S. Järvenpää and E. Somersalo, *Modeling anisotropic light propagation in a realistic model of the human head*, Appl. Optics **44**, 2005, pp. 2049-2057.
- [7] Jorge Llacer and Eugene Veklerov, *Feasible Images and Practical Stopping Rules for Iterative Algorithms in Emission Tomography*, IEEE Transactions on Medical Imaging, Vol. 8, No. 2, 1989, pp. 186-193.
- [8] L. B. Lucy, *An Iterative Technique for the Rectification of Observed Distributions*, The Astronomical Journal, **79** (1974), pp. 745-754.
- [9] V. A. Morozov, *On the solution of functional equations by the method of regularization*, Soviet Mathematics Doklady, vol. 7, 1966, pp. 414-417.
- [10] Kevin M. Perry and Stanley J. Reeves, *Generalized Cross-Validation as a Stopping Rule for the Richardson-Lucy Algorithm*, in The Restoration of HST Images and Spectra II. R.J. Hanisch and R.L. White, Eds., Space Telescope Science Institute, 1994, pp. 97-103.
- [11] Stanley J. Reeves, *Generalized Cross-Validation as a Stopping Rule for the Richardson-Lucy Algorithm*, International Journal of Imaging Systems and Technology, Vol. 6, 1995, pp. 387-391.
- [12] W. H. Richardson, *Bayesian-Based Iterative Method of Image Restoration*, Journal of the Optical Society of America **62** (1972), 55-59.
- [13] H. J. Trussell, *Convergence criteria of iterative restoration methods*, IEEE Transactions on Acoustics, Speech, and Signal Processing, ASSP-31, 1983, pp. 129-136.
- [14] C. R. Vogel, *Computational Methods for Inverse Problems*, SIAM, Philadelphia, 2002.
- [15] PET Wikipedia site: http://en.wikipedia.org/wiki/Positron_emission_tomography.