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# Modal Division and its Application to Medical Image Analysis.

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## Abstract

Statistical instability is the problem associated with the calculation of poorly defined variables from data corrupted by noise. The problem of statistical instability of numerical algorithms is well known in the image processing literature. Problems with instability of a small number of calculations is never worse than when attempting Fourier deconvolution. Each parameter in the Fourier domain affects every data point in the spatial domain so that unstable calculation of just one parameter distorts the solution for the entire space. The standard solution to this problem is often referred to as "optimal" or "Wiener" filtering. However, Wiener filtering is not found to yield good solutions in images and other authors have suggested alternative (empirical) techniques for solving the problem in practical situations. This paper explains the un-suitability of Wiener filtering for image deconvolution and defines a new technique based on an intuitive use of maximum likelihood, which we have called "modal arithmetic", and can be shown to generate the empirical methods used in positron emission tomography (PET) as a special case. The method is demonstrated on the deconvolution of 3D PET data.

## Introduction

Image reconstruction directly from back-projected images is still a method of choice for novel 3D PET systems (eg: PETRRA [1]), as spatial sampling accuracy of the system is retained whilst giving significant data size reduction. The reconstruction is normally carried out by 3D deconvolution of the system point response function. However, for noisy images this can yield unstable results so generally some form of constrained deconvolution is used.

Weiner filtering is based on a maximum likelihood derivation for the optimal linear filter which needs to be applied to data in order to give the minimum error in the spatial domain after deconvolution [2]. The technique involves estimating the noise in the power spectrum of the data (numerator) and setting any terms in the Fourier domain within some number of deviations from zero to that value. The problem with this approach is that it is still possible for very small values in the Fourier spectrum of the deconvolution kernel (denominator) to amplify residual noise (beyond the selected noise threshold) to very large values. The probability that this can happen increases as the scale of the Fourier space increases. Unfortunately, the number of Fourier terms in the FFT of an image is generally very large. Ultimately, the number of deviations from zero which must be used in order to ensure stable division is so great that the resulting deconvolution is compromised. In practical applications a technique which has been applied widely involves adding an offset term to the denominator. This limits the smallest value of the division and ensures a stable result but it is not clear how this technique is statistically justified compared to Wiener filtering. However, there is a more direct way of assessing the maximum likelihood value of a calculation which does not necessarily require the assumption of a linear filter solution. In the remainder of this paper we will examine the direct application of maximum likelihood to noisy denominators. We will show how the method most commonly used for the deconvolution of 3D PET data [3] follows from this alternative derivation with particular assumptions for the behavior of the data. The implications for design of image processing algorithms is far broader than this however, as the general approach can be applied to any non-linear calculation in order to regain computational stability.

## Methods

For division (eg:  $y = 1/x$ ), small errors on the data produce instabilities in computations involving large quantities of data. Error propagation shows that a small change in the input quantity  $\Delta_x$  will give an error on the corresponding output of

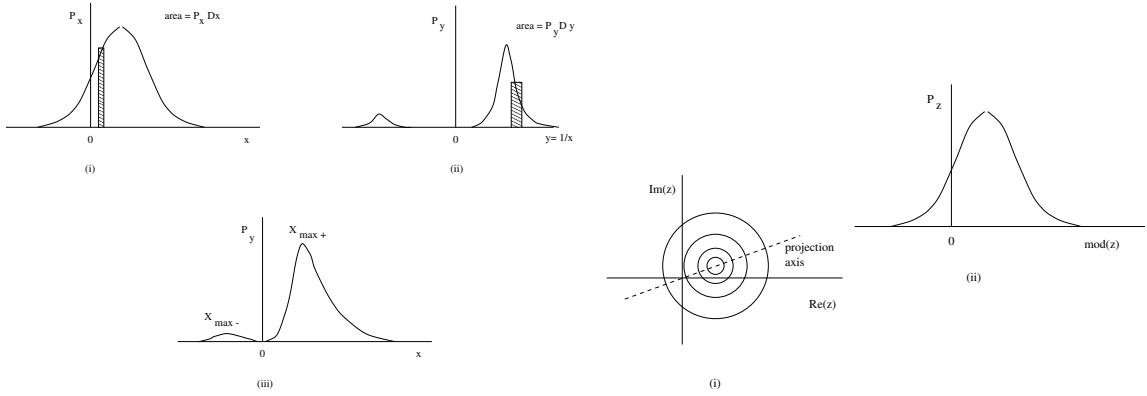
$$\Delta_y = \frac{\Delta_x}{x^2}$$

which is clearly unstable for values of  $x$  which are comparable to its error. This problem can be understood better by considering the distribution of computed values from the range of those available for input. We start by assuming a Gaussian distribution for the denominator.

$$P_x \Delta_x = A \exp(-(x - x_0)^2 / 2\sigma^2)$$

Where  $x_0$  is the central value of  $x$  with a standard deviation of  $\sigma$ . If we take a small area of data from the probability distribution for  $x$  (ie:  $P_x \Delta_x$ ), we can associate this with an equal number of solutions in the output space  $y$  (ie:  $P_y \Delta_y$ ) (figure 1 (a) (i) and (ii)) giving:

$$P_y = A x^2 \exp(-(x - x_0)^2 / 2\sigma^2)$$



(a) Probability distributions for  $x$  and  $y$ .

(b) Probability distributions for  $z$  and signed  $mod(z)$

Figure 1: Probability Distributions for a real and complex denominator.

This expected probability distribution for  $y$  as a function of  $x$  (figure 1(a)(iii)) can be differentiated to find its maxima. Setting this to zero we can determine the modal values of this distribution:

$$x^2 - x_0 x - 2\sigma^2 = 0 \quad \text{with} \quad x_{max} = \frac{x_0 \pm \sqrt{x_0^2 + 8\sigma^2}}{2}$$

which correspond to the positive and negative peaks due to the distribution of  $x$  spanning zero (figure 1(a)(i)). If we were to ask which value of  $y$  would be most likely to result from the division then the answer would be  $1/x_{max}$  selected with the same sign as the input value  $x_0$ . Taking this value as a replacement for the denominator provides a maximum likelihood technique of stabilising the process of division using knowledge of measurement accuracy and could best be described as **modal division**. Modal division can be used with impunity for calculations involving large quantities of noisy data without instability problems for values around zero, with the minimum denominator limited to a value of  $\sqrt{2}\sigma$ .

A simple symmetry argument can be used to show that the technique can be easily extended to complex numbers  $z$ , with equal independent Gaussian errors on both real and imaginary components (figure 1(b)(i)), by applying the correction to the magnitude of the complex number (figure 1(b)(ii)).

$$mod(z_{max}) = \frac{mod(z_0) + \sqrt{mod(z_0)^2 + 8\sigma^2}}{2} \quad \text{and} \quad z_{max} = z_0 \cdot mod(z_{max}) / mod(z_0)$$

The general method of modal arithmetic for a measured value with distribution  $D(x)$  and a non-linear function  $f(x)$  would be to find the solution  $x_{max}$  of

$$\partial \left[ \frac{D(x)}{\partial f(x) / \partial x} \right] / \partial x = 0$$

with the modal solution of  $f(x_{max})$ . Modal arithmetic is unconditionally stable, as peaks in probability distributions cannot occur at infinity. It also has much similarity with some approaches in statistics which advocate the use of the **mode** rather than the **mean** as the most robust indicator of a distributed variable.

It is not immediately obvious that the method of modal division can be applied to deconvolution. The standard approach proceeds as follows:

$$I = U.R \text{ implies } U = I/R = IR^*/(R^*R)$$

where  $I$  and  $U$  are the complex Fourier coefficients from the image data and signal source respectively, and  $R$  is a coefficient from the assumed convolution kernel. From Parseval's theorem and the orthogonality of the Fourier domain, we know that uniform independent Gaussian errors in the spatial domain correspond to uniform independent Gaussian errors in the spatial frequency domain. The errors on the data  $I$  are generally assumed to come from the measurement process, either in the spatial or spatial frequency domains. However, the observable error  $\sigma_I$  can just as easily be generated from noise in each component of the convolution kernel  $\sigma_R$ , ie:

$$\sigma_I^2 = \text{mod}(U)^2 \sigma_R^2$$

This change in the assumed image formation process makes no difference to the observed data but makes modal division appropriate <sup>1</sup>. Using this relationship we can compute the error on a coefficient in the kernel  $R$  needed to generate the expected error in the measured image <sup>2</sup>. We can then apply the method of modal division to Fourier deconvolution.

$$\text{mod}(R_{max}) = \frac{\text{mod}(R) + \sqrt{\text{mod}(R)^2 + 8\sigma_I^2/\text{mod}(U)^2}}{2}$$

This method can be implemented as an iterative calculation

$$\text{mod}(R_t) = \frac{\text{mod}(R_0) + \sqrt{\text{mod}(R_0)^2 + 8\sigma_I^2/\text{mod}(U_{t-1})^2}}{2}$$

$$U_t = IR_t^*/R_t^*R_t$$

with  $U_0 = I$  and  $R_0 = R$ . Since convolution generally involves attenuation of the value of coefficients (ie:  $I < U$ ), this is expected to be computationally stable as early iterations overestimate the error on  $R$ . Further, as the calculation involves only a slight modification to the computed values it is expected to converge rapidly.

## Results

The above theory is directly applicable to calculations in medical image processing involving a division of voxel values. One example of this is in the calculation of perfusion flow from relative cerebral blood volume (RCBV) and mean transit time (MTT) [4, 5]. However, the most convincing demonstration of the method is with Fourier deconvolution. One of the standard applications of this is in the deconvolution of 3D PET images after back projection. The expected deconvolution kernel is a symmetrical function with  $1/r^2$  dependency. PET data has Poisson noise characteristics and this leads to correlations in the noise in the spatial frequency domain. However, we need only know the individual distributions for each component in order to apply modal division. Treated separately, the co-efficients have Gaussian noise with equal variance as modelled above.

The method suggested by Chu and Tam in [3] is a constrained deconvolution which has been used by other groups (eg: [7]). It is derived from an assumption of smoothness in the reconstructed image and of the form

$$U'(\mathbf{p}) = \frac{I(\mathbf{p})}{R(\mathbf{p}) + \gamma p^4/R(\mathbf{p})}$$

<sup>1</sup>Clearly there is an infinite set of possible models with different levels of contribution to the statistical error from both sources but this model is the one which will result in the greatest stability.

<sup>2</sup>Interestingly, the resulting kernel error

$$\sigma_R^2 = \sigma_I^2/\text{mod}(U)^2$$

is also indicative of the accuracy to which this coefficient must be determined in order to attempt deconvolution, with the implication that contrary to conventional teaching we do not need highly accurate estimates of all kernel co-efficients in order to get stable results.

where  $U'(\mathbf{p})$  is an estimate of the constrained solution at spatial frequency  $\mathbf{p}$ ,  $\gamma$  is a constant proportional to the noise level and  $R(\mathbf{p})$  is real. The method is not defined for asymmetric kernel functions (ie: complex  $R(\mathbf{p})$ ). Assuming that  $R(\mathbf{p})$  is small (which would therefore be potentially a cause of instability) the correction terms in the two approaches can be directly compared, ie:

$$\sigma_I \sqrt{2R(\mathbf{p})^2 / \text{mod}(I(\mathbf{p}))^2} \approx \gamma p^4 / R(\mathbf{p}) \quad \text{implies} \quad \text{mod}(I(\mathbf{p})) \propto R(\mathbf{p})^2 p^{-4}$$

The scaling with noise is directly equivalent. The Chu and Tam result can be interpreted as equivalent to modal division only on the assumption of a typical relationship between the power spectra of the data and kernel. This result is in keeping with the assumptions of the original paper. The practical difference between the two approaches is that those occasions where the algorithm fails can often be recovered by adjusting the value of  $\gamma$ . For modal division, this parameter can be replaced by a value computed using error propagation.

Typical results from deconvolution of back-projected 3D PET images for the standard technique and modal division are given in Figure 2 below. The image is an 18-FDG (fluorodeoxy-glucose) scan of a mouse (Fluorine 18 positron emitter). The data were Acquired on the HIDAC (II) [6] scanner at the Paterson Institute for Cancer Research. The slice is 128x128 voxels, each of 1 mm side length. (from a 128x128x128 matrix). The scanner has two main rotating planar detectors: each with two HIDAC detection modules, of size 320mm x 320 mm with a detector separation of 714 mm. There is clearly very little difference between the final results which implies that the required relationship between the power spectra are indeed quite close. However, one would have to worry about the stability of the Chu and Tam method for other deconvolution kernels.

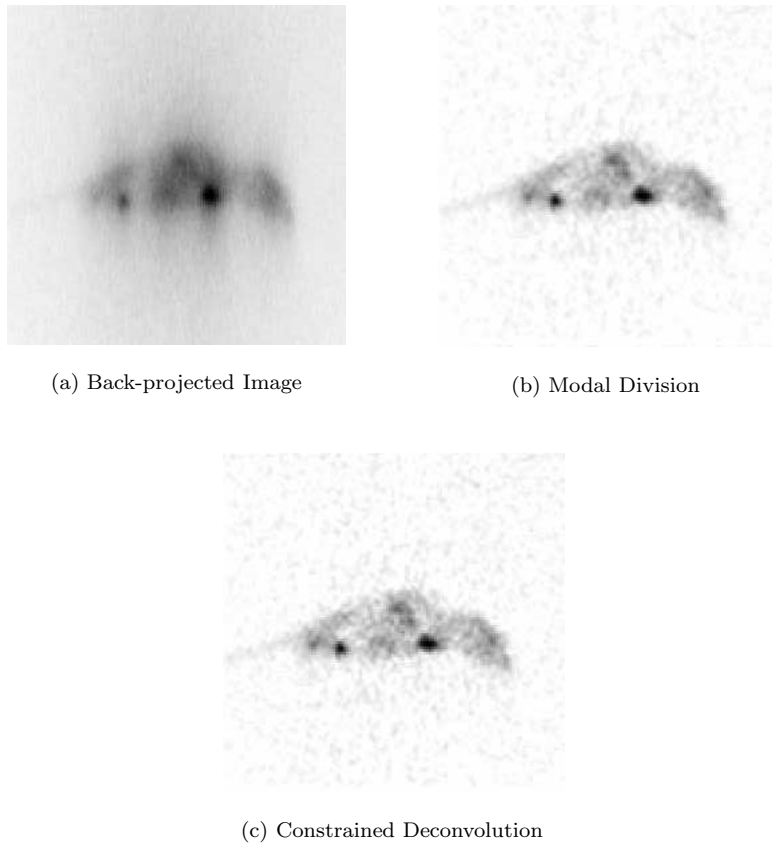


Figure 2: Performance of modal division and constrained deconvolution on PET data.

## Conclusions

The problem of statistical stability occurs frequently in medical image analysis but is probably never more obvious than in the deconvolution of image data, where denominators comparable to the noise level are frequent yet every coefficient must be computed stably in order to give an accurate result. Common

methods for dealing with such data based on maximum likelihood have key failings, while more ad-hoc techniques have often been more successful. This demonstrates that statistical methods have not yet been correctly applied to the problem. Ultimately, appropriate statistical methods should give the best performance. We have defined a new approach to the design of unconditionally stable algorithms based upon maximum likelihood which we call “modal arithmetic”. We have been able to show how the most common (practical) technique for deconvolution in the 3D PET images can be related to the method derived using this technique. The results obtained, do not demonstrate the new technique to be any better than the empirical method on this data. A more systematic evaluation is required if we wish to establish this. In fact we have recently been able to show that the convergence point of our iterative algorithm is the same as using Wiener Filtering. However, the results do illustrate the validity of this new methodology for designing stable computational processes. The basic approach to the implementation of non-linear calculations in noisy data sets has scope for general applicability. The method of modal image division is available within the TINA software which is available as open source from our web site [8].

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