Regularizing Direct Parametric Reconstruction for Dynamic PET with the Method of Sieves

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***Abstract*—This paper proposes regularization methods for direct parametric dynamic PET reconstruction, when the space-time activity function needs to be recovered from measurements. In case of high spatial and temporal resolution, the reconstruction is statistically poorly defined, requiring the inclusion of a priori information in the form of a penalty term or filtering. The method of sieves executes filtering in each iteration step, i.e. projects the actual estimate into the subspace of acceptable solutions, and has been successful in reconstructing static data. The objective of this paper is to generalize the filtering scheme for spatio-temporal reconstruction, taking into account that accurate kinetic models describing the temporal behavior are non-linear. Fast changes are impossible to distinguish from noise if only a small temporal window is examined, thus the simple extension to 4D does not provide acceptable results. We show that efficient filtering can be obtained if voxel based model parameters are modified according to the time activity functions of neighboring voxels belonging to the same anatomic region. As the dependence of the time activity function on the model parameters is non-linear for sophisticated kinetic models, the filtering step involves a non-linear parameter fitting, which can be solved analytically for the two-tissue compartment model. The presented method is compared to the application of a TV penalty of the voxel activities. The presented model is built into the TeraTomo$^{\text{TM}}$ system.**

I. Introduction

In dynamic Positron Emission Tomography (PET), we focus on the dynamic nature of biological processes, like accumulation and emptying drugs in certain organs. Generally, we assume that the radiotracer concentration in each voxel V in time t can be expressed by a common *kinetic model* $C(\mathbf{p}_V, t)$, where spatial dependent properties of voxel V are encoded in a low dimensional vector of kinetic parameters $\mathbf{p}_V$. Such models can be defined based on the mathematical description of the biological/chemimal processes or on compartment analysis [1], [6], [5]. The expected number of radioactive decays, i.e. number of positrons generated in voxel V and in time frame T covering $[t_T, t_{T+1})$ is

$$\tilde{x}_T(\mathbf{p}_V) = \int_{t_T}^{t_{T+1}} C(\mathbf{p}_V, t) \exp(-\mu t) \mathrm{d}t,$$

where μ is the decay rate of the radiotracer. The positron emitted at a decay may annihilate with an electron, when two oppositely directed gamma-photons are born, which might be detected by the tomograph. A PET/CT system collects the *events* of simultaneous photon incidents in detector pairs. An event is a composition of the identification of the detector pair, also called *Line Of Response* or *LOR*, and its time of occurrence. The state-of-the-art and previous work on direct estimation of kinetic parameters for dynamic PET are surveyed in review articles [4], [2].

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According to the concept of maximum-likelihood reconstruction, unknown parameters $\mathbf{p}$ are found to maximize the log-likelihood:

$$\mathbf{p} = \arg\max \log \mathcal{L}, \qquad \log \mathcal{L} = \sum_L \sum_T \left(y_{L,T} \log \tilde{y}_{L,T} - \tilde{y}_{L,T} \right) \tag{1}$$

where measured number of hits $y_{L,T}$ in LOR L in frame T follows a Poisson distribution of expectation $\tilde{y}_{L,T}$ that can be computed from the activity $\tilde{x}_T(\mathbf{p}_V)$ of voxels in frame T. The solution of the optimization problem usually iteratively updates the parameters of voxels.

II. Spatial filtering of time activity functions

There are various options to regularize the solution, which is essential in the case of inverse problems. One option is the modification of the optimization target in Equation 1 by a regularization term that penalizes unacceptable solutions having too high spatial or temporal variation.

In this paper, we use another option, called the *method of sieves* [3]. In this approach, the optimization target is not modified, but the iterated approximation is filtered in each iteration step. The objective of filtering is to find an acceptable solution that is close to the solution proposed by the iteration. Mathematically, this approach projects the current estimate into the subspace of acceptable solutions in each iteration. Filtering can also exploit anatomic information gathered by a CT or an MR.

For each voxel, we wish to set the time activity function to the weighted average of the those of the neighboring voxels of the same anatomic region. Weights $G(V', V)$ can be selected as a distance dependent Gaussian if V and V' belong to the same anatomic region and zero otherwise. Thus, our target filtered time activity function in voxel V is:

$$C(\mathbf{p}_V, t) \approx \frac{\sum_{V'} C(\mathbf{p}_{V'}, t) G(V', V)}{\sum_{V'} G(V', V)} = \sum_{V'} C(\mathbf{p}_{V'}, t) w(V', V)$$

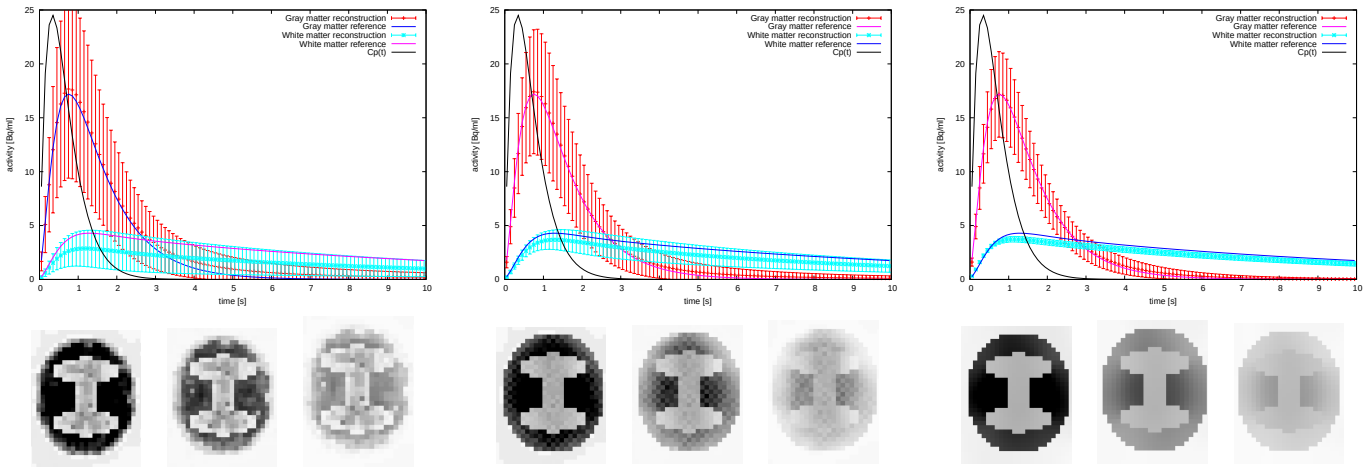
where $w(V', V)$ are the normalized weights that sum up to 1. Note that in the classical application of the method of sieves, this filtering is computed on scalars, but here we need to average functions. If the time activity curves were expressed as a linear combination of pre-defined basis functions, then the filtering of functions would be equivalent to the filtering of the parameters defining the time activity functions. However, sophisticated kinetic models are non-linear. For example, the popular *two-tissue compartment model* assumes the following concentration function:

$$C(\mathbf{p}, t) = (1 - f_v) \sum_{i=1}^{2} a_i \alpha_i \exp(-\alpha_i t) * C_p(t) + f_v C_w(t),$$

$$\mathbf{p} = (f_v, a_1, a_2, \alpha_1, \alpha_2),$$

where f_v is the fractional volume of blood, $*$ stands for convolution, $C_p(t)$ and $C_w(t)$ are the known activity function of the blood and the whole blood concentration function, respectively.

Clearly, filtering the parameters independently does not work for non-linear functions, because there is no guarantee that the resulting function will be in between the filtered functions.



no regularization | TV regularization, $\lambda = 0.1$ | method of sieves, $\sigma = 1.5$

Fig. 1. Reconstructed time activity curves showing the average and the standard deviation for the anatomic regions in $t = 1$, $t = 2$, and $t = 3$

In our filtering algorithm, f_v is handled separately and is filtered first. Having fixed its value, filtered parameters $(a_1, a_2, \alpha_1, \alpha_2)$ of voxel V must be obtained. As the blood input function is shared, the similarity of the time activity functions requires

$$(1 - f_v) \sum_{i=1}^{2} a_i \alpha_i \exp(-\alpha_i t) \approx$$

$$\sum_{V'} (1 - f_{v,V'}) \sum_{i=1}^{2} a_{i,V'} \alpha_{i,V'} \exp(-\alpha_{i,V'} t) w(V', V).$$

To find the filtered parameters, we require the integral of the two sides of this equation be equal, and also the equality of their values, first and second derivatives at $t = 0$, respectively, resulting in the following four non-linear equations for the four unknowns:

$$\sum_{i=1}^{2} \alpha_i^j a_i = A_j, \quad j = 0, 1, 2, 3,$$

where A_0, A_1, A_2, A_3 are weighted averages. Unknown parameters $(a_1, a_2, \alpha_1, \alpha_2)$ can analytically obtained by solving first a second order equation for α_1:

$$(A_0 A_2 - A_1^2)\alpha_1 - (A_1 A_2 - A_0 A_3)\alpha_1 + (A_1 A_3 - A_2^2) = 0,$$

and then using the following substitutions:

$$\alpha_2 = \frac{A_3 - A_2 \alpha_1}{A_2 - A_1 \alpha_1}, \quad a_2 = \frac{A_1 - A_0 \alpha_1}{\alpha_2 - \alpha_1}, \quad a_1 = A_0 - a_2.$$

III. Results

To examine the proposed method, we use a 2D mathematical tomograph model where the detector ring contains 90 detector crystals and each of them is of size 2.2 in voxel units and participates in 47 LORs connecting this crystal to crystals being in the opposite half circle, thus the total number of LORs is $90 \times 47/2 = 2115$. The voxel array to be reconstructed is in the middle of the ring and has 32×32 resolution, i.e. 1024 voxels. The measured data is obtained with Monte Carlo simulation of a brain model where there are three homogeneous regions, including the white matter, the gray matter, and the background. The simulation generated 16k hits in total, distributed in 100 frames covering a 10 second long interval. Note that this is a low statistic measurement where the average number of hits per frame per LOR is less than 0.08.

The measurements are reconstructed without any spatial regularization, with TV penalty on the activity values, and with the proposed method. The results are shown in Fig. 1. Note that TV penalty reduces both the bias and the variance of the reconstruction, but is poorer than the result obtained with the method of sieves. Efficient penalty based regularization algorithms use the *one-step-late option*, which has negligible computational overhead, but may prohibit convergence when the reguralization parameter λ is too strong. Here we used $\lambda = 0.1$, which is found to be optimal, i.e. lower values cause higher variance reconstructions, higher values divergence and stronger chess-pattern like artifacts. Thus, using the one-step-late option, the applicability of TV reguralization is limited. This is not the case for the method of sieves, where the homogeneity of anatomic regions can be enforced without limits by increasing the standard deviation of the position based Gaussian.

IV. Conclusions

In this paper we investigated the regularization problem of direct parametric PET reconstruction. We proposed the application of spatial averaging of the voxel-based time activity functions, i.e. the method of sieves, as a way of regularization. To implement the basic idea, we also addressed the problem of averaging non-linear functions in parameter space. The proposed method can use anatomic information about region boundaries and remains stable for aggressive filtering as well. In our fully-3D implementation all steps are implemented on the GPU where the added computational cost of filtering is negligible with respect to forward and back projection calculations.

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