# Physically Informed Neural Network for Non-Invasive Arterial Input Function Estimation In Dynamic PET Imaging

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## Abstract

The invasive measurement of the AIF for the full quantification of dynamic PET data limits its widespread use in clinical research studies. Current methods which estimate the AIF from imaging data are prone to large errors, even when based on NNs. This work aims to estimate the AIF from dynamic PET images using physically informed deep neural networks. To this end, we employ 3D convolutions where we exploit the different channels to encode time-dependent information, and exploit depthwise separable convolutional layers to significantly reduce parameter count. We find that the incorporation of prior knowledge in the form of differentiable equations allows accurate estimation of the AIF. This allows kinetic modelling which leads to good estimates of the distribution volume. This work can pave the way for removing the large invasivity constraint that currently limits quantitative PET applications.

**Keywords:** PINN, AIF, separable convolutions, quantitative PET imaging

## 1. Introduction

The translocator protein 18kDa (TSPO) is upregulated by activated microglia and macrophages, therefore representing a target for [11C]PBR28 Positron Emission Tomography (PET)-based *in vivo* imaging of neuroinflammation. Quantitative PET requires sampling of the Arterial Input Function (AIF) via invasive arterial cannulation, which comes with several challenges including e.g. higher clinical staff demands and additional patient burden. While it could be possible to estimate the AIF noninvasively through deep learning techniques, this is often hampered by 1) the need for large data sets 2) the data footprint 3D/4D medical images (which results in high computational burden and model parameter count). Here we aimed to estimate the AIF from a dynamic PET acquisition (i.e. a 4D image only) while employing a parameter efficient, Physically Informed Neural Network (PINN).

We inject *a priori* knowledge about the AIF time course (Karniadakis et al., 2021) while 4D dynamic PET images form the input for a set of depthwise separable convolutional layer. Time evolution is encoded in the channels, hence forgoing the use of 4D convolutional layers. Quantitative PET results obtained (in the test set) using the estimated *versus* real AIF are not statistically different, indicating that deep learning techniques may provide a valuable strategy to limit the need for arterial cannulation.

## 2. Material and methods

[$^{11}$C]PBR28 Positron Emission Tomography/ Magnetic Resonance Imaging (PET/MRI) of the brain was performed with a Siemens Biograph mMR on 50 individuals (22 females; 58.2/13.2 years old [mean/SD], 15 mCi of [$^{11}$C]PBR28, 90 minutes). Arterial blood samples were collected at 3-10s (first 3 minutes) and at 5, 10, 20, 30, 50, 70 and 90 minutes post-[$^{11}$C]PBR28 injection, and radio-metabolite-corrected AIFs were obtained for each subject. T1-weighted structural Magnetic Resonance Imaging (MRI) volumes were also acquired for anatomical localization and selection of Region Of Interests (ROIs).

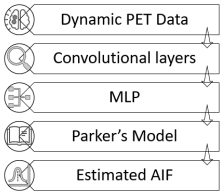


Figure 1: *Architecture overview*

Our network was trained to approximate the mapping function from the dynamic PET images to the parameters of the equation known as the Parker Model (PM), which describes the AIF as a mixture of two Gaussians and an exponential modulated by a sigmoid function (Parker et al., 2006):

$$\mathrm{AIF}(t) = \sum (\mathrm{A}_n = (\ _n\sqrt{2}\ ) \exp((-t - \mathrm{T}_n)^2 = 2\ \ ^2_n) + \quad \exp((-\ \ t) = (1 + \exp(-s(t - \ \ ))) \quad (1)$$

where $\mathrm{A}_n$, $\mathrm{T}_n$, and $_n$ are the scaling constants, centers, and widths of the nth Gaussian, and are the amplitude and decay constant of the exponential, $s$ and are the width and center of the sigmoids, respectively.

Our architecture (Figure 1) consisted of six depthwise separable 3D strided convolution layers which repeatedly downsample the dynamic 4D PET image by a factor of two. We employed 3D convolutional layers and included time information in the channels. The interaction between channels was split through the implementation of a depthwise separable 3D convolution, which consisted of the sequential application of depthwise and pointwise convolutions. This resulted in both a considerable reduction of parameter count (a factor of twenty) and a computation of spatiotemporal features thanks to the pointwise channel's interaction term. The convolution layers were followed by an average pooling layer with a kernel size of two. Features were then flattened and passed to a multilayer perceptron of depth 3 with hyperbolic tangent activation functions that mapped the features onto the ten parameters of the PM. The PM was integrated into the computational graph to output an AIF estimate over 200 evenly sampled time points which was compared to the original one during training (mean squared error loss, 80 : 20 train/test split). The model was trained on an NVIDIA A100 GPU (80GB RAM; batch size: 20, 2500 epochs, Adam optimizer, learning rate:1e - 4; reduced by 10% every 500 epochs). The network learns how to predict parameters of the PM model from the PET image. After training, the estimated AIF in the test set was used to model [$^{11}$C]PBR28 kinetics with the 2TCM With Irreversible Vascular Trapping (2TCM-1k) (Figure 2).

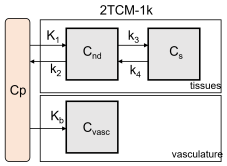


Figure 2: *Compartmental model. $C_p$: plasma compartment; $C_{nd}$/$C_s$: tissue compartments; $C_{vasc}$: vascular component.*

This resulted in the estimation of the distribution volume $v_T$ ($mL$=$cm^3$, proportional to receptor density and binding activity) from the model parameters as : $v_T = (K_1 = k_2)(1 + (k_3 = k_4))$ where the microparameters $K_1$ ($mL$=$cm^3$ per minute), $k_2$ (1/minute), $k_3$ (1/minute), and $k_4$ (1/minute) are the rate constants for tracer transport from plasma to tissue and