dPETSTEP

- Run your first simulation -

Introduction

dPETSTEP (https://github.com/CRossSchmidtlein/dPETSTEP) is a fast dynamic PET simulator designed for high throughput simulation of dynamic PET images. It allows full simulation of a user defined parametric image, kinetic model, input function, time sampling and more into realistic (noisy) dynamic PET-like images. Furthermore, the dynamic PET data can then be model fitted to produce parameter/parametric image estimates.

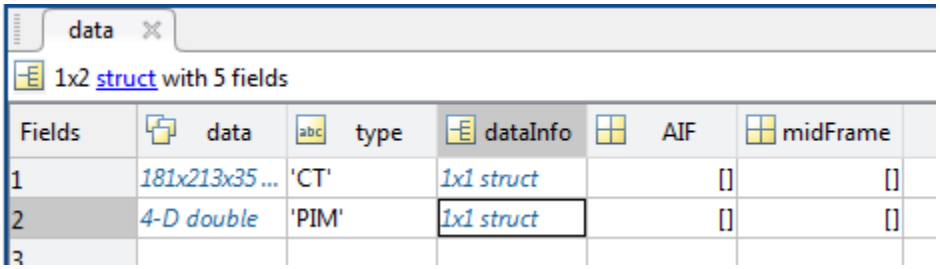
This application is written in MATLAB and designed as an extension of PETSTEP (https://github.com/CRossSchmidtlein/PETSTEP). Currently, MATLAB functions from PETSTEP are used by dPETSTEP, but there is no requirement of installing CERR (Computational Environment for Radiological Research, https://github.com/adityaapte/CERR).

Data structure

The data used by dPETSTEP should have a certain format, as will be specified below. It should contain three fields: data, type and dataInfo. It should contain two rows per field:

1. The first row should be the CT or mu-map of the object. Data should contain the 3D matrix of the object. Type should be “CT” or “mumap”.
2. The second row should be the parametric image of the object. Data should be the 4D (3 spatial + 1 parametric) matrix with the parametric object. Type should be “PIM”.

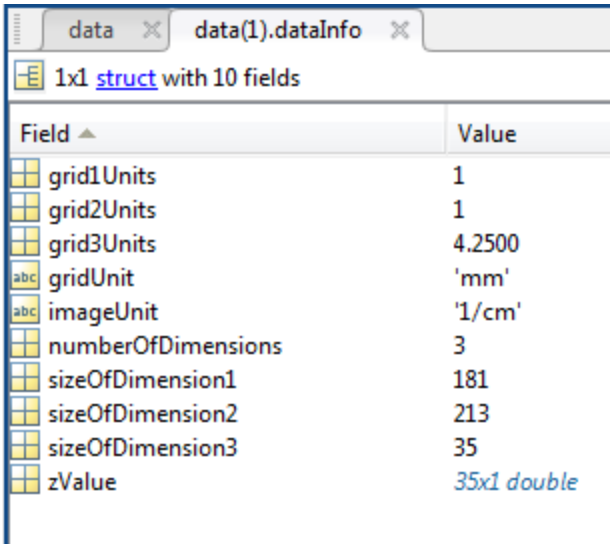
These data should be stored in a 1x2 structure named “data”:



In the example folder in the github repository, there is a *.mat-file with a sample data structure file. You can use that data as a starting point and just change the data and relevant information for your own simulation.

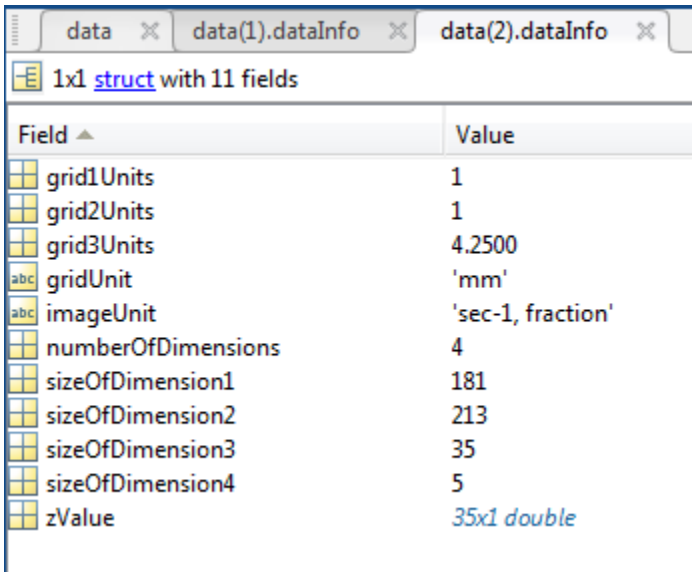
CT or mu-map

The dataInfo for the CT or mu-map should contain the fields as in the figure below. Currently, the grid units have to be in millimeters. For mu-maps, the unit should be 1/cm. The zValue is a vector with the mid slice positions in millimeters.



Parametric image

The dataInfo for the parametric image should look like below. The grid units should be in millimeters, and the rate constants should be in 1/sec. The zValue is a vector with the mid slice positions in millimeters.



Run a simulation

Once you have the input data structure set up properly according to above, you can start your simulation process. First however, there are a few things you need to do.

Kinetic modelling

1. You need to adjust all settings of the simulation according to your preference. Do this by opening “Dynamic_setSimParameters.m” and adjust the fields as you like.

   >> open Dynamic_setSimParameters.m

```
function simSet = Dynamic_setSimParameters(frame,Cif)
%*****************************************************************************************************
% Sets dPETSTEP simulation parameters.
%
% USAGE  : simSet = Dynamic_setSimParameters(frame,Cif)
%
% INPUT  : frame    Vector with start and end frame times in sec,
%                   [frameStart1; frameStart2=frameEnd1; frameStart3=frameEnd2;...].
%          Cif      Vector with input function to model (AIF or reference tissue TAC).
%
% OUTPUT : simSet  Structure with all simulation settings
%*****************************************************************************************************
% IH, 19/04/2016
%
% Copyright 2016, C. Ross Schmidtlein, on behalf of the dPETSTEP development team.
%
% This file is part of the Dynamic PET Simulator for Tracers via Emission Projection (dPETSTEP) software.
%
% dPETSTEP development has been led by:  Ida Häggström, Bradley J. Beattie and C. Ross Schmidtlein.
%
% dPETSTEP has been financially supported by the Cancer Research Foundation in Northern Sweden,
% the US National Institutes of Health and the National Cancer Institute under multiple grants.
%
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%
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%     it under the terms of the GNU General Public License as published by
%     the Free Software Foundation, either version 3 of the License, or
%     (at your option) any later version.
%
% dPETSTEP is distributed in the hope that it will be useful, but WITHOUT ANY WARRANTY;
% without even the implied warranty of MERCHANTABILITY or FITNESS FOR A PARTICULAR PURPOSE.
% See the GNU General Public License for more details.
%
% You should have received a copy of the GNU General Public License
% along with dPETSTEP.  If not, see <http://www.gnu.org/licenses/>.
%*****************************************************************************************************

%% Simulation parameters
simSet = struct;

% input parameters
simSet.CTscanNum  = 1;                  % CT  scan's ID : should be automated
simSet.PIMscanNum = 2;                  % Parametric image scan's ID : should be automated
simSet.PTscanNum  = 3;                  % Dynamic PET image scan's ID : should be automated

% count data
simSet.countSens      = (265/324)*6.44; % 3D sensitivity (counts/kBq/s) (GE DLS)
simSet.SF             = 0.289;          % scatter fraction S/(T+S)
simSet.RF             = 0.02;           % randoms fraction R/(T+S+R)
```

```
% Dynamic settings
simSet.frame          = frame;          % Vector with frame times in sec.
simSet.dwellTime      = diff(frame);    % Frame lengths.
simSet.Cif            = Cif;            % Vector with input function in Bq/cc. Either arterial input function.
                                        % or reference tissue TAC, depending on what model you use.
simSet.CifScaleFactor = 1;              % Scale factor to multiply the supplied input function with.
simSet.halflife       = 'none';         % Halflife of nuclide in sec, or 'none' for no decay.
simSet.timeStep       = 0.5;            % Convolution time step in sec.
simSet.interpMethod   = 'linear';       % Interpolation method.
simSet.kineticModel   = '2-Tissue';     % Desired kinetic model, '1-Tissue', '2-Tissue', 'FRTM', 'SRTM' or 'sumExp'.

% scanner charaterisitics
simSet.RingData   = 880;        % the diameter of the scanner ring (GE DLS)
simSet.tanBin     = 336;        % Sets inital projetion data size (GE DLS)
simSet.maxRingDiff= 11;         % Maximum allowed ring difference
simSet.psf        = 5.1;        % Assumes a PSF for the system, uses same for correction. FWHM.
simSet.blurT      = 5.1;        % DLS

% image reconstruction definitions
simSet.fovSize    = 128;        % size of dynamic image FOV in mm. Voxel size = fovSize/simSize.
simSet.simSize    = 128;        % matrix size of reconstructed image
simSet.zFilter    = [1 4 1];    % post recon Z-axis filter 3-point smoothing
                                % Heavy[ 1 2 1]/4, Standard[1 4 1]/6, Light[1 6 1]/8, None[0 1 0]
simSet.postFilter = 6;          % FWHM in (mm) of post reconstruction filter. FWHM = 2*sqrt(2*log(2))*sigma.
simSet.iterNUM    = 5;          % number of iterations
simSet.subNUM     = 16;         % number of subsets

% Biologic variability
simSet.addVariability   = false;  % Flag to add biologic variability or not
simSet.variabilityScale = 10;     % Scale factor of variability (variance of gaussian noise = image/scale)

% Reconstructions
simSet.FBP_OUT       = false;
simSet.OS_OUT        = false;
simSet.OSpsf_OUT     = false;

% number of replicate data sets
simSet.nREP       = 1;

end
```

2. You need to specify the frames of your simulation as input to Dynamic_setSimParameters; a vector called “frame”, unit (sec). f = number of frames.
   frame = [frameStart_1 ; frameEnd_1=frameStart_2 ; frameEnd_2=frameStart_3 ; … frameEnd_f].
3. For the second input, you specify the input function to your model, a vector called “Cif”. Should be the arterial input function for the 1-, and 2-Tissue models and sum of exponentials, and a reference tissue TAC for the FRTM and SRTM models, in unit (Bq/cc).
   Cif = [Cif_1 ; Cif_2; … ; Cif_f-1].
4. Finally, you need to specify a scale factor to scale number of counts in the sinogram. This factor is a scalar in unit (Bq), e.g. 1e6, and corresponds to the average activity in a frame. This factor determines the level of noise in the sinograms.

To run a simulation, simply run:

```
>>[data,simSet,FBP4D,OS4D,OSpsf4D,counts,countsNoise,nFWprompts,FWtrues,FWscatters,FWrandoms,wcc]=Dynamic_main_kineticModelling(data, frame, Cif, scaleFactor);
```

(See section Matlab functions below). This adds a pristine (noiseless) dynamic image based on your parametric image and settings to your structure “data”. It then simulates the dynamic PET from that dynamic pristine input. The data that is created is:

data	Same data structure as input, but with the pristine 4D image added to it.
simSet	Structure with simulation settings.
FBP4D	4D matrix with reconstructed dynamic FBP image.
OS4D	4D matrix with reconstructed dynamic OSEM image.
OSpsf4D	4D matrix with reconstructed dynamic OSEM image with PSF correction.
counts	Structure with the pristine sinogram counts.
countsNoise	Structure with the noisy sinogram counts.
nFWprompts	Noisy prompts sinogram.
FWtrue	Noiseless true sinogram.
FWscatters	Noiseless scatters sinogram.
FWrandoms	Noiseless randoms sinogram.
wcc	Well-counter-calibration factor to get unit Bq/cc.

Dynamic image

If you do not want to start with a parametric image, but instead only simulate a PET acquisition of your own input dynamic image, there is an option for that too.

1. Same as step 1 above under kinetic modeling. Set the aquisition parameters. Some settings will not be used (the ones related to parametric imaging).
2. Same as step 2 above. Specify what time sampling you used.
3. Same as step 4 above. Specify a scale factor to scale number of counts in the sinogram. This factor is a scalar in unit (Bq), e.g. 1e6, and corresponds to the average activity in a frame. This factor determines the level of noise in the sinograms.

To run a simulation, simply run:

```
>>[data,simSet,FBP4D,OS4D,OSpsf4D,counts,countsNoise,nFWprompts,FWtrues,FWscatters,FWrandoms,wcc]=Dynamic_main_dynamicImage(data, frame, scaleFactor);
```

Matlab functions

To run dPETSTEP, you will also need to download the MATLAB functions from PETSTEP (found in the PETSTEP repository on github).

The MATLAB functions in dPETSTEP (found in the dPETSTEP repository on github) are the following:

addVariability2PIM.m

```
%*****************************************************************************************************
%| Adds variability to an existing parametric image (PIM). Represents biological diversity.          |
%|                                                                                                   |
%| IH, 19/04/2016                                                                                    |
%|                                                                                                   |
%| m        = number of kinetic parameters.                                                          |
%| nx,ny,nz = image dimensions.                                                                      |
%|                                                                                                   |
%| USAGE  :  pim_var = addVariability2PIM('pim',pim,'scale',10).                                     |
%|                                                                                                   |
%| INPUT  :  pim        2 or 2D parametric image, one vector per voxel. Rate constants in unit       |
%|                      (s^-1).                                                                      |
%|                      pim = [nx*ny*nz*m].                                                          |
%|           scale      Scalar with amount of variability, sigma = pim/scale.                        |
%|                      (higher scale-->less variability).                                           |
%|                                                                                                   |
%| OUTPUT :  pim_var    2 or 2D variablility (~noise) parametric image, one vector per voxel. Rate   |
%|                      constants in unit (s^-1).                                                    |
%|                      pim_var = [nx*ny*nz*m].                                                      |
%|                                                                                                   |
%*****************************************************************************************************
```

calculateWeights.m

```
%*****************************************************************************************************
% Calculates frame weights = 1/variance according to user specified model.
%
% IH, 19/04/2016
%
% f = number of frames
%
% INPUT:    t        - mid frame (time) column vector [f-1,1], unit (sec).
%           C        - tissue TAC [f-1,1].
%           type     - type of weighting, string 'w1', 'w2'...
%           frameVar - frame variance, column vector [f-1,1].
%           halflife - halflife of nuclide in (sec), scalar.
%
%           Available weight model types are:
%           'ones' : uniform weighting (vector of ones)
%           'w1'   : 1/frameVariance
%           'w2'   : decayFactor^2
%           'w3'   : decayFactor * 1/(frameLength*TAC )
%           'w4'   : frameLength * exp(-lambda*t) / TAC
%           'w5'   : frameLength * exp(-lambda*t)
%
% OUTPUT:   w        - weight vector [f-1,1].
%*****************************************************************************************************
```

convertCT2mumap.m

```
%*********************************************************************************************************
% Converts the HU values of the CT to a mu-map (1/cm).
% Reference: C Burger et al., "PET attenuation coefficients from CT images:
% Experimental evaluation of the transformation of CT into PET 511-keV
% attenuation coefficients", EJNM 29(7), pp.922-927 (2002).
%
% IH, 19/04/2016
%
% USAGE  :  mumap = convertCT2mumap(CT).
%
% INPUT  :  CT      Matrix in Hounsfield units, size [x,y,z].
%
% OUTPUT :  mumap   Matrix in units (1/cm), size [x,y,z].
%*********************************************************************************************************
```

createDynamicPETfromParametricImage_matrix.m

```
%*********************************************************************************************************
%| Creates a 4D dynamic image of a 4D matrix with kinetic parameters (parametric image), using      |
%| a given blood input function or reference TAC, and frame vector. PIM = parametric image.        |
%|                                                                                                  |
%| IH, 19/04/2016                                                                                   |
%|                                                                                                  |
%| N = no of kinetic parameters.                                                                    |
%| f = no of frames.                                                                                |
%|                                                                                                  |
%| USAGE  :   dynamicImage = createDynamicPETfromParametricImage_matrix('paramImage',paramImage,... |
%|                                                        'model','2Tissue',...                     |
%|                                                        'Cif',[cif_1 cif_2...cif_f-1],...         |
%|                                                        'CifScaling',2,...                        |
%|                                                        'doDecay',halflife,...                    |
%|                                                        'frame',[f_1 f_2...f_f],...               |
%|                                                        'dt',0.5,...                              |
%|                                                        'interpMethod',interpMethod).             |
%|                                                                                                  |
%| INPUT  :   paramImage    4D matrix with parametric image - one parameter set per 3D              |
%|                          voxel, unit (1/s) for rate constants.                                   |
%|                          paramImage = [nx*ny*nz*N].                                              |
%|                          paramImage(x,y,z,:) = [N*1].                                            |
%|            model         String of desired kinetic model, e.g. '1Tissue' or '2Tissue'.           |
%|            frame         Vector with frame start and ends, unit (s).                             |
%|                          frame = [f*1].                                                          |
%|                          [frameStart1; frameStart2=frameEnd1; frameStart3=frameEnd2;...].        |
%|            Cif           Vector with input function to model (arterial or reference tissue),     |
%|                          unit (arbitrary), e.g. (Bq/cc).                                         |
%|                          Cif = [(f-1)*1].                                                        |
%|            dt            Scalar with time step length for calculations, unit (s). Smaller        |
%|                          step means a better calculation of the TACs, but a longer               |
%|                          computation time.                                                       |
%|            OPTIONAL :                                                                            |
%|            CifScaling    Scalar to multiply Cif with.                                            |
%|            doParallell   Optional flag to do parallell computing (1) or not (0)(default).       |
%|            doDecay       Optional string to add physical decay to TACs or not. Specify halflife  |
%|                          in (s) or leave out or specify 'none' to not add decay (default).       |
%|            interpMethod  Optional string with interpolation method (interp1). Default 'linear'. |
%|                                                                                                  |
%| OUTPUT :   dynamicImage  4D matrix with dynamic image (3D image with a 4th time                  |
%|                          dimension), unit (arbitrary, same as Cif (Cp or Cref).                  |
%|                          dynamicImage = [nx*ny*nz*(f-1)].                                        |
%|                                                                                                  |
%*********************************************************************************************************
```

Dynamic_buildSimFullData.m

```
%*****************************************************************************************************
%"Dynamic_buildSimFullData"
%   Builds un-noised PET projection data and attenuation projections
%
% CRS, 08/01/2013
% IH,  04/07/2016
%
% Usage:
%   [FWPTtrue,FWPTscatter,FWPTrandoms,FWAC,wcc] = Dynamic_buildSimFullData(refPT,muCT,psf,vox,countsTotal,SF,RF)
%       refPT       = reference PET image
%       FWAC        = forward projection of mumap
%       PSFsim      = Postfilter matched to simulation size
%       scatterK    = Scatter kernel matched to simulation size
%       vox         = voxel sizes, dimensions for input, simulation and output images
%       countsScale = mean total counts per active voxel
%       SF          = Scatter fraction
%       RF          = Randoms fraction
%       sensScale   = Sensitivity scale factor for each slice
%
%*****************************************************************************************************
```

Dynamic_main_dynamicImage.m

```
%*****************************************************************************************************
% Run a complete dynamic PET simulation.
%
% USAGE  : [data,simSet,FBP4D,OS4D,OSpsf4D,counts,countsNoise,nFWprompts,FWtrues,FWscatters,FWrandoms,wcc]
= Dynamic_main_dynamicImage(data,frame,scaleFactor)
%
% INPUT  : data         Structure with all simulation input data.
%          frame        Vector with start and end frame times in sec,
%                       [frameStart1; frameStart2=frameEnd1; frameStart3=frameEnd2;...].
%          scaleFactor  Scalar scalefactor for sinograms which determines noise level.
%
% OUTPUT : data         Structure with all simulation input data, updated.
%          simSet       Structure with simulation settings.
%          FBP4D        Reconstructed dynamic FBP image in (Bq/cc).
%          OS4D         Reconstructed dynamic OSEM image in (Bq/cc).
%          OSpsf4D      Reconstructed dynamic OSEM w/ PSF image in (Bq/cc).
%          counts       Pristine sinogram counts.
%          countsNoise  Noisy sinogram counts.
%          nFWprompts   Noisy prompts sinogram.
%          FWtrue       Noiseless true sinogram.
%          FWscatters   Noiseless scatters sinogram.
%          FWrandoms    Noiseless randoms sinogram.
%          wcc          Well-counter-calibration factor to get unit Bq/cc.
%*****************************************************************************************************
```

Dynamic_main_kineticModelling.m

```
%*************************************************************************************************
% Run a complete dynamic PET simulation.
%
% USAGE  : [data,simSet,FBP4D,OS4D,OSpsf4D,counts,countsNoise,nFWprompts,FWtrues,FWscatters,FWrandoms,wcc]
= Dynamic_main_kineticModelling(data,frame,Cif,scaleFactor)
%
% INPUT  : data         Structure with all simulation input data.
%          frame        Vector with start and end frame times in sec,
%                       [frameStart1; frameStart2=frameEnd1; frameStart3=frameEnd2;...].
%          Cif          Vector with input function to model (AIF or reference tissue TAC).
%          scaleFactor  Scalar scalefactor for sinograms which determines noise level.
%
% OUTPUT : data         Structure with all simulation input data, updated.
%          simSet       Structure with simulation settings.
%          FBP4D        Reconstructed dynamic FBP image in (Bq/cc).
%          OS4D         Reconstructed dynamic OSEM image in (Bq/cc).
%          OSpsf4D      Reconstructed dynamic OSEM w/ PSF image in (Bq/cc).
%          counts       Pristine sinogram counts.
%          countsNoise  Noisy sinogram counts.
%          nFWprompts   Noisy prompts sinogram.
%          FWtrue       Noiseless true sinogram.
%          FWscatters   Noiseless scatters sinogram.
%          FWrandoms    Noiseless randoms sinogram.
%          wcc          Well-counter-calibration factor to get unit Bq/cc.
%*************************************************************************************************
```

Dynamic_PETSTEP.m

```
%*************************************************************************************************
%| Simulates an FBP, OSEM and OSEMpsf image from a pristine image.                               |
%|                                                                                               |
%| IH, 26/09/2016                                                                                |
%|                                                                                               |
%| USAGE  :  output = Dynamic_PETSTEP(data,simSet,frameNo,vox,...                                |
%|                              PSFsim,PSFout,POST,scatterK,FWAC,initPT)                         |
%|                                                                                               |
%| INPUT  :  data           Structure with 4D PT and 3D CT data.                                 |
%|           simSet         Structure with all simulation settings.                              |
%|           frameNo        Scalar with what frame from data structure to use.                   |
%|           vox            Structure with voxel information for input, simulation, and ouput.   |
%|           PSFsim         Matrix with PSF kernel matched to simulation size.                   |
%|           PSFout         Matrix with PSF kernel matched to output size.                       |
%|           POST           Matrix with postfilter kernel matched to output size.                |
%|           scatterK       Matrix with scatter kernel.                                          |
%|           FWAC           Matrix with forward projection of mu-map.                            |
%|           initPT         Matrix with initial PT guess for iterative recon.                    |
%|                                                                                               |
%| OUTPUT :  FBP            Matrix with simulated FBP image.                                     |
%|           OS             Matrix with simulated OSEM image.                                    |
%|           OSpsf          Matrix with simulated PSF corrected OSEM image.                      |
%|           counts         Structure with pristine sinogram counts.                             |
%|           countsNoise    Structure with noised sinogram counts.                               |
%|           nFWprompts     Matrix with noisy prompt (total) counts sinogram.                    |
%|           FWtrues        Matrix with pristine true counts sinogram.                           |
%|           FWscatters     Matrix with pristine scatter counts sinogram.                        |
%|           FWrandoms      Matrix with pristine random counts sinogram.                         |
%|           wcc            2D matrix with well counter calibration factor per slice per frame.  |
%*************************************************************************************************
```

Dynamic_PETSTEP_overhead.m

```
%*************************************************************************************************
% Calculates voxel sizes, attenuation factors, initial PET etc.
%
% USAGE  : [vox,PSFsim,PSFout,POST,scatterK,FWAC,initPT,sensScale,activityConc] =
%              Dynamic_PETSTEP_overhead(data,simSet)
%
% INPUT  : data      Structure with CT/mumap and dynamic image
%          simSet    Structure with all simulation settings
%
% OUTPUT : vox          structure with voxel sizes
%          PSFsim       Matrix with system PSF kernel
%          PSFout       Matrix with PSF kernel for correction during reconstruction
%          POST         Matrix with Gaussian XY post filter kernel
%          scatterK     Matrix with scatter kernel
%          FWAC         Matrix with attenuation factors in sinogram space
%          initPT       Initial guess of PET image (disk of ones)
%          sensScale    Vector with sensitivity scale factor for all slices
%          activityConc Normalized activity conc. (with attenuation), to scale sinogram counts
%*************************************************************************************************
```

Dynamic_setSimParameters.m

```
%*************************************************************************************************
% Sets dPETSTEP simulation parameters.
%
% USAGE  : simSet = Dynamic_setSimParameters(frame,Cif,Cmean)
%
% INPUT  : frame    Vector with start and end frame times in sec,
%                   [frameStart1; frameStart2=frameEnd1; frameStart3=frameEnd2;...].
%          Cif      Vector with input function to model (AIF or reference tissue TAC).
%          Cmean    Average activity for each frame of the simulation in (Bq/cc).
%                   (Scales sinograms which in turn determines noise level).
%
% OUTPUT : simSet  Structure with all simulation settings
%*************************************************************************************************
```

fit_1Tissue_lsqnonlin.m

```
%*********************************************************************************************************
%| Fits a response TAC to the 1-tissue compartment model, from given time sampling, input function     |
%| and frame weights. Generates a vector of fitted parameters.                                         |
%|                                                                                                     |
%| IH, 19/04/2016                                                                                      |
%|                                                                                                     |
%| f  = number of frames.                                                                              |
%| np = number of model parameters = 2 or 3.                                                           |
%|                                                                                                     |
%| USAGE  :  p = fit_1Tissue_lsqnonlin(t,C,Cp,w,p0,dt,doPlot,lowerBounds,upperBounds,algorithm).       |
%|                                                                                                     |
%| INPUT  :  t             Vector of mid frame times (evenly sampled), size [(f-1),1], unit (s).       |
%|                         t = [t_1; t_2; ... ;t_f-1].                                                 |
%|           C             Vector with tissue TAC, size [(f-1),1], unit (arbitrary) e.g. (Bq/cc).      |
%|                         C = [C_1; C_2; ... ;C_f-1].                                                 |
%|           Cp            Vector with AIF values corresponding to frame mid times,                    |
%|                         size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                             |
%|                         Cp = [Cp_1; Cp_2; ... ;Cp_f-1].                                             |
%|           w             Vector with frame weights, size [(f-1),1].                                  |
%|                         w = [w_1; w_2; ... ;w_f-1].                                                 |
%|           p0            Vector with initial parameter guesses, unit rate const. (1/s). Size [1,np].|
%|                         p0 = [K1_0 k2_0 (Vp_0)].                                                    |
%|           dt            Scalar with frame duration of t, unit (s).                                  |
%|           doPlot        Flag to plot fitted solution (1) or not (0).                                |
%|           lowerBounds   Vector with lower bounds for estimate of p, size [1,np]. Default zero.     |
%|           upperBounds   Vector with upper bounds for estimate of p, size [1,np]. Default 100*p0.   |
%|           algorithm     String with desired fitting algorithm. Default 'trust-region-reflective'.   |
%|                                                                                                     |
%| OUTPUT :  p             Vector with fitted model parameters, size [1,np].                           |
%|                         p = [K1 k2 (Vp)].                                                           |
%|      |    __|_____________________                                                                 |
%|      |Cp |  |   K1    _________    |                                                                |
%|      |   |  |------>|         |   |                                                                |
%|      |   |  |<------|   C1    |   |                                                                |
%|      |   |Vp|   k2  |_________|   |                                                                |
%|      |   |__|_____________________| Cpet                                                           |
%|      |      |                                                                                       |
%|                                                                                                     |
%|   Theoretical 1-tissue model:                                                                       |
%|   *-----------------------------------------*                                                       |
%|   | C      = [ K1*exp(-k2*t) ] CONV [Cp]    |                                                       |
%|   | Cpet   = (1-Vp)*C + Vp*Cp               |                                                       |
%|   *-----------------------------------------*                                                       |
%|                                                                                                     |
%*********************************************************************************************************
```

fit_2Tissue_lsqnonlin.m

```
%*********************************************************************************************************
%| Fits a response TAC to the 2-tissue compartment model, from given time sampling, input function     |
%| and frame weights. Generates a vector of fitted parameters.                                         |
%|                                                                                                     |
%| IH, 19/04/2016                                                                                      |
%|                                                                                                     |
%| f  = number of frames.                                                                              |
%| np = number of model parameters = 4 or 5.                                                           |
%|                                                                                                     |
%| USAGE  :  p = fit_2Tissue_lsqnonlin(t,C,Cp,w,p0,dt,doPlot,lowerBounds,upperBounds,algorithm).       |
%|                                                                                                     |
%| INPUT  :  t             Vector of mid frame times (evenly sampled), size [(f-1),1], unit (s).       |
%|                         t = [t_1; t_2; ... ;t_f-1].                                                 |
%|           C             Vector with tissue TAC, size [(f-1),1], unit (arbitrary) e.g. (Bq/cc).      |
%|                         C = [C_1; C_2; ... ;C_f-1].                                                 |
%|           Cp            Vector with AIF values corresponding to frame mid times,                     |
%|                         size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                             |
%|                         Cp = [Cp_1; Cp_2; ... ;Cp_f-1].                                             |
%|           w             Vector with frame weights, size [(f-1),1].                                   |
%|                         w = [w_1; w_2; ... ;w_f-1].                                                 |
%|           p0            Vector with initial parameter guesses, unit rate const. (1/s). Size [1,np].|
%|                         p0 = [K1_0 k2_0 k3_0 k4_0 (Vp_0)].                                          |
%|           dt            Scalar with frame duration of t, unit (s).                                  |
%|           doPlot        Flag to plot fitted solution (1) or not (0).                                |
%|           lowerBounds   Vector with lower bounds for estimate of p, size [1,np]. Default zero.      |
%|           upperBounds   Vector with upper bounds for estimate of p, size [1,np]. Default 100*p0.    |
%|           algorithm     String with desired fitting algorithm. Default 'trust-region-reflective'.   |
%|                                                                                                     |
%| OUTPUT :  p             Vector with fitted model parameters, size [1,np].                           |
%|                         p = [K1 k2 k3 k4 (Vp)].                                                     |
%|      |    __|_____________________________________                                                 |
%|      |Cp |  |   K1    __________    k3    __________   |                                            |
%|      |   |  |------>|          |------>|          |  |                                            |
%|      |   |  |<------|   C1     |<------|   C2     |  |                                            |
%|      |   |Vp|   k2  |__________|  k4   |__________|  |                                            |
%|      |   |__|_____________________________________| Cpet                                       |
%|      |      |                                                                                     |
%|                                                                                                     |
%|   Theoretical 2-tissue model:                                                                       |
%|   *-----------------------------------------------------------------*                               |
%|   | alpha1 = 0.5*( k2+k3+k4 - sqrt( [k2+k3+k4]^2 - 4*k2*k4) )       |                               |
%|   | alpha2 = 0.5*( k2+k3+k4 + sqrt( [k2+k3+k4]^2 - 4*k2*k4) )       |                               |
%|   | C      = K1/(alpha2-alpha1)*[ (k3+k4-alpha1)*exp(-alpha1*t) +   |                               |
%|   |                (alpha2-k3-k4)*exp(-alpha2*t) ] CONV [ Cp ]      |                               |
%|   | Cpet   = (1-Vp)*C + Vp*Cp                                       |                               |
%|   *-----------------------------------------------------------------*                               |
%|                                                                                                     |
%*********************************************************************************************************
```

fit_FRTM_lsqnonlin.m

```
%*************************************************************************************************
%| Fits a response TAC to the FRTM compartment model, from given time sampling, reference tissue TAC   |
%| and frame weights. Generates a vector of fitted parameters.                                         |
%|                                                                                                     |
%| IH, 19/04/2016                                                                                      |
%|                                                                                                     |
%| f  = number of frames.                                                                              |
%| np = number of model parameters = 4.                                                                |
%|                                                                                                     |
%| USAGE  :  p = fit_FRTM_lsqnonlin(t,C,Cref,w,p0,dt,doPlot,lowerBounds,upperBounds,algorithm).        |
%|                                                                                                     |
%| INPUT  :  t              Vector of mid frame times (evenly sampled), size [(f-1),1], unit (s).      |
%|                          t = [t_1; t_2; ... ;t_f-1].                                                |
%|           C              Vector with tissue TAC, size [(f-1),1], unit (arbitrary) e.g. (Bq/cc).     |
%|                          C = [C_1; C_2; ... ;C_f-1].                                                |
%|           Cref           Vector with reference tissue TAC corresponding to frame mid times,          |
%|                          size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                            |
%|                          Cref = [Cref_1; Cref_2; ... ;Cref_f-1].                                    |
%|           w              Vector with frame weights, size [(f-1),1].                                  |
%|                          w = [w_1; w_2; ... ;w_f-1].                                                |
%|           p0             Vector with initial parameter guesses, unit rate const. (1/s). Size [1,np].|
%|                          p0 = [R1_0 k2_0 k3_0 BPnd_0].                                              |
%|           dt             Scalar with frame duration of t, unit (s).                                 |
%|           doPlot         Flag to plot fitted solution (1) or not (0).                               |
%|           lowerBounds    Vector with lower bounds for estimate of p, size [1,np]. Default zero.     |
%|           upperBounds    Vector with upper bounds for estimate of p, size [1,np]. Default 100*p0.   |
%|           algorithm      String with desired fitting algorithm. Default 'trust-region-reflective'.  |
%|                                                                                                     |
%| OUTPUT :  p              Vector with fitted model parameters, size [1,np].                          |
%|                          p = [R1 k2 k3 BPnd].                                                       |
%|    ___________________________________________                                                      |
%|   |                                           |                                                     |
%|   |  |    |   K1    _________    k3    _________   |                                                |
%|   |  | Cp |------>|         |------>|         |  |                                                |
%|   |  |    |<------|   C1    |<------|   C2    |  |                                                |
%|   |  |    |   k2  |_________|  k4   |_________|  |                                                |
%|   |__|____|_____________________________________| Tissue with specific binding, Cpet              |
%|    __|____|_____________________                                                                  |
%|   |  |    |   K1'   _________   |                                                                 |
%|   |  |    |------>|         |  |                                                                 |
%|   |  |    |<------|   C1'   |  |                                                                 |
%|   |  |    |   k2' |_________|  |                                                                 |
%|   |_____________________________| Reference tissue with non-specific binding, Cref                |
%|                                                                                                     |
%|   Theoretical FRTM:                                                                                 |
%|   *-------------------------------------------------------------------------------*                 |
%|   | R1     = K1/K1'                                                               |                 |
%|   | BPnd   = k3/k4                                                                |                 |
%|   | a      = (k3+k4-c)(c-r)/u                                                     |                 |
%|   | b      = (d-k3-k4)(d-r)/u                                                     |                 |
%|   | c      = (s+u)/2                                                              |                 |
%|   | d      = (s-u)/2                                                              |                 |
%|   | u      = sqrt(s^2-q)                                                          |                 |
%|   | q      = 4k2k4                                                                |                 |
%|   | r      = k2/R1                                                                |                 |
%|   | s      = k2+k3+k4                                                             |                 |
%|   | Cpet   = R1*Cref + R1*( [a*Cref] CONV [exp(-ct)] + [b*Cref] CONV [exp(-dt)] ) |                 |
%|   *-------------------------------------------------------------------------------*                 |
%|   Reference: A.A. Lammertsma et al., Comparison of methods for analysis of clinical                 |
%|   raclopride[11C]studies, J. Cereb. Blood Flow Metab. 16(1), 42-52 (1996).                          |
%|                                                                                                     |
%*************************************************************************************************
```

fit_SRTM_lsqnonlin.m

```
%*********************************************************************************************************
%| Fits a response TAC to the SRTM compartment model, from given time sampling, reference tissue TAC   |
%| and frame weights. Generates a vector of fitted parameters.                                          |
%|                                                                                                      |
%| IH, 19/04/2016                                                                                       |
%|                                                                                                      |
%| f  = number of frames.                                                                               |
%| np = number of model parameters = 3.                                                                 |
%|                                                                                                      |
%| USAGE  :  p = fit_SRTM_lsqnonlin(t,C,Cref,w,p0,dt,doPlot,lowerBounds,upperBounds,algorithm).         |
%|                                                                                                      |
%| INPUT  :  t             Vector of mid frame times (evenly sampled), size [(f-1),1], unit (s).      |
%|                         t = [t_1; t_2; ... ;t_f-1].                                                  |
%|           C             Vector with tissue TAC, size [(f-1),1], unit (arbitrary) e.g. (Bq/cc).      |
%|                         C = [C_1; C_2; ... ;C_f-1].                                                  |
%|           Cref          Vector with reference tissue TAC corresponding to frame mid times,          |
%|                         size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                              |
%|                         Cref = [Cref_1; Cref_2; ... ;Cref_f-1].                                      |
%|           w             Vector with frame weights, size [(f-1),1].                                   |
%|                         w = [w_1; w_2; ... ;w_f-1].                                                  |
%|           p0            Vector with initial parameter guesses, unit rate const. (1/s). Size [1,np].|
%|                         p0 = [R1_0 k2_0 BPnd_0].                                                     |
%|           dt            Scalar with frame duration of t, unit (s).                                   |
%|           doPlot        Flag to plot fitted solution (1) or not (0).                                 |
%|           lowerBounds   Vector with lower bounds for estimate of p, size [1,np]. Default zero.      |
%|           upperBounds   Vector with upper bounds for estimate of p, size [1,np]. Default 100*p0.    |
%|           algorithm     String with desired fitting algorithm. Default 'trust-region-reflective'.    |
%|                                                                                                      |
%| OUTPUT :  p             Vector with fitted model parameters, size [1,np].                            |
%|                         p = [R1 k2 BPnd].                                                            |
%|    ____________________________________                                                              |
%|   |                                    |                                                             |
%|   |  |    |   K1   ___________________  |                                                             |
%|   |  | Cp |------->|                   | |                                                             |
%|   |  |    |<-------|        C          | |                                                             |
%|   |  |    |   k2   |___________________| |                                                             |
%|   |__|____|_____________________________| Tissue with specific binding, Cpet                          |
%|     __|____|_____________________                                                                     |
%|   |  |    |   K1'  _________   |                                                                     |
%|   |  |    |------->|         |  |                                                                     |
%|   |  |    |<-------|   C1'   |  |                                                                     |
%|   |  |    |   k2'  |_________|  |                                                                     |
%|   |_____________________________| Reference tissue with non-specific binding, Cref                    |
%|                                                                                                      |
%|   Theoretical SRTM:                                                                                  |
%|   *-------------------------------------------------------------------------------*                  |
%|   | R1     = K1/K1'                                                               |                  |
%|   | BPnd   = k3/k4                                                                |                  |
%|   | Cpet   = R1*Cref + [ (k2-R1*k2/(1+BPnd))*Cref ] CONV [ exp(-k2*t/(1+BPnd)) ]  |                  |
%|   *-------------------------------------------------------------------------------*                  |
%|   Reference: A.A. Lammertsma and S.P. Hume, Simplified reference tissue model for PET receptor       |
%|   studies, Neuroimage 4, 153-158 (1996).                                                             |
%|                                                                                                      |
%*********************************************************************************************************
```

fit_sumExp_lsqnonlin.m

```
%*****************************************************************************************************
%| Fits a response TAC to an arbitrary sum of exponentials, from given time sampling, input function   |
%| and frame weights. Generates a vector of fitted parameters.                                         |
%|                                                                                                     |
%| IH, 19/04/2016                                                                                      |
%|                                                                                                     |
%| f  = number of frames.                                                                              |
%| N  = number of exponentials.                                                                        |
%| np = number of model parameters = 2N or 2N+1.                                                       |
%|                                                                                                     |
%| USAGE  :  p = fit_sumExp_lsqnonlin(t,C,Cp,w,p0,dt,doPlot,lowerBounds,upperBounds,algorithm).        |
%|                                                                                                     |
%| INPUT  :  t              Vector of mid frame times (evenly sampled), size [(f-1),1], unit (s).      |
%|                          t = [t_1; t_2; ... ;t_f-1].                                                |
%|           C              Vector with tissue TAC, size [(f-1),1], unit (arbitrary) e.g. (Bq/cc).     |
%|                          C = [C_1; C_2; ... ;C_f-1].                                                |
%|           Cp             Vector with AIF values corresponding to frame mid times,                    |
%|                          size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                            |
%|                          Cp = [Cp_1; Cp_2; ... ;Cp_f-1].                                            |
%|           w              Vector with frame weights, size [(f-1),1].                                  |
%|                          w = [w_1; w_2; ... ;w_f-1].                                                |
%|           p0             Vector with initial parameter guesses, unit rate const. (1/s). Size [1,np].|
%|                          p0 = [p0_1 p0_2 p0_3...p0_np].                                             |
%|           dt             Scalar with frame duration of t, unit (s).                                 |
%|           doPlot         Flag to plot fitted solution (1) or not (0).                               |
%|           lowerBounds    Vector with lower bounds for estimate of p, size [1,np]. Default zero.     |
%|           upperBounds    Vector with upper bounds for estimate of p, size [1,np]. Default 100*p0.   |
%|           algorithm      String with desired fitting algorithm. Default 'trust-region-reflective'.  |
%|                                                                                                     |
%| OUTPUT :  p              Vector with fitted model parameters, size [1,np].                          |
%|                          p = [p_1 p_2 p_3...p_np].                                                  |
%|      |    __|_____________________                                                                 |
%|      |Cp |  |   p1   _________    |                                                                |
%|      |   |  |------->|         |   |                                                                |
%|      |   |  |<-------|   C1    |   |                                                                |
%|      |   |  |   p2   |_________|   |                                                                |
%|      |   |  |   p3   _________    |                                                                |
%|      |   |  |------->|         |   |                                                                |
%|      |   |  |<-------|   C2    |   |                                                                |
%|      |   |  |   p4   |_________|   |                                                                |
%|      | p(2N+1)  .        .        |                                                                |
%|      |   |  |   .        .        | Cpet                                                           |
%|      .   .  .   .        .        .                                                                |
%|                                                                                                     |
%|   Theoretical model:                                                                                |
%|   C        = [ p(1)*exp(-p(2)*t) + p(3)*exp(-p(4)*t) + ... + p(2N-1)*exp(-p(2N)*t) ] CONV [ Cp ]    |
%|   Cpet     = (1-p(2N+1))*C + p(2N+1)*Cp                                                             |
%|                                                                                                     |
%*****************************************************************************************************
```

interpolateWeights.m

```
%*********************************************************************************************************
% IH, 19/04/2016
%
% USAGE:    w2 = interpolateWeights(t,w,t2)
%
% INPUT:    t    - mid frame (time) column vector
%           w    - weight vector
%           t2   - mid frame (time) column vector of interpolation time
%
% OUTPUT:   w2   - interpolated weight vector
%*********************************************************************************************************
```

kineticModel_1Tissue_matrix.m

```
%*********************************************************************************************************
%| Generates a response TAC corresponding to the 1-tissue compartment model from a given input of      |
%| kinetic parameters, frame vector and arterial input function.                                       |
%|                                                                                                     |
%| IH, 19/04/2016                                                                                      |
%|                                                                                                     |
%| f  = number of frames.                                                                              |
%| np = number of model parameters = 2.                                                                |
%| nv = number of voxels.                                                                              |
%|                                                                                                     |
%| USAGE  :  Cpet = kineticModel_1TissueModel_matrix(t,dt,Cp,p).                                       |
%|                                                                                                     |
%| INPUT  :  t             Matrix of mid frame times (evenly sampled), size [nv,(f-1)], unit (s).     |
%|                         t = [t_1,1 t_1,2 ... t_1,f-1 ]                                              |
%|                             [ ...      ...     ...   ]                                              |
%|                             [t_nv,1    ...   t_nv,f-1].                                             |
%|           dt            Scalar with frame duration of t, unit (s).                                  |
%|           Cp            Vector with AIF values corresponding to frame mid times,                    |
%|                         size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                             |
%|                         Cp = [Cp_1;Cp_2; ... ;Cp_f-1].                                              |
%|           p             Matrix of model parameter values, size [nv,np], unit rate constants (1/s). |
%|                         E.g. for the 1-tissue model: param(v,:) = [K1 k2].                          |
%|                         p = [p_1,1 p_1,2 ... p_1,np ]                                               |
%|                             [ ...      ...     ...  ]                                              |
%|                             [p_nv,1    ...   p_nv,np].                                              |
%|                                                                                                     |
%| OUTPUT :  Cpet          Matrix of response tissue TAC, size [nv,(f-1)], unit (same as Cp).          |
%|                         Cpet = [Cpet_1,1 Cpet_1,2 ... Cpet_1,f-1 ]                                  |
%|                                [Cpet_2,1 Cpet_2,2 ... Cpet_2,f-1 ]                                  |
%|                                [   ...            ... Cpet_nv,f-1].                                 |
%|                                                                                                     |
%|      |    |  | K1   _________   |                                                                    |
%|      | Cp |--|---->|         |  |                                                                    |
%|      |    |<-|-----|   C1    |  |                                                                    |
%|      |    |  | k2  |_________|  |                                                                    |
%|      |    |  |____________________| Cpet                                                           |
%|                                                                                                     |
%|   Theoretical 1-tissue model:                                                                       |
%|   *-----------------------------------------*                                                       |
%|   | Cpet   = [ K1*exp(-k2*t) ] CONV [Cp]      |                                                     |
%|   *-----------------------------------------*                                                       |
%|   Note! Blood spillover term is excluded here.                                                      |
%|                                                                                                     |
%*********************************************************************************************************
```

kineticModel_2Tissue_matrix.m

```
%*****************************************************************************************************
%| Generates a response TAC corresponding to the 2-tissue compartment model from a given input of     |
%| kinetic parameters, frame vector and arterial input function.                                      |
%|                                                                                                    |
%| IH, 19/04/2016                                                                                     |
%|                                                                                                    |
%| f  = number of frames.                                                                             |
%| np = number of model parameters = 4.                                                               |
%| nv = number of voxels.                                                                             |
%|                                                                                                    |
%| USAGE  :  Cpet = kineticModel_2TissueModel_matrix(t,dt,Cp,p).                                      |
%|                                                                                                    |
%| INPUT  :  t              Matrix of mid frame times (evenly sampled), size [nv,(f-1)], unit (s).    |
%|                          t = [t_1,1 t_1,2 ... t_1,f-1 ]                                            |
%|                              [ ...      ...     ...   ]                                            |
%|                              [t_nv,1    ...   t_nv,f-1].                                           |
%|           dt             Scalar with frame duration of t, unit (s).                                |
%|           Cp             Vector with AIF values corresponding to frame mid times,                  |
%|                          size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                           |
%|                          Cp = [Cp_1;Cp_2; ... ;Cp_f-1].                                            |
%|           p              Matrix of model parameter values, size [nv,np], unit rate constants (1/s). |
%|                          E.g. for the 2-tissue model: p(v,:) = [K1 k2 k3 k4].                      |
%|                          p = [p_1,1 p_1,2 ... p_1,np ]                                             |
%|                              [ ...      ...     ... ]                                              |
%|                              [p_nv,1    ...   p_nv,np].                                            |
%|                                                                                                    |
%| OUTPUT :  Cpet           Matrix of response tissue TAC, size [nv,(f-1)], unit (same as Cp).        |
%|                          Cpet = [Cpet_1,1 Cpet_1,2 ... Cpet_1,f-1 ]                                |
%|                                 [Cpet_2,1 Cpet_2,2 ... Cpet_2,f-1 ]                                |
%|                                 [   ...            ... Cpet_nv,f-1].                               |
%|                 ____________________________________                                               |
%|       |    |  | K1     _________     k3     _________    |                                         |
%|       | Cp |--|---->|         |------>|         |   |                                              |
%|       |    |<-|-----|   C1    |<------|   C2    |   |                                              |
%|       |    |  | k2  |_________|  k4   |_________|   |                                              |
%|       |    |  |____________________________________| Cpet                                          |
%|                                                                                                    |
%|   Theoretical 2-tissue model:                                                                      |
%|   *-----------------------------------------------------------------*                              |
%|   | alpha1 = 0.5*( k2+k3+k4 - sqrt( [k2+k3+k4]^2 - 4*k2*k4) )        |                              |
%|   | alpha2 = 0.5*( k2+k3+k4 + sqrt( [k2+k3+k4]^2 - 4*k2*k4) )        |                              |
%|   | Cpet   = K1/(alpha2-alpha1)*[ (k3+k4-alpha1)*exp(-alpha1*t) +    |                              |
%|   |                 (alpha2-k3-k4)*exp(-alpha2*t) ] CONV [ Cp ]       |                              |
%|   *-----------------------------------------------------------------*                              |
%|   Note! Blood spillover term is excluded here.                                                     |
%|                                                                                                    |
%*****************************************************************************************************
```

kineticModel_FRTM_matrix.m

```
%*************************************************************************************************************
%| Generates a response TAC corresponding to the full reference tissue compartment model (FRTM)              |
%| from a given vector of kinetic parameters, frame vector and reference TAC.                                 |
%|                                                                                                            |
%| IH, 19/04/2016                                                                                             |
%|                                                                                                            |
%| f  = number of frames.                                                                                     |
%| n  = number of compartments in tissue.                                                                     |
%| np = number of model parameters = 4.                                                                       |
%| nv = number of voxels.                                                                                     |
%|                                                                                                            |
%| USAGE  :  Cpet = kineticModel_FRTM_matrix(t,dt,Cref,p).                                                    |
%|                                                                                                            |
%| INPUT  :  t             Matrix of mid frame times (evenly sampled), size [nv,(f-1)], unit (s).             |
%|                         t = [t_1,1 t_1,2 ... t_1,f-1 ]                                                     |
%|                             [ ...      ...     ...   ]                                                     |
%|                             [t_nv,1    ...   t_nv,f-1].                                                    |
%|           dt            Scalar with frame duration of t, unit (s).                                         |
%|           Cref          Vector with reference tissue TAC corresponding to frame mid times,                  |
%|                         size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                                    |
%|                         Cref = [Cref_1;Cref_2; ... ;Cref_f-1].                                             |
%|           p             Matrix of model parameter values, size [nv,np], unit rate constants (1/s).         |
%|                         E.g. for the FRTM: param(v,:) = [R1 k2 k3 BPnd].                                   |
%|                         p = [p_1,1 p_1,2 ... p_1,np ]                                                      |
%|                             [ ...      ...     ...  ]                                                     |
%|                             [p_nv,1    ...   p_nv,np].                                                     |
%|                                                                                                            |
%| OUTPUT :  Cpet          Matrix of response tissue TAC, size [nv,(f-1)], unit (same as Cref).               |
%|                         Cpet = [Cpet_1,1 Cpet_1,2 ... Cpet_1,f-1 ]                                         |
%|                                [Cpet_2,1 Cpet_2,2 ... Cpet_2,f-1 ]                                         |
%|                                [   ...            ... Cpet_nv,f-1].                                        |
%|    ____________________________________________                                                            |
%|   |                                            |                                                           |
%|   |  |    |   K1    _________    k3    _______  |                                                           |
%|   |  | Cp |------>|         |------>|         |  |                                                           |
%|   |  |    |<------|   C1    |<------|   C2    |  |                                                           |
%|   |  |    |   k2  |_________|  k4   |_________|  |                                                           |
%|   |__|____|_____________________________________| Tissue with specific binding, Cpet                        |
%|    __|____|_____________________                                                                           |
%|   |  |    |   K1'   _________   |                                                                          |
%|   |  |    |------>|         |  |                                                                          |
%|   |  |    |<------|   C1'   |  |                                                                          |
%|   |  |    |   k2' |_________|  |                                                                          |
%|   |_____________________________| Reference tissue with non-specific binding, Cref                          |
%|                                                                                                            |
%|   Theoretical FRTM:                                                                                        |
%|   *-------------------------------------------------------------------------------*                        |
%|   | R1     = K1/K1'                                                               |                        |
%|   | BPnd   = k3/k4                                                                |                        |
%|   | a      = (k3+k4-c)(c-r)/u                                                     |                        |
%|   | b      = (d-k3-k4)(d-r)/u                                                     |                        |
%|   | c      = (s+u)/2                                                              |                        |
%|   | d      = (s-u)/2                                                              |                        |
%|   | u      = sqrt(s^2-q)                                                          |                        |
%|   | q      = 4k2k4                                                                |                        |
%|   | r      = k2/R1                                                                |                        |
%|   | s      = k2+k3+k4                                                             |                        |
%|   | Cpet   = R1*Cref + R1*( [a*Cref] CONV [exp(-ct)] + [b*Cref] CONV [exp(-dt)] ) |                        |
%|   *-------------------------------------------------------------------------------*                        |
%|   Reference: A.A. Lammertsma et al., Comparison of methods for analysis of clinical                        |
%|   raclopride[11C]studies, J. Cereb. Blood Flow Metab. 16(1), 42-52 (1996).                                 |
%|                                                                                                            |
%*************************************************************************************************************
```

kineticModel_SRTM_matrix.m

```
%*****************************************************************************************************
%| Generates a response TAC corresponding to the simplified reference tissue compartment model (SRTM)  |
%| from a given input of kinetic parameters, frame vector and reference TAC.                            |
%|                                                                                                      |
%| IH, 19/04/2016                                                                                       |
%|                                                                                                      |
%| f  = number of frames.                                                                               |
%| n  = number of compartments in tissue.                                                               |
%| np = number of model parameters = 3.                                                                 |
%| nv = number of voxels.                                                                               |
%|                                                                                                      |
%| USAGE  :  Cpet = kineticModel_SRTM_matrix(t,dt,Cref,p).                                              |
%|                                                                                                      |
%| INPUT  :  t              Matrix of mid frame times (evenly sampled), size [nv,(f-1)], unit (s).      |
%|                          t = [t_1,1 t_1,2 ... t_1,f-1 ]                                              |
%|                              [ ...      ...     ...   ]                                             |
%|                              [t_nv,1    ...   t_nv,f-1].                                            |
%|           dt             Scalar with frame duration of t, unit (s).                                  |
%|           Cref           Vector with reference tissue TAC corresponding to frame mid times,          |
%|                          size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                             |
%|                          Cref = [Cref_1;Cref_2; ... ;Cref_f-1].                                      |
%|           p              Matrix of model parameter values, size [nv,np], unit rate constants (1/s).  |
%|                          E.g. for the SRTM: param(v,:) = [R1 k2 BPnd].                               |
%|                          p = [p_1,1 p_1,2 ... p_1,np ]                                               |
%|                              [ ...      ...     ...  ]                                              |
%|                              [p_nv,1    ...   p_nv,np].                                             |
%|                                                                                                      |
%| OUTPUT :  Cpet           Matrix of response tissue TAC, size [nv,(f-1)], unit (same as Cref).        |
%|                          Cpet = [Cpet_1,1 Cpet_1,2 ... Cpet_1,f-1 ]                                  |
%|                                 [Cpet_2,1 Cpet_2,2 ... Cpet_2,f-1 ]                                  |
%|                                 [   ...            ... Cpet_nv,f-1].                                 |
%|    ____________________________________                                                              |
%|   |                                    |                                                             |
%|   |  |    |   K1   ___________________  |                                                             |
%|   |  | Cp |------>|                   | |                                                             |
%|   |  |    |<------|        C          | |                                                             |
%|   |  |    |   k2  |___________________| |                                                             |
%|   |__|____|_____________________________| Tissue with specific binding, Cpet                          |
%|    __|____|_____________________                                                                     |
%|   |  |    |   K1'  _________   |                                                                     |
%|   |  |    |------>|         |  |                                                                     |
%|   |  |    |<------|   C1'   |  |                                                                     |
%|   |  |    |   k2' |_________|  |                                                                     |
%|   |_____________________________| Reference tissue with non-specific binding, Cref                    |
%|                                                                                                      |
%|   Theoretical SRTM:                                                                                  |
%|   *-------------------------------------------------------------------------------*                  |
%|   | R1     = K1/K1'                                                               |                  |
%|   | BPnd   = k3/k4                                                                |                  |
%|   | Cpet   = R1*Cref + [ (k2-R1*k2/(1+BPnd))*Cref ] CONV [ exp(-k2*t/(1+BPnd)) ]  |                  |
%|   *-------------------------------------------------------------------------------*                  |
%|   Reference: A.A. Lammertsma and S.P. Hume, Simplified reference tissue model for PET receptor       |
%|   studies, Neuroimage 4, 153-158 (1996).                                                             |
%|                                                                                                      |
%*****************************************************************************************************
```

kineticModel_sumExp_matrix.m

```
%*********************************************************************************************************
%| Generates a response TAC corresponding to an arbitrary sum of exponentials, from a given input of   |
%| kinetic parameters, frame vector and arterial input function.                                        |
%|                                                                                                      |
%| IH, 19/04/2016                                                                                       |
%|                                                                                                      |
%| f  = number of frames.                                                                               |
%| np = number of model parameters.                                                                     |
%| nv = number of voxels.                                                                               |
%| N  = number of exponentials.                                                                         |
%|                                                                                                      |
%| USAGE  :  Cpet = kineticModel_sumExp_matrix(t,dt,Cp,p).                                              |
%|                                                                                                      |
%| INPUT  :  t             Matrix of mid frame times (evenly sampled), size [nv,(f-1)], unit (s).       |
%|                         t = [t_1,1 t_1,2 ... t_1,f-1 ]                                               |
%|                             [ ...      ...     ...   ]                                               |
%|                             [t_nv,1    ...   t_nv,f-1].                                              |
%|           dt            Scalar with frame duration of t, unit (s).                                   |
%|           Cp            Vector with AIF values corresponding to frame mid times,                     |
%|                         size [(f-1),1], unit (arbitrary), e.g. (Bq/cc).                              |
%|                         Cp = [Cp_1;Cp_2; ... ;Cp_f-1].                                               |
%|           p             Matrix of model parameter values, size [nv,np], unit rate constants (1/s).   |
%|                         p = [p_1,1 p_1,2 ... p_1,np ]                                                |
%|                             [ ...      ...     ...  ]                                                |
%|                             [p_nv,1    ...   p_nv,np].                                               |
%|                                                                                                      |
%| OUTPUT :  Cpet          Matrix of response tissue TAC, size [nv,(f-1)], unit (same as Cp).           |
%|                         Cpet = [Cpet_1,1 Cpet_1,2 ... Cpet_1,f-1 ]                                   |
%|                                [Cpet_2,1 Cpet_2,2 ... Cpet_2,f-1 ]                                   |
%|                                [   ...            ... Cpet_nv,f-1].                                  |
%|      |    |   ____________________                                                                   |
%|      | Cp |  |  p1    _________   |                                                                  |
%|      |    |--|----->|         |  |                                                                  |
%|      |    |<-|------|   C1    |  |                                                                  |
%|      |    |  |  p2  |_________|  |                                                                  |
%|      |    |  |  p3    _________  |                                                                  |
%|      |    |--|----->|         |  |                                                                  |
%|      |    |<-|------|   C2    |  |                                                                  |
%|      |    |  |  p4  |_________|  |                                                                  |
%|      |    |  |  .        .      |                                                                  |
%|      |    |  |  .        .      | Cpet                                                             |
%|      .    .  .  .        .      .                                                                  |
%|                                                                                                      |
%|   Theoretical sum of exponentials model:                                                             |
%|   *-------------------------------------------------------------------------------*                  |
%|   | Cpet =  [ p1*exp(-p2*t) + p3*exp(-p4*t) + ... + p2N-1*exp(-p2N*t) ] CONV [ Cp ]  |                  |
%|   *-------------------------------------------------------------------------------*                  |
%|   Note! Blood spillover term is excluded here.                                                       |
%|                                                                                                      |
%*********************************************************************************************************
```

modelFitting_main.m

```
%*********************************************************************************************
%| Fits the dynamic PET data to a kinetic model, producing parametric images (voxel-wise) or a set  |
%| of parameters for a ROI.                                                                         |
%|                                                                                                  |
%| IH, 19/04/2016                                                                                   |
%|                                                                                                  |
%| N = no of kinetic parameters.                                                                    |
%| f = no of frames.                                                                                |
%|                                                                                                  |
%| USAGE  :   paramImage = modelFitting_main('image',image,...                                      |
%|                                  'model','2tissue',...                                           |
%|                                  'midFrame',[f_1 f_2...f_f-1],...                                |
%|                                  'w',[w_1 w_2...w_f-1] or e.g. 'w1', 'ones',...                  |
%|                                  'p0',[p0_1 p0_2 ... p0_N],...                                   |
%|                                  'ROIMask',[nx,ny,nz],...                                        |
%|                                  'Cp',[cp_1 cp_2...cp_f-1],...                                   |
%|                                  'CpMask',[nx,ny,nz],...                                         |
%|                                  'Cref',[c_1 c_2...c_f-1],...                                    |
%|                                  'CrefMask',[nx,ny,nz],...                                       |
%|                                  'halflife', scalar in sec,...                                   |
%|                                  'noExp',scalar,...                                              |
%|                                  'interpMethod',string,...                                       |
%|                                  'solver',string,...                                             |
%|                                  'lowerBound', [lb_1 lb_2...lb_N],...                            |
%|                                  'upperBound', [ub_1 ub_2...ub_N].                               |
%|                                                                                                  |
%| INPUT  :   image         4D matrix with dynamic image, unit (arbitrary), e.g. (Bq/ml).           |
%|                          image = [nx,ny,nz,f-1].                                                 |
%|            model         String of desired kinetic model, '1Tissue', '2Tissue', 'FRTM', 'SRTM',  |
%|                          or 'sumExp'.                                                            |
%|            midFrame      Vector with mid frame times, unit (s).                                  |
%|                          midFrame = [f-1,1].                                                     |
%|            Cp            Vector with blood input function to model, unit (arbitrary), e.g.       |
%|                          (Bq/cc).                                                                |
%|                          Cp = [(f-1),1].                                                         |
%|            Cref          Vector with reference tissue TAC, unit (arbitrary), e.g. (Bq/cc). Used  |
%|                          for kinetic models FRTM and SRTM.                                       |
%|                          Cref = [(f-1),1].                                                       |
%|                          Cp = [(f-1),1].                                                         |
%|            OPTIONAL :                                                                            |
%|            ROIMask       3D matrix with image ROI mask, for an image-derived response function.  |
%|                          ROIMask = [nx,ny,nz].                                                   |
%|            CpMask        3D matrix with Cp ROI mask, for an image-derived input function.        |
%|                          CpMask = [nx,ny,nz].                                                    |
%|            CrefMask      3D matrix with Cref ROI mask, for an image-derived Cref.                 |
%|                          CrefMask = [nx,ny,nz].                                                  |
%|            w             String or vector with frame weights, unit (unitless).                   |
%|                          w = [(f-1),1], or string 'w1', 'w2',...,'w6' or 'ones' (default).       |
%|            p0            Vector with initial parameter guesses, unit (1/s) for rate constants.    |
%|                          p0 = [1,N]. Default 0.01 for all parameters.                            |
%|            halflife      Nuclide halflife in sec, for calculation of some weight types.          |
%|            noExp         Scalar between 1-inf. Number of exponentials for model 'sumExp'.        |
%|            interpMethod  String with interpolation method. Default 'linear'.                    |
%|            solver        String with desired solver algorith. Default []-->'trust-region-refl'.  |
%|            lowerBound    Vector with lower bound for parameters, unit (1/s) for rate constants.  |
%|                          lowerBound = [1,N]. Default 0 for all parameters.                       |
%|            upperBound    Vector with upper bound for parameters, unit (1/s) for rate constants.  |
%|                          upperBound = [1,N]. Default 100*p0.                                     |
%|                                                                                                  |
%| OUTPUT :   paramImage    1) No ROIMask: 4D matrix with parametric image (3D image with a 4th     |
%|                          parameter dimension), unit (1/s) for rate constants.                    |
%|                          paramImage = [nx,ny,nz,N].                                              |
%|                          2) ROIMask specified: vector of parameters for ROI.                     |
%|                          paramImage = [1,N].                                                     |
%|                                                                                                  |
%*********************************************************************************************
```

pickOutTACFromROI.m

```
%*********************************************************************************************************
% IH, 19/04/2016.
%
% USAGE :   [TACmatrix,TACvariance] = pickOutTACFromROI( image, roi, type ).
%
% INPUT :   image        Matrix with 4D image, [nx,ny,nz,f].
%           roi          Matrix with 3D roi, [nx,ny,nz].
%           type         string with desired type, "voxel" or "average".
%                           average - average TAC in ROI, [f,1].
%                           voxel   - each voxel TAC in ROI, [f,noVox].
%
% OUTPUT:   TACmatrix    Matrix with TAC from the ROI, average or each voxel, [f,1] or [f,noVox].
%           TACvariance  Matrix with ROI variance, [f,1].
%*********************************************************************************************************
```

recon_fbpSimData_nonUniformSliceSens.m

```
%*********************************************************************************************************
%"recon_fbpSimData_nonUniformSliceSens"
%   Reconstructs PET-like images via FBP for non-uniform axial sensitivity
%
% CRS, 08/01/2013
% IH,  19/04/2016
%
%Usage:
%   [FBP] = recon_fbpSimData_nonUniformSliceSens(nFWPTtotal,RS,CTAC,POST,wcc,radBin,tanBin,simSize,zSlice)
%       nFWPTtotal = Projection data
%       RS         = scatter + random projection reference data
%       CTAC       = CT attenuation correction data
%       POST       = FWHM of post filter
%       wcc        = "Well-counter correction"
%       vox        = radial bins, tanBin, simSize, zSlice
%
%*********************************************************************************************************
```

recon_osemSimData_nonUniformSliceSens.m

```
%*********************************************************************************************************
%"recon_osemSimData_nonUniformSliceSens"
%   Reconstructs PET-like images via OS-MLEM for non-uniform axial sensitivity
%
% CRS, 09/18/2013
% IH,  19/04/2016
%
%Usage:
%   [OS] = recon_osemSimData_nonUniformSliceSens(nFWPTtotal,RS,CTAC,POST,wcc,radBin,tanBin,
simSize,zSlice,iterNUM,reconType)
%       nFWPTtotal = Projection data
%       RS         = scatter + random projection reference data
%       CTAC       = CT attenuation correction data
%       POST       = FWHM of post filter
%       wcc        = "Well-counter correction"
%       radBin     = radial bins
%       tanBin     = projection bins
%       simSize    = Final image size
%       zSlice     = number of slices
%       iterNUM    = number of iterations
%       subNUM     = number of subsets
%
%*********************************************************************************************************
```

recon_osemPSFSimData_nonUniformSliceSens.m

```
%*********************************************************************************************************
%"recon_osemPSFSimData_nonUniformSliceSens"
%   Reconstructs PET-like images via OSEM w/ psf for non-uniform axial sensitivity
%
% CRS, 08/01/2013
% IH,  19/04/2016
%
%Usage:
%   [OS] = recon_osemPSFSimData_nonUniformSliceSens(nFWPTtotal,
RS,CTAC,PSF,POST,wcc,radBin,tanBin,simSize,zSlice,iterNUM,reconType)
%       nFWPTtotal = Projection data
%       RS         = scatter + random projection reference data
%       CTAC       = CT attenuation correction data
%       PSF        = FWHM of PSF
%       POST       = FWHM of post filter
%       wcc        = "Well-counter correction"
%       radBin     = radial bins
%       tanBin     = projection bins
%       simSize    = Final image size
%       zSlice     = number of slices
%       iterNUM    = number of iterations
%
%*********************************************************************************************************
```