Software Requirements Specification for 3dfim+

Mojdeh Sayari Nejad and Spencer Smith

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Contents

1 Reference Material

This section records information for easy reference.

1.1 Table of Units

For basic units in SI (Système International d'Unités) the symbol is given in the table below followed by a description of the unit with the SI name.

symbol	**unit**	**SI**
s	time	second

Table 1: Table of Units

3dfim+ calculates cross-correlation of two sequences of data. Correlation coefficients are not influenced by the units and the two sequences of data can be measured in different units. Indeed, the calculations for correlation coefficients were designed such that the units of measurement do not affect the calculation. As a result, we do not provide units for them.

1.2 Table of Notations

Through this document, some notations are used to define mathematical expressions. These notations are given below in table 2 followed by a description. Some of the notations are chosen from [1].

1.3 Table of Symbols

Table 3 summarizes the symbols used in this document. The symbols are listed in alphabetical order.

symbol	**type**	**description**
a	$\mathbb{R}$	variable
A	$\mathbb{R}^n$	sample dataset of size n
$Average$	$\mathbb{R}$	average quantity for fMRI dataset

b	$\mathbb{R}$	variable
B	$\mathbb{R}^n$	sample dataset of size n
base	$\mathbb{R}^n$	baseline signal
$Baseline$	$\mathbb{R}$	baseline quantity for fMRI dataset
$cval$	$\mathbb{R}$	a threshold variable
d	$\mathbb{N}^+$	sample size
f	$\mathbb{N}$	number of frames
k	$\mathbb{N}$	index of best ideal signal
M	$\mathbb{R}^{m\times n}$	data model consisting of baseline, orthogonal and ideal time series
MSE	$\mathbb{R}$	mean square error
p	$\mathbb{R}$	threshold for voxel's intensity
$pnum$	$\mathbb{W}$	degree of the polynomial in the baseline model
r	$\mathbb{R}^n$	ideal signal
r_k	$\mathbb{R}^n$	best ideal signal
s	$\mathbb{R}$	sample variance
sb	$\mathbb{R}^{m\times n\times p}$	sub-brick
slc	$\mathbb{R}^{m\times n}$	slice
SSE	$\mathbb{R}$	sum of squared errors
t	$\mathbb{R}$	time
$Topline$	$\mathbb{R}$	topline quantity for fMRI dataset
v	$\mathbb{R}$	voxel
X	$\mathbb{R}^{m\times n\times p\times q}$	3d+time dataset
α	$\mathbb{R}$	fit coefficient for ideal signal
β	$\mathbb{R}$	fit coefficient for baseline
β^*	$\mathbb{R}^n$	vector of fit coefficients
ϵ	$\mathbb{R}^n$	noise vector
γ	$\mathbb{R}$	fit coefficient for orthogonal time series
σ	$\mathbb{R}$	sample standard deviation
σ_r	$\mathbb{R}$	standard deviation of the residuals
ρ	$\mathbb{R}$	Pearson correlation coefficient
ρ_s	$\mathbb{R}$	Spearman correlation coefficient
ρ_q	$\mathbb{R}$	quadrant correlation coefficient
ϕ	$\mathbb{R}^n$	orthogonal time series

Table 3: Table of Symbols

symbol	Description
$\bar{}$	over bar indicating arithmetic mean
$\mathbb{N}$	set of natural numbers
$\mathbb{N}^n$	set of natural vectors of size n
$\mathbb{N}^{m\times n}$	set of natural 2D matrices of size $m \times n$
$\mathbb{R}$	set of real numbers
$\mathbb{R}^n$	sequence of real numbers (set of real vectors) of size n
$\mathbb{R}^{m\times n\times p}$	set of 3D real matrices of size $m \times n \times p$
$\mathbb{R}^{m\times n\times p\times q}$	sequence of length of q of 3D real matrices of size $m \times n \times p$
a_i	i^{th} entry of a matrix
a_{ij}	entry (i, j) of a 2D matrix
a_{ijk}	entry (i, j, k) of a 3D matrix
a_{ijkl}	entry (i, j, k) of a 3D matrix in a sequence of 3D matrices at time l
A^T	transpose of a matrix: $A^T_{ij} = A_{ji}$
rank(a_{ij},A)	rank of element (i, j) in a 2D matrix A

Table 2: Table of Notations

1.4 Abbreviations and Acronyms

Table 4 contains the abbreviations and acronyms used in this document.

symbol	description
2D	2-Dimensional
3D	3-Dimensional
3dfim+	3-Dimensional Functional Intensity Map+
4D	4-Dimensional
A	Assumption
AFNI	Analysis of Functional NeuroImages
DD	Data Definition
DICOM	Digital Imaging and Communications in Medicine
fMRI	functional Magnetic Resonance Imaging
GS	Goal Statement
IM	Instance Model
LC	Likely Change
LPI	Left-Posterior-Inferior

LPS	Left-Posterior-Superior
MRI	Functional magnetic resonance imaging
NIfTI	Neuroimaging Informatics Technology Initiative
R	Requirement
RAI	Right-Anterior-Inferior
RAS	Right-Anterior-Superior
SRS	Software Requirements Specification
T	Theoretical Model
WCS	World Coordinate System

Table 4: Abbreviations and Acronyms

2 Introduction

This document provides an overview of the Software Requirements Specification (SRS) for the program 3dfim+ [2]. 3dfim+ mainly calculates the cross-correlation of an ideal reference signal versus the measured fMRI time series for each voxel. The current section explains the purpose of this document, the scope of the software, the organization of the document and the characteristics of the intended readers.

2.1 Purpose of Document

The main purpose of this document is to provide sufficient information to understand what 3dfim+ does. The goals and theoretical models used in the 3dfim+ implementation are provided, with an emphasis on explicitly identifying assumptions and unambiguous definitions.

2.2 Scope of Requirements

The responsibilities of the user and the 3dfim+ are as follows:

- User Responsibilities: Users are responsible to provide appropriate inputs to the program and ensure that the inputs meet the assumptions mentioned in 4.2.1.
- 3dfim+ Responsibilities: Upon receiving appropriate inputs, the program is intended to compute the cross-correlation of each voxel's activity over time with a user specified reference time series. Other outputs are mentioned in R6 to R13.

2.3 Organization of Document

The organization of this document follows the template for an SRS for scientific computing software proposed by [3] and [4]. The presentation follows the standard pattern of presenting goals, theories, definitions and assumptions. The goal statements are refined to the theoretical models, and theoretical models to the instance models. For readers that would like a more bottom-up approach, they can start reading the instance models in Section 4.2.4 and trace back to find any additional information they require.

3 General System Description

This section provides general information about the system, identifies the interfaces between the system and its environment, and describes the user characteristics and the system constraints.

3.1 System Context

Figure 1 shows the system context. A circle represents an external entity outside the software, the user in this case. A rectangle represents the software system itself. Arrows are used to show the data flow between the system and its environment.

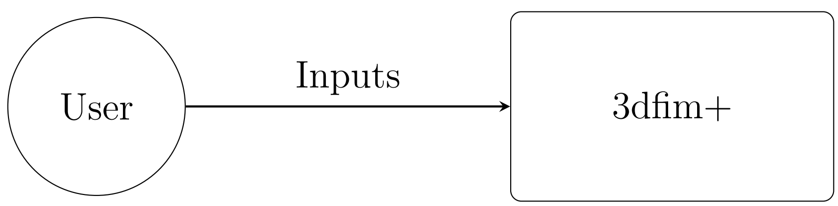


Figure 1: System Context

3dfim+ is mostly self-contained. The only external interaction is through the user interface. The responsibilities of the user and the system are as follows:

- User Responsibilities:
  - Provide the input data to the system
  - Ensure the input meets the necessary assumptions
  - Run the appropriate experiment to obtain the required data
- 3dfim+ Responsibilities:
  - Calculate the required outputs

3.2 User Characteristics

The end user of 3dfim+ should have an understanding of undergraduate Level 1 Linear Algebra.

3.3 System Constraints

Intended environment to run the program on are the Unix+X11+Motif systems [5].

4 Specific System Description

This section first presents the problem description, which gives a high-level view of the problem to be solved. This is followed by the solution characteristics specification, which presents the assumptions, theories, definitions and finally the instance models.

4.1 Problem Description

The main purpose of 3dfim+ is to calculate the cross-correlation between voxels and a reference signal over time. Other outputs of the program are mentioned in R6 to R13.

4.1.1 Background

This section provides information necessary to understand the correlation.

4.1.1.1 Basics of Correlation

Correlation is used to measure strength of association between two variables. Correlation coefficients are standardized; they vary between +1 and -1 and describe strength and direction of the association.

If a variable is correlated to itself, the resulting value is called autocorrelation or serial correlation. In this case the variable is being compared to itself with a time shift. Otherwise, if we have two different variables, the output is called cross-correlation.

If the value of the correlation coefficient is near to +1 or -1, there is a strong degree of association between the two variables. A value near to zero represents a weak correlation between the variables.

4.1.1.2 Visual Representation of Correlation

To study the possible correlation between two variables, we can produce a graph called scatter diagram or scattergram. Axes represent values of two variables, and corresponding values are shown by a dot. Figure 2 shows a sample of a scattergram of two sample variables a and b.

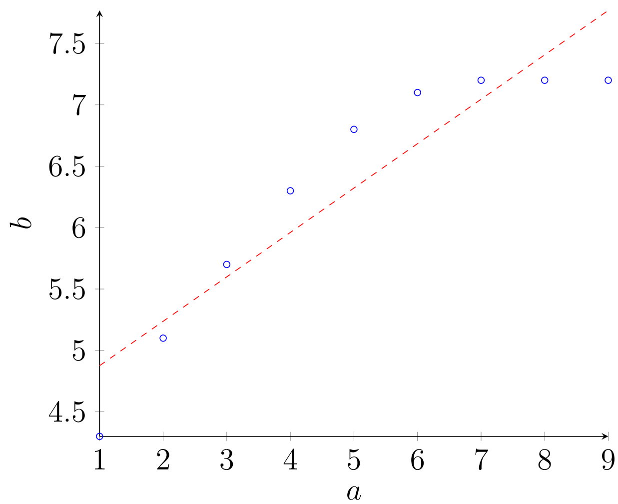


Figure 2: A sample of a scattergram and regression line of two variables a and b

The red dashed line in the graph shows linear regression, which represents the best-fit straight line through the points. The nearer the points are to this line, the stronger the association between the two variables is.

4.1.1.3 Different Types of Correlation

We can categorize correlation based on the nature of inputs and the relationship between them as follows:

- Positive and Negative Correlation: Positive correlation occurs when two variables change in the same direction. In other words, both variables either increase or decrease. A sample scattergram of a positive correlation is shown in Figure 3 .

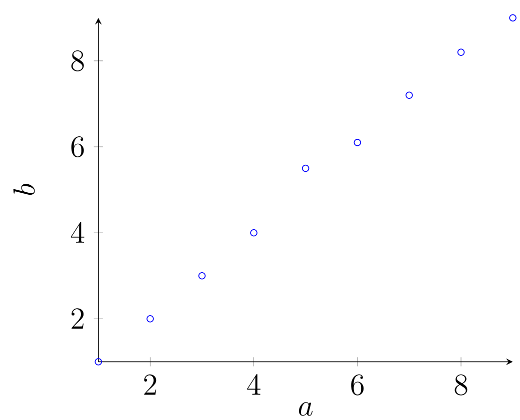


Figure 3: A sample positive correlation

There is a negative correlation between variables if one variable increases while the other decreases. In other words, two variables change in the opposite directions. A sample scattergram showing a negative correlation is shown in Figure 4.

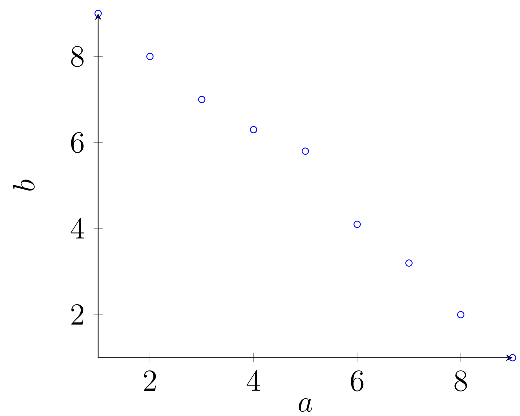


Figure 4: A sample negative correlation

- Linear versus Non-Linear Correlation: If the ratio between two variables remains the same, there exists a linear correlation between them. In this case, there is a straight line relationship between those variables. If the ratio does not remain constant over time, the correlation is called non-linear. When a relation is non-existent or random, correlation coefficients are near zero.

- Parametric versus Non-parametric Correlation: Parametric correlation uses data information such as mean and standard deviation while non-parametric correlation does not need such information. So if the data type is interval or ratio, we use a parametric estimation such as Pearson correlation coefficient and if the level of measurement is either ordinal or nominal, we use a non-parametric estimation, such as Spearman correlation coefficient. Moreover, to use a parametric correlation data distribution should be approximately normal. It is important to choose an appropriate correlation to get valid results.

- Pearson Correlation Coefficient: Pearson correlation is the most commonly used type of correlations. This correlation, signified by ρ, is a linear correlation used in statistics to measure the degree of linear relationship between paired data.

- Spearman Correlation Coefficient: Spearman correlation coefficient, denoted by ρ_S, is a statistical measure of the strength of a monotonic relationship between the observation ranks. We can consider this correlation as a non-parametric version of the Pearson correlation that measures the strength of association between two ranked variables. This rank-based estimator is highly efficient and is robust to outliers [6].

- Quadrant Correlation Coefficient: As we mentioned previously, an estimation procedure can be endowed with robustness properties by using a rank statistics [7]. Quadrant correlation coefficient is a non-parametric estimator that computes the correlation coefficient between the sign of deviations from medians using ranked data.

4.1.1.4 Effect Size

The correlation coefficient representing the strength of relationship between two variables is referred to as the effect size. We can use either Cohen's (1998) [8] or Evans (1996) [9] standard shown in Tables 5 and 6 respectively, to interpret the effect size.

Table 5: Cohen's effect size

Strength of Association	Positive Coefficient	Negative Coefficient
Small	0.1 to 0.29	-0.1 to -0.29
Medium	0.3 to 0.49	-0.3 to -0.49
Large	0.5 to 1	-0.5 to -1

Table 6: Evans' effect size

Strength of Association	Positive Coefficient	Negative Coefficient
Very Weak	0.00 to 0.19	0.00 to -0.19
Weak	0.20 to 0.39	-0.20 to -0.39
Moderate	0.40 to 0.59	-0.40 to -0.59
Strong	0.60 to 0.79	-0.60 to -0.79
Very Strong	0.8 to 1	-0.8 to -1

Note that correlation coefficient of 0 does not imply that there is no relationship between the variables. For example, a value of 0 for a Pearson correlation coefficient only indicates that there is no linear association between the variables. However, other relationships, such as quadratic relationship, can exist between them.

Also note that a coefficient of +1 means that there is no variation between the data points and the line of best fit.

4.1.2 Terminology Definition

This subsection provides definitions for the terms that are used in the subsequent sections with the purpose of reducing ambiguity and making it easier to understand the requirements.

- Arithmetic Mean: The arithmetic mean of a set of data, also referred to as mean or sample mean, is computed as the sum of all the values in the dataset divided by the count of all data points in the dataset.

- Variance: Variance is a measure of how far the numbers in a set are spread out. It measures the distance between each number in the set from the mean of the numbers in the set. It is calculated as the average of the squared differences between each number in the set and the mean.

- Standard Deviation: Standard deviation is a measure that is used to quantify the amount of variation of a set of data values. It is computed as the square root of the variance. Standard deviation is used when a sample of data from an entire population is available.

- Nominal Data: Nominal data also known as categorical data is a type of data that is categorized but there is no order between the categories.

- Ranked Data: Ranked data is a set of variables that for any two of them, one is ranked either equal to or lower than or higher than the other one. The relationship between these variables is called ranking. More information is provided in DD4.

- Ordinal Data: Ordinal type is when there is a clear ordering of variables, but the difference between values is inconsistent. Rating between 0 and 10 is an example of this kind of variables. The difference between rate 2 and 4 is not necessarily the same as the difference between rate 6 and 8.

- Interval Data: For an interval variable, order is important as for an ordinal variable. In addition, the interval between the values are equally spaced. For example, temperature is considered as an interval variable. The difference between 50 degrees and 60 degrees is the same as the difference between 70 degrees and 80 degrees.

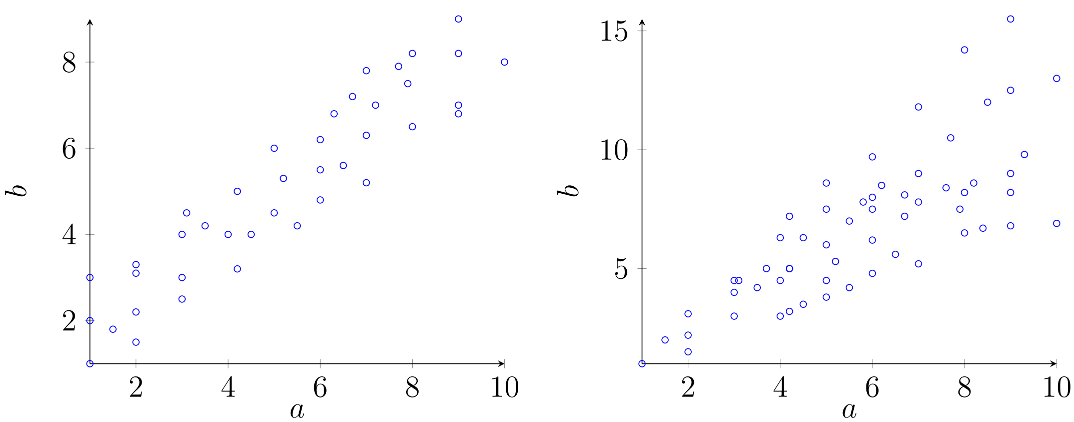
- Ratio Data: A ratio variable has all the properties of an interval variable. Moreover, when the value of the variable is equal to 0, it means that there is none of that variable. For example, a value of 0 for a variable such as height means we have no height. Note that ratio data can also be considered as an interval data and an ordinal data. In other words, ratio data $\subset$ interval data $\subset$ ordinal data.

  The definition of nominal, ordinal, interval, and ratio variables, known as level of measurement, was first developed by Stevens (1946) [10]. The level of measurement determines which statistical measures are appropriate for the specific need. Note that for calculating Pearson correlation coefficients, variables need to have a level of measurement at least equal to interval. The reason is that we need to compute mean of variables for Pearson correlation coefficients and computing an average is meaningful only when the intervals between values are equally spaced.

If data is ordinal, Spearman correlation coefficients or quadrant correlation coefficients are used instead.

- Homoscedasiticity: Homoscedacsiticity happens when both variables are normally distributed around the regression line. It means that the variances along the regression line remain similar while moving along the line.

  When using Pearson correlation coefficient as a measure, violation in homoscedasiticity may result in over-estimating the goodness of the fit. Figure 5 shows this characteristic.



(a) Homoscedasiticity

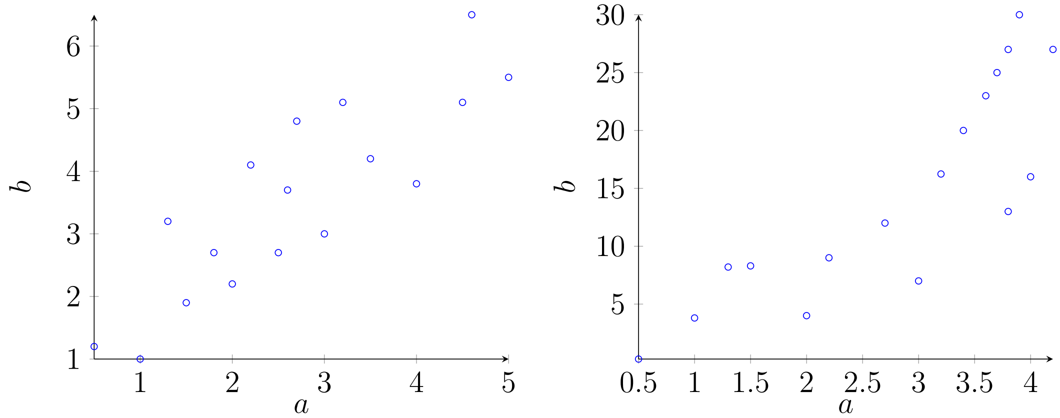
(b) Heteroscedasiticity

Figure 5

- Bivariate normal distribution: When each variable is normally distributed itself and is also normally distributed at all levels of the other variable, the distribution is bivariate normal. If this assumption is met, the only type of statistical relationship that can exist between the two variables is a linear relationship. However, if the assumption is violated, a non-linear relationship may exist. It is important to determine if a non-linear relationship exists between two variables before describing the results using Pearson correlation coefficient.

- Outlier: An outlier is a data point that does not follow the general pattern of the data and its value is extremely different from the rest of the data, such that it has a large effect on some parameters such as mean of the data and consequently on Pearson correlation coefficient and the regression line. Pearson correlation coefficient is sensitive to outliers, so if data point removal is not allowed, we should use a non-parametric estimation such as Spearman correlation coefficient.

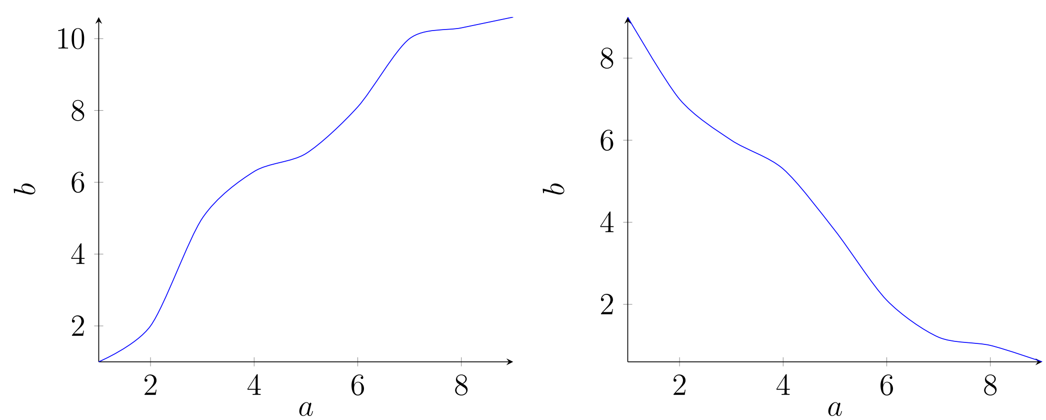
- Linearity: Linearity is a mathematical relationship between two variables that can be represented as a straight line. If the relationship between the variables is non-linear, Pearson correlation coefficient is not an appropriate statistic for measuring the association. Figure 6 visualizes this relationship.



(a) Linear (b) Nonlinear

Figure 6

- Monotonic function: Monotonic function $b(a)$ is a function where increasing in the value of a results in either always increasing or always decreasing in the value of b. Figure 7 visualizes this function.



(a) Monotonically increasing (b) Monotonically decreasing

Figure 7

4.1.3 Coordinate Systems

While working with medical images, it is necessary to be familiar with the different coordinate systems of the medical literarure and how data (voxels' orientation) is interpreted in different medical and non-medical software. Each coordinate system uses one or more numbers (coordinates) to uniquely determine the position of a point (in the medical context, we refer to each point as a voxel). The purpose of this section is to introduce some of the coordinate systems related to the medical imaging. There are different coordinate systems to represent data. A knowledge of the following coordinate systems is needed to be able to work with the medical images.

4.1.3.1 Cartesian Coordinate System

A Cartesian coordinate system is a coordinate system that specifies each point uniquely in a 2D plane by a pair of numerical coordinates or in a 3D space by three numerical coordinates. We assume a right-hand Cartesian coordinate system throughout this document.

4.1.3.2 World Coordinate System

World Coordinate System (WCS) is a Cartesian coordinate system that describes the physical coordinates associated with a model such as a MRI scanner or a patient. While each model has its own coordinate system, without a universal coordinate system such as WCS, they cannot interact with each other. For model interaction to be possible, their coordinate systems must be transformed into the WCS. Figure 10 shows the WCS corresponding space and axes.

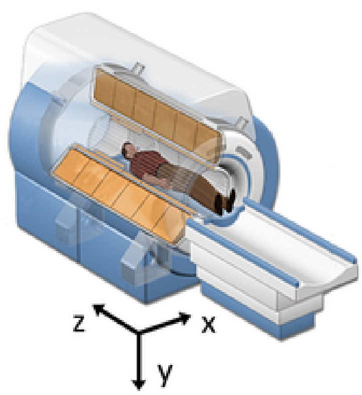


Figure 8: World Coordinate System Space and Axes [11]

4.1.3.3 Anatomical Coordinate System

Anatomical coordinate system, also known as patient coordinate system, is a right-handed 3D coordinate system which describes the standard anatomical position of a human using the following 3 orthogonal planes:

- Axial / Transverse plane: is a plane parallel to the ground that separates the body into head (superior) and tail (inferior) positions.

- Coronal / Frontal plane: is a plane perpendicular to the ground that divides the body into front (anterior) and back (posterior) positions.
- Sagittal / Median plane: is a plane that divides the body into right and left positions.

Figure 9 shows this coordinate system.

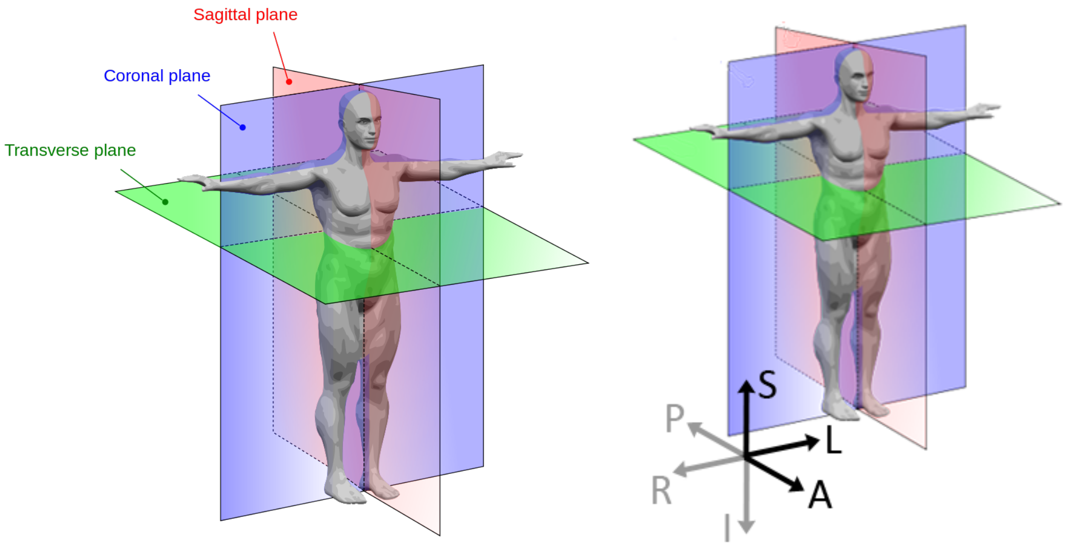


Figure 9: Anatomical Coordinate System Space and Axes [11]

Medical applications follow an anatomical coordinate system to store voxels in sequences. Depending on how the data is stored, this coordinate system can be divided into different bases. The most common ones are:

- LPS Coordinate System:

  The LPS coordinate system, also known as DICOM (patient) coordinate system, is a left-hand coordinate system used in DICOM images. In this system, voxels are ordered from left to right in a row, rows are ordered from posterior to anterior, and slices are stored from inferior to superior. In other words, it is an LPI system.
  LPS stands for Left-Posterior-Superior which indicates the directions that spatial axes are increasing.

- RAS Coordinate System:

  LPI is a right-hand coordinate system for voxel orientation. It stores voxels from right to left to create rows, rows from anterior to posterior to create slices and slices from superior to inferior to create volumes. This system is the preferred basis for Neurological applications such as 3dfim+ and is used in NIfTI files. The increasing position order is RAS.

4.1.3.4 Image Coordinate System

To specify locations in an image we need to know to which coordinate system it is referenced. Different software may use different orders as their index convention.

- Image Coordinate System for Matlab:

  In Matlab, index numbering starts at the upper left corner. To express the position of point (x, y, z), we should consider that the x axis increases from left to right, the y axis increases to the bottom and the z axis increases backward.

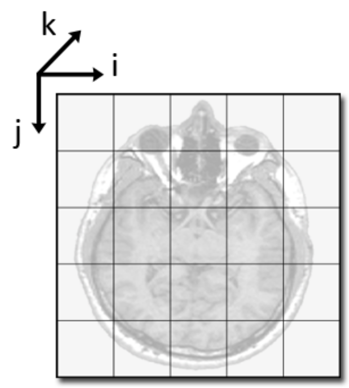


Figure 10: Image Coordinate System Space and Axes in Matlab [11]

- Image Coordinate System for AFNI:

  In AFNI, the lower left hand corner of the image is considered as the origin, which represents the position of the first voxel (0,0,0).

  If we are using different file formats and software, we need to transform their coordinate systems into WCS.

4.1.4 Physical System Description

We do not study the physical system for MRI or how the data is actually generated.

4.1.5 Goal Statements

Given an fMRI time series (DD6), one or more ideal time series (DD7) and zero or more orthogonal time series (DD13):

GS1: Estimate the Pearson correlation coefficients between the (best) ideal time series and the fMRI time series at each voxel over time.

GS2: Estimate the Spearman correlation coefficient between the (best) ideal time series and the fMRI time series at each voxel over time.

GS3: Estimate the quadrant correlation between the (best) ideal time series and the fMRI time series at each voxel over time.

GS4: In case of having multiple ideal signals, report the index number for the best ideal time series.

GS5: Calculate the percentage change in the fMRI time series due to the (best) ideal time series relative to the average for each voxel.

GS6: Calculate the percentage change in the fMRI time series due to the (best) ideal time series relative to the baseline for each voxel.

GS7: Calculate the fMRI time series baseline for each voxel.

GS8: Calculate the fMRI time series average for each voxel.

GS9: Calculate the percentage change in the fMRI time series due to the (best) ideal time series relative to the topline for each voxel.

GS10: Calculate the fMRI time series topline quantity for each voxel.

GS11: Calculate the standard deviation of the residuals at each voxel between the fMRI dataset and corresponding data estimation.

4.2 Solution Characteristics Specification

In this section, necessary information to understand the meaning of instance models, presented in subsection 4.2.4, is provided.

4.2.1 Assumptions

This section simplifies the original problem and helps in developing the theoretical model by filling in the missing information for the physical system. The numbers given in the square brackets refer to the theoretical model [T], data definition [DD], instance model [IM], or likely change [LC], in which the respective assumption is used.

The calculation of Pearson correlation coefficient requires the following data assumptions to hold:

A1: The variables should be either of type interval or ratio. In other words, they should be continuous, which is also known as quantitative variable. However, both variables do not need to be measured on the same scale; one can be of type interval while the other can be of type ratio [T1, IM1].

A2: There is a linear relationship between the two variables [T1, IM1].

A3: The variables are bivariately normally distributed [T1, IM1].

A4: Outliers are removed entirely or kept to a minimum [T1, IM1, LC1].

A5: The variables are homoscedastic [T1, IM1].

If data does not meet all of the above assumptions, then Spearman correlation coefficient or quadrant correlation coefficient can be used, if the data holds the following characteristics:

A6: The variables should be either of type interval, ratio or ordinal. However, both variables do not need to be measured on the same scale; one can be interval while the other is ratio [T2, T3, IM3, IM4].

A7: The variables should be monotonically related. One can check whether a monotonic relation exists between the two variables using a scattergram [T2, T3, IM3, IM4].

It is worth mentioning that Spearman correlation coefficient estimation is not very sensitive to outliers. Hence, if there are outliers in the data, the result should still be valid.

4.2.2 Theoretical Models

This section focuses on the general equations and laws that 3dfim+ is based on. In this document, we considered indexing starts from 1.

Number	T1
Name	Pearson
Label	**Calculating Pearson Correlation Coefficient**
Equation	$\rho(A,B) = \frac{\sum\limits_{i=1}^{n}(a_i-\bar{a})(b_i-\bar{b})}{[\sum\limits_{i=1}^{n}(a_i-\bar{a})^2 \sum\limits_{i=1}^{n}(b_i-\bar{b})^2]^{\frac{1}{2}}}$
Description	The equation calculates Pearson correlation coefficients ρ applied to two datasets $A : \mathbb{R}^n$ and $B : \mathbb{R}^n$ both of size n. $\bar{a}$ and $\bar{b}$ are sample means (DD1) of A and B, respectively. ρ is the Pearson correlation coefficient between A and B. The equation can be also written as: $\rho(A,B) = \frac{\sum\limits_{i=1}^{n} a_i b_i - n\bar{a}\bar{b}}{(n-1)\sigma_{a_i}\sigma_{b_i}}$ Where σ_a and σ_b are standard deviations (DD3). Assumptions A1, A2, A3, A4 and A5 must hold when calculating this correlation.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf http://www.statstutor.ac.uk/resources/uploaded/pearsons.pdf
Ref. By	IM1

Number	T2
Name	Spearman
Label	**Calculating Spearman Correlation Coefficient**
Equation	$\rho_s(A,B) = \frac{\sum_{i=1}^{n}(\text{rank}(a_i,A)-\frac{n+1}{2})(\text{rank}(b_i,B)-\frac{n+1}{2})}{\sqrt{\sum_{i=1}^{n}(\text{rank}(a_i,A)-\frac{n+1}{2})^2(\text{rank}(b_i,B)-\frac{n+1}{2})^2}}$
Description	This formula calculates Spearman correlation coefficient ρ_s applied to two sample datasets $A : \mathbb{R}^n$ and $B : \mathbb{R}^n$ both of size n. ρ_s is the Spearman correlation coefficient between A and B. $\text{rank}(a_i, A)$ and $\text{rank}(b_i, B)$ are rank functions (DD4). This formula can also be written as: $\rho_s(A,B) = 1 - \frac{6\sum_{i=1}^{n} h_i^2}{n(n^2-1)}$ h_i is the difference between paired ranked variables: $h_i = \text{rank}(a_i, A) - \text{rank}(b_i, B)$ Note that assumptions A6 and A7 must hold while calculating this correlation.
Source	http://www.statstutor.ac.uk/resources/uploaded/spearmans.pdf
Ref. By	IM3

Number	T3
Name	Quadrant
Label	**Calculating Quadrant Correlation Coefficient**
Equation	$\rho_q(A,B) = \frac{\sum\limits_{i=1}^{n}(\text{sign}(\text{rank}(a_i,A)-\frac{n+1}{2}))(\text{sign}(\text{rank}(b_i,B)-\frac{n+1}{2}))}{\sqrt{\sum\limits_{i=1}^{n}((\text{rank}(a_i,A)-\frac{n+1}{2}))^2((\text{rank}(b_i,B)-\frac{n+1}{2}))^2}}$
Description	This formula calculates the quadrant (sign) correlation coefficient ρ_q using the rank function (DD4) and sign function (DD5) applied to two sample datasets $A : \mathbb{R}^n$ and $B : \mathbb{R}^n$ both of size n. ρ_q is the quadrant correlation coefficient between A and B. Note that assumptions A6 and A7 must hold while calculating this correlation.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf https://books.google.ca/books?id=-058B6kg32sC&pg=PA19&lpg=PA19&dq=quadrant+correlation&source=bl&ots=diTd_d0tou&sig=vfZXlpyTf2BzVWYUAQYpZQSjiv4&hl=en&sa=X&ved=0ahUKEwi4g7DP45LSAhXpy4MKHfFPCU04ChDoAQg-MAY#v=onepage&q=quadrant%20correlation&f=false
Ref. By	IM4

Number	T4
Name	Linear Regression
Label	**Linear Regression Model**
Equation	$f(t, x) = x_1\omega_1(t) + x_2\omega_2(t) + \cdots + x_n\omega_n(t)$
Description	Regression is the task of finding the best fit for a model through a set of data points. Given data points (t_i, y_i) where $i = 1, \cdots, m$, we want to find the vector x of size n $(m > n)$ of parameters that gives the best fit to the data by the model function $f(t, x)$. The terms in the linear model $f(t, x)$ are either constant, i.e. $\omega_i(t) = 1$ or the product of a parameter x_i and a function $\omega_i(t)$. The above equation is called a linear regression equation and the fitting line that it generates is called line of best fit. If the data is linear, then the line of best fit is straight; otherwise, it is a curve. One of the common methods for estimating the linear regression is least squares method. (T8).
Source	[12]
Ref. By	T5, T8

Number	T5
Name	SSE
Label	**Sum of Squared Errors**
Equation	$SSE = \sum_{i=1}^{n} (y_i - f(t_i, x))^2$
Description	SSE is the sum of squared residuals. Here, the residual refers to the difference between the data y_i and the estimated value $f(t_i, x)$ (T4).
Source	https://en.wikipedia.org/wiki/Residual_sum_of_squares
Ref. By	T6, IM12

Number	T6
Name	MSE
Label	**Mean Squared Error**
Equation	$MSE = \frac{1}{n}(\sum_{i=1}^{n}(y_i - f(t_i, x))^2)$
Description	MSE is the mean of the SSE (T5).
Source	https://en.wikipedia.org/wiki/Mean_squared_error
Ref. By	T7, IM12

Number	T7
Name	Residuals Deviation
Label	**Standard Deviation of the Residuals**
Equation	$\sigma_r = \sqrt{MSE}$
Description	MSE is the mean squared error (T6).
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf https://brownmath.com/stat/infregr.htm
Ref. By	IM12

Number	T8
Name	Least Squares
Label	**Linear Least Squares**
Equation	$Ax \cong b$
Description	Given the best fit model $f(t, x)$ (T4) and data points (t_i, y_i), $i = 1, \cdots, m$, we want to find an estimation for x. Least squares tries to minimize the residual as follows: $$min \sum_{i=1}^{m} (y_i - f(t_i, x))^2$$ The matrix representation is $$b = Ax + \epsilon$$ Where: A is a $m \times n$ matrix with entries $a_{ij} = \omega_j(t_i)$, b is a $m \times 1$ vector where $b_i = y_i$, x is a $n \times 1$ vector of parameters, and ϵ is a $m \times 1$ vector of errors. If $m > n$, the system is overdetermined and there is no exact solution for x. Instead, our goal is to minimize some norm of the residual vector $r = b - Ax$ as a function of x : $$min \|Ax - b\|_2^2$$ If we use 2-norm as the approximation, the method is called least squares and takes the form of $Ax \cong b$. We can show that: $$\hat{x} = (A^T A)^{-1} A^T b$$ The estimated fit is then given by: $$\hat{b} = A\hat{x} = A(A^T A)^{-1} A^T b$$ The residual vector $\hat{\epsilon}$ is : $b - A\hat{x} = b - A(A^T A)^{-1} A^T b$.
Source	[12]
Ref. By	T4, IM12

4.2.3 Data Definitions

This section provides the mathematical formulas of the arithmetic concepts used in this document.

Number	DD1
Name	Mean
Label	**Calculating Arithmetic Mean**
Symbol	$\bar{}$
Equation	$\bar{a} = \frac{1}{d}\sum_{i=1}^{d} a_i$
Description	This formula calculates arithmetic mean, also referred as sample mean or mean for a dataset containing d values.
Source	http://mathworld.wolfram.com/ArithmeticMean.html
Ref. By	T1, IM1

Number	DD2
Name	Variance
Label	**Calculating Sample Variance**
Symbol	s^2
Equation	$s_a^2 = \frac{1}{d}\sum_{i=1}^{d}(a_i - \bar{a})^2$
Description	This formula calculates sample variance of a dataset containing d values.
Source	http://mathworld.wolfram.com/SampleVariance.html
Ref. By	DD3

Number	DD3
Name	Standard Deviation
Label	**Calculating Sample Standard Deviation**
Symbol	σ
Equation	$\sigma_a = \sqrt{s_a^2} = \sqrt{\frac{1}{d}\sum_{i=1}^{d}(a_i - \bar{a})^2}$
Description	This formula calculates sample standard deviation, that is the square root of the sample variance (DD2) when applied to a dataset containing d values.
Source	http://mathworld.wolfram.com/StandardDeviation.html
Ref. By	T1

Number	DD4
Name	Rank
Label	**Rank Function**
Symbol	rank()
Equation	$\text{rank} : \mathbb{R} \times \mathbb{R}^n \to \mathbb{N}$
Description	The rank of data points is determined by sorting them in an ascending order and assigning a value according to their position in the sorted list. If ties exist, the average of all of the tied positions is calculated as the rank. Mathematically, the rank of element a in dataset A is defined as follows: $\text{rank}(a, A) : \mathbb{R} \times \mathbb{R}^n \to \mathbb{N}$ $\text{rank}(a, A) \equiv \text{avg}(\text{indexSet}(a, \text{sort}(A)))$ $\text{indexSet}(a, B) : \mathbb{R} \times \mathbb{R}^n \to \text{ set of } \mathbb{N}$ $\text{indexSet}(a, B) \equiv \{j : \mathbb{N} \mid j \in [1..\lvert B \rvert] \wedge B_j = a : j\}$ $\text{sort}(A) : \mathbb{R}^n \to \mathbb{R}^n$ $\text{sort}(A) \equiv B : \mathbb{R}^n, \text{ such that}$ $\forall(a : \mathbb{R} \mid a \in A : \exists(b : \mathbb{R} \mid b \in B : b = a) \wedge \text{count}(a, A) = \text{count}(b, B)) \wedge \forall(i : \mathbb{N} \mid i \in [1..\lvert A \rvert - 1] : B_i \leq B_{i+1})$ $\text{count}(a, A) : \mathbb{R} \times \mathbb{R}^n \to \mathbb{N}$ $\text{count}(a, A) : +(x : \mathbb{N} \mid x \in A \wedge x = a : 1)$ $\text{avg}(C) : \text{ set of } \mathbb{N} \to \mathbb{R}$ $\text{avg}(C) \equiv +(x : \mathbb{N} \mid x \in C : x)/\lvert C \rvert$ The above equations use the Gries and Schneider notation [13, p. 143] for set building and evaluation of an operator applied over a set of values. Specifically, the expression $(*x : X \mid R : P)$ means application of the operator $*$ to the values P for all x of type X for which range R is true. In the above equations, the $*$ operators include $\forall$, $\exists$ and $+$ are used.
Source	https://en.wikipedia.org/wiki/Ranking
Ref. By	T2, T3

Number	DD5
Name	Sign
Label	**Sign Function**
Symbol	sign()
Equation	$$\text{sign(a)} = \begin{cases} 1 & a > 0 \\ 0 & a = 0 \\ -1 & a < 0 \end{cases}$$
Description	Given a variable a, the sign function returns 1 if a is positive, 0 if a is equal to zero, and -1 if a is negative.
Source	https://en.wikipedia.org/wiki/Sign_function
Ref. By	T3

Number	DD6
Name	3d+time
Label	**Mathematical Representation of 3d+time Dataset**
Symbol	$X : \mathbb{R}^{m \times n \times p \times q}$
Equation	-
Description	3d+time datasets are 4D datasets that have a temporal component, a time dimension that is the time intervals during scanning, collecting and concatenating datasets together. 3d+time datasets are the basic units of the fMRI.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	GS1, DD8, DD14, DD16, DD17, DD19, IM1, IM2, IM3, IM4, IM9, IM10, R1

Number	DD7
Name	Ideal Signal
Label	**Mathematical Representation of Ideal (Reference) Signal (Time Series)**
Symbol	$r : \mathbb{R}^n$
Equation	-
Description	Ideal signal is a waveform of choice.
Source	https://en.wikipedia.org/wiki/Square_wave
Ref. By	GS1, DD16, IM1, IM2, IM3, IM4, IM6, IM9, IM10, IM12, R1, R7, R8, R11

Number	DD8
Name	Sub-brick
Label	**Sub-brick**
Symbol	$\text{sb} : \mathbb{R}^{m \times n \times p}$
Equation	-
Description	A dataset (DD6) is comprised of one or more sub-bricks. Each sub-brick is a 3D array of numbers.
Source	https://msu.edu/~zhuda/fmri_class/labs/lab2/afni01_intro.pdf
Ref. By	DD9

Number	DD9
Name	Slice
Label	**Slice**
Symbol	slc : $\mathbb{R}^{m \times n}$
Equation	-
Description	A sub-brick (DD8) consists of slices. Each move in the Z plane is considered as one slice.
Source	https://msu.edu/~zhuda/fmri_class/labs/lab2/afni01_intro.pdf
Ref. By	DD10

Number	DD10
Name	Voxel
Label	**Voxel**
Symbol	$v : \mathbb{R}$
Equation	–
Description	A slice (DD9) consists of $n \times n$ voxels. A real number is assigned to each voxel which reports its activation significance. Figure 11 is provided for a better understanding.
Source	https://msu.edu/~zhuda/fmri_class/labs/lab2/afni01_intro.pdf
Ref. By	GS1

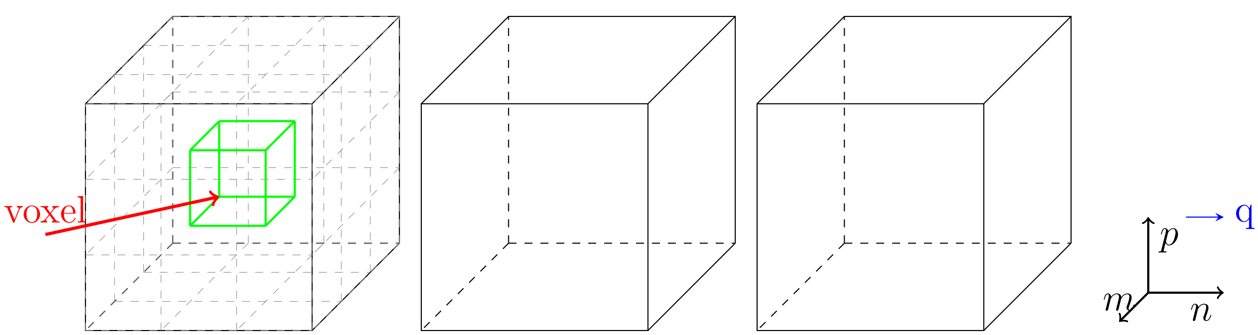


Figure 11: 3x3x3 dataset consisting of 3 sub-bricks

Number	DD11
Name	Baseline
Label	**Baseline Model**
Symbol	base: $\mathbb{R}^n \to \mathbb{R}^n$
Equation	$\text{base}(x) = a_n x^n + a_{n-1} x^{n-1} + \cdots + a_2 x + a_1$
Description	The average signal level from which a signal departs and to which it returns. Baseline is modeled as a function of time. *pnum* (DD12) is used to set the degree of the polynomial in baseline model.
Source	http://dalspace.library.dal.ca/bitstream/handle/10222/37440/Rukhshinda-Jabeen-MSc-CHEM-August-2013.pdf?sequence=6
Ref. By	DD13, IM2, IM6, IM7, IM8

Number	DD12
Name	Polynomial Degree
Label	**Polynomial Degree of Baseline Model**
Symbol	*pnum*: $\mathbb{W}$
Equation	-
Description	*pnum* indicates the degree of the polynomial in the baseline model. For example, $pnum = 0$ indicates a constant baseline, $pnum = 1$ is used to model a linear baseline and $pnum = 2$ removes any quadratic trend in data and so on. The default of the 3dfim+ is $pnum = 1$.
Source	https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dfim+.html
Ref. By	DD11, IM2, IM6, IM7, IM8, R1, IM12

Number	DD13
Name	Orthogonal
Label	**Orthogonal Time Series**
Symbol	$\phi : \mathbb{R}^n$
Equation	-
Description	Time series that is perpendicular to the baseline (DD11). Two polynomials are orthogonal if their inner product is zero. We define an inner product for two functions by integrating their product. $$\int_a^b \phi(x)\text{base}(x)dx = 0$$
Source	https://www.johndcook.com/OrthogonalPolynomials.pdf
Ref. By	GS1, IM2, IM6, IM7, IM8, IM12, R1

Number	DD14
Name	Threshold
Label	**Threshold For Voxels' Intensity**
Symbol	$p : \mathbb{R}; 0 \leq p \leq 1.0$
Equation	-
Description	p is a variable between 0 and 1. By default $p = 0.0999$. 3dfim+ calculates the average image intensity for the first sub-brick of the X (DD6) in the time series and then excludes any voxel whose intensity is less than $p *$ average. This process decreases the run time of the program.
Source	https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dfim+.html
Ref. By	R1

Number	DD15
Name	Correlation Coefficient Comparing Value
Label	**Comparing Value For Correlation Coefficient Screen Display**
Symbol	$cval : \mathbb{R};\ 0 \leq cval \leq 1$
Equation	-
Description	*cval* is used to control the correlation coefficient values displayed on the user's screen as the output of the program 3dfim+. The correlation coefficient value for each voxel is printed on the screen only if the absolute value of the computed correlation coefficient is greater than or equal to *cval*.
Source	https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dfim+.html
Ref. By	R1

Number	DD16
Name	Best Ideal
Label	**Best Ideal Signal**
Symbol	$r_k : \mathbb{R}^n$
Equation	-
Description	When multiple ideal signals (DD7) are defined, each of them is separately correlated with the dataset A (DD6). For each voxel, one of the signals is the most highly correlated one to that voxel's activity. We call this signal the best ideal signal for that voxel. Consider the g ideal signals $r_1, r_2, \cdots, r_g$. For each voxel: $$r_k = \underset{\substack{r_i \\ i=1\cdots g}}{\operatorname{argmax}} \mid \rho(A, r_i) \mid \text{ (DD18)}$$ In this case, r_k is the best ideal signal.
Source	https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dfim+.html
Ref. By	GS1, DD17, IM5, IM6, IM7, IM8, IM9, IM10, R6, R7, R8, R11

Number	DD17
Name	Best Index
Label	**Index of Best Ideal Signal**
Symbol	$k : \mathbb{N}$
Equation	-
Description	The index of the best ideal signal (DD16) is called the best index. Consider the g ideal signals $r_1, r_2, \cdots, r_g$ and a dataset A (DD6). For each voxel: $$r_k = \underset{i=1\cdots g}{\underset{r_i}{\text{argmax}}} \mid \rho(A, r_i) \mid \text{(DD18)}$$ In this case, the kth ideal signal is the best ideal signal and k is the best index.
Source	https://afni.nimh.nih.gov/pub/dist/doc/program_help/3dfim+.html
Ref. By	R6, IM5

Number	DD18
Name	argmax
Label	**Argmax Function**
Symbol	argmax: $(\mathbb{R} \rightarrow \mathbb{R}) \rightarrow (\mathbb{R} \rightarrow \mathbb{R})$
Equation	-
Description	Given a function f defined on a set D, argmax function is defined as follows: $$\underset{x \in D}{\text{argmax}} f(x) := \{x \mid \forall y \in D : f(x) \geq f(y)\}$$
Source	https://www.cs.ubc.ca/~schmidtm/Documents/2016_540_Argmax.pdf
Ref. By	DD16, DD17, IM5

Number	DD19
Name	Peak
Label	**Peak to Peak**
Symbol	$pp() : \mathbb{R}$
Equation	$pp(A) = \max_{i=1\cdots n}(a_i) - \min_{i=1\cdots n}(a_i)$ where $a_i \in A$
Description	Peak to peak function calculates the variation among the elements in a dataset (DD6).
Source	-
Ref. By	IM9, IM10, IM11

4.2.4 Instance Models

In this section, we express the 3dfim+ functionality mathematically.

The goal GS1 to GS11 is solved by IM1 to IM12.

Number	IM1
Name	Pearson Model
Label	**Calculating Pearson Correlation Coefficient Between the Reference Signal and the Input Dataset**
Input	$X : \mathbb{R}^{m \times n \times p \times q}$, $r : \mathbb{R}^q$
Output	$\rho_{ijk}(X, r) = \frac{\sum_{l=1}^{q}(x_{ijkl} - \bar{x}_{ijk})(r_l - \bar{r})}{[\sum_{l=1}^{q}(x_{ijkl} - \bar{x}_{ijk})^2 (r_l - \bar{r})^2]^{\frac{1}{2}}}$
Description	The formula calculates the Pearson correlation coefficient (T1) between the ideal time series r (DD7) and the 3d+time dataset X (DD6). $\bar{x}_{ijk}$ and $\bar{r}$ are sample means (DD1) defining as follows: $\bar{x}_{ijk} = \frac{\sum_{l=1}^{q} x_{ijkl}}{q}$ $\bar{r} = \frac{\sum_{i=1}^{q} r_i}{q}$ Note that assumptions A1, A2, A3, A4 and A5 must hold while calculating this correlation. We also assumed that $r = r_k$ (DD16) in case of having more than one ideal signal.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R2, R3, LC2

Number	IM2
Name	fMRI Dataset Model
Label	**Mathematical Model of Measured fMRI Dataset To Find Fit Coefficients**
Input	X, $\phi_i \in \mathbb{R}^q$, $r_i \in \mathbb{R}^q$
Output	$\beta_{ijk}^T = [\beta_0, \beta_1, \cdots, \gamma_1, \gamma_2, \cdots, \alpha_1, \alpha_2, \cdots]^T$
Description	Correlation analysis of each voxel's time series in X (DD6) with reference signal(s) r_i (DD7) where: $$M = \begin{bmatrix} 1 & 1 & \cdots & \phi_{1_1} & \cdots & r_{1_1} & \cdots \\ 1 & 2 & \cdots & \phi_{1_2} & \cdots & r_{1_2} & \cdots \\ 1 & 3 & \cdots & \phi_{1_3} & \cdots & r_{1_3} & \cdots \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots & \ddots \\ 1 & f & \cdots & \phi_{1_f} & \cdots & r_{1_f} & \cdots \end{bmatrix}$$ $$X_{ijk} = y_{ijk} = \begin{bmatrix} y_1 \\ y_2 \\ y_3 \\ \vdots \\ y_f \end{bmatrix} \beta_{ijk}^* = \begin{bmatrix} \beta_0 \\ \beta_1 \\ \vdots \\ \gamma_1 \\ \gamma_2 \\ \vdots \\ \alpha_1 \\ \alpha_2 \\ \vdots \end{bmatrix} \epsilon_{ijk} = \begin{bmatrix} \epsilon_1 \\ \epsilon_2 \\ \vdots \\ \epsilon_f \end{bmatrix}$$ The equation can be also written as: $X_{ijk} = M\beta_{ijk}^* + \epsilon_{ijk}$ where: M is the data model consisting of baseline (DD11), orthogonal time series ϕ_i's (DD13) and ideal time series r_i's (DD7). β_{ijk}^{*T} is the vector of unknown fit coefficients for each voxel v_{ijk}. ϵ_{ijk} is the noise at a specific voxel v_{ijk} over time. α 's are the fit coefficient for ideal signals. β's are the fit coefficient for baseline. γ's are the fit coefficient for orthogonal time series.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	IM6, IM7, IM8, R2, R12

The fMRI data we get from brain activity can be modeled as a factor of the model M. The data is composed of baseline, orthogonal time series, reference signal time series and noise. In the X matrix, the first columns indicate baseline (DD11) of the signals we get from each voxel's activity. The first column is for the constant baseline, the second column indicates the linear baseline, etc. $pnum$ (DD12) indicates the degree of the baseline polynomial. After baseline columns, we have orthogonal time series (DD13) columns shown by ϕ's. We can have zero or more orthogonal time series. The next columns are for the reference time series. We can define one or more ideal time series.

Number	IM3
Name	Spearman Model
Label	**Calculating Spearman Correlation Coefficient Between the Reference Signal and the Input Dataset**
Input	$X : \mathbb{R}^{m \times n \times p \times q}$, $r : \mathbb{R}^q$
Output	$\rho_{s_{ijk}}(X, r) = \frac{\sum_{l=1}^{q}(\text{rank}(x_{ijkl}, X_{kl}) - \frac{q+1}{2})(\text{rank}(r_l, r) - \frac{q+1}{2})}{\sqrt{\sum_{l=1}^{q}(\text{rank}(x_{ijkl}, X_{kl}) - \frac{d+1}{2})^2 (\text{rank}(r_l, r) - \frac{q+1}{2})^2}}$
Description	The above formula calculates Spearman correlation coefficient (T2) between the ideal time series r (DD7) and the 3d+time dataset X (DD6). Assumptions A6 and A7 must hold while calculating this correlation.
Source	`http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf`
Ref. By	R4

Number	IM4
Name	Quadrant Model
Label	**Calculating Quadrant Correlation Coefficient Between the Reference Signal and the Input Dataset**
Input	$X : \mathbb{R}^{m\times n\times p\times q}$, $r : \mathbb{R}^q$
Output	$\rho_{q_{ijk}}(X, r) = \frac{\sum_{l=1}^{q}(\text{sign}(\text{rank}(x_{ijkl}, X_{kl}) - \frac{q+1}{2}))(\text{sign}(\text{rank}(r_l, r) - \frac{q+1}{2}))}{\sqrt{\sum_{l=1}^{q}((\text{rank}(x_{ijkl}, X_{kl}) - \frac{q+1}{2}))^2((\text{rank}(r_l, r) - \frac{q+1}{2}))^2}}$
Description	The above formula calculates quadrant correlation coefficient between the ideal time series r (DD7) and the 3d+time dataset X (DD6). Note that assumptions A6 and A7 must hold while calculating this correlation.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R5

Number	IM5
Name	Best Index Model
Label	**Finding the Index of the Most Highly Correlated Ideal Time Series with the Dataset**
Input	$X : \mathbb{R}^{m\times n\times p\times q}$, $r_i : \mathbb{R}^q$
Output	$k : \mathbb{N}$ such that $r_k = \underset{\substack{r_i \\ i=1\cdots g}}{\text{argmax}} \mid \rho(X, r_i) \mid$
Description	The program gives an integer upon requesting the best index. argmax (DD18) returns the best ideal signal r_k (DD16) and index k is the best index (DD17).
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R6

Number	IM6
Name	Baseline Quantity
Label	**Calculating Baseline Quantity for fMRI Dataset**
Input	$X : \mathbb{R}^{m \times n \times p \times q}$, $r_i : \mathbb{R}^q$
Output	$Baseline = \sum_{i=1}^{c} \beta_i . avg(\text{base}_i) + \sum_{j=1}^{h} \gamma_j . avg(\phi_i) + \hat{\alpha}.\min(r_k)$
Description	The program returns a real number for the *Baseline* computed as mentioned in the output above. We assume that the polynomial baseline model is of order c ($pnum = c$ (DD12)) and we have h orthogonal time series (DD13). base_i indicates the baseline model (DD11) of degree i. $avg()$ function calculates the average value of its input over time. $\hat{\alpha}$ is the fit coefficient for the (best) ideal time series (DD16). min() function outputs the minimum value of the (best) ideal time series (DD7) over time. β and γ are defined in IM2.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	IM9, R7, R9

Number	IM7
Name	Average Quantity
Label	**Calculating Average Quantity for fMRI Dataset**
Input	$X : \mathbb{R}^{m \times n \times p \times q}$, $r_i : \mathbb{R}^q$
Output	$Average = \sum_{i=1}^{c} \beta_i.avg(\text{base}_i) + \sum_{j=1}^{h} \gamma_j.avg(\phi_i) + \hat{\alpha}.avg(r_k)$
Description	The program returns a real number for the *Average* computed based on the formula mentioned in the output. We assume that the polynomial baseline model is of order c ($pnum = c$ (DD12)) and we have h orthogonal time series (DD13). base_i indicates the baseline model (DD11) of degree i. $avg()$ function calculates the average value of its input over time. $\hat{\alpha}$ is the fit coefficient for the (best) ideal time series (DD16). β and γ are defined in IM2.
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	IM10, R8, R10

Number	IM8
Name	Topline Quantity
Label	**Calculating Topline Quantity for fMRI Dataset**
Input	$X : \mathbb{R}^{m \times n \times p \times q}$, $r_i : \mathbb{R}^q$
Output	$Topline = \sum_{i=1}^{c} \beta_i.avg(\text{base}_i) + \sum_{j=1}^{h} \gamma_j.avg(\phi_i) + \hat{\alpha}.\max(r_k)$
Description	The program returns a real number for the *Topline* computed based on the above formula. We assume that the polynomial baseline model is of order c ($pnum = c$ (DD12)) and we have h orthogonal time series (DD13). base_i indicates the baseline model (DD11) of degree i. $avg()$ function calculates the average value of its input over time. $\hat{\alpha}$ is the fit coefficient for the (best) ideal time series (DD16). max() function outputs the maximum value of the (best) ideal time series (DD16) over time. β and γ are defined in IM2.
Source	`http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf`
Ref. By	IM11, R11, R12

Number	IM9
Name	Baseline Percentage Change
Label	**Calculating Percentage Change in the fMRI Dataset Relative to Baseline**
Input	*Baseline* (IM6), $r_i : \mathbb{R}^q$
Output	$\%base = 100.\frac{\hat{\alpha}.pp(r_k)}{Baseline}$
Description	The formula calculates the percentage change in the fMRI dataset (DD6) due to the (best) ideal time series (DD7, DD16) relative to the *Baseline*(IM6) for each voxel. $\hat{\alpha}$ is the fit coefficient for the (best) ideal time series. $pp()$ is the peak to peak function (DD19) which calculates the variation of the (best) ideal time series as follows: $$pp(r_k) = \max_{j=1\cdots d}(r_{k_j}) - \min_{j=1\cdots d}(r_{k_j})$$
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R7

Number	IM10
Name	Average Percentage Change
Label	**Calculating Percentage Change in the fMRI Dataset Relative to Average**
Input	*Average* (IM7), $r_i : \mathbb{R}^q$
Output	$\%avg = 100.\frac{\hat{\alpha}.pp(r_k)}{Average}$
Description	The formula calculates the percentage change in the fMRI dataset (DD6) due to the (best) ideal time series (DD7, DD16) relative to the *Average* (IM7) for each voxel. $\hat{\alpha}$ is the fit coefficient for the (best) ideal time series. $pp()$ is the peak to peak function (DD19) which calculates the variation of the (best) ideal time series as follows: $$pp(r_k) = \max_{j=1 \cdots d}(r_{k_j}) - \min_{j=1 \cdots d}(r_{k_j})$$
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R8

Number	IM11
Name	Topline Percentage Change
Label	**Calculating Percentage Change in the fMRI Dataset Relative to Topline**
Input	$\mathit{Topline}$(IM8), $r_i : \mathbb{R}^q$
Output	$\%top = 100.\frac{\hat{\alpha}.pp(r_k)}{\mathit{Topline}}$
Description	The formula calculates the percentage change in the fMRI dataset (DD6) due to the (best) ideal time series (DD7, DD16) relative to the *Topline* (IM8) for each voxel. $\hat{\alpha}$ is the fit coefficient for the (best) ideal time series. $pp()$ is the peak to peak function (DD19) which calculates the variation of the (best) ideal time series as follows: $$pp(r_k) = \max_{j=1\cdots d}(r_{k_j}) - \min_{j=1\cdots d}(r_{k_j})$$
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R11

Number	IM12
Name	Standard Deviation of the Residuals
Label	**Calculating The Standard Deviation of the Residuals at Each Voxel Between the fMRI Dataset and Corresponding Data Estimation**
Input	$X : \mathbb{R}^{m\times n\times p\times q}$, $\phi_i : \mathbb{R}^q$, $r_i : \mathbb{R}^q$
Output	$\hat{\sigma}_{ijk} = \sqrt{\frac{\sum_{l=1}^{q}(X_{ijkl}-\hat{X}_{ijkl})^2}{q-n_b-n_o-n_i}}$
Description	Extending the theoretical model T8 to the fMRI dataset, we have: $$\hat{X}_{ijkl} = (M^T M)^{-1} M^T X_{ijkl}$$ Using theoretical models T5, T6 and T7 we can calculate thestandard deviation of the residuals: $$\hat{\sigma}_{ijk} = \sqrt{\frac{\sum_{l=1}^{q}(X_{ijkl}-\hat{X}_{ijkl})^2}{q - pnum - n_o - n_i}}$$ Where: $pnum$ is the polynomial degree (DD12), n_o is the number of orthogonal time series (DD13), and n_i depends on the number of ideal time series (DD7) such that: $$n_i = \begin{cases} 1 \text{ if we have 1 ideal time series} \\ 2 \text{ if we have more than one ideal time series} \end{cases}$$
Source	http://homepage.usask.ca/~ges125/fMRI/AFNIdoc/3dfim+.pdf
Ref. By	R13

4.2.5 Data Constraints

Data constraints on the input are as follows:

- Dimensions of reference signals (DD7) and orthogonal time series (DD13) should match.

Data constraints on the output are as follows:

- Correlation coefficients ρ (IM1),ρ_s (IM3),ρ_q (IM4) must lie between -1 and 1.

4.2.6 Properties of a Correct Solution

Whether we use Pearson, Spearman or quadratic correlation coefficient estimation, the value of the computed correlation coefficients should be between -1 and 1.

5 Requirements

This section provides functional and non-functional requirements for 3dfim+.

5.1 Functional Requirements

R1: Input the following functions, data and parameters:

symbol	description
X	fMRI data as a 3d+time dataset in NIfTI format (DD6)
$pnum$	degree of the polynomial in the baseline model (DD12)
ϕ	orthogonal time series function(s) (DD13)
r	reference time series function(s) (DD7)
p	threshold for voxels' intensity (DD14)
$cval$	comparing value for correlation coefficient screen display (DD15)

R2: Use the inputs in R1 to estimate the vector of unknown parameters β (IM2) at each voxel (from IM2).

R3: Calculate the Pearson correlation coefficient at each voxel between X and (best) r (from IM1).

R4: Calculate the Spearman correlation coefficient at each voxel between X and (best) r (from IM3).

R5: Calculate the quadrant correlation coefficient at each voxel between X and (best) r (from IM4).

R6: In case of having multiple ideal signals r, report the index number k (DD17) for the best ideal time series r_k (DD16) (from IM5).

R7: Calculate the percentage change in X due to the (best) ideal time series (DD7, DD16) relative to the *Baseline* (IM6) for each voxel (from IM9).

R8: Calculate the percentage change in X due to the (best) ideal time series (DD7, DD16) relative to the *Average* (IM7) for each voxel (from IM10).

R9: Calculate the fMRI dataset X *Baseline* quantity for each voxel (from IM6).

R10: Calculate the fMRI dataset X *Average* quantity for each voxel (from IM7).

R11: Calculate the percentage change in X due to the (best) ideal time series (DD7, DD16) relative to the *Topline* (IM8) for each voxel (from IM11).

R12: Calculate the fMRI dataset X *Topline* quantity for each voxel (IM8).

R13: Calculate the standard deviation of the residuals at each voxel between the fMRI dataset and corresponding data estimation (from IM12).

5.2 Non-functional Requirements

Considering the use of this program in the research, as well as keeping an eye on its future use in the clinical practice, the priority non-functional requirements are correctness, reliability, verifiability, understandability, reusability and maintainability.

6 Likely Changes

LC1: A4 - Although outliers can have deleterious effects on statistical analyses, some people prefer not to exclude them reasoning the outliers are parts of the dataset.

LC2: IM1 - There are other methods of calculating correlation coefficients such as Kendall rank correlation which is likely to be used instead of Pearson correlation. Input data assumptions might be different from method to method.

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