

3D Medical Image Processing Laboratory



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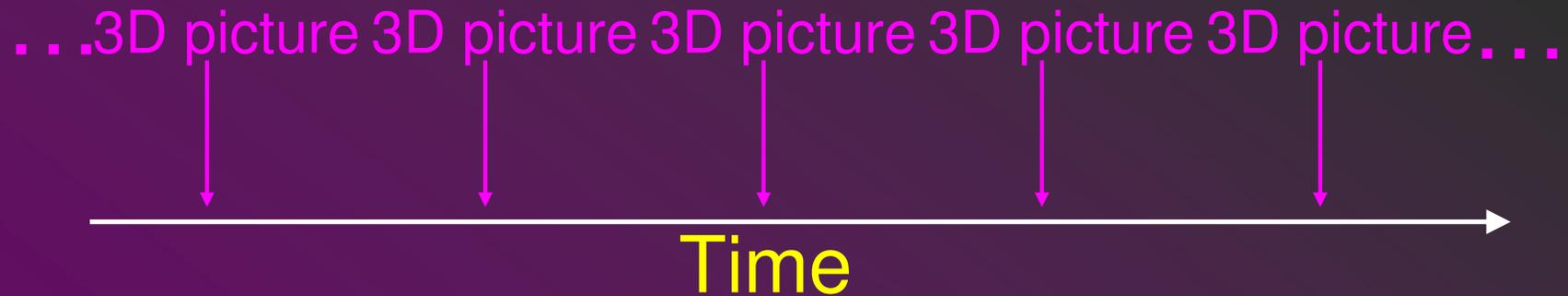
Factor Analysis in Nuclear Medicine

Goal of the Lecture

- **Familiarize**
- **Caution**
- **Interest**

Dynamic Imaging

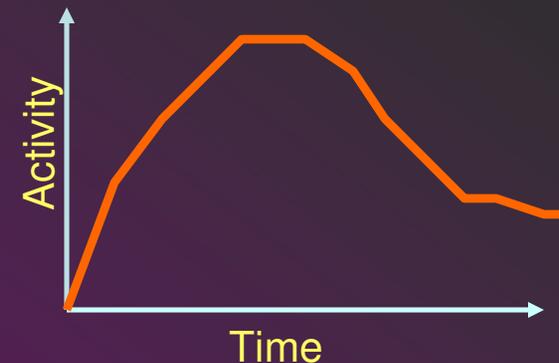
- 4 Dimensions



Terminology

Factor Analysis = Factor Analysis of Dynamic Structures (FADS)

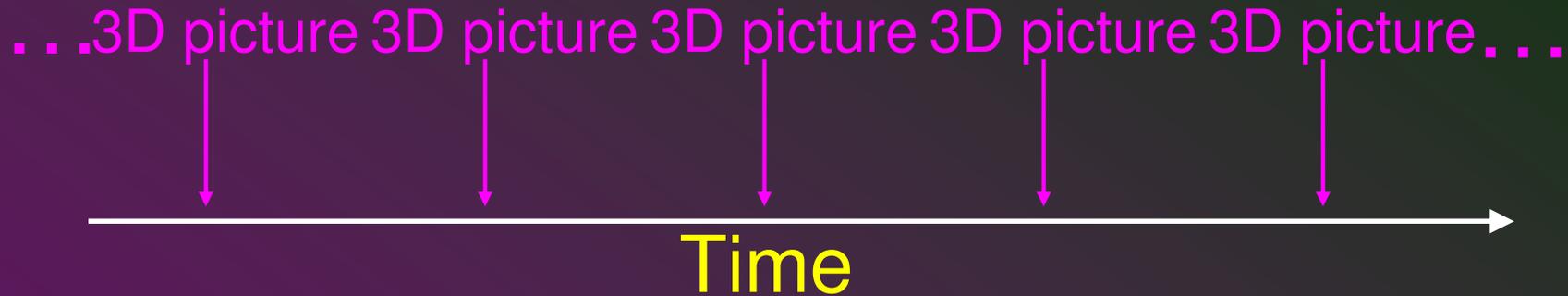
Time Activity Curve (TAC)



Factor Model of Dynamic Data

- Factor model assumes that in the image there are groups of pixels that have the same time behavior
- Examples of such groups: Liver, heart, heart defect *etc.*

Factor Analysis



↓ Factor analysis

1. Spatial definitions of groups with the same differential uptake (*e.g.* Liver, heart *etc.*)
2. TACs corresponding to these groups

Definitions

- Factor Analysis finds groups of pixels that have a similar time uptake, and also determines the corresponding TAC
- Number of groups is predetermined (usually up to 4)

A factor is the TAC that corresponds to a group

A factor coefficient image is a spatial definition of a group

Factor Analysis - Math

Image from
dynamic
sequence acquired
at time t

= Image of factor
coefficients for first
factor times value of
first factor for time t

+ Image of factor
coefficients for
second factor times
value of second factor
for time t + ...

$$\mathbf{I}(t) = \mathbf{C}_1 F_1(t) + \mathbf{C}_2 F_2(t) + \dots$$

$$\mathbf{I} = \mathbf{C} \mathbf{F}$$

Factor Analysis - Matrices

Dynamic sequence = Factor coefficients x Factor

$$N \begin{matrix} M \\ \mathbf{I} \end{matrix} = N \begin{matrix} K \\ \mathbf{C} \end{matrix} \mathbf{F} \begin{matrix} K \\ M \end{matrix}$$

N Number of pixels in each dynamic image (*e.g.* 128x128x30)

M Number of dynamic images (*e.g.* 100)

K Number of factors (*e.g.* 4)

Goal

$$\mathbf{I} = \mathbf{C} \mathbf{F}$$

The goal of performing FADS is to obtain matrix **C** and matrix **F** from matrix **I**

Reminder:

Matrix C corresponds to image of the organs with similar uptake (in cardiac imaging it could be heart tissue, left or right blood pool, liver...)

Matrix F corresponds to time behavior of those regions

Matrix I is the measured dynamic sequence

Non-Negativity

$$\mathbf{I} = \mathbf{C} \mathbf{F}$$

Elements of matrix **C** and matrix **F** have physiological interpretation, so they cannot be negative.

Reminder:

Matrix C corresponds to image of the organs with similar uptake (in cardiac imaging it could be heart tissue, left or right blood pool, liver...)

Matrix F corresponds to time behavior of those regions

Matrix I is the measured dynamic sequence

Question & Answer

$$\mathbf{I} = \mathbf{C} \mathbf{F}$$

Is it hard to get non-negative matrices C and F using above equation ? **Not really**

Reminder:

Matrix C corresponds to image of the organs with similar uptake (in cardiac imaging it could be heart tissue, left or right blood pool, liver...)

Matrix F corresponds to time behavior of those regions

Matrix I is the measured dynamic sequence

Simple Solution

$$\mathbf{I} = \mathbf{C} \mathbf{F}$$

Methods of solving of the above using principal component (PC) analysis

The method: do Singular Value Decomposition (SVD)

Correspondence

$$\text{FA} \quad \begin{matrix} & M \\ N & \mathbf{I} \end{matrix} = \begin{matrix} & K \\ N & \mathbf{C} \end{matrix} = \mathbf{F} \begin{matrix} & M \\ K & \mathbf{C} \end{matrix}$$

$$\text{SVD} \quad \begin{matrix} & M \\ N & \mathbf{I} \end{matrix} = \begin{matrix} & M \\ N & \mathbf{U} \end{matrix} \begin{matrix} & M \\ M & \mathbf{W} \end{matrix} \mathbf{V}^T \begin{matrix} & M \\ M & \mathbf{V} \end{matrix}$$

Correspondence II

SVD

$$\begin{matrix} & M \\ N & \mathbf{I} \end{matrix} = \begin{matrix} & M \\ N & \mathbf{U} \end{matrix} \begin{matrix} M \\ \mathbf{W} \end{matrix} \mathbf{V}^T \begin{matrix} & M \\ M & \mathbf{V} \end{matrix}$$

Only K singular values are non-zero if \mathbf{I} is described by factor model

$$\begin{matrix} & M \\ N & \mathbf{I} \end{matrix} = \begin{matrix} & K \\ N & \mathbf{U} \end{matrix} \mathbf{W} \mathbf{V}^T \begin{matrix} & M \\ K & \mathbf{V} \end{matrix}$$

“Exact” match

FA

$$\begin{matrix} & M \\ N & \mathbf{I} \end{matrix} = \begin{matrix} & K \\ N & \mathbf{C} \end{matrix} \begin{matrix} & & M \\ \mathbf{F} & \mathbf{K} & \mathbf{M} \end{matrix}$$

SVD

$$\begin{matrix} & M \\ N & \mathbf{I} \end{matrix} = \begin{matrix} & K \\ N & \mathbf{U} \end{matrix} \begin{matrix} & & M \\ \mathbf{W} & \mathbf{V}^T & \mathbf{K} & \mathbf{M} \end{matrix}$$

PCA

Performing SVD on dynamic data is called in the literature:

Principal Component Analysis
(PCA)

$$\mathbf{I} = \mathbf{U} \mathbf{w} \mathbf{V}^T$$

\mathbf{U} Defines *Principal Components*

FA - Exact Match - Revisited

FA

$$N \begin{matrix} M \\ \mathbf{I} \end{matrix} = N \begin{matrix} K \\ \mathbf{C} \end{matrix} \mathbf{F} \begin{matrix} M \\ K \end{matrix}$$

SVD

$$N \begin{matrix} M \\ \mathbf{I} \end{matrix} = N \begin{matrix} K \\ \mathbf{U} \end{matrix} \mathbf{w} \mathbf{V}^T \begin{matrix} M \\ K \end{matrix}$$

PCA [?] = FA

$$\mathbf{C} \neq \mathbf{U}$$

$$\mathbf{F} \neq \mathbf{w}\mathbf{V}^T$$

\mathbf{C} and \mathbf{F} non-negative, whereas both \mathbf{U}
and $\mathbf{w}\mathbf{V}^T$ have negative values

$$\tilde{\mathbf{V}} := \mathbf{w}\mathbf{V}^T$$

How to get FA solution from PCA

$$\text{SVD: } \mathbf{I} = \mathbf{U} \mathbf{\tilde{V}}$$



How ?

$$\mathbf{I} = \mathbf{C} \mathbf{F}$$

Oblique Rotation

$$1. \mathbf{I} = \mathbf{U} \tilde{\mathbf{V}}$$

$$2. \mathbf{I} = \mathbf{U} \mathbf{R} \mathbf{R}^{-1} \tilde{\mathbf{V}}$$

$$N \begin{array}{|c|} \hline M \\ \hline \mathbf{I} \\ \hline \end{array} = N \begin{array}{|c|} \hline K \\ \hline \mathbf{U} \mathbf{R} \square \square \mathbf{R}^{-1} \tilde{\mathbf{V}} \\ \hline \end{array} K \begin{array}{|c|} \hline M \\ \hline \end{array}$$

Rotation matrix:

$$\mathbf{R} = \begin{array}{|c|} \hline K \\ \hline \square K \\ \hline \end{array}$$

Methods of finding R

1. Apex Seeking

- Iterative algorithm (Di Paola et al 1980 *IEEE Trans. Nucl. Sci.*) is used in order to find R^{-1} , such that elements of $F = R^{-1}\tilde{V}$ the factors are non-negative.
- Factor coefficients C are found using:

$$C = (IF^T)(FF^T)^{-1}$$

Methods of finding \mathbf{R}

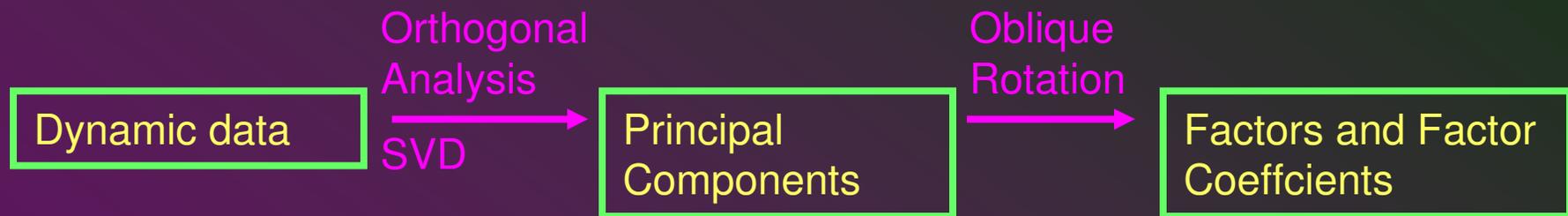
2. Minimization of the negativity

Minimizing of:
$$f(\mathbf{R}) = \sum_{i,k=1}^{N,K} H(C_{ik}) + \sum_{j,k}^{M,K} H(F_{kj})$$

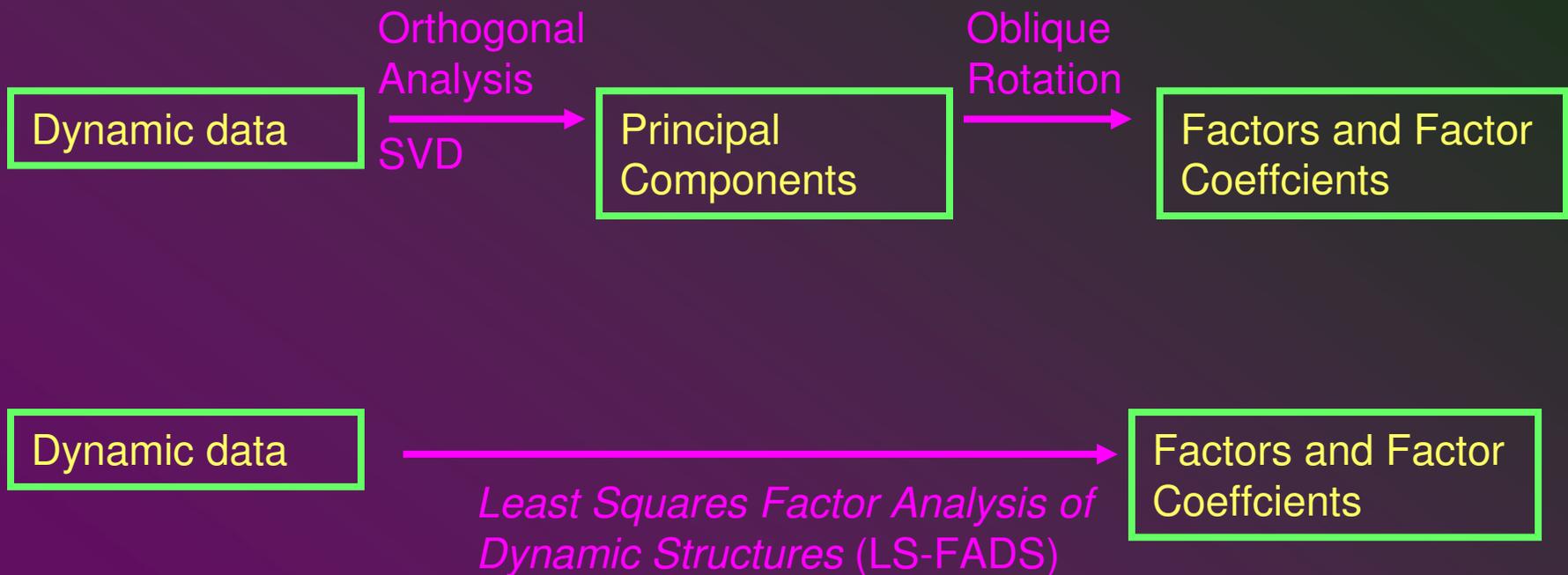
where: $\mathbf{C} = \mathbf{UR}$ and $\mathbf{F} = \mathbf{R}^{-1}\tilde{\mathbf{V}}$

$$H(x) = \begin{cases} 0 & \text{for } x \geq 0 \\ x^2 & \text{for } x < 0 \end{cases}$$

Factor Analysis



Least Squares Factor Analysis



Least Squares Factor Analysis

Least Squares method – minimize squared difference between the data and the model

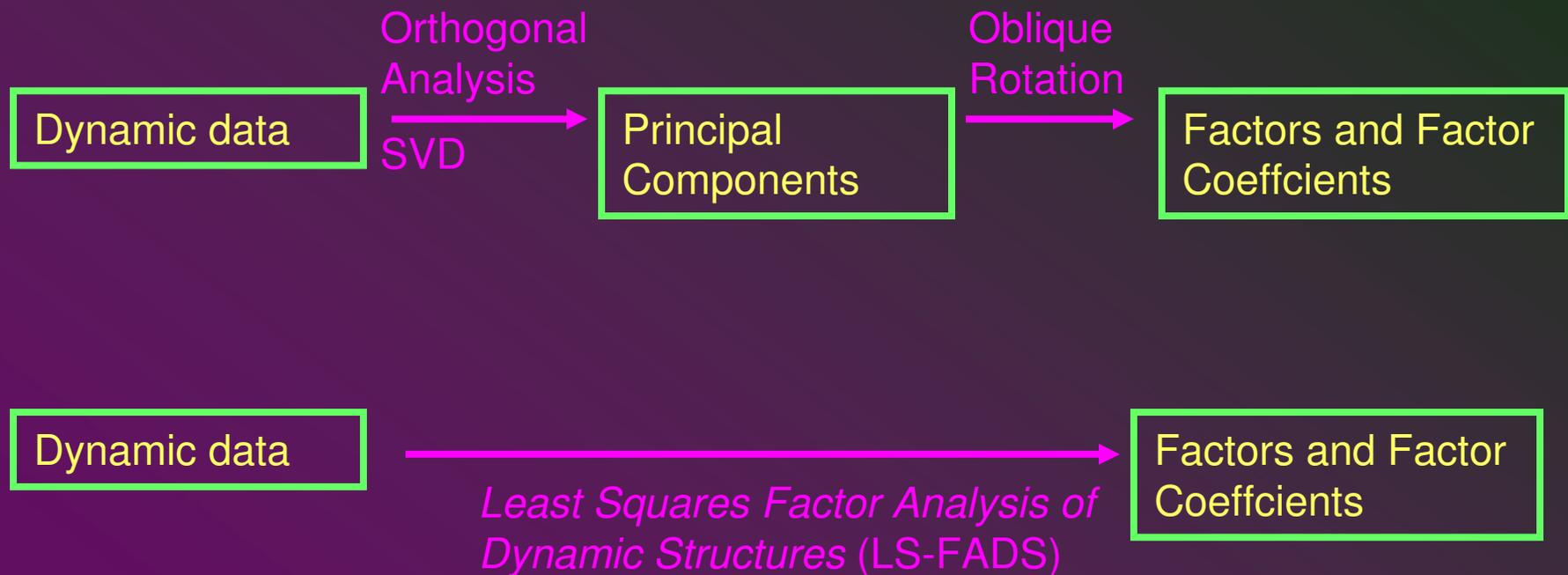
Least Squares Factor Analysis

$$f_{\text{LS}}(\mathbf{C}, \mathbf{F}) = \sum_{i,j=1}^{N,M} \left(\sum_{k=1}^K C_{ik} F_{kj} - I_{ij} \right)^2$$

The non-negativity is enforced by the following term —

$$f_{\text{nneg}}(\mathbf{C}, \mathbf{F}) = \sum_{i,k=1}^{N,K} H(C_{ik}) + \sum_{j,k=1}^{M,K} H(F_{kj})$$

Least Squares Factor Analysis



Non-Uniqueness

Non-uniqueness example

Demonstration of the non-uniqueness for 2 factor model. Matrices C_1, C_2, F_1, F_2 are non-negative

$$I = C_1 F_1 + C_2 F_2 \quad (1)$$

$$I = C_1 F_1 + C_2 F_2 + a C_1 F_2 - a C_1 F_2 \quad (2)$$

$$I = C_1 (F_1 - a F_2) + (C_2 + a C_1) F_2 \quad (3)$$

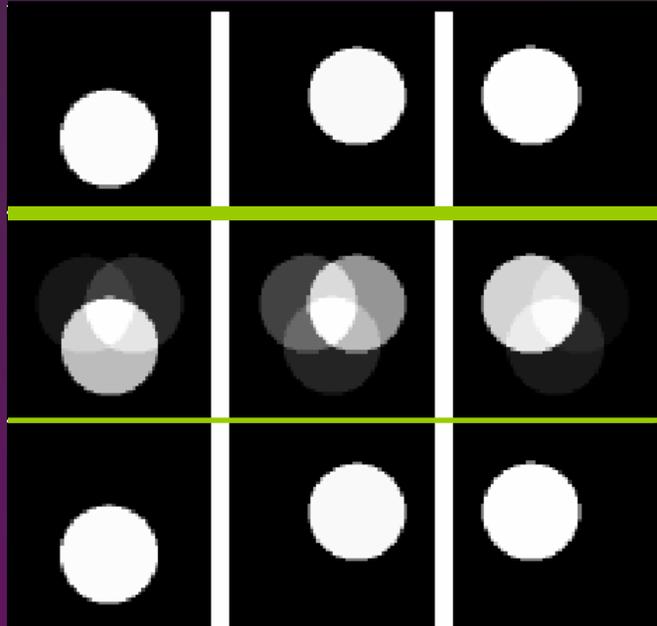
$$I = C_1 F'_1 + C'_2 F_2 \quad (4)$$

Matrices $C_1, C'_2 = C_2 + a C_1, F'_1 = F_1 - a F_2, F_2$ are equally good as long as non-negative

Caution

Factor analysis is not
quantitative technique if
non-uniqueness is not
addressed

FADS examples

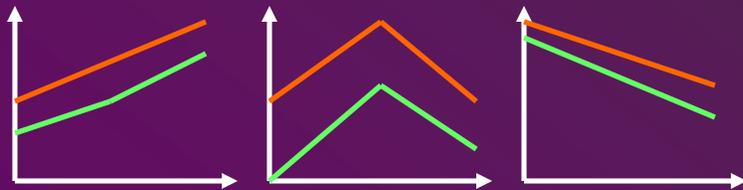


Original

LS-FADS

PLS-FADS

Computer
Simulation



LS-FADS

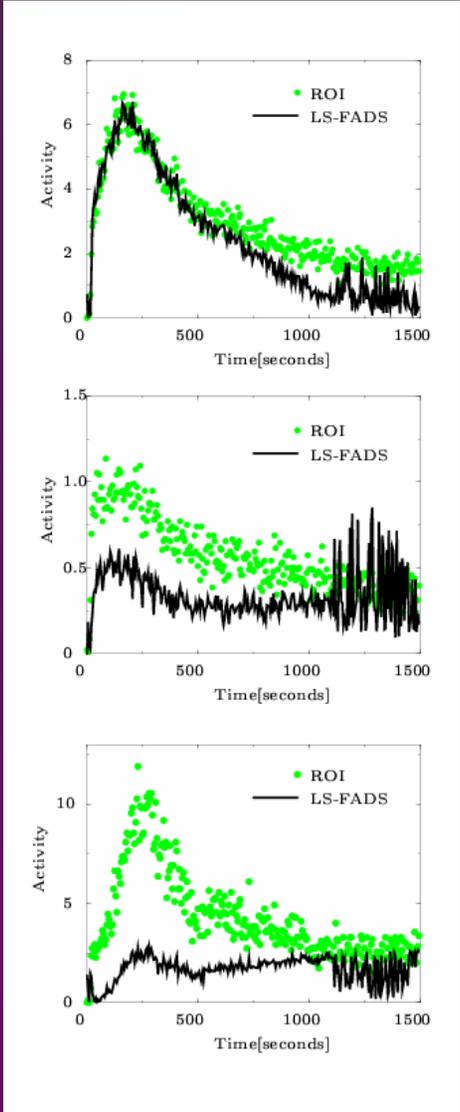
More Caution

**Factor analysis is not
qualitative technique if
non-uniqueness is not
addressed**

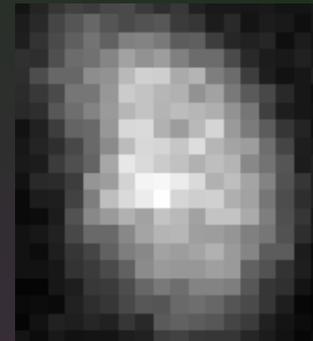
FADS example

Patient kidney $^{99m}\text{Tc-MAG3}$

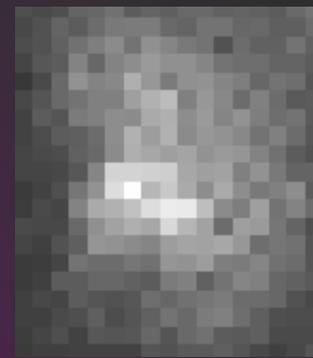
Factors



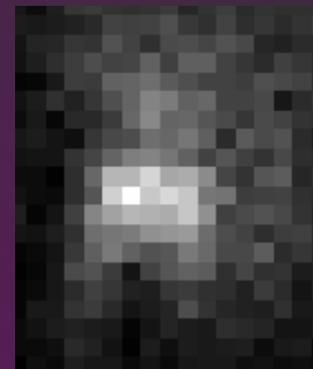
Cortex



Background

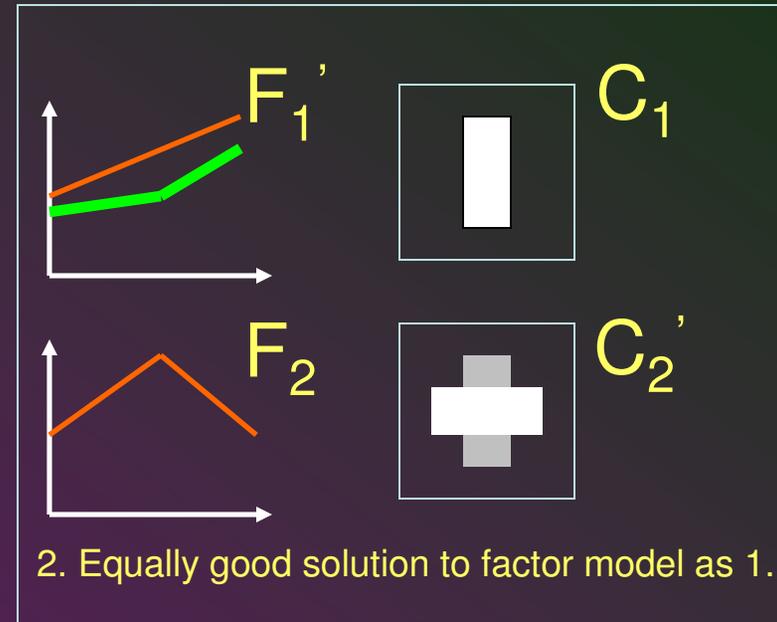
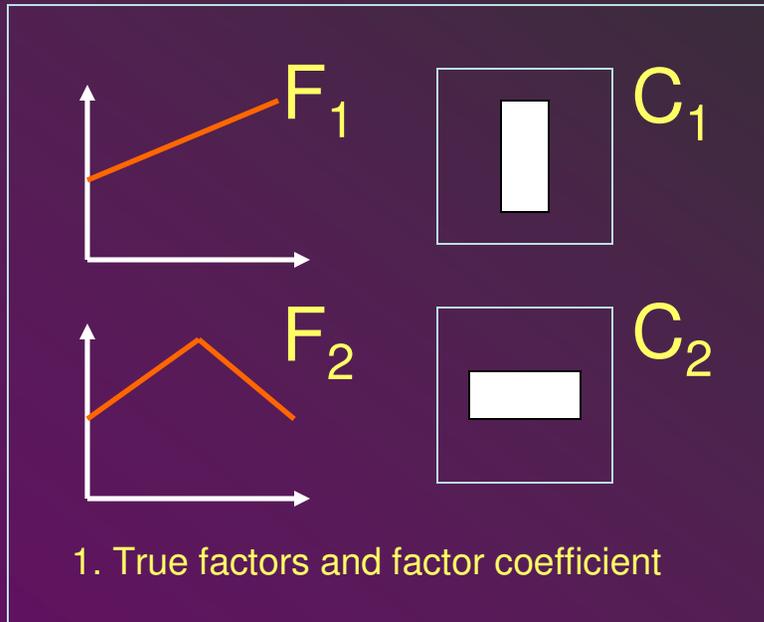


Ureter



Factor Coefficients

Non-uniqueness Manifestation



$$C_1, C_2,$$

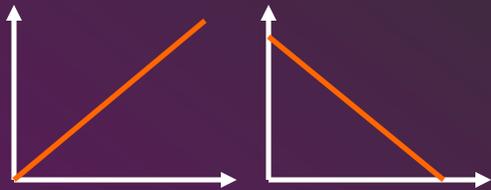
$$F_1, F_2$$

$$C_1, C'_2 = C_2 + aC_1,$$

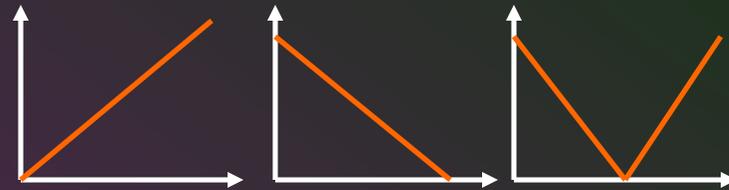
$$F'_1 = F_1 - aF_2, F_2$$

Interesting Conclusion

2-factor set



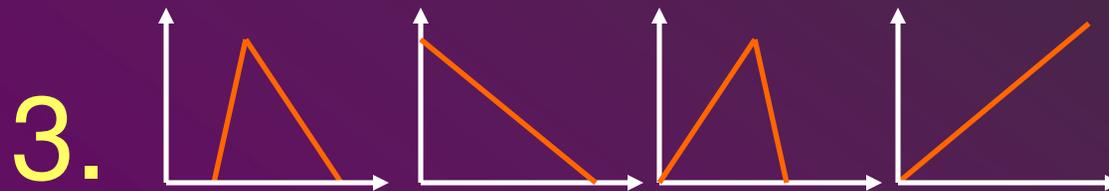
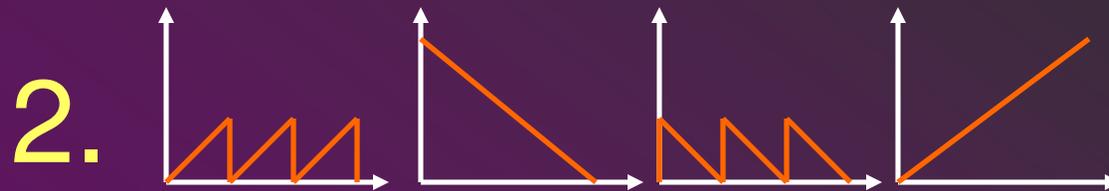
3 factor set



Since it is impossible to subtract any of these curves from any other without violating non-negativity, these factor sets give a unique solution to FADS if images of the factor coefficients do not completely overlap.

Quiz

Which of these will give unique solution ?



Non-Uniqueness Manifestation

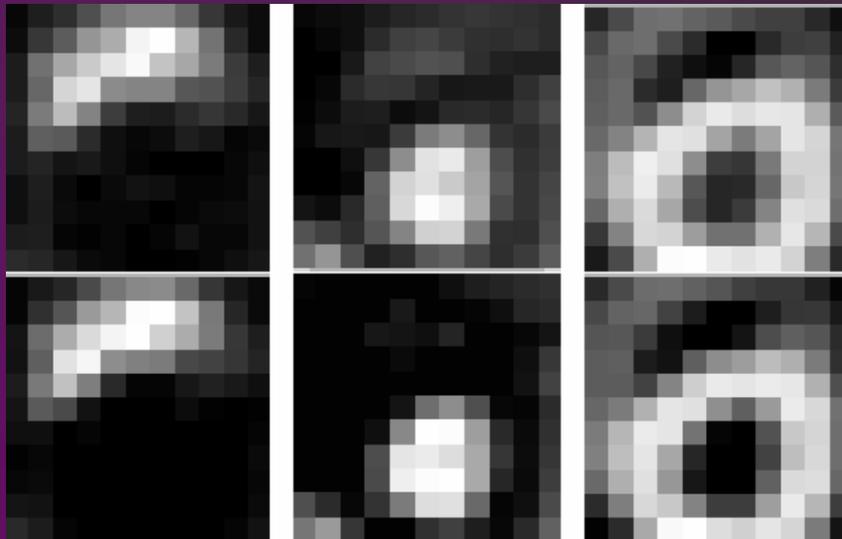
Cardiac canine

^{99m}Tc -Teboroxime

RV

LV

Tissue



LS-FADS

PLS-FADS (with non-uniqueness correction)

IMAGING PROTOCOL

FAST SPECT 179 image dynamic series. Images taken every 7 seconds at rest and stress

Non-Uniqueness Manifestation

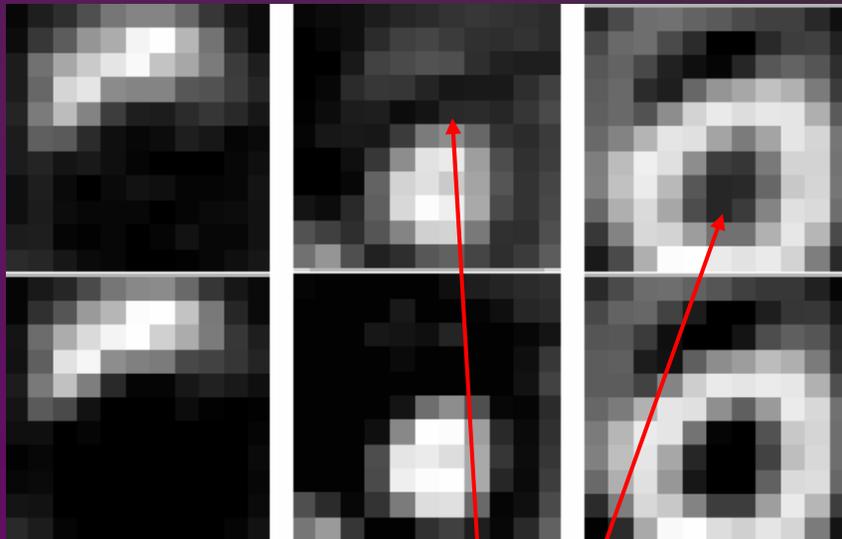
Cardiac canine

^{99m}Tc -Teboroxime

RV

LV

Tissue



LS-FADS

PLS-FADS (with non-uniqueness correction)

Decreased contrast

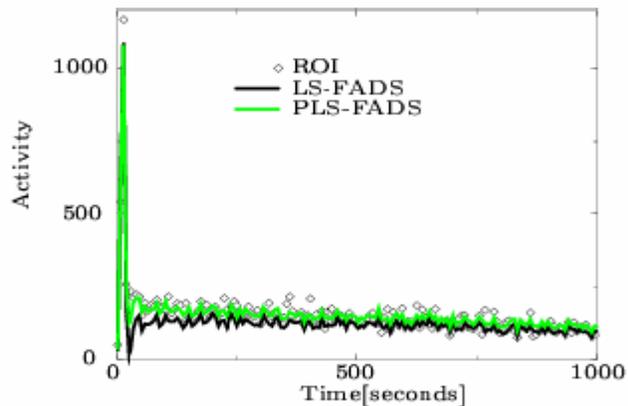
Non-Uniqueness Manifestation

RV

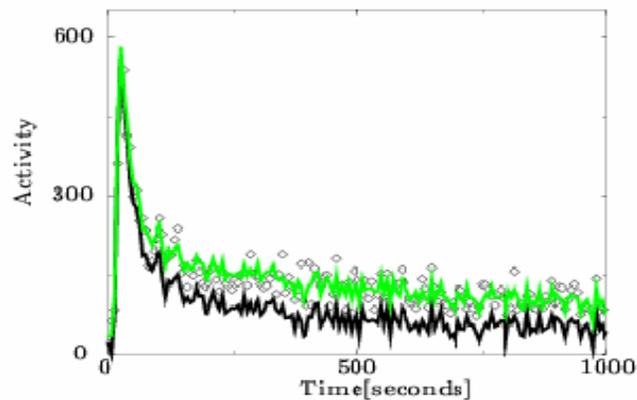
Cardiac canine

^{99m}Tc -Teboroxime

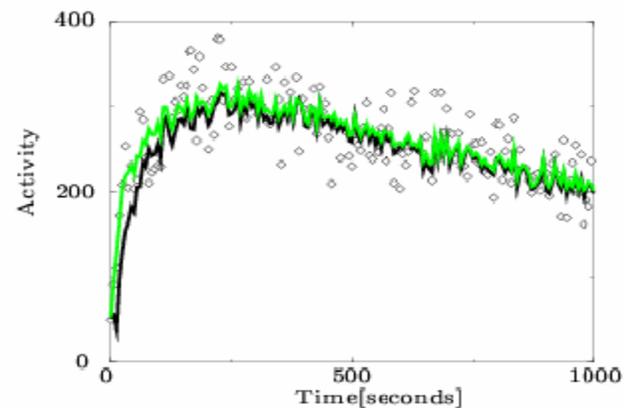
(A)



(B)



(C)



LV

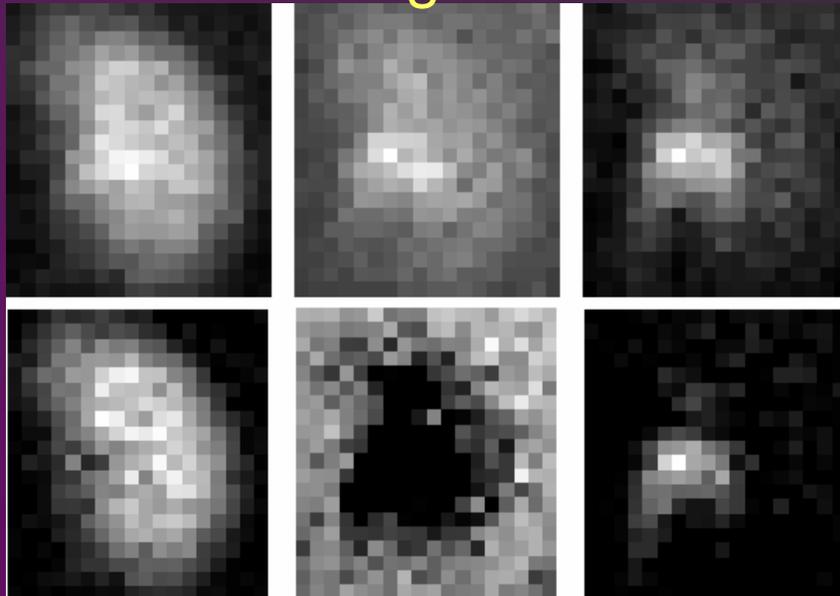
Tissue

Non-uniqueness

Kidney

^{99m}Tc -MAG3

Cortex Background Ureter



LS-FADS

PLS-FADS (with non-uniqueness correction)

IMAGING PROTOCOL

Planar - 300 image dynamic series.
Images taken every 5 seconds.

Non-uniqueness

LS-FADS PLS-FADS

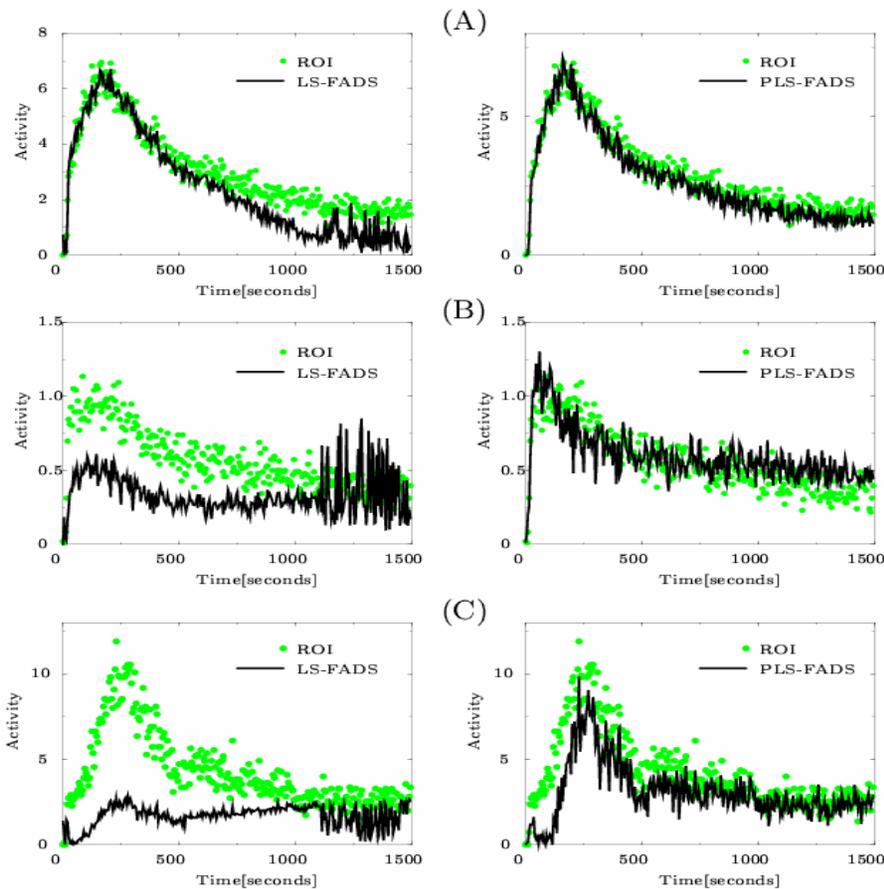
Patient kidney

^{99m}Tc -MAG3

Cortex

Background

Ureter



Examples of the FADS Applications

FADS examples

Patient cardiac

^{99m}Tc -Teboroxime

Summed

LV

RV

Tissue

Liver

Summed - Liver

IMAGING PROTOCOL

FAST SPECT - 90 image dynamic series. Images taken every 11 seconds in rest and stress

PLS-FADS

FADS examples

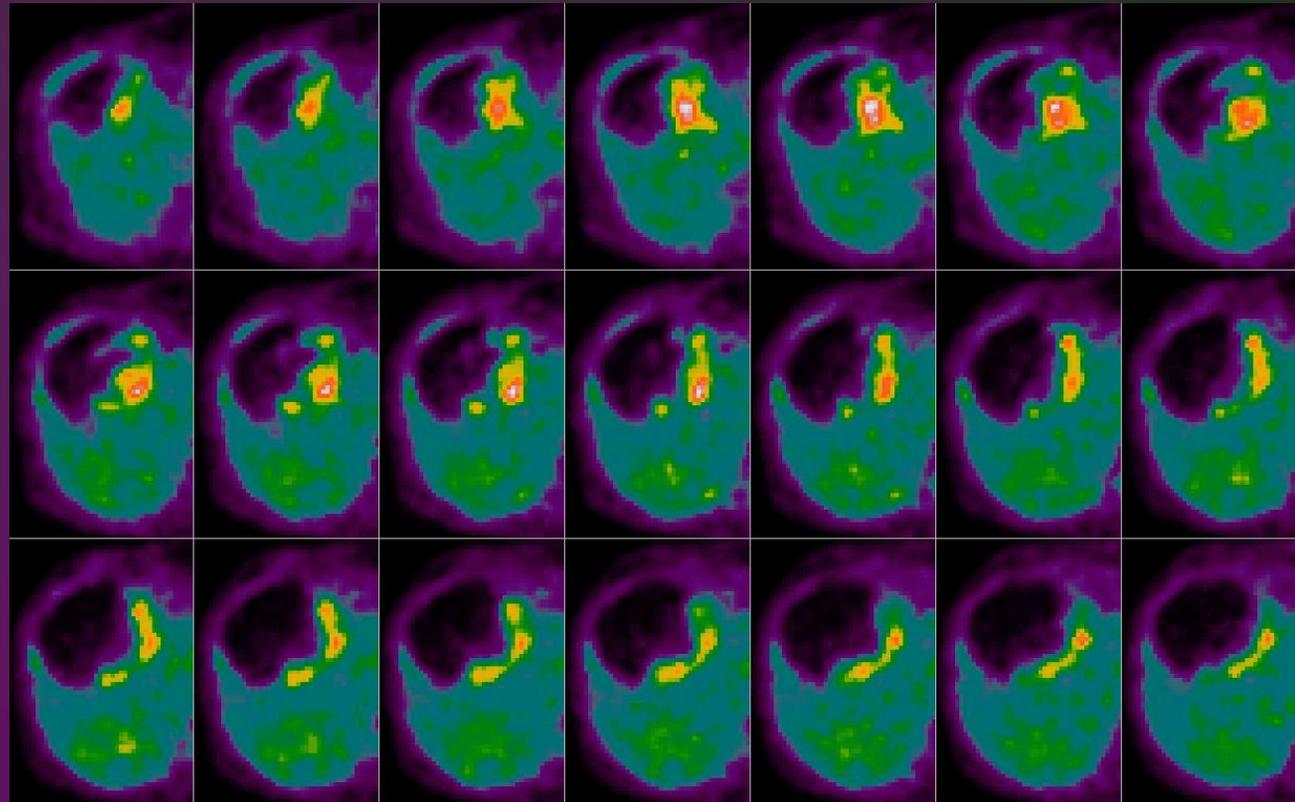
IMAGING PROTOCOL

PET - 30 image dynamic series
Images taken over variable
periods.

Patient liver

^{18}F -FDG

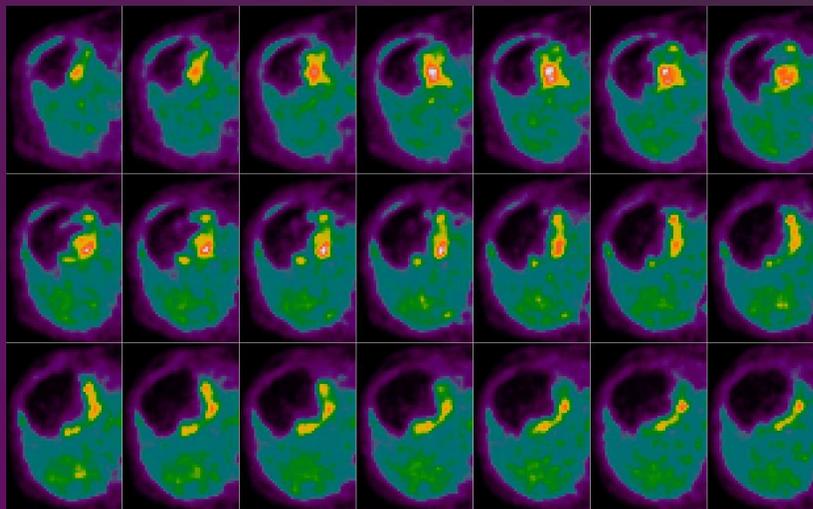
21 slices of
summed image
(right lobe of the
liver)



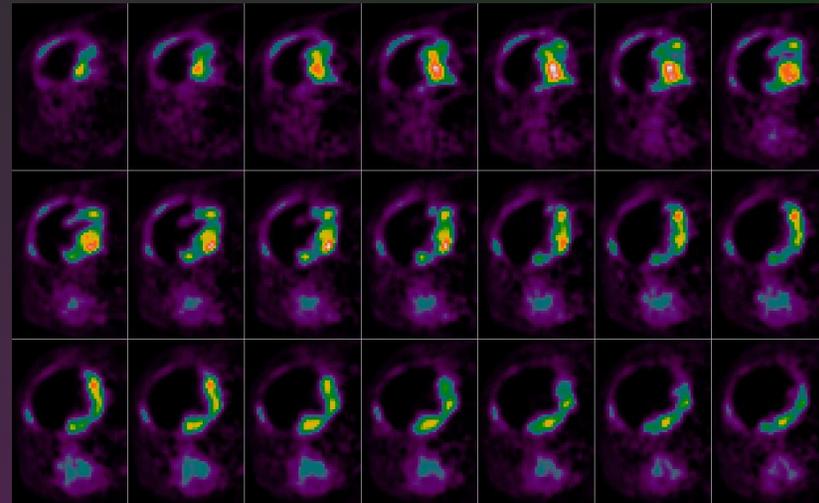
FADS examples

Patient liver ^{18}F -FDG

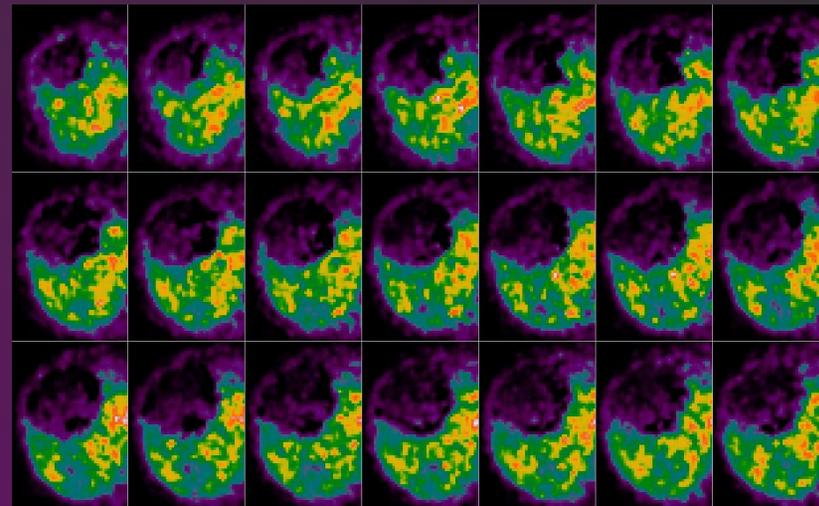
Summed



Tumor

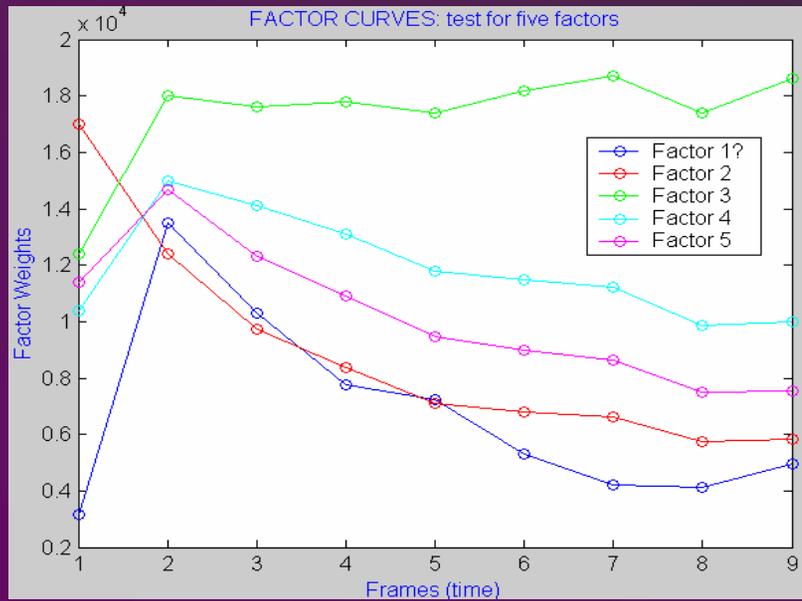
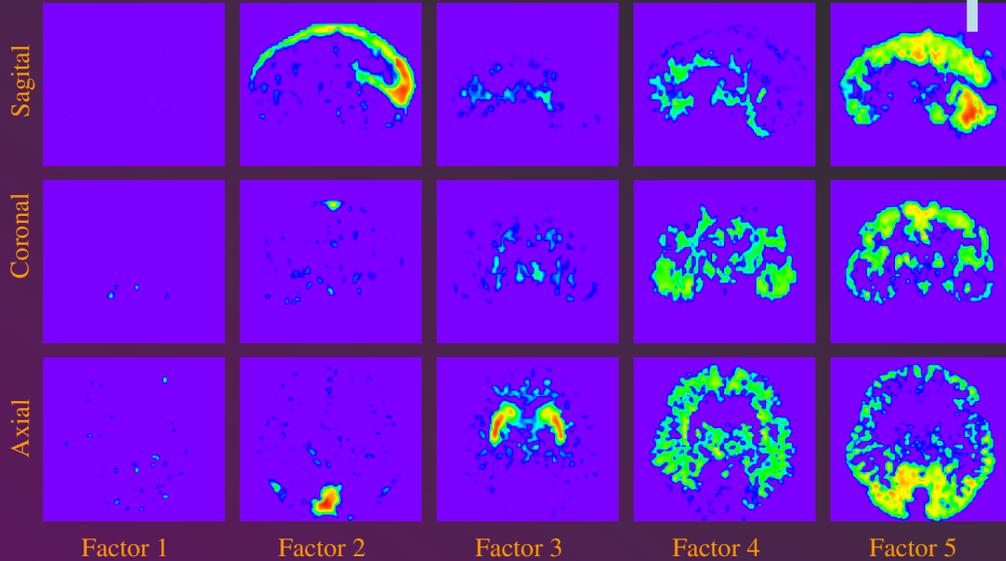


Normal tissue



FADS examples

Patient brain
fDOPA



Summary

- Excellent for image segmentation and separation of the overlapped regions
- Very good for extraction of TACs (better than ROI measurements)
- Semi-automatic...

“... and they are all this only if you know how to avoid their dangers”

taken from “My Life as a Nuclear Medicine Physicist”

Summary

- **HOWEVER**

“... and they are all this only if you know how to avoid their dangers”

taken from “My Life as a Nuclear Medicine Physicist”

Summary

- **Non-uniqueness has to be addressed**

“... and they are all this only if you know how to avoid their dangers”

taken from “My Life as a Nuclear Medicine Physicist”

Summary

- How to avoid the non-uniqueness dangers?

1. Sitek et al. *IEEE Trans. Med. Imag.* 2002 21 216-225
2. Sitek et al. *Phys. Med. Biol.* 2000 45 2619-2638
3. + non-uniqueness references cited there

References

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- Houston *Phys Med Biol* **29** 1109-1116 1984
- Nirjan et al *Phys Med Biol* **31** 1107-1117 1986
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- Sitek et al *IEEE Trans Nucl Sci* **46** 2227-2232 1999
- Sitek et al *IEEE Trans Med Imag* 2002 **21** 216-225
- Sitek et al *Phys Med Biol* 2000 **45** 2619-2638

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Thank you