

GENERALIZED FACTOR ANALYSIS OF MEDICAL IMAGE SERIES (FAMIS) FOR ACCURATE QUANTITATION

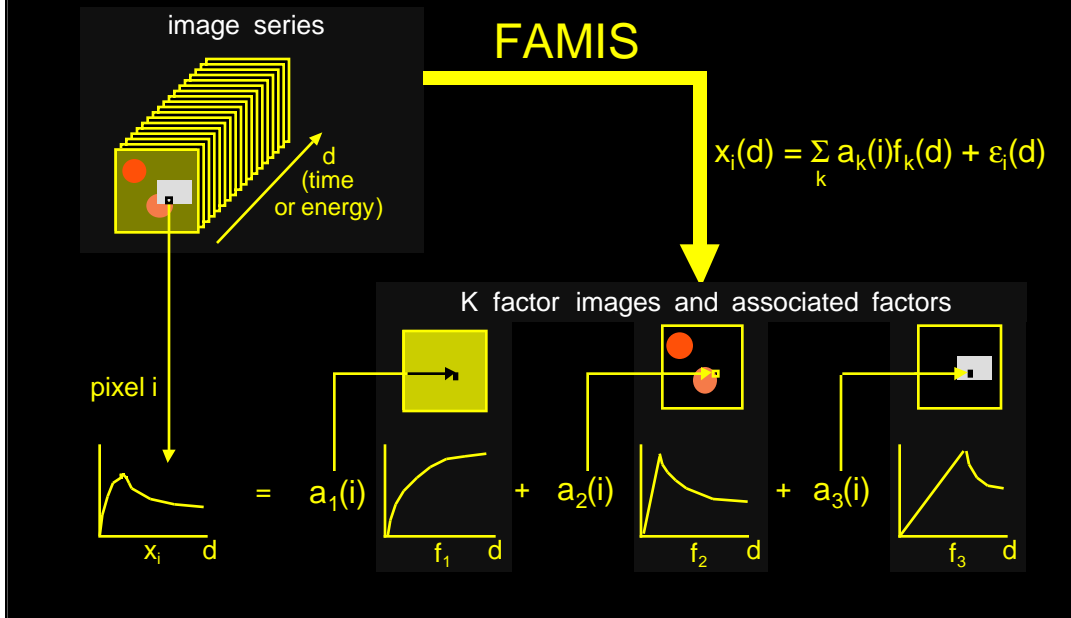
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Mister Chairmen, Ladies and Gentlemen,

Introduction: FAMIS model



Factor Analysis of Medical Image Sequences has been introduced in the eighties in Nuclear Medicine as a tool to summarize the relevant information underlying a dynamic or spectral image series by few images and associated curves, called factors.

Indeed, FAMIS decomposes an image series, which can be indexed by time or energy, into few factor images and associated curves, so that the curve associated to any pixel in the series can be expressed as a linear combination of these factors. The weight associated with each factor corresponds to the pixel intensity in the associated factor image, and each factor image therefore represents the spatial distribution of the signal following the associated curve.

This linear model can be written as follows, where x_i represents the curve associated with pixel i , a_k represents the weights associated to each curve and f_k represents the factor. As this linear model is always an approximation of real data, for instance because of noise, there is an error term in the model.

Although FAMIS is still used and studied in the medical imaging community, it has not gained wide acceptance yet for several reasons.

Purpose

Is FAMIS quantitative ?

- Which phenomena introduce biases in FAMIS ?
- How can these biases be reduced ?

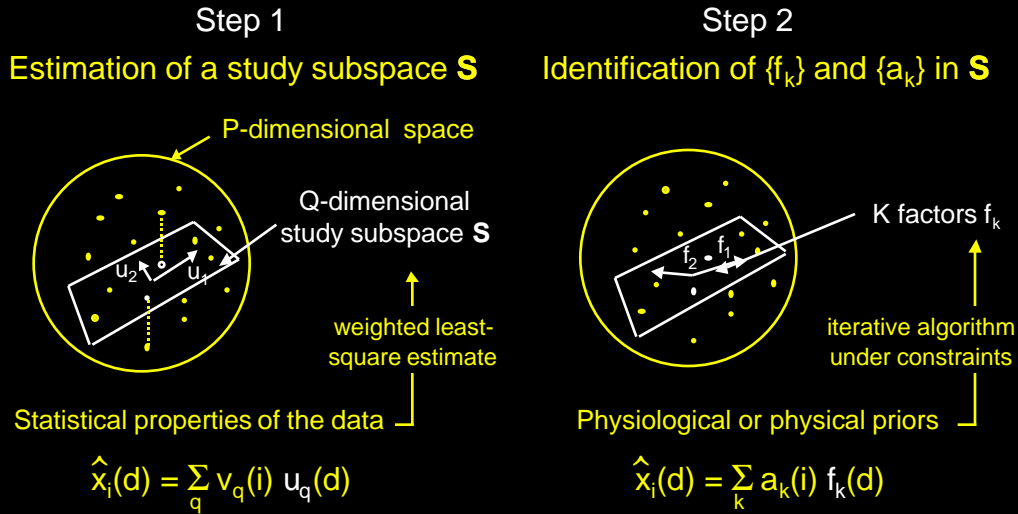
One of these reasons is that it is not well understood whether FAMIS is a quantitative approach.

In this talk, we will show which phenomena actually introduce quantitative biases in FAMIS.

We will then propose solutions to reduce these biases so that accurate quantitation can be achieved with FAMIS.

Theory: FAMIS solution

$$x_i(d) = \sum_k a_k(i) f_k(d) + \varepsilon_i(d)$$



To understand where quantitative biases can come from in FAMIS, let me briefly recall how FAMIS is solved. FAMIS includes two major steps:

- first, a study subspace is determined in which all relevant information is supposed to be represented.
- second, the factor and factor images are identified in this study subspace.

For the rest of the talk, it is important to well understand the notion of study subspace. When the original data is a series of P images, these data lie in a P-dimensional space. However, there is often a space of lower dimension Q in which all the relevant information underlying the original series is well represented. This is what we call the study subspace, represented by this plane here. This subspace is conventionally estimated in a weighted least square sense, so that it minimizes the mean square differences between the original data and the projection of the data on this space. The appropriate weights are chosen as a function of the statistical properties of the data.

In the study subspace, the relevant part of the data, written \hat{x} here, can be written as a linear combination of the orthogonal basis vectors u .

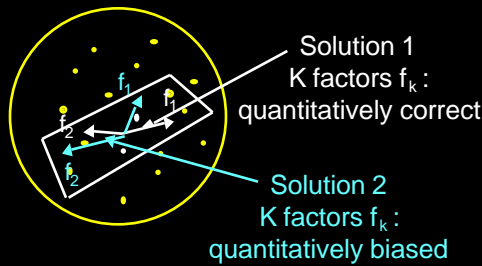
The second step of FAMIS consists in finding the K factors f that will have a physiological or physical interpretation in the subspace \mathbf{S} . To locate these factors, physiological or physical priors related to the factors and the associated images are used as constraints in an iterative procedure that minimizes the discrepancy between the model and the data. Once the factors f have been identified, a least square regression is used to estimate the corresponding a_k coefficients that give the factor images.

Theory: quantitative biases in FAMIS

$$x_i(d) = \sum_k a_k(i) f_k(d) + \varepsilon_i(d)$$

Insufficient priors

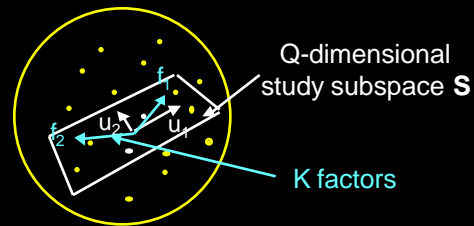
Several solutions satisfy the priors



➔ introduce more priors in FAMIS !

K = Q assumption

No solution in a K-dimensional subspace



Algorithmic advantage:

$$f_k(d) = \sum_q \beta_{kq} u_q(d)$$

↑
K x K matrix inversion

Now, what can introduce quantitative biases in FAMIS ?

One well known source of bias is that one does not have enough priors to use as constraints when solving FAMIS model. In that case, several solutions can satisfy the model, and the solution found by the algorithm might not be necessarily the physiologically or physically meaningful solution. The only way to reduce such biases is to introduce more priors in FAMIS model, so that there is a unique solution compatible with both the data and the priors.

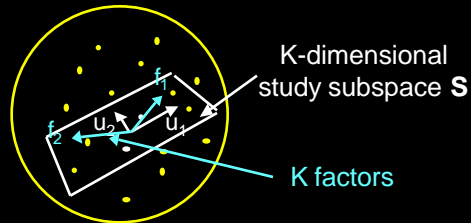
We recently found another potential source of bias in FAMIS. Indeed, FAMIS model always assumes that the dimension Q of the study subspace is identical to the number K of factors to be estimated. We will show in the following that in fact, there might be no solution in a study subspace of dimension K, and that the solution might be in a study subspace of dimension greater than K. The assumption K=Q has been introduced for algorithmic reasons. Indeed, FAMIS algorithm involves the inversion of the matrix representing the coordinates of the factors in the study subspace. If K=Q, this matrix is a square matrix which facilitates the inversion.

This assumption has never really been questioned to date, and we will show in the following that it can yield quantitative biases in FAMIS.

Theory: generalized FAMIS

$$x_i(d) = \sum_k a_k(i) f_k(d) + \varepsilon_i(d)$$

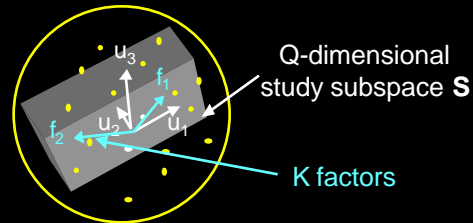
FAMIS: $K = Q$



$$f_k(d) = \sum_{k'} \beta_{kk'} u_{k'}(d)$$

Inversion of a square matrix $K \times K$

Generalized FAMIS: $K \leq Q$



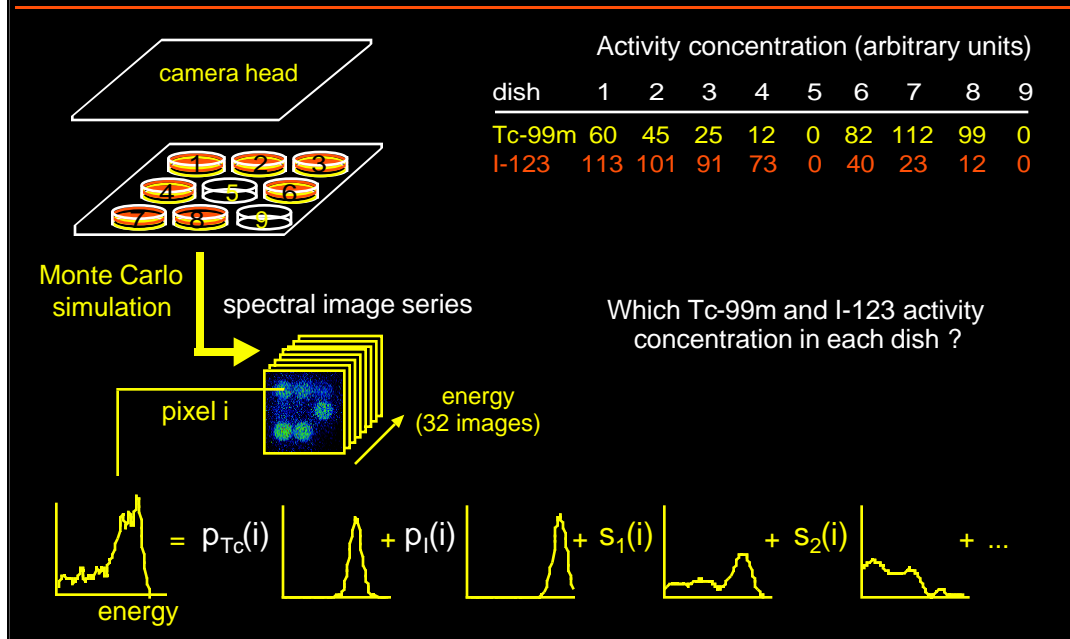
$$f_k(d) = \sum_q \beta_{kq} u_q(d)$$

Inversion of a rectangular matrix $K \times Q$

To show that it might be beneficial not to make this assumption, we had to find a way to change the algorithm so that it can be solved even if K is different from Q . What was needed was to replace the inversion of a square matrix by the inversion of a rectangular matrix, i.e. to use a generalized matrix inversion instead of a simple matrix inversion.

Solving FAMIS with this generalized matrix inversion is what we call generalized FAMIS solution. Generalized FAMIS makes it possible to estimate K factors in a Q -dimensional space with Q greater than K .

Example: a planar Tc-99m / I-123 dual-isotope study



Now, enough for the theory, let's go to an example that will demonstrate the insufficiency of a study space of dimension K .

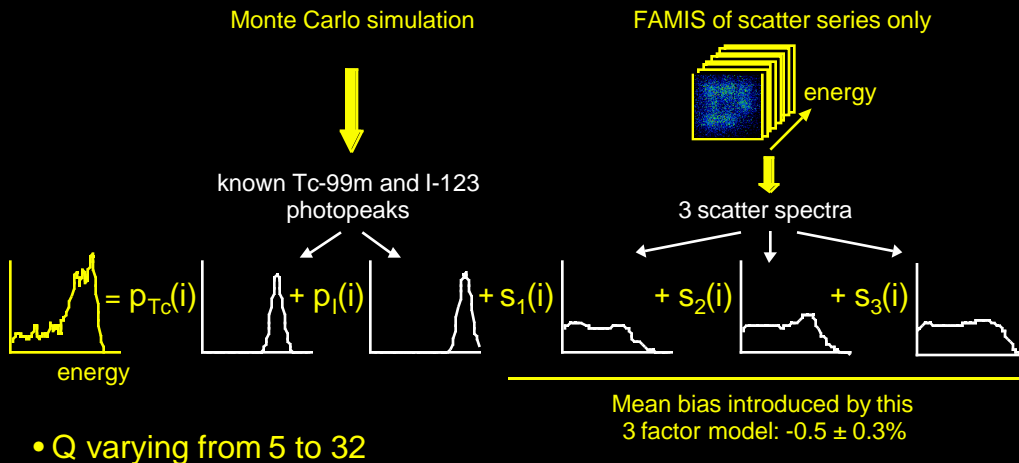
We used a Monte Carlo simulation of a dual-isotope Tc-99m / I-123 planar acquisition. The phantom consisted in 9 Petri dishes containing different mixtures of Tc-99m and I-123. The problem of quantitation here was to estimate the respective concentration of Tc-99m and I-123 in the different dishes.

The Monte Carlo simulation yielded a series of 32 spectral images, so that the energy spectrum of the photons detected in each pixel could be calculated. In this example, FAMIS model applies to the spectral image series and assumes that each energy spectrum can be written as a linear combination of a primary Tc-99m spectrum, a primary I-123 spectrum and several scatter spectra.

Solving FAMIS model will give us the number of photons following the primary Tc-99m and I-123 spectra in each pixel, from which one can deduce the Tc-99m and I-123 activity concentration in each dish.

Example: focussing on the study subspace dimension

- Estimation of 5 spectra, i.e., $K=5$
- Strong priors to remove biases caused by insufficient priors



Using these data, we performed several analyses.

In all cases, we estimated 5 factors, i.e. $K=5$.

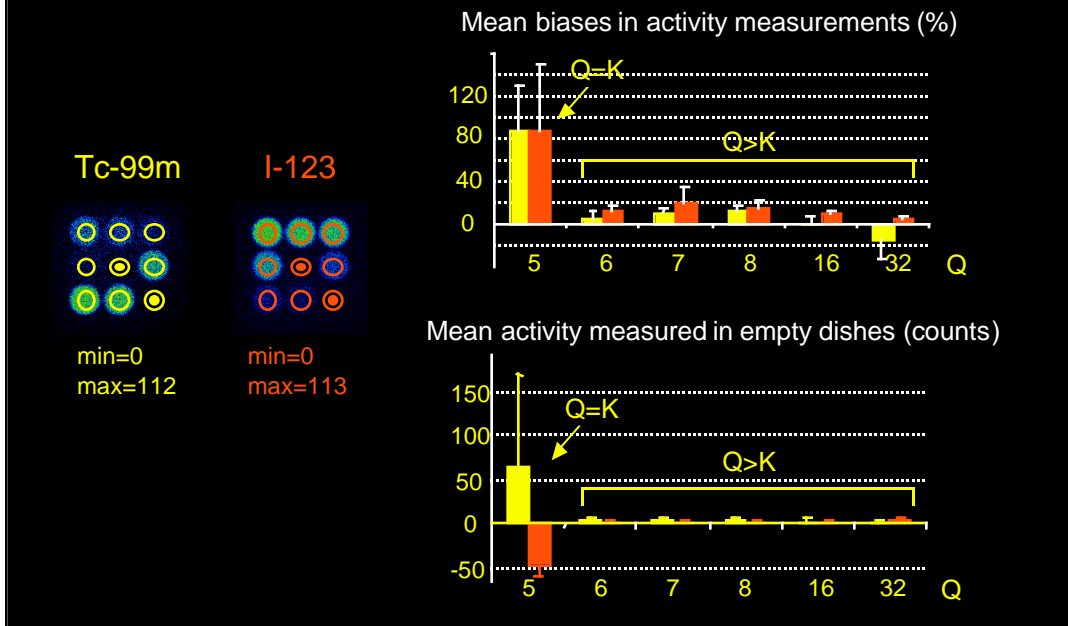
Remember that there might be 2 sources of biases in FAMIS: insufficient priors or $K=Q$. To make sure quantitative bias would not be introduced by insufficient priors, we used strong priors in the analysis, i.e. we assumed we had precise knowledge about the expected factors.

Indeed, as this was a Monte Carlo simulation, we knew perfectly the primary Tc-99m and I-123 spectra and used these as priors.

To determine which scatter spectra should be used, we analysed the spectral series corresponding to scatter photons only using a 3 factor analysis. This gave 3 scatter spectra that we used as priors when we analysed the whole series. We checked that the error made by decomposing scatter as a linear combination of these 3 spectra was less than 1%.

Using these 5 priors as constraints in FAMIS, we performed several FAMIS with different values of Q.

Example: biases in activity measurements



Here are the plots of the mean bias in activity measured in the primary Tc-99m and primary I-123 images estimated by FAMIS, as a function of the dimension Q of the study subspace. The mean bias was calculated on the dishes circled here, in yellow for the Tc-99m images and in orange for the I-123 image. One can see that quantitation was largely biased for $Q=K=5$. In this example, increasing the subspace dimension by just 1, i.e. $Q=6$, improved quantitation a lot. As soon as the study subspace was large enough to satisfy the priors, the quantitative bias did not change much.

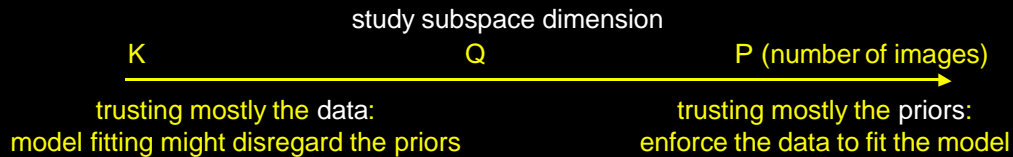
Here are the numbers of counts measured in the Tc-99m and I-123 factor images in regions in which there were a priori no counts, shown here. Again, one can see that quantitation in these regions was wrong with $Q=K$, and became correct from $Q=6$. Again, quantitative accuracy did not change much with the dimension Q .

Discussion

- Conventional FAMIS: K factors \rightarrow study subspace dimension $Q = K$
Not always true: sometimes $Q > K$
- How to know ?
Check whether priors are satisfied

prior	mean value in negative pixels		
	$K=Q=5$	$K=5, Q=6$	$K=5, Q=16$
0	-123	-17	-13

- Trade-off



So in summary, conventional FAMIS always assumes that the number of factors to be estimated is identical to the dimension of the study subspace. We found that this hypothesis was not always correct and that one could need a study subspace of dimension greater than K to estimate K factors.

An important point is how can we know in advance the appropriate dimension of the study subspace?

From our experience, it appears that if the priors are not properly verified in a Q -dimensional subspace, it often indicates that this subspace is not large enough, and Q should be increased until the priors are properly satisfied. When the priors are satisfied, this usually indicates that the study subspace is appropriate and will not be a source of bias in the analysis. For instance, in our previous example in which we should not observe any negative values in the primary images, we found that the average values in negative pixels was -123 with $Q=5$, and then decreased to -17 with $Q=6$, and remained stable for larger values of Q .

Another rule of thumb is that the choice of Q is a trade-off between the confidence associated with the model, i.e. the priors, and the confidence associated with the data. The lower Q , the more you trust the data and get a solution that will fit the data well but might disregard the priors, the greater Q , the more you trust the priors and get a solution that enforces the data to fit the priors.

Conclusion

Priors poorly met in FAMIS ?
Quantitative bias in FAMIS ?

1. Question the validity of your priors and of your data
2. If you trust both your priors and your data, make $Q > K$!

So in conclusion, when using FAMIS, do not take the assumption $K=Q$ for granted anymore. If you find that your priors about the data are poorly met or that you get large quantitative bias:

- first, question the validity of your priors and the validity of your data.
- second, if you trust your priors well enough, increase the dimension of the study subspace so that you can get a better match between the FAMIS solution and your priors. This should contribute to reduce the quantitative biases you may have observed when using FAMIS.

Thank you for your attention.