



HAL
open science

Appendix Alzheimer's Disease Modelling and Staging through Independent Gaussian Process Analysis of Spatio-Temporal Brain Changes

Clement Abi Nader, Nicholas Ayache, Philippe Robert, Marco Lorenzi

► **To cite this version:**

Clement Abi Nader, Nicholas Ayache, Philippe Robert, Marco Lorenzi. Appendix Alzheimer's Disease Modelling and Staging through Independent Gaussian Process Analysis of Spatio-Temporal Brain Changes. 2018. hal-01849180

HAL Id: hal-01849180

<https://hal.science/hal-01849180v1>

Submitted on 26 Jul 2018

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Appendix

Alzheimer's Disease Modelling and Staging through Independent Gaussian Process Analysis of Spatio-Temporal Brain Changes

Clement Abi Nader¹, Nicholas Ayache¹, Philippe Robert^{2,3}, and Marco Lorenzi¹

¹ *UCA, Inria Sophia Antipolis, Epione Research Project*

² *UCA, CoBTeK*

³ *Centre Memoire, CHU de Nice*

A. Lower bound derivation

In this section we detail the derivation of the lower bound :

$$\begin{aligned} \log(p(Y, C|\sigma, \lambda)) &= \log\left[\int_A \int_S \int_{S'} p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S, S'|\lambda)dAdSdS'\right] \\ &= \log\left[\int_A \int_S \int_{S'} p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S'|S, \lambda)p(S)dAdSdS'\right] \end{aligned} \quad (1)$$

If we know S this completely determines S', thus we have $\int p(S'|S, \lambda)dS' = 1$ which gives us :

$$\begin{aligned} \log(p(Y, C|\sigma, \lambda)) &= \log\left[\int_A \int_S p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S)dAdS\right] \\ &= \log\left[\int_A \int_S p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S) \frac{q_1(A)q_2(S)}{q_1(A)q_2(S)} dAdS\right] \\ &= \log\left[\mathbb{E}_{A \sim q_1, S \sim q_2} \left[\frac{p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S)}{q_1(A)q_2(S)}\right]\right] \\ &\geq \mathbb{E}_{A \sim q_1, S \sim q_2} \left[\log\left[\frac{p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S)}{q_1(A)q_2(S)}\right]\right] \end{aligned} \quad (2)$$

This is obtained thanks to Jensen's inequality. Finally this leads us to :

$$\begin{aligned} \mathbb{E}_{A \sim q_1, S \sim q_2} \left[\log\left[\frac{p(Y|A, S, \sigma)p(C|S', \lambda)p(A)p(S)}{q_1(A)q_2(S)}\right]\right] &= \mathbb{E}_{A \sim q_1, S \sim q_2} [\log[p(Y|A, S, \sigma)]] \\ &\quad + \mathbb{E}_{S \sim q_2} [\log(P(C|S', \lambda))] \\ &\quad - \mathcal{D}[q_1(A|Y)||p(A)] \\ &\quad - \mathcal{D}[q_2(S|Y)||p(S)] \end{aligned} \quad (3)$$

Independent Gaussian Process Analysis

In the Method section we introduced the approximation $q_1(A) = \prod_{n=1}^{Ns} \mathcal{N}(\mu_n, \Sigma(\alpha, \beta))$.

The covariance matrix is shared by all the spatial processes which gives us the set of spatial parameters :

$$\psi = \{\mu_n, n \in [1, Ns], \alpha, \beta\} \quad (4)$$

Following [5] we introduce for each GP two vectors, Ω_n with a prior $p(\Omega_n) = \mathcal{N}(0, \frac{1}{l_n}I)$ for each element and W_n with a prior $p(W_n) = \mathcal{N}(0, I)$, such that $S_n(t) = \Phi(t\Omega_n)W_n$. Where Φ is chosen to obtain a RBF kernel as explained in [5]. We define the approximated distributions $q_3(W_n) = \prod_j \mathcal{N}(m_{n,j}, s_{n,j}^2)$ and $q_4(\Omega_n) = \prod_j \mathcal{N}(\alpha_{n,j}, \beta_{n,j}^2)$ of $p(W_n)$ and $p(\Omega_n)$. Using these approximations and following [5], we can derive a lower bound for S with the same technique than above. We have the set of temporal parameters :

$$\theta = \{m_n, s_n, \alpha_n, \beta_n, l_n, n \in [1, Ns]\} \quad (5)$$

Now we can obtain every term of (3). The Kullback-Leibler of a multivariate Gaussian has a closed-form :

$$\mathcal{D}[q_1(A|X)||p(A)] = \frac{1}{2} \sum_{n=1}^{Ns} Tr(\Sigma) + \mu_n^T \mu_n - F - \log[det(\Sigma)] \quad (6)$$

Using the factorized form of q_2 and the fact that the different Gaussian processes are independent from each other we can write :

$$\mathcal{D}[q_2(S|X)||p(S)] = \sum_{n=1}^{Ns} \mathcal{D}[q_3(W_n)|p(W_n)] + \mathcal{D}[q_4(\Omega_n)|p(\Omega_n)] \quad (7)$$

Since the approximations q_3 and q_4 and their respective priors are normally distributed we have an analytic formula for both Kullback-Leibler divergences.

$$\mathcal{D}[q_3(W_n)|p(W_n)] = \frac{1}{2} \sum_j s_{n,j}^2 + \mu_{n,j}^2 - 1 - \log(s_{n,j}^2) \quad (8)$$

$$\mathcal{D}[q_4(\Omega_n)|p(\Omega_n)] = \frac{1}{2} \sum_j \beta_{n,j}^2 l_n + \alpha_{n,j}^2 l_n - 1 - \log(\beta_{n,j}^2 l_n) \quad (9)$$

As in [10] we employ the reparameterization trick to have an efficient way of sampling the expectations of (3). Thus we have :

$$\begin{aligned} - W_{n,j} &= m_{n,j} + s_{n,j} * \epsilon_{n,j} \\ - \Omega_{n,j} &= \alpha_{n,j} + \beta_{n,j} * \zeta_{n,j} \\ - A_n &= \mu_n + \Sigma_n^{\frac{1}{2}} * \kappa_n \end{aligned}$$

Which gives us :

$$\mathbb{E}_{A \sim q_1, S \sim q_2}[\log(p(Y|A, S, \sigma))] = \mathbb{E}_{\epsilon, \zeta, \kappa}[\log(p(Y|m, s, \alpha, \beta, \mu, \Sigma, \sigma))] \quad (10)$$

$$\mathbb{E}_{S \sim q_2}[\log(p(C|S', \lambda))] = \mathbb{E}_{\epsilon, \zeta}[\log(p(C|m, s, \alpha, \beta, \lambda))] \quad (11)$$

Where $\epsilon_{n,j} \sim \mathcal{N}(0, 1)$, $\zeta_{n,j} \sim \mathcal{N}(0, 1)$ and $\kappa_n \sim \mathcal{N}(0, I)$.

B. Kronecker factorization

Here we detail how to split the covariance matrix in a Kronecker product of three matrices along each spatial dimensions. We have :

$$\Sigma_{i,j}(\alpha, \beta) = \alpha \exp\left(-\frac{\|u_i - u_j\|^2}{2\beta}\right) \quad (12)$$

We can use the separability properties of the exponential to decompose the covariance between two locations $u_i = (x_i, y_i, z_i)$ and $u_j = (x_j, y_j, z_j)$:

$$\Sigma_{i,j}(\alpha, \beta) = \alpha \exp\left(-\frac{(x_i - x_j)^2}{2\beta}\right) \exp\left(-\frac{(y_i - y_j)^2}{2\beta}\right) \exp\left(-\frac{(z_i - z_j)^2}{2\beta}\right) \quad (13)$$

So Σ can be decomposed into the Kronecker product of 1D processes :

$$\Sigma = \Sigma_x \otimes \Sigma_y \otimes \Sigma_z \quad (14)$$

Allowing us to deal with large-size matrices.

C. Comparison with ICA

We performed a comparison of our algorithm with ICA on a similar example than in 3.1. However the data was generated in a simplified setting since ICA can't be applied when the time associated to each image is unknown. To do so we assigned the ground truth parameter t_p beforehand. The goal was to compare the separation performances of both our algorithm and ICA, on data generated with three latent spatio-temporal processes. In Figure 1 we observe that the sources estimated by ICA are more noisy and uncertain than the ones estimated by our method, highlighting the performances of our algorithm in terms of sources separation.

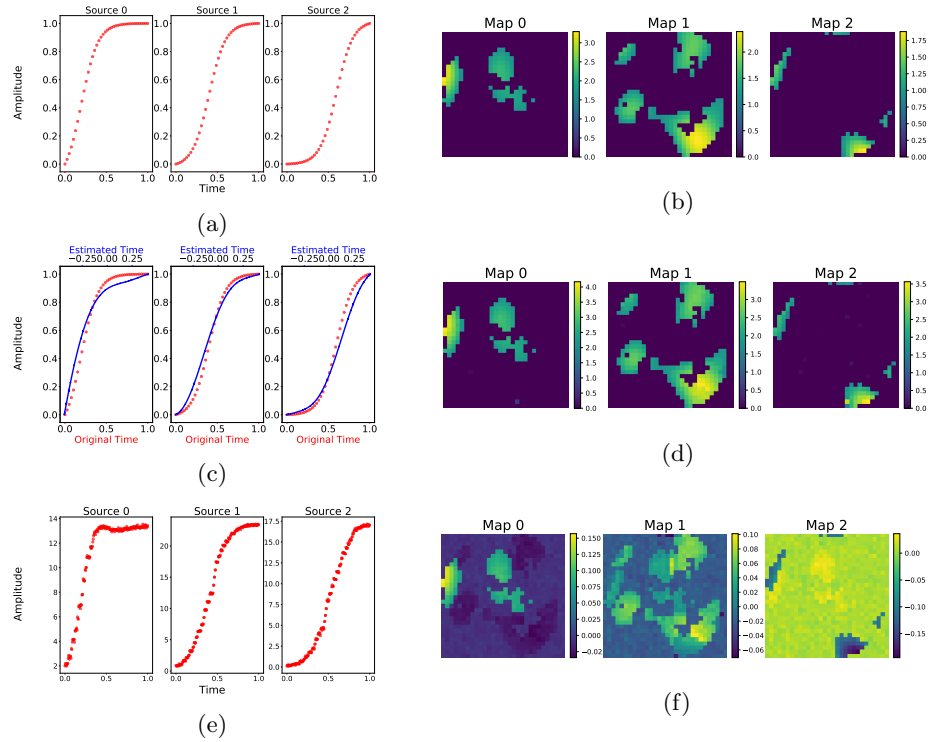


Fig. 1: First Row : Raw sources. Second Row : Sources estimated by our method. Third Row : Sources estimated by ICA.

D. ADNI

Data collection and sharing for this project was funded by the Alzheimer's Disease Neuroimaging Initiative (ADNI) and DOD ADNI. ADNI is funded by the National Institute on Aging, the National Institute of Biomedical Imaging and Bioengineering, and through generous contributions from the following: AbbVie, Alzheimer's Association; Alzheimer's Drug Discovery Foundation; Araclon Biotech; BioClinica, Inc.; Biogen; Bristol-Myers Squibb Company; CereSpir, Inc.; Cogstate; Eisai Inc.; Elan Pharmaceuticals, Inc.; Eli Lilly and Company; EuroImmun; F. Hoffmann-La Roche Ltd and its affiliated company Genentech, Inc.; Fujirebio; GE Healthcare; IXICO Ltd.; Janssen Alzheimer Immunotherapy Research & Development, LLC.; Johnson & Johnson Pharmaceutical Research & Development LLC.; Lumosity; Lundbeck; Merck & Co., Inc.; Meso Scale Diagnostics, LLC.; NeuroRx Research; Neurotrack Technologies; Novartis Pharmaceuticals Corporation; Pfizer Inc.; Piramal Imaging; Servier; Takeda Pharmaceutical Company; and Transition Therapeutics. The Canadian Institutes of Health Research is providing funds to support ADNI clinical sites in Canada. Private sector contributions are facilitated by the Foundation for the National Institutes of Health (www.fnih.org). The grantee organization is the Northern California Institute for Research and Education, and the study is coordinated by the Alzheimer's Therapeutic Research Institute at the University of Southern California. ADNI data are disseminated by the Laboratory for Neuro Imaging at the University of Southern California.