Supplementary Material II: Generalized Additive Models

This document contains supplementary material related to the description of generalized additive models in Section 2 of the article "Meta-Analysis of Generalized Additive Models in Neuroimaging Studies" by Sørensen et al.

Construction of GAMs from Basis Functions

Figure 1 illustrates how a smooth function is constructed from four cubic regression splines using equation (2). The left panel shows the splines $b_{1s}(x), \dots, b_{4s}(x)$, and the colored dots indicate the knot location of the respective spline. The colored curves in the right panel shows the contribution from each spline to the sum in (2) when using weights $(\gamma_{1s}, \gamma_{2s}, \gamma_{3s}, \gamma_{4s}) = (1, 0.2, -0.2, 0.5)$, and the black curve shows the resulting smooth function $f_s(x)$.

As a concrete example of the notation introduced in equation (1), consider a model with a continuous variable x_1 and a group variable x_2 taking on the values $\{0, 1\}$. A GAM with a univariate smooth term for x_1, an offset effect for x_2, and a smooth interaction term is represented by

$$y = \beta_0 + f_1(x_1) + \beta_2 x_2 + f(x_1)x_2 + \epsilon,$$

where $f_2(x_2) = \beta_2 x_2$ is the offset effect and $f_3(x_1, x_2) = f(x_1)x_2$ is the interaction term, in which $f(x_1)$ is some smooth function modeling how $f_1(x_1)$ differs between $x_2 = 1$ and $x_2 = 0$.

Smoothing

With second derivative penalization, the optimal weights (γ_{ks} in equation (2)) for a GAM are defined by the values minimizing the loss function

$$\sum_{i=1}^{n} \left\{ y_i - \beta_0 - \sum_{s=1}^{S} f_s\left(\mathcal{X}_{s,i}\right) \right\}^2 + \sum_{s=1}^{S} \lambda_s \int \left\{ f_s''\left(\mathcal{X}_s\right) \right\}^2 \mathrm{d}\mathcal{X}_s, \qquad (1)$$

where λ_s is the smoothing parameter for the sth term and the interval is computed over the range of $\mathcal{X}_s$ in the sample. An optimal value of $\boldsymbol{\lambda} = (\lambda_1, \dots, \lambda_s)'$ can be obtained using, e.g., generalized cross-validation, restricted maximum likelihood, or marginal maximum likelihood. For GAMMs with a random effect

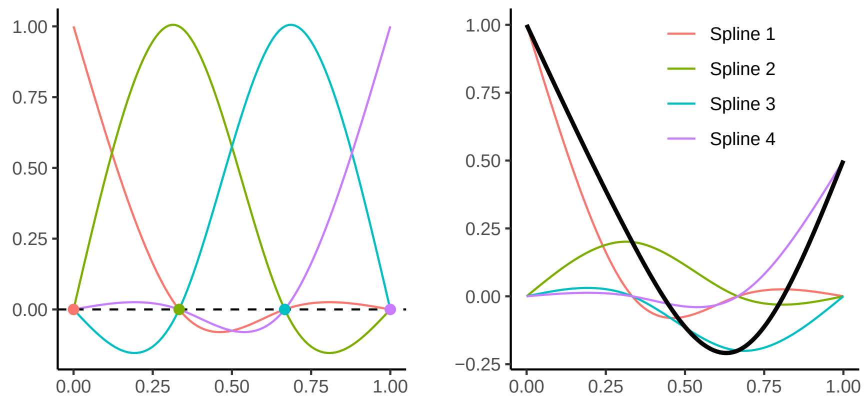

Figure 1: **Constructing a smooth function from splines.** The left panel shows four cubic regression splines, with knot locations indicated by the colored dots. The right panel shows the contribution from each spline when using weights $(\gamma_{1s}, \gamma_{2s}, \gamma_{3s}, \gamma_{4s}) = (1, 0.2, -0.2, 0.5)$, and the black curve shows the resulting smooth function $f_s(x)$.

term, e.g. for analysis of data with repeated measurements, a reparametrization is required in order to obtain (1), by expressing the random effects as smooth terms (Wood, 2017, Ch. 6.8). Alternatively, and typically more efficient with longitudinal data, the GAMM can be formulated as a mixed model by expressing the smooth terms as a combination of fixed and random effects (Lin and Zhang, 1999; Wood, 2004), allowing the use of software for linear mixed models. However, also in this case the smooth terms are penalized as suggested by equation (1).

Figure 2 shows the impact of the smoothing parameter λ on the lifespan hippocampal volume curves from Figure 1. The fits were computed using 50 cubic regression splines with knots equally spaced over the range of age values in the data. The optimal smoothing parameter λ was estimated to 434. The black line represents this optimal value, which appropriately captures the nonlinearities without being too wiggly. The gray curves show a range of fits with λ between 1 and 10^7. The curves with low smoothing follow the same overall trend as the optimal curve, but are quite wiggly, particularly during late adolescence and early adulthood. On the other hand, the curves with high λ are smooth, but do not capture the actual nonlinearity in the data.

References

Lin, X. and Zhang, D. (1999). Inference in generalized additive mixed models by using smoothing splines. *Journal of the Royal Statistical Society: Series*

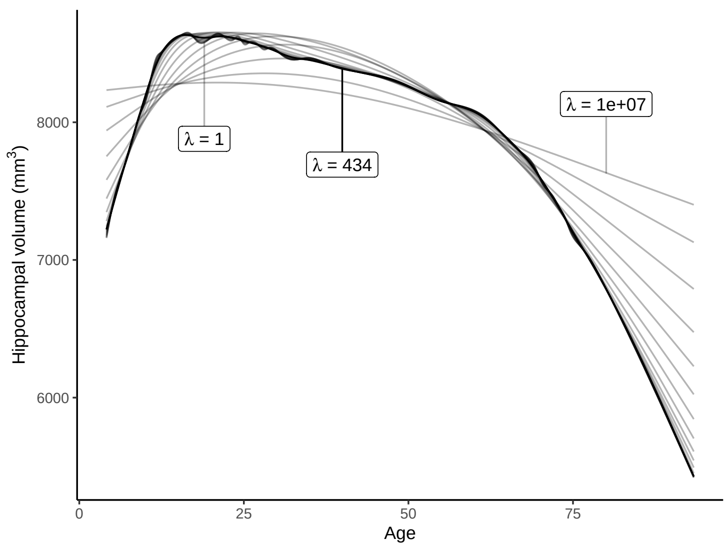

Figure 2: **Smoothing parameter controls wiggliness.** Impact of the smoothing parameter λ on the lifespan trajectories of hippocampal volume from Figure 1. The black line shows the fit corresponding to $\lambda = 434$, which is optimal in terms of maximizing the restricted maximum likelihood. The gray lines show a range of fits with λ between 1 and 10^7. The annotations show the function estimates in each extreme end of the range of smoothing parameters, as well as the optimal estimate.

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