

# 000 001 002 003 004 005 006 007 008 009 010 011 012 013 014 015 016 017 018 019 020 021 022 023 024 NASH: NEURAL ADAPTIVE SHRINKAGE FOR STRUC- TURED HIGH-DIMENSIONAL REGRESSION

005 **Anonymous authors**

006 Paper under double-blind review

## 009 ABSTRACT

012 Sparse linear regression is a fundamental tool in data analysis. However, traditional  
013 approaches often fall short when covariates exhibit structure or arise from hetero-  
014 geneous sources. In biomedical applications, covariates may stem from distinct  
015 modalities or be structured according to an underlying graph. We introduce *Neural*  
016 *Adaptive Shrinkage* (Nash), a unified framework that integrates covariate-specific  
017 side information into sparse regression via neural networks. Nash adaptively mod-  
018 ulates penalties on a per-covariate basis, learning to tailor regularization without  
019 cross-validation. We develop a variational inference algorithm for efficient training  
020 and establish connections to empirical Bayes regression. Experiments on real  
021 data demonstrate that Nash can improve accuracy and adaptability over existing  
022 methods.

## 025 1 INTRODUCTION

028 Regularization techniques for linear models have been central in data analysis for decades (Hoerl &  
029 Kennard, 1970; Tibshirani, 1996; Zou & Hastie, 2005). They remain central in modern data analysis  
030 as they are competitive approaches when the sample size is limited and the covariates are high-  
031 dimensional (Horvath & Raj, 2018; Bohlin et al., 2016; Horvath & Raj, 2018; Haftorn et al., 2021).  
032 Despite their popularity, these methods often fall short when dealing with heterogeneous covariates  
033 that exhibit structural properties, such as nominal, ordinal, spatial, or graphical data. Classical  
034 regularization methods like Lasso (Tibshirani, 1996) typically apply uniform penalties across all  
035 covariates, which can be suboptimal when diverse predictor types are present in the covariate matrix  
036 (e.g., different genetic modalities). Real-world problems often benefit from tailored regularization  
037 that leverages the covariate side information, such as geographical proximity (Devriendt et al.,  
038 2021) or type biological measurements (Boulesteix et al., 2017). On the other hand, the existing  
039 methods that leverage covariate side information (Tibshirani et al., 2005; Yuan & Lin, 2006; Yu  
040 et al., 2016; Boulesteix et al., 2017) are often limited by their application-specific nature and reliance  
041 on cumbersome cross-validation for hyperparameter selection (Tibshirani et al., 2005; Yuan & Lin,  
042 2006).

043 In this work, we introduce *neural adaptive shrinkage* (Nash), a novel regression model framework  
044 that can leverage neural networks to automatically learn the form of the penalty and select the amount  
045 of regularization without using cross-validation or approximate methods. Hence, alleviating the  
046 limitations listed above. We fit Nash using a novel variational inference empirical Bayes (VEB)  
047 method called split VEB, originally introduced for smoothing over-dispersed Poisson counts (Xie,  
048 2023), that we adapt here for high-dimensional Gaussian linear models. When no side information  
049 is available, our approach corresponds to optimizing the lower bound of a recently proposed model  
050 by Kim et al. (2024) and has similar computation complexity  $O((n + K)p)$ . However, our learning  
051 algorithm is much simpler than the one proposed by Kim et al. (2024) and allows easy integration  
052 of machine learning approaches for penalty learning (e.g., neural net, xgboost Chen & Guestrin  
053 (2016)). Hence, Nash is both an extremely efficient high-dimensional regression method when no  
side information is present and a very flexible alternative when side information is available. We  
demonstrate that Nash is a highly competitive framework through a comprehensive study on real data  
examples.

054 2 PREVIOUS WORKS AND CONTRIBUTION  
055  
056

057 **Previous works** have mostly focused on two main types of side information on the covariate. The  
058 first type corresponds to groups (e.g. DNA methylation vs genotype data (Boulesteix et al., 2017)) or  
059 hierarchical information on the covariate; these works include group Lasso (Yuan & Lin, 2006) and  
060 other of its variations (Gertheiss & Tutz, 2010; Tutz & Oelker, 2017; Oelker & Tutz, 2017) and the  
061 IPF Lasso (Boulesteix et al., 2017). Essentially, these methods extend classical regularized techniques  
062 for linear models by using different additive sub-penalties that depend on the group/hierarchy of the  
063 covariates. The second type of covariate side information leveraged in penalized regression is graphs  
064 (Tibshirani et al., 2005; Tibshirani & Taylor, 2011). Spanning from simple L0 graph filtering problem  
065 such as Fused Lasso (Tibshirani et al., 2005) to more complex graphical structure that can be handled  
066 by the GEN Lasso (Tibshirani & Taylor, 2011) and more recent variations (Yu et al., 2016; Devriendt  
067 et al., 2021) that can fit a mix of the different penalties above within a single framework.

068 **Our contribution.** While combining neural networks with linear regression is not new (Okoh  
069 et al., 2018; Nalisnick et al., 2019; Lemhadri et al., 2021), existing methods focus on hybrid models  
070 (Okoh et al., 2018; Nalisnick et al., 2019) or learning link functions (Lemhadri et al., 2021) rather  
071 than learn the penalty itself. Our work differs substantially from the previous works listed above.  
072 To our knowledge, this is the first work to propose the use of a neural network to incorporate  
073 covariate side information when learning the penalty function in linear regression. Our work is  
074 much more assumption-lean compared to previous works, as Nash can leverage any side information  
075 that is processable by a neural net. Additionally, we propose a novel low-complexity variational  
076 approximation for empirical Bayes in multiple linear regression. The resulting learning algorithm is a  
077 simple and effective iterative procedure, akin to ADMM or proximal algorithms (Polson et al., 2015).  
078

079 3 PROBLEM DEFINITION  
080  
081082 3.1 VARIATIONAL EMPIRICAL BAYES FOR THE NASH MODEL  
083

084 The Nash model is defined as follows:

$$086 \mathbf{y} | \mathbf{X}, \boldsymbol{\beta}, \sigma^2 \sim N(\mathbf{X}\boldsymbol{\beta}, \sigma^2) \quad (1)$$

$$087 \beta_j \sim N(b_j, \sigma_0^2) \quad (2)$$

$$088 b_j \sim g(\mathbf{d}_j, \boldsymbol{\theta}) \quad (3)$$

091 where  $\mathbf{y}$  is a response vector of length  $n$ ,  $\mathbf{X}$  is an  $n \times p$  matrix, where  $p$  can be much larger than  
092  $n$  (i.e.,  $p \gg n$ ), and  $\mathbf{x}_j$  is the  $j^{th}$  column of  $\mathbf{X}$ . The terms  $\sigma^2 > 0$  and  $\sigma_0^2 > 0$  are strictly positive  
093 variance parameters. The vector  $\mathbf{d}_j$  corresponds to side information on column  $j$ . The function  $g(\cdot, \cdot)$   
094 belongs to a certain class of functions  $\mathcal{G}$  and takes  $\mathbf{d}_j$  (side information) as its first argument and  
095  $\boldsymbol{\theta}$  (parameters) as its second argument. For any tuple  $(\mathbf{d}_j, \boldsymbol{\theta})$ ,  $g(\mathbf{d}_j, \boldsymbol{\theta})$  defines a distribution with a  
096 density, denoted as  $g(b_j; \mathbf{d}_j, \boldsymbol{\theta})$  at the point  $b_j$ .

097 For simplicity, we assume that  $\mathbf{y}$  is scaled, centered with unit variance, and similarly that each  
098 columns of  $\mathbf{X}$  (i.e.,  $\|\mathbf{x}_j\| = 1$  and  $\mathbb{E}(x_j) = 0$  for all  $j = 1, \dots, p$ ). Note that we do not model  
099 the intercept in equation 1, as centering  $\mathbf{y}$  and  $\mathbf{X}$  prior to model fitting accounts for it, and it is  
100 straightforward to recover the effect for the unscaled  $\mathbf{X}$  (Chipman et al., 2001).

101 We assume that for each predictor  $\mathbf{x}_j$  in  $\mathbf{X}$ , we observe some side information  $\mathbf{d}_j$ . We intentionally  
102 remain vague on the form of the side information  $\mathbf{d}_j$ , with the only constraint being that  $\mathbf{d}_1, \dots, \mathbf{d}_p$   
103 can be processed by a neural network (e.g., images, tokens, graph matrices). For ease of presentation,  
104 we assume that we can store  $\mathbf{d}_1, \dots, \mathbf{d}_p$  in a matrix  $\mathbf{D}$  of size  $p \times k$ . The case without any side  
105 information can be recovered by setting  $\mathbf{d}_1 = \mathbf{d}_2 = \dots = \mathbf{d}_p$ , i.e., constant side information.

106 Assuming that  $\sigma^2$  and  $\sigma_0^2$  are known, solving equation 1 in an Empirical Bayes (EB) fashion involves  
107 the following steps:

108 1. Learning the parameter  $\theta$  of the function  $g(\cdot, \cdot) \in \mathcal{G}$  via maximum marginal likelihood  $\mathcal{L}(\theta)$   
 109

$$110 \quad \hat{\theta} = \arg \max_{\theta} \mathcal{L}(\theta) \quad (4)$$

$$112 \quad = \arg \max_{\theta} \int p(\mathbf{y}|\mathbf{X}, \beta, \sigma^2) \prod_j p(\beta_j|b_j, \sigma_0^2) g(b_j; \mathbf{d}_j, \theta) db_j \quad (5)$$

115 2. Compute the posterior distribution

$$116 \quad p_{\text{post}}(\beta, \mathbf{b}) = p(\beta, \mathbf{b}|\mathbf{y}, \mathbf{X}, \mathbf{D}, \sigma^2) \propto p(\mathbf{y}|\mathbf{X}, \beta, \sigma^2) \prod_j p(\beta_j|b_j, \sigma_0^2) g(b_j; \mathbf{d}_j, \hat{\theta}) \quad (6)$$

119 Wang & Stephens (2021) and Kim et al. (2024) study similar problems in the case where  $g$  does  
 120 not depend on side information  $\mathbf{d}$  (i.e.,  $g(\mathbf{d}_j, \theta) = g(\theta)$  for all  $j$ ). They note that even in this case,  
 121 both steps described above are computationally intractable except in some very special cases. This  
 122 problem becomes even more challenging when we allow the prior  $g$  to depend on side information.  
 123

### 124 3.2 SPLIT VARIATIONAL INFERENCE

126 Given that we aim to fit model equation 1 in a tractable and efficient way, we propose fitting equation 1  
 127 via split VEB (Xie, 2023) using a candidate posterior of the form:

$$130 \quad q(\beta, \mathbf{b}) = \prod_j^P q_{\beta_j}(\beta_j) q_{b_j}(b_j) \quad (7)$$

133 The main idea behind split VEB is to decouple the prior/penalty learning step (step 1) from the  
 134 posterior computation step (step 2). Our primary quantity of interest is the posterior of  $\mathbf{b}$ . However,  
 135 using  $\mathbf{b}$  directly in the linear predictor results in a coupled prior/posterior update as in Kim et al.  
 136 (2024). To alleviate this problem, we essentially introduce a latent variable  $\beta$  that allows splitting the  
 137 ELBO into two parts that are separately updated (see equation 8). At a high level, split VEB allows  
 138 deriving a coordinate ascent that essentially iterates between solving two simple problems similar to  
 139 optimization techniques (e.g., ADMM or proximal algorithms Polson et al. (2015)).  
 140

141 **Form of the ELBO** Using the candidate posteriors of the form 7 leads to an ELBO of the following  
 142 form for the Nash model

$$145 \quad F(q_{\beta}, q_{\mathbf{b}}, g, \sigma^2, \sigma_0^2)_{\text{Nash}} = \sum_i \mathbb{E}_{q(\beta, \mathbf{b})} \left[ \log \frac{p(y_i|\mathbf{x}_i, \beta, \sigma^2)}{q_{\beta}(\beta)} \right] + \sum_j \mathbb{E}_{q(\beta, \mathbf{b})} \left[ \log p(\beta_j|b_j, \sigma_0^2) \right] + \quad (8)$$

$$148 \quad \sum_j \mathbb{E}_{q(\beta, \mathbf{b})} \left[ \log \frac{g(b_j; \mathbf{d}_j, \theta)}{q_{b_j}(b_j)} \right] \quad (9)$$

152 Where  $q(\beta, \mathbf{b})$  is the mean-field variational distribution as defined in 7.

154 **High-Level Coordinate Ascent Update for Nash** Let  $\bar{\beta}_j = \mathbb{E}_q(\beta_j)$  denote the expected value of  
 155  $\beta_j$  with respect to  $q$ , and  $\bar{b}_j = \mathbb{E}_q(b_j)$  denote the expected value of  $b_j$ . We define  $\bar{\mathbf{r}} = \mathbf{y} - \mathbf{X}\bar{\beta}$  as  
 156 the vector of expected residuals with respect to  $q$ . Let  $\mathbf{X}_{-j}$  be the design matrix excluding the  $j^{\text{th}}$   
 157 column, and  $q_{-j}$  denote all factors  $q_{j'}$  except factor  $j$ . The expected residuals accounting for the  
 158 linear effect of all variables other than  $j$  are given by:

$$161 \quad \bar{r}_j = \mathbf{y} - \mathbf{X}_{-j}\bar{\beta}_{-j} = \mathbf{y} - \sum_{j' \neq j} \mathbf{x}_{j'}\bar{\beta}_{j'} \quad (10)$$

162  
163 1. **Update for  $q_{\beta_j}^*$ :** the coordinate ascent update  $q_{\beta_j}^* = \arg \max_{q_{\beta_j}} F_{\text{Nash}}(g, q, \sigma^2, g, q, \sigma_0^2)$  is  
164 obtained by computing the posterior using

$$165 \quad p(\bar{\mathbf{r}}_j | \mathbf{x}_j, \beta_j, \sigma) p(\beta_j | \bar{b}_j, \sigma_0^2)$$

166 This is a simple posterior computation due to conjugacy and has a closed form that only  
167 requires computing the ordinary least square (OLS) regression of  $\mathbf{x}_j$  on  $\bar{\mathbf{r}}_j$  (see section  
168 3.2.1).

169 2. **Update for  $(g^*, q_b^*)$ :** The coordinate ascent update  
170

$$171 \quad (g^*, q_b^*) = \arg \max_{g, q_b} F(q_{\beta}, q_b, g; \sigma^2)_{\text{Nash}}$$

173 is obtained by fitting a neural net with the following objective function:

$$174 \quad \hat{\boldsymbol{\theta}} = \arg \max_{\boldsymbol{\theta}} \mathcal{L}(\boldsymbol{\theta}) \quad (11)$$

$$175 \quad = \arg \max_{\boldsymbol{\theta}} \prod_{j=1}^p \int \mathcal{N}(\bar{\beta}_j; b_j, \sigma_0^2) g(b_j; \mathbf{d}_j, \boldsymbol{\theta}) db_j \quad (12)$$

179 Then, by computing the posterior of  
180

$$181 \quad p(b_j | \bar{\beta}_j, \mathbf{d}_j, \sigma_0^2) \propto \mathcal{N}(\bar{\beta}_j; b_j, \sigma_0^2) g(b_j; \mathbf{d}_j, \hat{\boldsymbol{\theta}})$$

183 for each  $b_j$ , which is also a simple posterior computation.

184 3. **Update for  $\sigma^2, \sigma_0^2$**

$$185 \quad (a) (\sigma^2)^* = \arg \max_{\sigma^2} F(q_{\beta}, q_b, g, \sigma^2, \sigma_0^2)_{\text{Nash}}$$

$$186 \quad (b) (\sigma_0^2)^* = \arg \max_{\sigma_0^2} F(q_{\beta}, q_b, g, \sigma^2, \sigma_0^2)_{\text{Nash}}$$

188 The first step is a direct consequence of the work by Kim et al. (2024) (see Appendix for more details),  
189 the second step results from our splitting approach, and the last step is a standard coordinate ascent  
190 variational inference (CAVI) step. We provide the closed-form formulas for both  $\sigma^2$  and  $\sigma_0^2$  in the  
191 supplementary section A.1, and we describe the overall learning process in the Appendix, Algorithm  
192 1.

193 **Choice of  $\mathcal{G}$**  For clarity, suppose that  $g(\cdot, \cdot)$  belong to a family of distributions  $\mathcal{G}$  that have the  
194 following form:  
195

$$196 \quad g(\mathbf{d}_j, \boldsymbol{\theta}) = \sum_{m=0}^M \pi_m(\mathbf{d}_j, \boldsymbol{\theta}) g_m \quad (13)$$

$$197 \quad \pi(\mathbf{d}_j, \boldsymbol{\theta}) = (\pi_0(\mathbf{d}_j, \boldsymbol{\theta}), \dots, \pi_M(\mathbf{d}_j, \boldsymbol{\theta})) \quad (14)$$

202 where  $g_m$  are fixed known distributions (e.g.,  $g_0 = \delta_0$  and  $g_m = \mathcal{N}(0, \sigma_m^2)$  with  $\sigma_m^2 < \sigma_{m+1}^2$  for all  
203  $m > 0$ ). Then  $\pi(\cdot, \boldsymbol{\theta})$  is a neural network that takes side information  $\mathbf{d}_j$  as input and outputs a vector  
204 of probabilities  $(\pi_0(\mathbf{d}_j, \boldsymbol{\theta}), \dots, \pi_M(\mathbf{d}_j, \boldsymbol{\theta}))$  that sum to 1 (e.g., using a softmax function). Under  
205 this model, the loss for  $\boldsymbol{\theta}$  has the following simple form:  
206

$$208 \quad \hat{\boldsymbol{\theta}} = \arg \max_{\boldsymbol{\theta}} \sum_{j=1}^P \log \sum_{m=0}^M \pi_m(\mathbf{d}_j, \boldsymbol{\theta}) L_{jm} \quad (15)$$

211 where  $L_{jm}$  is defined as:  
212

$$214 \quad L_{jm} = \int p(\bar{\beta}_j | b_j) g_m(b_j) db_j \quad (16)$$

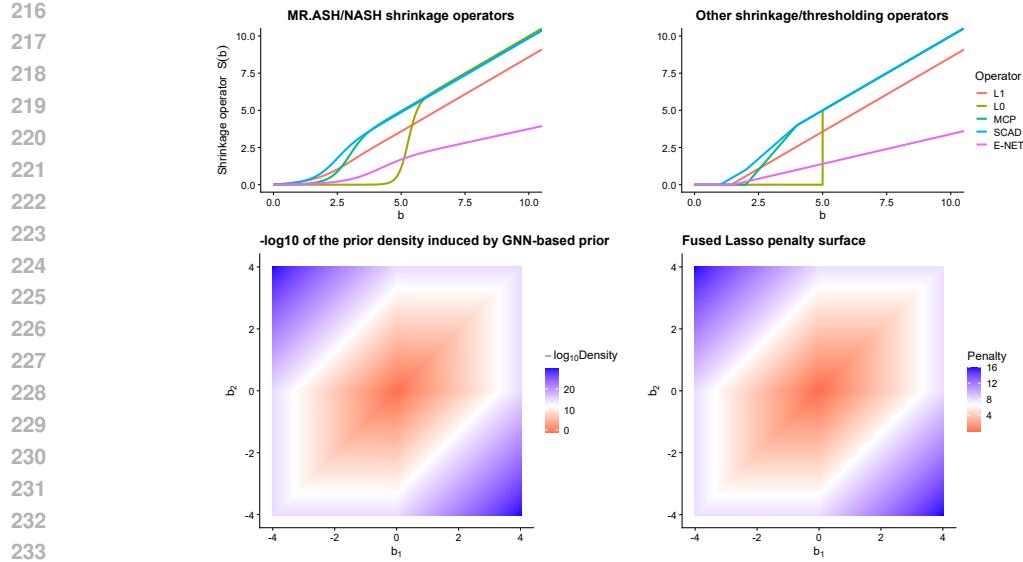


Figure 1: Upper panel: Adaptation of Figure 1 from Kim et al. (2024), showcasing that posterior mean shrinkage operators (left panel) for different choices of  $\sigma_1^2, \dots, \sigma_M^2$  and  $\pi_0, \dots, \pi_M$  can mimic the shrinkage operators from some commonly used penalties (right-hand panel). Bottom panel left: Illustration of how Nash can mimic fused Lasso penalty when used with a graph neural net prior-based. The left image presents the induced prior density from equation 24, allowing Nash to mimic the fused Lasso penalty (using  $s_1 = 0.45$  and  $s_2 = 0.15$ ). Bottom right panel, penalty surface of the fused Lasso (i.e.,  $|b_1| + |b_2| + |b_1 - b_2|$ ).

This represents the marginal likelihood of  $\bar{\beta}_j$  under mixture component  $m$ . For Gaussian mixture components  $g_m = \mathcal{N}(0, \sigma_m^2)$ , we have:

$$L_{jm} = \mathcal{N}(\hat{\beta}_j; 0, \sigma_0^2 + \sigma_m^2) \quad (17)$$

These integrals often cannot be computed analytically for other priors and error models. However,  $(L_{jm})$  are simple one-dimensional integrals that are fast to approximate. It is straightforward to extend this model to use more complex distribution mixtures such as Mixture Density Networks Bishop (1994) or Graph Mixture Density Networks Errica et al. (2021) (see section 4 for more details). More generally,  $g(\cdot, \cdot)$  can be any probabilistic model (e.g., Gaussian Process, but potentially more complex models) for which the loss in 12 can be evaluated and the posterior  $p(b_j | \bar{\beta}_j, \mathbf{d}_i, \sigma_0^2) \propto \mathcal{N}(\bar{\beta}_j; b_j, \sigma_0^2)g(b_i; \mathbf{d}_i, \hat{\theta})$  can be computed. For computational efficiency, it is useful that both of these steps can be evaluated via closed-form formulas. Note that when  $g$  does not depend on the covariate, then step 2) in the coordinate ascent described above corresponds to an empirical Bayes normal mean problem (EBNM; see Willwerscheid et al. (2024) for an overview, and (Robbins, 1956; Efron, 1971; Stephens, 2017) for classical statistical papers on this topic). In this case, fitting  $g$  as in 13 with fixed  $g_m(\cdot)$  distributions corresponds to estimating the mixture proportions for the different mixture components  $g_m(\cdot)$ . Using fixed distributions is particularly practical as it allows efficient estimation of the mixture components  $(\pi_0, \dots, \pi_M)$  via sequential quadratic programming, which is often achieved in sub-linear time (in terms of  $p$ ), see Kim et al. (2019).

### 3.2.1 ON THE UPDATE FOR $\beta$

A careful reader will notice that the update for  $\beta$  can actually be solved exactly, without using an approximate posterior as in 7. Split VEB leads to an update for  $\beta$  that corresponds to a Bayesian ridge regression  $\mathbf{y} | \mathbf{X}, \beta, \sigma^2 \sim N(\mathbf{X}\beta, \sigma^2)$  with a prior on  $\beta \sim N(\mathbf{b}, \sigma_0^2 I_p)$ . The posterior of  $\beta$  has a well-known closed form (Hoerl & Kennard, 1970). However, computing this posterior requires inverting a matrix, resulting in  $O(np^2 + p^3)$  operations to compute the exact posterior (or  $O(n^2p + n^3)$  operations using the dual form, via Woodbury formula (Saunders et al., 1998)). Because of conjugacy

and the assumption that the columns of  $\mathbf{X}$  are centered and scaled, the update at iteration  $t + 1$  for  $\beta_j$  under 7 is given by  $\beta_j^{t+1} = \omega \mathbf{x}_j^\top \bar{\mathbf{r}}_j^{t+1} + (1 - \omega) \bar{b}_j^t$ . Here,  $\bar{\mathbf{r}}_j^{t+1}$  is the expected residual at iteration  $t + 1$  as defined in 10,  $\bar{b}_j^t$  is the posterior mean of  $b_j$  under 7 at iteration  $t$ , and  $\mathbf{x}_j^\top \bar{\mathbf{r}}_j$  corresponds to the maximum likelihood estimate (MLE) of the effect of  $\mathbf{x}_j$  on  $\bar{\mathbf{r}}_j^{t+1}$  due to scaling. The term  $\omega$  is defined as  $\omega = \frac{(n-1)\sigma_0^2}{\sigma^2 + (n-1)\sigma_0^2}$  as due to scaling  $\mathbf{x}_j^\top \mathbf{x}_j = n - 1$ . Therefore, each update for a  $\beta_j$  corresponds to a scalar product between two vectors, resulting in a coordinate ascent algorithm that has a complexity of  $O(np)$ , which is significantly smaller than  $O(n^2p + n^3)$  or  $O(np^2 + p^3)$ .

### 3.2.2 AN AUTOREGRESSIVE UPDATE FOR $g$ WITH AUTO-ADAPTIVE DAMPENING

Given that in practice both  $\sigma^2$  and  $\sigma_0^2$  are being updated (see steps 3a and 3b in the coordinate ascent algorithm above), the resulting updates for  $g$  and  $q_b$  correspond to fitting a series of autoregressive covariate-moderated empirical Bayes normal mean problems (cEBNM) that have the following form:

$$\omega_t \hat{\beta}_{jMLE}^{t+1} + (1 - \omega_t) \bar{b}_j^t \sim N(b_j^{t+1}, \sigma_{0,t}^2), \quad (18)$$

$$b_j^{t+1} \sim g(\mathbf{d}_j, \boldsymbol{\theta}^{t+1}). \quad (19)$$

Here,  $\omega_t = \frac{(n-1)\sigma_{0t}^2}{\sigma_t^2 + (n-1)\sigma_{0t}^2}$ , where  $\sigma_{0t}$  is the value of  $\sigma_0^2$  at iteration  $t$  (the same goes for  $\sigma_t^2$ ). Equation 18 arises from basic Bayesian computation, yet it leads to an update that is simple to interpret. At each update for  $g$  and  $q_b$ , the model uses a proportion  $\omega_t$  of novel evidence while retaining  $1 - \omega_t$  of the previous update. Given that  $\sigma_t^2$  and  $\sigma_{0t}^2$  are maximized by Nash's ELBO, the parameter  $\omega_t$  can be viewed as a data-driven dampening parameter for learning  $g$  and  $q_b$ .

### 3.3 COMPARISON AND CONNECTION WITH MR.ASH

Our work is closely related to the multiple regression with adaptive shrinkage (mr.ash) proposed by Kim et al. (2024), but it differs in two key aspects. The most notable difference is that mr.ash cannot handle side information. A more technical yet important difference is our learning algorithm. Kim et al. (2024) use a standard CAVI for fitting VEB approximation of mr.ash, which results in a coordinate ascent algorithm that requires updating the prior  $g$  whenever updating  $q_{b_j}$ . Thus mr.ash's update for  $g$  corresponds to an M-step (Dempster et al., 1977). Because the posterior and the prior learning steps are not decoupled in the mr.ash variational formulation, the resulting CAVI requires updating the prior  $g$ ,  $p$  times per CAVI update. Split VEB allows decoupling these two problems, leading to a coordinate ascent for Nash that is notably more efficient, as it only requires updating the prior  $g$  once per coordinate ascent update. While this nuance may appear subtle at first, it turns out to be crucial when side information is present. Using split VEB allows fitting Nash with a single update of the neural net parameters  $\theta(g(\cdot, \theta))$  per coordinate ascent update iteration. In contrast, adapting mr.ash would require updating the neural net  $p$  times per CAVI update, which is not practical when  $p$  is large.

$$\text{mr.ash} \quad \text{Nash, without side information} \quad (20)$$

$$\mathbf{y} | \mathbf{X}, \mathbf{b}, \sigma^2 \sim N(\mathbf{X}\mathbf{b}, \sigma^2) \quad \mathbf{y} | \mathbf{X}, \boldsymbol{\beta}, \sigma^2 \sim N(\mathbf{X}\boldsymbol{\beta}, \sigma^2) \quad (21)$$

$$b_j \sim g \quad \beta_j \sim N(b_j, \sigma_0^2) \quad (22)$$

$$b_j \sim g \quad (23)$$

These two works are related, as fitting Nash with split VEB when no side information is provided corresponds to optimizing a lower bound of mr.ash's Evidence Lower Bound (ELBO), when using  $g \in \mathcal{G}$  from the same family of distributions when fitting both models (see section A.2 for a formal proof). We also provide in supplementary material **Algorithm 2** a high-level description of the key differences between Nash and mr.ash fitting procedures.

## 324 4 CONNECTION TO PENALIZED LINEAR REGRESSION AND BEYOND

326 Kim et al. (2024) showed that mr.ash (and therefore Nash) can be viewed as a penalized linear  
 327 regression (PLR) problem. When using an adaptive shrinkage prior (ash, (Stephens, 2017)) of the  
 328 form  $g = \pi_0 \delta_0 + \sum_{m=1}^M \pi_m N(0, \sigma_m^2)$ , different choices of  $(\pi_0, \dots, \pi_M)$  corresponding to different  
 329 penalties such as Ridge regression (Hoerl & Kennard, 1970), L0Learn (Hazimeh et al., 2023), Lasso  
 330 (Tibshirani, 1996), Elastic Net (Zou & Hastie, 2005), the smoothly clipped absolute deviation (SCAD)  
 331 penalty, and the minimax concave penalty (MCP) (Breheny & Huang, 2011). The advantage of  
 332 mr.ash and Nash is that the user doesn't need to specify the penalty, as the model learns the mixture  
 333  $(\hat{\pi}_0, \dots, \hat{\pi}_M)$  that best fits the data via EB. (Kim et al., 2024) proposed the concept of a shrinkage  
 334 operator to properly establish the connection between EB multiple linear regression and PLR, which  
 335 we depict in figure 1. We further build on this idea by suggesting that some parameterizations of  
 336 Nash (detailed below) can be viewed as extensions to previous PLR methods with side information.

337 **Group-Based and Hierarchical Penalty** Several approaches have been developed to modulate  
 338 the penalty based on groups or hierarchical structures of the data. Examples include the Group  
 339 Lasso (Yuan & Lin, 2006), which uses a penalty of the form  $\lambda_1 \|b\|_1 + \lambda_2 \sum_{k \in \mathcal{K}} \sqrt{d_k} \|b_k\|_2$ , and  
 340 the IPF-Lasso Boulesteix et al. (2017) with a penalty of the form  $\lambda \sum_{k \in \mathcal{K}} \sum_{j \in k} \omega_k |b_j|$ , where  $\mathcal{K}$   
 341 corresponds to the different groups or clusters. These cases are easily handled by Nash, as they  
 342 simply correspond to fitting an ash prior per group/cluster/category. This is achieved using a prior of  
 343 the form  $g_k(\cdot) = \pi_{0k} \delta_0 + \sum_{m=1}^M \pi_{mk} N(0, \sigma_m^2)$  for each  $k$ . In other words the side information  $\mathbf{d}_j$   
 344 for the covariate  $\mathbf{x}_j$  is a vector of length  $\mathcal{K}$  with binary entries, where the  $k^{\text{th}}$  entry of  $\mathbf{d}_j$  is set to 1 if  
 345 covariate  $j$  belongs to group  $k$ . Thus, the model  $\pi : \mathbf{d}_j \rightarrow (\pi_0(\mathbf{d}_j), \dots, \pi_M(\mathbf{d}_j))$  is a multinomial  
 346 regression that is straightforward to fit using standard machine learning routines. Unlike the Group  
 347 Lasso or the IPF-Lasso, Nash can naturally fit different penalty types to different groups (e.g., fitting  
 348 an  $L_1$  like penalty on group 1 and fitting an  $L_2$  like penalty on group 2).

349 **Fused Lasso and Graph-Based Penalty** The Fused Lasso (Tibshirani et al., 2005) aims to balance  
 350 sparsity and smoothness covariates using a penalty of the form  $\sum_{j=1}^p |b_j| \leq s_1$  and  $\sum_{j=2}^p |b_j -$   
 351  $b_{j-1}| \leq s_2$ . Bayesian versions Casella et al. (2010); Betancourt et al. (2017) have been proposed. We  
 352 extend these with graph neural networks (GNNs) to handle more complex dependencies. Classical  
 353 Bayesian Fused Lasso Casella et al. (2010) can be reframed using a trivial graphical neural networks  
 354 (GNN) (Kipf & Welling, 2017). Here,  $\mathbf{d}_j = \mathbf{d}_j^{t+1}$  is the graph (a line in the Fused Lasso case)  
 355 with nodes storing  $\beta_{j,MLE}^{t+1}$  and  $\bar{b}_j^t$ . As the model converges,  $\bar{b}_j^{t+1} \approx \bar{b}_{j+1}^t$ , aligning with classic  
 356 formulations. We propose the EB Fused Lasso formulation:

$$g_{\text{fused}}(\mathbf{d}_j) = z L(0, s_1) L(l(\mathbf{d}_j), s_2) L(r(\mathbf{d}_j), s_2) \quad (24)$$

357 Here,  $L(\mu, s_0)$  is a Laplace distribution centered at  $\mu$  with scale  $s_0$ , and  $z$  is a normalization constant.  
 358 Functions  $r(\mathbf{d}_j) = \bar{b}_{j-1}^t$  and  $l(\mathbf{d}_j) = \bar{b}_{j+1}^t$  are trivial GNNs, allowing different strengths for previous  
 359 and next values. Posterior moments for  $b_j$  can be approximated via Gauss-Hermite quadrature.  
 360 Hyperparameters  $(s_1, s_2)$  are learned by maximizing the marginal log likelihood.

361 For an arbitrary graph, model 24 becomes computationally challenging as computing the posterior  
 362 under a product of  $k > 3$  Laplace distributions, as it quickly becomes computationally demanding to  
 363 approximate. We propose a **generalized EB Fused Lasso** :

$$g_{\text{fused}}(\mathbf{d}_j) = z L(0, s_1) L(v_1(\mathbf{d}_j), s_2(\mathbf{d}_j)) \quad (25)$$

364 Here,  $v_1(\mathbf{d}_j)$ ,  $(\mathbf{d}_j)$  is the output of a GNN output controlling  $b_j$ 's smoothness with respect to the  
 365 graph structure. This simplifies normalization computation and integral approximation as it only uses  
 366 two Laplace distributions.

367 Note that different variations of the Fused Lasso have been proposed, such as the Sparse Regression  
 368 Incorporating Graphical Structure Among Predictors (SRIG) Yu et al. (2016) or the Graph-Guided  
 369 Fused Lasso (GGFL) Chen et al. (2010). The SRIG and GGFL penalties can also be mimicked by  
 370 adapting the prior 72 using Normal instead of Laplace.

371 **Beyond Regularization** We also provide an implementation of Nash that uses penalties based on  
 372 Mixture Density Networks (MDN) (Bishop, 1994) and Graph Mixture Density Networks (GMDN)  
 373 (Errica et al., 2021). The formulation is as follows:

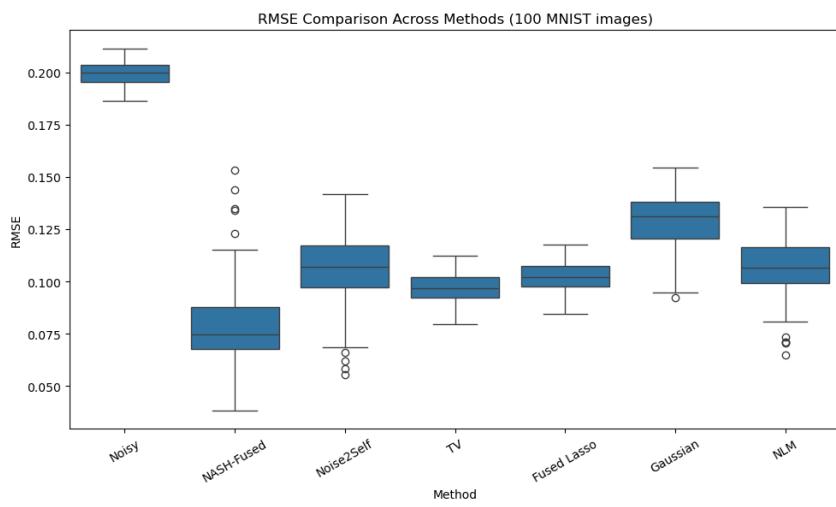
378  
379  
380  
381

$$g(j, \theta) = \pi_0(\mathbf{d}_j)\delta_0 + \sum_k \pi_k(\mathbf{d}_j)N(\mu_k(\mathbf{d}_j), \sigma_k^2(\mathbf{d}_j)) \quad (26)$$

382 Here,  $(\pi_k(\mathbf{d}_j))$ ,  $(\mu_k(\mathbf{d}_j))$ ,  $(\sigma_k^2(\mathbf{d}_j))$  are the outputs of the (graph) MDN, as described in Bishop  
383 (1994) and in Errica et al. (2021). These parameterizations allow the model to actually push the  
384 values of  $b_j$  away from 0. Enabling Nash to be used as a "self-supervised" biased regression where  
385 the bias (here  $\mu_k(\mathbf{d}_j)$ ) is automatically learned from the data.

386  
387

## 5 NUMERICAL EXPERIMENT

388  
389  
390  
391  
392  
393  
394  
395  
396  
397  
398  
399  
400  
401  
402  
403  
404  
405

406

Figure 2: Performances of the different approaches for denoising MNIST image in terms of RMSE.

407  
408  
409  
410  
411  
412  
413

We evaluate Nash prediction performance on 4 real data sets that have side information. In each of these datasets, we also benchmark the performance of mr.ash, Lasso, the elastic net (Enet) with  $\alpha = 0.5$ , ridge regression, and when the data display group/hierarchical side information, we also benchmark the ipf Lasso. We benchmark 2 versions of Nash: i) Nash without side information and ii) Nash-mdn equation 26. We also benchmark the performance of xgboost (Chen & Guestrin, 2016), and multi-layer perceptron (MLP) with L2 regularization.

414  
415  
416  
417  
418  
419

We selected a range of real datasets that spans from small data set and with a limited number of covariates (e.g. Air Passenger data ) to larger data set scale such as epigenetic age prediction with nearly 500,000 predictors. We detail these datasets and the preprocessing in A.3. In most of our experiments, we proceed as follows: we remove at random 20% of the data for testing purposes, run the different methods on the remaining data, and evaluate the performance of each method in terms of root mean squared error (RMSE).

420  
421  
422  
423  
424  
425  
426  
427  
428  
429  
430  
431

- **SNP500:** we used daily return from of the **AAPL** symbols from SNP500 using other assets daily return. For each asset used in the predictor, we obtained the type of industry in which this asset is part of (e.g., Technology, Communication Services, Healthcare, Equity Funds ) and used it as side information.
- **Airpassenger:** we added noise to the Airpassenger data set and used the measurement time point as side information.
- **GSE40279:** we used methylation data from individuals measurement ( $p = 489, 503$ ) to predict the age of the subject (Bohlin et al., 2016; Horvath & Raj, 2018). We use methylation probe annotation as side information.
- **TCGA:** we predict individual normalized *BRCA1* gene expression (an important gene in breast cancer) expression level using the other genes. We use gene pathways from KEGG pathway as side information.

Method	SNP500	Airpassenger	GSE40279	TCGA
Dimension ( $n \times p$ )	$235 \times 85$	$144 \times 144$	$679 \times 489,503$	$1,212 \times 18,300$
Side info	group	time	probe type	pathway
Ridge	0.070 (0.065; 0.076)	33.0 (31.0; 35.0)	7.21 (6.83; 7.58)	0.536 (0.472; 0.599)
Enet	0.071 (0.066; 0.078)	30.2 (29.5; 30.9)	5.28 (5.02; 5.56)	0.466 (0.411; 0.522)
Lasso	0.093 (0.087; 0.100)	49.2 (48.7; 49.7)	5.39 (5.08; 5.71)	0.465 (0.412; 0.518)
mr.ash	0.082 (0.076; 0.088)	20.2 (19.1; 21.3)	5.25 (5.01; 5.71)	0.449 (0.405; 0.493)
XGBoost	0.062 (0.053; 0.069)	18.2 (17.2; 19.1)	6.17 (5.83; 6.52)	0.549 (0.494; 0.604)
MLP	0.441 (0.361; 0.521)	59.5 (58.3; 60.8)	13.62 (13.08; 14.15)	0.457 (0.349; 0.566)
ipf-Lasso	0.066 (0.060; 0.072)	NA	<b>5.06</b> (4.81; 5.33)	0.443 (0.393; 0.473)
Nash.no.cov	0.084 (0.079; 0.089)	19.7 (18.6; 20.7)	5.27 (5.01; 5.53)	0.457 (0.412; 0.504)
Nash.mdn	<b>0.058</b> (0.053; 0.0643)	<b>17.7</b> (17.1; 18.2)	5.12 (4.77; 5.47)	<b>0.435</b> (0.387; 0.483)

Table 1: Comparison of methods across datasets using RMSE. Parentheses denote 95% confidence intervals based on Gaussian approximations. ipf-Lasso cannot handle time as side information, so we put NA for the Airpassenger experiment.

## 5.1 DENOISING MNIST IMAGES

We evaluate the performance of Nash-fused 24 using a simple 2-layer message passing GNN to remove Gaussian noise in images compared to methods for image denoising that only use a **single image** (as opposed to models trained on other images like diffusion model), such as fused-lasso (Tibshirani et al., 2005), Total Variation (TV) Denoising Chambolle (2004), Non-Local Means (NLM ) (Buades et al., 2005), Gaussian Filtering (Gonzalez & Woods, 2002), Median Filtering (Huang et al., 1979), and Noise2Self (Batson & Royer, 2019) of denoising noisy grayscale images from the MNIST dataset. Nash-fused was run treating each image as a 2D grid graph, where each pixel is a node connected to its 4-nearest neighbors, and Nosie2Self was run using a convolutional neural net, which is substantially slower than Nash-fused. The true signal is the clean MNIST digit image scaled to [0,1], and additive Gaussian noise with standard deviation of  $\sigma = 0.2$  was applied to produce the observed noisy image. The experiment is repeated over 100 randomly selected MNIST images. For each method, we report the root mean squared error (RMSE) between the denoised image and the ground truth. Results are summarized as boxplots in Figure 2 additional experiments using convolutional neural nets are presented in supplementary material in Figure 3. Examples of denoised images using Nash-fused in the Appendix (see figure5-11)

## 6 DISCUSSION

We proposed Nash, a novel high-dimensional regression framework that integrates covariate-specific side information into the estimation process using neural networks. Nash adaptively learns structured penalties in a nonparametric fashion, enabling flexible regularization without the need for cross-validation. Our method generalizes and extends existing approaches that incorporate side information, offering a unified and more expressive framework. We also proposed a new learning algorithm, split variational empirical Bayes (split VEB), which decouples prior learning from posterior inference, allowing for efficient and scalable optimization. This algorithm naturally connects to and simplifies a recently proposed variational Empirical Bayes approach(Kim et al., 2024), while supporting far richer prior families, including those parameterized by deep neural networks.

To our knowledge, Nash is the first regression method that models the prior distribution over regression effects as a direct function of side information, enabling automatic, data-driven regularization across diverse structures such as groups, time, and graphs. Through extensive experiments on real and synthetic datasets, we demonstrated that Nash consistently performs competitively and can outperform existing methods tailored to handle a **specific** type of side information.

## REFERENCES

Joshua Batson and Laurent Royer. Noise2Self: Blind Denoising by Self-Supervision. In Kamalika Chaudhuri and Ruslan Salakhutdinov (eds.), *Proceedings of the 36th International Conference on Machine Learning*, volume 97 of *Proceedings of Machine Learning Research*, pp. 524–533. PMLR, 2019.

486 Brenda Betancourt, Abel Rodríguez, and Naomi Boyd. Bayesian Fused Lasso Regression for  
 487 Dynamic Binary Networks. *Journal of Computational and Graphical Statistics*, October  
 488 2017. ISSN 1061-8600. URL <https://www.tandfonline.com/doi/full/10.1080/10618600.2017.1341323>. Publisher: Taylor & Francis.  
 489

490 Christopher M. Bishop. Mixture Density Networks. Technical Report NCRG/94/004, Aston  
 491 University, Birmingham, UK, 1994. URL [https://publications.aston.ac.uk/id/eprint/373/1/NCRG\\_94\\_004.pdf](https://publications.aston.ac.uk/id/eprint/373/1/NCRG_94_004.pdf).  
 492

493 J. Bohlin, S. E. Håberg, P. Magnus, S. E. Reese, H. K. Gjessing, M. C. Magnus, C. L. Parr, C. M. Page,  
 494 S. J. London, and W. Nystad. Prediction of gestational age based on genome-wide differentially  
 495 methylated regions. *Genome Biology*, 17(1):207, October 2016. ISSN 1474-760X. doi: 10.1186/s13059-016-1063-4. URL <https://doi.org/10.1186/s13059-016-1063-4>.  
 496

497 Anne-Laure Boulesteix, Riccardo De Bin, Xiaoyu Jiang, and Mathias Fuchs. IPF-LASSO: Integrative  
 498 L1-Penalized Regression with Penalty Factors for Prediction Based on Multi-Omics Data.  
 499 *Computational and Mathematical Methods in Medicine*, 2017:7691937, 2017. ISSN 1748-6718.  
 500 doi: 10.1155/2017/7691937.  
 501

502 Patrick Breheny and Jian Huang. Coordinate descent algorithms for nonconvex pen-  
 503 alized regression, with applications to biological feature selection. *The Annals of Applied Statistics*, 5(1):232–253, March 2011. ISSN 1932-6157, 1941-  
 504 7330. doi: 10.1214/10-AOAS388. URL <https://projecteuclid.org/journals/annals-of-applied-statistics/volume-5/issue-1/Coordinate-descent-algorithms-for-nonconvex-penalized-regression-with-applications-10.1214/10-AOAS388.full>. Publisher: Institute of Mathematical Statistics.  
 505

506 A. Buades, B. Coll, and J.-M. Morel. A non-local algorithm for image denoising. In *2005 IEEE  
 507 Computer Society Conference on Computer Vision and Pattern Recognition (CVPR'05)*, volume 2,  
 508 pp. 60–65 vol. 2, June 2005. doi: 10.1109/CVPR.2005.38. URL <https://ieeexplore.ieee.org/document/1467423>. ISSN: 1063-6919.  
 509

510 George Casella, Malay Ghosh, Jeff Gill, and Minjung Kyung. Penalized regres-  
 511 sion, standard errors, and Bayesian lassos. *Bayesian Analysis*, 5(2):369–411, June  
 512 2010. ISSN 1936-0975, 1931-6690. doi: 10.1214/10-BA607. URL <https://projecteuclid.org/journals/bayesian-analysis/volume-5/issue-2/Penalized-regression-standard-errors-and-Bayesian-lassos/10.1214/10-BA607.full>. Publisher: International Society for Bayesian Analysis.  
 513

514 Antonin Chambolle. An algorithm for total variation minimization and applications. *Journal of  
 515 Mathematical Imaging and Vision*, 20(1-2):89–97, 2004. Publisher: Springer.  
 516

517 Tianqi Chen and Carlos Guestrin. XGBoost: A Scalable Tree Boosting System. In *Proceedings of  
 518 the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*,  
 519 pp. 785–794, San Francisco California USA, August 2016. ACM. ISBN 978-1-4503-4232-2.  
 520 doi: 10.1145/2939672.2939785. URL <https://dl.acm.org/doi/10.1145/2939672.2939785>.  
 521

522 Xi Chen, Seyoung Kim, Qihang Lin, Jaime G. Carbonell, and Eric P. Xing. Graph-Structured  
 523 Multi-task Regression and an Efficient Optimization Method for General Fused Lasso, May 2010.  
 524 URL <http://arxiv.org/abs/1005.3579>. arXiv:1005.3579 [stat].  
 525

526 Hugh Chipman, Edward I. George, and Robert E. McCulloch. The Practical Implementation of  
 527 Bayesian Model Selection. In *Model Selection*, volume 38 of *IMS Lecture Notes – Monograph  
 528 Series*, pp. 65–116. Institute of Mathematical Statistics, 2001.  
 529

530 Ran Cui, Roy A. Elzur, Masahiro Kanai, Jacob C. Ullrich, Omer Weissbrod, Mark J. Daly,  
 531 Benjamin M. Neale, Zhou Fan, and Hilary K. Finucane. Improving fine-mapping by mod-  
 532 eling infinitesimal effects. *Nature Genetics*, 56(1):162–169, January 2024. ISSN 1546-  
 533 1718. doi: 10.1038/s41588-023-01597-3. URL <https://www.nature.com/articles/s41588-023-01597-3>. Publisher: Nature Publishing Group.  
 534

535

540 A. P. Dempster, N. M. Laird, and D. B. Rubin. Maximum Likelihood from Incomplete Data via the  
 541 EM Algorithm. *Journal of the Royal Statistical Society. Series B (Methodological)*, 39(1):1–38,  
 542 1977. ISSN 0035-9246. URL <https://www.jstor.org/stable/2984875>.

543 Sander Devriendt, Katrien Antonio, Tom Reynkens, and Roel Verbelen. Sparse Regression with  
 544 Multi-type Regularized Feature Modeling. *Insurance: Mathematics and Economics*, 96:248–  
 545 261, January 2021. ISSN 01676687. doi: 10.1016/j.insmatheco.2020.11.010. URL [http://arxiv.org/abs/1810.03136](https://arxiv.org/abs/1810.03136). arXiv:1810.03136 [stat].

546 Bradley Efron. Bayes, Oracle Bayes and Empirical Bayes. *Statistical Science*, 34  
 547 (2):177–201, May 2019. ISSN 0883-4237, 2168-8745. doi: 10.1214/18-STS674.  
 548 URL <https://projecteuclid.org/journals/statistical-science/volume-34/issue-2/Bayes-Oracle-Bayes-and-Empirical-Bayes/10.1214/18-STS674.full>. Publisher: Institute of Mathematical Statistics.

549 Federico Errica, Davide Bacci, and Alessio Micheli. Graph Mixture Density Networks. In *Proceed-  
 550 ings of the 38th International Conference on Machine Learning*, volume 139 of *Proceedings of  
 551 Machine Learning Research*, pp. 3025–3035. PMLR, 2021. URL <https://proceedings.mlr.press/v139/errica21a.html>.

552 Jan Gertheiss and Gerhard Tutz. Sparse modeling of categorial explanatory variables.  
 553 *The Annals of Applied Statistics*, 4(4):2150–2180, December 2010. ISSN 1932-  
 554 6157, 1941-7330. doi: 10.1214/10-AOAS355. URL <https://projecteuclid.org/journals/annals-of-applied-statistics/volume-4/issue-4/Sparse-modeling-of-categorial-explanatory-variables/10.1214/10-AOAS355.full>. Publisher: Institute of Mathematical Statistics.

555 Rafael C. Gonzalez and Richard E. Woods. *Digital Image Processing*. Prentice Hall, Upper Saddle  
 556 River, NJ, USA, 2nd edition, 2002.

557 Kristine L. Haftorn, Yunsung Lee, William R. P. Denault, Christian M. Page, Haakon E. Nustad,  
 558 Robert Lyle, Håkon K. Gjessing, Anni Malmberg, Maria C. Magnus, Øyvind Næss, Darina  
 559 Czamara, Katri Räikkönen, Jari Lahti, Per Magnus, Siri E. Håberg, Astanand Jugessur, and Jon  
 560 Bohlin. An EPIC predictor of gestational age and its application to newborns conceived by assisted  
 561 reproductive technologies. *Clinical Epigenetics*, 13(1):82, April 2021. ISSN 1868-7083. doi: 10.  
 562 1186/s13148-021-01055-z. URL <https://doi.org/10.1186/s13148-021-01055-z>.

563 Hussein Hazimeh, Rahul Mazumder, and Tim Nonet. L0Learn: A Scalable Package for Sparse  
 564 Learning using L0 Regularization. *Journal of Machine Learning Research*, 24(205):1–8, 2023.  
 565 ISSN 1533-7928. URL <http://jmlr.org/papers/v24/22-0189.html>.

566 Arthur E. Hoerl and Robert W. Kennard. Ridge Regression: Biased Estimation for Nonorthog-  
 567 onal Problems. *Technometrics*, 12(1):55–67, 1970. ISSN 0040-1706. doi: 10.2307/1267351.  
 568 URL <https://www.jstor.org/stable/1267351>. Publisher: [Taylor & Francis, Ltd.,  
 569 American Statistical Association, American Society for Quality].

570 Steve Horvath and Kenneth Raj. DNA methylation-based biomarkers and the epigenetic  
 571 clock theory of ageing. *Nature Reviews Genetics*, 19(6):371, June 2018. ISSN 1471-  
 572 0064. doi: 10.1038/s41576-018-0004-3. URL <https://www.nature.com/articles/s41576-018-0004-3>.

573 T. Huang, G. Yang, and G. Tang. A fast two-dimensional median filtering algorithm. *IEEE Transac-  
 574 tions on Acoustics, Speech, and Signal Processing*, 27(1):13–18, February 1979. ISSN 0096-3518.  
 575 doi: 10.1109/TASSP.1979.1163188. URL <https://ieeexplore.ieee.org/document/1163188>.

576 Youngseok Kim, Peter Carbonetto, Matthew Stephens, and Mihai Anitescu. A Fast Algorithm for  
 577 Maximum Likelihood Estimation of Mixture Proportions Using Sequential Quadratic Programming.  
 578 *Journal of Computational and Graphical Statistics*, 0(0):1–13, November 2019. ISSN 1061-8600.  
 579 doi: 10.1080/10618600.2019.1689985. URL <https://doi.org/10.1080/10618600.2019.1689985>.

594 Youngseok Kim, Wei Wang, Peter Carbonetto, and Matthew Stephens. A flexible empirical Bayes  
 595 approach to multiple linear regression and connections with penalized regression. *Journal of*  
 596 *Machine Learning Research*, 25(185):1–59, 2024. ISSN 1533-7928. URL <http://jmlr.org/papers/v25/22-0953.html>.  
 597

598 Thomas N Kipf and Max Welling. SEMI-SUPERVISED CLASSIFICATION WITH GRAPH  
 599 CONVOLUTIONAL NETWORKS. 2017.

601 Ismael Lemhadri, Feng Ruan, Louis Abraham, and Robert Tibshirani. LassoNet: A Neural Network  
 602 with Feature Sparsity. *Journal of Machine Learning Research*, 22(127):1–29, 2021. ISSN  
 603 1533-7928. URL <http://jmlr.org/papers/v22/20-848.html>.

604 Eric Nalisnick, Akihiro Matsukawa, Yee Whye Teh, Dilan Gorur, and Balaji Lakshminarayanan.  
 605 Hybrid Models with Deep and Invertible Features. In *Proceedings of the 36th International Conference*  
 606 *on Machine Learning*, pp. 4723–4732. PMLR, May 2019. URL <https://proceedings.mlr.press/v97/nalisnick19b.html>. ISSN: 2640-3498.

607

608 Margret-Ruth Oelker and Gerhard Tutz. A uniform framework for the combination of penalties  
 609 in generalized structured models. *Advances in Data Analysis and Classification*, 11(1):97–120,  
 610 March 2017. ISSN 1862-5355. doi: 10.1007/s11634-015-0205-y. URL <https://doi.org/10.1007/s11634-015-0205-y>.

611

612 D. I. Okoh, G. K. Seemala, A. B. Rabiu, J. Uwamahoro, J. B. Habarulema, and M. Ag-  
 613 garwal. A Hybrid Regression-Neural Network (HR-NN) Method for Forecasting the So-  
 614 lar Activity. *Space Weather*, 16(9):1424–1436, 2018. ISSN 1542-7390. doi: 10.1029/  
 615 2018SW001907. URL <https://onlinelibrary.wiley.com/doi/abs/10.1029/2018SW001907>.  
 616

617

618 Nicholas G. Polson, James G. Scott, and Brandon T. Willard. Proximal Algorithms  
 619 in Statistics and Machine Learning. *Statistical Science*, 30(4):559–581, November  
 620 2015. ISSN 0883-4237, 2168-8745. doi: 10.1214/15-STS530. URL <https://projecteuclid.org/journals/statistical-science/volume-30/issue-4/Proximal-Algorithms-in-Statistics-and-Machine-Learning/10.1214/15-STS530.full>. Publisher: Institute of Mathematical Statistics.

621

622

623

624

625 Herbert Robbins. An Empirical Bayes Approach to Statistics. *Proceedings of the Third Berkeley  
 626 Symposium on Mathematical Statistics and Probability, Volume 1: Contributions to the Theory  
 627 of Statistics*, 3.1:157–164, January 1956. URL <https://projecteuclid.org/ebooks/berkeley-symposium-on-mathematical-statistics-and-probability/Proceedings-of-the-Third-Berkeley-Symposium-on-Mathematical-Statistics-and/Chapter/An-Empirical-Bayes-Approach-to-Statistics/bsmsp/1200501653>. Publisher: University of California Press.

626

627

628

629

630

631

632 Craig Saunders, Alexander Gammerman, and Volodya Vovk. Ridge Regression Learning Algorithm  
 633 in Dual Variables. In *Proceedings of the 15th International Conference on Machine Learning*  
 634 (ICML), pp. 515–521. Morgan Kaufmann, 1998. URL [https://eprints.soton.ac.uk/258942/1/Dualrr\\_ICML98.pdf](https://eprints.soton.ac.uk/258942/1/Dualrr_ICML98.pdf).

635

636

637

638

639

640

641

642

643

644

645

646

647

648

649

650

651

652

653

654

655

656

657

658

659

660

661

662

663

664

665

666

667

668

669

670

671

672

673

674

675

676

677

678

679

680

681

682

683

684

685

686

687

688

689

690

691

692

693

694

695

696

697

698

699

700

701

702

703

704

705

706

707

708

709

710

711

712

713

714

715

716

717

718

719

720

721

722

723

724

725

726

727

728

729

730

731

732

733

734

735

736

737

738

739

740

741

742

743

744

745

746

747

748

749

750

751

752

753

754

755

756

757

758

759

760

761

762

763

764

765

766

767

768

769

770

771

772

773

774

775

776

777

778

779

780

781

782

783

784

785

786

787

788

789

790

791

792

793

794

795

796

797

798

799

800

801

802

803

804

805

806

807

808

809

810

811

812

813

814

815

816

817

818

819

820

821

822

823

824

825

826

827

828

829

830

831

832

833

834

835

836

837

838

839

840

841

842

843

844

845

846

847

848

849

850

851

852

853

854

855

856

857

858

859

860

861

862

863

864

865

866

867

868

869

870

871

872

873

874

875

876

877

878

879

880

881

882

883

884

885

886

887

888

889

890

891

892

893

894

895

896

897

898

899

900

901

902

903

904

905

906

907

908

909

910

911

912

913

914

915

916

917

918

919

920

921

922

923

924

925

926

927

928

929

930

931

932

933

934

935

936

937

938

939

940

941

942

943

944

945

946

947

948

949

950

951

952

953

954

955

956

957

958

959

960

961

962

963

964

965

966

967

968

969

970

971

972

973

974

975

976

977

978

979

980

981

982

983

984

985

986

987

988

989

990

991

992

993

994

995

996

997

998

999

999

648 Ryan J. Tibshirani and Jonathan Taylor. The solution path of the generalized lasso. *The Annals of*  
 649 *Statistics*, 39(3):1335–1371, June 2011. ISSN 0090-5364, 2168-8966. doi: 10.1214/11-AOS878.  
 650 URL <https://projecteuclid.org/journals/annals-of-statistics/volume-39/issue-3/The-solution-path-of-the-generalized-lasso/10.1214/11-AOS878.full>. Publisher: Institute of Mathematical Statistics.

653 Gerhard Tutz and Margret-Ruth Oelker. Modelling Clustered Heterogeneity: Fixed Effects, Random  
 654 Effects and Mixtures. *International Statistical Review*, 85(2):204–227, 2017. ISSN 1751-5823.  
 655 doi: 10.1111/insr.12161. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/insr.12161>. \_eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1111/insr.12161>.

656 Wei Wang and Matthew Stephens. Empirical Bayes Matrix Factorization. *Journal of Machine Learning  
 657 Research*, 22(120):1–40, 2021. ISSN 1533-7928. URL <http://jmlr.org/papers/v22/20-589.html>.

658 Jason Willwerscheid, Peter Carbonetto, and Matthew Stephens. ebnm: An R Package for Solving the  
 659 Empirical Bayes Normal Means Problem Using a Variety of Prior Families, March 2024. URL  
 660 <http://arxiv.org/abs/2110.00152>. arXiv:2110.00152 [stat].

661 Dongyue Xie. *Empirical Bayes methods for count data*. PhD thesis, 2023.

662 Guan Yu, , and Yufeng Liu. Sparse Regression Incorporating Graphical Structure Among  
 663 Predictors. *Journal of the American Statistical Association*, 111(514):707–720, April  
 664 2016. ISSN 0162-1459. doi: 10.1080/01621459.2015.1034319. URL <https://doi.org/10.1080/01621459.2015.1034319>. Publisher: ASA Website \_eprint:  
 665 <https://doi.org/10.1080/01621459.2015.1034319>.

666 Ming Yuan and Yi Lin. Model selection and estimation in regression with grouped vari-  
 667 ables. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 68(1):  
 668 49–67, 2006. ISSN 1467-9868. doi: 10.1111/j.1467-9868.2005.00532.x. URL <https://onlinelibrary.wiley.com/doi/abs/10.1111/j.1467-9868.2005.00532.x>.  
 669 \_eprint: <https://onlinelibrary.wiley.com/doi/pdf/10.1111/j.1467-9868.2005.00532.x>.

670 Hui Zou and Trevor Hastie. Regularization and Variable Selection Via the Elastic Net. *Journal of  
 671 the Royal Statistical Society Series B: Statistical Methodology*, 67(2):301–320, April 2005. ISSN  
 672 1369-7412, 1467-9868. doi: 10.1111/j.1467-9868.2005.00503.x. URL <https://academic.oup.com/jrssb/article/67/2/301/7109482>.

## 681 A APPENDIX

### 682 A.1 DETAILED SPLIT VEB FOR THE NASH MODEL

683 The Nash model with side information can be written as:

$$684 \mathbf{y} | \mathbf{X}, \boldsymbol{\beta}, \sigma^2 \sim N(\mathbf{X}\boldsymbol{\beta}, \sigma^2) \quad (27)$$

$$685 \beta_j \sim N(b_j, \sigma_0^2) \quad (28)$$

$$686 b_j \sim g(\cdot; \mathbf{d}_j, \theta) \quad (29)$$

687 As noted in our manuscript we restrict our search to posterior of the form

$$688 q(\boldsymbol{\beta}, \mathbf{b}) = \prod_j^P q_{\beta_j}(\beta_j) q_{b_j}(b_j) \quad (30)$$

689 The overall evidence lower bound (ELBO) for the Nash model is

$$690 F(q_{\boldsymbol{\beta}}, q_{\mathbf{b}}, g; \sigma^2, \sigma_0^2)_{Nash} = \sum_i \mathbb{E} \log \frac{p(y_i | \mathbf{x}_i, \boldsymbol{\beta}, \sigma^2)}{q_{\boldsymbol{\beta}}(\boldsymbol{\beta})} + \sum_j \mathbb{E} \log p(\beta_j | b_j, \sigma_0^2) + \quad (31)$$

$$691 \sum_j \mathbb{E} \log \frac{g(b_j; \mathbf{d}_j, \theta)}{q_{b_j}(b_j)} \quad (32)$$

692 Our coordinate-ascent algorithm iterates between the updating  $q_{\boldsymbol{\beta}}$  and updating  $(q_{\mathbf{b}}, g(\cdot, \cdot, \theta))$ .

702 A.1.1 UPDATE FOR  $q_{\beta_j}$   
703704 Note that given that when  $q_b, g(\cdot, \cdot, \theta)$  are fixed then the ELBO Nash model for  $q_{\beta_j}, j = 1, \dots, P$  is  
705

706 
$$F(q_{\beta_j})_{Nash} = \mathbb{E} \log(p(\mathbf{y} | \mathbf{x}_j, \beta_j, \mathbf{X}_{-j}, \boldsymbol{\beta}_{-j}, \sigma^2) + \mathbb{E} \log p(\beta_j | \bar{b}_j, \sigma_0^2) - \mathbb{E} \log q_{\beta_j} \quad (33)$$

707 
$$= \mathbb{E} \log(p(\bar{r}_j | \mathbf{x}_j, \beta_j, \sigma^2) + \mathbb{E} \log p(\beta_j | \bar{b}_j, \sigma_0^2) - \mathbb{E} \log q_{\beta_j} \quad (34)$$

708 where  $\bar{r}_j = \mathbf{y} - \mathbf{X}_{-j} \bar{\beta}_{-j}$ , this is direct consequence of Proposition 1 of Kim et al. (2024)), so the  
709 and so  $q_{\beta_j}^* = \max F(q_{\beta_j})$  is given by computing the posterior of the following simple model  
710

712 
$$\bar{r}_j = \mathbf{x}_j \beta_j + \varepsilon \quad (35)$$

713 
$$\beta_j \sim \mathcal{N}(\bar{b}_j, \sigma_0^2) \quad (36)$$

715 
$$\varepsilon \sim \mathcal{N}(0, \sigma^2) \quad (37)$$

717 By conjugacy, the posterior distribution of  $\beta_j$  has the following form  $\beta_j | \bar{r}_j, \mathbf{x}_j \sim \mathcal{N}(\bar{\beta}_j, s_j^2)$  with  
718 posterior variance  $s_j^2 = \left( \frac{\mathbf{x}_j^t \mathbf{x}_j}{\sigma^2} + \frac{1}{\sigma_0^2} \right)^{-1}$  and posterior mean  $\bar{\beta}_j = s_j^2 \left( \frac{\mathbf{x}_j^t \bar{r}_j}{\sigma^2} + \frac{\bar{b}_j}{\sigma_0^2} \right)$ . In practice  
719 given that the column of  $\mathbf{X}$  are centered  $\mathbf{x}_j^t \mathbf{x}_j^t = n - 1$  for all  $j = 1, \dots, p$ .  
720722 A.1.2 UPDATE FOR  $q_b$  AND  $g$ 723 Given  $q_{\beta}$  and  $\sigma^2$ , the ELBO for the Nash model  
724

726 
$$F(q_b, g(\cdot, \cdot, \theta))_{Nash} = \sum_j \mathbb{E} \log p(\bar{\beta}_j | b_j, \sigma_0^2) + \sum_j \mathbb{E} \log \frac{g(b_j; \mathbf{d}_j, \theta)}{q_{b_j}(b_j)} \quad (38)$$

729 This ELBO corresponds to a so-called (covariate)moderated normal mean problem (see (Stephens,  
730 2017; Willwerscheid et al., 2024)) that we detail below  
731732 **The cEBNM problem** Given  $p$  observations  $\bar{\beta}_j \in \mathbb{R}$  with known standard deviations  $s_j^2 > 0$ ,  
733  $j = 1, \dots, p$ , the normal means model (Stephens, 2017) is  
734

735 
$$\bar{\beta}_j \stackrel{\text{ind.}}{\sim} N(b_j, \sigma_0^2), \quad (39)$$

737 where the "true" means  $b_j \in \mathbb{R}$  are unknown. We further assume that  
738

739 
$$b_j \stackrel{\text{i.i.d.}}{\sim} g \in \mathcal{G}, \quad (40)$$

740 where  $\mathcal{G}$  is some prespecified family of probability distributions. The empirical Bayes (EB) approach  
741 to fitting this model exploits the fact that the noisy observations  $\bar{\beta}_j$ , contain not only information  
742 about the underlying means  $b_j$  but also about how the means are collectively distributed (i.e.,  $g$ ). EB  
743 approaches "borrow information" across the observations to estimate  $g$ , typically by maximizing the  
744 marginal log-likelihood. The unknown means  $b_j$  are generally estimated by their posterior mean.745 We adapt EBNM to a covariate-moderated setting (covariate moderated EBNM, cEBNM), where we  
746 allow the prior for the  $j$ -th unknown mean to depend on additional data  $\mathbf{d}_j$ ,  
747

748 
$$b_j \stackrel{\text{ind.}}{\sim} g(\mathbf{d}_j, \boldsymbol{\theta}) \in \mathcal{G}, \quad (41)$$

749 so that each combination of  $\boldsymbol{\theta}$  and  $\mathbf{d}_j$  maps to an element of  $\mathcal{G}$ . We refer to this modified EBNM  
750 model as "covariate-moderated EBNM" (cEBNM).  
751752 Solving the cEBNM problem, therefore, involves two key computations:  
753754 **1. Estimate the model parameters.** Compute  
755

756 
$$\hat{\boldsymbol{\theta}} := \arg \max_{\boldsymbol{\theta} \in \mathbb{R}^m} \mathcal{L}(\boldsymbol{\theta}), \quad (42)$$

756 where  $\mathcal{L}(\boldsymbol{\theta})$  denotes the marginal likelihood,  
 757

758

$$759 \mathcal{L}(\boldsymbol{\theta}) := p(\bar{\boldsymbol{\beta}} \mid \mathbf{s}, \boldsymbol{\theta}, \mathbf{D}) = \prod_{j=1}^p \int \mathcal{N}(\bar{\beta}_j; b_j, \sigma_0^2) g(b_j; \mathbf{d}_j, \boldsymbol{\theta}) db_j, \quad (43)$$

760

761 in which  $\bar{\boldsymbol{\beta}} = (\bar{\beta}_1, \dots, \bar{\beta}_p)$ ,  $\mathbf{s} = (s_1, \dots, s_n)$ ,  $\mathbf{D}$  is a matrix storing  $\mathbf{d}_1, \dots, \mathbf{d}_p$ , and  $\mathcal{N}(\bar{\beta}_j; b_j, \sigma_0^2)$   
 762 denotes the density of  $\mathcal{N}(b_j, \sigma_0^2)$  at  $\bar{\beta}_j$ , and  $g(b_j; \mathbf{d}_j, \boldsymbol{\theta})$  denotes the density of  $g(\mathbf{d}_j, \boldsymbol{\theta})$  at  $b_j$ .  
 763

764

765 **2. Compute posterior summaries.** Compute summaries from the posterior distributions, such as  
 766 the posterior means  $\bar{b}_j := \mathbb{E}[b_j \mid \bar{\boldsymbol{\beta}}_j, s_j, \hat{\boldsymbol{\theta}}, \mathbf{D}]$ , using the estimated prior,  
 767

768

$$769 p(b_j \mid \bar{\boldsymbol{\beta}}_j, s_j, \hat{\boldsymbol{\theta}}, \mathbf{D}) \propto \mathcal{N}(\hat{\beta}_j; b_j, \sigma_0^2) g(b_j; \mathbf{d}_j, \hat{\boldsymbol{\theta}}). \quad (44)$$

770

771 In summary, solving the cEBNM problem consists of finding a mapping from known quantities  
 772  $(\bar{\boldsymbol{\beta}}, \mathbf{s}, \mathbf{D})$  to a tuple  $(\hat{\boldsymbol{\theta}}, q)$ , where each  $(\mathbf{d}_j, \hat{\boldsymbol{\theta}})$  maps to an element  $g(\mathbf{d}_j, \boldsymbol{\theta}) \in \mathcal{G}$ , and  $q$  is the posterior  
 773 distribution of the unobserved  $\mathbf{b}$  given  $(\bar{\boldsymbol{\beta}}, \mathbf{s}, \mathbf{D})$ . We denote this mapping as  
 774

775

$$776 \text{cEBNM}(\hat{\boldsymbol{\beta}}, \mathbf{s}, \mathbf{D}) = (\hat{\boldsymbol{\theta}}, q). \quad (45)$$

777

778 Any prior family is admissible under the cEBMF framework so long as 45 is computable.  
 779

780

#### 781 A.1.3 UPDATE FOR $\sigma$ AND $\sigma_0^2$

782

783 The update for  $\sigma$  and  $\sigma_0^2$  are obtained by simply maximizing the ELBO  $F(q_{\boldsymbol{\beta}}, q_{\mathbf{b}}, g; \sigma^2, \sigma_0^2)_{Nash}$   
 784 with respect to  $\sigma$  and  $\sigma_0^2$ , i.e;  
 785

786

$$787 (\sigma^2)^* = \arg \max_{\sigma^2} F(q_{\boldsymbol{\beta}}, q_{\mathbf{b}}, g; \sigma^2, \sigma_0^2)_{Nash} \quad (46)$$

788

$$789 (\sigma_0^2)^* = \arg \max_{\sigma_0^2} F(q_{\boldsymbol{\beta}}, q_{\mathbf{b}}, g; \sigma^2, \sigma_0^2)_{Nash} \quad (47)$$

790

791 It turns out that using results from (Wang & Stephens, 2021) and Kim et al. (2024) that the update for  
 792

793

$$801 \sigma^2 = \frac{\|\mathbf{y} - \mathbf{X}\boldsymbol{\beta}\| + \boldsymbol{\beta}^t(\boldsymbol{\beta}_{MLE} - \boldsymbol{\beta}) + \sigma^2 p}{n + p} \quad (48)$$

802

$$803 \sigma_0^2 = \frac{\|\mathbf{y} - \mathbf{X}\mathbf{b}\| + \mathbf{b}^t(\boldsymbol{\beta} - \mathbf{b}) + \sigma_0^2 p \left(1 - \frac{\sum_j \pi_0(\mathbf{d}_j)}{p}\right)}{n + p \left(1 - \frac{\sum_j \pi_0(\mathbf{d}_j)}{p}\right)} \quad (49)$$

804

805

806

807

808

809

Where  $\boldsymbol{\beta}_{MLE}$  is the vector of  $\mathbf{x}_j^t \bar{\mathbf{r}}_j$  as defined in the section A.1.1.

## A.2 NASH OPTIMIZES A LOWER BOUND OF MR.ASH ELBO

The derivations below are adapted from Section 4.2.1 of Xie (2023). While Xie (2023) studies a different problem (smoothing Poisson counts), we draw inspiration from this work and adapt it to the high-dimensional Gaussian setting. In this section, we show that in the absence of side information, Nash optimizes a lower bound of the mr.ash evidence lower bound (ELBO).

Recall the two models, mr.ash and Nash:

mr.ash Nash (51)

$$y|X, b, \sigma^2 \sim N(Xb, \sigma^2) \quad y|X, \beta, \sigma^2 \sim N(X\beta, \sigma^2) \quad (52)$$

$$b_j \sim g(\cdot) \quad \beta_j \sim N(b_j, \sigma_0^2) \quad (53)$$

$$b_j \sim g(.) \quad (54)$$

We consider the case without side information, recall that both approach restrict their search to posteriors of the form

mr.ash Nash (55)

$$q(\mathbf{b}) = \prod_j^P q_{b_j}(b_j) \quad q(\boldsymbol{\beta}, \mathbf{b}) = \prod_j^P q_{\beta_j}(\beta_j) q_{b_j}(b_j) \quad (56)$$

So the corresponding ELBO for the two models are

$$F(q_{\beta}, g; \sigma^2)_{mr.ash} = \sum_i \mathbb{E} \log \frac{p(y_i | \mathbf{x}_i, \mathbf{b}, \sigma^2)}{q_b(\mathbf{b})} + \sum_j \mathbb{E} \log \frac{g(b_j)}{q_{b_j}(b_j)} \quad (57)$$

$$F(q_{\beta}, q_b, g; \sigma^2 \sigma_0^2)_{Nash} = \sum_i \mathbb{E} \log \frac{p(y_i | \mathbf{x}_i, \beta, \sigma^2)}{q_{\beta}(\beta)} + \sum_j \mathbb{E} \log p(\beta_j | b_j, \sigma_0^2) + \sum_j \mathbb{E} \log \frac{g(b_j)}{q_{b_j}(b_j)} \quad (58)$$

Below we show that the profiled ELBO  $F(q_\beta, g; \sigma^2)_{Nash} = \max_{q_\beta} F(q_\beta, q_\beta, g; \sigma^2)_{Nash}$  is a lower bound for  $F(q_\beta, g; \sigma^2)_{mr.ash}$ .

864 A.2.1 ELBO FOR  $b_j$  IN THE NASH MODEL  
865866 The introduction of latent variable  $\beta_j$  induces a marginal density of  $b_j$  as  
867

868 
$$\log p(\mathbf{y}|\mathbf{x}, b_j, \sigma^2, \sigma_0^2) = \log \int p(\mathbf{y}|\mathbf{X}, \beta_j, \sigma^2) N(\beta_j, b_j, \sigma_0^2) g(b_j) d\beta_j \quad (59)$$
  
869

870 We denote  $\log p(\mathbf{y}|\mathbf{x}, b_j, \sigma_0^2)$  by  $\log f(b_j)$ . Before demonstrating that Nash optimizes a lower bound  
871 for the mr.ash approximation, we first introduce a lemma.  
872873 **Lemma** *The second order derivative of  $\log f(\cdot)$  with respect to  $b$  is lower bounded by  $-1/\sigma_0^2$ .*  
874875 *Proof.* The second derivative of  $\log f(b)$  is  
876

877 
$$\frac{d^2 \log f(b_j)}{db_j^2} = \frac{f''(b_j)}{f(b_j)} - \left( \frac{f'(b_j)}{f(b_j)} \right)^2 \quad (60)$$
  
878

879 where  
880

881 
$$f'(b_j) = \frac{1}{\sigma_0^2} f(b_j) \int \beta p(\beta | b_j) g(b_j) d\beta - \frac{\beta}{\sigma_0^2} f(b_j) = \frac{1}{\sigma_0^2} f(b_j) (\mathbb{E}(\beta) - b_j),$$
  
882

883 
$$f''(b_j) = \frac{1}{(\sigma_0^2)^2} f(b_j) (\mathbb{E}(\beta^2) - b_j \mathbb{E}(\beta)) - \frac{1}{\sigma_0^2} f(b_j) - \frac{b_j}{\sigma_0^2} \quad (61)$$
  
884

885 
$$= f(b_j) \left( \frac{1}{(\sigma_0^2)^2} \mathbb{E}(\beta^2) - \frac{2b_j}{(\sigma_0^2)^2} \mathbb{E}(\beta) - \frac{1}{\sigma_0^2} + \frac{b_j^2}{(\sigma_0^2)^2} \right) \quad (62)$$
  
886

887 where the expectation are under  $p(\beta_j | \mathbf{y}, \mathbf{X}, b_j, \sigma, \sigma_0^2)$   
888889 Substituting  $f'(b_j)$  and  $f''(b_j)$ , we have  
890

891 
$$\frac{d^2 \log f(b_j)}{db_j^2} = -\frac{1}{\sigma_0^2} + \frac{1}{(\sigma_0^2)^2} (\mathbb{E}(\beta^2) - \mathbb{E}(\beta)^2) \geq -\frac{1}{\sigma_0^2} \quad (63)$$
  
892

893 The primary objective is to perform inference on  $b_j$ , the most straightforward approach is to regard  
894 the marginal distribution as the prior of  $b_j$  and maximize the corresponding ELBO,  
895

896 
$$\tilde{F}(q_{\beta_j}, \sigma^2) = \mathbb{E} \log \frac{p(\mathbf{y}|\mathbf{X}, \beta_j, \beta_{-j})}{q_{\beta_j}} + \mathbb{E} \log f(\beta_j; g, \sigma^2). \quad (9)$$
  
897

898 The following theorem shows that the ELBO function maximized by the splitting approach is a lower  
899 bound of  $F(q_{\beta_j}; \sigma^2)$ .  
900901 **Theorem A.1.** *The profiled ELBO function  $F(q_{b_j}; \sigma^2, \sigma_0^2) = \max_{q_{\beta_j}} F(q_{\beta_j}, q_{b_j}; \sigma^2, \sigma_0^2)_{Nash}$  is a  
902 lower bound of  $F(q_{b_j}; \sigma^2)_{mr.ash}$ .*  
903904 *Proof.* The ELBO of Nash for  $\beta_j, b_j$  is  
905

906 
$$F(q_{\beta_j}, q_{b_j}; \sigma^2, \sigma_0^2)_{Nash} = \mathbb{E} \log p(\mathbf{y}|\mathbf{X}, \beta_j, \beta_{-j}) + \mathbb{E} \log \frac{N(\beta_j, \bar{b}_j, \sigma_0^2)}{q_{\beta_j}(\beta_j)} + \mathbb{E} \log \frac{g(b_j)}{q_{b_j}} - \frac{V_{q_{b_j}}}{2\sigma_0^2} \quad (64)$$
  
907

908 
$$= \mathbb{E} \log p(\mathbf{r}_j | \mathbf{X}_j, \beta_j) + \mathbb{E} \log \frac{N(\beta_j, \bar{b}_j, \sigma_0^2)}{q_{\beta_j}(\beta_j)} + \mathbb{E} \log \frac{g(b_j)}{q_{b_j}} - \frac{V_{q_{b_j}}}{2\sigma_0^2} \quad (65)$$
  
909

910 Where  $\mathbf{r}_j = \mathbf{y} - \mathbf{X}_{-j} \beta_{-j}$ ,  $\bar{b}_j = \mathbb{E}_{q_{b_j}}(b_j)$  and  $V_{q_{b_j}} = \mathbb{E}_{q_{b_j}}(b - \bar{b})$   
911912 Therefore the profiled Nash ELBO for  $q_{b_j}, g$  is  
913

914 
$$F(b_j, g; \sigma^2, \sigma_0^2) = \max_{q_{\beta_j}} F(q_{\beta_j}, q_{b_j}; \sigma^2, \sigma_0^2)_{Nash} \quad (66)$$
  
915

916 
$$= \log p(\mathbf{r}_j | \bar{b}_j, \sigma^2) + \mathbb{E} \log \frac{g(b_j)}{q_{b_j}} - \frac{V_{q_{b_j}}}{2\sigma_0^2} \quad (67)$$
  
917

918 The ELBO  $F(q_{\beta_j}, q_{b_j}; \sigma^2, \sigma_0^2)_{Nash}$  reach its maximum over  $q_{\beta_j}$  at  $q_{\beta_j}^* = p(\beta_j | r_j, \bar{b}_j, \sigma_0^2)$   
 919

920 A second order Taylor series expansion of  $F(q_{b_j}, g; \sigma^2)_{mr.ash}$  in around  $\bar{b}_j$  gives  
 921

$$922 \quad F(q_{b_j}; \sigma^2)_{mr.ash} = \mathbb{E} \log p(\mathbf{y} | \mathbf{X}, b_j, \mathbf{b}_{-j}, \sigma^2, \sigma_0^2) + \mathbb{E} \log \frac{g(b)}{q_b} \quad (68)$$

$$924 \quad = \log p(\mathbf{r}_{-j} | b_j, \sigma^2, \sigma_0^2) + \frac{1}{2} \left( \frac{d^2 f(b)}{db^2} \right) \Big|_{b=\bar{b}} V_{q_b} + \mathbb{E} \log \frac{g(b)}{q_b} \quad (69)$$

$$926 \quad \geq \log p(\mathbf{r}_{-j} | b_j, \sigma^2, \sigma_0^2) - \frac{1}{2\sigma_0^2} V_{q_b} + \mathbb{E} \log \frac{g(b)}{q_b} \quad (70)$$

$$928 \quad = \max_{q_{\beta_j}} F(q_{\beta_j}, q_{b_j}; \sigma^2, \sigma_0^2)_{Nash} \quad (71)$$

930 where  $\theta$  is between  $\hat{\beta}$  and  $\beta$ . The first inequality holds due to the Lemma above, and the second  
 931 inequality is due to the definition of ELBO.  $\square$   
 932

933  
 934  
 935  
 936  
 937  
 938  
 939  
 940  
 941  
 942  
 943  
 944  
 945  
 946  
 947  
 948  
 949  
 950  
 951  
 952  
 953  
 954  
 955  
 956  
 957  
 958  
 959  
 960  
 961  
 962  
 963  
 964  
 965  
 966  
 967  
 968  
 969  
 970  
 971

972 A.3 REAL DATA EXPERIMENT  
973974 A.3.1 GROUP-BASED AND HIERARCHICAL SIDE INFORMATION  
975976 This section clarifies the construction of  $(X, y)$ , the definition of the side information  $d_j$ , the neural  
977 architecture used to parameterize the prior, and how the prior induces covariate-specific shrinkage.  
978 This applies to the datasets *SNP500*, *GSE40279*, and *TCGA*.979 **Side information.** In group-structured regression, each covariate  $j$  belongs to a group  $k(j) \in$   
980  $\{1, \dots, K\}$ . We encode this using a one-hot vector.  
981

982 
$$d_j \in \{0, 1\}^K, \quad d_{j,k} = 1 \iff j \in \text{group } k.$$
  
983

984 This representation allows the prior on coefficient  $b_j$  to depend explicitly on the group membership  
985 of covariate  $j$ .986 **Prior parameterization.** We use a mixture density network (MDN) to produce the group-specific  
987 shrinkage prior  
988

989 
$$g(b_j \mid d_j, \theta) = \pi_0(d_j) \delta_0 + \sum_{k=1}^M \pi_k(d_j) N(\mu_k(d_j), \sigma_k^2(d_j)),$$
  
990  
991

992 with  $g_0 = \delta_0$  fixed. The MDN learns the smooth mapping  $d_j \mapsto \{\pi_k(d_j), \mu_k(d_j), \sigma_k^2(d_j)\}$  so that  
993 different groups receive different shrinkage patterns.  
994995 **Neural network architecture.** The MDN is implemented as a fully connected feed-forward network  
996 with three affine layers and ReLU activations. Given  $d_j \in \mathbb{R}^q$ , the network computes  
997

998 
$$h_1 = \text{ReLU}(W_1 d_j + b_1), \quad h_2 = \text{ReLU}(W_2 h_1 + b_2),$$
  
999 
$$\pi(d_j; \theta) = \text{Softmax}(W_3 h_2 + b_3).$$
  
1000

1001 Here,  
1002

1003 
$$W_1 \in \mathbb{R}^{H \times q}, \quad W_2 \in \mathbb{R}^{H \times H}, \quad W_3 \in \mathbb{R}^{(M+1) \times H},$$
  
1004 and we use  $H = 32$  in all experiments. The final layer outputs the  $(M+1)$  mixture weights for the  
1005 spike-and-slab prior, along with  $2M$  linear outputs for the means and log-variances of the continuous  
1006 mixture components.  
1007

1008 All networks in this section are trained using the Adam optimizer with a learning rate  $10^{-3}$  for 100  
1009 epochs.  
10101009 A.3.2 CONTINUOUS SIDE INFORMATION  
10101011 In the *AirPassengers* application, the side information associated with each coefficient is continuous  
1012 rather than categorical. This section clarifies how the side information  $d_j$  is constructed and how the  
1013 MDN adapts shrinkage continuously across covariates.1014 **Side information.** When covariates are associated with continuous metadata—such as time, spatial  
1015 location, or continuous annotations—we encode each covariate  $j$  using a real-valued feature vector  
1016

1017 
$$d_j \in \mathbb{R}^q,$$
  
1018

1019 where  $q$  depends on the application. Examples include (i)  $d_j = t_j$  for time-indexed covariates,  
1020 (ii)  $d_j = (x_j, y_j)$  for 2D spatial structure, and (iii) multi-dimensional continuous annotations. This  
1021 allows the prior strength and sparsity pattern to vary smoothly as a function of  $d_j$ .1022 **Prior parameterization via an MDN.** The mixture density network used here is identical to the  
1023 architecture described in Section A.3.1. It outputs the mixture weights and mixture parameters as  
1024 continuous functions of  $d_j$ .  
10251026 All MDNs in this section are trained using Adam with a learning rate  $10^{-3}$  for 100 epochs.

1026 A.3.3 GRAPH-BASED SIDE INFORMATION  
1027

1028 In the MNIST denoising experiment, the covariates correspond to pixels on a two-dimensional grid.  
1029 This induces a natural graph structure that the prior can exploit to encourage spatial smoothness while  
1030 allowing for sharp boundaries and local adaptivity. Below we describe the construction of the side  
1031 information  $d_j$ , the graph  $G = (V, E)$ , and the neural architecture used to parameterize the fused  
1032 prior.

1033

1034 **Side information from 2D coordinates.** Each coefficient  $b_j$  corresponds to a pixel located at  
1035  $(d_{j1}, d_{j2})$  on an  $n \times n$  grid. We encode its spatial position as the normalized coordinate pair

1036

$$1037 \quad d_j = (d_{j1}/n, d_{j2}/n),$$

1038

1039 so that both components lie in  $[0, 1]$ . This representation allows the prior to vary smoothly across  
1040 both spatial dimensions.

1040

1041

1042 **Graph construction.** We equip the pixel grid with a 4-nearest-neighbor graph:

1043

$$1044 \quad E = \{(j, k) : k \in \text{Nbh}(j)\}, \quad \text{Nbh}(j) = \{\text{up, down, left, right}\}.$$

1045

1046 This graph encodes local spatial adjacency and enables the use of message passing to incorporate  
1047 information from neighboring pixels.

1047

1048

1049 **Fused-Laplace prior.** To encourage piecewise smoothness, we employ a fused-Laplace shrinkage  
1050 prior of the form

1050

$$1051 \quad g_{\text{fused}}(d_j) = z L(0, s_1) L(v_1(d_j), s_2(d_j)), \quad (72)$$

1052

1053

1054

1055

1056 where  $L(\mu, s)$  denotes a Laplace distribution with location  $\mu$  and scale  $s$ , and  $z$  is a normalizing  
1057 constant. The first factor shrinks  $b_j$  toward zero, while the second penalizes the local difference  $v_1(d_j)$   
1058 between  $b_j$  and its neighbors. Learning  $(s_1, s_2(d_j), v_1(d_j))$  produces a data-adaptive analogue of the  
1059 fused lasso.

1060

1061

1062 **Neural parameterization via a 2-layer message-passing GNN.** The parameters of the fused prior

1063

$$(s_1, v_1(d_j), s_2(d_j))$$

1064

1065

1066

1067 are produced by a *two-layer message-passing neural network* (MPNN) operating on the graph  
1068  $G = (V, E)$ . Let  $h_j^{(0)} = d_j$  denote the initial node features. The GNN performs two rounds of  
1069 message passing:

1070

1071

1072

$$h_j^{(1)} = \text{ReLU} \left( W_1 h_j^{(0)} + \sum_{k \in \text{Nbh}(j)} W_{\text{msg}} h_k^{(0)} \right),$$

1073

1074

1075

$$h_j^{(2)} = \text{ReLU} \left( W_2 h_j^{(1)} + \sum_{k \in \text{Nbh}(j)} W'_{\text{msg}} h_k^{(1)} \right).$$

1076

1077

1078

1079 A final linear layer produces the prior parameters:

1080

1081

1082

$$(s_1, s_2(d_j), v_1(d_j)) = \text{Softplus} \left( W_3 h_j^{(2)} + b_3 \right).$$

1083

1084

1085

1086 This architecture allows the shrinkage strength  $s_1$ , the smoothness scale  $s_2(d_j)$ , and the fused-lasso  
1087 direction  $v_1(d_j)$  to depend not only on the spatial coordinates of pixel  $j$ , but also on the features of  
1088 its neighbors through message passing.

1089

1090

1091 We use  $H = 64$  hidden dimensions and train all GNNs using the Adam optimizer with learning rate  
1092  $10^{-3}$  for 100 epochs.

1080

## A.3.4 OTHER METHODS

1081

1082

1083

1084

1085

1086

1087

1088

1089

1090

1091

1092

1093

1094

1095

1096

1097

1098

1099

1100

1101

1102

1103

1104

1105

1106

1107

1108

1109

1110

1111

1112

1113

1114

1115

1116

1117

1118

1119

1120

1121

1122

1123

1124

1125

1126

1127

1128

1129

1130

1131

1132

1133

**MLP/Feed forward neural network:** We trained a feed-forward neural network (NN) as a baseline for comparison. The network consists of three fully connected layers: an input layer followed by two hidden layers of sizes 128 and 64, each with ReLU activation. The output is a single linear unit predicting a continuous response. The input features were standardized to zero mean and unit variance based on the training set. The model was trained using the Adam optimizer with a learning rate of 0.001 and mean squared error (MSE) loss. Each model was trained for 100 epochs using all training samples in batch mode. Training and evaluation were implemented in PyTorch. RMSE was computed on each test split, and average RMSE across the 10 folds is reported.

**xgboost:** We trained gradient-boosted decision trees using the xgboost *R* package with default hyperparameters. Specifically, we used root mean square error as objective for regression. Each model was trained using 50 boosting iterations (default parameter) with a maximum tree depth of 6 and a learning rate (eta) of 0.3.

**MNIST** We evaluated seven denoising methods on the MNIST dataset with additive Gaussian noise of standard deviation  $\sigma = 0.2$ , applied independently to each pixel. Each method was applied to 20 randomly selected test images, and performance was measured using root mean squared error (RMSE) against the clean image. The Noise2Self model was a convolutional neural network (CNN) with three convolutional layers:  $\text{Conv}_{1 \rightarrow 32} \rightarrow \text{ReLU} \rightarrow \text{Conv}_{32 \rightarrow 32} \rightarrow \text{ReLU} \rightarrow \text{Conv}_{32 \rightarrow 1}$ . It was trained using masked pixel regression, where approximately 10% of pixels were randomly set to zero during each training iteration and the model was trained to reconstruct them. The loss was computed only over masked pixels using mean squared error. We trained the Noise2Self model for 5 epochs using the Adam optimizer with a learning rate of  $10^{-3}$  and batch size 64.

The Nash-fused was trained using a message passing GNN representing each image as a 784-node graph corresponding to a  $28 \times 28$  grid, with 4-neighbor connectivity and node features consisting of the noisy intensity and normalized spatial coordinates. The underlying graph neural network had two hidden layers with ReLU activations. We trained Nash-fused separately for each image using 300 steps of gradient descent with the Adam optimizer and learning rate  $10^{-2}$ .

Classical baselines included total variation (TV) denoising, fused lasso, Gaussian smoothing, and non-local means (NLM). TV denoising used regularization weight 0.1. Fused lasso was formulated as a convex optimization problem with an  $\ell_2$  data fidelity term and isotropic TV penalty, solved using cvxpy with the SCS solver. Gaussian filtering used a fixed kernel with standard deviation  $\sigma = 1$ . NLM used the implementation from skimage.restoration with parameters  $h = 1.15 \cdot \hat{\sigma}$  (where  $\hat{\sigma}$  is estimated from the image), patch size 3, and patch distance 5.

**CNN:** We also included a small convolutional neural network as a baseline for image denoising. The model receives a noisy  $28 \times 28$  grayscale image and predicts a clean version of the same dimensions. Its architecture consists of four convolutional layers with ReLU nonlinearities, following a standard encoder-decoder design: Conv1:  $1 \rightarrow 32$  filters, kernel  $3 \times 3$ , padding 1, ReLU; Conv2:  $32 \rightarrow 64$  filters, kernel  $3 \times 3$ , padding 1, ReLU; Conv3:  $64 \rightarrow 32$  filters, kernel  $3 \times 3$ , padding 1, ReLU; Conv4:  $32 \rightarrow 1$  filter, kernel  $3 \times 3$ , padding 1, linear output.

The model is trained via mean squared error (MSE) between predicted and true clean pixels, using Adam optimizer with a learning rate of  $10^{-3}$  using five epochs, on a single image. See Figure 3

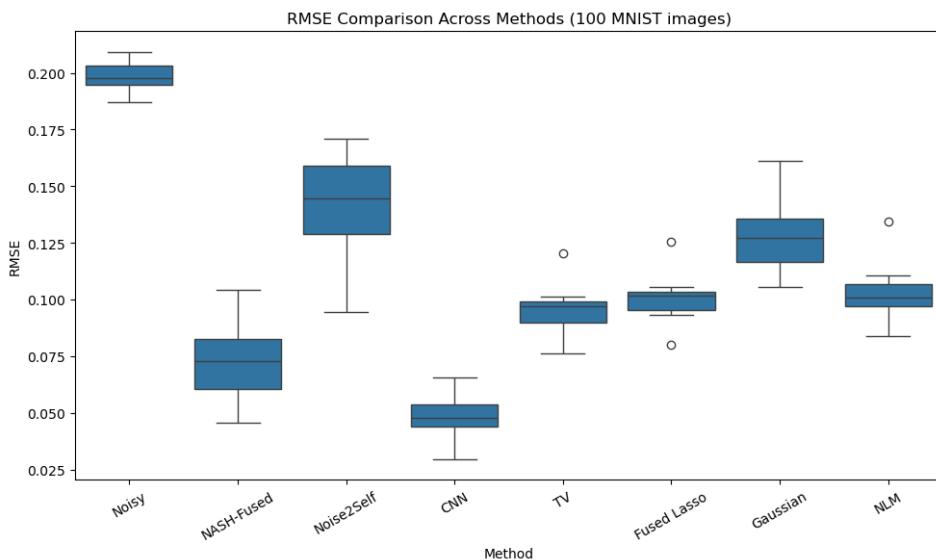


Figure 3: performances of the different approaches for denoising 100 MNIST images in terms of RMSE.

#### A.4 COMPARISON WITH MR.ASH

In figure 4a, we showcase a couple of examples where we compare Nash and mr.ash both in terms of ELBO and fitted performance. The ELBO of Nash is particularly cumbersome to compute, as it requires storing a large number of parameters ( $O(MP)$ , where  $M$  is the number of mixture components in the prior and  $P$  is the number of covariates). In the example below, we display Mr.ash  $ELBO_{mr.ash} + \sum_j \mathbb{E} \log \frac{p(\beta_j | b_j, \sigma_0^2)}{q_\beta(\beta)}$ . In practice we monitor convergence as in mr.ash Kim et al. (2024) (and other commonly used variational method such as SuSiE-inf Cui et al. (2024)) by stopping the iteration when  $\|\beta^{t+1} - \beta^t\|_2^2 < 1e - 6$ . In **Algorithm 2** below, we also provide a high-level description of the differences between Nash and mr.ash.

1166  
1167  
1168  
1169  
1170  
1171  
1172  
1173  
1174  
1175  
1176  
1177  
1178  
1179  
1180  
1181  
1182  
1183  
1184  
1185  
1186  
1187

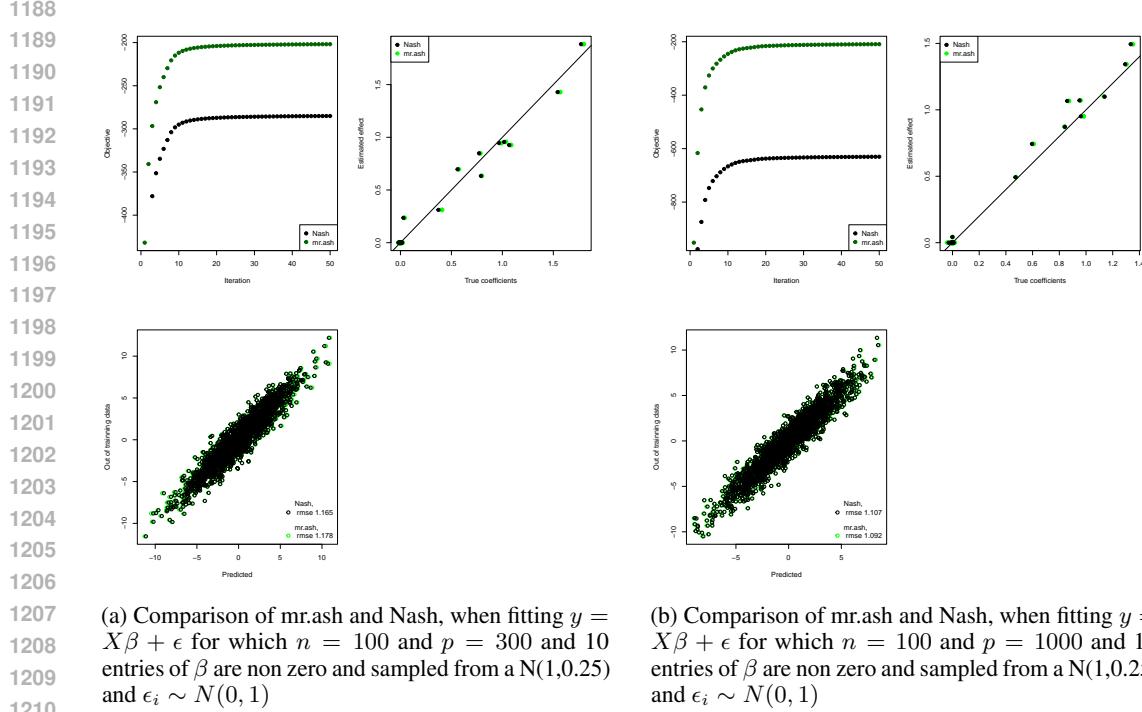


Figure 4: Comparison of mr.ash and Nash in two case examples

**Algorithm 2:** Side-by-side pseudo-code comparison of the learning procedures for `mr.ash` and `Nash`. We highlight in red the main computational differences between `mr.ash` and `Nash`

---

**mr.ash**


---

**Require:**  $X, y$ , prior model  $g(\theta)$ .

- 1: **repeat**
- 2:   **for**  $j = 1$  to  $p$  **do**
- 3:      $\bar{r}_j \leftarrow \bar{r} + x_j \bar{b}_j$
- 4:      $\tilde{b}_j \leftarrow x_j^\top \bar{r}_j$
- 5:     Update  $\bar{b}_j$  given  $\tilde{b}_j$
- 6:     Update  $g(\hat{\theta})$  given  $\tilde{b}_j$  (M-step)
- 7:      $\bar{r} \leftarrow \bar{r}_j - x_j \bar{b}_j$
- 8:   **end for**
- 9:   Update  $g(\hat{\theta})$  using  $(\tilde{b}_j)_{j=1,\dots,P}$  (E-step)
- 10: **until** convergence

---

**Nash**


---

**Require:**  $X, y$ , prior model  $g(\theta)$ .

- 1: **repeat**
- 2:   **for**  $j = 1$  to  $p$  **do**
- 3:      $\bar{r}_j = y - \sum_{j' \neq j} x_{j'} \bar{\beta}_{j'}$
- 4:      $\tilde{\beta}_j = x_j^\top \bar{r}_j$
- 5:     Update  $\bar{\beta}_j$  given  $\tilde{\beta}_j$
- 6:      $\bar{r} \leftarrow \bar{r}_j - x_j \bar{\beta}_j$
- 8:   **end for**
- 9:   Update  $g(\hat{\theta})$  using  $(\tilde{\beta}_j)_{j=1,\dots,P}$
- 10: **until** convergence

---

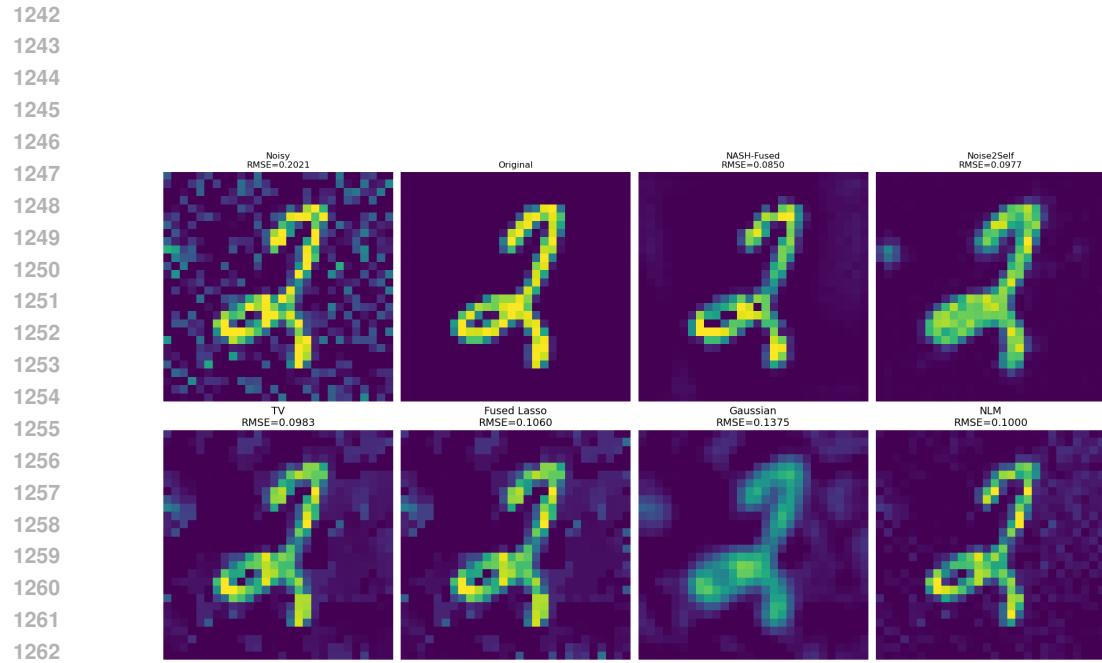


Figure 5: Additional denoised image

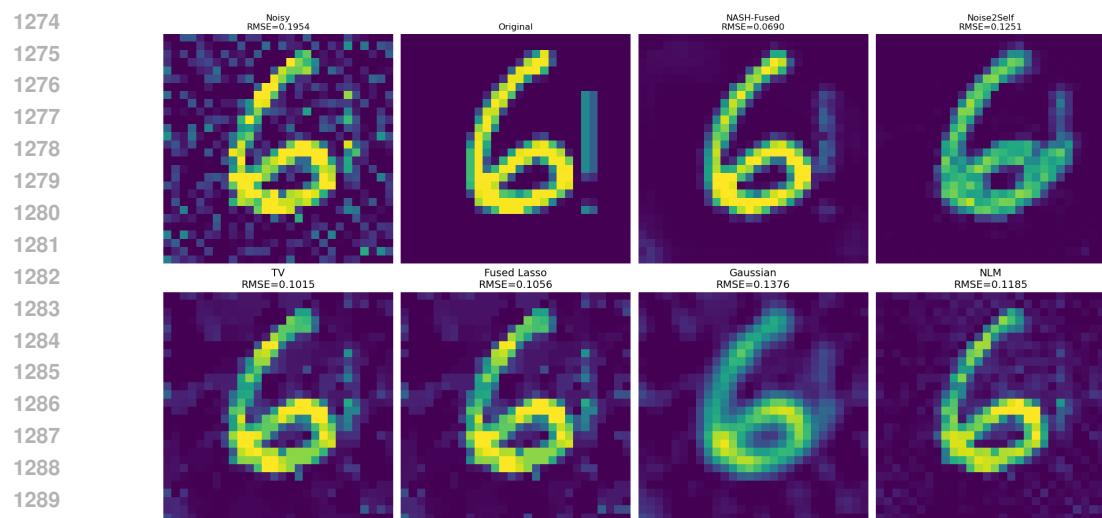


Figure 6: Additional denoised image

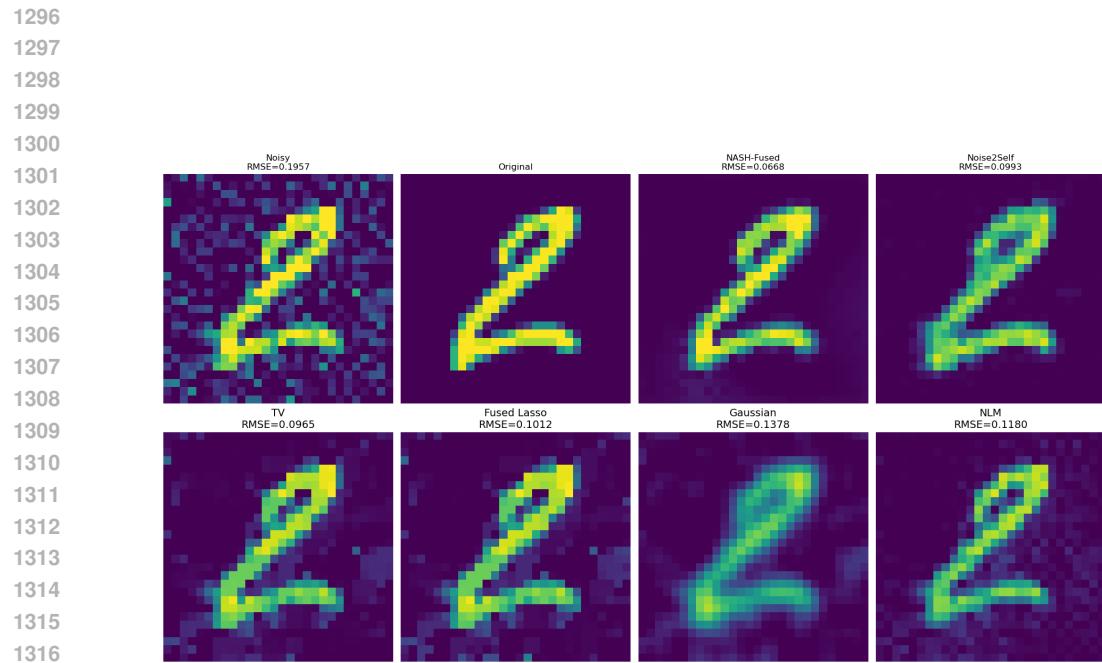


Figure 7: Additional denoised image

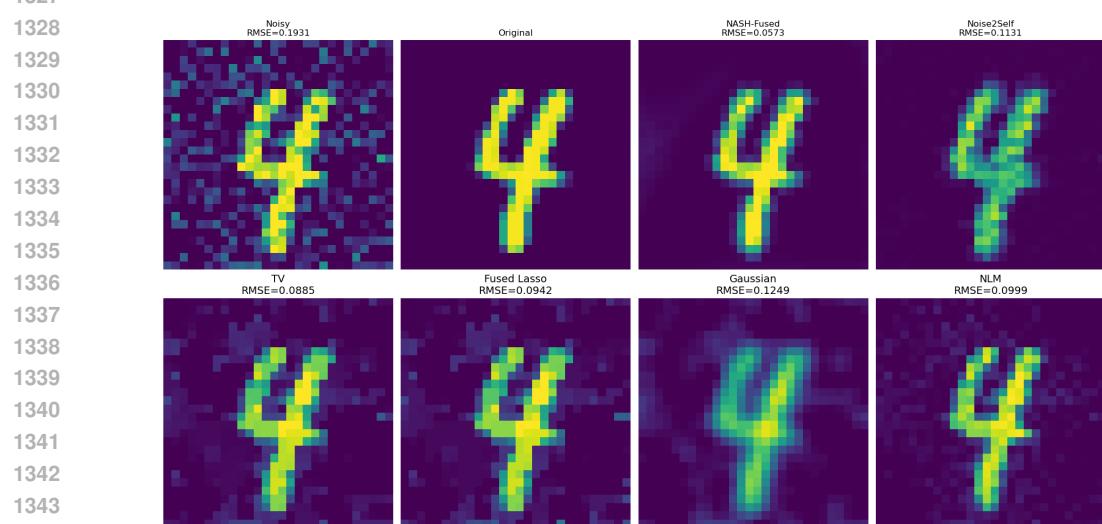


Figure 8: Additional denoised image

1344  
1345  
1346  
1347  
1348  
1349

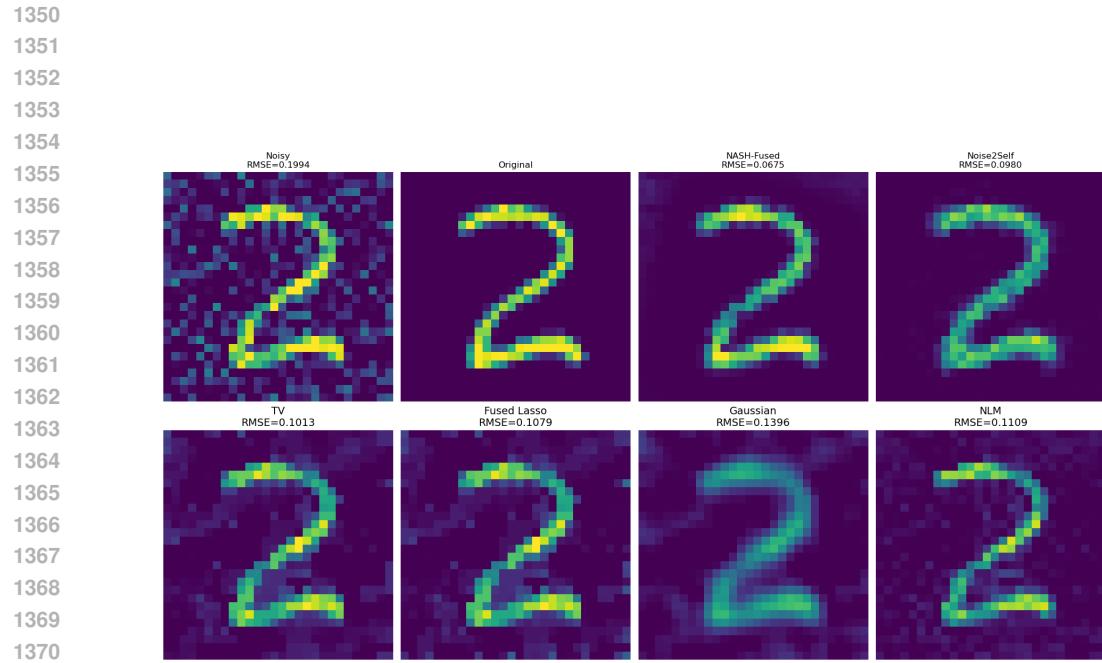


Figure 9: Additional denoised image

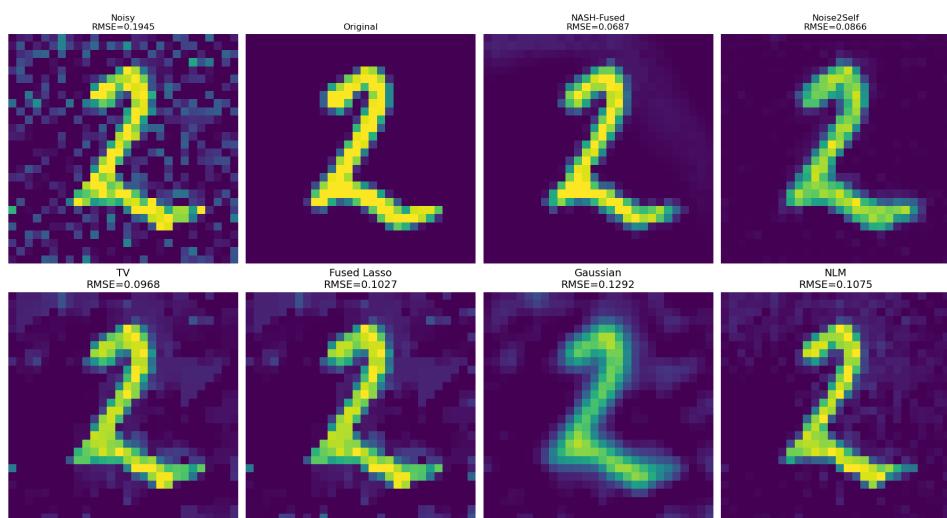


Figure 10: Additional denoised image

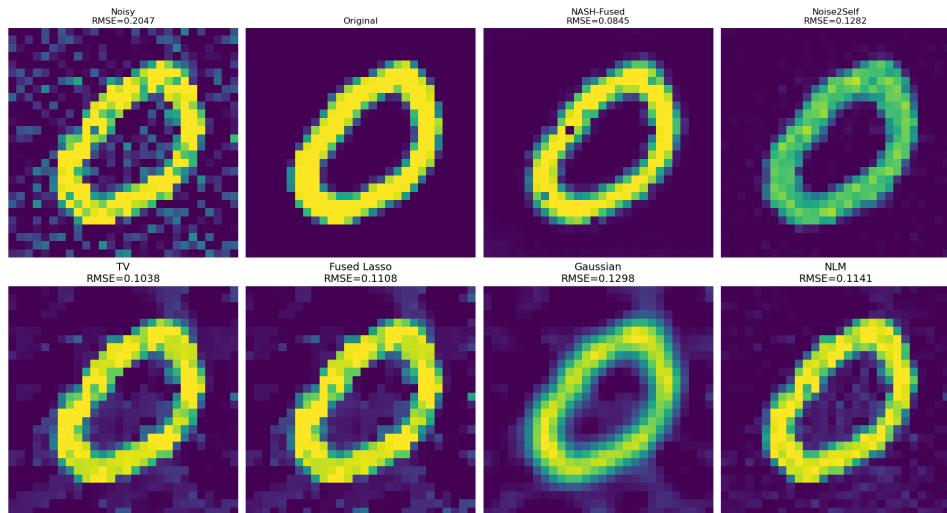


Figure 11: Additional denoised image

1404  
1405  
1406  
1407  
1408  
1409  
1410  
1411  
1412  
1413  
1414  
1415  
1416  
1417  
1418  
1419  
1420  
1421  
1422  
1423  
1424  
1425  
1426  
1427  
1428  
1429  
1430  
1431  
1432  
1433  
1434  
1435  
1436  
1437  
1438  
1439  
1440  
1441  
1442  
1443  
1444  
1445  
1446  
1447  
1448  
1449  
1450  
1451  
1452  
1453  
1454  
1455  
1456  
1457