A Flexible Empirical Bayes Approach to Multiple Linear Regression and Connections with Penalized Regression

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Abstract

We introduce a new empirical Bayes approach for large-scale multiple linear regression. Our approach combines two key ideas: (i) the use of flexible “adaptive shrinkage” priors, which approximate the nonparametric family of scale mixture of normal distributions by a finite mixture of normal distributions; and (ii) the use of variational approximations to efficiently estimate prior hyperparameters and compute approximate posteriors. Combining these two ideas results in fast and flexible methods, with computational speed comparable to fast penalized regression methods such as the Lasso, and with superior prediction accuracy across a wide range of scenarios. Furthermore, we show that the posterior mean from our method can be interpreted as solving a penalized regression problem, with the precise form of the penalty function being learned from the data by directly solving an optimization problem (rather than being tuned by cross-validation). Our methods are implemented in an R package, mr.ash.alpha, available from https://github.com/stephenslab/mr.ash.alpha

Keywords:  Empirical Bayes, variational inference, normal means, penalized linear regression, nonconvex optimization

1. Introduction

Multiple linear regression is one of the oldest statistical methods for relating an outcome variable to predictor variables, dating back at least to the eighteenth century (Stigler, 1984). In recent decades, data sets have grown rapidly in size, with the number of predictor variables often exceeding the number of observations. Fitting even simple models such as multiple linear regression to large data sets raises interesting research challenges; among these challenges, a key question is how to estimate parameters to avoid overfitting. A
great variety of approaches have been proposed, including approaches based on penalized least squares criteria (e.g., Hoerl and Kennard, 1970; Tibshirani, 1996; Fan and Li, 2011; Miller, 2002; Zou and Hastie, 2005; Zhang, 2010; Hazimeh and Mazumder, 2020), and many Bayesian approaches (e.g., Mitchell and Beauchamp, 1988; George and McCulloch, 1993; Meuwissen et al., 2001; Park and Casella, 2008; Carvalho et al., 2010; Guan and Stephens, 2011; Habier et al., 2011; Carbonetto and Stephens, 2012; Zhou et al., 2013; Wang et al., 2020; Drugowitsch, 2013; Ray and Szabó, 2021; Zabad et al., 2022). The approaches differ in the choice of penalty function or prior distribution for the regression coefficients, and in the algorithm used to arrive at estimates of the coefficients. Despite considerable past work, fitting multiple linear regression models remains an active research area.

The many different approaches to this problem naturally have strengths and weaknesses. For example, ridge regression (an $L_2$-penalty; Hoerl and Kennard, 1970; Tikhonov, 1963) has the advantages of simplicity and competitive prediction accuracy in “dense” settings that involve many predictors with non-zero effects. However, it is not well adapted to “sparse” settings where a small number of non-zero coefficients dominate. The Lasso ($L_1$-penalty; Tibshirani, 1996) is also computationally convenient, involving a simple convex optimization problem and a single tuning parameter, and behaves better in sparse settings than ridge regression. However, prediction accuracy of the Lasso is limited by its tendency to “overshrink” large effects (e.g., Su et al., 2017). The Elastic Net (Zou and Hastie, 2005) combines some of the advantages of ridge regression and the Lasso, and in its most general form includes both as special cases; however this general form also introduces an additional tuning parameter that results in (non-trivial) additional computation expense. Non-convex penalties—examples include the $L_0$-penalty (Miller, 2002; Hazimeh and Mazumder, 2020), SCAD (Fan and Li, 2011) and MCP (Zhang, 2010)—can also give better prediction performance in sparse settings, but this comes with the challenge of solving a non-convex optimization problem. Bayesian methods, by using flexible priors, have the potential to achieve excellent prediction accuracy in sparse and dense settings (e.g., Guan and Stephens, 2011; Zeng et al., 2018; Zhou et al., 2013), but have some practical drawbacks; model fitting typically involves a Markov chain Monte Carlo (MCMC) scheme with a potentially high computational burden, and convergence of the Markov chain can be difficult to diagnose, particularly for non-expert users. In summary, when choosing among existing methods, one must confront tradeoffs between prediction accuracy, flexibility, and computational convenience.

In this paper, we develop an approach to multiple linear regression that aims to combine the best features of existing methods: it is fast, comparable in speed to the cross-validated Lasso; it is flexible, capable of adapting to sparse and dense settings; it is self-tuning, with no need for user-specified hyperparameters; and, in our numerical studies, its prediction accuracy is competitive with the best methods against which we compared, and in a wide range of regression settings. Furthermore, we show that our method has a dual interpretation as both a penalized regression method and a Bayesian regression method, thereby providing a conceptual bridge between these two approaches.

Our method is based on an empirical Bayes (Robbins, 1964; Efron, 2019) (EB) approach to multiple regression, in which the regression coefficients are assumed independently drawn from some prior distribution that is estimated from the data. Empirical Bayes is, in many ways, a natural approach for attempting to attain the benefits of Bayesian methods while
addressing some of their computational challenges. However, previous EB approaches to multiple regression have either focused on relatively inflexible priors, or have been met with considerable computational challenges. For example, Nebebe and Stroud (1986) developed an EB approach with a normal prior—effectively EB Ridge regression—which makes computations easy, but is not well adapted to sparse settings. In contrast, George and Foster (2000) consider the point-normal prior (sometimes called a “spike-and-slab” prior), which is considerably more flexible, but makes computation difficult. George and Foster (2000) make several approximations, including use of “conditional maximum likelihood” (CML), which conditions on a single best model (that is, the subset of predictors with non-zero coefficients) instead of summing over all models as a conventional likelihood would. However, even the CML approximation is intractable, because finding the best model is intractable, and further approximations are required. Building on this work, Yuan and Lin (2005) also uses the CML approximation to perform EB estimation for spike-and-slab priors, but they replace the normal slab with a Laplace (double-exponential) slab. To address computational difficulties, they reduce the model’s flexibility; specifically, they constrain the two parameters of the prior to connect it to the Lasso in an interesting way, then they exploit this connection to make inferences more tractable.

Here we propose a different EB approach that is both more flexible than these previous EB approaches, and more computationally scalable. This new EB approach has two key components. First, to increase flexibility we borrow the “adaptive shrinkage” priors used in Stephens (2016); specifically, we use the scale mixture of normals version of these priors. This prior family includes most of popular choices of the priors that have been used in Bayesian regression, including normal, Laplace, point-normal, point-Laplace, point-t, normal-inverse-gamma and horseshoe priors (Hoerl and Kennard, 1970; George and McCulloch, 1997; Meuwissen et al., 2001, 2009; Habier et al., 2011). Increasing model flexibility typically means greater computational expense, but in this case the use of the adaptive shrinkage priors actually simplifies many computations, essentially because the scale mixture family is a convex family. Second, to make computations tractable, we exploit the variational approximation (VA) methods for multiple regression from Carbonetto and Stephens (2012). Although these VA methods are approximations, they improve on the CML approximation because they sum over a large set of plausible models rather than simply selecting a single best model. The main limitation of this VA approach is that, in sparse settings with very highly correlated predictors, it will give only one of the correlated predictors a non-negligible coefficient (Carbonetto and Stephens, 2012). This limitation, which is shared by several other existing methods, including the Lasso and $L_0$-penalized regression, does not greatly affect prediction accuracy. However, it does limit the conclusions that can be drawn about confidence in the selected variables. Consequently, other methods (e.g., Wang et al., 2020) may be preferred when the main goal is variable selection for scientific interpretation, rather than for prediction. Since our approach combines EB ideas with variational approximations, we refer to it as an “variational EB” (VEB) approach.

Although based on Bayesian ideas, our VEB approach can also be viewed as a penalized linear regression (PLR) method, and the algorithm we use can be viewed as a coordinate-ascent algorithm for fitting a PLR. However, in contrast to existing PLR methods which assume a relatively restrictive class of penalty functions, usually with just one or two parameters that are tuned by cross-validation, our VEB approach has a much more flexible family of
penalty functions (corresponding to our flexible family of priors), and the form of the penalty function is adapted to the data. While one might expect that this flexibility comes at a greater computational cost, in fact the VEB approach has a similar computational burden to methods such as Lasso tuning a single parameter by cross-validation, and is substantially faster than methods such as the Elastic Net that tune two parameters by cross-validation. Our methods are implemented as an R package, mr.ash.alpha (“Multiple Regression with Adaptive SHrinkage priors”), available at https://github.com/stephenslab/mr.ash.alpha.

1.1 Organization of the Paper

The remainder of this paper is organized as follows. Section 2 gives background, describes the mathematical setup, and outlines our approach. Section 3 describes the VEB methods and optimization algorithms in detail. Section 4 draws connections between our VEB approach and penalized approaches. Section 5 gives results from numerical studies comparing prediction performance of different methods for multiple linear regression, including our VEB approach. Section 6 summarizes the contributions of this work and discusses future directions.

1.2 Notations and Conventions

We write vectors in bold, lowercase letters e.g., $b$, and matrices in bold, uppercase letters, e.g., $X$. We use $\mathbb{R}^n$ to denote the set of real-valued vectors of length $n$, $\mathbb{R}_+^n$ for the set of real non-negative vectors of length $n$, we use $\mathbb{R}^{m \times n}$ to denote the set of real $m \times n$ matrices, and $S^n = \{x \in \mathbb{R}_+^n : \sum_{i=1}^n x_i = 1\}$ denotes the $n$-dimensional simplex. We use $x_j$ to denote the $j$th column of matrix $X$. We write sets and families in calligraphic font, e.g., $G$. We use $N(x; \mu, \Sigma)$ to denote the probability density of the multivariate normal distribution at $x \in \mathbb{R}^n$ with mean $\mu \in \mathbb{R}^n$ and $n \times n$ covariance matrix $\Sigma$. We use $I_n$ to denote the $n \times n$ identity matrix. Finally, $\|x\|$ denotes the $L_2$-norm of vector $x \in \mathbb{R}^n$, $\|x\| = \sqrt{x^T x}$, and $\|x\|_\infty$ denotes the $L$-infinity norm of $x$, $\|x\|_\infty = \max\{|x_1|, \ldots, |x_n|\}$.

2. Outline and Preliminaries

2.1 Empirical Bayes Linear Regression

We consider the multiple linear regression model,

$$y \mid X, b, \sigma^2 \sim N(Xb, \sigma^2 I_n),$$

(1)

where $y \in \mathbb{R}^n$ is a vector of responses, $X \in \mathbb{R}^{n \times p}$ is a design matrix whose columns contain predictors $x_1, \ldots, x_p \in \mathbb{R}^n$, $b \in \mathbb{R}^p$ is a vector of regression coefficients, and $\sigma^2 \geq 0$ is the variance of the residual errors. While an intercept is not explicitly included in (1), it is easily accounted for by centering $y$ and the columns of $X$ prior to model fitting (Chipman et al., 2001); see also Section 3.3. To simplify presentation, we will assume throughout the main text of the paper that the columns of $X$ are rescaled so that $\|x_j\| = 1$, for $j = 1, \ldots, p$. However, all our methods and results can be extended to the unscaled case, and Appendix B includes these extensions.
Flexible empirical Bayes regression

We assume a prior distribution in which the scaled regression coefficients, \( b_j / \sigma \), are independent and identically distributed (i.i.d.) from some distribution with density \( g \),

\[
\begin{align*}
b_j & \sim \text{i.i.d.} g, \\
b_j | g, \sigma^2 & \sim g, \\
\end{align*}
\]

where \( g_\sigma(b_j) \triangleq g(b_j / \sigma) / \sigma \) is the \( \sigma \)-scaled prior on the regression coefficients. Formulating the prior in terms of the scaled coefficients may help reduce issues with multi-modality; see Park and Casella (2008) for example. (The scaled prior also provides computational benefits in the “fully Bayesian” regression setting; see, for example, Chipman et al. 2001; George and McCulloch 1997; Liang et al. 2008 for arguments in favour of the scaled prior.)

All our methods can also be applied, with minor modifications, to work with the unscaled prior \( b_j | g \sim g \). Although our methods apply more generally, we focus on priors, \( g \), that are scale mixtures of normals—this choice is computationally attractive while also preserves flexibility.

Specifically, following Stephens (2016), we assume \( g \in \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2) \), where

\[
\mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2) \triangleq \left\{ g = \sum_{k=1}^{K} \pi_k N(0, \sigma_k^2) : \pi \in S^K \right\},
\]

and where \( 0 \leq \sigma_1^2 < \cdots < \sigma_K^2 < \infty \) is a pre-specified grid of component variances, and \( \pi_1, \ldots, \pi_K \) are unknown mixture proportions. Typically, the first variance \( \sigma_1^2 \) would be set exactly to zero to allow for a sparse regression model. (Here we adopt the convention that \( N(0, 0) = \delta_0 \), the Dirac “delta” mass at zero). By making this grid of variances sufficiently wide and dense, the prior family \( \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2) \) can approximate, with arbitrary accuracy, the nonparametric family of all the scale mixtures of zero-mean normal distributions. This nonparametric family, which we denote by \( \mathcal{G}_{\text{SMN}} \), includes most popular distributions used as priors in Bayesian regression models, motivated by different applications, including normal (“ridge regression”) (Hoerl and Kennard, 1970), point-normal (“spike and slab”) (Chipman et al., 2001; George and McCulloch, 1993, 1997; Mitchell and Beauchamp, 1988), double-exponential or Laplace (Figueiredo, 2003; Park and Casella, 2008; Hans, 2009; Tibshirani, 1996), horseshoe (Carvalho et al., 2010), the normal-inverse-gamma prior (Meuwissen et al., 2009; Habier et al., 2011), mixture of two normals (BSLMM) (Zhou et al., 2013), and the mixture of four zero-centered normals with different variances (BayesR) suggested by Moser et al. (2015). It is helpful to think of \( g \in \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2) \) as determining a set of mixture proportions \( \pi = (\pi_1, \ldots, \pi_K) \) and component variances \( \sigma_1^2, \ldots, \sigma_K^2 \) of a normal mixture. For \( g \in \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2) \), we can therefore write the \( \sigma \)-scaled prior (2) as

\[
b_j | g, \sigma^2 \sim \sum_{k=1}^{K} \pi_k N(0, \sigma^2 \sigma_k^2). \tag{4}
\]

It is also convenient for derivations to introduce the standard augmented-variable representation of this mixture:

\[
\begin{align*}
p(\gamma_j = k | g) &= \pi_k, \\
b_j | g, \gamma_j = k &\sim N(0, \sigma^2 \sigma_k^2), \tag{5}
\end{align*}
\]

where the discrete latent variable \( \gamma_j \in \{1, \ldots, K\} \) indicates which mixture component gave rise to \( b_j \).
A standard EB approach to fitting the regression model (1, 2) would involve the following two steps:

1. Estimate the prior density, \( g \), and the error variance, \( \sigma^2 \), by maximizing the marginal likelihood:
\[
(\hat{g}, \hat{\sigma}^2) = \arg \max_{g \in \mathcal{G}, \sigma^2 \in \mathbb{R}_+} p(y \mid X, g, \sigma^2)
= \arg \max_{g \in \mathcal{G}, \sigma^2 \in \mathbb{R}_+} \log \int p(y \mid X, b, \sigma^2) p(b \mid g, \sigma^2) \, db.
\] (6)

2. Infer \( b \) based on its posterior distribution,
\[
p_{\text{post}}(b \mid y, X, \hat{g}, \hat{\sigma}^2) \propto p(y \mid X, b, \hat{\sigma}^2) p(b \mid \hat{g}, \hat{\sigma}^2).
\] (7)

In particular, for prediction one typically estimates \( b_j \) by its posterior mean,
\[
E(b_j \mid X, y, \hat{g}, \hat{\sigma}^2) = E_{\text{post}}(b_j).
\]

Unfortunately, both steps are computationally impractical due to intractable integrals or very large sums, or both, except in special cases. For parameter estimation (Step 1), the optimization is hard due to the intractable, high-dimensional integral in the marginal likelihood. For posterior inference (Step 2), computation of the posterior (7) involves an intractable normalization constant (also the marginal likelihood), and computation of the posterior expectations may involve additional intractable integrals.

To circumvent the intractability of these steps, we use a mean-field variational approximation (Blei et al., 2017; Jordan et al., 1999; Wainwright and Jordan, 2008). Mean-field variational approximations have been previously used to implement (approximate) EB methods: the idea is mentioned explicitly in Blei et al. (2003), although earlier work implemented similar ideas (e.g., Saul and Jordan, 1996; Ghahramani and Hinton, 2000). From an algorithmic perspective, these variational approaches to EB end up solving Steps 1 and 2 iteratively because the variational approximation introduces an interdependency between the parameter estimation (Step 1) and posterior computation (Step 2). This iterative procedure can be understood as solving a single optimization problem (described in Section 3), and is a version of the generalized EM framework of Neal and Hinton (1998). Because of their close connection to EM, such algorithms are sometimes referred to as “variational EM” algorithms, although this terminology can be confusing as it has been used in other ways; for example, the “variational Bayesian EM” of Beal and Ghahramani (2003) is not the same as the approach we use here.

While variational methods have previously been used to fit Bayesian linear regression models (Girolami, 2001; Logsdon et al., 2010; Carbonetto and Stephens, 2012; Wang et al., 2020; You et al., 2014; Ren et al., 2011), they have not been used to implement an EB method, and not with the flexible class of priors (3) we consider here. (Independent of our work, Zabad et al. 2022 recently used a VEB approach with less flexible priors.) Our work here arises from the combination of two earlier ideas: (1) the use of variational approximation techniques for fast posterior computation in large-scale linear regression (Carbonetto and Stephens, 2012); and (2) the use of a flexible class of priors (3), which was originally proposed in Stephens (2016) for performing EB inference in a simpler, but related,
problem—the “normal means problem” (Efron and Morris, 1973; Johnstone and Silverman, 2004; Sun and Stephens, 2018). The combination of these two ideas results in methods that are simpler, faster, more flexible, and generally more accurate than those in Carbonetto and Stephens (2012). Before describing the new methods in detail, we first briefly review the two key ideas—variational inference for linear regression, and flexible priors for the normal means problem—that provide the building blocks for our approach.

2.2 The Empirical Bayes Normal Means Model

The normal means (NM) model is a model for a sequence $y_1, \ldots, y_n$ of observations in which each observation is normally distributed with unknown mean $b_j$ and known variance $\sigma^2$:

$$y_j \mid b_j, \sigma^2 \sim N(b_j, \sigma^2), \quad j = 1, \ldots, n.$$  

(8)

This can be viewed as a special case of the multiple regression model (1) in which $X = I_n$ and $\sigma^2$ is known. (See Appendix A for a more general definition allowing for variances that differ among observations $j$.) Stephens (2016) provides methods to fit the NM model (8) by EB (i.e., Steps 1 and 2 above, but with $\sigma^2$ fixed) for various prior classes $b_j \sim g_\sigma$ (2), with a focus on the scale mixtures of normals (4). We briefly review the fitting procedures here.

In Step 1, estimating the prior $g$ is simplified by the use of a fixed grid of variances in (4), which means that only the mixture proportions $\pi$ need to be estimated. This is done by maximizing the (marginal) likelihood under the NM model (8). Due to the conjugacy of the normal mixture prior (4) and the normal likelihood (8), the marginal likelihood has a simple, analytical form,

$$p^{\text{NM}}(y \mid g, \sigma^2) = \prod_{j=1}^p \sum_{k=1}^K \pi_k L_{jk},$$  

(9)

where $L_{jk}$ denotes the likelihood for each mixture component,

$$L_{jk} \triangleq p(y_j \mid g, \sigma^2, \gamma_j = k) = \frac{\pi_k L_{jk}}{\sum_{k'=1}^K \pi_{k'} L_{jk'}}.$$  

(10)

Thus, maximum-likelihood estimation of the mixture weights $\pi$ can be written as

$$\hat{\pi} = \arg\max_{\pi \in \mathbb{S}^K} \sum_{j=1}^p \log \sum_{k=1}^K \pi_k L_{jk},$$  

(11)

which is a convex optimization problem, and can be solved efficiently using convex optimization techniques (Koenker and Mizera, 2014; Kim et al., 2020), or more simply by iterating the following Expectation Maximization (EM) updates (Dempster et al., 1977):

E-step $\phi_{jk} \leftarrow \phi_k(y_j; g, \sigma^2) \triangleq p(\gamma_j = k \mid y_j, g, \sigma^2) = \frac{\pi_k L_{jk}}{\sum_{k'=1}^K \pi_{k'} L_{jk'}}.$  

(12)

M-step $\pi_k \leftarrow \frac{1}{p} \sum_{j=1}^p \phi_{jk}, \quad k = 1, \ldots, K.$  

(13)
The posterior mixture assignment probabilities, $\phi_{jk}$, are sometimes referred to as the “responsibilities” (e.g., Hastie et al. 2009).

Step 2, computing the posterior distribution, is also straightforward, again due to the independence of the observations and the conjugacy of the normal (mixture) prior with the normal likelihood:

$$p_{\text{NM}}^{\text{post}}(b_j, \gamma_j = k \mid y_j, g, \sigma^2) = p(\gamma_j = k \mid y_j, g, \sigma^2) p(b_j \mid y_j, g, \sigma^2, \gamma_j = k) = \phi_{jk} N(b_j; \mu_{jk}, s_{jk}^2),$$

(14)

in which $\phi_{jk} = \phi_k(y_j; g, \sigma^2)$ and the component posterior means and posterior variances are

$$\mu_{jk} \triangleq \mu_k(y_j; g, \sigma^2) = \frac{\sigma^2_k}{1 + \sigma^2_k} \times y_j;$$

(15)

$$s_{jk}^2 \triangleq s_k^2(y_j; g, \sigma^2) = \frac{\sigma^2}{1 + \sigma^2_k} \times \sigma^2.$$  

(16)

(Although the posterior variances do not depend on $y_j$, we write them as $s_k^2(y_j; g, \sigma^2)$ for notational consistency.) Summing the component posterior (14) over $k$ then yields an analytic expression for the posterior mean of $b_j$,

$$p_{\text{NM}}^{\text{post}}(b_j \mid y_j, g, \sigma^2) = \sum_{k=1}^{K} \phi_{jk} N(b_j; \mu_{jk}, s_{jk}).$$

(17)

### 2.3 Variational Inference for Linear Regression

Following previous work (e.g., Carbonetto and Stephens, 2012) we use a variational approximation (VA) to perform approximate Bayesian inference for multiple linear regression. The key idea of the VA is to approximate the intractable posterior distribution,

$$p_{\text{post}}(b, \gamma) \triangleq p(b, \gamma \mid X, y, g, \sigma^2)$$

(18)

by an approximate posterior, $q$, drawn from some family $Q$ that is chosen to make computations tractable. A common strategy is to take $Q$ to be a set of distributions that factorize in a convenient way (e.g., Bishop, 2006; Blei et al., 2017). In particular, Carbonetto and Stephens (2012) follow this strategy with the family

$$Q = \{ q : q(b, \gamma) = \prod_{j=1}^{p} q_j(b_j, \gamma_j) \}.$$  

(19)

In words, the variational posterior $q(b, \gamma)$ factorizes into a product over individual factors $q_j(b_j, \gamma_j)$, $j = 1, \ldots, p$.

Selecting a $q$ within the chosen family $Q$ then proceeds as an optimization problem,

$$\hat{q}_{g,\sigma^2} \triangleq \arg \min_{q \in Q} D_{\text{KL}}(q \parallel p_{\text{post}})$$

$$= \arg \min_{q \in Q} \int q(b, \gamma) \log \left\{ \frac{q(b, \gamma)}{p_{\text{post}}(b, \gamma)} \right\} db,$$

(20)
where $D_{KL}(q \parallel p)$ denotes the Kullback-Leibler (K-L) divergence from a distribution $q$ to a distribution $p$ (Kullback and Leibler, 1951). The notation $\hat{q}_{g,\sigma^2}$ makes clear the dependency of $\hat{q}$ on $g, \sigma^2$, just as $p_{\text{post}}$ depends on $g, \sigma^2$. In words, the aim is to find an approximate posterior $\hat{q}_{g,\sigma^2}$ within the variational family $Q$ that best fits the true posterior, where the quality of the fit is measured by the K-L divergence.

Because $D_{KL}(q \parallel p_{\text{post}})$ is itself computationally intractable, the optimization problem (20) is usually recast as an equivalent maximization problem (Jordan et al., 1999; Bishop, 2006; Blei et al., 2017),

$$\hat{q}_{g,\sigma^2} \triangleq \arg \max_{q \in Q} F(q, g, \sigma^2),$$

(21)

where

$$F(q, g, \sigma^2) \triangleq \log p(y \mid X, g, \sigma^2) - D_{KL}(q \parallel p_{\text{post}}).$$

(22)

This is often called the “Evidence Lower Bound” (ELBO) because it is a lower-bound for the “evidence,” $\log p(y \mid X, g, \sigma^2)$. (The K-L divergence term is always non-negative.) Although each of the terms on the right hand side of (22) are themselves intractable, some cancelling out occurs to make $F$ more tractable. (See Appendix B) Carbonetto and Stephens (2012) derive an algorithm to solve for $\hat{q}$ when the prior, $g$, is point-normal—that is, $g = \pi_0 \delta_0 + (1 - \pi_0)N(0, \sigma_0^2)$. This can be viewed as a special case of our approach, with $K = 2, \sigma_1^2 = 0, \sigma_2^2 = \sigma_b^2$.

To deal with the fact that $g$ and $\sigma^2$ are unknown, Carbonetto and Stephens (2012) perform approximate Bayesian inference for these parameters (specifically, for $\pi_0, \sigma_b^2, \sigma^2$). They do this by treating $F(\hat{q}_{g,\sigma^2}, g, \sigma^2)$ as a direct approximation to the evidence. That is, they use the approximation

$$p(y \mid X, g, \sigma^2) \approx \exp\{F(\hat{q}_{g,\sigma^2}, g, \sigma^2)\},$$

and combine this approximate likelihood with a prior on $g, \sigma^2$ to arrive at an approximate posterior distribution for $g, \sigma^2$. This approach of computing an approximate posterior distribution for $g, \sigma^2$ is computationally burdensome because it requires many optimizations of (21). Our approach, which we describe next, greatly simplifies this by simultaneously fitting $q, g, \sigma^2$.

3. Variational Empirical Bayes Multiple Linear Regression

With these preliminaries, our approach is straightforward to describe. In short, we combine the EB methods from Stephens (2016) for the NM problem with the VA from Carbonetto and Stephens (2012) for the multiple regression problem. The resulting VEB method reduces to solving the following optimization problem:

$$\maximize_{q \in Q, \ g \in G(\sigma_1^2, \ldots, \sigma_K^2), \ \sigma^2 \in \mathbb{R}_+} F(q, g, \sigma^2),$$

(23)

where $F(q, g, \sigma^2)$ is defined in (22). We denote a (local) solution to this problem by $(\hat{q}, \hat{g}, \hat{\sigma}^2)$. 
Algorithm 1 Coordinate ascent for fitting VEB model (outline only).

Require: Data $X \in \mathbb{R}^{n \times p}, y \in \mathbb{R}^n$, and initial estimates $q_1, \ldots, q_p, g, \sigma^2$.

repeat
  for $j \leftarrow 1$ to $p$ do
    $q_j \leftarrow \arg\max_{q_j} F(q, g, \sigma^2)$
  end for
  $g \leftarrow \arg\max_{g \in G} F(q, g, \sigma^2)$
  $\sigma^2 \leftarrow \arg\max_{\sigma^2 \in \mathbb{R}^+} F(q, g, \sigma^2)$
until termination criterion is met
return $q_1, \ldots, q_p, g, \sigma^2$.

The standard (but intractible) EB procedure (6, 7) corresponds to solving (23) with no constraint on $q$ (Wang et al., 2020, e.g. see Supplement of). By constraining $q$ to be “fully factorized” (19) the optimization problem becomes tractable. We call this approach “variational EB” (VEB) to emphasise the fact that it is a modification to the standard EB approach with a variational approximation to the posterior.

While our work is closely connected to Carbonetto and Stephens (2012), there are two key differences compared with that previous work: our work replaces the point-normal prior with the more flexible normal scale mixture family, $G(\sigma^2_1, \ldots, \sigma^2_K)$; and it replaces the numerical integration over $g, \sigma^2$ with a maximization over $g$ and $\sigma^2$ (as is conventional in EB methods). These modifications lead to substantial algorithmic simplifications and computational speedups without sacrificing prediction performance (see Section 5).

3.1 Coordinate Ascent Algorithm

The approximating distribution $q$ decomposes as a product over the individual coefficients $b_j$, for $j = 1, \ldots, p$ (19). This allows for the development of a coordinatewise algorithm for solving the optimization problem (23)—also known as CAVI, short for “coordinate ascent variational inference” (Blei et al., 2017; Bishop, 2006)—in which each update improves the ELBO by adjusting a single parameter while keeping the other parameters fixed. These coordinatewise updates are iterated until some termination criterion is met. A sketch of the generic coordinate ascent algorithm, with few assumptions made, is given in Algorithm 1.

The key result of this section—and a key benefit of the VEB approach—is that each step of Algorithm 1 involves only simple analytic computations from the EB normal means model (2, 8):

(i) The update for each $q_j$ involves computing a posterior distribution (17) under the normal means model.

(ii) The update for $g$ involves running a single M-step update (13) for the normal means model, in which the exact posterior probabilities are replaced with approximate posterior probabilities.
(iii) The coordinatewise update for the residual variance, $\sigma^2$, also has a simple, closed-form solution. These results are summarized in the following proposition.

We emphasize that these properties are the result of making only a single assumption that $q$ factorizes as a product over the coordinates $j$ (19). No other assumptions are needed.

**Proposition 1 (Coordinate ascent updates for VEB)** Assume $x_j^T x_j = 1$, for $j = 1, \ldots, p$, let $\bar{b}_j = \mathbb{E}(b_j)$, $\bar{b} = \mathbb{E}(b)$ be the expected values of $b_j, b$ with respect to $q$, $\bar{r} = y - X\bar{b} \in \mathbb{R}^n$ is the vector of expected residuals with respect to $q$, $X_{-j}$ denotes the design matrix $X$ excluding the $j$th column, $q_{-j}$ is shorthand for all factors $q_{j'}$ other than $q_j$, and $\bar{r}_j \in \mathbb{R}^n$ is the vector of expected residual accounting for linear effects of all variables other than $j$,

$$\bar{r}_j \triangleq y - X_{-j}\bar{b}_{-j} = y - \sum_{j' \neq j} x_j' \bar{b}_{j'}.$$  

Additionally, we use $\tilde{b}_j \triangleq x_j^T \bar{r}_j = \bar{b}_j + x_j^T \bar{r}$ to denote the ordinary least squares (OLS) estimate of the coefficient $b_j$ when the residuals $\bar{r}_j$ are regressed against $x_j$. Then we have the following results:

(i) The coordinate ascent update $q_j^* \triangleq \arg \max_{q_j} F(q, g, \sigma^2)$ is obtained by the posterior distribution for $b_j, \gamma_j$ under the normal means model (2, 8) in which the observation $y_j$ is replaced by the OLS estimate of $b_j$; that is,

$$q_j^*(b_j) = p_{\text{post}}^{\text{NM}}(b_j; \tilde{b}_j, g, \sigma^2).$$

In particular, the posterior distribution at the maximum is

$$q_j^*(b_j, \gamma_j = k) = \phi_{jk}^* N(b_j; \mu_{jk}^*, (s_{jk}^*)^*),$$

in which

$$\mu_{jk}^* = \mu_k(\tilde{b}_j; g, \sigma^2)$$

$$s_{jk}^* = s_k^2(\tilde{b}_j; g, \sigma^2)$$

$$\phi_{jk}^* = \phi_k(\tilde{b}_j; g, \sigma^2).$$

See eqs. 12, 14, 15 and 17 for the definitions of $\mu_k, s_k^2, \phi_k$ and $p_{\text{post}}^{\text{NM}}$.

(ii) The coordinate ascent update

$$g^* \triangleq \arg \max_{g \in \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2)} F(q, g, \sigma^2)$$

is achieved by setting

$$g^* = \sum_{k=1}^K \pi_k^* N(0, \sigma_k^2)$$

$$\pi_k^* = \frac{1}{p} \sum_{j=1}^p q_j(\gamma_j = k), \quad k = 1, \ldots, K.$$
(iii) Assume that $q_1, \ldots, q_p$ and $g$ are updated as in (i) and (ii) above, and $\sigma_1^2 = 0$. Then the coordinate ascent update

$$(\sigma^2)^* \triangleq \arg \max_{\sigma^2 \in \mathbb{R}^+} F(q, g, \sigma^2)$$

is achieved with

$$(\sigma^2)^* = \frac{||\bar{r}||^2 + \sum_{j=1}^{p} \text{Var}_q(b_j) + \sum_{j=1}^{p} \sum_{k=2}^{K} \phi_{jk} \mathbb{E}[b_j | \gamma_j = k] / \sigma_k^2}{n + p - \sum_{j=1}^{p} \phi_{jk}}$$

or with the simpler update formula

$$(\sigma^2)^* = \frac{||\bar{r}||^2 + \bar{b}^T(\bar{b} - \tilde{b}) + \sigma^2 p(1 - \pi_1^*)}{n + p(1 - \pi_1^*)}.$$ (31)

Note if $\pi$ is not updated using (29), $\pi_1^*$ using can be substituted with $\sum_{j=1}^{p} \phi_{1}(\tilde{b}_j; g, \sigma^2) / p$ in (31).

**Proof** See Appendix B.

Applying these expressions to the generic algorithm (Algorithm 1) results in Algorithm 2, which implements the VEB method with the scale mixture of normals prior. This algorithm is simple to use, having relatively few tuning parameters—the only tuning parameters are the number of mixture components, $K$, and $\sigma_1^2, \ldots, \sigma_K^2$ controlling the prior variances. For these tuning parameters we provide sensible defaults that should provide reasonably good performance in a wide range of settings (see Section 3.3.2).

A single iteration of the outer (“repeat-until”) loop implements the two-stage EB fitting procedure: the first part, the inner-loop over the coordinates $j = 1, \ldots, p$, is the posterior inference step (Step 2 of the procedure in Section 2.1), and can be viewed as an approximate E step; the second part estimates the model parameters, $g, \sigma^2$, and can be thought of as an approximate M step.

Algorithm 2 involves iteratively solving for the maximum of each parameter subject to all other parameters being fixed, so every update is guaranteed to increase the objective, $F$. The algorithm is also guaranteed to converge to a stationary point of $F$, a result summarized by the following proposition (this is analogous to Proposition 1 of Breheny and Huang (2011), which establishes convergence of the coordinate descent updates for the SCAD and MCP penalties):

**Proposition 2 (Convergence of coordinate ascent for VEB)** The sequence of iterates

$$\{q^{(t)}, g^{(t)}, (\sigma^2)^{(t)}\}, \quad t = 0, 1, 2, \ldots,$$

generated by Algorithm 2 converge monotonically to a local maximum of $F$ (22).

**Proof** See Appendix D.
Algorithm 2 Coordinate ascent for fitting VEB model (in detail).

Require: Data $X \in \mathbb{R}^{n \times p}$, $y \in \mathbb{R}^n$; number of mixture components, $K$; prior variances, $\sigma_1^2 < \cdots < \sigma_K^2$, with $\sigma_1^2 = 0$; initial estimates $\bar{b}, \pi, \sigma^2$.

$\bar{r} = y - X \bar{b}$ (compute mean residuals)

$t \leftarrow 0$

repeat

for $j \leftarrow 1$ to $p$ do

$\bar{r}_j = \bar{r} + x_j \bar{b}_j$ (disregard $j$th effect in residuals)

$\bar{b}_j \leftarrow x_j^T \bar{r}_j$ (compute OLS estimate)

for $k \leftarrow 1$ to $K$ do

$\phi_{jk} \leftarrow \phi_k(\bar{b}_j; g, \sigma^2)$

$\mu_{jk} \leftarrow \mu_k(\bar{b}_j; g, \sigma^2)$

end for

$\bar{b}_j \leftarrow \sum_{k=1}^{K} \phi_{jk} \mu_{jk}$.

$\bar{r} \leftarrow \bar{r} - x_j \bar{b}_j$. (update mean residuals)

end for

for $k \leftarrow 1$ to $K$ do

$\pi_k \leftarrow \sum_{j=1}^{p} \phi_{jk} / p$.

end for

$\sigma^2 \leftarrow \frac{||\bar{r}||^2 + \bar{b}^T (\bar{b} - \bar{b}) + \sigma^2 p(1 - \pi_1)}{n + p(1 - \pi_1)}$ (update $\sigma^2$; eq. 31)

$t \leftarrow t + 1$

until termination criterion is met

return $\bar{b}, \pi, \sigma^2$

While the structure of Algorithm 2 is the same as Algorithm 1, we have organized the computations in Algorithm 2 to limit redundant operations and reduce memory requirements. We have assumed $||x_j|| = 1$ here to simplify the formulae and focus attention on the high-level structure of the algorithm; a more general implementation that does not require this assumption is given in the appendix; see in particular Algorithm 4 in Appendix B.4.

An attractive feature of Algorithm 2 is that the computation scales linearly in the number of samples ($n$) and the number of predictors ($p$), with a computational complexity of $O((n + K)p)$ per outer-loop iteration—specifically, this is the computational complexity for performing a single update of $q_1, \ldots, q_p$, $g$ and $\sigma^2$. This means that this method’s flexibility does not come at a high computational cost, and in practice the method can be applied to very large data sets. In our experiments below we assess this empirically by simulating data sets of different sizes.

A second key feature of the algorithm is that, beyond storing the data matrix, $X$, the vector of posterior mean coefficients, $\bar{b}$, is sufficient to uniquely define $q$. (If the full posterior $q(b, \gamma)$ is desired, it can be recovered at any time from $\pi, \sigma^2$ and $\bar{b}$ by running a single round of the coordinate ascent updates for $q_1, \ldots, q_p$.) This means that the algorithm’s memory requirements are only $O(n + p + K)$; in our implementation, only the posterior means $\bar{b}$, OLS estimates $\bar{b}$ and expected residuals $\bar{r}$ need to be stored. This also means that the model fit can be easily initialized from another linear regression method since only
is needed to initialize the coordinate ascent updates for $q$. By exploiting this feature, we show that simple initialization strategies can yield better fits and with less effort.

We have implemented Algorithm 2, solving (23) with prior family $G = G(\sigma_1^2, \ldots, \sigma_K^2)$, in an R package, mr\_ash\_alpha, and we refer to this method as Mr.ASH (“Multiple regression with Adaptive SHrinkage priors”).

### 3.2 Accuracy of VEB and Exactness for Orthogonal Predictors

Carbonetto and Stephens (2012) note that their VA approach provides the exact posterior distribution when the columns of $X$ are orthogonal. Here we extend this result, showing that in this special case the VEB method recovers the ordinary empirical Bayes method.

**Proposition 3** When $X$ has orthogonal columns, solving the VEB problem (23) is mathematically equivalent to the usual EB two-step procedure (6, 7).

**Proof** See Appendix D.

In brief, this result follows from the fact that, when $X$ has orthogonal columns, the (exact) posterior distribution for $b$ factorizes as (19), and therefore the mean-field assumption (19) is not an approximation. More precisely, $\hat{q} = p_{\text{post}}$ when $\hat{q} = \arg\max_{q \in Q} F(q, g, \sigma^2)$, and therefore the ELBO $\max_{q \in Q} F(q, g, \sigma^2)$ is equal to the marginal log-likelihood $\log p(y | X, g, \sigma^2)$. By contrast, the CML approach to approximating EB inference used in George and Foster (2000); Yuan and Lin (2005) is not exact even in the case of orthogonal columns.

Proposition 3 suggests that our VEB method should be accurate when the columns of $X$ are close to orthogonal; e.g., when the columns are approximately independent with mean zero. It also suggests that the approximation may be less accurate for very highly correlated columns. However, Carbonetto and Stephens (2012) discuss this issue in depth, and explain that, even though the VA for $b$ is inaccurate for highly correlated columns, the estimated hyperparameters (here which is the prior $g$) can nonetheless be very accurate. They also note that, when two predictors are highly correlated with one another, and also predictive of $y$, the VA tends to give just one of them an appreciable estimated coefficient. This is similar to the behaviour of many PLR methods, including the Lasso, but different from other numerical approaches to approximating posteriors, such as MCMC. While this behaviour is undesirable when the main aim is to select variables for scientific interpretation, this behaviour does not necessarily harm prediction accuracy. Thus, the VEB approach may be expected to perform well for prediction even in settings where the assumptions of the mean-field variational approximation are clearly violated. Our numerical studies (Section 5) confirm this.

### 3.3 Practical Issues and Extensions

In this subsection we discuss some practical implementation issues and potential extensions of this method.

#### 3.3.1 Intercept

In multiple regression applications, it is common to include an intercept term that is not regularized in the same way as other variables. A common approach, and the approach we
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3.3.2 Selection of Grid for Prior Variances

Following Stephens (2016), we choose a grid \( \{\sigma_1^2, \ldots, \sigma_K^2\} \) that is sufficiently broad and dense that results do not change much if the grid is made broader and denser; the aim is to choose a \( G(\sigma_1^2, \ldots, \sigma_K^2) \) that closely approximates \( G_{\text{SMN}} \). Specifically, we set the lower end of the grid to be \( \sigma_1^2 = 0 \), which is a point mass at zero, and we set the largest prior variance to be \( \sigma_K^2 \approx n \) so that the prior variance of \( x_j b_j \) is close to \( \sigma^2 \) (recall, we assumed \( x_j^T x_j = 1 \), so \( \text{Var}(x_j) \approx 1/n \) when \( x_j \) is centered). We have found a grid of 20 points spanning this range to be sufficient to achieve reliable prediction performance across many settings (see Section 5). Based on these considerations, unless otherwise stated we use the following settings for the prior variances: \( K = 20, \sigma_k^2 = n(2^{(k-1)/20} - 1)^2 \).

In rare cases, \( \text{Var}(x_j b_j) \) may be larger than \( \sigma^2 \) for some \( j \). In that case, we may need a larger \( \sigma_K^2 \) to avoid underestimating, or “overshrinking”, the effect \( b_j \). Therefore, we suggest checking that the final estimate of \( \pi_K \) is negligible and, if not the grid may need to be made wider.

3.3.3 Initialization and Update Order

Except in special cases, maximizing \( F \) is a non-convex optimization problem, and so although Algorithm 2 is guaranteed to converge, the solution obtained may depend on initialization of \( \bar{b}, \pi, \sigma^2 \), as well as the order in which the coordinate ascent updates cycle through the coordinates \( j \in \{1, \ldots, p\} \) (e.g., Carbonetto and Stephens, 2012; Ray and Szabó, 2021). Therefore, we experimented with different initialization and update orderings.

The simplest initialization for \( \bar{b} \) is \((0, \ldots, 0)^T\). We call this the “null initialization.” Another initialization, used in Zhang et al. (2012) for example, is to initialize \( \bar{b} \) to the lasso solution \( \hat{b}^{\text{lasso}} \) (after choosing the Lasso penalty strength via cross-validation). Given \( \bar{b} \), we initialize the other parameters to \( \sigma^2 = \|y - X\bar{b}\|^2/n, \pi = (1/K, \ldots, 1/K) \). In our experiments (Section 5.5.6), we found that the \( \bar{b} = \hat{b}^{\text{lasso}} \) initialization usually lead to better performance than the null initialization in cases where the columns of \( X \) were highly correlated, and in other cases the null and lasso initializations performed similarly.

In our initial investigations we did not find any systematic benefit to different update orderings when the posterior mean coefficients were initialized to \( \bar{b} = \hat{b}^{\text{lasso}} \). Therefore, unless otherwise stated, in our experiments we performed the coordinate ascent updates in increasing order from 1 to \( p \).

3.3.4 Termination Criterion

Since one of our primary aims is to accurately estimate \( g \), we stop optimizing only when the change in \( \pi \) between two successive iterations is small; specifically, at iteration \( t \) the algorithm terminates if \( \|\pi^{(t)} - \pi^{(t-1)}\|_\infty \) is less than \( K \times 10^{-8} \).

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3.3.5 Computing the ELBO

Although Algorithm 2 optimizes the ELBO, $F$, computing the ELBO is actually not necessary. However, it is often useful to compute the ELBO, for example to monitor progress of the coordinate ascent updates. The ELBO can also act as an approximate marginal likelihood, which can be used, say, to compare evidence for models with different priors or different hyperparameter settings. See the appendix for analytic expressions for the ELBO. These expressions includes additional posterior quantities which are not explicitly computed in Algorithm 2 but all the expressions needed to compute these quantities are given in Sections 2 and 3.

3.3.6 Extension to Other Mixture Prior Families

We have focussed on $G = G(\sigma_1^2, \ldots, \sigma_K^2)$, the family of finite mixtures of zero-mean normals, because computations with normal mixtures are particularly simple, fast, and numerically stable. Another reason to use the family of scale mixtures of normals is that this family includes most prior distributions previously used for multiple regression, and so we expect this family of priors to suffice for most practical applications. Nonetheless, we note that Algorithm 2 can be adapted to accommodate other prior families of the form $G = \{g = \sum_{k=1}^K \pi_k g_k : \pi \in S^K\}$, with fixed mixture components $g_1, \ldots, g_K$. When choosing $G$, there are two important practical points to consider: (i) the convolution of $g_k$ with a normal likelihood should be numerically tractable, ideally with an analytic expression; (ii) the posterior mean in the normal means model with prior $b_j \sim g_k$ should be easy to compute. Examples of fixed mixture components $g_k$ satisfying (i) and (ii) include point masses, uniform distributions and Laplace distributions.

3.3.7 Estimation and Inference

Here we focus on using multiple regression for prediction. For this purpose a natural estimate of the regression parameter is the posterior mean, which is estimated by the expectation of $\hat{q}$. This posterior mean is not strictly sparse, even if the prior $g$ is sparse, (although it may have many entries near zero). If a sparse solution is desired then the posterior median of $\hat{q}$ may be used (Johnstone and Silverman, 2004), which is typically sparse if the (estimated) prior is sufficiently sparse. (We do not recommend use of the posterior mode as it does not have such a good decision-theoretic justification as median or mean).

3.3.8 Variable selection

As we mentioned, our focus here is on developing flexible multiple regression methods for accurate prediction. In other work (Carbonetto and Stephens, 2012; Wang et al., 2020), we have focussed more on using multiple regression models for variable selection—that is, the problem of identifying which variables explain variation in the outcome. Even though the variable selection problem is not our focus here, we note that, when $\sigma_i^2 = 0$, the posterior inclusion probability $\text{PIP}(j) = 1 - \phi_{j1}$ provides a simple way to quantify the probability that variable $j$ has a nonzero effect on the outcome, $y$. We caution, however, that this quantity is very much approximate in the sense that it does not properly account for correlations among the variables; for example, a variable $j$ that is strongly correlated with other variables with
high PIPs could potentially be good predictors of $\mathbf{y}$ even if $\text{PIP}(j)$ itself is small. The other point of caution is that the PIPs can be sensitive to the choice of grid, so these posterior inclusion probabilities should only be used as a rough guide for identifying “important” variables. See Wang et al. (2020) for a more principled treatment of the variable selection problem based on similar models.

4. Variational Empirical Bayes and Penalized Linear Regression

Here we explain how the (approximate) posterior mean computed by our VEB approach can be viewed as solving a penalized linear regression (PLR) in which the form of the penalty is flexible and adaptive.

4.1 Penalties and Shrinkage Operators

PLR methods estimate the regression coefficients by minimizing a penalized squared-loss function:

$$
\text{minimize} \quad h_\rho(\mathbf{b}) \triangleq \frac{1}{2} \| \mathbf{y} - \mathbf{Xb} \|^2 + \sum_{j=1}^{p} \rho(b_j),
$$

for some penalty function $\rho : \mathbb{R} \to \mathbb{R}$.

The PLR problem (32) is often tackled using coordinate descent algorithms (e.g., Friedman et al., 2010; Wu and Lange, 2008; Breheny and Huang, 2011; Hazimeh and Mazumder, 2020); that is, by iterating over the coordinates of $b_1, \ldots, b_p$ sequentially, at each iteration solving (32) for one coordinate $b_j$ while keeping the remaining coordinates fixed. Assuming the columns of $\mathbf{X}$ are scaled such that $x_j^T x_j = 1$, the solution for the $j$th coordinate is achieved by

$$
b_j \leftarrow S_{\rho}(b_j + x_j^T (\mathbf{y} - \mathbf{Xb})),
$$

where

$$
S_{\rho}(y) \triangleq \arg \min_{b \in \mathbb{R}} \frac{1}{2} (y - b)^2 + \rho(b),
$$

is the shrinkage operator for penalty $\rho$ (it is also referred to as the univariate proximal operator with respect to $\rho$; Parikh and Boyd 2014). Some commonly used penalty functions include the $L_2$-penalty (Ridge; Hoerl and Kennard 1970), the $L_0$-penalty (Miller, 2002), the $L_1$-penalty (Lasso; Tibshirani 1996), the Elastic Net (E-NET; Zou and Hastie 2005), the Smoothly Clipped Absolute Deviation (SCAD; Fan and Li 2011) and the Minimax Concave Penalty (MCP; Zhang 2010). These penalty functions, and their corresponding shrinkage operators, are summarized in Table 1. Studying the shrinkage operator $S_\rho$ is often helpful for understanding the behaviour of its corresponding penalty, $\rho$. For example, the shrinkage operators for the $L_0$ and $L_1$ penalties both have a “thresholding” property in which coefficients $b$ less than some value are driven to zero, and this thresholding property tends to produce sparse solutions to (32), (see the right-hand side of Figure 1 for an illustration).

In the next section, we show that our VEB approach can be interpreted as solving a PLR problem with a penalty function, $\rho_{g, \sigma}$, that depends on the prior $g_{\sigma}$ and the residual variance $\sigma^2$. This penalty function has a corresponding shrinkage operator, denoted by $S_{g, \sigma}$, that has a particular simple form and interpretation—it is the posterior mean under
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| method                     | penalty function, \( \rho(t) \) | shrinkage operator, \( S_{\rho}(t) \) |
|---------------------------|----------------------------------|----------------------------------------|
| normal shrinkage          | \( \lambda t^2 / 2 \)           | \( \frac{t^2}{1+\lambda} \)          |
| (Ridge, \( L_2 \)-penalty)|                                  |                                        |
| hard thresholding         | \( \lambda \times \mathbb{I}\{|t| > 0\} \) | \[ \begin{cases} t & \text{if } t < -\lambda, \\ t & \text{if } t > \lambda, \\ 0 & \text{otherwise} \end{cases} \] |
| (best subset, \( L_0 \)-penalty)|                               |                                        |
| soft thresholding         | \( \lambda |t| \)                 | \( S_{\text{soft,} \lambda} \triangleq \begin{cases} t + \lambda & \text{if } t < -\lambda, \\ t - \lambda & \text{if } t > \lambda, \\ 0 & \text{otherwise} \end{cases} \) |
| (Lasso, \( L_1 \)-penalty)|                                  |                                        |
| Elastic Net (E-NET)       | \((1 - \eta)\lambda t^2 / 2 + \eta \lambda |t| \) | \( S_{\text{soft,} \eta \lambda / a}(t / a), \) \( a = 1 + (1 - \eta) \lambda \) |
| Minimax Concave Penalty (MCP) | \( \begin{cases} \lambda |t| - t^2/(2\eta) & \text{if } |t| \leq \eta \lambda, \\ \eta \lambda^2 / 2 & \text{otherwise} \end{cases} \) | \( S_{\text{soft,} \lambda}(t), \) \( \text{if } |t| \leq \eta \lambda, \) \( t \), \( \text{otherwise} \) |
| Smoothly Clipped Absolute Deviation (SCAD) | \( \begin{cases} \lambda |t| & \text{if } |t| \leq 2\lambda, \\ \lambda^2(\eta + 1)/2 & \text{if } |t| > \eta \lambda, \\ \frac{\eta |t| - (t^2 + \lambda^2)/\eta - 1}{t} & \text{otherwise} \end{cases} \) | \( S_{\text{soft,} \lambda}(t), \) \( \text{if } |t| \leq 2\lambda, \) \( t \), \( \text{if } |t| > \eta \lambda, \) \( \frac{S_{\text{soft,} \eta \lambda / a}(t / a)}{1/(\eta - 1)} \), \( \text{otherwise} \) |

Table 1: Examples of penalty functions and their corresponding shrinkage operators.

A normal means model. This shrinkage operator \( S_{g_\sigma, \sigma} \) is important for developing these arguments, so before continuing we define it more formally:

**Definition 4 (Normal Means Posterior Mean Operator)** We define the normal means posterior mean operator, \( S_{f, \sigma} : \mathbb{R} \rightarrow \mathbb{R} \), as the mapping

\[
S_{f, \sigma}(y) \triangleq \mathbb{E}_{\text{NM}}(b \mid y, f, \sigma^2)
\]

in which \( \mathbb{E}_{\text{NM}} \) denotes the expectation under the following normal means model with prior \( f \) and variance \( \sigma^2 \),

\[
y \mid b \sim N(b, \sigma^2) \\
b \sim f.
\]

From (17), \( S_{g_\sigma, \sigma} \) has a simple analytic form when \( f = g_\sigma, g \in \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2) \):

\[
S_{g_\sigma, \sigma}(y) = \sum_{k=1}^{K} \phi_k(y; g, \sigma^2) \mu_k(y; g, \sigma^2).
\]

It is easy to show that \( S_{g_\sigma, \sigma} \) is an odd function and is monotonic in \( y \). Also, \( S_{g_\sigma, \sigma} \) is a shrinkage operator, in that \( |S_{g_\sigma, \sigma}(y)| \leq |y| \); see Lemma 12 in the appendix.

The behavior of the shrinkage operator \( S_{g_\sigma, \sigma} \) naturally depends on the prior. For example, the more mass the prior places near zero, the stronger the shrinkage tends toward zero. Our VEB method estimates the prior from within a flexible family capable of capturing a wide range of scenarios; consequently, the corresponding shrinkage operator is also
estimated from a flexible family of shrinkage operators. Indeed, given a suitable choice of the prior, the shrinkage operator $S_{g_0,\alpha}$ can mimic, qualitatively, the behaviour of many commonly used shrinkage operators; see Figure 1 for an illustration.

From a high-level perspective, one can view our VEB approach as a PLR method that tries to improve accuracy by adapting the shrinkage operator to a given data set. This process is analogous to estimating the tuning parameters in regular PLR methods, which is usually done by cross-validation (CV) (e.g., Friedman et al., 2010; Breheny and Huang, 2011). However, our VEB approach dispenses with cross-validation, and makes it possible to efficiently tune across a much wider range of shrinkage operators. Indeed, whereas traditional PLR methods use just one or two tuning parameters, ours has $K$ degrees of freedom (parameters $\pi_1, \ldots, \pi_K$ and $\sigma^2$). Further, in practice the computational burden of the VEB approach is similar to methods that tune a single tuning parameter by CV, and is much lower than methods that tune two tuning parameters by CV (see Section 5.5).

4.2 VEB as Penalized Linear Regression

Having providing some intuition for the connection between our VEB approach and PLR, now we develop a more formal connection between the two. An obvious difference between the PLR problem (32) and our VEB approach is that the PLR directly estimates the regression coefficients $b \in \mathbb{R}^p$ by optimizing an objective function $h_\rho(b)$, whereas our VEB method estimates the regression coefficients indirectly—it first estimates the approximate posterior distributions $q_1, \ldots, q_p$ by optimizing an objective function (the ELBO, $F$), then it estimates the regression coefficients by $b = \bar{b}$, where $\bar{b}_j$ is the mean of $q_j$. 

---

**Figure 1:** Examples of posterior mean shrinkage operators for different $g \in G(\sigma_1^2, \ldots, \sigma_K^2)$ (left-hand panel) and $\sigma^2$ chosen to mimic the shrinkage operators from commonly used penalties (right-hand panel).
Therefore, the first step in connecting VEB with PLR is to write our VEB approach as an optimization over the regression coefficients, $\mathbf{b}$, rather than an optimization over (approximate) posterior distributions, $q$. We do this by defining an objective function $h$ as follows,

$$h(\mathbf{b}, g, \sigma^2) \triangleq \left\{ \max_{q \in Q, \mathbb{E}_q[\mathbf{b}] = \mathbf{b}} F(q, g, \sigma^2) \right\},$$

in which we introduce an additional constraint that the expected value of $\mathbf{b}$ with respect to $q$ must be $\mathbf{b}$. (The negative sign is introduced here simply to help make the connection with PLR, which is usually framed with a loss function to be minimized (see eq. 32) rather than with an objective to be maximized.)

Any algorithm for optimizing $F$ over $q$ (and possibly $g, \sigma^2$) also provides a way to optimize $h$ over $\mathbf{b}$ (and possibly $g, \sigma^2$). This claim is formalized by the following proposition.

**Proposition 5 (Computing Posterior Mean as an Optimization Problem)** Let $\hat{q}, \hat{g}, \hat{\sigma}^2$ be a solution to

$$\hat{q}, \hat{g}, \hat{\sigma}^2 = \arg \max_{q \in Q, g \in \mathcal{G}, \sigma^2 \in \mathcal{T}} F(q, g, \sigma^2),$$

where $Q$ is the variational mean-field family of approximate posterior distributions (19), $\mathcal{G}$ is any family of prior distributions on $\mathbf{b} \in \mathbb{R}$, and $\mathcal{T}$ is any subset of $\mathbb{R}_+$. (This general formulation allows, as a special case, $g, \sigma^2$ to be fixed rather than estimated by taking both $\mathcal{G}$ and $\mathcal{T}$ be singleton sets.) Let $\mathbf{b}$ denote the expected value of $\mathbf{b}$ with respect to $\hat{q}$. Then $\hat{b}, \hat{g}, \hat{\sigma}^2$ also solves the following optimization problem:

$$\hat{b}, \hat{g}, \hat{\sigma}^2 = \arg \min_{\mathbf{b} \in \mathbb{R}^p, g \in \mathcal{G}, \sigma^2 \in \mathcal{T}} h(\mathbf{b}, g, \sigma^2).$$

**Proof** See Appendix D.

The final step to connecting VEB with PLR is to show that the objective function $h$ has the form of a penalized squared-loss function. This is claimed in the following proposition.

**Theorem 6 (VEB as a Penalized Log-likelihood)** The objective function $h$ defined in (38) has the form of a PLR,

$$h(\mathbf{b}, g, \sigma^2) = \frac{1}{2\sigma^2} ||\mathbf{y} - \mathbf{X}\mathbf{b}||^2 + \frac{1}{\sigma^2} \sum_{j=1}^{p} \rho_{g, \sigma}(\bar{b}_j) + \frac{n-p}{2} \log(2\pi\sigma^2),$$

in which the penalty function $\rho_{f, \sigma}$ satisfies

$$\rho_{f, \sigma}(S_{f, \sigma}(y)) = -\sigma^2 \ell_{\text{NM}}(y; f, \sigma^2) - (y - S_{f, \sigma}(y))^2 / 2.$$  

and

$$(\rho_{f, \sigma})'(S_{f, \sigma}(y)) = (y - S_{f, \sigma}(y)).$$

Here, $\ell_{\text{NM}}(y; f, \sigma^2)$ denotes the marginal log-likelihood under the NM model (36), $\ell_{\text{NM}}(y; f, \sigma^2) \triangleq \log p(y | f, \sigma^2)$, and $S_{f, \sigma}$ denotes the shrinkage operator (35). From this it follows that the normal means posterior mean shrinkage operator $S_{f, \sigma}$ (35) can be also written as $S_{\rho_{f, \sigma}}$ (34), a shrinkage operator for penalty $\rho_{f, \sigma}$.
Algorithm 3 Coordinate Ascent Iterative Shrinkage Algorithm for Variational Posterior Mean (with fixed $g, \sigma^2$)

Require: $X \in \mathbb{R}^{n \times p}, y \in \mathbb{R}^n, \sigma^2 > 0,$ prior $g$, and initial estimates $\bar{b}$.

repeat
    for $j \leftarrow 1$ to $p$ do
        $\bar{b}_j \leftarrow S_{g, \sigma}(\bar{b}_j + x_j^T(y - X\bar{b}))$
    end for
until convergence criteria is met

Output: $\bar{b}$

Proof See Appendix D.

Note that explicit computation of $\rho_{f, \sigma}(\bar{b})$ for a given $\bar{b}$ in (40) would require us to recover $y$ via the inverse shrinkage operator, $y = S_{f, \sigma}^{-1}(\bar{b})$. We know that this inverse exists because the shrinkage operator (37) is strictly increasing. However, we do not have an analytic expression for this inverse.

4.2.1 Special Case When $g$ and $\sigma^2$ Are Fixed

The special case where $g$ and $\sigma^2$ are fixed is particularly simple and helpful for intuition. In this case, the VEB approach is solving a PLR problem with fixed penalty $\rho_{g, \sigma}$ and shrinkage operator $S_{g, \sigma}$. This leads to a very simple coordinate ascent algorithm (Algorithm 3). Compare this simple algorithm with the inner loop of Algorithm 2, which maximizes the ELBO, $F$, over each $q_j$ in turn. The key computation in the inner loop is computation of the posterior mean, $\bar{b}_j$. (When $g$ and $\sigma^2$ are fixed, the other computations in the inner loop such as computing $\phi_{jk}$ and $\mu_{jk}$ are needed only to compute $\bar{b}_j$.) Further, from Proposition 1, this value is computed as the posterior mean under a simple normal means model, which is given by the shrinkage operator $S_{g, \sigma}$.

In summary, for fixed $g, \sigma^2$, Algorithm 2 can be reframed as a coordinate ascent algorithm for PLR, which is Algorithm 3.

4.2.2 Special Case of a Normal Prior (Ridge Regression)

When the prior, $g$, is a fixed normal distribution with zero mean, the NM posterior mean shrinkage operator $S_{g, \sigma}$ is the same as the ridge regression (or $L_2$) shrinkage operator (Table 1), and the penalty function $\rho_{g, \sigma}$ is the $L_2$-penalty. Thus, in this special case, Algorithm 3 is solving ridge regression (i.e., PLR with $L_2$-penalty), which is a convex optimization problem. Furthermore, in this special case Algorithm 3 converges to the true posterior mean of $b$ because the posterior is multivariate normal, and therefore the posterior mean is equal to the posterior mode. Thus, in this special case, even though the variational posterior...
approximation $q$ does not exactly match the true posterior—because the true posterior does not factorize as in (19)—the variational posterior mean recovers the true posterior mean.

4.2.3 Posterior Mean vs. Posterior Mode

Traditional PLR approaches are sometimes motivated from a Bayesian perspective as computing a posterior mode estimate for $b$—i.e., a maximum a posteriori, or MAP, estimate—in which the penalty term corresponds to some prior on $b$. For example, the Lasso is the MAP with a Laplace prior (Figueiredo, 2003). By contrast, the variational approach seeks the posterior mean, not the posterior mode. For example, the variational approach with a Laplace prior would not lead to the usual Lasso estimate—it would be closer to the posterior mean from the Bayesian Lasso (Park and Casella, 2008). Our formulation of the (approximate) posterior mean as solving a PLR is new and, as far as we are aware, may be useful in other settings.

From a Bayesian decision-theoretic perspective (e.g., Chapter 4 of Berger 1985), the posterior mean for $b$ has much better theoretical support than the posterior mode; not only does it minimize the expected mean-squared-error in $b$, it also minimizes the expected mean-squared-error in the predicted, or “fitted,” responses $\hat{y}_i = (x_{i1}, \ldots, x_{ip})^T b$. By contrast, the posterior mode has very little support as an estimator for $b$, particularly when predicting $y$ is the main goal. For example, for a sparse prior such as the spike-and-slab prior Mitchell and Beauchamp (1988) that has non-zero mass on zero, the posterior mode is always $b = 0$, which will generally provide poor prediction performance. (Also, if $b_{\text{mode}}$ is the posterior mode of $b$, then $(x_{i1}, \ldots, x_{ip})^T b_{\text{mode}}$ is not generally the posterior mode of the fitted value $\hat{y}_i$.)

5. Numerical Experiments

Having argued above for the benefits of a variational empirical Bayes (VEB) approach to multiple linear regression, here we assess these benefits empirically. In the remainder, we refer to the proposed VEB approach as multiple regression with adaptive shrinkage priors, or “Mr.ASH” for short.

In the experiments, we considered the task of predicting $y$ in unseen test examples after fitting a linear regression model to training data, and we compared the accuracy of the predictions generated by the different methods (see Section 5.3). Our goal was to evaluate the methods in a wide range of simulated data sets to better understand when these methods work well and when they work poorly, and why (see Section 5.1). Our expectation was that the methods with the least flexible priors or penalties will achieve good performance in settings where the prior or penalty are well-suited to the data, and will perform poorly in other settings. The most flexible methods, by contrast, should perform competitively in a wider variety of settings.

Methods compared include classic methods such as ridge regression and the Lasso, and more recently developed methods based on both penalized linear regression ideas (e.g., SCAD Breheny and Huang 2011) and Bayesian ideas (e.g., Bayesian Lasso Park and Casella 2008) The methods compared in the experiments are summarized in Table 2 (see Section 5.2 for more details).
### Table 2: Overview of the methods compared.

| method       | R package | brief description                                                                                                                                 |
|--------------|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------|
| Mr.ASH       | mr.ash.alpha | VEB method proposed in this paper                                                                                                               |
| Ridge        | glmnet    | ridge regression; PLR with $L_2$-penalty (Friedman et al., 2010; Hoerl and Kennard, 1970)                                                       |
| Lasso        | glmnet    | PLR with $L_1$-penalty (Friedman et al., 2010; Tibshirani, 1996).                                                                                  |
| E-Net        | glmnet    | the Elastic Net; PLR with linear combination of $L_1$ and $L_2$ penalties (Friedman et al., 2010; Zou and Hastie, 2005)                             |
| SCAD         | ncvreg    | PLR with smoothly clipped absolute deviation penalty (Breheny and Huang, 2011)                                                                   |
| MCP          | ncvreg    | PLR with minimax concave penalty (Breheny and Huang, 2011)                                                                                      |
| L0Learn      | L0Learn   | PLR with $L_0$-penalty (Hazimeh and Mazumder, 2020)                                                                                              |
| BayesB       | BGLR      | MCMC with $b_i \sim (1 - \pi)\delta_0 + \pi\sigma_0 t_i$ prior (Meuwissen et al., 2001; Pérez and de Los Campos, 2014)                           |
| B-Lasso      | BGLR      | Bayesian Lasso; MCMC with scaled Laplace prior on coefficients $b_j$ (Park and Casella, 2008; Pérez and de Los Campos, 2014)                       |
| SuSiE        | susieR    | variational inference for “sum of single effects” (SuSiE) model, with normal priors on “single effects” $b_i$ (Wang et al., 2020)                 |
| varbvs       | varbvs    | variational inference with $b_i \sim (1 - \pi)\delta_0 + \pi N(0, \sigma^2 \sigma_i^2)$ prior (Carbonetto and Stephens, 2012; Carbonetto et al., 2017) |

#### 5.1 Design of the Simulations

To test the methods in a range of settings, we designed four sets of simulations, which we refer to as “Experiment 1” through “Experiment 4.” In each set of simulations, we varied one aspect of the simulated data sets while keeping the other aspects fixed:

- In Experiment 1, we varied the “sparsity level”—that is, the proportion of number with non-zero coefficients. We denote this number by $s$, so that $s = 1$ is the sparsest model (with only a single non-zero coefficient), and $s = p$ is the densest model (all variables produce a change in $y$).

- In Experiment 2, we varied the “total signal strength”—more precisely, the proportion of variance in the response $y$ that is explained by $X$ (we refer to this parameter as “PVE”, short for “proportion of variance explained”).

- In Experiment 3, we considered different distributions for the non-zero coefficients. We use $h$ to denote the distribution that was used to simulate the non-zero effects.

- In Experiment 4, we varied the number of predictors, $p$.

We took the following steps to simulate each data set:

- First, we generated the $n \times p$ design matrix, $X$. We considered three types of design matrices: (1) independent variables, in which the individual observations $x_{ij}$ were simulated i.i.d. from the standard normal distribution; (2) correlated variables, in which
each row of $X$ was an independent draw from the multivariate normal distribution with mean zero and a covariance matrix diagonal entries set to 1 and off-diagonal entries set to $\rho \in [0,1]$; (3) real genotype data—to simulate data with realistic correlation patterns, we also took $X$ to be the genotype data from the the Genotype-Tissue Expression (GTEx) project (GTEx Consortium, 2017). Specifically, we used the data sets generated by Wang et al. (2020). In these data sets, the variables are genetic variants (specifically, single nucleotide polymorphisms, or “SNPs”), and these SNPs exhibit complex correlation patterns, with some pairs of SNPs being very highly correlated, with correlations near 1 or $-1$. Each genotype matrix $X$ drawn from the GTEx data contained the genotypes of all SNPs within 1 Megabase (Mb) of a gene’s transcription start site after filtering out SNPs with minor allele frequencies less than 5% (see Wang et al. 2020 for details). We randomly selected 20 GTEx data sets for our simulations (among the thousands of data sets used in Wang et al. 2020). Unless otherwise stated, we simulated independent variables with $n = 500$ and $p = 1,000$. For the genotype data sets, $n = 287$, and $p$ ranged from 4,012 to 8,760.

- Next, we selected the $s$ non-zero coefficients uniformly at random among the $p$ variables. When not explicitly stated, we set $s = 20$.

- We simulated the coefficients $b_j$ for the $s$ selected variables i.i.d. from some distribution, $h$. We used the following distributions: standard normal; uniform on $[-1,1]$; double-exponential (Laplace) distribution centered at zero with variance $2\lambda^2$, $\lambda = 1$ Gelman et al. (2013); $t$-distribution with 1, 2, 4 and 8 degrees of freedom; and a point mass (so that all coefficients were the same). Unless stated otherwise, we simulated the coefficients from the standard normal.

- Finally, we simulated the responses $y_i = \sum_{j=1}^{p} x_{ij} b_j + e$, $e \sim N(0, \sigma^2)$, in which $\sigma^2$ was set to $\sigma^2 = \text{Var}(Xb) \times \frac{1}{\text{PVE}}$ to hit the target PVE. Unless otherwise stated we used a target PVE of 0.5.

We repeated the simulations 20 times for each parameter setting in each experiment.

The test sets used to evaluate the model fits were generated in the exact same way as the training sets (with the same coefficients $b$), and the test sets were always the same size as the training sets.

### 5.2 Methods Compared

A large number of multiple regression methods have been proposed in the literature and it is infeasible to compare all of them. In our experiments, we focussed on the most prominent methods that capture a wide range of approaches—these methods are distinguished by different choices of penalties or priors, different modeling assumptions, and/or different model fitting strategies (point estimation or approximate posterior inference via MCMC or variational methods). Other important considerations when deciding which methods to evaluate was whether the method was implemented in R (R Core Team, 2019) and whether the software was well maintained and well documented. The methods compared in our experiments are summarized in Table 2. Here we briefly describe the different methods and comment on their possible strengths and weaknesses:
• Ridge regression (Ridge; Hoerl and Kennard 1970) and the Bayesian Lasso (B-Lasso; Park and Casella 2008) are well adapted to dense signals, so should be competitive in such settings. On the other hand, they may perform poorly for sparse signals.

• By contrast, L0Learn (Hazimeh and Mazumder, 2020) and SuSiE (Wang et al., 2020) are very well adapted to sparse signals, so they should perform well in such settings, but may perform poorly for dense signals.

• The Lasso (Tibshirani, 1996) is a very widely used PLR method in part because it is fast and computing the Lasso estimator is a convex optimization problem. On the other hand, the Lasso estimates can suffer from bias by overshrinking the strongest signals (e.g., Su et al., 2017; Javanmard and Montanari, 2018).

• The Elastic Net (E-NET; Zou and Hastie 2005) is another convex PLR method with two tuning parameters, which makes it more flexible than the Lasso and Ridge—indeed, it includes both as special cases. The E-NET may therefore perform well across a wider range of settings, at the cost of increased computation for parameter selection.

• SCAD and MCP are based on non-convex penalties that were designed to address bias in the Lasso estimates (Breheny and Huang, 2011). They might therefore outperform Lasso, possibly at a cost of some additional computation. Since these methods were primarily developed with sparse regression in mind, they may not adapt well to dense signals.

• BayesB is a Bayesian regression method with a “spike-and-slab” prior, in which the “slab” is a $t$ distribution (Meuwissen et al., 2001). It has the potential to perform well for both sparse and dense signals provided the Markov chain is simulated long enough so as to adequately explore the posterior distribution.

• varbvs (Carbonetto and Stephens, 2012; Carbonetto et al., 2017) and Mr.ASH both compute approximate posteriors using the same mean field variational approximation. Compared to varbvs, Mr.ASH features a more flexible prior, and uses a simpler and more efficient empirical Bayes approach to estimate the prior. Mr.ASH also uses an initialization based on the Lasso, which, as we show below, can improve the model fit, particularly when the predictors are strongly correlated. We expect Mr.ASH to outperform varbvs some settings, particularly in “dense” settings when many of the predictors affect the outcome, or when the predictors are strongly correlated.

One complicating factor is that most methods have many options and tuning parameters. Even the use of a relatively straightforward method such as the Lasso involves several choices, sometimes with inherent tradeoffs in runtime vs. prediction accuracy: number of folds to use in the cross-validation step; what criterion to use for selecting the optimal penalty strength parameter; whether to “relax” the fit; etc. With so many methods to compare, we did not attempt to find the optimal tuning parameters. Instead, we applied these methods “out of the box”; that is, we used the software’s default settings unless the defaults were unreasonable. We deviated from this rule-of-thumb in only two cases: for the E-NET, we tuned both of the penalty parameters, $\alpha$ and $\lambda$, by cross-validation (in glmnet,
by default, only $\lambda$ is estimated by cross-validation); for SuSiE, we set the maximum number of single effects to $L = 20$ since many of the data sets were simulated with more than 10 non-zero coefficients. (Increasing $L$ further could improve SuSiE’s performance, particularly for dense signals, but doing so would also increase the computational cost.)

5.3 Evaluation

Each method returns $\hat{b}$, an estimate of the regression coefficients. To evaluate this estimate, we predicted responses in a collection of unseen test examples, $\hat{y}_{test} = X_{test}\hat{b}$, and we measured the accuracy of these predictions by the root mean squared error,

$$\text{RMSE}(y_{test}, \hat{y}_{test}) \triangleq \frac{\|y_{test} - \hat{y}_{test}\|}{\sqrt{n}}.$$  (42)

A problem with reporting the “raw” RMSE metric directly is that the RMSE will vary greatly depending on the difficulty of the data set, which will sometimes make it difficult to summarize results across simulations. For example, data sets simulated from dense models with low PVE will are the most challenging, and therefore the RMSE for these data sets will typically be much higher than data sets simulated from sparse models with high PVE. To account for this, we instead report a scaled RMSE metric,

$$\text{RMSE-scaled}(y_{test} - \hat{y}_{test}) \triangleq \frac{\text{RMSE}(y_{test}, \hat{y}_{test})}{\text{RMSE}(\hat{b} = 0)},$$  (43)

where $\text{RMSE}(\hat{b} = 0) \triangleq \sigma/\sqrt{1 - \text{PVE}}$ denotes the expected RMSE for the null predictor, $\hat{b} = 0$. This scaled RMSE measure is also easier to interpret: the expected scaled RMSE of the “oracle” predictor, in which $\hat{b}$ is the set of coefficients used to simulate the data, is $\sqrt{1 - \text{PVE}}$, and therefore in the best case the scaled RMSE is expected to be $\sqrt{1 - \text{PVE}}$, and in the worst case it is expected to be near 1. However, for understanding the results, it is important to keep in mind that an increase (or decrease) in the scaled RMSE does not necessarily imply an increase (or decrease) in the (absolute) RMSE.

5.4 Software Availability

Mr.ASH is implemented in the R package mr.ash.alpha, and is available at https://github.com/stephenslab/mr.ash.alpha (In the experiments, we used mr.ash.alpha version 0.1-33 (git commit id 0845778). The source code and analysis steps used to generate the results of our numerical experiments are included in a separate repository on GitHub, https://github.com/stephenslab/mr-ash-workflow.

5.5 Results

Results of Experiments 1–4 are presented in Sections 5.5.1 through 5.5.4. After that, we review these results at a high level (Section 5.5.5), then we look more closely at the effect of initialization and update order on Mr.ASH’s performance (Section 5.5.6).

5.5.1 Experiment 1—Varying the Sparsity Level

In the first set of simulations, we varied $s$, the number of nonzero predictors, which controls the model sparsity when $p$ is fixed. Varying $s$ highlights differences in performance between
Flexible empirical Bayes regression

Figure 2: Results from Experiment 1 in which the sparsity level, $s$, was varied. Each point shows the prediction error (scaled RMSE) averaged over the 20 simulations at that setting.

methods that are well suited to a particular level of sparsity versus methods that more flexibly adapt to different sparsity levels (Figures 2 and 3). For example, L0Learn and SuSiE are well adapted to sparse settings, and therefore generally performed poorly in dense settings; by contrast, Ridge and B-Lasso are well adapted to dense settings, and therefore
Figure 3: Results from Experiment 1 in which the sparsity level, $s$, was varied. Each point shows the prediction error (scaled RMSE) averaged over the 20 simulations at that setting. Note that the Mr.ASH results shown in this figure are the same as in Figure 2; we have added them to this figure for a common point of reference.

performed poorly in sparse settings. The other methods performed more consistently across sparsity levels. In particular, the Lasso and E-NET methods performed somewhat similarly,
with E-NET being consistently slightly better, but there was a distinct performance gap between these two methods and the best performing method in each setting. The non-convex penalty-based methods, MCP and SCAD, also performed similarly to one another, and were competitive in many settings, with the exception of the dense-signal data sets in some scenarios (e.g., in the low-dimension settings, with \( p = 200 \) non-zero coefficients). Mr.ASH was competitive at all sparsity levels, consistently achieving performance close to the best-performing method. Also, Mr.ASH outperformed other methods in data sets with correlated predictors, with a couple exceptions: B-Lasso had better prediction accuracy in settings with the densest signals, and SuSiE achieved better prediction accuracy in the sparest signal settings. One possible explanation for this is that the mean-field variational approximation used by Mr.ASH may contribute to some loss of accuracy in settings with correlated predictors (B-Lasso uses MCMC to compute the posterior estimates, and SuSiE uses a different variational approximation entirely that can deal with strong correlations). Overall, these results illustrate the versatility of Mr.ASH, and the effectiveness of the VEB approach to adapt to different sparsity levels by adapting the prior (and therefore penalty) to the data.

We highlight two other interesting trends that emerged from this first experiment. First, the BayesB method performed consistently poorly in the scenarios with correlated predictors. In principle, correlated predictors should not cause problems for Bayesian methods such as BayesB, so we suspect this is a numerical issue; perhaps the default MCMC settings were not appropriate for all data sets. Second, although varbvs is based on the same variational approximation as Mr.ASH, its prediction accuracy was generally worse than Mr.ASH. This is particularly evident in the dense-signal data sets—perhaps because the varbvs hyperparameters were chosen to favor sparsity—and in correlated-predictor data sets, probably because, unlike Mr.ASH, in varbvs little effort made to seek a careful initialization, which can be helpful in data sets with correlations among predictors. (We investigate the importance of careful initialization in more detail in Section 5.5.6.)

### 5.5.2 Experiment 2—Varying the Total Signal Strength

In contrast to the first experiment, we do not expect that the methods will have systematically different performance as the total signal strength (PVE) changes. In sparse scenarios (top two rows in Figure 4), this expectation is confirmed; the curves showing performance of different methods generally do not cross over, and Mr.ASH is consistently one of the most accurate methods. The results on data sets generated from dense signals (bottom two rows in Figure 4), however, reveal a different story; some of the methods that performed competitively at moderate PVEs were no longer performing as competitively at high PVEs. This includes, surprisingly, Mr.ASH, which obtained remarkably similar accuracy to varbvs and SCAD in these simulations. This occurred despite the fact that Mr.ASH should, in principle, adapt well to both sparse and dense signals (consider that Mr.ASH includes ridge regression as a special case, and the ridge regression estimates yield better predictions in the dense data sets). We infer from these findings that the VEB approach to selecting the penalty introduces some error or bias. We discuss this point further below, but, in brief, we believe this issue arises because the variational approximation used by Mr.ASH has the
Figure 4: Results from Experiment 2 in which the total signal strength (PVE) was varied. Each point shows the prediction error (scaled RMSE) averaged over the 20 simulations at that setting. The Mr.ASH results were added to all the plots for a common point of reference.

The good performance of BayesB in these simulations suggests an advantage of MCMC over the variational approximation in dense scenarios.

effect of penalizing dense priors. Also, the good performance of BayesB in these simulations suggests an advantage of MCMC over the variational approximation in dense scenarios.
Flexible empirical Bayes regression

Figure 5: Results from Experiment 3 in which the signal distribution ($h$) was varied. Each point shows the prediction error (scaled RMSE) averaged over the 20 simulations at that setting. The Mr.ASH results were added to all the plots for a common point of reference. The results are arranged along the horizontal axis in each plot in such a way that the simulations with the greatest variation in the coefficients are toward the left of the plot.

5.5.3 Experiment 3—Varying the Signal Distribution

Similar to the previous experiment, in this experiment we find that the distribution used to simulate the coefficients, $h$, has little effect on relative performance in sparse settings, but
Table 3: Average runtime (in seconds) of each method in the first three experiments. The “Mr.ASH” runtime includes running Lasso to initialize the estimates; the runtime for Mr.ASH without a Lasso initialization is given by the number in parentheses.

| Method      | 7.78 | 16.07 | 18.79 | 20.37 (15.05) | 22.00 | 23.59 | 24.80 | 33.76 | 35.04 | 54.98 | 223.66 |
|-------------|------|-------|-------|---------------|-------|-------|-------|-------|-------|-------|--------|
| L0Learn     |      |       |       |               |       |       |       |       |       |       |        |
| B-Lasso     |      |       |       |               |       |       |       |       |       |       |        |
| Lasso       |      |       |       |               |       |       |       |       |       |       |        |
| Mr.ASH      |      |       |       |               |       |       |       |       |       |       |        |
| MCP         |      |       |       |               |       |       |       |       |       |       |        |
| SuSiE       |      |       |       |               |       |       |       |       |       |       |        |
| BayesB      |      |       |       |               |       |       |       |       |       |       |        |
| Ridge       |      |       |       |               |       |       |       |       |       |       |        |
| SCAD        |      |       |       |               |       |       |       |       |       |       |        |
| varbvs      |      |       |       |               |       |       |       |       |       |       |        |
| E-Net       |      |       |       |               |       |       |       |       |       |       |        |

can have a considerable effect in dense settings. In particular, in dense settings in which many variables affect $y$, Ridge struggles to accurately estimate the coefficients simulated with long-tailed distributions such as $t$-distribution with 1 degree of freedom ($t_1$). Consider that when $h$ is long-tailed, often a small number of coefficients will dominate, and the normal prior in ridge regression is poorly suited for this case. B-Lasso is more robust than Ridge to this issue, which is expected since B-Lasso uses a longer-tailed Laplace prior for the coefficients.

5.5.4 Experiment 4—Varying the Number of Predictors

In the fourth set of simulations, we looked at not only prediction accuracy, but also how the computational complexity scales with the number of predictors, $p$. The runtimes we report are based on running the experiments in R 3.5.1 (R Core Team, 2019) on a machine with a quad-core 2.6 GHZ Intel Core i7 processor and 16 GB of memory. R was installed from macOS binaries and we used the BLAS libraries that were distributed with R.

The results on prediction accuracy and runtime are summarized in Figure 6. The runtime results show that, with the software settings used here, all the methods scale similarly with the number of predictors, $p$. E-NET was considerably slower than the other methods because we tuned both of the Elastic Net parameters by cross-validation, whereas other methods involved tuning only a single parameter by CV. (E-NET could be run faster by tuning only one parameter, but at the risk of losing some prediction accuracy.) Fitting the Mr.ASH prior involves tuning a large number of parameters, but because it tunes these parameters via a (variational) empirical Bayes approach rather than by CV, Mr.ASH ends up being roughly as fast as methods that tune a single parameter by CV. This is one benefit to (variational) EB over CV.

An important detail that isn’t apparent from the results shown in Figure 6 is that a large fraction of the effort in running Mr.ASH was actually due to running Lasso (recall, we used Lasso to initialize coordinate ascent for Mr.ASH). This is because the Lasso initialization was often very good, and therefore often greatly reduced the number of iterations required for the Mr.ASH coordinate ascent updates to settle on a stationary point of the ELBO (within the specified tolerance).

Remarkably, the methods that computed posterior estimates using MCMC—B-Lasso and BayesB—also scaled similarly to the PLR and variational-based methods. (We say this is remarkable because many Monte Carlo methods, particularly MCMC methods, have a reputation for being very computationally intensive.) This was because the software implementations of these methods set, by default, the length of the simulated Markov chain to be proportional to $p$. (Also, the per-iteration cost of simulating the Markov chain is
independent of \( p \) when the model configurations are sparse.) However, as \( p \) increased, the prediction accuracy for these methods was no longer as good as the other methods. For B-Lasso, this is probably due to the fact that we fixed \( s \), the number of non-zero coefficients, in these simulations, so simulations with larger \( p \) involved sparse models, and B-Lasso, as we observed in earlier experiments, was less competitive in sparse settings. For BayesB, the reduction in prediction accuracy may instead reflect a failure of the Markov chain to adequately explore the posterior distribution, and perhaps better performance could be achieved by running the MCMC longer (at the cost of increasing the computational cost).
Figure 7: Summary of results from Experiments 1–4, in which the simulations are grouped slightly differently to emphasize common trends. To highlight differences in performance among the methods, the boxplots summarize the distribution of RMSEs relative to the best performing method in each simulation (see text for details). The horizontal line inside each box depicts the median; the dot depicts the mean; and the upper and lower lines defining the box give the interquartile range.

Nonetheless, it is interesting to note that BayesB obtained better prediction accuracy than the Lasso at roughly the same computational effort as the Lasso.

To summarize, Mr.ASH consistently achieved the best prediction accuracy in these simulations, with computational effort that was on par with or considerably less than the other methods.
5.5.5 Summary of the Results

The four experiments highlighted some differences in performance and behaviour among the multiple regression models. In Figure 7, we provide a higher level summary of the methods’ performance across all four of these experiments. To produce this summary, for each simulation $t$ we calculated the relative prediction accuracy as the ratio of the RMSE to the best RMSE achieved in that simulation among all the methods compared; $\text{RRMSE}_tm = \frac{\text{RMSE}_tm}{\min_{m'} \text{RMSE}_{tm'}}$, where $\text{RMSE}_{tm}$ is the root mean squared error (42) in the predictions generated by model $m$ for the test set in simulation $t$. Defined in this way, the RRMSE cannot be smaller than 1, and the most accurate method in a given simulation has an RRMSE of 1.

Figure 7 highlights the consistently good prediction accuracy of Mr.ASH compared with the other methods across a range of data sets; in Groups A, C and D, Mr.ASH’s performance is the best, or close to the best, among all methods compared, and is rarely much worse than the best method. In Group B—simulations with correlated predictors—the benefits of Mr.ASH are more mixed. Yet even in these simulations Mr.ASH remains competitive, achieving an average prediction accuracy that is among the best. This good accuracy is also obtained efficiently, with a computational effort that is not much greater than the fastest methods such as L0Learn and the Lasso (Table 3).

5.5.6 Impact of Initialization and Order of Updates on Prediction Accuracy

Since Mr.ASH is solving a non-convex optimization problem, and therefore is only guaranteed to converge to a locally optimal solution (except in special cases), the quality of
the solution—and hence the accuracy of the predictions—can be sensitive to initialization. This situation is similar to other methods such as SCAD that solve nonconvex optimization problems, but different from methods such as Lasso that solve a convex optimization problem, and therefore are guaranteed to end up with the same final estimates irrespective of initialization (provided of course that the algorithm is given enough time to converge to the solution). Additionally, the order in which the coordinatewise updates are performed can also affect which local solution the Mr.ASH algorithm converges to (Rav and Szabó, 2021).

For these non-convex optimization problems, sometimes a “smart” initialization or update order can lead to better local solutions. From experience, we have found that initializing Mr.ASH to the cross-validated Lasso estimate of \( \hat{b} \) seems to work well, and does not greatly increase computational effort. Here, we investigate more systematically the benefits of a careful initialization. Specifically, we compared the following four Mr.ASH variants in our simulations:

- **“Null” initialization.** The posterior mean coefficients \( \bar{b} \) are all initialized to zero, and the individual coordinates \( j \) are updated in a random order. By “random order”, we mean a random permutation of the indices 1, 2, …, \( p \). A new random permutation is generated for each iteration of the algorithm (that is, for each iteration of the repeat-until loop in Algorithm 2).

- **Lasso initialization.** The posterior mean coefficients are set to \( b = \hat{b}_{\text{lasso}} \) as described in Section 3.3.3, and the individual coordinates \( j \) are updated in a random order.

- **Lasso update order.** The coordinates \( j \) are updated in the order that they are estimated to have nonzero coefficients as the strength of the Lasso penalty is decreased. We call this the “Lasso update order,” and it can be understood as the order in which the coefficients “enter the Lasso path” (Su et al., 2017). Note that determining the Lasso update order typically takes less effort than computing \( \hat{b}_{\text{lasso}} \) because the cross-validation step is avoided.

- **Lasso initialization and Lasso update order.** Both the Lasso initialization \( \bar{b} = \hat{b}_{\text{lasso}} \) and Lasso update order are used.

(Initialization of \( \sigma^2, \pi \) is described in Section 3.3.3.)

To assess the benefits of these four initialization and update order strategies, we simulated data sets with varying degrees of correlations among the predictors (columns of \( X \)), and compared the performance of the four Mr.ASH variants. The results of these simulations are summarized in Figure 8. The smart initialization and update ordering provided little benefit when the variables were not correlated, or only weakly correlated, but produced considerable gains in prediction accuracy when the variables were strongly correlated. Interestingly, once the coefficients were initialized to the Lasso estimates, \( b = \hat{b}_{\text{Lasso}} \), there was no additional benefit to updating the coordinates using the Lasso update order. Therefore, initializing the coefficients to the cross-validated Lasso estimates is a simple way to improve the performance of Mr.ASH.
6. Discussion

We have presented a new VEB method for multiple linear regression, with a focus on fast and accurate prediction. This VEB method combines flexible shrinkage priors with variational methods for efficient posterior computations. Variational methods and EB methods are sometimes disparaged because of their tendency to understate uncertainty compared with “fully Bayesian” methods; see Morris (1983), Wang and Titterington (2005) and references therein for discussion. However, in some applications uncertainty is of secondary importance compared with speed and accuracy of point estimates. For example, speed and accuracy is often important when multiple regression is used simply to build an accurate predictor for downstream use—see Gamazon et al. (2015) for one such application—and our VEB approach seems particularly attractive for such uses.

A natural next step would be to produce similar VEB methods for non-Gaussian (i.e., generalized) linear models (McCullagh and Nelder, 1989). Extension of our methods to logistic regression should be possible via additional approximations that allow for efficient analytic computations (Carbonetto and Stephens, 2012; Carbonetto et al., 2017; Jaakkola and Jordan, 2000; Marlin et al., 2011; Bishop, 2006; Wang and Blei, 2013). Extension to other types of outcome distributions and link functions should also be possible but may require more work.

Our work also illustrates the benefits of an EB approach in an important and well studied statistical problem. While there is much theoretical (Johnstone and Silverman, 2004) and empirical (Efron, 2008) support for the benefits of EB approaches, EB approaches have not been widely adopted outside of some specific research topics such as wavelet shrinkage (Johnstone and Silverman, 2005) and moderated estimation in gene expression studies (Smyth, 2004; Lu and Stephens, 2016; Zhu et al., 2019). Recent work has highlighted the potential for EB methods in other applications, including smoothing non-Gaussian data (Xing et al., 2021), multiple testing (Stephens, 2016; Sun and Stephens, 2018; Urbut et al., 2019; Gerard and Stephens, 2020), matrix factorization and sparse factor analysis (Wang and Stephens, 2021), and additive models (Wang et al., 2020). We hope that these examples, including our work here, will inspire readers to apply EB approaches to new problems.

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Appendix A. More General Formulation of the Normal Means model

In Section 2.2 we defined the normal means (NM) model for the special case when all observations have the same variance. This special case was sufficient to develop the VEB methods with the assumption that $x_j^T x_j = 1, j = 1, \ldots, p$. Here, we extend the NM model to allow for observation-specific variances, which is needed to generalize the VEB method to cases in which the $x_j^T x_j = 1$ assumption no longer holds.

A.1 The Normal Means Model

Let $\text{NM}_p(f, s^2)$ denote the normal means model with prior $f$ and observation-specific variances $s^2 = (s^2_1, \ldots, s^2_p) \in \mathbb{R}_+^p: \begin{align} y_j \mid b_j, s^2_j \sim N(b_j, s^2_j), \quad & \quad \text{such that } y_j, b_j \in \mathbb{R}, j = 1, \ldots, p. \\ b_j \mid f & \sim f, \quad j = 1, \ldots, p, \end{align}$

such that $y_j, b_j \in \mathbb{R}, j = 1, \ldots, p$.

Here we assume priors that are mixtures of normals, $f \in \mathcal{G}(u^2_1, \ldots, u^2_K)$, $u^2_k \geq 0, k = 1, \ldots, K$, so that any prior can be written as

$$ b_j \sim \sum_{k=1}^K \pi_k N(0, u^2_k), $$

such that $\pi = (\pi_1, \ldots, \pi_K) \in S^K$. As in (45), it is helpful in the derivations to make use of the latent variable representation:

$$ b_j \mid f, \gamma_j = k \sim N(0, u^2_k) \quad (45) $$

$$ p(\gamma_j = k \mid f) = \pi_k, \quad (46) $$

with $\gamma_j \in \{1, \ldots, K\}, j = 1, \ldots, p$. We write the joint prior for $b_j, \gamma_j$ as

$$ p_{\text{prior}}(b_j, \gamma_j = k) \triangleq p(b_j, \gamma_j = k \mid f) = \pi_k N(b_j; 0, u^2_k). \quad (47) $$

In the expressions below we sometimes write the joint prior as $p_{\text{prior}}(f)$ to make its dependence on $f$ explicit.

Note that the definition of the NM model given in the main text (Section 2.2), with prior (4), is a special case of these definitions and can be obtained with the substitutions $s^2_j \leftarrow \sigma^2, j = 1, \ldots, p$ and $u_k \leftarrow \sigma^2 u^2_k, k = 1, \ldots, K$.

A.2 Posterior Distribution under Normal Means Model with One Observation

Let $q^{\text{NM}}(b, \gamma \mid y, f, s^2)$ denote the posterior distribution of $b, \gamma$ under the normal means model $\text{NM}_1(f, s^2)$ with a single observation, $p = 1,$

$$ y \mid b, s^2 \sim N(b, s^2) \quad \begin{align} b \mid f & \sim f. \end{align} $$
For a mixture of normals prior, \( f \in G(u_1^2, \ldots, u_K^2) \), the posterior distribution of \( b, \gamma \) and the marginal posterior distribution of \( b \) can be written as

\[
p^{\text{NM}}(b, \gamma = k \mid y, f, s^2) = \phi_{1k} \mathcal{N}(b; \mu_{1k}, s_{1k}^2),
\]

\[
p^{\text{NM}}(b \mid y, f, s^2) = \sum_{k=1}^{K} p^{\text{NM}}(b, \gamma = k \mid y, f, s^2),
\]

(48)

in which the posterior component means \( \mu_{1k} \), variances \( s_{1k}^2 \), responsibilities \( \phi_{1k} \), and component (marginal) likelihoods \( L_k \) are, respectively,

\[
\mu_{1k} \triangleq \mu_{1k}(y; f, s^2) = \frac{u_k^2}{s^2 + u_k^2} \times y \tag{49}
\]

\[
s_{1k}^2 \triangleq s_{1k}^2(y; f, s^2) = \frac{s^2 u_k^2}{s^2 + u_k^2} \tag{50}
\]

\[
\phi_{1k} \triangleq \phi_{1k}(y; f, s^2) = \frac{\pi_k L_k}{\sum_{k'=1}^{K} \pi_{k'} L_{k'}} \tag{51}
\]

\[
L_k \triangleq L_k(y; f, s^2) = p(y \mid f, s^2, \gamma = k) = \int p(y \mid b, s^2) p(b \mid f, \gamma = k) \, db \tag{52}
\]

The posterior expressions for the NM model given in the main text (14, 15, 16, 17) can be recovered from these more general expressions here with the substitutions \( s_j^2 \leftarrow \sigma^2 \), \( u_k \leftarrow \sigma^2 s_k^2 \).

### A.3 Evidence Lower Bound for Normal Means Model with One Observation

Given some probability density on \( b \in \mathbb{R} \), denoted by \( q \), the ELBO for the normal means model \( \text{NM}_1(f, s^2) \) with observation \( y \) is

\[
F_1^{\text{NM}}(q, f, s^2; y) = \log p(y \mid f, s^2) - D_{\text{KL}}(q \parallel p^{\text{NM}})
\]

\[
= \mathbb{E}_q[\log p(y \mid b, s^2)] - D_{\text{KL}}(q \parallel p_{\text{prior}}(f))
\]

\[
= -\frac{1}{2} \log(2\pi s^2) - \frac{1}{2s^2} \mathbb{E}_q[(y - b)^2] - D_{\text{KL}}(q \parallel p_{\text{prior}}(f)).
\]

(53)

With this expression, we state the following basic result.

**Lemma 7 (Normal Means Posterior as maximum of ELBO)** The posterior distribution (48) under the NM model \( \text{NM}_1(f, s^2) \) with observation \( y \) maximizes the ELBO (53); that is,

\[
p^{\text{NM}} = \arg \max_q -\frac{1}{2s^2} \mathbb{E}_q[(y - b)^2] - D_{\text{KL}}(q \parallel p_{\text{prior}}(f)).
\]

From this lemma it follows that any \( q \) maximizing the ELBO (53) must have the following form:

\[
q(b) = \sum_{k=1}^{K} \phi_{1k} \mathcal{N}(b; \mu_{1k}, s_{1k}^2),
\]

(54)

with \( \phi_{1k} \geq 0, \mu_{1k} \in \mathbb{R}, s_{1k}^2 > 0, k = 1, \ldots, K \).
For any $q$ of the form (54), the ELBO (53) has an analytic expression, which we derive in part by making use of the formula for the K-L divergence between two normal distributions (Hastie et al., 2009):

$$F_{1}^{NM}(q, f, s^2) = \mathbb{E}_{q}[\log p(y | b, s^2)] - D_{KL}(q \parallel p_{prior}(f)),$$

in which

$$\mathbb{E}_{q}[\log p(y | b, s^2)] = -\frac{1}{2} \log(2\pi s^2) - \frac{(y - \bar{b})^2}{2s^2} - \frac{1}{2s^2} \sum_{k=1}^{K} [\phi_{1k}(\mu_{1k}^2 + s_{1k}^2) - \bar{b}^2]$$

and

$$D_{KL}(q \parallel p_{prior}(f)) = \sum_{k=1}^{K} \phi_{1k} \log \left( \frac{\phi_{1k}}{\pi_k} \right) - \frac{1}{2} \sum_{k=2}^{K} \phi_{1k} \left[ 1 + \log \left( \frac{s_{1k}^2}{u_{k}^2} \right) - \frac{\mu_{1k}^2 + s_{1k}^2}{u_{k}^2} \right],$$

where $\bar{b}$ is the posterior mean of $b$ with respect to $q$, $\bar{b} = \frac{\sum_{k=1}^{K} \phi_{1k} \mu_{1k}}{\sum_{k=1}^{K} \phi_{1k}}$. Here we have assumed that the first component in the prior mixture is a point mass at zero ($\sigma_{1}^2 = 0$).

### A.4 ELBO for Normal Means Model with Multiple Observations

Now we extend the above results for the single-observation NM model to the NM model multiple observations, $NM_p(f, s^2)$. Since the $b_j$'s are independent under the posterior, the ELBO is simply the sum of the ELBOs for the single-observation NM models:

$$F^{NM}(q, f, s^2) = \sum_{j=1}^{p} F_{1}^{NM}(q_j, f, s_{j}^2).$$

From Lemma 7, the $q$ that maximizes the ELBO is

$$q(b) = \prod_{j=1}^{p} q_j(b_j)$$

$$q_j(b_j) = p^{NM}(b_j | y_j, f, s_{j}^2),$$

It also follows that any $q$ maximizing the ELBO (56) must have the following form:

$$q(b) = \prod_{j=1}^{p} q_j(b_j)$$

$$q_j(b_j) = \sum_{k=1}^{K} \phi_{1jk} N(b_j; \mu_{1jk}, s_{1jk}^2),$$

in which $\phi_{1jk} \geq 0$, $\mu_{1jk} \in \mathbb{R}$, $s_{1jk}^2 > 0$, $j = 1, \ldots, p$, $k = 1, \ldots, K$. For any $q$ of the form (57), the analytic expression for the ELBO (56) is easily obtained by applying the analytic expression for the single-observation NM model (55).
Appendix B. Derivation of Algorithm 2 and Proof of Proposition 1

We prove Proposition 1 by proving a slightly more general proposition that does not require that \( x_j^T x_j = 1 \) for all \( j = 1, \ldots, p \).

Proposition 8 Let \( d_j = x_j^T x_j, \; j = 1, \ldots, p \), and let
\[
\tilde{b}_j \triangleq x_j^T \bar{r}_j / d_j
\]
denote the ordinary least squares (OLS) estimate of the coefficient \( b_j \) when the residuals \( \bar{r}_j \) are regressed against \( x_j \). See Proposition 1 for more notation. Then we have the following results:

(i) The coordinate ascent update \( q_j^* \triangleq \arg \max_{q_j} F(q, g, \sigma^2) \) is obtained by
\[
q_j^*(b_j) = p^{\text{NM}}(b_j; \tilde{b}_j, g, \sigma^2 / d_j)
\]
in which \( p^{\text{NM}} \), defined in (48), is the posterior distribution of \( b_j \) under the following NM model:
\[
\begin{align*}
\tilde{b} \mid b, \sigma^2 & \sim N(b, \sigma^2 / d_j) \\
b \mid g, \sigma^2 & \sim g_{\sigma}.
\end{align*}
\]

(ii) The coordinate ascent update
\[
g^* \triangleq \arg \max_{g \in \mathcal{G}(\sigma_1^2, \ldots, \sigma_K^2)} F(q, g, \sigma^2)
\]
is achieved by setting
\[
\begin{align*}
g^* &= \sum_{k=1}^K \pi_k^* N(0, \sigma_k^2) \\
\pi_k^* &= \frac{1}{p} \sum_{j=1}^p q_j(\gamma_j = k), \quad k = 1, \ldots, K.
\end{align*}
\]

In particular, if \( q_j \) is updated as in (i) above, so that \( q_j(b_j) = p^{\text{NM}}(b_j; \tilde{b}_j, g, \sigma^2 / d_j) \), then \( q_j(\gamma_j = k) \) is equal to the responsibility \( \phi_k(b_j; g, \sigma^2 / d_j) \) (51).

(iii) Using the parameterization of \( q \) in (57), and assuming that \( g \) is updated as in (ii) above, and \( \sigma_1^2 = 0 \), the coordinate ascent update
\[
(\sigma^2)^* \triangleq \arg \max_{\sigma^2 \in \mathbb{R}_+} F(q, g, \sigma^2)
\]
is achieved by setting
\[
(\sigma^2)^* = \left\lfloor \bar{r} \right\rfloor^2 + \sum_{j=1}^p \text{Var}_q(b_j) + \sum_{j=1}^p \sum_{k=2}^K \mathbb{E}[b_j \mid \gamma_j = k] / \sigma_k^2
\]
\[
= \left\lfloor \bar{r} \right\rfloor^2 + \sum_{j=1}^p \sum_{k=2}^K \phi_{jk}(d_j + 1 / \sigma_k^2)(\mu_{jk}^2 + s_{jk}^2) - \sum_{j=1}^p d_j \tilde{b}_j^2
\]
\[
= \frac{\left\lfloor \bar{r} \right\rfloor^2 + \sum_{j=1}^p \sum_{k=2}^K \phi_{jk}(d_j + 1 / \sigma_k^2)(\mu_{jk}^2 + s_{jk}^2) - \sum_{j=1}^p d_j \tilde{b}_j^2}{n + p(1 - \pi_1^*)}.
\]
in which $\bar{b}_j = \sum_{k=1}^K \phi_{1jk} \mu_{1jk}$, $j = 1, \ldots, p$. Additionally, if $q_1, \ldots, q_p$ are updated as in (i) above, we obtain the simpler update formula

$$
(\sigma^2)^* = \frac{\|r\|^2 + \bar{b}^T D(\bar{b} - \bar{b}) + \sigma^2 p(1 - \pi_1)}{n + p(1 - \pi_1)},
$$

(60)

where $D$ is the $p \times p$ diagonal matrix with diagonal entries $d_1, \ldots, d_p$.

Note that Proposition 1 is a special case of this proposition when $d_j = 1$, for $j = 1, \ldots, p$.

In the next sections, we prove parts (i), (ii) and (iii) of Proposition 8. These proofs start from the ELBO (21), which for convenience, we reproduce here:

$$
F(q, g, \sigma^2) = \mathbb{E}_q \log p(y \mid X, g, \sigma^2) - D_{KL}(q \parallel p_{\text{post}}).
$$

From Bayes’ rule,

$$
p_{\text{post}}(b) = \frac{p(y \mid X, b, \sigma^2) p(b \mid g, \sigma^2)}{\int p(y \mid X, b, \sigma^2) p(b \mid g, \sigma^2) \, db},
$$

we can write the ELBO as

$$
F(q, g, \sigma^2) = \mathbb{E}_q[\log p(y \mid X, b, \sigma^2)] - \sum_{j=1}^p D_{KL}(q_j \parallel p_{\text{prior}}).
$$

(61)

Next, using the property that $q$ factorizes over the individual coordinates $j = 1, \ldots, p$, we have

$$
F(q, g, \sigma^2) = -\frac{n}{2} \log(2\pi \sigma^2) - \frac{1}{2\sigma^2} \mathbb{E}_q[\|y - Xb\|^2] - \sum_{j=1}^p D_{KL}(q_j \parallel p_{\text{prior}}).
$$

(62)

**B.1 Update for $q_j$**

The coordinate ascent update for $q_j$ involves solving the following optimization problem:

$$
q_j^* = \arg \max_{q_j} F(q, g, \sigma^2).
$$

(63)

From the ELBO expression (61), this is equivalent to solving

$$
q_j^* = \arg \max_{q_j} \mathbb{E}_q[\log p(y \mid X, b, \sigma^2)] - D_{KL}(q_j \parallel p_{\text{prior}})
$$

(64)

By rearranging terms, it can be shown that this is equivalent to solving

$$
q_j^* = \arg \max_{q_j} -\frac{d_j}{2\sigma^2} \mathbb{E}_q[\|\bar{b}_j - b_j\|^2] - D_{KL}(q_j \parallel p_{\text{prior}}).
$$

(65)

The right-hand side of (65) is the ELBO for the NM model (59); that is, if we ignore constant terms, the ELBO in (53) recovers (65) by making the substitutions $y \leftarrow \bar{b}_j$, $s^2 \leftarrow \sigma^2/d_j$, $f \leftarrow g_{\sigma}$. And therefore from Lemma 7—and specifically from (54)—we have

$$
q_j^*(b_j) = p_{\text{NM}}(b_j \mid \bar{b}_j, g_{\sigma}, \sigma^2/d_j)
$$

$$
= \sum_{k=1}^K \phi_{1jk} N(b_j; \mu_{1jk}, s_{1jk}^2),
$$

(66)

(67)
in which
\[
\phi_{1jk} = \phi_{1k}(\tilde{b}_j, g_\sigma, \sigma^2/d_j)
\]
\[
\mu_{1jk} = \mu_{1k}(\tilde{b}_j, g_\sigma, \sigma^2/d_j)
\]
\[
s^2_{1jk} = s^2_{1k}(\tilde{b}_j, g_\sigma, \sigma^2/d_j).
\]

This proves part (i) of Proposition 8.

**B.2 Update for \(g\)**

The coordinate ascent update for \(g\) involves solving the following optimization problem:

\[
g^* \leftarrow \arg\max_{g \in \mathcal{G}} F(q, g, \sigma^2).
\] (68)

Recall, for the mixture prior with fixed mixture components, fitting \(g\) reduces to fitting the mixture weights, \(\pi\). Since \(\pi\) only appears in the ELBO in the K-L divergence term with respect to the prior, solving (68) is equivalent to solving

\[
\pi^* = \arg\min_{\pi \in \mathcal{S}^K} \sum_{j=1}^{p} D_{\text{KL}}(q_j || p_{\text{prior}}),
\]

and this simplifies further:

\[
\pi^* = \arg\max_{\pi \in \mathcal{S}^K} \sum_{j=1}^{p} \sum_{k=1}^{K} \phi_{jk} \log \pi_k.
\]

This basic optimization problem has the following analytic solution:

\[
\pi^*_k = \frac{1}{p} \sum_{j=1}^{p} \phi_{jk}, \quad k = 1, \ldots, K.
\]

This proves part (ii) of Proposition 8.

This update can be thought of as an approximate M step update for the mixture weights in which the posterior probabilities (the “responsibilities”) are computed approximately based on the variational approximation \(q\).

**B.3 Update for \(\sigma^2\)**

The coordinate ascent update for the residual variance \(\sigma^2\) is the solution to

\[
(\sigma^2)^* = \arg\max_{\sigma^2 \in \mathbb{R}_+} F(q, g, \sigma^2).
\] (69)

From earlier results, the ELBO for any \(q\) parameterized as (57) works out to

\[
F(q, g, \sigma^2) = \mathbb{E}_q[\log p(y | \mathbf{X}, \mathbf{b}, \sigma^2)] - \sum_{j=1}^{p} D_{\text{KL}}(q_j || p_{\text{prior}})
\] (70)
in which

\[
E_q[\log p(y \mid X, b, \sigma^2)] = -\frac{n}{2} \log(2\pi\sigma^2) - \frac{1}{2\sigma^2} \|y - X\bar{b}\|^2 \\
- \frac{1}{2\sigma^2} \sum_{j=1}^{p} d_j \left[ \sum_{k=1}^{K} \phi_{1jk}(\mu_{1jk} + s_{1jk}^2) - \bar{\theta}_j^2 \right]
\]

(71)

\[
D_{\text{KL}}(q_j \| p_{\text{prior}}) = \sum_{k=1}^{K} \phi_{1jk} \log \frac{\phi_{1jk}}{\pi_k} - \frac{1}{2} \sum_{k=2}^{K} \phi_{1jk} \left[ 1 + \log \frac{s_{1jk}^2}{\sigma^2\sigma_k^2} - \frac{s_{1jk}^2 + \mu_{1jk}^2}{\sigma^2\sigma_k^2} \right],
\]

(72)

and \(\bar{b}_j = \sum_{k=1}^{K} \phi_{1jk} \mu_{1jk}\). Taking the partial derivative of \(F\) with respect to \(\sigma^2\), then solving for \(\sigma^2\), yields the following update for \(\sigma^2\):

\[
(\sigma^2)^* = \frac{\|y - X\bar{b}\|^2 + \sum_{j=1}^{p} \sum_{k=2}^{K} \phi_{1jk}(d_j + 1/\sigma_k^2)(\mu_{1jk}^2 + s_{1jk}^2) - \sum_{j=1}^{p} d_j \bar{b}_j^2}{n + p(1 - \pi_1)}.
\]

(73)

When \(\sigma^2\) is updated following updates to the \(q_j\)'s, we can simplify this expression by noting the specific form of the posterior means and variances,

\[
s_{1jk}^2 = \frac{\sigma^2}{d_j + 1/\sigma_k^2},
\]

\[
\mu_{1jk} = \frac{d_j \bar{b}_j}{d_j + 1/\sigma_k^2},
\]

for \(k = 2, \ldots, K\), which gives

\[
(\sigma^2)^* = \frac{\|y - X\bar{b}\|^2 + \sum_{j=1}^{p} \sum_{k=2}^{K} \phi_{1jk}(\mu_{1jk} d_j \bar{b}_j + \sigma^2) - \sum_{j=1}^{p} d_j \bar{b}_j^2}{n + p(1 - \pi_1)}
\]

\[
= \frac{\|y - X\bar{b}\|^2 + \sum_{j=1}^{p} d_j \bar{b}_j(\tilde{b}_j - \bar{b}_j) + p(1 - \pi_1)\sigma^2}{n + p(1 - \pi_1)}.
\]

This proves part (iii) of Proposition 8.

B.4 More details on the VEB algorithm

Further details about the implementation of the VEB algorithm are given in Algorithm 4. Note that, unlike Algorithm 2, Algorithm 4 does not require that \(x_j^T x_j = 1, j = 1, \ldots, p\).

Appendix C. VEB as a PLR

C.1 Normal Means as a Penalized Estimation Problem

In this section, we formulate the normal means problem with one observation, \(\text{NM}_1(f, s^2)\), as penalized estimation problem. Specifically, we will express the posterior mean of \(b\) under the NM model as a solution to a penalized least squares problem. The results derived here for the single-observation NM model are used below to derive results for the multiple linear regression model.
Algorithm 4 Coordinate ascent for fitting VEB model (with more details).

Require: Data $X \in \mathbb{R}^{n \times p}, y \in \mathbb{R}^n$; number of mixture components, $K$; prior variances, $\sigma_1^2 < \cdots < \sigma_K^2$, with $\sigma_1^2 = 0$; initial estimates $b, \pi, \sigma^2$.

$r \leftarrow y - Xb$ (compute mean residuals)

$t \leftarrow 0$

for $j \leftarrow 1 \text{ to } p$ do

$d_j = x_j^T x_j$

end for

repeat

$\pi^{(\text{new})} \leftarrow 0.$

for $j \leftarrow 1 \text{ to } p$ do

$\tilde{b}_j \leftarrow \tilde{b}_j^{(t)} + x_j^T r/d_j$ (compute OLS estimate)

for $k \leftarrow 1 \text{ to } K$ do

$\phi_{jk} \leftarrow \frac{\pi_k}{1 + d_j \sigma_k^2} \exp \left\{ \frac{1}{2\sigma^2} \times \frac{d_j^2 \tilde{b}_j^2}{d_j + 1/\sigma_k^2} \right\}$ (update $q_j$)

$\pi^{(\text{new})}_k \leftarrow \pi^{(\text{new})} + \phi_{jk}$

end for

$z_j \leftarrow \sum_{k=1}^K \phi_{jk}$

for $k \leftarrow 1 \text{ to } K$ do

$\phi_{jk} \leftarrow \phi_{jk} / z_j$

$\pi^{(\text{new})}_k \leftarrow \pi^{(\text{new})} + \phi_{jk}$

end for

$\bar{b}_j^{(\text{new})} \leftarrow \sum_{k=1}^K \phi_{jk} \times \frac{d_j}{d_j + 1/\sigma_k^2} \times \tilde{b}_j$ (update posterior mean of $b_j$)

$\bar{r} \leftarrow \bar{r} - x_j (\bar{b}_j^{(\text{new})} - \tilde{b}_j)$ (update mean residuals)

end for

$\pi \leftarrow \pi^{(\text{new})} / p$ (update $\pi$; eq. 29)

$\sigma^2 \leftarrow \frac{||\bar{r}||^2 + \sum_{j=1}^p d_j \bar{b}_j (\bar{b}_j - \tilde{b}_j) + \sigma^2 p (1 - \pi_1)}{n + p (1 - \pi_1)}$ (update $\sigma^2$; eq. 31)

$t \leftarrow t + 1.$

until convergence criteria is met

return $\bar{b}, \pi, \sigma^2$

Recall that $F_{NM}(q, f, s^2; y)$ denotes the ELBO for the NM model (see 53). From this we define

$$- h_{NM}(\bar{b}, f, s^2; y) \triangleq \max_{q: \mathbb{E}_q(b) = \bar{b}} F_{NM}(q, f, s^2; y).$$ (74)

As a reminder, $F_{NM}(q, f, s^2; y)$ attains its maximum over $q$ at $q = p_{\text{post}}^{NM}$, which is the (exact) posterior; analogously, $h_{NM}(\bar{b}, f, s^2; y)$ attains its minimum over $\bar{b}$ at $\bar{b} = S_{f,s}(y)$, which is the posterior mean of $b$ under the NM1 $(f, s^2)$ model (refer to Definition 4).
Further, at their respective optima these two functions recover the marginal likelihood:

\[
\log p(y \mid f, s^2) = F(p_{\text{post}}^{\text{NM}}, f, s^2; y) = \max_q F^{\text{NM}}(q, f, s^2; y) = \max_{b \in \mathbb{R}} \max_{q : \mathbb{E}_q(b) = b} F^{\text{NM}}(q, f, s^2; y) = \max_{b \in \mathbb{R}} -h^{\text{NM}}(\bar{b}, f, s^2; y) = -h^{\text{NM}}(S_{f,s}(y), f, s^2; y).
\]

With these definitions we can express the posterior mean for \(b\) as the solution to a real-valued optimization problem:

\[
S_{f,s}(y) = \arg \min_b h^{\text{NM}}(\bar{b}, f, s^2; y).
\]

The following lemma states that this can be understood as optimizing a penalized loss function, and gives an explicit form for the penalty term.

**Lemma 9** \(h^{\text{NM}}(\bar{b}, f, s^2; y)\) can be written as a penalized loss function,

\[
h^{\text{NM}}(\bar{b}, f, s^2; y) = \frac{1}{2s^2}(y - \bar{b})^2 + \frac{1}{s^2} \rho_{f,s}(\bar{b}),
\]

in which the penalty term is

\[
\rho_{f,s}(\bar{b}) \triangleq \min_{q : \mathbb{E}_q(b) = \bar{b}} \frac{1}{2} \mathbb{E}_q(\mathbb{E}_q(b) + s^2 D_{\text{KL}}(q \parallel p_{\text{prior}}(f))) + \frac{s^2}{2} \log(2\pi s^2).
\]

For any \(y \in \mathbb{R}\), this penalty term satisfies

\[
\rho_{f,s}(S_{f,s}(y)) = -s^2 \ell^{\text{NM}}(y; f, s^2) - (y - S_{f,s}(y))^2/2,
\]

and

\[
(\rho_{f,s})'(S_{f,s}(y)) = (y - S_{f,s}(y))
\]

in which \(\ell^{\text{NM}}(y; f, s^2)\) is the marginal log-likelihood \(\ell^{\text{NM}}(y; f, s^2) = \log p(y \mid f, s^2)\) for the single-observation normal means model, NM\(_1(f, s^2)\).

**Proof** From (53), we have

\[
F^{\text{NM}}(q, f, s^2; y) = \frac{1}{2} \log(2\pi s^2) - \frac{1}{2s^2} \mathbb{E}_q[(y - b)^2] - D_{\text{KL}}(q \parallel p_{\text{prior}}(f))
\]

\[
= -\frac{1}{2s^2}(y - \mathbb{E}_q(b))^2 - \left[ \frac{1}{2s^2} \mathbb{E}_q(b) + D_{\text{KL}}(q \parallel p_{\text{prior}}(f)) + \frac{1}{2} \log(2\pi s^2) \right].
\]

Expressions (75) and (76) follow from definition (74).
Expression (77) is obtained by substituting $\bar{b} = S_{f,s}(y)$ into (75) and rearranging, noting that $h(\bar{b}, f, s^2; y)$ attains it minimum at this $\bar{b}$, and therefore it recovers the marginal log-likelihood,

$$-h_{NM}(S_{f,s}(y), f, s^2; y) = \ell_{NM}(y; f, s^2).$$

Expression (78) is a consequence of the fact that $h_{NM}(\bar{b}, f, s^2; y)$ attains its minimum at $\bar{b} = S_{f,s}(y)$ for any $y \in \mathbb{R}$; that is,

$$S_{f,s}(y) = \arg \min_{\bar{b} \in \mathbb{R}} h_{NM}(\bar{b}, f, s^2; y).$$

Therefore, the derivative of (75) with respect to $\bar{b}$ at $\bar{b} = S_{f,s}(y)$ must be zero. Finally, (79) is obtained by applying Tweedie’s formula (Efron, 2011).

### C.2 VEB as a Penalized Regression Problem

Here we consider the ELBO for multiple linear regression (22), defining

$$h(\bar{b}, g, \sigma^2) \triangleq \max_{q: \mathbb{E}_q(b) = \bar{b}} F(q, g, \sigma^2). \quad (80)$$

We begin with the following basic lemma.

**Lemma 10** If the distribution $q(b)$ factorizes as $q(b) = \prod_{j=1}^{p} q_j(b_j)$, then

$$\mathbb{E}_q[\|y - Xb\|^2] = \|y - X\bar{b}\|^2 + \sum_{j=1}^{p} d_j \text{Var}_{q_j}(b_j),$$

where $\bar{b} = \mathbb{E}_q(b)$ and $d_j \triangleq x_j^T x_j$.

**Proof**

$$\mathbb{E}_q[\|y - Xb\|^2] = \mathbb{E}_q[\|y - Xb + X(\bar{b} - b)\|^2]$$

$$= \|y - X\bar{b}\|^2 + \mathbb{E}_q[\|X(\bar{b} - b)\|^2]$$

$$= \|y - X\bar{b}\|^2 + \mathbb{E}_q[(\bar{b} - b)^T X^T X (\bar{b} - b)]$$

$$= \|y - X\bar{b}\|^2 + \text{tr}(X^T X \text{Cov}_q(b))$$

$$= \|y - X\bar{b}\|^2 + \sum_{j=1}^{p} d_j \text{Var}_{q_j}(b_j).$$

In the following proposition, we express the ELBO for multiple line regression as a penalized loss function.

**Proposition 11** $h(\bar{b}, g, \sigma^2)$ defined in (38) can be written as a penalized loss function,

$$h(\bar{b}, g, \sigma^2) = \frac{1}{2\sigma^2} \|y - X\bar{b}\|^2 + \frac{1}{\sigma^2} \sum_{j=1}^{p} d_j \rho_{g, s_j}(\bar{b}_j) + \frac{1}{2} \sum_{j=1}^{p} \log(d_j) + \frac{n - p}{2} \log(2\pi \sigma^2), \quad (81)$$

using the penalty function $\rho_{f,s}$ defined in (76) in Lemma 9, and defining $s_j^2 \triangleq \sigma^2/d_j$, $j = 1, \ldots, p$. Note that when $d_j = 1$, $k = 1, \ldots, p$, this expression simplifies to (39).
Proof From Lemma 10, we have

\[
\begin{align*}
\log(h(\bar{b}, g, \sigma^2)) &= \frac{n}{2} \log(2\pi \sigma^2) + \frac{1}{2\sigma^2} \sum_{j=1}^{p} D_{KL}(q_j \parallel p_{prior}(g_\sigma)) \\
&= \frac{n}{2} \log(2\pi \sigma^2) + \frac{1}{2\sigma^2} \sum_{j=1}^{p} \sigma_j^2 \text{Var}_{q_j}(b_j) + \sum_{j=1}^{p} D_{KL}(q_j \parallel p_{prior}(g_\sigma)).
\end{align*}
\]

Therefore,

\[
\begin{align*}
\log(h(\bar{b}, g, \sigma^2)) &= \max_{q : E_q(b) = \bar{b}} F(q, g, \sigma^2) \\
&= \frac{n}{2} \log(2\pi \sigma^2) + \frac{1}{2\sigma^2} \|y - X\bar{b}\|^2 \\
&\quad + \sum_{j=1}^{p} \frac{d_j}{\sigma_j^2} \times \min_{q_i : E_{q_i}(b_i) = \bar{b}_i} \left\{ \frac{1}{2} \text{Var}_{q_i}(b_i) + \frac{\sigma_i^2}{d_j} D_{KL}(q_i \parallel p_{prior}(g_\sigma)) \right\} \\
&= \frac{1}{2\sigma^2} \|y - X\bar{b}\|^2 + \sum_{j=1}^{p} \frac{d_j}{\sigma_j^2} \left[ \rho_{g_\sigma,s_j}(\bar{b}_j) - \frac{\sigma_j^2 \log(2\pi \sigma_j^2/d_j)}{2d_j} \right] + \frac{n}{2} \log(2\pi \sigma^2) \\
&= \frac{1}{2\sigma^2} \|y - X\bar{b}\|^2 + \sum_{j=1}^{p} \frac{d_j}{\sigma_j^2} \rho_{g_\sigma,s_j}(\bar{b}_j) + \frac{1}{2} \sum_{j=1}^{p} \log(d_j) + \frac{n - p}{2} \log(2\pi \sigma^2).
\end{align*}
\]

Appendix D. Additional proofs

D.1 Proof of Proposition 2

By Proposition 2.7.1 of Bertsekas (1999), the sequence of iterates \(\{q^{(t)}, g^{(t)}, (\sigma^2)^{(t)}\}\), \(t = 0, 1, 2, \ldots\), generated by Algorithm 2 converges monotonically to a stationary point of the ELBO, \(F(22)\), provided that \(F(22)\) is continuously differentiable, and each coordinate update, \(\arg \max_{q_j} F(q_1^{(t+1)}, \ldots, q_{j-1}^{(t+1)}, q_j, q_{j+1}^{(t)}, \ldots, q_p^{(t)}, g^{(t)}, (\sigma^2)^{(t)})\), \(j = 1, \ldots, p\)

is finite and uniquely determined. A sufficient condition for \(F(22)\) to be continuously differentiable and for the coordinate ascent updates (see Proposition 1 or Proposition 8) to have a unique solution is that \(0 < \sigma^2 < \infty\), \(\pi_k > 0\) for all \(k = 1, \ldots, K\), and \(0 \leq \sigma_1^2 < \cdots < \sigma_K^2 < \infty\). This completes the proof.
D.2 Proof of Proposition 3

The ELBO

\[ F(q, g, \sigma^2) = \int \int q(b, \gamma) \log \left\{ \frac{p(y \mid X, b, \sigma^2) p(b, \gamma \mid g, \sigma^2)}{q(b, \gamma)} \right\} \, db \, d\gamma \]

is maximized with respect to \( q \) when \( q(b, \gamma) \propto p(y \mid X, b, \sigma^2) p(b, \gamma \mid g, \sigma^2) \). This follows from the equality condition of Jensen’s inequality (Jordan et al., 1999). When the columnns of \( X \) are orthogonal, the posterior factorizes over the individual coordinates \( j \),

\[
p(b, \gamma \mid X, y, g, \sigma^2) \propto p(b, \gamma \mid g, \sigma^2) p(y \mid X, b, \sigma^2) \propto p(\prod_{j=1}^{p} (b_j, \gamma_j \mid g, \sigma^2)) \times \exp \left\{ -\frac{(b_j - x_j^T y)^2}{2\sigma^2} \right\}.
\]

Therefore, when \( X \) has orthogonal columnns, the best \( q \), even with the restriction of being fully factorized (19), is able to recover the exact posterior since the exact posterior also factorizes over the coordinates \( j = 1, \ldots, p \).

D.3 Proof of Proposition 5

First, we note that

\[ F(\hat{q}, \hat{g}, \hat{\sigma}^2) = \max_{q \in Q} F(q, \hat{g}, \hat{\sigma}^2) = -h(\hat{b}, \hat{g}, \hat{\sigma}^2). \]

Hence, for any \( \tilde{b} \in \mathbb{R}^p \), we have

\[
-h(\tilde{b}, g, \sigma^2) = \max_{q \in Q, \mathbb{E}_q[b] = \tilde{b}} F(q, g, \sigma^2) \\
\leq \max_{q \in Q} F(q, g, \sigma^2) \\
\leq \max_{q \in Q, g \in G, \sigma^2 \in T} F(q, g, \sigma^2) \\
= F(\hat{\tilde{b}}, \hat{g}, \hat{\sigma}^2) \\
= -h(\hat{\tilde{b}}, \hat{g}, \hat{\sigma}^2).
\]

This proves that

\[ \hat{\tilde{b}}, \hat{g}, \hat{\sigma}^2 = \arg \min_{\tilde{b} \in \mathbb{R}^p, g \in G, \sigma^2 \in T} h(\tilde{b}, g, \sigma^2). \]

D.4 Proof of Theorem 6

The proof of the first part of Theorem 6 follows immediately from Proposition 11 and Lemma 9 by letting \( d_j = 1 \) for \( j = 1, \ldots, p \).

To show that that \( S_{\rho_f, \sigma}(y) = S_{f, \sigma}(y) \), we start with the definition of \( S_f \) in (34), which gives

\[ S_{\rho_f, \sigma}(y) = \arg \min_{b \in \mathbb{R}} \frac{1}{2} (y - b)^2 + \rho_f, \sigma(b). \]
To solve for the argmin on the right-hand side, we differentiate with respect to $b$ and set the derivative to zero,

$$\rho'_{f,\sigma}(b) = (y - b).$$

From (41), this derivative vanishes when $b = S_{f,\sigma}(y)$. This shows that $S_{\rho,\sigma}(y) = S_{f,\sigma}(y)$.

**D.5 Mathematical Properties of the Posterior Mean Shrinkage Operator**

**Lemma 12** Let $f$ be a symmetric unimodal distribution on $\mathbb{R}$ with a mode at zero, and assume $\sigma^2 > 0$. Then the NM posterior mean operator $S_{f,\sigma}(y)$ defined in (35) is symmetric, non-negative, and non-decreasing on $y \in \mathbb{R}$, and $S_{f,\sigma}(y) \leq y$ on $y \in (0, \infty)$. That is, $S_{f,\sigma}$ is a shrinkage operator that shrinks towards zero.

**Proof** For convenience, we restate the NM model here, originally defined in (36):

$$y \mid b, \sigma^2 \sim \mathcal{N}(b, \sigma^2)$$

$$b \sim f.$$

The marginal likelihood for this model is

$$\ell_{\text{NM}}(y; f, \sigma^2) \triangleq \log p(y \mid f, \sigma^2)$$

$$= \int p(y \mid b, \sigma^2) p(b) \, db$$

$$= \int \mathcal{N}(y; b, \sigma^2) f(b) \, db.$$

By Khintchine’s representation theorem (Dharmadhikari and Joag-Dev, 1988), $f$ can be represented as mixture of uniform distributions,

$$f(b) = \int_0^\infty \frac{\mathbb{I}\{|b| < t\}}{2t} p(t) \, dt$$

for some (possibly improper) univariate mixing density $p(t)$. Let $p(b \mid t)$ be the density function of the uniform distribution on $[-t, t]$. Then we have

$$p(y \mid f, \sigma^2) = \int p(y \mid b, \sigma^2) p(b \mid f, \sigma^2) \, db$$

$$= \int_0^\infty \left[ \int p(y \mid b, \sigma^2) p(b \mid t) \, db \right] \times p(t) \, dt$$

$$= \int_0^\infty p(y \mid \sigma^2, t) p(t) \, dt,$$

(82)

where

$$p(y \mid \sigma^2, t) = \int p(y \mid b, \sigma^2) p(b \mid t) \, db$$

$$= \frac{1}{2t} \left[ \Phi \left( \frac{t - y}{\sigma} \right) + \Phi \left( \frac{t + y}{\sigma} \right) - 1 \right],$$

(83)

and where $\Phi(x)$ denotes the normal cumulative distribution function. Note that, from (36), $p(y \mid b, \sigma^2) = \mathcal{N}(y; b, \sigma^2)$. Since $\Phi(t + y) + \Phi(t - y)$ is non-increasing in $y \in (0, \infty)$ for any $t \geq 0$, $p(y \mid \sigma^2, t)$ is also non-increasing in $y \in (0, \infty)$ for any $t \geq 0$. This implies that $p(y \mid \sigma^2, t)$ is unimodal with a mode at zero, and therefore $p(y \mid f, \sigma^2)$ must also be
Flexible empirical Bayes regression

unimodal with a mode at zero since it is a mixture of unimodal distributions that all have modes at zero.

From (79), which was obtained by applying Tweedie’s formula, we have that

\[ S_{f,\sigma}(y) = y + \sigma^2 \ell'_{NM}(y; f, \sigma) \leq y, \]

in which the inequality is obtained by noting that \( \ell_{NM}(y; f, \sigma) \) is non-increasing in \( y \in (0, \infty) \). And since \( \ell_{NM}(y; f, \sigma^2) \) is symmetric about zero, the shrinkage operator must be an odd function; i.e., \( S_{f,\sigma}(y) = -S_{f,\sigma}(-y) \).

It remains to show that \( S_{f,\sigma}(y) \) is non-decreasing on \( y \in \mathbb{R}_+ \). Since \( p(y \mid b, \sigma^2) = N(y; b, \sigma^2) \) and \( p(b \mid t) \) is the uniform distribution on interval \([-t, t]\), the posterior density is truncated normal:

\[
p(b \mid y, \sigma^2, t) \propto p(y \mid b, \sigma^2) p(b \mid t)
= N_{[-t,t]}(b; y, s^2)
\]

where \( N_{[-t,t]}(x; \mu, s^2) = N(x; \mu, s^2) \mathbb{I}\{x < t\} \) denotes the probability density of the normal distribution with mean \( \mu \) and variance \( s^2 \) truncated to the interval \( x \in [-t, t] \). Clearly, the expected value of the truncated normal,

\[
E[X] = \mu + s \times \frac{N(\mu + t; 0, s^2) - N(\mu - t; 0, s^2)}{\Phi((t - \mu)/s) - \Phi(-(t + \mu)/s)},
\]

is non-decreasing with respect to \( \mu \), for all \( \mu \in \mathbb{R}, t > 0 \). To show this, we simply note that the derivative of the expected value with respect to \( \mu \) is always positive: \( \frac{\partial}{\partial \mu}E[X] = \text{Var}(X)/s^2 > 0 \). Therefore, \( S_{f,\sigma} \) is a mixture of non-decreasing functions on \( \mathbb{R}_+ \). This completes the proof.

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