

Introduction to Bayesian Linear Regression, Posterior Inference, and MCMC

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Overview

- **Classical Linear Regression**
 - Model, inference, and limitations
- **Bayesian Linear Regression**
 - Motivation, priors, and posteriors
 - Conditional posteriors and inference
- **Computation and Applications**
 - MCMC and Gibbs sampling
 - Diagnostics and R implementation

Introduction

- **Bayesian Linear Regression (BLR)** extends classical regression by incorporating **prior information** and producing **posterior distributions** over model parameters.
- **Advantages:**
 - Handles **high-dimensional** and **small-sample** problems.
 - Provides **full uncertainty quantification**.
 - Enables **regularization** and integration of **prior biological knowledge**.

Applications in Genomics

- **Bayesian Linear Regression (BLR)** is widely applied in quantitative genetics and genomics.
- **Common use cases:**
 - Genome-Wide Association Studies (**GWAS**) and **fine-mapping** of causal variants.
 - **Genetic prediction** and **heritability estimation**.
 - **Pathway** and **gene-set enrichment** analyses.
 - Integrative **multi-omics** modeling (genome, transcriptome, epigenome).

Classical Linear Regression

Model

$$y = X\beta + e, \quad e \sim \mathcal{N}(0, \sigma^2 I_n)$$

- y : outcomes
- X : design matrix
- β : coefficients
- e : are the residuals
- σ^2 : residual variance

Estimation

Regression effects:

$$\hat{\beta} = (X^{\top} X)^{-1} X^{\top} y$$

Residual variance:

$$\hat{\sigma}^2 = \frac{1}{n - p} \sum_i (y_i - x_i^{\top} \hat{\beta})^2$$

Inference via standard errors and t -tests, confidence intervals, and prediction intervals.

Limitations

- No explicit control over **effect size distribution**
- Sensitive when **collinearity** is high
- **Not identifiable** when $p > n$
- Uncertainty largely **asymptotic** unless normality assumptions hold

Why Bayesian Linear Regression?

- Combines **likelihood** and **prior** to form the **posterior**.
- Priors express beliefs about **effect sizes**:
 - Normal \rightarrow many small effects
 - Spike-and-slab \rightarrow sparse effects
- Acts as a **regularizer**:
 - Shrinks small/noisy effects toward 0
 - Preserves large, important effects
- **Stable when** $p > n$ due to prior information.
- Provides **full posterior distributions** for β and σ^2 .

Overview: Bayesian Linear Regression

- Combines data and prior knowledge using **Bayes' rule**.
- Uses **conjugate priors** to yield closed-form full conditionals.
- Employs **Gibbs sampling** to approximate the posterior distribution.
- Estimates **parameters, uncertainty, and predictions** from posterior draws.

Bayesian Linear Regression with Gaussian Priors

Bayesian linear regression starts with the same model structure as classical linear regression.

$$y = X\beta + e, \quad e \sim \mathcal{N}(0, \sigma^2 I_n)$$

- y : $n \times 1$ vector of observed outcomes
- X : $n \times p$ design matrix of predictors
- β : $p \times 1$ vector of unknown coefficients
- e : Gaussian noise with mean 0 and variance σ^2

Likelihood in Bayesian Linear Regression

Because the residuals are Gaussian, it follows that the marginal distribution of y is:

$$e \sim \mathcal{N}(0, \sigma^2 I_n)$$

The marginal distribution of y is:

$$y \sim \mathcal{N}(X\beta, \sigma^2 I_n)$$

This defines the **likelihood** the probability of the observed data given parameters β and σ^2 :

$$p(y \mid X, \beta, \sigma^2) = \mathcal{N}(X\beta, \sigma^2 I_n)$$

Introducing Priors

In Bayesian linear regression, we specify **prior distributions** that express our beliefs about parameters before seeing the data.

A common **conjugate prior** for the regression coefficients is:

$$\beta \mid \sigma_b^2 \sim \mathcal{N}(0, \sigma_b^2 I_p)$$

This reflects the belief that most effect sizes are small and centered near zero — consistent with the **polygenic assumption** in genetics.

Role of the Prior Variance σ_b^2

The parameter σ_b^2 acts as a **shrinkage (regularization) parameter**:

- Small $\sigma_b^2 \rightarrow$ stronger shrinkage toward zero.
- Large $\sigma_b^2 \rightarrow$ weaker shrinkage, allowing larger effects.

It controls the **strength of regularization** and is often treated as an **unknown hyperparameter** estimated from the data.

Priors on Variance Components

We also place priors on the variance components to complete the hierarchical model.

$$\sigma_b^2 \mid S_b, v_b \sim S_b \chi^{-2}(v_b), \quad \sigma^2 \mid S, v \sim S \chi^{-2}(v)$$

Here:

- S_b and v_b are user-defined hyperparameters that control the prior distribution on the **variance of regression coefficients**.
- S and v are hyperparameters for the **residual variance** σ^2 .

Conjugate Priors and Regularization

Conjugate priors keep posteriors in the same family (e.g., scaled inverse-chi-squared), allowing **closed-form Gibbs updates**.

They also serve as **regularizers**:

- The prior on β shrinks small or noisy effects toward zero.
- Priors on variance components prevent overfitting, especially when $p > n$.

Thus, conjugate priors make Bayesian linear regression **efficient** and **stable**.

Posterior Distribution

In Bayesian analysis, we combine the **likelihood** and **priors** using Bayes' rule to obtain the **joint posterior**:

$$p(\beta, \sigma_b^2, \sigma^2 \mid y) \propto p(y \mid \beta, \sigma^2) p(\beta \mid \sigma_b^2) p(\sigma_b^2) p(\sigma^2)$$

This posterior captures all **updated knowledge** about the unknown parameters after observing the data.

It forms the basis for computing **posterior means**, **credible intervals**, and **predictions**.

Conjugacy and Gibbs Sampling

With **conjugate priors**, each parameter's **full conditional distribution** has a closed-form solution.

This makes **Gibbs sampling** a natural and efficient inference method.

- Parameters are updated one at a time, each from its conditional posterior.
- The resulting Markov chain explores the **joint posterior** of $(\beta, \sigma_b^2, \sigma^2)$.

Gibbs sampling thus provides an easy way to approximate the full posterior in Bayesian linear regression.

Full Conditional for β

Given σ^2 , σ_b^2 , and the data y , the regression coefficients have a **multivariate normal** conditional posterior:

$$\beta \mid \sigma^2, \sigma_b^2, y \sim \mathcal{N}(\mu_\beta, \Sigma_\beta)$$

where

$$\Sigma_\beta = \left(\frac{X^\top X}{\sigma^2} + \frac{I}{\sigma_b^2} \right)^{-1}, \quad \mu_\beta = \Sigma_\beta \frac{X^\top y}{\sigma^2}$$

This distribution represents our **updated belief** about β after observing the data, while holding σ_b^2 and σ^2 fixed.

Comparison to Classical OLS

In classical regression, the OLS estimator is

$$\hat{\beta}_{\text{OLS}} = (X^\top X)^{-1} X^\top y, \quad y \sim \mathcal{N}(X\beta, \sigma^2 I)$$

The estimate of β is **independent of** σ^2 ,
since σ^2 only scales the likelihood, not its maximum.

In Bayesian regression, σ^2 appears explicitly in the posterior:

$$\Sigma_\beta = \left(\frac{X^\top X}{\sigma^2} + \frac{I}{\sigma_b^2} \right)^{-1}, \quad \mu_\beta = \Sigma_\beta \frac{X^\top y}{\sigma^2}$$

The term $\frac{I}{\sigma_b^2}$ introduces **shrinkage**, regularizing estimates and stabilizing inference especially when $p > n$ or predictors are highly correlated.

Thus, the Bayesian posterior mean is a **regularized, uncertainty-aware generalization** of OLS.

Full Conditional for β_j

Instead of sampling β jointly, we can update each coefficient β_j **one at a time**, holding all others fixed efficient for large p or spike-and-slab models.

Let X_j be the j th column of X and define the **partial residual**:

$$r_j = y - X_{-j}\beta_{-j}$$

Then the conditional posterior for β_j is univariate normal:

$$\beta_j \mid D \sim \mathcal{N}\left(\frac{X_j^\top r_j}{X_j^\top X_j + \sigma^2/\sigma_b^2}, \frac{\sigma^2}{X_j^\top X_j + \sigma^2/\sigma_b^2}\right)$$

This corresponds to a **regularized least-squares update**. Residual updates **avoid matrix inversion**, scale to high dimensions, and extend naturally to **sparse (spike-and-slab)** models.

Full Conditional for σ_b^2

The conditional distribution of the **prior variance** σ_b^2 , given β and the hyperparameters, is a **scaled inverse-chi-squared**:

$$\sigma_b^2 \mid \beta \sim \tilde{S}_b \chi^{-2}(\tilde{v}_b)$$

where

$$\tilde{v}_b = v_b + p, \quad \tilde{S}_b = \frac{\beta^\top \beta + v_b S_b}{\tilde{v}_b}$$

At each Gibbs iteration, σ_b^2 is sampled directly given β . This update reflects our revised belief about the **variability of effect sizes** after observing the current posterior draw of β .

Full Conditional for σ^2

The conditional distribution of the **residual variance** σ^2 , given β and the data, is also **scaled inverse-chi-squared**:

$$\sigma^2 \mid \beta, y \sim \tilde{S} \chi^{-2}(\tilde{v})$$

where

$$\tilde{v} = v + n, \quad \tilde{S} = \frac{(y - X\beta)^\top (y - X\beta) + vS}{\tilde{v}}$$

At each Gibbs iteration, σ^2 is sampled directly given β . This captures our updated belief about the **residual variability** after accounting for the current linear predictor $X\beta$.

Gibbs Sampling: Motivation

Bayesian inference often involves **complex posteriors** that lack closed-form solutions. To approximate these, we use **Markov Chain Monte Carlo (MCMC)** methods.

MCMC builds a **Markov chain** whose stationary distribution is the target posterior. Once the chain has **converged**, its samples can be used to estimate:

- Posterior means, variances, and credible intervals
- Predictive distributions
- Other functions of interest

Among MCMC algorithms, the **Gibbs sampler** is especially useful when all **full conditional distributions** are available in **closed form**.

Gibbs Sampling: The Algorithm

For Bayesian linear regression with conjugate priors, the joint posterior is:

$$p(\beta, \sigma_b^2, \sigma^2 \mid y) \propto p(y \mid \beta, \sigma^2) p(\beta \mid \sigma_b^2) p(\sigma_b^2) p(\sigma^2)$$

We iteratively draw from the following **full conditionals**:

1. Sample $\beta \mid \sigma_b^2, \sigma^2, y$
2. Sample $\sigma_b^2 \mid \beta$
3. Sample $\sigma^2 \mid \beta, y$

Each step updates one parameter given the latest values of the others. Repeating this sequence yields samples from the **joint posterior** $p(\beta, \sigma_b^2, \sigma^2 \mid y)$.

Because each conditional is **standard** (Normal or scaled inverse- χ^2), Gibbs sampling is both **efficient** and **easy to implement**.

Posterior Summaries

After running the Gibbs sampler, we obtain posterior draws $\{\theta^{(t)}\}_{t=1}^T$ for parameters such as β_j , σ^2 , or σ_b^2 .

We summarize the posterior distribution via:

- **Posterior mean**

$$\mathbb{E}[\theta \mid y] \approx \frac{1}{T} \sum_{t=1}^T \theta^{(t)}$$

- **Posterior median:** the median of $\theta^{(t)}$
- **Credible interval (95%)**

$$[\theta]_{0.025}, [\theta]_{0.975}$$

These summaries describe the most probable values of θ and their uncertainty after combining data and prior beliefs.

Estimating Uncertainty

Bayesian inference provides **full posterior distributions**, not just point estimates. Uncertainty is quantified directly from the posterior samples:

- **Posterior standard deviation**

$$\text{SD}(\theta \mid y) \approx \sqrt{\frac{1}{T-1} \sum_{t=1}^T (\theta^{(t)} - \bar{\theta})^2}$$

The **width** of the credible interval reflects this uncertainty. Parameters with broader posteriors are estimated with less precision, and the degree of uncertainty depends on both the data and the prior.

Posterior Prediction

Given a new observation x_{new} , we can predict using posterior draws:

1. Compute predicted means for each sample:

$$\hat{y}_{\text{new}}^{(t)} = x_{\text{new}}^{\top} \beta^{(t)}$$

2. Add residual uncertainty:

$$y_{\text{new}}^{(t)} \sim \mathcal{N}(x_{\text{new}}^{\top} \beta^{(t)}, \sigma^2(t))$$

The resulting samples $\{y_{\text{new}}^{(t)}\}$ form a **posterior predictive distribution**, from which we can derive **predictive intervals** and evaluate **predictive accuracy**.

Model Checking and Hypothesis Testing

Posterior samples enable rich **model diagnostics** and **hypothesis testing**:

- **Posterior probability of an event**

$$\Pr(\beta_j \neq 0 \mid y) \approx \frac{1}{T} \sum_{t=1}^T \mathbf{1}(\beta_j^{(t)} \neq 0)$$

- **Posterior predictive checks**

Simulate new datasets using posterior draws and compare them to the observed data to assess model fit.

- **Model comparison**

Bayes factors and marginal likelihoods can be approximated to formally test or compare competing models.

These tools extend Bayesian inference beyond estimation to **model validation**, **uncertainty quantification**, and **decision-making**.

Convergence Diagnostics

Before interpreting MCMC results, we must check that the Gibbs sampler has **converged** to the target posterior distribution.

Convergence diagnostics assess whether the Markov chain has reached its **stationary distribution** and is producing valid samples.

Two basic strategies are:

- **Burn-in** – Discard early iterations (e.g., first 1000) to remove dependence on starting values.
- **Thinning** – Keep every k -th sample to reduce autocorrelation.

These steps improve sample quality and ensure reliable posterior summaries.

Trace Plots

A simple yet powerful diagnostic is the **trace plot**, showing sampled parameter values $\theta^{(t)}$ over iterations t .

- A **converged chain** fluctuates around a stable mean — no trend or drift.
- Multiple chains from different starting points should **overlap** and **mix well**.

Trace plots help detect: - Lack of stationarity (upward/downward trends) - Poor mixing or multimodality - Burn-in issues

Visual inspection is often the **first step** in assessing convergence.

Autocorrelation

Samples from a Gibbs sampler are **correlated**, especially for tightly coupled parameters.

The **autocorrelation function (ACF)** quantifies dependence across lags k :

$$\hat{\rho}_k = \frac{\sum_{t=1}^{T-k} (\theta^{(t)} - \bar{\theta})(\theta^{(t+k)} - \bar{\theta})}{\sum_{t=1}^T (\theta^{(t)} - \bar{\theta})^2}$$

- High $\hat{\rho}_k \rightarrow$ slow mixing and fewer effective samples
- Low $\hat{\rho}_k \rightarrow$ better mixing and faster convergence

Reducing autocorrelation may require **more iterations**, **reparameterization**, or **thinning** the chain.

Effective Sample Size (ESS)

Autocorrelation reduces the number of *independent* samples obtained.

The **effective sample size (ESS)** adjusts for this:

$$\text{ESS}(\theta) = \frac{T}{1 + 2 \sum_{k=1}^K \hat{\rho}_k}$$

- Small ESS \rightarrow chain is highly correlated, less informative
- Rule of thumb: ESS > 100 per parameter for stable inference

ESS provides a quantitative measure of **sampling efficiency** and helps determine whether more iterations are needed.

Gelman–Rubin Diagnostic (\hat{R})

When running multiple chains, the **Gelman–Rubin statistic** compares between-chain and within-chain variability.

For m chains with T iterations each:

$$W = \frac{1}{m} \sum_{i=1}^m s_i^2, \quad B = \frac{T}{m-1} \sum_{i=1}^m (\bar{\theta}_i - \bar{\bar{\theta}})^2$$

The potential scale reduction factor:

$$\hat{R} = \sqrt{\frac{\hat{V}}{W}}, \quad \hat{V} = \frac{T-1}{T} W + \frac{1}{T} B$$

- $\hat{R} \approx 1 \rightarrow$ convergence achieved
- $\hat{R} > 1.1 \rightarrow$ chains have **not converged**

Geweke Diagnostic

The **Geweke test** checks whether early and late portions of a single chain have the same mean, indicating **stationarity**.

$$Z = \frac{\bar{\theta}_A - \bar{\theta}_B}{\sqrt{\text{Var}(\bar{\theta}_A) + \text{Var}(\bar{\theta}_B)}}$$

Typically:

- Segment A = first 10% of the chain
- Segment B = last 50% of the chain

Under convergence, $Z \sim \mathcal{N}(0, 1)$.

- $|Z| \leq 2 \rightarrow$ chain likely stationary
- $|Z| > 2 \rightarrow$ potential non-convergence

These diagnostics ensure that posterior summaries reflect the **true target distribution**.

Spike-and-Slab Bayesian Linear Regression

As in classical BLR, the outcome is modeled as:

$$y = Xb + e, \quad e \sim \mathcal{N}(0, \sigma^2 I_n)$$

where y is the $n \times 1$ response, X the design matrix, b the regression coefficients, and σ^2 the residual variance.

This defines the **likelihood**:

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

The goal is to estimate b and identify which predictors truly contribute to y .

Motivation for the Spike-and-Slab Prior

In standard Bayesian linear regression:

$$\beta_j \sim \mathcal{N}(0, \sigma_b^2)$$

This **Gaussian (shrinkage) prior** assumes all predictors have small effects, but it does **not allow exact zeros** — limiting variable selection.

The **spike-and-slab prior** addresses this by mixing two components:

- A **spike** at zero \rightarrow excluded predictors
- A **slab** (wide normal) \rightarrow active predictors

This yields **sparse**, interpretable models that select relevant variables.

The Spike-and-Slab Mixture Prior

Each regression effect is drawn from a two-component mixture:

$$p(b_i \mid \sigma_b^2, \pi) = \pi \mathcal{N}(0, \sigma_b^2) + (1 - \pi) \delta_0$$

where:

- π = prior probability that b_i is non-zero
- δ_0 = point mass at zero

Thus, with probability π a predictor is active (slab), and with probability $1 - \pi$ it is excluded (spike).

Advantages of Spike-and-Slab Priors

This hierarchical mixture prior provides several benefits:

- **Sparsity** — allows exact zeros for irrelevant predictors
- **Interpretability** — binary indicators give posterior inclusion probabilities (PIPs)
- **Adaptivity** — the inclusion probability π is learned from the data
- **Balance** — captures both strong signals (detection) and small effects (prediction)

Hence, spike-and-slab models combine **variable selection** with **Bayesian uncertainty quantification**.

Hierarchical Representation

We express each effect as:

$$b_i = \alpha_i \delta_i$$

where:

$$\alpha_i \mid \sigma_b^2 \sim \mathcal{N}(0, \sigma_b^2), \quad \delta_i \mid \pi \sim \text{Bernoulli}(\pi)$$

- α_i : effect size when predictor is included
- δ_i : binary inclusion indicator (0 or 1)

Marginalizing over δ_i yields the spike-and-slab mixture prior above.

Prior for the Inclusion Probability π

The overall sparsity level is controlled by π , assigned a **Beta prior**:

$$\pi \sim \text{Beta}(\alpha, \beta)$$

- Small α , large $\beta \rightarrow$ favor sparser models
- $\alpha = \beta = 1 \rightarrow$ uniform prior
- Larger $\alpha \rightarrow$ denser models

This prior lets the **data determine the degree of sparsity**.

Priors for Variance Components

Variance parameters use **scaled inverse-chi-squared** priors:

$$\sigma_b^2 \sim S_b \chi^{-2}(v_b), \quad \sigma^2 \sim S \chi^{-2}(v)$$

These are conjugate, providing closed-form conditional updates. Hyperparameters (S_b, v_b) and (S, v) encode prior beliefs about effect size variability and residual noise.

Joint Posterior Structure

Combining the likelihood and priors, the joint posterior is:

$$p(\mu, \alpha, \delta, \pi, \sigma_b^2, \sigma^2 \mid y) \propto p(y \mid \mu, \alpha, \delta, \sigma^2) p(\alpha \mid \sigma_b^2) p(\delta \mid \pi) p(\pi) p(\sigma_b^2) p(\sigma^2)$$

This captures our **updated beliefs** about effects, inclusion indicators, and variance components.

Gibbs Sampling for Spike-and-Slab BLR

Inference proceeds via **Gibbs sampling**, cycling through these conditional updates:

1. $\alpha \mid D$
2. $\delta \mid D$
3. $\pi \mid D$
4. $\sigma_b^2 \mid D$
5. $\sigma^2 \mid D$

Each has a **standard distribution** (Normal, Bernoulli, Beta, scaled- χ^{-2}). Iterating these updates generates samples from the joint posterior.

Posterior Inclusion Probabilities

The **posterior inclusion probability (PIP)** measures how likely each predictor is truly associated with y :

$$\widehat{\Pr}(\delta_i = 1 \mid y) = \frac{1}{T} \sum_{t=1}^T \delta_i^{(t)}$$

- High PIP \rightarrow predictor is likely important
- Low PIP \rightarrow predictor likely irrelevant

PIPs summarize **variable relevance** and drive **Bayesian feature selection**.

Summary of Bayesian Linear Regression

Bayesian Linear Regression combines **likelihood** and **prior** to form the **posterior**, enabling principled modeling, regularization, and uncertainty quantification.

- Inference via **MCMC** (often **Gibbs sampling**) with posterior draws for **means**, **credible intervals**, and **predictions**.
- **Spike-and-slab priors** enable **sparsity** and **variable selection**, assigning **exact zeros** to irrelevant predictors and identifying key variables via **posterior inclusion probabilities (PIPs)**.
- **Conjugate and mixture priors** yield **efficient** and **robust inference**, even when $p > n$.
- With **proper convergence checks**, Bayesian models provide **stable and reliable inference** across a wide range of data settings.

Applications in Genomics

We have now seen the basic framework of **Bayesian Linear Regression (BLR)**

and will illustrate how it provides a **unified approach** for analyzing genetic and genomic data.

- **Genome-Wide Association Studies (GWAS)** and **fine-mapping** of causal variants.
- **Genetic prediction** and **heritability estimation**.
- **Pathway** and **gene-set enrichment** analyses.
- Integrative **multi-omics** modeling (genome, transcriptome, epigenome).

These examples show how BLR connects **statistical modeling** with **biological interpretation** in quantitative genetics.