

# Introduction to Bayesian Linear Regression, Posterior Inference, and MCMC

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# Introduction (Applications and motivation in genomics and healthcare)

**Bayesian Linear Regression Models** provide a flexible statistical framework for modeling complex biological and healthcare data.

They support key applications such as:

- **Genome-wide association studies (GWAS)** and **fine-mapping** of causal variants
- **Polygenic risk scoring (PRS)** for predicting complex traits and disease risk
- **Gene and pathway enrichment analyses** to test biological hypotheses
- **Integrative multi-omics modeling** across the genome, transcriptome, epigenome, and proteome
- Applications to **registry-based healthcare data**, enabling population-level **risk prediction** and **disease modeling**

# Introduction (Definition and advantages of BLR)

- **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**.

# Overview (Structure of the session)

- **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

# Classical Linear Regression

The standard linear regression model, which assumes that the observed outcomes can be expressed as a linear combination of predictors plus random noise:

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

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

## Estimation

Given the linear model, we can estimate the regression coefficients and residual variance using the method of ordinary least squares (OLS), which minimizes the sum of squared residuals:

Regression effects:

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

Residual variance:

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

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

## Limitations

While ordinary least squares estimation is simple and widely used, it has several important limitations that motivate the use of regularized or Bayesian approaches:

- 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?

The Bayesian framework extends linear regression by incorporating prior beliefs about the model parameters and updating them with observed data through Bayes' theorem:

- 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  $\beta$  and  $\sigma^2$ .

# 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
- $\beta$ :  $p \times 1$  vector of unknown coefficients
- $e$ : Gaussian noise with mean 0 and variance  $\sigma^2$

## Likelihood in Bayesian Linear Regression

Because the residuals are assumed to be Gaussian,

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

it follows that the **response vector**  $y$  follows a multivariate normal distribution:

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

This defines the **likelihood**, i.e. the probability of the observed data given the model parameters  $\beta$  and  $\sigma^2$ :

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

## Introducing Priors

In Bayesian linear regression, we specify **prior distributions** to express our beliefs about the model parameters before observing 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 expresses the belief that most effect sizes are small and centered around zero — consistent with the **polygenic assumption** often used in genetics.

Using **conjugate priors** ensures that the **posterior distributions** remain in the same family as the priors (e.g., scaled inverse-chi-squared for variance parameters), enabling **closed-form Gibbs sampling updates**.

## Role of the Prior Variance $\sigma_b^2$

The parameter  $\sigma_b^2$  acts as a **shrinkage** (or **regularization**) parameter:

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

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

## Priors on Variance Components

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

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

- $S_b$  and  $v_b$  are hyperparameters that control the prior distribution for the **effect size variance**  $\sigma_b^2$ .
- $S$  and  $v$  are hyperparameters for the **residual variance**  $\sigma^2$ .

These scaled inverse-chi-squared priors ensure conjugacy, enabling **closed-form updates** for the variance parameters in Gibbs sampling.

### Typical choices:

- Small degrees of freedom (e.g.,  $v_b = v = 4$ ) give weakly informative, heavy-tailed priors.
- Scale parameters  $S_b$  and  $S$  are often set based on expected variance magnitudes (e.g., empirical estimates).

## Posterior Distribution

In Bayesian linear regression, we combine the **likelihood** and **prior distributions** using **Bayes' rule** to obtain the **joint posterior**:

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

The posterior distribution represents all **updated knowledge** about the unknown parameters after observing the data.

It serves as the foundation for computing **posterior means**, **credible intervals**, and **predictions**.

In practice, the posterior is often too complex to evaluate directly, so we use **sampling-based methods** such as Gibbs sampling to approximate it.

# 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 $\beta$

Given  $\sigma^2$ ,  $\sigma_b^2$ , 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  $\beta$  after observing the data, while holding  $\sigma_b^2$  and  $\sigma^2$  fixed.

## Comparison to Classical OLS

In classical regression, the OLS estimator is

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

The estimate of  $\beta$  is **independent of**  $\sigma^2$ , since  $\sigma^2$  only scales the likelihood, not its maximum.

In Bayesian regression,  $\sigma^2$  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 $\beta_j$

Instead of sampling  $\beta$  jointly, we can update each coefficient  $\beta_j$  **one at a time**, holding all others fixed efficiently.

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  $\beta_j$  is univariate normal:

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

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 $\sigma_b^2$

The conditional distribution of the **prior variance**  $\sigma_b^2$ , given  $\beta$  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,  $\sigma_b^2$  is sampled directly given  $\beta$ . This update reflects our revised belief about the **variability of effect sizes** after observing the current posterior draw of  $\beta$ .

## Full Conditional for $\sigma^2$

The conditional distribution of the **residual variance**  $\sigma^2$ , given  $\beta$  and the data, is also **scaled inverse-chi-squared**:

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

where

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

At each Gibbs iteration,  $\sigma^2$  is sampled directly given  $\beta$ . 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:

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

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

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

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

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

## Posterior Summaries

After running the Gibbs sampler, we obtain a sequence of posterior draws  $\{\theta^{(t)}\}_{t=1}^T$  for parameters such as  $\beta_j$ ,  $\sigma^2$ , or  $\sigma_b^2$ , where  $T$  denotes the total number of MCMC iterations (after burn-in).

We can summarize the posterior distribution using:

- **Posterior mean**

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

- **Posterior median:** the median of  $\{\theta^{(t)}\}$
- **95% credible interval:** the interval between the 2.5th and 97.5th percentiles of  $\{\theta^{(t)}\}$

These summaries describe the most probable values of  $\theta$  and their associated uncertainty after combining data with 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  $x_{\text{new}}$ , 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:

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

The potential scale reduction factor:

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

Values of  $\hat{R}$  close to 1 indicate convergence, whereas  $\hat{R} > 1.1$  suggests that the chains have not yet 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**.

# 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 that all predictors have small effects but does **not allow exact zeros**, limiting its ability to perform variable selection.

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

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

This formulation produces **sparse**, interpretable models that automatically select the most relevant variables.

# Spike-and-Slab Bayesian Linear Regression

As in classical Bayesian linear regression, 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 vector,  $X$  is the  $n \times p$  design matrix of predictors,  $b$  is the  $p \times 1$  vector of regression coefficients, and  $\sigma^2$  is 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 determine which predictors truly contribute to explaining variation in  $y$ .

# The Spike-and-Slab Mixture Prior

Each regression coefficient  $b_i$  is drawn from a **two-component mixture prior**:

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

where:

- $\pi$  is the **prior probability** that  $b_i$  is nonzero (active predictor)
- $\delta_0$  is a **point mass at zero** (excluded predictor)

Thus, with probability  $\pi$  a predictor belongs to the **slab** (included), and with probability  $1 - \pi$  it belongs to the **spike** (excluded).

This prior induces **sparsity**, allowing the model to automatically select relevant predictors while shrinking others exactly to zero.

## Hierarchical (Indicator) Representation

The spike-and-slab prior can be expressed hierarchically by introducing a **binary inclusion indicator**  $\delta_i$ :

$$b_i = \alpha_i \delta_i$$

where

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

- $\alpha_i$ : effect size when the predictor is **included**
- $\delta_i$ : binary variable indicating **inclusion (1)** or **exclusion (0)**

This representation separates **effect size** ( $\alpha_i$ ) from **inclusion** ( $\delta_i$ ), making inference straightforward via Gibbs sampling. Marginalizing over  $\delta_i$  recovers the **spike-and-slab mixture prior** defined earlier.

## Prior for the Inclusion Probability $\pi$

The overall **sparsity level** of the model is controlled by  $\pi$ , which represents the prior probability that a predictor is included.

We assign  $\pi$  a **Beta prior**:

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

- Small  $\alpha$  and large  $\beta \rightarrow$  favor **sparser models**
- $\alpha = \beta = 1 \rightarrow$  **uniform prior** (no preference)
- Larger  $\alpha \rightarrow$  favor **denser models**

This prior allows the **data to inform the degree of sparsity** through posterior updating of  $\pi$ .

## Priors for Variance Components

Variance parameters are typically assigned **scaled inverse-chi-squared** priors:

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

These priors are **conjugate**, yielding **closed-form conditional updates** for both variance components.

The hyperparameters  $(S_b, v_b)$  and  $(S, v)$  encode prior beliefs about the variability of **effect sizes** and **residual noise**, respectively.

In the spike-and-slab model, the **sum of squares** for updating  $\sigma_b^2$  is computed only over the **included effects**, i.e.,

$$\sum_{i:\delta_i=1} \alpha_i^2,$$

ensuring that the variance of inactive predictors (where  $\delta_i = 0$ ) does not influence the estimate of  $\sigma_b^2$ .

## Joint Posterior Structure

As in Bayesian linear regression with normal priors, we combine the **likelihood** and **priors** to obtain the **joint posterior** over all model parameters:

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

This captures our **updated beliefs** about effect sizes, inclusion indicators, and variance components after observing the data.

The inference procedure follows the same principle as for standard BLR — we use **Gibbs sampling** to draw from each parameter's full conditional distribution.

Next, we derive these **full conditional distributions** from the joint posterior.

# Gibbs Sampling: The Algorithm (Spike-and-Slab BLR)

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

1. Sample  $\alpha \mid \delta, \sigma_b^2, \sigma^2, y$
2. Sample  $\delta \mid \alpha, \pi, y$
3. Sample  $\pi \mid \delta$
4. Sample  $\sigma_b^2 \mid \alpha, \delta$
5. Sample  $\sigma^2 \mid \alpha, \delta, y$

Each step updates one parameter block given the others, and iterating the sequence yields samples from the joint posterior. Since all conditionals have **standard forms** (Normal, Bernoulli, Beta, scaled inverse- $\chi^2$ ), Gibbs sampling is **straightforward and efficient**.

## Posterior Inclusion Probabilities

The **posterior inclusion probability (PIP)** quantifies how likely each predictor is to be **included in the model** (i.e., truly associated with  $y$ ):

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

- **High PIP** → predictor is likely important
- **Low PIP** → predictor is likely irrelevant

PIPs provide a direct measure of **variable relevance** and form the basis for **Bayesian feature selection**.

# Advantages of Spike-and-Slab Priors

This hierarchical mixture prior offers several key benefits:

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

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

# Summary of Bayesian Linear Regression

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

- Inference is performed via **MCMC**, typically **Gibbs sampling**, producing posterior draws for **means**, **credible intervals**, and **predictions**.
- **Spike-and-slab priors** introduce **sparsity** and support **variable selection**, assigning **exact zeros** to irrelevant predictors and identifying key variables through **posterior inclusion probabilities (PIPs)**.
- **Conjugate** and **mixture** priors allow for **efficient** and **robust inference**, even when  $p > n$ .
- With appropriate **convergence diagnostics**, Bayesian models yield **stable and reliable inference** across diverse data settings.

# Applications in Genomics

We have now covered 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

These applications demonstrate how BLR connects **statistical modeling** with **biological interpretation** in quantitative genetics.