calculated based on # reads in cells

$S_J \cdot q_{iJ}$ → Funct° of $\vec{\beta_i}$ & $\vec{x_J}$

calculated previously

Final estimate of LFC

$$\vec{\beta_i} = \underset{\vec{\beta}}{\arg\max}\left(\sum_{J} \log_{NB}(K_{iJ}, M_J(\vec{\beta}), \alpha_i) + \underbrace{\Lambda(\vec{\beta})}_{}\right)$$

samples

Ridge penalty term

+ $M_J(\vec{\beta}) = S_{iJ}\, e^{\Sigma_r x_{Jr} \cdot \beta_r}$

+ $\Lambda(\vec{\beta}) = \sum_r \frac{-\beta_r^2}{2\sigma_r^2}$ → log likelihood of β, given the prior $\beta_r \sim N(0, \sigma_r^2)$

→ this is calculated based on the emp distribut° of β_r^{MLE} based on the original framework "Empirical prior estimate"

"Iteratively reweighted ridge regression"

Say we want to sample $X \sim \pi(x)$ where $\pi(x) \propto \Phi(x) I(x \geq c)$

① what's the exact form of $\pi(x)$, out of curiosity

② How to most effectively do rejection sampling on $X \sim \pi(x)$?

Answer

① We need $1 = \int_{-\infty}^{+\infty} \Phi(x) I(x \geq c) \cdot \mathscr{C}\, dx$, where $\mathscr{C}$ is a normality constant

Find $\mathscr{C}$

$$\frac{1}{\mathscr{C}} = \int_c^{+\infty} \Phi(x)\, dx = \underbrace{\int_c^{+\infty} \frac{1}{\sqrt{2\pi}}\, e^{\left(\frac{-1}{2}\frac{x^2}{\sigma^2}\right)} dx}_{\text{This has to be calculated numerically}}$$

, maybe by the fact that $e^{x^2} = 1 + x^2 + \frac{x^4}{2} + \frac{x^6}{3!} + \frac{x^8}{4!} + \cdots$

Taylor's series

② How to most effectively sample from $\pi(x)$?

"Rejection sampling"

Let's say we choose $g(x) = \lambda e^{-\lambda(x-c)}$ where $x \in [c, +\infty)$

Goal. Find λ to be the optimal for efficient sampling

Say $M \cdot g(x) \geq \Phi(x)\ \forall x \geq c$

$$\Leftrightarrow M \geq \frac{\Phi(x)}{g(x)} = \frac{\frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}}{\lambda e^{-\lambda(x-c)}} = \frac{1}{\sqrt{2\pi}\cdot\lambda}\, e^{-\frac{x^2}{2} + \lambda x - \lambda c}$$

$y = F(x) = 1 - e^{-\lambda x}, x \geq 0$

Now write $x = 1 - e^{-\lambda y}$ and find the form of y

$$e^{-\lambda y} = 1 - x$$

$$-\lambda y = \ln(1-x)$$

$$y = \frac{\ln(1-x)}{-\lambda}$$

$y = 0, x < 0$

I WTS $P(X \leq x) = U$

w

$$P(X \leq x) = F(x) = U$$

$$x = F^{-1}(U)$$

We want to first find x the maximize $M = \frac{\Phi(x)}{g(x)}$ nom. as close to denom. as possible

$$\Leftrightarrow \underset{x}{\operatorname{argmax}} \; -\frac{x^2}{2} + \lambda x - \lambda c$$

$$= \underset{x}{\operatorname{argmax}} \; -\frac{x^2}{2} + 2\lambda x \cdot \frac{1}{\sqrt{2}} \cdot \frac{1}{2} - \frac{\lambda^2}{4} + \frac{\lambda^2}{4} - \lambda c$$

$$= \underset{x}{\operatorname{argmax}} \; -\left(\frac{x}{\sqrt{2}} - \frac{\lambda}{2}\right)^2 + \frac{\lambda^2}{4} - \lambda c \leq \frac{\lambda^2}{4} - \lambda c$$

$$\Leftrightarrow x = \frac{\lambda}{\sqrt{2}}$$

$Mg(x) \geq \Phi(x)$, minimize M to ↑ eff. in sampling

Now, we want to minimize M as a function of λ

$$M = \frac{1}{\sqrt{2\pi}\lambda} e^{\lambda^2/4 - \lambda c}$$

→ Calculate $\frac{\partial M}{\partial \lambda} = 0$ Solve → Find λ as a function of c