Bayesian statistics
and the borrowing of strength
in high-dimensional data analysis

Aad van der Vaart
Mathematical Institute
Leiden University

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Optimal method to recover $\theta$:

$$\hat{\theta} = \overline{X}_n = \frac{1}{n} \sum_{i=1}^{n} X_i.$$
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**Principles:**
- Maximum likelihood
- Objective Bayes
- Equivariant

**Criteria:**
- Minimum variance unbiased
- Admissible for symmetric loss
- Minimal risk equivariant
- Minimax
AIM: determine $\theta^1, \ldots, \theta^p$

MEASUREMENTS: $X^j_1, \ldots, X^j_n \overset{iid}{\sim} N(\theta^j, 1)$, for $j = 1, \ldots, p$.

We assume NOT:

- relations between $\theta^1, \ldots, \theta^p$.
- dependence between measurements.
Multidimensional measurements with errors (Stein, 1956)

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MEASUREMENTS: $X_1^j, \ldots, X_n^j \overset{iid}{\sim} \mathcal{N}(\theta^j, 1)$, for $j = 1, \ldots, p$.

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THEOREM [Stein, 1956]
If $p \geq 3$, then $(X_1^n, X_2^n, \ldots, X_p^n)$ is inadmissible: there exists $(T^1, \ldots, T^p)$ with, for all $\theta^1, \ldots, \theta^p$:

$$\sum_{j=1}^{p} \mathbb{E}(T^j - \theta^j)^2 < \sum_{j=1}^{p} \mathbb{E}(X_n^j - \theta^j)^2.$$
Intermezzo: Bayes’s rule (Bayes, 1763)

**BAYES’S RULE**
If a variable $\theta$ follows a probability distribution $\Pi$ and given $\theta$ a variable $X$ follows a probability density $x \mapsto p(x \mid \theta)$, then $\theta$ given $X$ follows the distribution:

$$d\Pi(\theta \mid X) \propto p(X \mid \theta) d\Pi(\theta).$$
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Bayesian statistics:

- $d\Pi(\cdot)$ models the a-priori uncertainty about the parameter $\theta$.
- $d\Pi(\cdot \mid X)$ the a-posteriori uncertainty.
WORKING HYPOTHESIS: $$(\theta^1, \theta^2, \ldots, \theta^p) \sim \Pi.$$
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Then \((X_j^i, \theta_j: i = 1, \ldots, n, j = 1, \ldots, p)\) follow a joint probability distribution.

Bayes’s rule gives a conditional distribution

\[ (\theta^j: j = 1, \ldots, p) \mid (X_j^i: i = 1, \ldots, n, j = 1, \ldots, p) \]

and hence expected values

\[ T^j(\Pi) := E(\theta^j \mid X_j^i: i = 1, \ldots, n, j = 1, \ldots, p). \]

Estimate \(\Pi\) from the data and use \(T^j(\hat{\Pi})\) (or use a hyper prior).
AIM: determine $\theta^1, \ldots, \theta^p$

MEASUREMENTS: $X^j_1, \ldots, X^j_n \overset{iid}{\sim} N(\theta^j, 1)$, for $j = 1, \ldots, p$.

WORKING HYPOTHESIS: $\theta^1, \ldots, \theta^p \overset{iid}{\sim} N(0, A)$.

If we knew $A$, then we might use the Bayes estimator $A/(A + 1)\bar{X}^j_n$. 
Empirical Bayes method: example
(James, Stein)

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Under the working hypothesis $\bar{X}^j_n \sim iid N(0, A + 1/n)$.

This suggests the estimate $\hat{A} = \sum_j \bar{X}^j_n^2 / (p - 2) - 1/n$. 
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If we knew $A$, then we might use the *Bayes estimator* $A/(A + 1)\overline{X^j_n}$.

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This suggests the estimate $\hat{A} = \sum_j \overline{X^j_n}^2 / (p - 2) - 1/n$.

$\hat{A}/(\hat{A} + 1)\overline{X^j_n}$ beats the MLE.

Not only under the working hypothesis, but for *any* $\theta^1, \ldots, \theta^p$. 
Nonparametric empirical Bayes method
(Zhang, 2009)

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WORKING HYPOTHESIS: $\theta^1, \ldots, \theta^p \overset{iid}{\sim} G$.

Then $X_n^j$ has marginal density $x \mapsto \int \sqrt{n} \phi((x - s) \sqrt{n}) \, dG(s)$, and nonparametric maximum likelihood estimator for $G$ is:

$$\hat{G} = \arg\max_G \prod_{j=1}^p \int \sqrt{n} \phi((X_n^j - s) \sqrt{n}) \, dG(s).$$
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(An analogous full Bayes analysis would put a Dirichlet prior on $G$.)
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Bayesian assumptions on parameters are often *working hypotheses*, not based on scientific theory.

Frequentist Bayesian theory tries to validate (or not) the resulting procedures in a general, non-Bayesian framework, taking account that priors can be partly *misspecified*.

Bayesian methods are promising for high-dimensional data, but their performance is poorly understood at the present time.
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**OUTLOOK:**
- In high dimensions the potential gain is large.
- A-priori knowledge should make this gain even bigger.

Sparsity

Consider many parameters $\theta^1, \theta^2, \ldots, \theta^p$, but suppose most are actually (near) zero.

Sparsity prior:

- Choose $s$ from prior $\pi_n$ on $\{0, 1, 2, \ldots, p\}$ with exponential decrease.
- Choose $S \subset \{0, 1, \ldots, p\}$ of size $|S| = s$ at random.
- Choose $(\theta_i: i \in S)$ from density $g_S$ on $\mathbb{R}^S$ (and set other $\theta_i$ zero).

**THEOREM** [Castillo, vdV, 2013]

This achieves the *minimax benchmark*: for $s = \#(j: \theta^j \neq 0)$,

$$\mathbb{E} \sum_{j=1}^{p} (T^j - \theta^j)^2 \asymp \frac{s}{n} \sqrt{\log \frac{s}{n}}.$$

Compare to: $\mathbb{E} \sum_{j=1}^{p} \left( \frac{X^j_n}{n} - \theta^j \right)^2 = \frac{p}{n}$. 
Uncertainty quantification and multiplicity correction

The Bayesian analysis results in a posterior distribution on \((\theta^1, \ldots, \theta^p)\), and hence in \textit{marginal posterior distributions} of every \(\theta^j\).

Credible intervals can be used for overall uncertainty quantification (?).
$Y_{i,j}$: RNA expression count of tag $i = 1, \ldots, p$ in tissue $j = 1, \ldots, n$.

$x_j$: covariates of tissue $j$.

\[
Y_{i,j} \sim \text{(zero-inflated) negative binomial, with}
\]

\[
EY_{i,j} = e^{\alpha_i + \beta_i x_j}, \quad \text{var } Y_{i,j} = EY_{i,j} \left(1 + EY_{i,j} e^{-\phi_i}\right).
\]

Simple Bayesian model: $\alpha_i \perp \beta_i \perp \phi_i$ with

\[
\alpha_i \sim F, \quad \beta_i \sim G_\tau, \quad \phi_i \sim H_\tau.
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Efficient empirical Bayes approach to estimate $\tau$: calculate marginal posteriors $\Pi^{\beta_i}$ of $\beta_1, \ldots, \beta_p$ and $\Pi^{\phi_i}$ of $\phi_1, \ldots, \phi_p$ given $\tau$ and equate

\[
\frac{1}{p} \sum_{i=1}^{p} \Pi^{\beta_i}(\cdot | Y_{i1}, \ldots, Y_{in}, \tau) = G_\tau(\cdot), \quad \frac{1}{p} \sum_{i=1}^{p} \Pi^{\phi_i}(\cdot | Y_{i1}, \ldots, Y_{in}, \tau) = H_\tau(\cdot).
\]
Even seemingly unrelated analyses can *borrow strength* from each other.

Gains can be particularly big if the data is big.

Bayesian thinking provides methods that can achieve this.

These methods may be computationally challenging.

There is much to be learned about the validity of these methods, in particular their uncertainty quantification.
Large scale testing by empirical Bayes

For every out of 30 000 genes test statistically whether its expression differs in cancer and normal tissues.
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Assume:

- A gene is expressed with probability $\pi$.
- The $p$-value of the gene’s test is random if not expressed; otherwise from some $f$. 
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Are the 30 000 tests connected?

Assume:
- A gene is expressed with probability $\pi$.
- The $p$-value of the gene’s test is random if not expressed; otherwise from some $f$.

Now estimate $\pi$ and $f$ from the data and compute

$$P(\text{gene is expressed} \mid \text{ALL DATA}).$$
**THEOREM**
Given ‘flat priors’ on the $s_n \ll p$ nonzero coefficients,

$$E_{\theta_0} \left\| \Pi_n (\cdot | Y^n) - \sum_S \hat{w}_S N (\hat{\theta}_S, \Gamma_{S}^{-1}) \otimes \delta_{S^c} \right\| \to 0,$$

for $\hat{\theta}_S$ the LS estimator for model $S$, $\Gamma_S^{-1}$ its covariance, and

$$\hat{w}_S \propto \frac{\pi_p (s)}{(p^s)} \left( \frac{\lambda \sqrt{2\pi}}{2} \right)^s |\Gamma_S|^{-1/2} e^{\frac{1}{2} \| X S \hat{\theta}_S \|^2_2} 1_{|S| \leq 4s_n, \| \theta_{0,S^c} \|_1 \leq s_n \sqrt{\log p/\| X \|}}.$$ 

**COROLLARY**
Given consistent model selection, mixture can be replaced by

$$N (\hat{\theta}_{S_{\theta_0}}, \Gamma_{S_{\theta_0}}^{-1}).$$