Bayesian Model Specification

4: Dealing With Model Uncertainty

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Getting From the Context and Design to the Model

Definition. In **model specification, optimal** $=\{$**conditioning** only on **propositions rendered true** by the **context** of the **problem** and the **design** of the **data-gathering process**, while **at the same time ensuring** that the **set of conditioning propositions** includes **all relevant problem context**$\}$.

This seems **hard to achieve**; for **example**, in the **IHGA case study**, **visualizing** the **data set before it arrives**, it would look like the **table shell** presented back on **page 2** of **Part 1** of the **Lecture Notes**:

	Number of Hospitalizations						
Group	0	1	...	k	n	Mean	SD
Control	n_{C0}	n_{C1}	...	n_{Ck}	$n_C = 287$	$\bar{y}_C$	s_C
Treatment	n_{T0}	n_{T1}	...	n_{Tk}	$n_T = 285$	$\bar{y}_T$	s_T

The **problem context** and **design** make this **table shell** something **You can condition on**, and the **lack of previous trials with IHGA** (this was the **first time** it was **implemented anywhere**) implies that **You can also condition** on a **diffuse choice** for $p(\theta|\mathcal{B})$ (with **572 observations**, it **won't matter much** how this **diffuseness** is **specified**), but **context** and **design** don't seem to have **anything to say** about the **predictive (sampling) distribution** $p(D|\theta\,\mathcal{B})$.

Model Uncertainty

In **problems** of **realistic complexity** You'll generally **notice** that (a) You're **uncertain** about θ but (b) You're also **uncertain** about how to **quantify Your uncertainty about θ, i.e., You** have **model uncertainty**.

Cox's Theorem says that You can draw **logically-consistent inferences** about an **unknown** θ, given **data** D and **background information** $\mathcal{B}$, by **specifying** $M = \{p(\theta|M\,\mathcal{B}), p(D|\theta\,M\,\mathcal{B})\}$, but **item (b)** in the previous paragraph implies that there will typically be **more than one such plausible** M; what should You **do** about this?

It would be **nice** to be able to **solve the inference problem** by using **Bayes's Theorem** to **compute** $p(\theta|D\,\mathcal{M}_{all}\,\mathcal{B})$, where $\mathcal{M}_{all}$ is the set of **all possible models**, but this is **not feasible**: just as **Kolmogorov** had to **resort to** σ**-fields** because the **set of all subsets** of an Ω with **uncountably many elements** is **too big** to **meaningfully assign probabilities** to **all of the subsets**, with a **finite data set** D, $\mathcal{M}_{all}$ is **too big** for D to permit **meaningful plausibility assessment** of **all the models** in $\mathcal{M}_{all}$.

Having adopted the **Calibration Principle**, it **makes sense** to talk about an **underlying data-generating model** M_{DG}, which is **unknown to You** (more on this below).

An Ensemble $\mathcal{M}$ of Models

Not being able to **compute** $p(\theta|D\,\mathcal{M}_{all}\,\mathcal{B})$, in practice the **best** You can do is to **compute** $p(\theta|D\,\mathcal{M}\,\mathcal{B})$, where $\mathcal{M}$ is an **ensemble of models** (**finite** or **countably** or **uncountably infinite**) chosen **"well"** by You, where **"well"** can and should be **brought into focus** by the **Calibration Principle** (and some of the other **Principles** to be introduced **later**): evidently what You **want**, among other things, is for $\mathcal{M}$ to **contain one or more models** that are **identical (or at least close)** to M_{DG}.

Suppose **initially**, for the sake of **discussion**, that You've **identified** such an **ensemble** (I'll present some **ideas** for how to do this later) and that it turns out to be **finite**: $\mathcal{M} = (M_1, \ldots, M_k)$ for $2 \leq k < \infty$; **what next?**

Are You **supposed** to try to **choose** one of these **models** (the **model selection problem**) and **discard** the rest, or **combine** them in some way (if so, **how?**), or **what?**

Solving the model uncertainty problem. People used to **"solve"** the problem of what to do about **model uncertainty** by **ignoring** it: it was **common**, at least through the **mid-1990s**, to

Dealing With Model Uncertainty

(a) use the **data** D to conduct a **search** among **possible models**, settling on a **single (apparently) "best" model** M^* arising from the **search**, and then

(b) draw **inferences** about θ **pretending** that M^* "$=$" M_{DG}.

This of course can lead to **quite bad calibration**, almost always in the **direction** of **pretending You know more than You actually do**, so that, e.g., Your **nominal 90% posterior predictive intervals** for **data values not used in the modeling process** would typically include **substantially fewer than 90%** of the actual **observations**.

The M^* approach **"solves"** the problem of how to **specify** $\mathcal{M}$ by setting $\mathcal{M} = \{M^*\}$; I'll continue to **postpone** for the moment how You might do a **better job** of **arriving at** $\mathcal{M}$.

Having **chosen** $\mathcal{M}$ in some way, how can You **assess** Your **uncertainty across the models** in $\mathcal{M}$, and appropriately **propagate** this through to Your **uncertainty** about θ, in a **well-calibrated** way?

I'm aware of **three approaches** to **improved assessment and propagation of model uncertainty**: **BMA, BNP, CCV**.

BMA, BNP

• **Bayesian model averaging (BMA):** If **interest** focuses on **something** that has the **same meaning across all the models** in $\mathcal{M}$ — for example, a set of **future data values** D^* to be **predicted** — **calculation** reveals (e.g., Leamer, 1978) that

$$p(D^*|D\,\mathcal{M}\,\mathcal{B}) = \int_{\mathcal{M}} p(D^*|D\,M\,\mathcal{B})\,p(M|D\,\mathcal{M}\,\mathcal{B})\,dM\,, \qquad (1)$$

which is **eminently reasonable**: equation **(1)** tells You to form a **weighted average** of Your **conditional predictive distributions** $p(D^*|D\,M\,\mathcal{B})$, given particular **models** $M \in \mathcal{M}$, **weighted** by those models' **posterior probabilities** $p(M|D\,\mathcal{M}\,\mathcal{B})$.

This **approach** typically provides **(substantially) better calibration** than that obtained by the M^* **method**.

• **Bayesian nonparametric (BNP) modeling:** The **BMA integral** in (1) can be thought of as an **approximation** to the **(unattainable?) ideal** of **averaging over all worthwhile models**; a **better approximation** to this **ideal** can often be achieved with **Bayesian nonparametric modeling**, which dates back to **de Finetti (1937)**.

Exchangeability

Continuing the **Kaiser example** on **page 14 (Part 1)**, suppose You also **observe** (for each of the $n = 112$ **randomly-sampled patients** from the **population** $\mathbb{P}$ of $N = 8{,}561$ **heart-attack patients**) a **real-valued conceptually-continuous quality-of-care score** y_i, and (following **de Finetti**) You're thinking about Your **predictive distribution** $p(y_1 \ldots y_n|\mathcal{B})$ for these scores **before any data have arrived**.

de Finetti pointed out that, if You have **no covariate information** about the **patients**, Your **predictive distribution** $p(y_1 \ldots y_n|\mathcal{B})$ should **remain the same** under **arbitrary permutation** of the **order** in which the **patients** are **listed**, and he **coined** the **term exchangeability** to describe this **state of uncertainty**.

He (and later **Diaconis/Freedman**) went on to **prove** that, if Your judgment of **exchangeability** extends from $(y_1 \ldots y_n)$ to $(y_1 \ldots y_N)$ (as it certainly **should** here, given the **random sampling**) and $N \gg n$ (as is **true** here), then all **logically-internally-consistent predictive distributions** can **approximately** be expressed **hierarchically** as follows:

Bayesian Nonparametric (BNP) Modeling

letting F stand for the **empirical CDF** of the **population values** $(y_1 \ldots y_N)$, the **hierarchical model** is (for $i = 1, \ldots, n$)

$$\left\{ \begin{array}{rcl} (F|\mathcal{B}) & \sim & p(F|\mathcal{B}) \\ (y_i|F\,\mathcal{B}) & \overset{\text{IID}}{\sim} & F \end{array} \right\}.$$

This requires placing a **scientifically-appropriate prior distribution** $p(F|\mathcal{B})$ on the **set $\mathcal{F}$ of all CDFs** on $\Re$, which **de Finetti** didn't know how to do in **1937**; thanks to work by **Freedman, Ferguson, Lavine, Escobar/West**, and others, **two methods** for doing this **sensibly** — **Pólya trees** and **Dirichlet-process (DP) priors** — are now in **routine use**: this — placing **distributions** on **function spaces** — is **Bayesian nonparametric** (BNP) modeling.

IHGA Example, Revisited: Once again **visualizing** the **IHGA data set before it arrives**, here's the **table shell** one more time:

	Number of Hospitalizations						
Group	0	1	...	k	n	Mean	SD
Control	n_{C0}	n_{C1}	...	n_{Ck}	$n_C = 287$	$\bar{y}_C$	s_C
Treatment	n_{T0}	n_{T1}	...	n_{Tk}	$n_T = 285$	$\bar{y}_T$	s_T

BNP Case Study

Letting (as before) μ_C and μ_T be the **mean hospitalization rates** (per two years) in the **population** $\mathcal{P}$ (of **all elderly non-institutionalized people** in **Denmark** in the **early 1980**s) under the C and T **conditions**, respectively, the **inferential quantity of main interest** is still $\theta = \frac{\mu_T - \mu_C}{\mu_C}$ (or this could be **redefined without loss** as $\theta = \frac{\mu_T}{\mu_C}$); how can You draw **valid and accurate inferences** about θ while **coping with Your uncertainty** about the **population** C and T **CDFs** — call them F_C and F_T, respectively — of **numbers of hospitalizations** per person (per two years)?

One approach: **Bayesian qualitative-quantitative inference** (Draper 2013): **exchangeability** implies a **multinomial sampling distribution** on the **qualitative outcome variable** with **category labels** 0, 1, . . . , and this permits **optimal model specification** here (this **approach** treats the **hospitalization outcome categorically** but permits **quantitative inference** about θ).

Another approach: **Bayesian nonparametric modeling** — it turns out that **DP priors** put **all their mass** on **discrete distributions**, so **one BNP model** for this data set would involve placing **parallel DPs priors** on F_C and F_T; see **KKD (2008)** for details on the **results**.

BNP Case Study (continued)

To serve as the **basis** of the M^* **(cheating) approach** (in which You **look at the data** for **inspiration** on **which models to fit**), here's a **table** of the **actual data values**:

Group	Number of Hospitalizations 0	1	2	3	4	5	6	7	n	Mean	SD
Control	138	77	46	12	8	4	0	2	287	**0.944**	1.24
Treatment	147	83	37	13	3	1	1	0	285	**0.768**	1.01

Evidently **(description)** IHGA **lowered** the **mean hospitalization rate** (for **these elderly Danish people**, at least) by $(0.944 - 0.768) = \mathbf{0.176}$, which is a $\left\{100\left(\frac{0.768-0.944}{0.944}\right) \doteq\right\}$ **19%** reduction from the **control level**, a difference that's **large in clinical terms**, but (**inference**) how **strong** is the **evidence** for a **positive effect** in $\mathcal{P} = \{$all people **similar** to those in the **experiment**$\}$?

It's **natural** to think **initially** of **parallel Poisson**(λ_C) and Poisson(λ_T) modeling (M_1), but there's **substantial over-dispersion**: the C and T **variance-to-mean ratios** are $\frac{1.24^2}{0.944} \doteq \mathbf{1.63}$ and $\frac{1.01^2}{0.768} \doteq \mathbf{1.33}$.

Bayesian Parametric Modeling

Unfortunately we have **no covariates** to help **explain** the **extra-Poisson variability**, and there's **little information external** to the **data set** about the **treatment effect**; this latter **state of knowledge** is expressed in **prior distributions** on **parameters** by making them **diffuse** (i.e., ensuring they have **large variability** to express **substantial uncertainty**).

In this **situation** You could fit **parallel Negative Binomial models** (M_2), but a **parametric choice** that more readily **generalizes** is obtained by letting $(x_i, y_i) = (\text{C/T status, outcome})$ — so that $x_i = 1$ if **Treatment**, 0 if **Control** and $y_i =$ the **number of hospitalizations** — for person $i = 1, \ldots, n$ and considering the **random-effects Poisson regression model** (M_3):

$$\begin{aligned} (y_i|\lambda_i\, M_3\, \mathcal{B}) &\overset{\text{indep}}{\sim} \text{Poisson}(\lambda_i) \\ \log(\lambda_i) &= \gamma_0 + \gamma_1 x_i + \epsilon_i \\ (\epsilon_i|\sigma_\epsilon^2\, M_3\, \mathcal{B}) &\overset{\text{IID}}{\sim} N\left(0, \sigma_\epsilon^2\right) \\ \left(\gamma_0\, \gamma_1\, \sigma_\epsilon^2|M_3\, \mathcal{B}\right) &\sim \text{diffuse.} \end{aligned} \tag{2}$$

In this model the **unknown** of **main policy interest** is

BNP Example

$\theta = \frac{\text{population } \bar{T}}{\text{population } \bar{C}} = e^{\gamma_1}$; the **other parameters** can be collected in a **vector** $\eta = (\gamma_0, \sigma_\epsilon^2)$; and the **random effects** ϵ_i can be thought of as **proxying** for the **combined main effect** $\sum_{j=2}^{J} \gamma_j (x_{ij} - \bar{x}_j)$ of all the **unobserved relevant covariates** (**age, baseline health status**, ...).

The **first line** of (2) makes **good scientific sense** (the y_i are **counts** of **relatively rare events**), but the **Gaussian assumption** for the **random effects** is **conventional** and **not driven by the science**; a potentially **better model** (M_4) is obtained by putting a **prior distribution** on the **CDF** of the ϵ_i that's **centered** at the $N\left(0, \sigma_\epsilon^2\right)$ **distribution** but that expresses **substantial prior uncertainty** about the **Gaussian assumption**:

$$
\begin{aligned}
(y_i | \lambda_i \, M_4 \, \mathcal{B}) &\overset{\text{indep}}{\sim} \text{Poisson}(\lambda_i) \\
\log(\lambda_i) &= \gamma_0 + \gamma_1 x_i + \epsilon_i \qquad (3) \\
(\epsilon_i | F \, M_4 \, \mathcal{B}) &\overset{\text{IID}}{\sim} F \\
(F | \alpha \, \sigma_\epsilon^2 \, M_4 \, \mathcal{B}) &\sim DP(\alpha, F_0), \;\; F_0 = N(0, \sigma_\epsilon^2) \\
\left(\gamma_0 \, \gamma_1 \, \sigma_\epsilon^2 | M_4 \, \mathcal{B}\right) &\sim \text{diffuse}; \;\; (\alpha | M_4) \sim \text{small positive}\,.
\end{aligned}
$$

Dirichlet-Process Mixture Modeling

Many **Bayesian prior distributions** $p(\theta|M_j\,\mathcal{B})$ have **two user-friendly inputs**: a **quantity** θ_0 that **acts like** a **prior estimate** of the **unknown** θ, and a **number** n_0 that **behaves like** a **prior sample size** (i.e., a **measure** of **how tightly the prior is concentrated** around θ_0); **DP priors** are **no exception to this pattern**.

In equation (3), $DP(\alpha, F_0)$ is a **Dirichlet-process prior** on F with **prior estimate** $F_0 = N(0, \sigma_\epsilon^2)$ and a **quantity** (α) that behaves something like a **prior sample size**; this is referred to as **Dirichlet-process mixture modeling**, because (3) is a **mixture model** — each **person** in the study has her/his **own** λ, drawn from F_C (control) or F_T (treatment) — in which **uncertainty** about F_C and F_T is **quantified** via a **DP**.

NB **Bayesian model averaging** (BMA) with a **finite set of models** can be regarded as a **crude approximation** to what **Bayesian nonparametric** (BNP) modeling is **trying** to do, namely **average over Your uncertainty in model space** to provide an **honest representation** of Your **overall uncertainty** that **doesn't condition on things You don't know are true**.

Cross-Validation

• **Calibration cross-validation (CCV)**: The way the **IHGA example** unfolded looks **a lot** like the M^* **approach** I **condemned** previously: I used the **entire data set** to suggest which models to **consider**.

This has the **(strong) potential** to **underestimate uncertainty**; **Bayesians** (like **everybody else**) need to be able to **look at the data** to **suggest alternative models**, but **all of us** need to do so in a way that's **well-calibrated**.

Cross-validation — **partitioning** the data (e.g., **exchangeably**) into **subsets** used for **different tasks** (**modeling**, **validation**, ...) can **help**.

— The M^* **approach** is an example of what might be called **1CV** (**one-fold cross-validation**): You use the **entire data set** D both to **model** and to **see how good the model is** (this is clearly **inadequate**).

— **2CV** (**two-fold cross-validation**) is **frequently used**: You (a) **partition** the data into **modeling** (M) and **validation** (V) **subsets**, (b) use M to explore a **variety of models** until You've found a **"good"** one M^*, and (c) see how well M^* **validates** in V (a **useful Bayesian way** to do this is to **use the data** in M

Calibration Cross-Validation (CCV)

to construct **posterior predictive distributions** for **all of the data values** in V and see how the **latter compare** with the **former**).

2CV is **a lot better** than **1CV**, but **what** do You do (as **frequently** happens) if M^* **doesn't validate well** in V?

— **CCV** (**calibration cross-validation**): going out **one more term** in the **Taylor series** (so to speak),

(a) **partition** the data into **modeling** (M), **validation** (V) and **calibration** (C) **subsets**,

(b) use M to explore a **variety of models** until You've found **one or more plausible candidates** $\mathcal{M} = \{M_1, \ldots, M_m\}$,

(c) see **how well** the models in $\mathcal{M}$ **validate** in V,

(d) if **none of** them do, **iterate (b) and (c)** until You do get **good validation**, and

(e) **fit** the **best model** in $\mathcal{M}$ (or, better, **use BMA**) on the **data** in M + V, and report both (i) **inferential conclusions** based on **this fit** and (ii) the **quality of predictive calibration** of **Your model/ensemble**) in C.

CCV (continued)

The **goal** with this **method** is both

(1) a **good answer**, to the **main scientific question**, that has **paid a reasonable price** for **model uncertainty** (the **inferential answer** is based only on M + V, making Your **uncertainty bands wider**) and

(2) an **indication** of how **well calibrated** {the **iterative fitting process** yielding the **answer** in (1)} is in C (a **good proxy** for **future data**).

You can use **decision theory** (Draper and Southwood, 2013) to decide **how much data** to put in each of M, V and C: the **more important calibration** is to You, the **more data** You want to put in C, but **only up to a point**, because getting a **good answer** to the **scientific question** is also **important** to You.

This is **related** to the **machine-learning** practice (e.g., **Hastie, Tibshirani, Friedman** [HTF] 2009) of **Train/Validation/Test** partitioning, with one **improvement** (**decision theory** provides an **optimal way** to choose the **data subset sizes**); I **don't agree** with HTF that this can **only be done with large data sets**: it's even **more important** to do it with **small** and **medium-size data sets** (You just need to work with **multiple (M, V, C) partitions** and **average**).

Modeling Algorithm

CCV provides a way to **pay** the **right price** for **hunting around in the data** for **good models**, motivating the following **modeling algorithm**:

(a) Start at a model M_0 (how choose?); set the current model $M_{\text{current}} \leftarrow M_0$ and the current model ensemble $\mathcal{M}_{\text{current}} \leftarrow \{M_0\}$.

(b) If M_{current} is good enough to stop (how decide?), return $\mathcal{M}_{\text{current}}$; else

(c) Generate a new candidate model M_{new} (how choose?) and set $\mathcal{M}_{\text{current}} \leftarrow \mathcal{M}_{\text{current}} \cup M_{\text{new}}$.

(d) If M_{new} is better than M_{current} (how decide?), set $M_{\text{current}} \leftarrow M_{\text{new}}$.

(e) Go to (b).

For **human analysts** the **choice** in **(a)** is **not hard**, although it **might not be easy to automate** in **full generality**; for **humans** the **choice** in **(c)** demands **creativity**, and as a **profession**, at present, we have **no principled way** to **automate** it; here I want to **focus** on the **questions** in (b) and (d):

$\boxed{Q_1}$: Is M_1 **better** than M_2? $\boxed{Q_2}$: Is M_1 **good enough**?

The Modeling-As-Decision Principle

These questions **sound fundamental** but **are not**: better **for what purpose**? Good enough **for what purpose**? This **implies** (see, e.g., Bernardo and Smith, 1995; Draper, 1996; Key et al., 1999) a

Modeling-As-Decision Principle: Making clear the **purpose to which the modeling will be put** transforms **model specification** into a **decision problem**, which should be solved by **maximizing expected utility** with a **utility function tailored** to the **specific problem** under study.

Some **examples** of this may be found (e.g., Draper and Fouskakis, 2008: **variable selection** in **generalized linear models** under **cost constraints**), but this is **hard work**; there's a **powerful desire** for **generic model-comparison methods** whose **utility structure** may provide a **decent approximation** to **problem-specific utility elicitation**.

Two such **methods** are **Bayes factors** and **log scores**.

- **Bayes factors.** It looks **natural** to **compare models** on the basis of their **posterior probabilities**; from **Bayes's Theorem** in **odds form**,

Bayes Factors

$$\frac{p(M_2|D\,\mathcal{B})}{p(M_1|D\,\mathcal{B})} = \left[\frac{p(M_2|\mathcal{B})}{p(M_1|\mathcal{B})}\right] \cdot \left[\frac{p(D|M_2\,\mathcal{B})}{p(D|M_1\,\mathcal{B})}\right]; \tag{4}$$

the **first term** on the right is just the **prior odds** in favor of M_2 over M_1, and the **second term** on the right is called the **Bayes factor**, so in words equation (4) says

$$\left(\begin{array}{c}\textbf{posterior}\\ \textbf{odds}\\ \text{for } M_2\\ \text{over } M_1\end{array}\right) = \left(\begin{array}{c}\textbf{prior odds}\\ \text{for } M_2\\ \text{over } M_1\end{array}\right) \cdot \left(\begin{array}{c}\textbf{Bayes factor}\\ \text{for } M_2\\ \text{over } M_1\end{array}\right). \tag{5}$$

(**Bayes factors** seem to have **first** been **considered** by **Turing** and **Good** ($\sim$ **1941**), as part of the effort to **break the German Enigma codes**.)

Odds o are related to **probabilities** p via $o = \frac{p}{1-p}$ and $p = \frac{o}{1+o}$; these are **monotone increasing transformations**, so the **decision rules** {choose M_2 over M_1 if the **posterior odds** for M_2 are greater} and {choose M_2 over M_1 if $p(M_2|D\,\mathcal{B}) > p(M_1|D\,\mathcal{B})$} are **equivalent**.

Decision-Theoretic Basis for Bayes Factors

This approach does have a **decision-theoretic basis**, but it's rather **odd**: if You pretend that the **only possible data-generating mechanisms** are $\mathcal{M} = \{M_1, \ldots, M_m\}$ for finite m, and You pretend that one of the models in $\mathcal{M}$ must be the **true data-generating mechanism** M_{DG}, and You pretend that the **utility function**

$$U(M, M_{DG}) = \left\{ \begin{array}{cc} 1 & \text{if } M = M_{DG} \\ 0 & \text{otherwise} \end{array} \right\} \tag{6}$$

reflects Your **real-world values**, then it's **decision-theoretically optimal** to choose the model in $\mathcal{M}$ with the **highest posterior probability** (i.e., that choice **maximizes expected utility**).

If it's **scientifically appropriate** to take the **prior model probabilities** $p(M_j|\mathcal{B})$ to be **equal**, this rule reduces to **choosing the model with the highest Bayes factor in favor of it**; this can be found by (a) **computing the Bayes factor** in favor of M_2 over M_1,

$$BF(M_2 \text{ over } M_1|D\,\mathcal{B}) = \frac{p(D|M_2\,\mathcal{B})}{p(D|M_1\,\mathcal{B})}, \tag{7}$$

Parametric Model Comparison

favoring M_2 if $BF(M_2 \text{ over } M_1|D\,\mathcal{B}) > 1$, i.e., if $p(D|M_2\,\mathcal{B}) > p(D|M_1\,\mathcal{B})$, and calling the **better model** M^*; (b) **computing the Bayes factor** in favor of M^* over M_3, calling the **better model** M^*; and so on up through M_m.

Notice that there's **something else** a bit **funny** about this: $p(D|M_j\,\mathcal{B})$ is the **prior** **(not posterior) predictive distribution** for the data set D under model M_j, so the **Bayes factor rule** tells You to **choose the model that does the best job of predicting the data before any data arrives**.

Let's look at the **general problem** of **parametric model comparison**, in which model M_j has **its own parameter vector** γ_j (of length k_j), where $\gamma_j = (\theta, \eta_j)$, and is **specified** by

$$M_j : \left\{ \begin{array}{c} (\gamma_j|M_j\,\mathcal{B}) \sim p(\gamma_j|M_j\,\mathcal{B}) \\ (D|\gamma_j\,M_j\,\mathcal{B}) \sim p(D|\gamma_j\,M_j\,\mathcal{B}) \end{array} \right\}. \tag{8}$$

Here the quantity $p(D|M_j\,\mathcal{B})$ that **defines the Bayes factor** is

Integrated Likelihoods

$$p(D|M_j\,\mathcal{B}) = \int p(D|\gamma_j\,M_j\,\mathcal{B})\,p(\gamma_j|M_j\,\mathcal{B})\,d\gamma_j\,; \tag{9}$$

this is called an **integrated likelihood** (or **marginal likelihood**) because it tells You to take a **weighted average** of the **sampling distribution/likelihood** $p(D|\gamma_j\,M_j\,\mathcal{B})$, but **NB** **weighted by the** **prior** for γ_j in model M_j; as noted above, this may seem **surprising**, but it's **correct**, and it can lead to **trouble**, as follows.

The first trouble is **technical**: the **integral** in (9) can be **difficult to compute**, and may not even be easy to **approximate**.

The second thing to **notice** is that (9) can be **rewritten** as

$$p(D|M_j\,\mathcal{B}) = E_{(\gamma_j|M_j\,\mathcal{B})}\;p(D|\gamma_j\,M_j\,\mathcal{B})\,. \tag{10}$$

In other words the **integrated likelihood** is the **expectation** of the **sampling distribution** over the **prior** for γ_j in model M_j (evaluated at the **observed data set** D).

A few **additional words** about **prior distributions** on **parameters**:

Instability of Bayes Factors

A **distribution (density)** for a **real-valued parameter** θ that summarizes the **information**

$\{\theta$ is **highly likely** to be **near** $\theta_0\}$

will have **most of its mass** concentrated **near** θ_0, whereas the **information**

$\{$**not much is known** about $\theta\}$

would correspond to a **density** that's rather **flat** (or **diffuse**) across a broad range of θ values; thus when the **scientific context** offers **little information** about γ_j **external** to the data set D, this translates into a **diffuse prior** on γ_j, and this spells **trouble** for **Bayes factors**:

$$p(D|M_j\,\mathcal{B}) = E_{(\gamma_j|M_j\,\mathcal{B})}\; p(D|\gamma_j\,M_j\,\mathcal{B})\,.$$

You can see that if the **available information** implies that $p(\gamma_j|M_j\,\mathcal{B})$ should be **diffuse**, the **expectation** defining the **integrated likelihood** can be **highly unstable** with respect to **small details** in how the **diffuseness is specified**.

Example: **Integer-valued** data set $D = (y_1\ \ldots\ y_n)$; $\bar{y} = \frac{1}{n}\sum_{i=1}^{n} y_i$;

Instability of Bayes Factors (continued)

$M_1 =$ **Geometric**(θ_1) likelihood with a **Beta**(α_1, β_1) prior on θ_1;

$M_2 =$ **Poisson**(θ_2) likelihood with a **Gamma**(α_2, β_2) prior on θ_2.

The **Bayes factor** in favor of M_1 over M_2 turns out to be

$$\frac{\Gamma(\alpha_1+\beta_1)\,\Gamma(n+\alpha_1)\,\Gamma(n\bar{y}+\beta_1)\,\Gamma(\alpha_2)\,(n+\beta_2)^{n\bar{y}+\alpha_2}\left(\prod_{i=1}^{n} y_i!\right)}{\Gamma(\alpha_1)\,\Gamma(\beta_1)\,\Gamma(n+n\bar{y}+\alpha_1+\beta_1)\,\Gamma(n\bar{y}+\alpha_2)\,\beta_2^{\alpha_2}}. \quad (11)$$

With **standard diffuse priors** — take $(\alpha_1, \beta_1) = (1, 1)$ and $(\alpha_2, \beta_2) = (\epsilon, \epsilon)$ for some $\epsilon > 0$ — the **Bayes factor** reduces to

$$\frac{\Gamma(n+1)\,\Gamma(n\bar{y}+1)\,\Gamma(\epsilon)\,(n+\epsilon)^{n\bar{y}+\epsilon}\left(\prod_{i=1}^{n} y_i!\right)}{\Gamma(n+n\bar{y}+2)\,\Gamma(n\bar{y}+\epsilon)\,\epsilon^{\epsilon}}. \quad (12)$$

This goes to $+\infty$ as $\epsilon \downarrow 0$, i.e., You can make the evidence in **favor** of the **Geometric model** over the **Poisson** as **large** as You want, **no matter what the data says**, as a function of a quantity near 0 that **scientifically** You have **no basis** to specify.

If instead You **fix and bound** (α_2, β_2) away from 0 and let $(\alpha_1, \beta_1) \downarrow 0$, You can **completely reverse** this and make the evidence in **favor** of the **Poisson model** over the **Geometric** as **large** as You want (for **any** y).

Approximating Integrated Likelihoods

The **bottom line** is that, when **scientific context** suggests **diffuse priors** on the **parameter vectors** in the **models** being **compared**, the **integrated likelihood values** that are at the **heart** of **Bayes factors** can be **hideously sensitive** to **small arbitrary details** in how the **diffuseness** is **specified**.

This has been **well-known** for quite awhile now, and it's given rise to **an amazing amount of fumbling around**, as people who like **Bayes factors** have tried to find a way to **fix** the problem: at this point the **list of attempts** includes {**partial, intrinsic, fractional**} **Bayes factors, well-calibrated priors, conventional priors, intrinsic priors, expected posterior priors**, ... (e.g., Pericchi 2004), and all of them **exhibit** a level of **ad-hockery** that's **otherwise absent** from the **Bayesian paradigm**.

Approximating integrated likelihoods. The **goal** is

$$p(D|M_j\,\mathcal{B}) = \int p(D|\gamma_j\,M_j\,\mathcal{B})\,p(\gamma_j|M_j\,\mathcal{B})\,d\gamma_j\,; \tag{13}$$

maybe there's an **analytic approximation** to this that will suggest how to **avoid trouble**.

Laplace Approximation

Laplace (1785) already faced this problem **225 years ago**, and he offered a **solution** that's often useful, which people now call a **Laplace approximation** in his honor (it's an **example** of what's also known in the **applied mathematics literature** as a **saddle-point approximation**).

Noticing that the **integrand** $P^*(\gamma_j) \equiv p(D|\gamma_j\, M_j\, \mathcal{B})\, p(\gamma_j|M_j\, \mathcal{B})$ in $p(D|M_j\, \mathcal{B})$ is an **un-normalized version** of the **posterior distribution** $p(\gamma_j|D\, M_j\, \mathcal{B})$, and appealing to a **Bayesian version** of the **Central Limit Theorem** — which says that **with a lot of data**, such a **posterior distribution** should be **close to Gaussian**, **centered** at the **posterior mode** $\hat{\gamma}_j$ — You can see that (with a **large sample size** n) $\log P^*(\gamma_j)$ should be **close to quadratic** around that mode; the **Laplace idea** is to take a **Taylor expansion** of $\log P^*(\gamma_j)$ around $\hat{\gamma}_j$ and **retain** only the terms out to **second order**; the result is

$$\begin{aligned} \log p(D|M_j\, \mathcal{B}) \quad = \quad & \log p(D|\hat{\gamma}_j\, M_j\, \mathcal{B}) + \log p(\hat{\gamma}_j|M_j\, \mathcal{B}) \\ & + \frac{k_j}{2} \log 2\pi - \frac{1}{2} \log |\hat{I}_j| + O\left(\frac{1}{n}\right) ; \end{aligned} \tag{14}$$

here $\hat{\gamma}_j$ is the **maximum likelihood estimate** of the **parameter vector** γ_j under **model** M_j and $\hat{I}_j$ is the **observed information matrix** under M_j.

BIC

Notice that the **prior** on γ_j in model M_j enters into this **approximation** through $\log p(\hat{\gamma}_j | M_j \mathcal{B})$, and this is a term that **won't go away with more data**: as n increases this term is $O(1)$.

Using a **less precise Taylor expansion**, Schwarz (1978) obtained a **different approximation** that's the **basis** of what has come to be **known** as the **Bayesian information criterion (BIC)**:

$$\log p(y | M_j \mathcal{B}) = \log p(y | \hat{\gamma}_j M_j \mathcal{B}) - \frac{k_j}{2} \log n + O(1). \tag{15}$$

People often work with a **multiple** of this for **model comparison**:

$$BIC(M_j | D \mathcal{B}) = -2 \log p(D | \hat{\gamma}_j M_j \mathcal{B}) + k_j \log n \tag{16}$$

(the -2 **multiplier** comes from **deviance** considerations); **multiplying** by **−2** induces a **search** (with this approach) for **models** with **small BIC**.

This **model-comparison method** makes an **explicit trade-off** between **model complexity** (which **goes up** with k_j at a $\log n$ rate) — and model **lack of fit** (through the $-2 \log p(D | \hat{\gamma}_j M_j \mathcal{B})$ **term**).

BIC and the Unit-Information Prior

BIC is called an **information criterion** because it resembles **AIC** (Akaike, 1974). which was derived using **information-theoretic** reasoning:

$$AIC(M_j|D\,\mathcal{B}) = -2\log p(D|\hat{\gamma}_j\,M_j\,\mathcal{B}) + 2\,k_j\,. \tag{17}$$

AIC penalizes **model complexity** at a **linear rate** in k_j and so can have **different behavior** than **BIC**, especially with moderate to large n (**BIC** tends to choose **simpler models**; more on this later).

It's possible to work out what **implied prior BIC is using**, from the point of view of the **Laplace approximation**; the result is

$$(\gamma_j|M_j\,\mathcal{B}) \sim N_{k_j}(\hat{\gamma}_j, n\hat{I}_j^{-1}). \tag{18}$$

In the **literature** this is called a **unit-information prior**, because in **large samples** it corresponds to the **prior** being **equivalent to 1 new observation** yielding the **same sufficient statistics** as the **observed data**.

This **prior** is **data-determined**, but this **effect** is **close to negligible** even with only **moderate** n.

Bayes Factors; Log Scores

The BIC **approximation** to Bayes factors has the **extremely desirable property** that it's **free** of the **hideous instability** of **integrated likelihoods** with respect to **tiny details**, in how **diffuse priors** are specified, that **do not arise directly from the science of the problem**; in my view, if You're going to use **Bayes factors** to **choose** among **models**, You're **well advised** to use a **method like BIC** that **protects You from Yourself** in **mis-specifying those tiny details**.

I said back on **page 18** that there are **two generic utility-based model-comparison methods**: **Bayes factors** and **log scores**.

- **Log scores** are **based on** the

Prediction Principle: **Good models** make **good predictions**, and **bad models** make **bad predictions**; that's one **scientifically important** way You know a **model** is **good** or **bad**.

This suggests developing a **generic utility structure** based on **predictive accuracy**: consider first a **setting** in which $D = y = (y_1 \ldots y_n)$ for real-valued y_i and the **models** to be **compared** are (as before)

Log Scores

$$M_j\text{:} \left\{ \begin{array}{c} (\gamma_j | M_j \, \mathcal{B}) \sim p(\gamma_j | M_j \, \mathcal{B}) \\ (y | \gamma_j \, M_j \, \mathcal{B}) \sim p(y | \gamma_j \, M_j \, \mathcal{B}) \end{array} \right\} . \tag{19}$$

When **comparing** a **(future) data value** y^* with the **predictive distribution** $p(\cdot | y \, M_j \, \mathcal{B})$ for it under M_j, it's **been shown** that (under **reasonable optimality criteria**) all optimal **scores** measuring the **discrepancy** between y^* and $p(\cdot | y \, M_j \, \mathcal{B})$ are **linear functions** of $\log p(y^* | y \, M_j \, \mathcal{B})$ (the **log** of the **height** of the **predictive distribution** at the **observed value** y^*).

Using this **fact**, perhaps the most **natural-looking** form for a **composite measure** of **predictive accuracy** of M_j is a **cross-validated** version of the resulting **log score**,

$$LS_{CV}(M_j | y \, \mathcal{B}) = \frac{1}{n} \sum_{i=1}^{n} \log p(y_i | y_{-i} \, M_j \, \mathcal{B}) \, , \tag{20}$$

in which y_{-i} is the y **vector** with observation i **omitted**.

Somewhat **surprisingly**, Draper and Krnjajić (2010) have shown that a **full-sample log score** that **omits** the **leave-one-out idea**,

Full-Sample Log Score

$$LS_{FS}(M_j|y\,\mathcal{B}) = \frac{1}{n}\sum_{i=1}^{n} \log p(y_i|y\,M_j\,\mathcal{B})\,, \tag{21}$$

made **operational** with the **rule** {favor M_2 over M_1 if $LS_{FS}(M_2|y\,\mathcal{B}) > LS_{FS}(M_1|y\,\mathcal{B})$}, can have **better small-sample model discrimination ability** than LS_{CV} (in addition to being **faster** to **approximate** in a **stable** way).

If, in the spirit of **calibration**, You're prepared to **think about** an **underlying data-generating model** M_{DG}, LS_{FS} also has a **nice interpretation** as an **approximation** to the **Kullback-Leibler divergence** between M_{DG} and $p(\cdot|y\,M_j\,\mathcal{B})$, in which M_{DG} is **approximated** by the **empirical CDF**:

$$\begin{aligned} KL[p(\cdot|y\,M_j\,\mathcal{B})||M_{DG}] &= E_{M_{DG}} \log M_{DG} - E_{M_{DG}} \log p(\cdot|y\,M_j\,\mathcal{B}) \\ &\doteq E_{M_{DG}} \log M_{DG} - LS_{FS}(M_j|y\,\mathcal{B})\,; \end{aligned} \tag{22}$$

the **first term** on the **right side** of (22) is **constant** in $p(\cdot|y\,M_j\,\mathcal{B})$, so **minimizing** $KL[p(\cdot|y\,M_j\,\mathcal{B}||M_{DG})]$ is **approximately the same** as **maximizing** LS_{FS}.

Bayes Factors/BIC Versus Log Scores

What follows is a **sketch** of **recent results** (Draper, 2013) based on **simulation experiments** with **realistic sample sizes**; in my view **standard asymptotic calculations — choosing between** the **models** in $\mathcal{M} = \{M_1, M_2\}$ as $n \to \infty$ with $\mathcal{M}$ **remaining fixed —** are **essentially irrelevant** in **calibration studies**, for **two reasons**:

(1) With **increasing** n, You'll want $\mathcal{M}$ to **grow** to **satisfy Your desire** to do a **better job** of **capturing real-world complexities**, and

(2) **Data** usually **accumulate over time**, and with **increasing** n it **becomes more likely** that the **real-world process** You're modeling is **not stationary**.

• **Versions** of **Bayes factors** that **behave sensibly** with **diffuse priors** on the **model parameters** (e.g., **intrinsic Bayes factors**: Berger and Pericchi, 1996, and **more recent** cousins) tend to have **model discrimination performance similar** to that of **BIC** in **calibration** (**repeated-sampling** with **known** M_{DG}) **environments**; I'll show **results** for **BIC** here.

Example: Consider **assessing** the **performance** of a **drug**, for **lowering**

Clinical Trial to Quantify Improvement

systolic blood pressure (SBP) in **hypertensive** patients, in a **phase–II clinical trial**, and suppose that a **Gaussian sampling distribution** for the **outcome variable** is **reasonable** (possibly after **transformation**).

Two **frequent designs** in **settings** of this type have as their goals **quantifying improvement** and **establishing bio-equivalence**.

• (**quantifying improvement**) Here You want to **estimate** the **mean decline** in **blood pressure** under this drug, and it would be **natural** to choose a **repeated-measures (pre-post) experiment**, in which **SBP values** are obtained for **each patient**, both **before** and **after** taking the drug for a **sufficiently long** period of time for its **effect** to become **apparent**.

Let θ stand for the **mean difference** $(SBP_{before} - SBP_{after})$ in the **population** of **patients** to which it's **appropriate** to **generalize** from the **patients** in Your **trial**, and let $D = y = (y_1 \ \ldots \ y_n)$. where y_i is the **observed difference** $(SBP_{before} - SBP_{after})$ for **patient** i $(i = 1, \ldots, n)$.

The **real-world purpose** of this **experiment** is to **decide** whether to **take the drug forward** to **phase III**; under the **weight** of **20th-century**

Decision, Not Inference

inertia (in which **decision-making** was **strongly** — and **incorrectly** — **subordinated** to **inference**), Your **first impulse** might be to **treat this** as an **inferential problem** about θ, but **it's not**; it's a **decision problem** that **involves** θ.

This is an **example** of the

- **Decision-Versus-Inference Principle:** We should all **get out of the habit** of **using inferential methods** to **make decisions**: their **implicit utility structure** is often **far from optimal**.

The **action space** here is $\mathcal{A} = (a_1, a_2) =$ (**don't take the drug forward to phase III**, **do take it forward**), and a **sensible utility function** $U(a_j, \theta)$ should be **continuous** and **monotonically increasing** in θ over a **broad range** of **positive** θ values (the **bigger** the **SBP decline** for **hypertensive patients** who **start** at (say) **160 mmHg**, the **better**, up to a **drop** of about **40 mmHg**, **beyond** which the **drug** starts inducing **fainting spells**).

However, to **facilitate** a **comparison** between **BIC** and **log scores**, here I'll **compare two models** M_1 and M_2 that **dichotomize** the θ range,

Models For Quantifying Improvement

but not at 0: despite a **century** of **textbook claims** to the **contrary**, **there's nothing special about $\theta = 0$ in this setting**, and in fact You **know scientifically** that θ is **not exactly 0** (because the **outcome variable** in **this experiment** is **conceptually continuous**).

What **matters** here is whether $\theta > \Delta$, where Δ is a **practical significance improvement threshold** below which the drug is **not worth advancing** into **phase III** (for example, **any drug** that did not **lower SBP** for **severely hypertensive patients** — those whose **pre-drug values** average **160 mmHg** or more — by **at least 15 mmHg** would **not deserve further attention**).

With **little information** about θ **external** to this **experimental data set**, what **counts** in this **situation** is the **comparison** of the following **two models**:

$$M_1: \left\{ \begin{array}{ccc} (\theta|\mathcal{B}) & \sim & \text{diffuse for } \theta \leq \Delta \\ (y_i|\theta\,\mathcal{B}) & \overset{\text{IID}}{\sim} & N(\theta, \sigma^2) \end{array} \right\} \quad \text{and} \tag{23}$$

$$M_2: \left\{ \begin{array}{ccc} (\theta|\mathcal{B}) & \sim & \text{diffuse for } \theta > \Delta \\ (y_i|\theta\,\mathcal{B}) & \overset{\text{IID}}{\sim} & N(\theta, \sigma^2) \end{array} \right\}, \tag{24}$$

Quantifying Improvement: Model Comparison Methods

in which **for simplicity** I'll take σ^2 to be **known** (the **results** are **similar** with σ^2 **learned** from the **data**).

This gives rise to **three model-selection methods** that can be **compared calibratively**:

- **Full-sample log scores**: **choose** M_2 if $LS_{FS}(M_2|y\,\mathcal{B}) > LS_{FS}(M_1|y\,\mathcal{B})$.

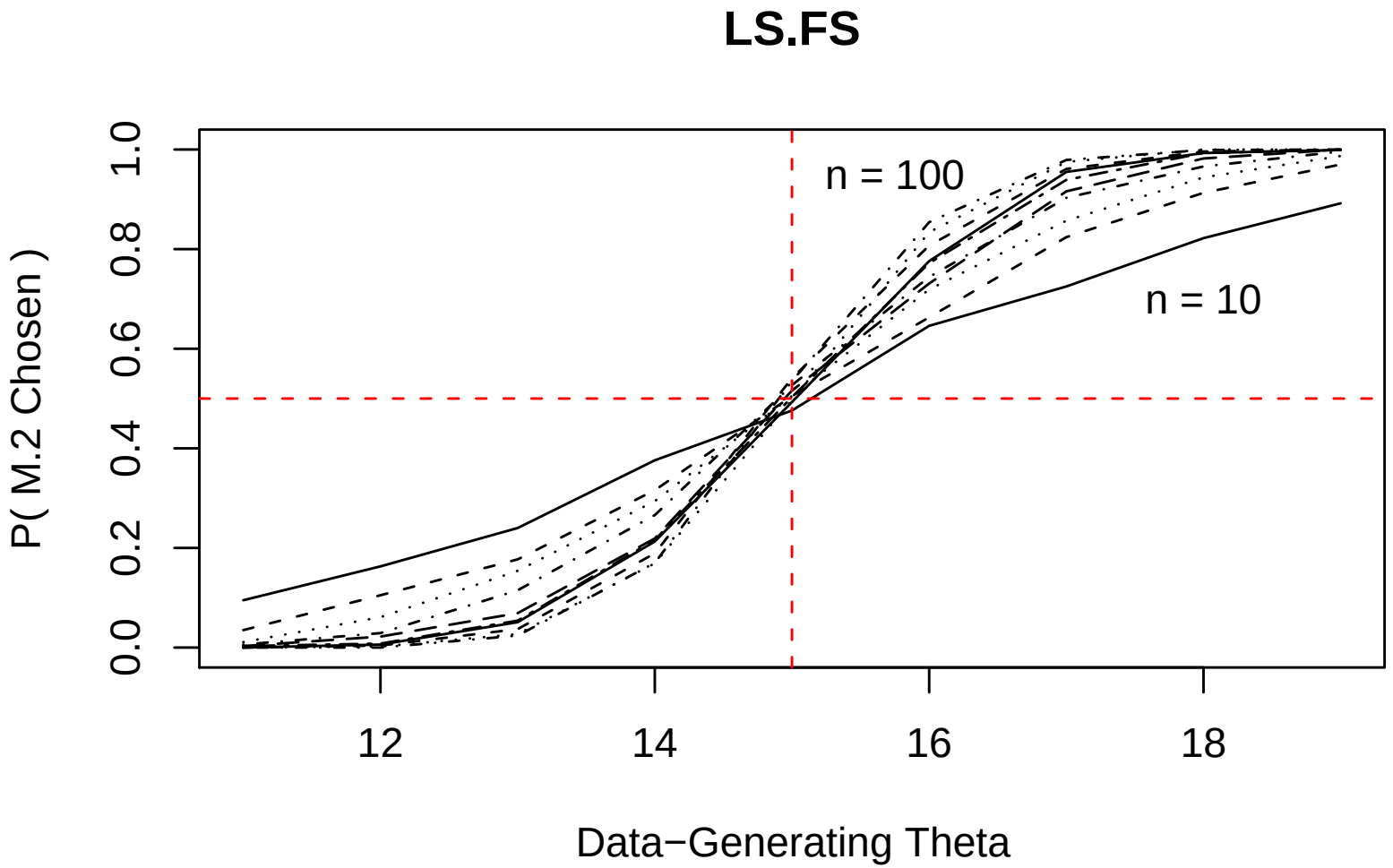
- **Posterior probability**: let $M^* = \{(\theta|\mathcal{B}) \sim \text{diffuse on } \Re, (y_i|\theta\,\mathcal{B}) \overset{\text{IID}}{\sim} N(\theta, \sigma^2)\}$ and **choose** M_2 if $p(\theta > \Delta|y\,M^*\,\mathcal{B}) > 0.5$.

- **BIC**: **choose** M_2 if $BIC(M_2|y\,\mathcal{B}) < BIC(M_1|y\,\mathcal{B})$.

Simulation experiment details, based on the **SBP drug trial**: $\Delta = 15$; $\sigma = 10$; $n = 10, 20, \ldots, 100$; **data-generating** $\theta_{DG} = 11, 12, \ldots, 19$; $\alpha = 0.05$; 1,000 **simulation replications**; **Monte-Carlo approximations** of the **predictive ordinates** in LS_{FS} based on **10,000 posterior draws**.

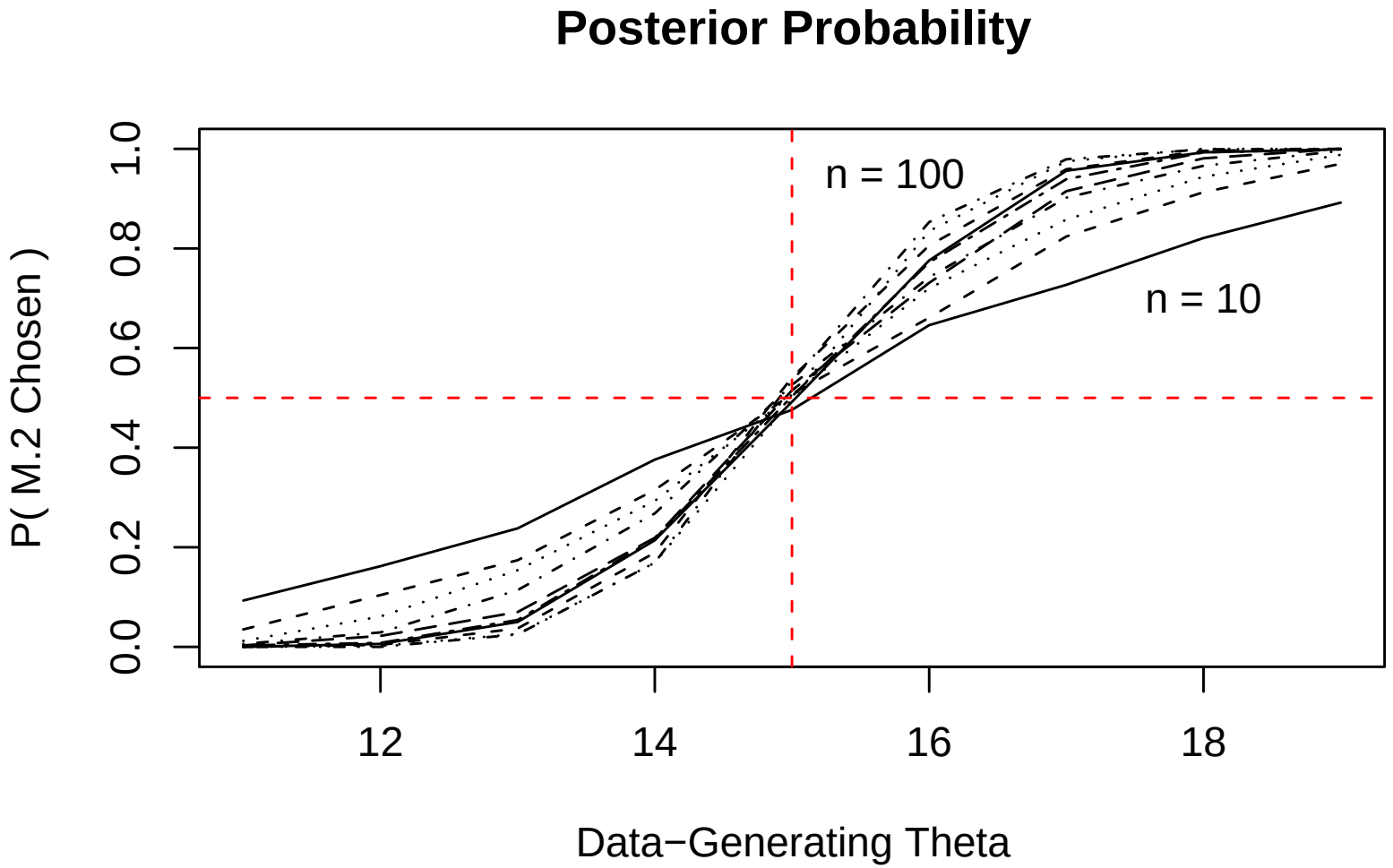
The **figures** below give **Monte-Carlo estimates** of the **probability that M_2 is chosen**.

LS_{FS} Results: Quantifying Improvement



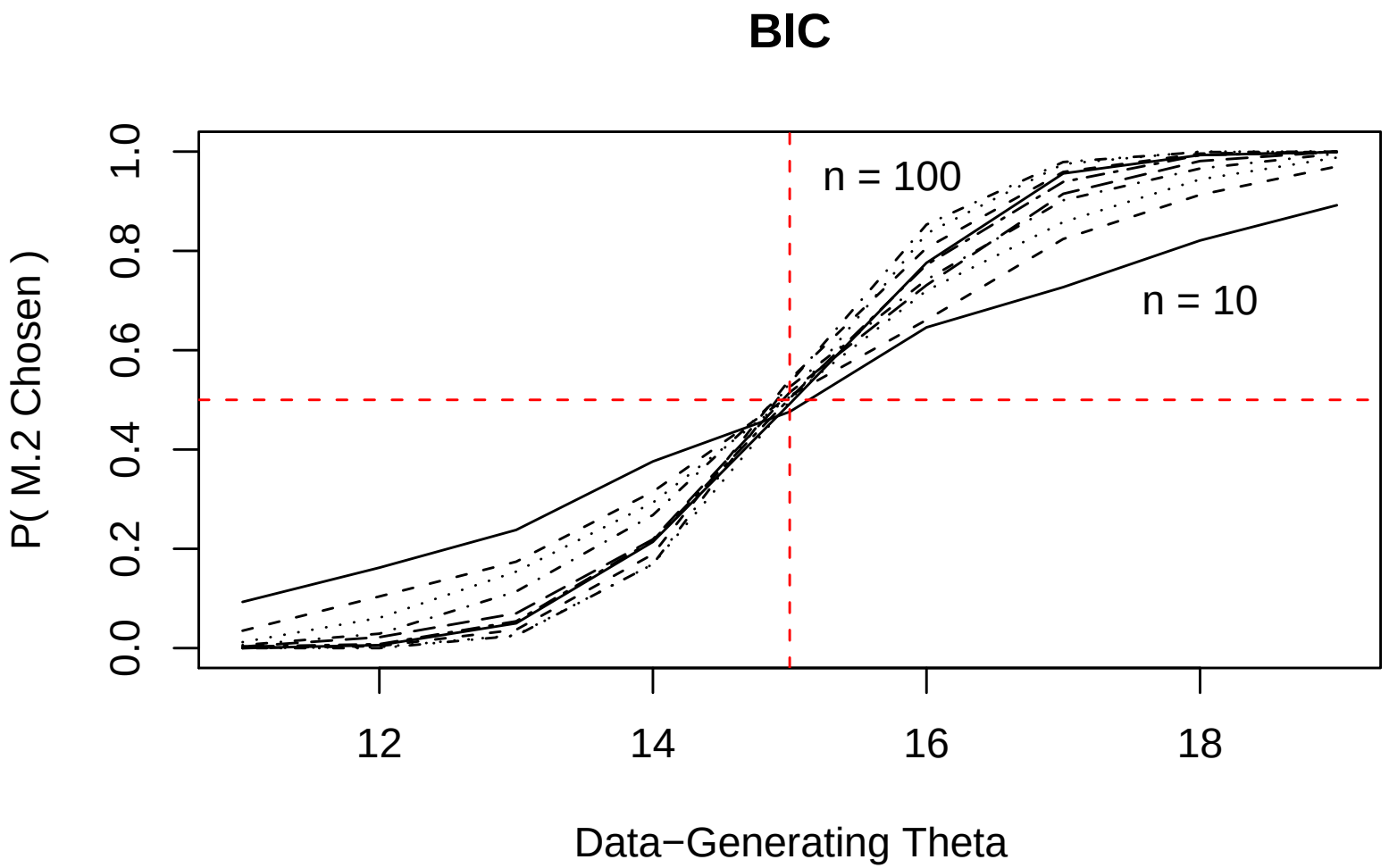
This **exhibits all** the **monotonicities** that it **should**, and **correctly yields 0.5** for all n with $\theta_{DG} = 15$.

Posterior Probability Results: Quantifying Improvement



Even though the LS_{FS} and **posterior-probability methods** are **quite different**, their **information-processing** in **discriminating** between M_1 and M_2 is **identical** to within $\pm$**0.003** (**well within simulation noise** with **1,000 replications**).

BIC Results: Quantifying Improvement



Here **BIC** and the **posterior-probability approach** are **algebraically identical**, making the **model-discrimination performance** of **all three approaches** the **same** in **this problem**.

Establishing Bio-Equivalence

• **(establishing bio-equivalence)** In this case there's a **previous hypertension drug** B (call the **new drug** A) and You're wondering if the **mean effects** of the **two drugs** are **close enough** to regard them as **bio-equivalent**.

A **good design** here would again have a **repeated-measures** character, in which **each patient's SBP** is measured **four times**: **before** and **after** taking drug A, and **before** and **after** taking drug B (allowing **enough time** to elapse between **taking the two drugs** for the **effects** of the **first drug** to **disappear**).

Let θ stand for the **mean difference**

$$[(SBP_{before,A} - SBP_{after,A}) - (SBP_{before,B} - SBP_{after,B})] \qquad (25)$$

in the **population** of **patients** to which it's **appropriate** to **generalize** from the **patients in Your trial**, and let y_i be the **corresponding difference** for patient i $(i = 1, \ldots, n)$.

Again in this **setting** there's **nothing special** about $\theta = 0$, and **as before** You **know scientifically** that θ is **not exactly 0**;

Bio-Equivalence Modeling

what **matters** here is whether $|\theta| \leq \lambda$, where $\lambda > 0$ is a **practical significance bio-equivalence threshold** (e.g., **5 mmHg**).

Assuming **as before** a **Gaussian sampling story** and **little information** about θ **external** to this **experimental data set**, what **counts** here is a **comparison** of

$$M_3: \left\{ \begin{array}{ccc} (\theta|\mathcal{B}) & \sim & \text{diffuse for } |\theta| \leq \lambda \\ (y_i|\theta\,\mathcal{B}) & \overset{\text{IID}}{\sim} & N(\theta, \sigma^2) \end{array} \right\} \quad \text{and} \tag{26}$$

$$M_4: \left\{ \begin{array}{ccc} (\theta|\mathcal{B}) & \sim & \text{diffuse for } |\theta| > \lambda \\ (y_i|\theta\,\mathcal{B}) & \overset{\text{IID}}{\sim} & N(\theta, \sigma^2) \end{array} \right\}, \tag{27}$$

in which σ^2 is again taken for **simplicity** to be **known**.

A **natural alternative** to **BIC** and LS_{FS} here is again based on **posterior probabilities**: as before, let $M^* = \{(\theta|\mathcal{B}) \sim \text{diffuse on } \Re, (y_i|\theta\,\mathcal{B}) \overset{\text{IID}}{\sim} N(\theta, \sigma^2)\}$, but this time **favor** M_4 over M_3 if $p(|\theta| > \lambda | y\, M^*\, \mathcal{B}) > 0.5$.

As before, a **careful real-world choice** between M_3 and M_4 in **this case** would be **based** on a **utility function** that **quantified** the

Bio-Equivalence Model Comparison

costs and benefits of

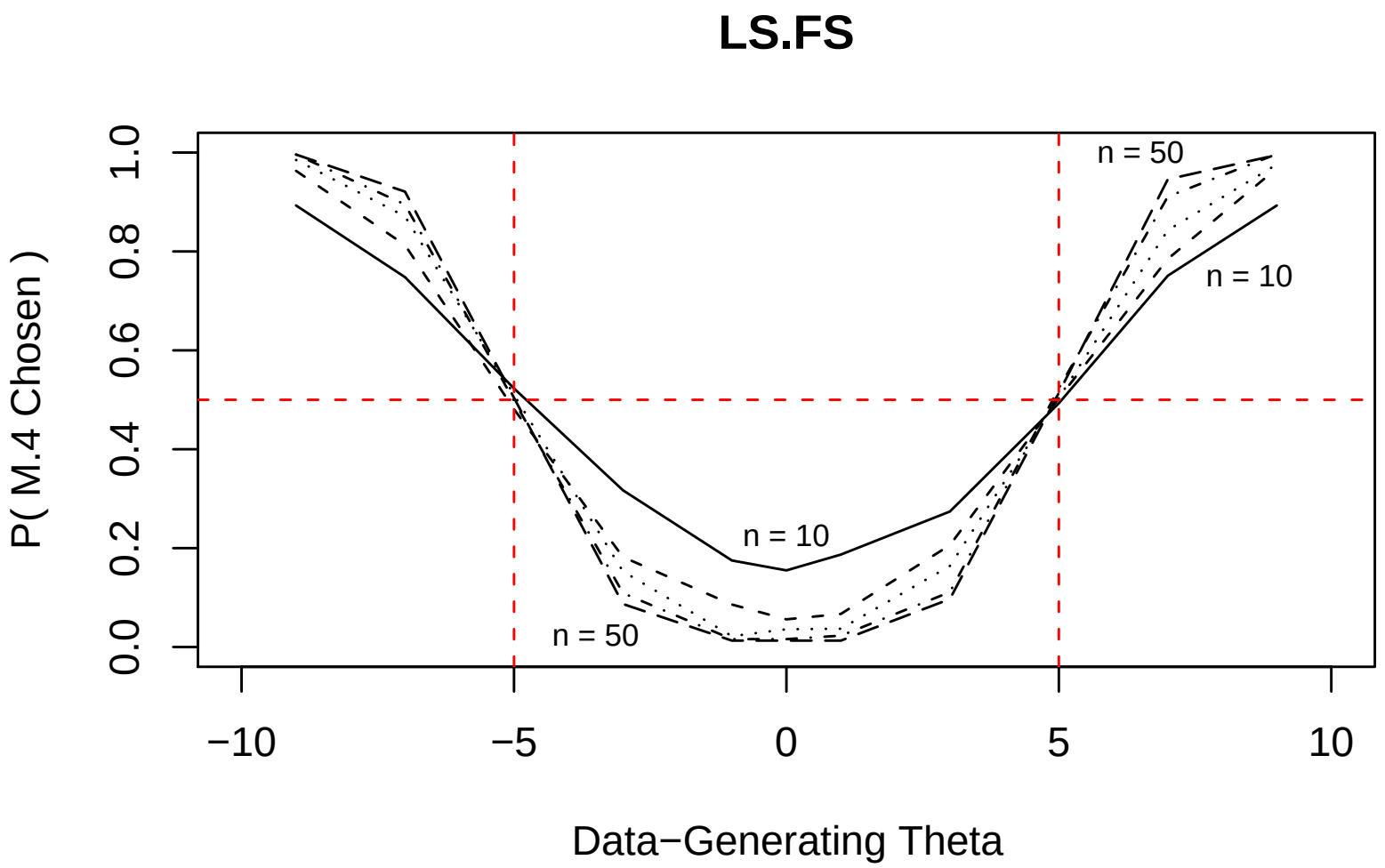
{**claiming** the two drugs were **bio-equivalent** when they **were**,
concluding that they were **bio-equivalent** when they **were not**,
deciding that they were **not bio-equivalent** when they **were**,
judging that they were **not bio-equivalent** when they were **not**},

but here I'll again simply **compare** the **calibrative performance** of LS_{FS}, **posterior probabilities**, and **BIC**.

Simulation experiment details, based on the **SBP drug trial**: $\lambda = 5$; $\sigma = 10$; $n = 10, 20, \ldots, 100$; **data-generating** $\theta_{DG} = \{-9, -7, -5, -3, -1, 0, 1, 3, 5, 7, 9\}$; $\alpha = 0.05$; **1,000 simulation replications**, $M =$ **10,000 Monte-Carlo draws** for LS_{FS}.

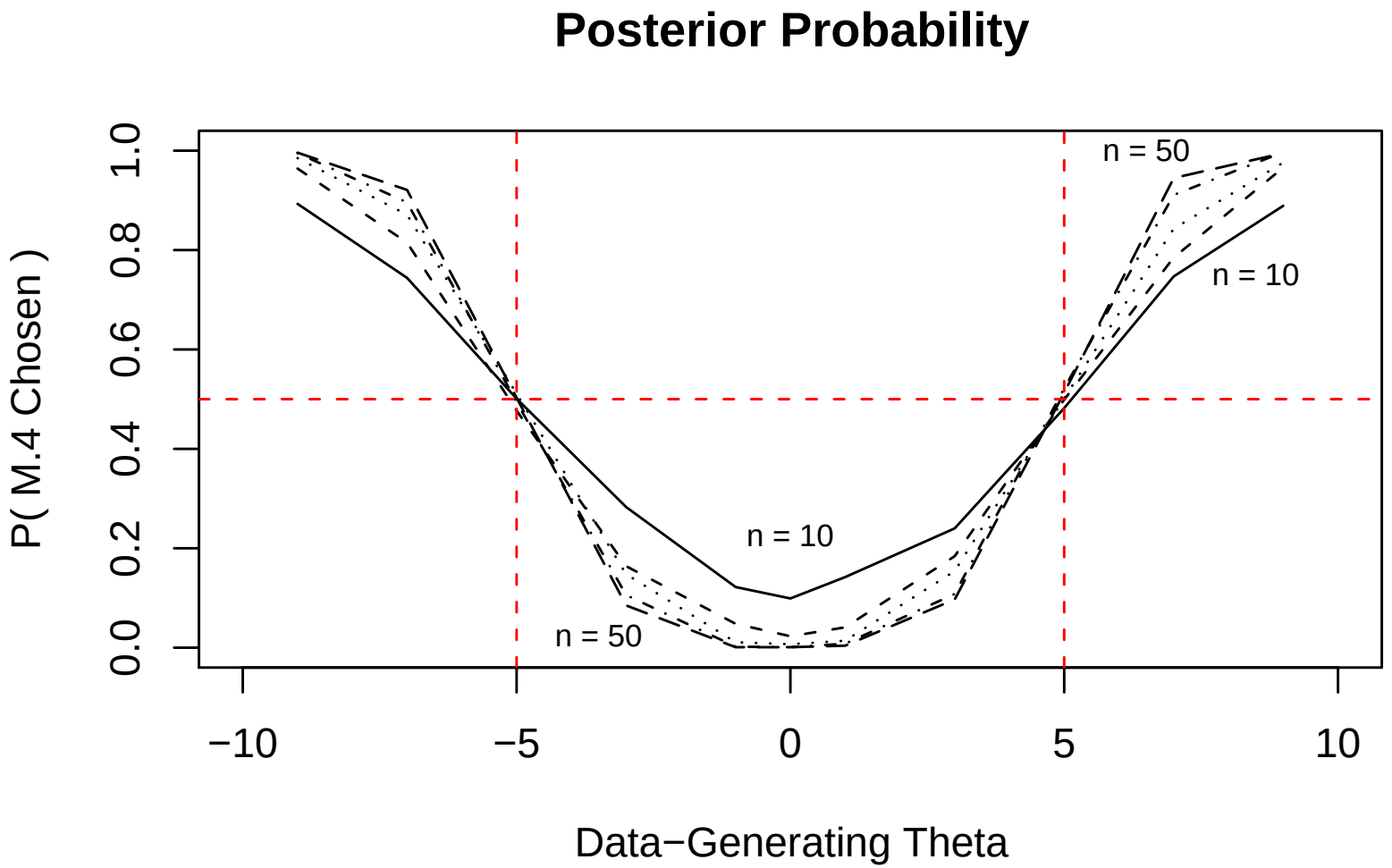
NB It has **previously been established** that when **making** the **(unrealistic) sharp-null comparison** $\theta = 0$ versus $\theta \neq 0$ in the **context** of $(y_i|\theta\, \mathcal{B}) \overset{\text{IID}}{\sim} N(\theta, \sigma^2)$, as $n \to \infty$ LS_{FS} **selects** the $\theta \neq 0$ **model** with **probability** $\to$ **1** even when $\theta_{DG} = 0$; this **"inconsistency of log scores at the null model"** has been **used by some people** as a **reason** to **dismiss log scores** as a **model-comparison method**.

LS_{FS} Results: Bio-Equivalence



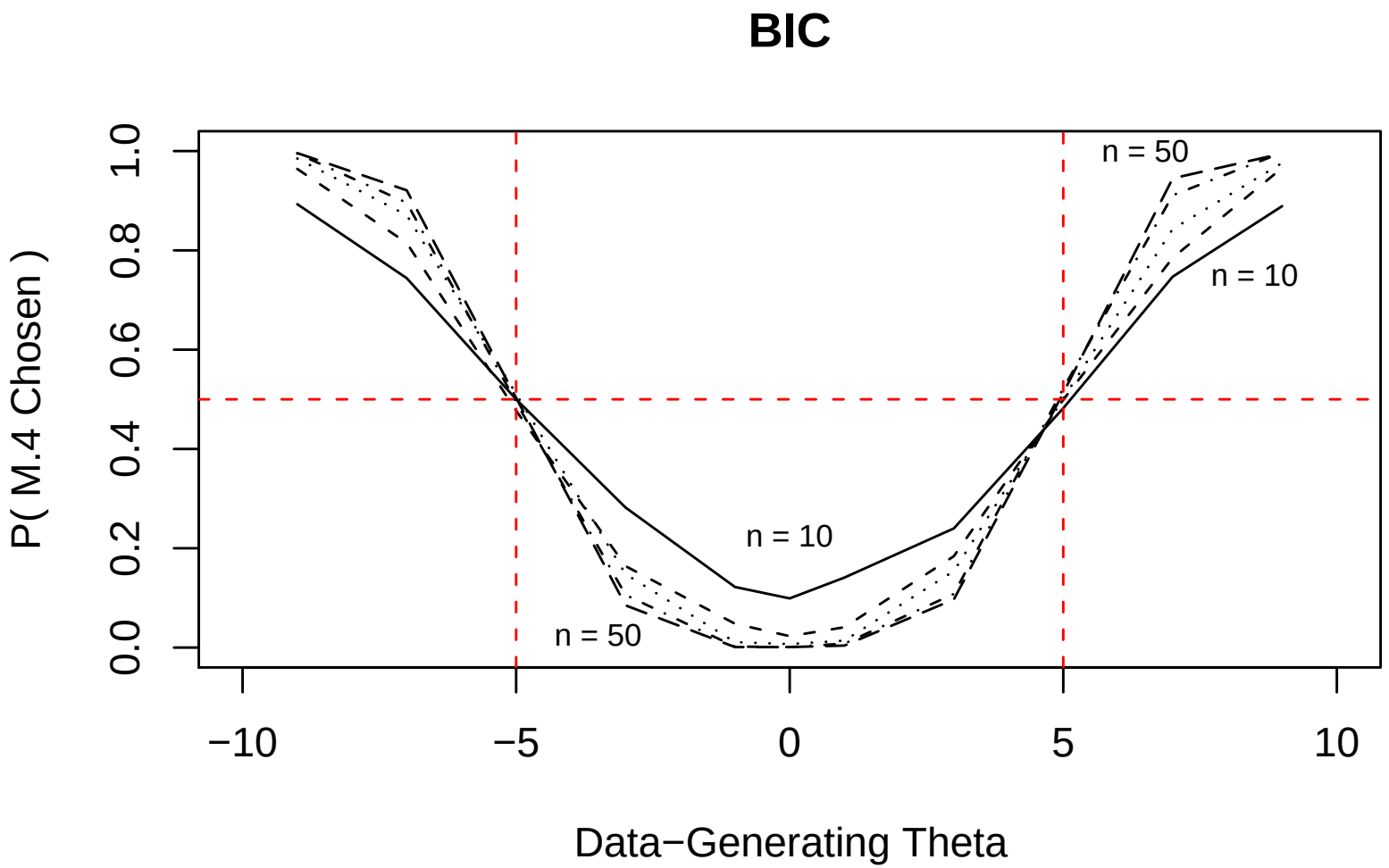
In this **more realistic setting**, comparing $|\theta| \leq \lambda$ versus $|\theta| > \lambda$ with $\lambda > 0$, LS_{FS} has the **correct large-sample behavior**, **both** when $|\theta_{DG}| \leq \lambda$ and when $|\theta_{DG}| > \lambda$.

Posterior Probability Results: Bio-Equivalence



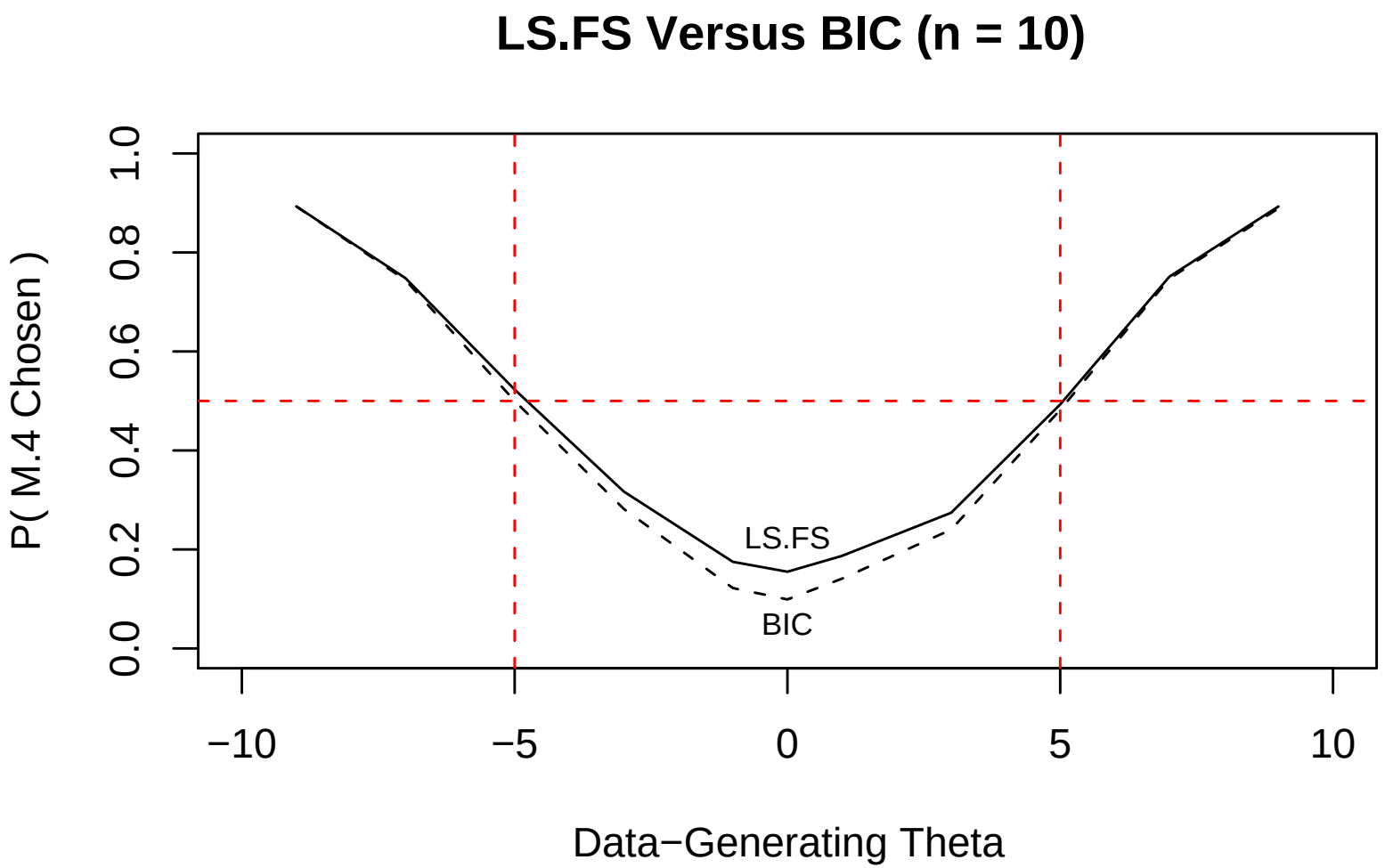
The **qualitative behavior** of the LS_{FS} and **posterior-probability methods** is **identical**, although there are some **numerical differences** (**highlighted** later).

BIC Results: Bio-Equivalence



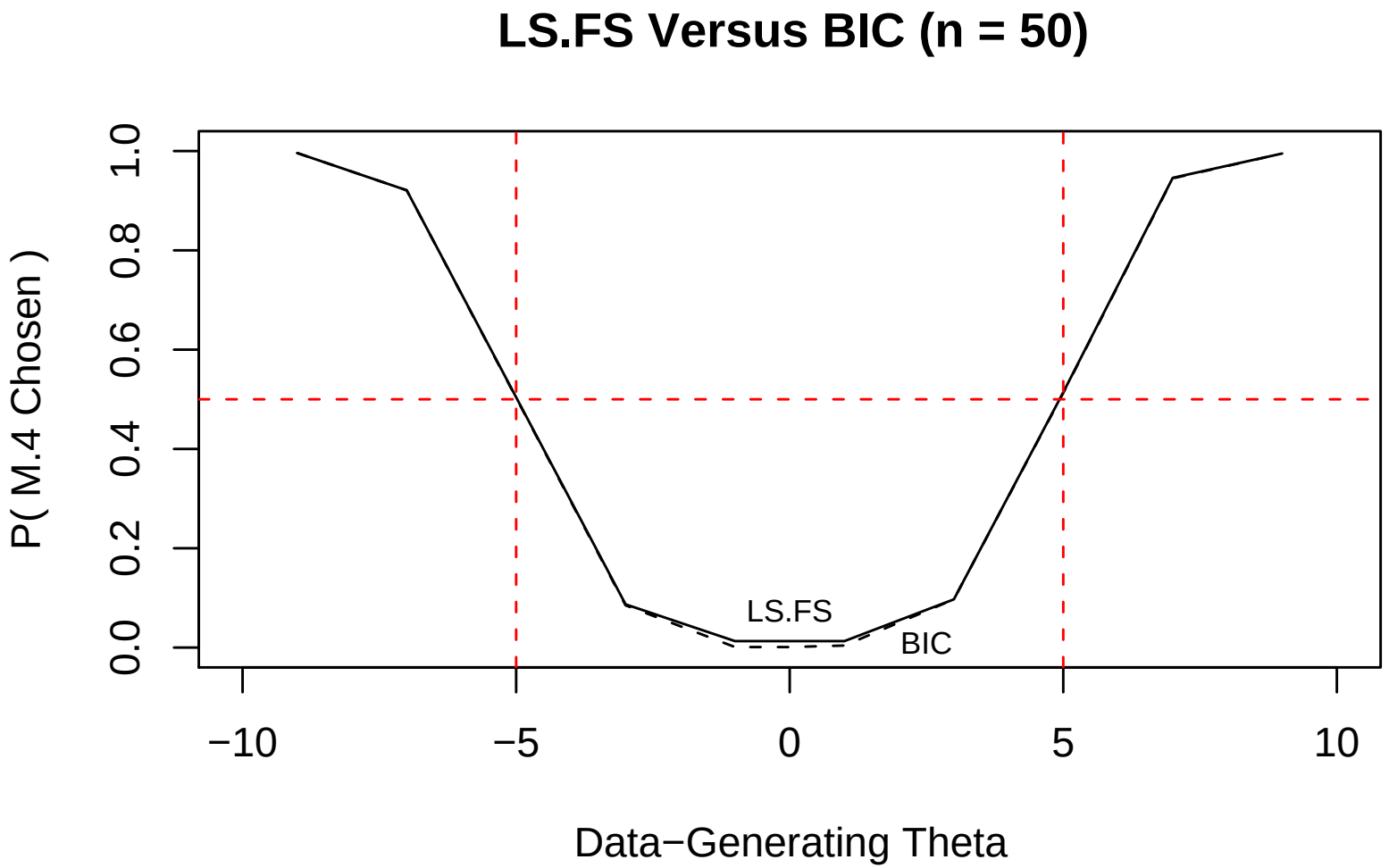
In the **quantifying-improvement** case, the **BIC** and **posterior-probability methods** were **algebraically identical**; here they **nearly coincide** (**differences** of $\pm$ **0.001** with **1,000 simulation repetitions**).

LS_{FS} Versus BIC Results: Bio-Equivalence



If You call **choosing** M_4: $|\theta| > \lambda$ when $|\theta_{DG}| \leq \lambda$ a **false-positive** error and **choosing** M_3: $|\theta| \leq \lambda$ when $|\theta_{DG}| > \lambda$ a **false-negative** mistake, with $n = 10$ there's a **trade-off**: LS_{FS} has more **false positives** and BIC has more **false negatives**.

LS_{FS} Versus BIC Results: Bio-Equivalence



By the time You **reach** $n = 50$ in **this problem**, LS_{FS} and BIC are **essentially equivalent**.

The Decision-Versus-Inference Principle, Revisited

In the **context** of the **quantifying-improvement example**, the **real-world purpose** of the **experiment** was to **decide whether or not** to **take** the drug **forward** to **phase III**.

Suppose that You **tried** to **solve** this **decision problem** with a **popular inferential tool: frequentist hypothesis-testing** of H_0: $\theta \leq \Delta$ versus H_A: $\theta > \Delta$ at **significance level** α.

Decision-theoretically this is **already wrong**; as **noted** back on **page 34**, the **utility function** should **actually** be **continuous** in θ rather than **artificially dichotomizing** Θ into $(-\infty, \Delta]$ and (Δ, ∞).

Even if You **temporarily** buy into this **incorrect dichotomization**, to **solve the problem properly** You'd have to **quantify the real-world consequences** of **each** of the **cells** in this **table specifying** $U(a, \theta)$ (here $u_{ij} \geq 0$):

	Truth	
Action	$\theta \leq \Delta$	$\theta > \Delta$
a_1 **(stop)**	u_{11}	$-u_{12}$
a_2 **(phase III)**	$-u_{21}$	u_{22}

Decision-Theory (Not Inference) For Decision Problems

Action	**Truth**	
	$\theta \leq \Delta$	$\theta > \Delta$
a_1 (**stop**)	u_{11}	$-u_{12}$
a_2 (**phase III**)	$-u_{21}$	u_{22}

- u_{11} is the **gain** from **correctly not taking the drug forward** to **phase III** (this is clearly **0**);
- u_{12} is the **loss** from **incorrectly failing to take the drug forward** to **phase III**;
- u_{21} is the **loss** from **incorrectly taking the drug forward** to **phase III**;
- u_{22} is the **gain** from **correctly taking the drug forward** to **phase III**.

The **optimal Bayesian decision** turns out to be: **choose** a_2 (go **forward to phase III**) iff

$$P(\theta > \Delta | y\, \mathcal{B}) \geq \frac{u_{21}}{u_{12} + u_{21} + u_{22}} = u^* \,. \tag{28}$$

The **frequentist (hypothesis-testing) inferential approach** is **equivalent** to this **only if**

Optimal Decision-Making in Phase-II Trials

$$\alpha = 1 - u^* = \frac{u_{12} + u_{22}}{u_{12} + u_{21} + u_{22}} \,. \tag{29}$$

The **implicit trade-off** between **false positives and false negatives** in BIC and LS_{FS} — and the **built-in trade-off** in **level–α hypothesis-testing** for any **given** α — may be **close to optimal** or **not**, according to the **real-world values** of $\{u_{12}, u_{21}, u_{22}\}$.

In **phase-II clinical trials** or **micro-array experiments**, when You're **screening many drugs** or **genes** for those that **may lead** to an **effective treatment** and — from the **drug company's point of view** — a **false-negative error** (of **failing to move forward** with a **drug** or **gene** that's actually **worth further investigation**) can be **much more costly** than a **false-positive mistake**, this **corresponds** to $u_{12} \gg u_{21}$ and **leads** in the **hypothesis-testing approach** in **phase-II trials** to a **willingness** to use **(much) larger** α **values** than the **conventional 0.01** or **0.05**, something that **good frequentist biostatisticians** have **long known intuitively**.

(In **work** I've done with a **Swiss pharmaceutical company**, this **approach** led to α **values** on the order of **0.45**, which is **close** to the **implicit trade-off** in **BIC** and LS_{FS}.)

For People Who Like to Test Sharp-Null Hypotheses

An **extreme example** of the **false-positive/false-negative differences** between LS_{FS} and **BIC** in **this setting** may be **obtained**, albeit **unwisely**, by **letting** $\lambda \downarrow 0$.

This is **unwise** here (and is **often unwise**) because it **amounts**, in **frequentist language**, to **testing** the **sharp-null hypothesis** H_0: $\theta = 0$ against the **alternative** H_A: $\theta \neq 0$.

It's **necessary** to **distinguish** between **problems** in which there **is or is not** a **structural singleton** in the **(continuous)** set Θ of **possible values** of θ: **settings** where it's **scientifically important** to **distinguish** between $\theta = \theta_0$ and $\theta \neq \theta_0$ — an **example** would be **discriminating** between {**these two genes** are on **different chromosomes** (the **strength** θ of their **genetic linkage** is $\theta_0 = 0$)} and {**these two genes** are on the **same chromosome** ($\theta > 0$)}.

Sharp-null testing without **structural singletons** is **always unwise** because

(a) **You already know** from **scientific context**, when the **outcome variable** is **continuous**, that H_0 is **false**, and **(relatedly)**

Testing Sharp-Null Hypotheses (continued)

(b) it's **silly** from a **measurement point of view**: with a **(conditionally) IID** $N(\theta, \sigma^2)$ **sample** of size n, your **measuring instrument** $\bar{y}$ is only **accurate** to **resolution** $\frac{\sigma}{\sqrt{n}} > 0$; **claiming** to be **able** to **discriminate** between $\theta = 0$ and $\theta \neq 0$ — with **realistic values** of n — is like **someone** with a **scale** that's **only accurate** to the **nearest ounce** telling You that Your **wedding ring** has **1 gram** (0.035 ounce) **less gold in it** than the **jeweler claims** it does.

Nevertheless, **for people who like to test sharp-null hypotheses**, here are some **results**: here I'm **comparing** the **models** ($i = 1, \ldots, n$)

$$M_5: \left\{ \begin{array}{ccc} (\sigma^2|\mathcal{B}) & \sim & \text{diffuse on } (0, \text{large}) \\ (y_i|\sigma^2\,\mathcal{B}) & \overset{\text{IID}}{\sim} & N(0, \sigma^2) \end{array} \right\} \quad \text{and} \qquad (30)$$

$$M_6: \left\{ \begin{array}{ccc} (\theta\,\sigma^2|\mathcal{B}) & \sim & \text{diffuse on } (-\text{large}, \text{large}) \times (0, \text{large}) \\ (y_i|\theta\,\sigma^2\,\mathcal{B}) & \overset{\text{IID}}{\sim} & N(\theta, \sigma^2) \end{array} \right\}, \qquad (31)$$

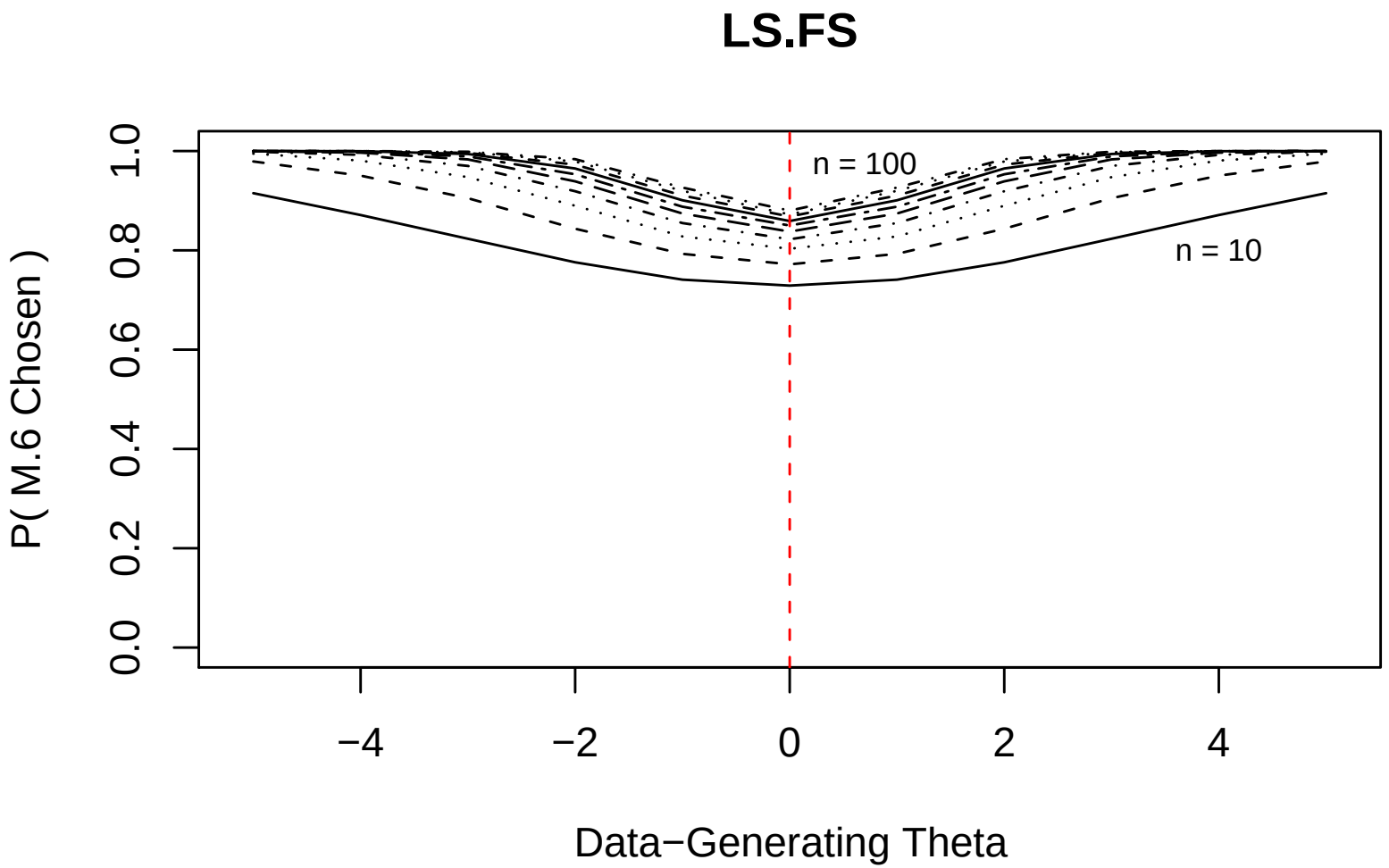
In **this case** a **natural Bayesian competitor** to **BIC** and LS_{FS} would be to **construct** the **central** $100(1-\alpha)\%$ **posterior interval** for θ under M_6 and **choose** M_6 if **this interval doesn't contain 0**.

Testing Sharp-Null Hypotheses (continued)

Simulation experiment details: **data-generating** $\sigma_{DG} = 10$; $n = 10, 20, \ldots, 100$; **data-generating** $\theta_{DG} = \{0, 1, \ldots, 5\}$; **1,000 simulation replications**, $M =$ **100,000 Monte-Carlo draws** for LS_{FS}; the **figures** below give **Monte-Carlo estimates** of the **probability that M_6 is chosen**.

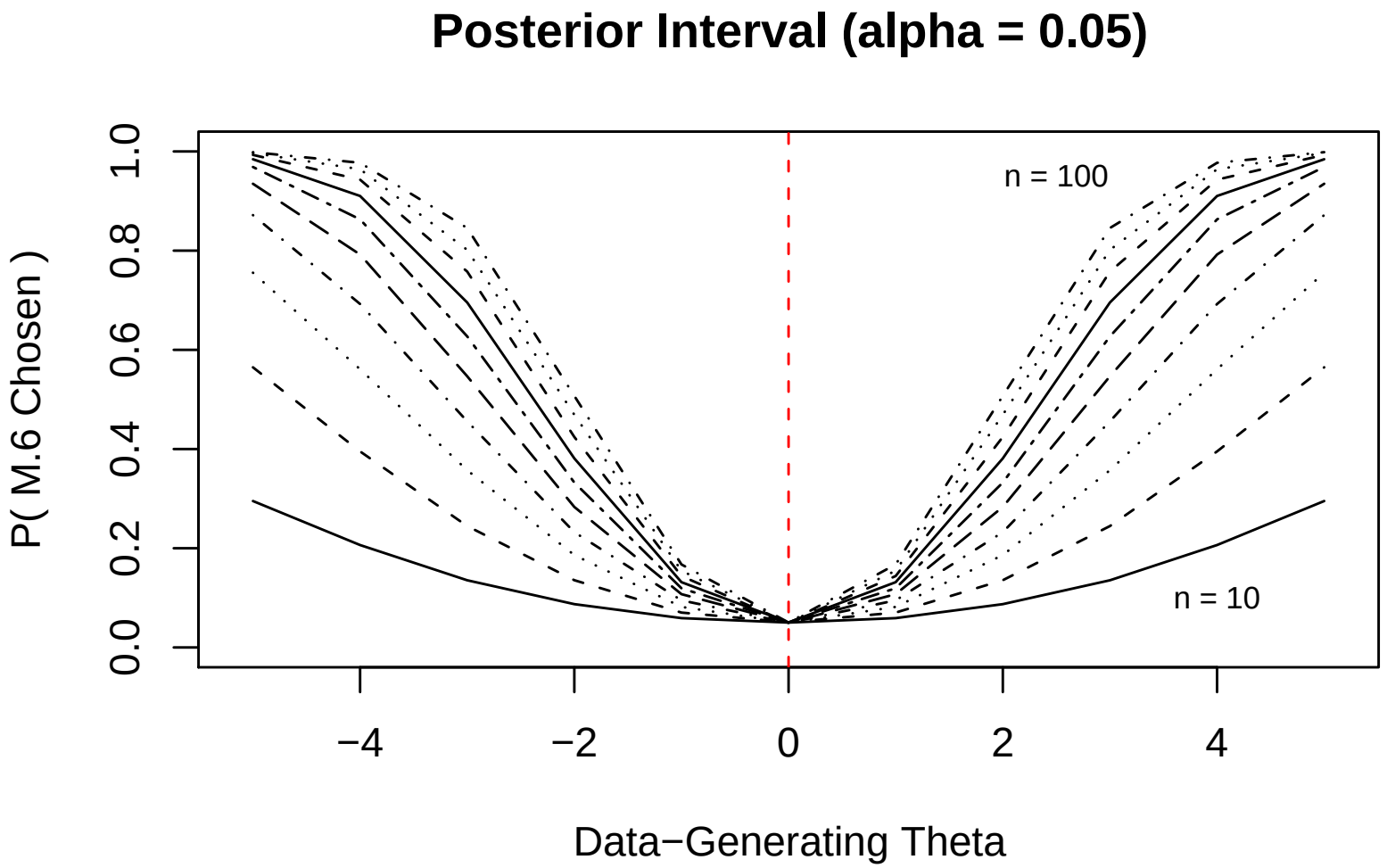
As before, let's call **choosing** M_6: $\theta \neq 0$ when $\theta_{DG} = 0$ a **false-positive** error and **choosing** M_5: $\theta = 0$ when $\theta_{DG} \neq 0$ a **false-negative** mistake.

LS_{FS} Results: Sharp-Null Testing



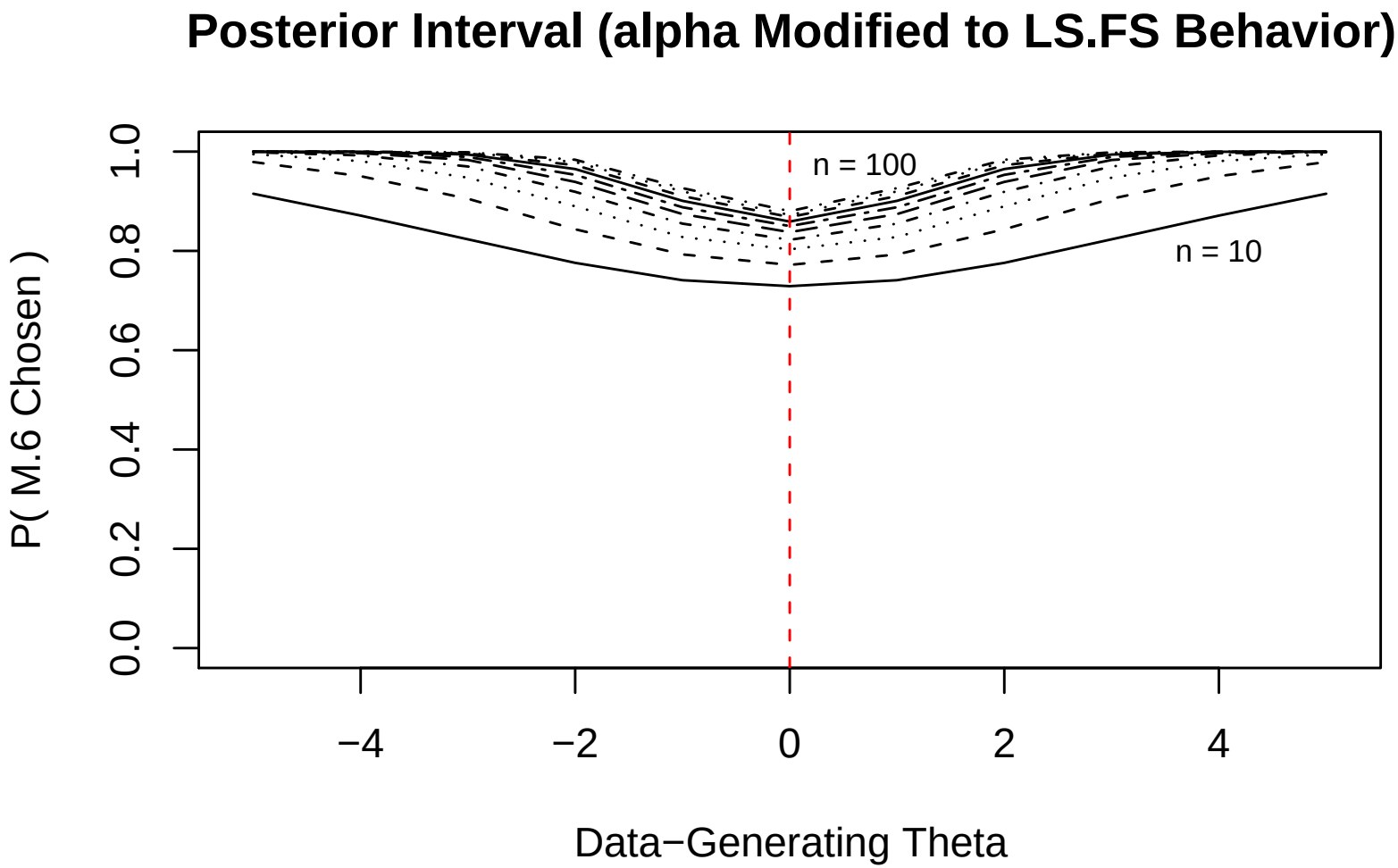
In the **limit** as $\lambda \downarrow 0$, the LS_{FS} **approach** makes **hardly any false-negative errors** but **quite a lot of false-positive mistakes**.

Interval ($\alpha = 0.05$) Results: Sharp-Null Testing



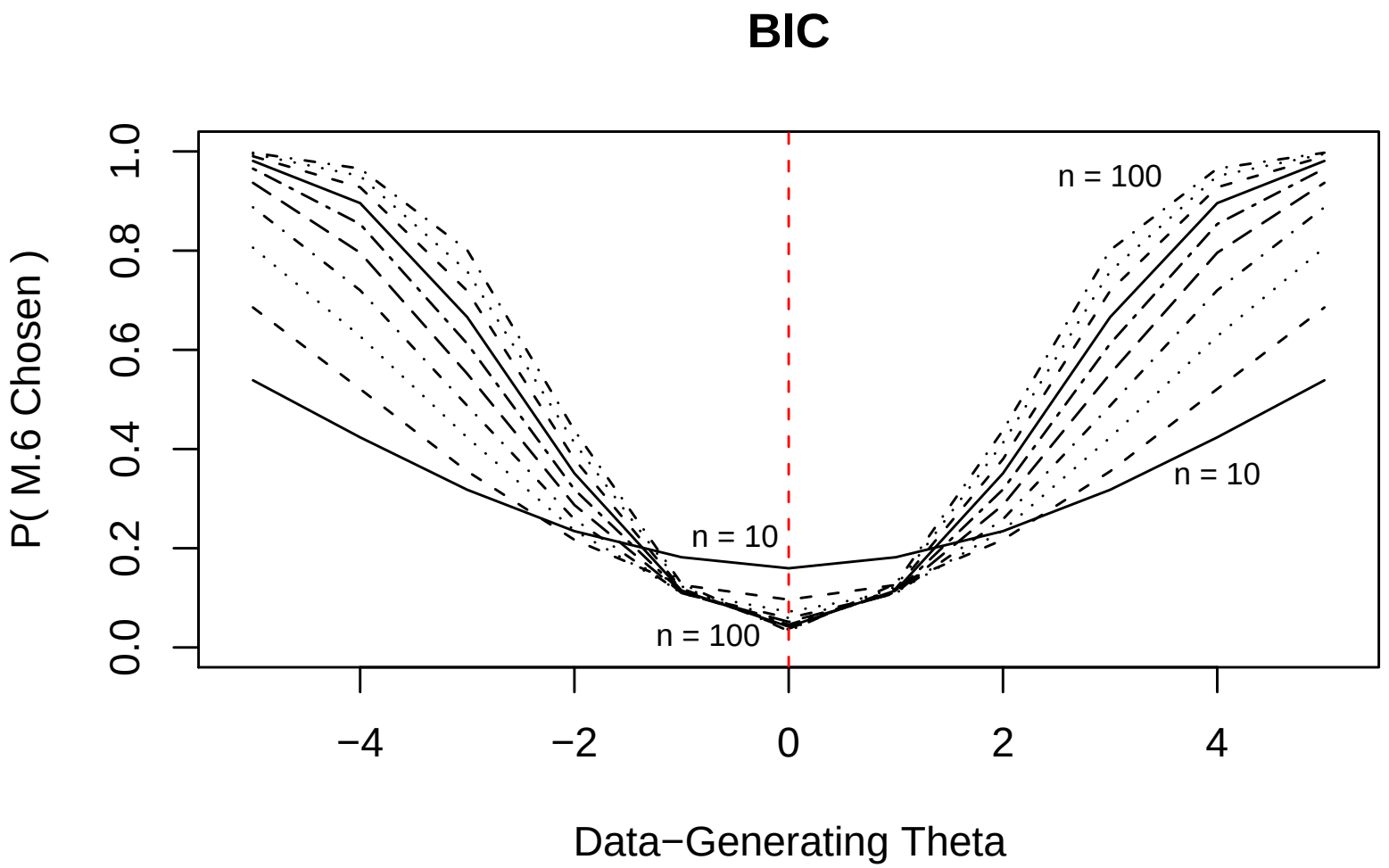
The **behavior** of the **posterior interval approach** is of course **quite different**: it makes **many false-negative errors** because its **rate of false-positive mistakes** is **fixed at 0.05**.

Interval (α Modified to LS_{FS} Behavior) Results



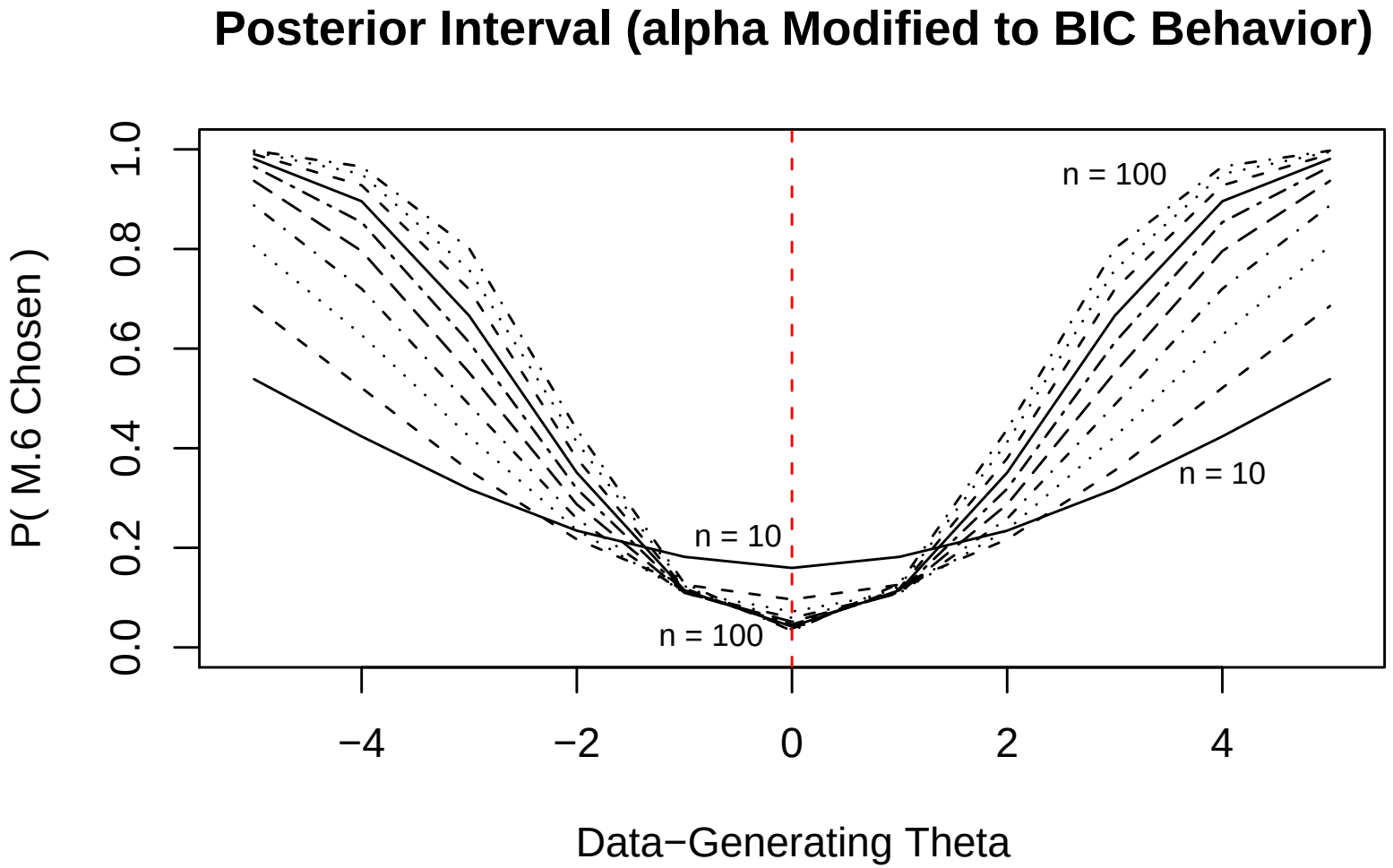
When the **interval method** is **modified** so that α **matches** the LS_{FS} **behavior** at $\theta_{DG} = 0$ (letting α **vary** with n), the **two approaches** have **identical model-discrimination ability**.

BIC Results: Sharp-Null Testing



BIC's behavior is **quite different** from that of LS_{FS} and **fixed-α posterior intervals**: its **false-positive rate decreases** as n grows, but it **suffers a high false-negative rate** to **achieve** this **goal**.

Interval (α Modified to BIC Behavior) Results



When the **interval method** is **modified** so that α **matches** the **BIC behavior** at $\theta_{DG} = 0$ (again letting α **vary** with n), the **two approaches** have **identical model-discrimination ability**.

LS_{FS} Versus BIC: Geometric Versus Poisson

As another **model-comparison example**, suppose You have an **integer-valued** data set $D = y = (y_1 \ldots y_n)$ and You wish to **compare**

$M_7 =$ **Geometric**(θ_1) **sampling distribution** with a **Beta**(α_1, β_1) **prior** on θ_1, and

$M_8 =$ **Poisson**(θ_2) **sampling distribution** with a **Gamma**(α_2, β_2) **prior** on θ_2.

LS_{FS} and **BIC** both have **closed-form expressions** in this **situation**: with $s = \sum_{i=1} y_i$ and $\hat{\theta}_1 = \frac{\alpha_1 + n}{\alpha_1 + \beta_1 + s + n}$,

$$\begin{aligned} LS_{FS}(M_7|y\,\mathcal{B}) \quad = \quad & \log\Gamma(\alpha_1 + n + \beta_1 + s) + \log\Gamma(\alpha_1 + n + 1) \\ & - \log\Gamma(\alpha_1 + n) - \log\Gamma(\beta_1 + s) \\ & + \frac{1}{n}\sum_{i=1}^{n}[\log\Gamma(\beta_1 + s + y_i) \\ & - \log\Gamma(\alpha_1 + n + \beta_1 + s + y_i + 1)]\,, \end{aligned} \tag{32}$$

$$BIC(M_7|y\,\mathcal{B}) = -2[n\log\hat{\theta}_1 + s\log(1 - \hat{\theta}_1)] + \log n\,, \tag{33}$$

Geometric Versus Poisson (continued)

$$
\begin{aligned}
LS_{FS}(M_8|y\,\mathcal{B}) \;=\; & (\alpha_2+s)\log(\beta_2+n) - \log\Gamma(\alpha_2+s) \\
& -(\alpha_2+s)\log(\beta_2+n+1) \qquad (34) \\
& +\frac{1}{n}\sum_{i=1}^{n}[\log\Gamma(\alpha_2+s+y_i) - y_i\log(\beta_2+n+1) \\
& -\log\Gamma(y_i+1)]\,, \text{ and}
\end{aligned}
$$

$$
BIC(M_8|y\,\mathcal{B}) = -2[s\log\hat{\theta}_2 - n\,\hat{\theta}_2 - \sum_{i=1}^{n}\log(y_i!)] + \log n\,, \qquad (35)
$$

$$
\text{where } \hat{\theta}_2 = \tfrac{\alpha_2+s}{\beta_2+n}.
$$

Simulation details: $n = \{10, 20, 40, 80\}$, $\alpha_1 = \beta_1 = \alpha_2 = \beta_2 = 0.01$, **1,000 simulation replications**; it **turns out** that with $(\theta_1)_{DG} = 0.5$ (Geometric) and $(\theta_2)_{DG} = 1.0$ (Poisson), **both data-generating distributions** are **monotonically decreasing** and **not easy to tell apart by eye**.

Let's call **choosing** M_8 (Poisson) when $M_{DG} =$ **Geometric** a **false-Poisson** error and **choosing** M_7 (Geometric) when $M_{DG} =$ **Poisson** a **false-Geometric** mistake.

Geometric Versus Poisson (continued)

The **table below** records the **Monte-Carlo probability** that the **Poisson model** was **chosen**.

M.DG = Poisson

n	LS.FS	BIC
10	0.8967	0.8661
20	0.9185	0.8906
40	0.9515	0.9363
80	0.9846	0.9813

M.DG = Geometric

n	LS.FS	BIC
10	0.4857	0.4341
20	0.3152	0.2671
40	0.1537	0.1314
80	0.0464	0.0407

Both methods make **more false-Poisson errors** than **false-Geometric mistakes**; the **results reveal once again** that **neither BIC nor** LS_{FS} **uniformly dominates** — each has a **different pattern** of **false-Poisson** and **false-Geometric** errors (LS_{FS} **correctly identifies** the **Poisson more often** than **BIC** does, but **as a result BIC gets** the **Geometric right more often** than LS_{FS}).

Properties of LS_{FS}

• **Log scores** are **entirely free** from the **diffuse-prior** problems **bedeviling Bayes factors:**

$$LS_{FS}(M_j|y\,\mathcal{B}) = \frac{1}{n}\sum_{i=1}^{n} \log p(y_i|y\,M_j\,\mathcal{B})\,,$$

in which

$$\begin{aligned} p(y_i|y\,M_j\,\mathcal{B}) &= \int p(y_i|\gamma_j\,M_j\,\mathcal{B})\,p(\gamma_j|y\,M_j\,\mathcal{B})\,d\gamma_j \qquad (36)\\ &= E_{(\gamma_j|y\,M_j\,\mathcal{B})}p(y_i|\gamma_j\,M_j\,\mathcal{B})\,; \end{aligned}$$

this **expectation** is over the **posterior (not the prior) distribution** for the **parameter vector** γ_j in **model** M_j, and is therefore **completely stable** with respect to **small variations** in how **prior diffuseness** (if **scientifically called for**) is **specified**, even with only **moderate** n.

• Following the **Modeling-As-Decision Principle**, the **decision-theoretic justification** for **Bayes factors** involves **not only the Bayes factors themselves** but also the **prior model probabilities**, which can be **hard to specify** in a **scientifically-meaningful way**: under the **Bayes-factor (possibly unrealistic) 0/1 utility structure**,

Properties of LS_{FS} (continued)

You're supposed to **choose the model** with the **highest posterior probability**, not the one with the **biggest Bayes factor**.

By contrast, **specification** of **prior model probabilities** doesn't arise with **log scores**, which have a **direct decision-theoretic justification** based on the **Prediction Principle**.

- It may **seem** that **log scores** have no **penalty** for **unnecessary model complexity**, but this is **not true**: for example, if **one of Your models** carries around a lot of **unnecessary parameters**, this will **needlessly inflate** its **predictive variances**, making the **heights** of its **predictive densities go down**, thereby **lowering its log score**.

- It may **also seem** that the **behavioral rule** based on **posterior Bayes factors** (Aitkin 1991) is the same as the **rule** based on LS_{FS}, which **favors model** M_j over $M_{j'}$ if

$$n\, LS_{FS}(M_j|y, \mathcal{B}) > n\, LS_{FS}(M_{j'}|y, \mathcal{B}). \tag{37}$$

But this is **not true either**: for example, in the **common situation** in which the **data set** D consists of **observations** y_i that are **conditionally IID** from $p(y_i|\eta_j, M_j, \mathcal{B})$ under M_j,

Summary

$$nLS_{FS}(M_j|y,\mathcal{B}) = \log \prod_{i=1}^{n} \left[\int p(y_i|\eta_j, M_j, \mathcal{B})\, p(\eta_j|y, M_j, \mathcal{B})\, d\eta_j \right], \quad (38)$$

and this is **not the same as**

$$\log \int \left[\prod_{i=1}^{n} p(y_i|\eta_j, M_j, \mathcal{B}) \right] p(\eta_j|y, M_j, \mathcal{B})\, d\eta_j = \bar{L}_j^{PBF} \quad (39)$$

because the **product** and **integral operators do not commute**.

- Some **take-away messages:**

— In the **bio-equivalence** example, even when You **(unwisely) let** $\lambda \downarrow 0$, thereby **testing a sharp-null hypothesis**, the **asymptotic behavior** of **log scores** is **irrelevant**; what **counts** is the **behavior** of **log scores** and **Bayes factors** with **Your sample size** and the **models being compared**, and **for any given** n it's **not possible to say** that the **false-positive/false-negative trade-off** built into **Bayes factors** is **universally better for all applied problems** than the **false-positive/false-negative trade-off** built into **log scores**,

Summary (continued)

or **vice versa** — You have to **think it through** in each problem.

For instance, the **tendency** of **log scores** to **choose the "bigger" model** in a **nested-model comparison** is **exactly the right qualitative behavior** in the following **two examples** (and **many more such examples exist**):

— **Variable selection** in **searching through many compounds or genes** to **find successful treatments**: here a **false-positive mistake** (taking an **ineffective compound or gene forward** to the **next level of investigation**) **costs** the **drug company** $\$C$, but a **false-negative error** (**failing to move forward** with a **successful treatment**, in a **highly-competitive market**) **costs** $\$k\,C$ with $k =$ **10–100**.

— In a **two-arm clinical-trial** setting, consider the **random-effects Poisson regression model**

$$\begin{aligned} (y_i|\lambda_i, \mathcal{B}) &\overset{\text{indep}}{\sim} \text{Poisson}(\lambda_i) \\ \log \lambda_i &= \beta_0 + \beta_1 x_i + e_i \\ (e_i|\sigma_e^2, \mathcal{B}) &\overset{\text{IID}}{\sim} N(0, \sigma_e^2)\,, \quad (\beta_0, \beta_1, \sigma_e^2) \sim \text{diffuse}\,, \end{aligned} \tag{40}$$

Summary (continued)

where the y_i are **counts** of a **relatively rare event** and x_i is **1** for the **treatment group** and **0** for **control**; You would consider **fitting this model** instead of its **fixed-effects counterpart**, obtained by **setting** $\sigma_e^2 = 0$, to **describe unexplainable heterogeneity (Poisson over-dispersion)**.

In this **setting, Bayes factors** will make the **mistake** of $\{$**telling You that** $\sigma_e^2 = 0$ **when it's not**$\}$ **more often** than **log scores**, and **log scores** will make the **error** of $\{$**telling You that** $\sigma_e^2 > 0$ **when it's actually 0**$\}$ **more often** than **Bayes factors**, but the **former mistake** is **much worse** than the **latter**, because You will **underpropagate uncertainty** about the **fixed effect** β_1, which is the **whole point of the investigation**.

- **All through this discussion** it's **vital** to **keep in mind** that

the **gold standard** for **false-positive/false-negative behavior** is provided **neither by Bayes factors nor by log scores** but instead by **Bayesian decision theory in Your problem**.

Summary (continued)

- **Asymptotic conclusions** are **often misleading**: while it's **true** that

Old Theorem: $P_{\theta_{DG}=0}(LS_{FS} \text{ chooses } \theta = 0) \to 0 \text{ as } n \to \infty,$

it's **also true** that

New Theorem (Draper, 2013): for any $\lambda > 0$,
$P_{|\theta_{DG}| \le \lambda}(LS_{FS} \text{ chooses } |\theta| \le \lambda) \to 1 \text{ as } n \to \infty,$

and the **second theorem** would seem to **call the relevance of the first theorem into question**.

- As a **profession**, we need to **strengthen** the progression

Principles → Axioms → Theorems

in **optimal model specification**; the **Calibration Principle,** the **Modeling-As-Decision Principle**, the **Prediction Principle** and the **Decision-Versus-Inference Principle** seem **helpful** in **moving toward this goal**.

Is M_1 Good Enough?

What about $\boxed{Q_2}$: **Is M_1 good enough**?

As **discussed previously**, by the **Modeling-As-Decision Principle** a **full judgment of adequacy** requires **real-world input** ("To what **purpose** will the model be put?"), so it's **not possible** to propose **generic methodology** to answer Q_2 (apart from **maximizing expected utility**, with a **utility function** that's **appropriately tailored** to the **problem at hand**), but the **somewhat related question**

$\boxed{Q_{2'}}$: **Could** the **data have arisen** from **model** M_j?

can be **answered in a general way** by **simulating** from M_j **many times**, developing a **distribution** of (e.g.) LS_{FS} values, and seeing how **unusual** the **actual data set's log score** is in **this distribution**.

This is **related** to the **posterior predictive model-checking** method of Gelman et al. (1996), which **produces** a P-value.

However, **this sort of thing** needs to be **done carefully** (Draper 1996), or the result will be **poor calibration**; indeed, Bayarri and Berger (2000) and Robins et al. (2000) have **demonstrated** that the

Is M_1 Good Enough? (continued)

Gelman et al. procedure may be **(sharply) conservative**: You may get $P = \mathbf{0.4}$ from Gelman et al. (indicating that **Your model is fine**) when a **well-calibrated** version of **their idea** would have $P = \mathbf{0.04}$ (indicating that it's **not fine**).

Using a **modification** of an **idea** suggested by Robins et al., Draper and Krnjajić (2010) have **developed** a **simulation-based method** for **accurately calibrating** the **log-score scale** (I'd be happy to **send You the paper**).

How should You **judge how unusual** the **actual data set's log score** is in **the simulation distribution**?

In all of **Bayesian inference**, **prediction** and **decision-making**, except for **calibration concerns**, there's **no need** for P-**values**, but — since this is a **calibrative question** — it's **no surprise** that **tail areas** (or **something else equally ad-hoc**, such as the **ratio** of the **attained height** to the **maximum height** of the **simulation distribution**) arise.

I don't see how to **avoid this ad-hockery** except by **directly answering** Q_2 **with decision theory** (instead of **answering** $Q_{2'}$ **with a tail area**).

Summary

• I've offered an **axiomatization** of **inferential, predictive** and **decision-theoretic statistics** based on **information, not belief**, and **RT Cox's** (1946) notion of **probability** as a measure of the **weight of evidence** in favor of the **truth** of a **true-false proposition** whose **truth status** is **uncertain** for You.

• **Cox's Theorem** lays out a **progression** from

Principles → **Axioms** → **Theorem**

to **prove** that **Bayesian reasoning** is **justified** under natural **logical consistency** assumptions; for me this **secures** the **foundations of applied probability**.

• But **Cox's Theorem does not go far enough** for **statistical work** in **science**, in **two ways** related to **model specification**:

— **Nothing** in its **consequences** requires You to
pay attention to how often You get the right answer,
which is a **basic scientific concern**, and

Summary (continued)

— it **doesn't offer any advice** on how to **specify the required ingredients**: with θ as the **unknown** of principal interest, $\mathcal{B}$ as Your **relevant background assumptions and judgments**, and an **information source (data set)** D relevant to **decreasing Your uncertainty** about θ, the ingredients are

$*$ $\{p(\theta|\mathcal{B}), p(D|\theta\,\mathcal{B})\}$ for **inference** and **prediction**, and

$*$ in addition $\{\mathcal{A}, U(a,\theta)\}$ for **decision**, where $\mathcal{A}$ is **Your set of available actions** and $U(a,\theta)$ is **Your utility function** (mapping from **actions** a and unknown θ to **real-valued consequences**).

• To **secure the foundations of statistics**, work is needed laying out the **logical progression**

Principles $\rightarrow$ **Axioms** $\rightarrow$ **Theorems**

for **model specification**; **progress** in this area is **part** of the **Theory of Applied Statistics**.

• A **Calibration Principle** helps address the **first** of the **two deficiencies** above:

Summary (continued)

Calibration Principle: In **model specification**, You should pay attention to **how often You get the right answer**, by creating situations in which **You know what the right answer is** and seeing **how often Your methods recover known truth**.

Interest in **calibration** can be seen to be **natural** in **Bayesian work** by thinking **decision-theoretically**, with a **utility function** that **rewards** both **quality of scientific conclusions** and **good calibration** of the **modeling process yielding** those **conclusions**.

• In problems of **realistic complexity** You'll generally notice that (a) You're **uncertain** about θ but (b) You're also **uncertain** about how to **quantify Your uncertainty about θ, i.e., You** have **model uncertainty**.

• This **acknowledgment** of Your **model uncertainty** implies a willingness by You to **consider two or more models** in an **ensemble** $\mathcal{M} = \{M_1, M_2, \dots\}$, which gives rise immediately to **two questions**:

Q_1: Is M_1 **better** than M_2? Q_2: Is M_1 **good enough**?

Summary (continued)

• These questions **sound fundamental** but **are not**: better **for what purpose**? Good enough **for what purpose**? To address the **second** of the **two deficiencies** above (**lack of guidance** from **Cox's Theorem** on **model specification**), this **implies** a

Modeling-As-Decision Principle: Making clear the **purpose to which the modeling will be put** transforms **model specification** into a **decision problem**, solvable by **maximizing expected utility** with a **utility function tailored** to the **specific problem** under study.

This **solves** the **model-specification problem** but is **hard work**; there's a **powerful desire** for **generic model-comparison methods** whose **utility structure** may provide a **decent approximation** to **problem-specific utility elicitation**.

Two such methods are **Bayes factors** (whose **utility justification** is **less than compelling**) and **log scores**, which are based on the

Prediction Principle: **Good models** make **good predictions**, and **bad models** make **bad predictions**; that's one **scientifically important** way You know a **model** is **good** or **bad**.

Summary (continued)

- I'm aware of **three approaches** to improved **assessment** and **propagation** of **model uncertainty**: **Bayesian model averaging** (BMA), **Bayesian nonparametric** (BNP) modeling, and **calibration (3-fold) cross-validation** (CCV).

- **CCV** provides a way to **pay** the **right price** for **hunting around in the data** for **good models**, motivating the following **modeling algorithm**:

(a) Start at a model M_0 (how choose?); set the current model $M_{\text{current}} \leftarrow M_0$ and the current model ensemble $\mathcal{M}_{\text{current}} \leftarrow \{M_0\}$.

(b) If M_{current} is good enough to stop (how decide?), return $\mathcal{M}_{\text{current}}$; else

(c) Generate a new candidate model M_{new} (how choose?) and set $\mathcal{M}_{\text{current}} \leftarrow \mathcal{M}_{\text{current}} \cup M_{\text{new}}$.

(d) If M_{new} is better than M_{current} (how decide?), set $M_{\text{current}} \leftarrow M_{\text{new}}$.

(e) Go to (b).

- For the **choice** in **(a)**, there's usually a **default off-the-shelf initial model** based on the **structure** of the **data set** D and the **scientific context**.

Summary (continued)

• In **manual model search** the **choice** in **(c)** is typically based on the **results** of a variety of **diagnostics**, with the **new model** suggested by **deficiencies** revealed in this way; at present, we have **no better way** to **automate this choice** in many cases than **choosing** M_{new} **at random** (I offer **no new ideas** on this topic **today**).

• In **comparing** M_1 with M_2 (the **choice** in (d)), consider a **calibrative scenario** in which the the **data-generating model** M_{DG} is **one** or the **other** of $\mathcal{M} = \{M_1, M_2\}$ (apart from **parameter estimation**), and call $\{$choosing M_2 when $M_{DG} = M_1\}$ a **false positive** and $\{$choosing M_1 when $M_{DG} = M_2\}$ a **false negative**; then

— The **right way** to do this, following the **Modeling-As-Decision Principle**, is to build a **utility function** by **quantifying** the **real-world consequences** of

$\{$choosing M_1 when $M_{DG} = M_1$, choosing M_1 when $M_{DG} = M_2$, choosing M_2 when $M_{DG} = M_1$, choosing M_2 when $M_{DG} = M_2\}$

and **maximize expected utility**.

Summary (continued)

— If instead You **contemplate** using **Bayes factors/BIC** or **log scores**, it is **not the case** that **one** of these two methods **uniformly dominates the other** in **calibrative performance**; in **some settings** they behave the **same**, in others **(for Your sample size)** they will have a **different balance of false positives and false negatives**; it's a good idea to **investigate this** before **settling on one method or the other**.

• See Draper and Krnjajić (2013) for a **method** for **answering the question** $Q_{2'}$**: Could the data have arisen from model** M_j**?** in a **well-calibrated way**.

• **CCV** provides an **approach** to finding a **good ensemble** $\mathcal{M}$ **of models**, and gives You a **decent opportunity** both to **arrive at good answers** to **Your main scientific questions** and to **evaluate the calibration** of the **iterative modeling process** that **led You to Your answers**.

• **Decision-Versus-Inference Principle:** We should all **get out of the habit** of **using inferential methods** to **make decisions**: their **implicit utility structure** is often **far from optimal**.

Another Unsolved Foundational Problem

• One more **unsolved foundational problem**: how can **good decisions** be arrived at when **"You"** is a **collective of individuals**, all with **their own utility functions** that imply **partial cooperation** and **partial competition**?

Example: **Allocation** of **finite resources** by **two or more people** who have **agreed to band together** in some sense (i.e., **politics**, at the level of **family** or **nation** or ...).

An instance of this: **Defining** and **funding good quality of health care** — the **actors** in the drama include

{**patient**, **doctor**, **hospital**, **state** and **local regulatory bodies**, **federal regulatory system**};

all are in **partial agreement** and **partial disagreement** on how (and how many) **resources** should be **allocated** to the **problem** of addressing **this patient's immediate health needs**.

(But that's for **another day**, as is the topic of **Bayesian computing** with **large data sets**.)

Cromwell's Rule, Part 1: Inference and Prediction

The **following two facts** are **easy consequences** of the **definition** of **conditional probability**: for **any two propositions** A and B and **any background information** $\mathcal{B}$:

- **Cromwell's Rule, Part 1(a)** **If** $P(A|\mathcal{B}) = 0$ **then** $P(A|B\,\mathcal{B}) = 0$ **for all** B for which $P(A|B\,\mathcal{B})$ is **defined** (i.e., for **which** $P(B|\mathcal{B}) > 0$).

- **Cromwell's Rule, Part 1(b)** **If** $P(A|\mathcal{B}) = 1$ **then** $P(A|B\,\mathcal{B}) = 1$ **for all** B for which $P(A|B\,\mathcal{B})$ is **defined** (i.e., for **which** $P(B|\mathcal{B}) > 0$).

To see the **implications** of **these facts**, let A be a **proposition** about **something unknown** to **You**, such as $(\theta < 0)$, and **let** B be a **proposition** about **Your data set** D, such as $(y_1 = 3, y_2 = -0.4, \ldots, y_n = 6.9)$.

Then Part 1(a) of **Cromwell's Rule says** that **any proposition about** the **unknown** θ to which **You give prior probability 0** **must** **have posterior probability 0, no matter how the data set** D **comes out**, and **Part 1(b)** of **Cromwell's Rule says** the **same thing with 0 replaced by 1**.

Cromwell's Rule Part 1 (continued)

Bayes's Theorem is **supposed to be** a **piece of machinery** that **permits You** to **learn, about unknowns from new data**, in an **optimal way**; **Cromwell's Rule Part 1 says** that **if You dogmatically place prior probability 0** or **1 on something, no learning is possible** when **new data** values arrive.

This is **obviously a way** to **break the Bayes's Theorem learning machine**, so the **practical consequence** of **Cromwell's Rule Part 1** is **captured** in the **following piece of advice**:

You should try hard never to put prior probability 0 or 1 on anything that might later have posterior probability between 0 and 1, depending on how new information comes out.

This has **direct consequences** for **Bayesian model specification: for example, consider** the **NB10 data set** from **Day 1, for which (by exchangeability) Your basic sampling model** for the **data values** $y = (y_1, \ldots, y_n)$ **before You see the data** is $(y_i | F\, \mathcal{B}) \overset{\text{IID}}{\sim} F$ for **some (unknown) CDF** F.

Cromwell's Rule Part 1 (continued)

If, before You see the data, You put all Your modeling eggs in the **Gaussian basket**, so that **You replace** $(y_i|F\,\mathcal{B}) \overset{\text{IID}}{\sim} F$ **with** $(y_i|\mu\,\sigma\,\mathcal{B}) \overset{\text{IID}}{\sim} N(\mu, \sigma^2)$, **this means that You've placed all of your prior probability on the Gaussian family**, thereby **implicitly giving prior probability 0 to all non-Gaussian behavior** (such as **multimodality, skewness** and/or **heavy tails**).

Now what do You do when **the data set arrives** and — as in the **case** of the **NB10 data — demonstrates much heavier tails** than the **Gaussian family** can **accommodate**?

Strictly speaking, by **Cromwell's Rule Part 1(a), all such non-Gaussian behavior must have posterior probability 0**, and **yet** the **data set clearly makes You wish** that **You hadn't been so dogmatic** in **Your "prior on model space."**

Going back and **changing Your prior on model space based on how the data set came out** is a **clear violation** of the **dichotomization** {**information internal to** D**, information external to** D}, which was **part** of the **axiomatization** in the **Day 3 (Part 1) Lecture Notes**:

Cromwell's Rule, Part 2: Decision-Making

in effect, **when You do this You're using the data twice — once** in **specifying** the **prior** on **model space**, and **again** in **updating that prior** with the **data set** D — and the **typical consequence** will be **understatement** of **Your actual uncertainty**.

I see only two ways out of **this dilemma**:

- **Bayesian nonparametric methods**, which — when **used properly** — give **positive prior probability to all possible CDFs** F), and

- **Calibration cross-validation**, which (1) **allows You to "cheat"** by **looking at the data** and **changing Your prior on model space** but (2) **forces You** to **pay** an **appropriate price for having done so**.

Cromwell's Rule, Part 2: **Part 1** of **Cromwell's Rule** is about **inference** and **prediction**; **Part 2 concerns decision-making**, and it **also** has a **part (a)** and a **part b)**, which **give advice** on **how to specify Your action space** $\mathcal{A}$ and **Your utility function** $U(a, \theta)$ **(respectively)**.

Cromwell's Rule, Part 2 (continued)

- **Cromwell's Rule, Part 2(a):** In **enumerating** the **possible actions** $\{a_1, a_2, \dots\}$ while **specifying** Your **action space** $\mathcal{A}$ in the **problem** $\mathbb{P}$ on which **You're working, You should try hard not to omit any action a_i that might turn out to be optimal if it's included in $\mathcal{A}$.**

The **point** is that **Bayesian decision theory only optimizes over the possible actions You remember to put in $\mathcal{A}$: if You forget a feasible action a_i that (unknown to You) is better than all of the actions in Your current $\mathcal{A}$, maximization of expected utility cannot protect You from this omission.**

Example: **HIV screening** with ***ELISA*** and **Western Blot (Day 1, Lecture Notes Part 1)**. In that **case study** it was **tempting** to **think** that the **only two possible actions** were $a_1 = \{$**test the blood sample with ELISA**$\}$ and $a_2 = \{$**test the blood sample with Western Blot**$\}$, but a **third action** — $a_3 = \{$**test half of the blood sample with ELISA; if negative, declare HIV negative; if positive, test the other half of the blood sample with Western Blot**$\}$ — **turned out** to **dominate** the **others**.

Cromwell's Rule, Part 2 (continued)

Example: **People** at **eBay** are **constantly running randomized controlled trials** on the **eBay web experience, looking** for **variations** on **things** like **(i) search algorithms** and **(ii)** {**presentation of items for sale to the users**} that **may create** a **better marketplace**.

Having run an **experiment** in which the **control group gets** the **current best eBay website** and the **treatment group gets** {**the current best eBay website plus a particular intervention** I}, thereby **obtaining** a **data set** D, the **unknown** θ is {**what the future would be like, as far as important outcome variables (such as user satisfaction) are concerned, if intervention** I **is or is not implemented**}, and it **appears** that **there are only two possible actions**: $a_1 =$ {**implement** I} and $a_2 =$ {**don't implement** I}.

However, as with the **HIV case study**, there's a **third possible action** that **has** an **adaptive flavor**: **perhaps there's still too much uncertainty**, on the **basis** of D, to **make** a **good choice between** a_1 and a_2, so **(if You're not** in a **tremendous hurry** to **choose**) **why not include** $a_3 =$ {**get more data before deciding**} in Your $\mathcal{A}$?

Cromwell's Rule, Part 2 (continued)

Bayesian sequential experimental design and **analysis** has this **adaptive character** — **get some data, see if the optimal choice is clearcut yet, if so make it, if not get more data** — and **have been shown** to **yield results** with **good false-positive** and **false-negative rates** that **involve collecting (far) less data** than **approaches** with **sample sizes** that are **fixed** at the **design stage**.

- **Cromwell's Rule, Part 2(a):** In **specifying Your utility function** for the **problem** $\mathbb{P}$ on which **You're working, You should try hard** to **ensure** that

(1) **Your vector** of **unknowns** θ **contains all relevant unknowns**, and

(2) **Your utility function** $U(a, \theta)$ **captures all relevant costs** and **benefits** to be **balanced against each other**.

The **point** is that

- **any relevant unknown** that **You mistakenly omit** from θ has **no opportunity** to **influence Your decision**; the **result** will often be **decisions** that **don't hedge sufficiently against uncertainty**,

Cromwell's Rule, Part 2 (continued)

because **omitting** a **relevant unknown** is **tantamount** to **pretending that it's known**; and

• **any relevant cost** or **benefit** that **You mistakenly omit** from $U(a, \theta)$ **has no opportunity** to **influence** the **optimal trade-off between costs** and **benefits**, and **(dramatically) sub-optimal decisions can result when this happens**.

In **enumerating** the **relevant costs** and **benefits, You'll have to fight against** the following **three basic human tendencies**:

(1) **Things** that are **easy** to **measure tend to get measured; things** that are **hard** to **measure tend to get ignored**.

With respect to a **particular cost** or **benefit**, the **classifications** $C_1 =$ {**important, not important**} and $C_2 =$ {**hard to quantify, easy to quantify**} **have nothing to do with each other; including** or **omitting costs** and **benefits solely** on the **basis** of C_2 **provides no assurance** that the **included costs** and **benefits** are **correct** with **respect** to C_1.

Cromwell's Rule, Part 2 (continued)

(2) **People** with **optimistic world views tend** to **exaggerate benefits** and **downplay costs**; **pessimists tend** to **make** the **opposite mistakes; not many people get this right unless they're on the lookout for it**.

(3) If **costs** and **benefits** are **balanced against each other additively** in **Your utility function**, You'll **typically find it relatively easy** to **choose** the **scale on which** to **quantify** the **costs** (e.g., in **monetary terms**), but **it may then be quite difficult** to **quantify** the **benefits** on the **same scale**.

Example: The **new drug *Olysio*** (***simeprevir*, approved for use** in the **U.S.** in **Nov 2013**) has been **shown** to be **quite effective** at **reducing** the **viral load** of **Hepatitis C patients, permitting their livers** to **begin** to **heal, as long** as the **drug** is **taken** for **at least three months**.

The **drug company** that **markets *Olysio*, Janssen**, has **set** the **wholesale price** of a **12-week supply** of **this drug** at **$66,360** (about **£41,000**).

Cromwell's Rule, Part 2 (continued)

Q: **Should** the **NHS decide** to **approve** ***Olysio*** for **routine treatment** of **Hepatitis C** in the **UK**?

The **cost term** in the **NHS's utility function clearly comes out** in £; to **trade this off against** the **health benefits** (e.g., **lengthened life span, better quality of life**), the **NHS** has to be **prepared** to **measure those benefits** in **monetary terms, leading** to **unpleasant questions** such as **"What's the monetary value of human life?"**

Example: **Draper (1995) examines** an **attempt by economists** in **1980** to **predict future oil prices** over the **horizon 1981–2020; many companies** and **governments routinely make investment decisions** based on **such predictions**.

The **OPEC oil embargo** of **1973–74 created** a **large spike in oil prices, because demand stayed constant** and **supply dramatically dropped; this was** the **first time anything like that had ever occurred**.

Cromwell's Rule, Part 2 (continued)

If You had undertaken the **1980 predictive exercise mentioned above prior to 1973, You** would have had no **straightforward way** to **include** {**Will another OPEC oil embargo occur, and if so when?**} as **part** of the **unknowns** in **Your** θ **vector**, but **You would have no excuse** for **omitting this unknown after 1973–74**, and **indeed this omission could lead** to a **dramatic understatement** of **Your future uncertainty** about the **price of oil, causing You** to **make decisions that fail** to **hedge sufficiently against** the **totality of Your uncertainty**.

Example: **You're about** to **make** a **long drive by car**, and **You're wondering about** the **optimal driving speed**: the **faster You drive** the **quicker You get** to **Your destination (good)**, but **undesirable outomes increase in probability as You speed up (bad)**.

The **action space clearly consists** of **possible speeds** (that was **easy**), but **what about** θ and $U(a, \theta)$?

As a **first pass, You might include** in θ **only** the **unknown** {**will You get a speeding ticket?**}, in which case **Your utility function** would have **only two terms**, which could be **combined additively**:

Cromwell's Rule, Part 2 (continued)

a **benefit (quantified** in **monetary terms)** based on **how short the journey is**, and a **cost (also expressed** in **money)** based on **what happens** if **You get a ticket (You have to pay** a **fine**, and **Your insurance costs may rise**).

I've found that **this formulation typically leads** to a **recommendation** to **drive quite rapidly**.

However, a **number** of **additional relevant unknowns** have been **omitted** from this **first-pass specification** of $\mathcal{A}$ and $U(a, \theta)$:

• {**Will You get into an accident?**} If so, {**How serious is the accident?**} {**How badly is Your car damaged?**} {**Does the accident injure or kill You?**} If **other people** are **involved** in the **accident,** {**How badly is their vehicle damaged?**} {**Does the accident injure or kill any of them?**}

Increasingly unfavorable answers to **all of these questions will all result in additional cost terms** in **Your utility function**, with the **result** that **Your optimal driving speed** will **monotonically decrease as You increase** the **realism** of **Your utility specification**.