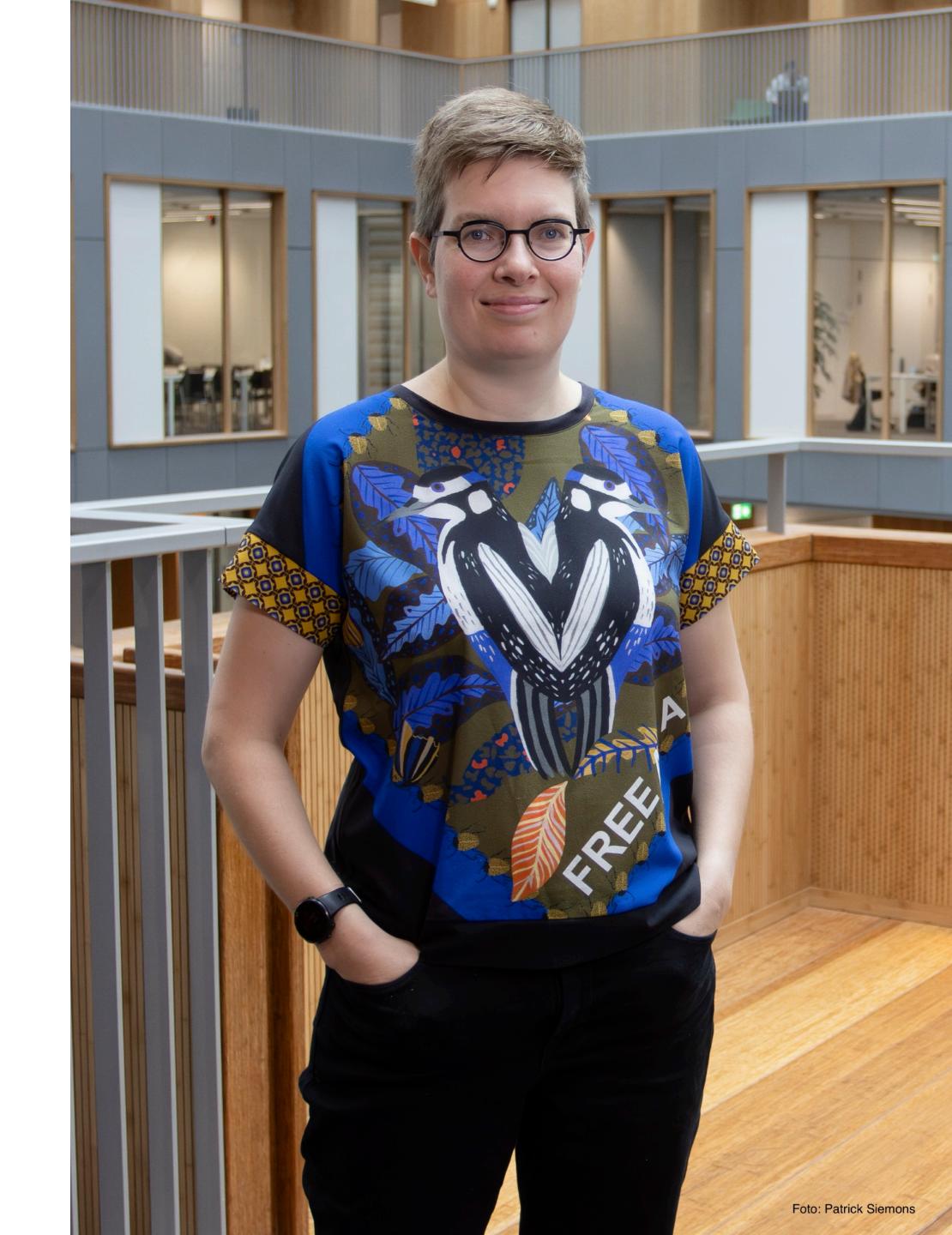
E-values

OBayes 2025 Tutorial

Dr. Rianne de Heide

Introduction

- @ University of Twente The Netherlands
- Mathematical Statistics, Machine Learning Theory
- Co-developed new theory of hypothesis testing with e-values
- Recognition: PhD thesis prize, Cor Baayen Early Career Researcher Award, NWO VENI & M2 grants, Bernoulli Society New Researcher Award 2025



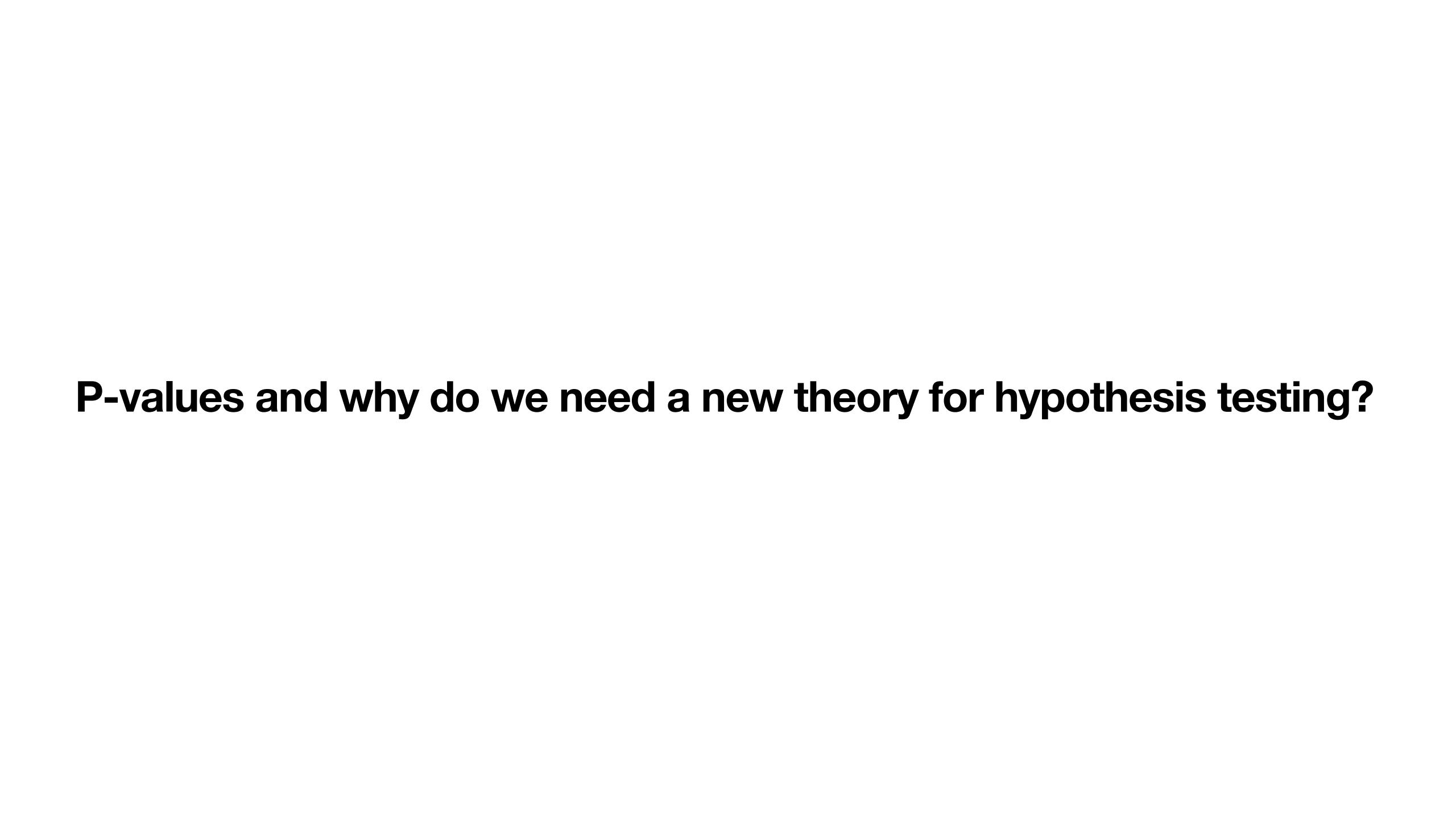
Menu

p-values and why do we need a new theory for hypothesis testing?

e-values

A trial

Another e-value highlight: multiple testing



P-values

• History: Karl Pearson (1900) and Ronald Fisher (1925)





Why do we need a new theory for hypothesis testing?

• 100 years later: replicability crisis in social and medical science

- Medicine: J. Ioannidis, Why most published research findings are false, PLoS Medicine 2(8) (2005).
- Social Science: 270 authors, Estimating the reproducibility of psychological science, Science 349 (6251), 2015.

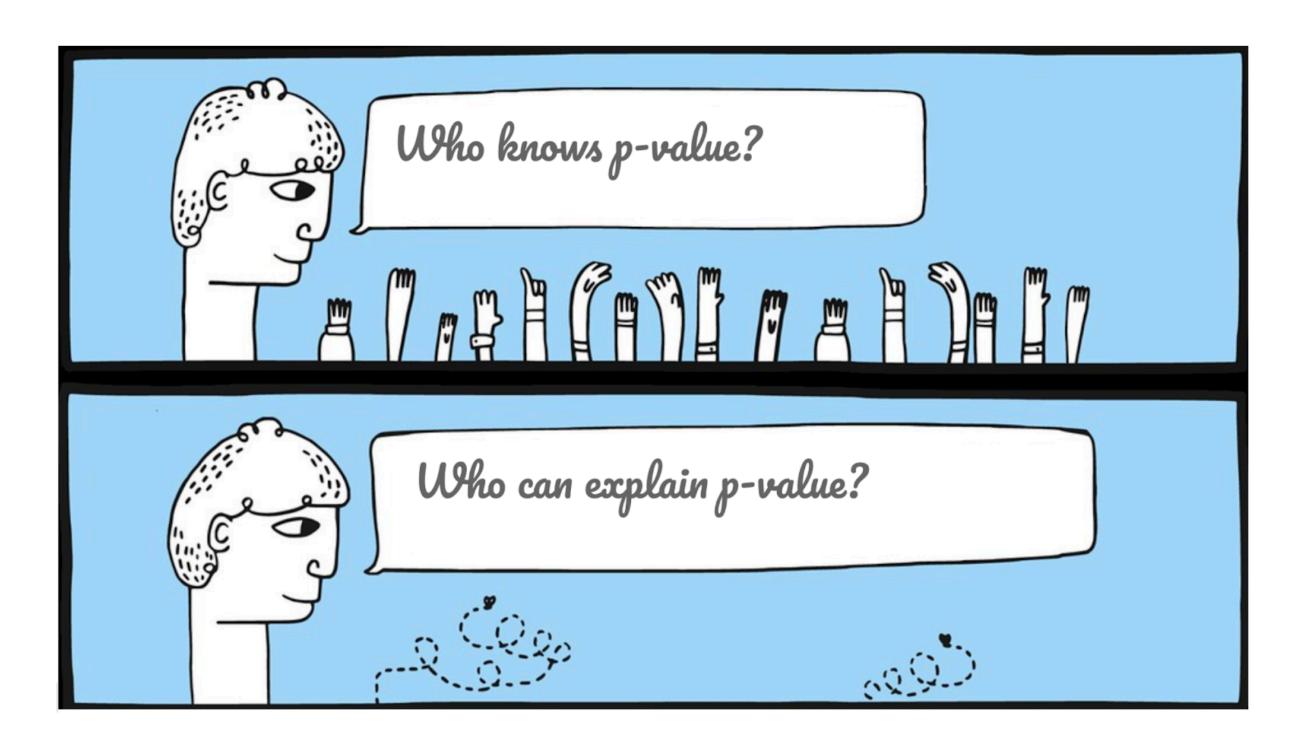
Why do we need a new theory for hypothesis testing?

Reproducibility crisis in social and medical science

Causes:

- publication bias
- fraud
- lab environment vs. natural environment
- use of p-values

We wish to test a null hypothesis \mathcal{H}_0 , often in contrast with an alternative hypothesis \mathcal{H}_1 .



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P-value:

- "Probability under the null hypothesis of obtaining a real-valued test statistic at least as extreme as the one obtained"
- "The P-value is the smallest level of significance that would lead to rejection of the null hypothesis H0 with the given data."
- "P-value is the level of marginal significance within a statistical hypothesis test, representing the probability of the occurrence of a given event."
- "A p-value, or probability value, is a number describing how likely it is that your data would have occurred by random chance."

What do doctors know about statistics?

A controlled trial of a new treatment led to the conclusion that it is significantly better than placebo: p < 0.05. Which of the following statements do you prefer? menti.com 3125 6009

- A. It has been proved that the treatment is better than placebo.
- B. If the treatment is not effective, there is less than 5 percent chance of obtaining such results.
- C. The observed effect of the treatment is so large that there is less than 5 percent chance that the treatment is no better than placebo.
- D. I do not really know what a p-value is and do not want to guess.

What do doctors know about statistics?

A controlled trial of a new treatment led to the conclusion that it is significantly better than placebo: p < 0.05. Which of the following statements do you prefer?

- A. It has been proved that the treatment is better than placebo. 20%
- B. If the treatment is not effective, there is less than 5 percent chance of obtaining such results. 13%
- C. The observed effect of the treatment is so large that there is less than 5 percent chance that the treatment is no better than placebo. 51%
- D. I do not really know what a p-value is and do not want to guess. 16%

Definition of the p-value

A p-value p is a random variable (i.e. a function) such that for every $P \in \mathcal{H}_0$, for $\alpha \in [0,1]$,

$$P(p \le \alpha) \le \alpha$$
.

• The p-value gives the probability of observing this data, or more extreme data, given that the null hypothesis is true. Notation: $P(X^n | \mathcal{H}_0)$.

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• But that is the quantity we are interested in, right?

• Suppose you are doing a trial on 70 subjects. The p-value is promising but just not significant (p = 0.06). Your boss says there is some more money for adding 10 more subjects to the trial. What do you do?

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- A) You add 10 subjects to the study, and you calculate a new p-value based on the total data, i.e. 80 subjects.
- B) You calculate a new p-value for the 10 new subjects, and you multiply that p-value by 0.06, the p-value from the first 70 subjects.
- C) You say to your boss: sorry, this is not possible. You are left with your p-value of 0.06, and you cannot conclude any significant result from your research.
- D) You calculate a new p-value for the new 10 subjects, and you use a method they also use in meta-analyses to combine the p-values.

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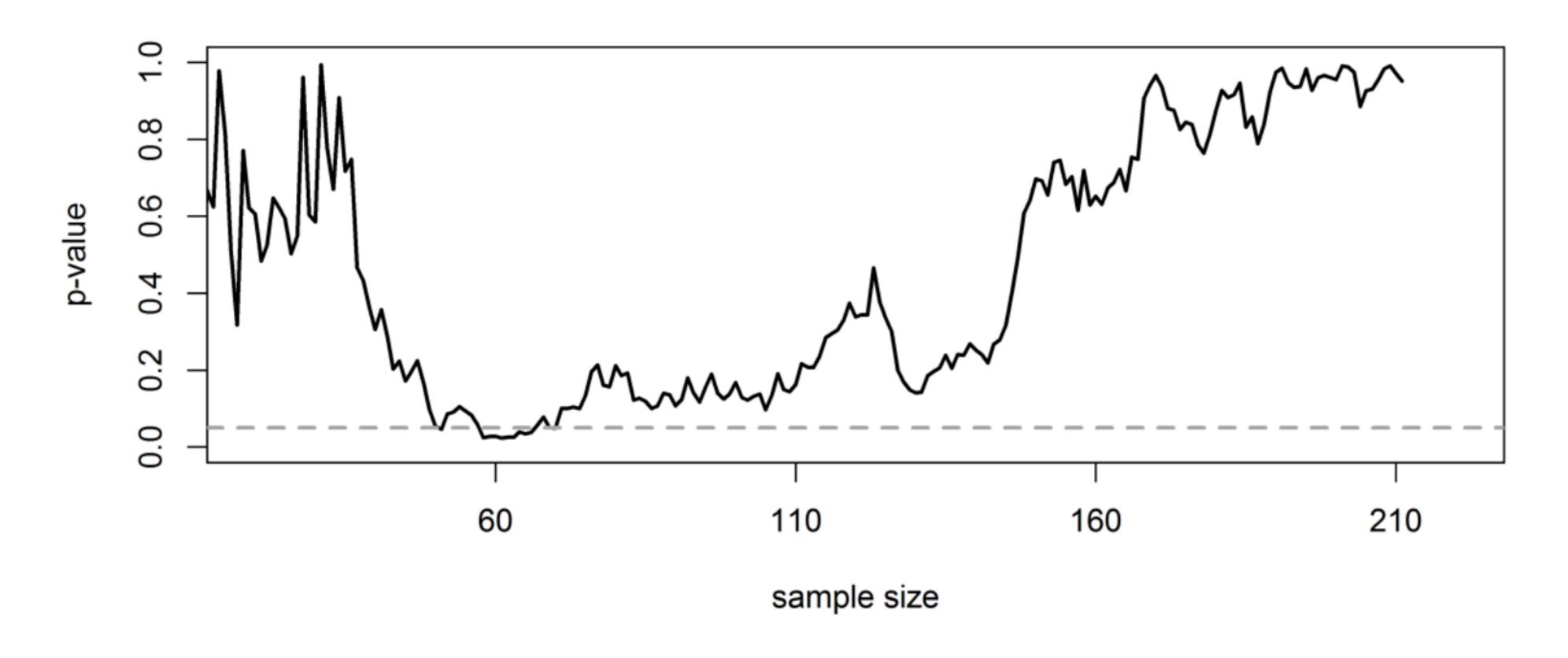
• John et al (2012): 55% of psychologists admits to "Deciding whether to collect more data after looking to see whether the results were significant".

 This is called optional stopping, and invalidates p-values and their error guarantees

Type I error guarantee

Fix $\alpha \in (0,1)$, then

 $\mathbb{P}(\text{reject }\mathcal{H}_0) \leq \alpha$



$$\mathbb{P}(\exists t \in \mathbb{N} : p_t < \alpha) = 1$$

Other disadvantages with p-values

Combining evidence from different (possibly dependent) studies

Hospitals A and B perform similar trials, and they report p-values p_A and p_B . How to combine the evidence?

A meta-analysis is done. However, the subsequent studies were only done because the previous studies were promising, so there is a complicated (and unknown) dependency. How to combine the evidence?

Other disadvantages with p-values

 Combining evidence from different (possibly dependent) studies (e.g. two different populations; meta-analysis)

• Limited applicability: unknown probabilities (counterfactuals)

Consider two weather forecasters A and B. On sunny days, $P_A(\text{RAIN}) \geq P_B(\text{RAIN})$, and on rainy days their accuracy is approximately the same. Is B better than A? We can't do this with p-values.

Other disadvantages with p-values

 Combining evidence from different (possibly dependent) studies (e.g. two different populations; meta-analysis)

• Limited applicability: unknown probabilities (counterfactuals)

Consider two weather forecasters A and B. On sunny days, $P_A(\text{RAIN}) \geq P_B(\text{RAIN})$. Is B better than A?

• Interpretational problems: misunderstanding (hence misuse) of p-values

E-values, e-processes and e-value based multiple testing

Hypothesis testing

- We assume that there is some distribution P^* that is generating data $X := (X_1, X_2, ...)$.
- We wish to test a null hypothesis $H_0: P^* \in \mathcal{P}$, where \mathcal{P} is a set of probability distributions on some sample space.
- Often (but not always), we test H_0 in contrast with an alternative hypothesis $H_1: P^* \in \mathcal{Q}$, where \mathcal{Q} is again a set of probability distributions, on the same sample space as \mathscr{P} .

The e-variable

• Definition: e-variable

An e-variable E for \mathscr{P} is a non-negative random variable satisfying $\mathbb{E}_P[E] \leq 1$ for all $P \in \mathscr{P}$.

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An e-variable E for \mathscr{P} is a non-negative random variable satisfying $\mathbb{E}_P[E] \leq 1$ for all $P \in \mathscr{P}$.

• The value taken by the e-variable after observing the data is called the e-value. However, often, as also happens with the infamous p-value (p-variable), the random variable E itself is also often called e-value.

Tests and the type I error guarantee

Definition: binary test

A binary test ϕ is a $\{0,1\}$ -valued random variable. The type-I error of a test ϕ for P is $\mathbb{E}_P[\phi]$. A test has level $\alpha \in [0,1]$ for \mathscr{P} if its type-I error is at most α for every $P \in \mathscr{P}$.

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Markov's inequality for e-variables

Let E be an e-variable for \mathscr{P} . We have $P(E \geq 1/\alpha) \leq \alpha$ for all $P \in \mathscr{P}$ and $\alpha \in (0,1]$. Hence, $\mathbf{1}_{\{E \geq 1/\alpha\}}$ is a binary test of level α .

The e-process: any-time valid inference (1)

 Any-time valid inference is a new paradigm for sequential testing (or estimation) that allows the statistician to stop at any arbitrary stopping time, possibly not anticipated or specified in advance.

E-processes are the central object for any-time valid inference

The e-process: any-time valid inference (2)

- E-processes are the central object for any-time valid inference
- Filtrations are important
- A filtration is an increasing nested sequence of sigma-algebra's, which we denote with $\mathfrak{F}:=(\mathcal{F}_t)_{t>0}$.
- A sequence of random variables $(Y_t)_{t\geq 0}$ is called a process if it is adapted to a filtration \mathfrak{F} , that means that every Y_t is measurable with respect to \mathscr{F}_t .
- A stopping time (or rule) τ is a nonnegative integer valued random variable such that $\{\tau \leq t\} \in \mathcal{F}_t$ for each $t \geq 0$. Let \mathcal{T} be the set of all stopping times.

The e-process: any-time valid inference (3)

Definition: e-process

A nonnegative process E is called an e-process if it satisfies $\mathbb{E}_P[E_\tau] \leq 1$ for any stopping time $\tau \in \mathcal{T}$ and any $P \in \mathcal{P}$.

 (There is an equivalent definition that an e-process is a process upper bounded by a family of test martingales.)

Intermezzo: Why are filtrations important?

Pérez-Ortiz, Lardy, De Heide, Grünwald - AoS '24

- Suppose data X_1, X_2, \ldots is sample from $\mathcal{N}(\mu, \sigma^2)$, and let $\delta = \mu/\sigma$. Consider testing $\mathcal{H}_0: \delta = \delta_0$ vs. $\mathcal{H}_1: \delta = \delta_1$
- Let $\mathbb F$ be the `full' data filtration, and let $\mathbb G$ denote the scale-invariant **coarsening** of $\mathbb F$: $\mathscr G_t = \sigma\Big(\frac{X_1}{|X_1|},...,\frac{X_t}{|X_1|}\Big), \forall t$
- In \mathbb{G} , an (in a certain sense optimal) e-process $(e_t)_{t>0}$ for this problem can be derived.
- This process is not an e-process w.r.t. F:

If
$$\tau^{\mathbb{F}} = 1 + \mathbf{1}\{|X_1| \in [0.44, 1.7]\}$$
, then $\mathbb{E}[e_{\tau^{\mathbb{F}}}] \approx 1.19 > 1$.

The e-process: any-time valid inference (4)

Ville's inequality

If E is an e-process for \mathscr{P} , then

$$P\big(\,\exists\, t\in\mathbb{N}: E_t\geq\frac{1}{\alpha}\big)\leq\alpha\text{ for every }P\in\mathscr{P}\text{ and }\alpha\in[0,1]$$

$$\Leftrightarrow \sup_{P \in \mathscr{P}} \left(\sup_{t \in \mathbb{N}} E_t \ge \frac{1}{\alpha} \right) \le \alpha \text{ for every } \alpha \in [0,1].$$

What are good e-variables?

ullet E-variable: non-negative random variable E satisfying

for all
$$P \in \mathcal{H}_0$$
: $\mathbb{E}_P[E] \leq 1$.

- But what is a good e-variable?
- GROW: Growth-Rate Optimal (in Worst case): the e-value E^* that achieves

```
\max_{E:E \text{ is an e-value}} \min_{P \in \mathcal{H}_1} \mathbb{E}_P[\log E]
```

Safe Testing (Grünwald, De Heide, Koolen) - JRSS-B 2024

 $\text{ The GROW e-value } \underbrace{E_{W_1}^*}_{W_1} \text{ exists (for composite } \mathscr{H}_0 \text{), and satisfies } \\ \mathbb{E}_{Z \sim P_{W_1}} [\log E_{W_1}^*] = \sup_{E \in \mathscr{E}} \mathbb{E}_{Z \sim P_{W_1}} [\log E] = \inf_{W_0 \in \mathscr{W}_0} D(P_{W_1} \parallel P_{W_0})$

- if the inf is achieved by some W_0° , the GROW e-value takes a simple form: $E_{W_1}^*=p_{W_1}(Z)/p_{W_0^\circ}(Z)$
- GROW e-values $E_{\mathcal{W}_1}^* = p_{W_1^*}(Z)/p_{W_0^*}(Z)$ can be found by a double KL-minimization problem $\min_{W_1 \in \mathcal{W}_1} \min_{W_0 \in \mathcal{W}_0} D(P_{W_1} \parallel P_{W_0})$ and they satisfy

$$\inf_{W \in \mathcal{W}_1} \mathbb{E}_{Z \sim P_W} [\log E_{\mathcal{W}_1}^*] = \sup_{E \in \mathcal{E}} \inf_{W \in \mathcal{W}_1} \mathbb{E}_{Z \sim P_W} [\log E] = D(P_{W_1^*} \parallel P_{W_0^*})$$

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 - fMRI: 200.000 voxels
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- Examples:
 - testing whether some of 20.000 genes are linked to a disease
 - fMRI: 100.000 voxels
 - DNA methylation: 500.000 sites
- We need other measures of acceptance/rejection errors.
- We need statistical procedures to control these measures of errors.

Notation

- Goal of a multiple testing procedure: choose a collection $\mathcal R$ of hypotheses to reject (often termed: discoveries)
- Errors that can be made:
 - Type I (false positives): rejected and true
 - Type II (false negatives): not rejected and false

	True	False	Total
Rejected Not rejected	V	$oldsymbol{U}$	\boldsymbol{R}
Not rejected	$m_0 - V$	$m_1 - U$	m-R
Total	m_0	m_1	m

Error rates

- . False discovery proportion (FDP) $Q = \begin{cases} V/R & \text{if } R > 0 \\ 0 & \text{otherwise} \end{cases}$
 - i.e. the proportion of false rejections among the rejections.
- In general $\mathcal R$ is random, so both V and Q are random variables, so we must focus on relevant aspects of their distribution.
- Family-wise error (FWER) = P(V > 0) = P(Q > 0)
- False Discovery Rate (FDR) = $\mathbb{E}(Q)$

e-BH (Wang & Ramdas, JRSS-B 2022)

- Associate each H_j with e-value e_j .
- Let $e_{[k]}$ be the kth order statistic of e_1, \ldots, e_K , from the largest to the smallest.
- Define the test procedure which rejects hypotheses with the largest k_e^\star e-values, where

$$k_e^* = \max \left\{ k \in [K] : \frac{ke_{[k]}}{K} \ge \frac{1}{\alpha} \right\}.$$

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- This procedure controls the FDR at level α even under unknown arbitrary dependence between the e-values.
- BH and BY are special cases of e-BH.

Aproblem

Testing a single hypothesis: no problem

- One e-process: E_1, E_2, \dots
- Suppose we already gathered E_{t+1} before properly evaluating E_t .
- If $E_t \ge 1/\alpha$ but $E_{t+1} < 1/\alpha$, we can still go back to E_t and reject H_0 , because Ville's inequality states

$$\sup_{P \in \mathscr{P}} \left(\sup_{t \in \mathbb{N}} E_t \ge \frac{1}{\alpha} \right) \le \alpha$$

• Let's focus on e-BH for FDR control.

• Consider K parallel e-processes E_t^1, \ldots, E_t^K

• e-BH guarantees: $\sup_{t} \text{FDR}(E_t^1, ..., E_t^K) \leq \alpha$

• Consider K=2, then e-BH rejects any hypothesis for which the e-value exceeds $2/\alpha$, and both hypotheses if both e-values exceed $1/\alpha$.

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- Consider K=2, then e-BH rejects any hypothesis for which the e-value exceeds $2/\alpha$, and both hypotheses if both e-values exceed $1/\alpha$.
- Suppose that at time t we have $1/\alpha \le E_t^1 < 2/\alpha$ and $E_t^2 < 1/\alpha$.
- Gathering more data for both e-processes, we could arrive at

$$E_{t+1}^1 < 1/\alpha \text{ and } 1/\alpha \le E_{t+1}^2 < 2/\alpha.$$

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- Gathering more data for both e-processes, we could arrive at

$$E_{t+1}^1 < 1/\alpha \text{ and } 1/\alpha \le E_{t+1}^2 < 2/\alpha.$$

• Now, if we would not have gathered one more data point for E^1 , then we would have rejected both hypotheses.

FDR control for e-processes

- e-BH guarantees: $\sup_{t} \text{FDR} \left(E_t^1, ..., E_t^K \right) \leq \alpha$
- But we would like to control:

$$FDR\left(\sup_{t} E_{t}^{1}, ..., \sup_{t} E_{t}^{K}\right) \leq \alpha$$

- We would like to argue that this is the proper FDR criterion for e-processes.
- (Note: in this talk I focus on FDR with e-BH, but we can show the same for other methods and FWER.)

A proposition

Working with the running maxima of e-processes

. Clearly, if we work with $M^k_t := \max_{1 \leq s \leq t} E^k_s$, the running maximum processes,

we obtain a non-decreasing sequence of sets of rejected hypotheses.

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we obtain a non-decreasing sequence of sets of rejected hypotheses.

• The running maximum process is not an e-process itself, therefore we cannot straightforwardly prove FDR control.

• In case the e-processes are independent, $1/M_t^k$ is a valid p-value (p-process), thus, we obtain FDR control via classical BH.

Proposition

(Tavyrikov, Goeman, De Heide, '25)

Proposition

The cumulative maximum e-BH procedure applied to arbitrarily dependent e-processes does not control the FDR at level α .

• Proof: example on the next slide.

Proof

$$E_t^1 = X_0^1 \prod_{s=1}^t e_s^1, \quad E_t^2 = X_0^2 \prod_{s=1}^t e_s^2$$
 with probability $1 - 2\alpha$,
$$(X_0^1, X_0^2) \sim \begin{cases} (0,0), & \text{with probability } 1 - 2\alpha, \\ \left(\frac{1}{2\alpha}, \frac{1}{2\alpha}\right), & \text{with probability } 2\alpha, \end{cases}$$

and the increments (e_s^1, e_s^2) are distributed as

$$\begin{cases} \left(\frac{1}{2}, \frac{1}{2}\right), & \text{with probability } \frac{1}{3}, \\ \left(2, \frac{1}{2}\right), & \text{with probability } \frac{1}{3}, \\ \left(\frac{1}{2}, 2\right), & \text{with probability } \frac{1}{3}. \end{cases}$$

Proof

$$E_t^1 = X_0^1 \prod_{s=1}^t e_s^1, \quad E_t^2 = X_0^2 \prod_{s=1}^t e_s^2$$

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These are valid e-processes, i.e. $\mathbb{E}[E_t^1] = \mathbb{E}[E_t^2] = 1$ at all times.

They are not independent.

Rejection happens for the event
$$E_t^1 \ge \frac{2}{\alpha}$$
, $E_t^2 \ge \frac{2}{\alpha}$, or both $E_t^1, E_t^2 \ge \frac{1}{\alpha}$

Simulations show that the FDR of the running maxima of these processes is 1.08α .

Asolution

Adjusters

• An (admissible) adjuster is an increasing function $A:[1,\infty]\to[1,\infty]$ that is right-continuous, $A(\infty)=\lim_{e\to\infty}A(e)=\infty$ and $\int_1^\infty A(e)/e^2\mathrm{d}e=1$.

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- . If $M^k_t := \sup_{1 \leq s \leq t} E^k_s$ is the running maximum of an e-process, then
 - $(A(M_t^k))_{t>0}$ is also an e-process.

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- . If $M^k_t := \sup_{1 \leq s \leq t} E^k_s$ is the running maximum of an e-process, then
 - $(A(M_t^k))_{t>0}$ is also an e-process.
- Since the adjusted process is non-decreasing, it will never result in regretting having collected more evidence.

The adjusted running maximum process has FDR-sup $\leq \pi_0 \alpha$ (Tavyrikov, Goeman, De Heide, '25)

Let $\mathscr{R}^{e-BH}(e)$ denote the e-BH rejection set based on a set of e-values

 $\mathbf{e} = e_{t_1}^1, \dots, e_{t_K}^K$, which can be obtained from different time points t_1, \dots, t_K .

I.e., $j \in \mathcal{R}^{\mathbf{e}-\mathsf{BH}}(\mathbf{e})$ if and only if $e^j_{t_j} > m/(\alpha \mid \mathcal{R}^{\mathbf{e}-\mathsf{BH}}(\mathbf{e}) \mid)$. Let A be an adjuster,

so that
$$A\left(\sup_{t\leq s}(e_t^j)\right)$$
 is an adjusted running maximum process.

The adjusted running maximum process has FDR-sup $\leq \pi_0 \alpha$ (Tavyrikov, Goeman, De Heide, '25)

Then the FDR-sup at time s is

$$\mathsf{FDR-sup}_{s} = \sum_{j \in H_{0}} \frac{1 \left\{ A \left(\mathsf{sup}_{t \leq s}(e_{t}^{j}) \right) \geq \frac{K}{\alpha \, | \, \mathscr{R}\mathsf{e-BH}(\mathbf{e}) \, |} \right\}}{|\, \mathscr{R}\mathsf{e-BH}(\mathbf{e}) \, | \, \vee \, 1}$$

$$\leq \sum_{j \in H_0} \mathbb{E} \left[A \left(\sup_{t \leq s} (e_t^j) \right) \frac{\alpha \frac{|\mathscr{R}^{\mathsf{e-BH}}(\mathbf{e})|}{|\mathscr{R}^{\mathsf{e-BH}}(\mathbf{e})| \vee 1} \right] \leq \frac{\alpha}{K} \sum_{j \in H_0} \mathbb{E} \left[A \left(\sup_{t \leq s} (e_t^j) \right) \right] \leq \frac{K_0}{K} \alpha.$$

Do we need adjusters?

Theorem (informal): The function is necessarily an adjuster, as long as it is an increasing function that maps the running maximum process to an e-process.

Advantages of e-values

- Any-time valid testing (validity under optional stopping)
- Easy combination (several studies/meta analysis)
- ullet Easy interpretation: betting. High e-value is more evidence against H_0
- E-values can be constructed from different paradigms: frequentist, objective Bayesian, subjective Bayesian, strict Neyman-Pearsonian, and others
- Many interesting properties, e.g. in multiple testing allowing for general dependence in FDR methods, derandomization of knock-offs, etc.

Exciting new result: bringing closure to FDR

With Jelle Goeman, Aldo Solari, Aaditya Ramdas, Neil Xu, Lasse Fischer

- Necessary and sufficient principle for multiple testing methods controlling an expected loss (think of FDR)
- Every such multiple testing method is a special case of a general closed testing procedure based on e-values.
- Uniform improvements of these methods
- Simultaneous error control
- Post-hoc flexibility for the user choice of alpha, target error rate, and sometimes even nominal error rate
- Restricted combinations possible exploiting logical relationships between hypotheses

The e-Partitioning Principle of False Discovery Rate Control

J Goeman, R de Heide, A Solari - arXiv preprint arXiv:2504.15946, 2025

Bringing closure to FDR control: beating the e-Benjamini-Hochberg procedure

Z Xu, L Fischer, A Ramdas - arXiv preprint arXiv:2504.11759, 2025

The future of e-values

• Many groups studying e-values now (in mathematical statistics, probability theory): e.g. CWI, CMU, ETH, Waterloo, London, Stanford, Twente...



Questions?

References

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