E-values

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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

Foto: Patrick Siemons

Menu

- p-values and why do we need a new theory for hypothesis testing?
- E-values, e-processes and e-value based multiple testing
- A problem
- A proposition
- A solution

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

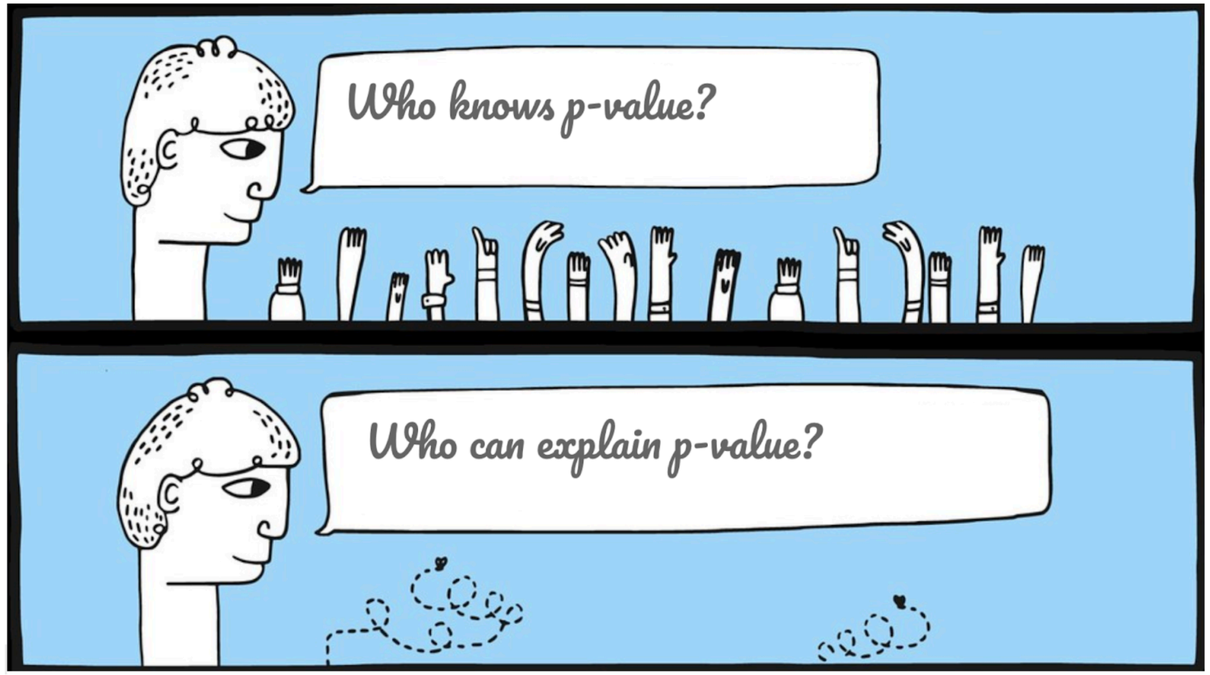
Reproducibility crisis in social and medical science

Causes:

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

What is a p-value actually?

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



What is a p-value actually?

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

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 5550 2085**

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 $P \in \mathscr{H}_0$, for $\alpha \in [0,1]$,

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

What is a p-value actually?

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

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

Stopping rules and p-values

- 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 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.

Stopping rules and p-values

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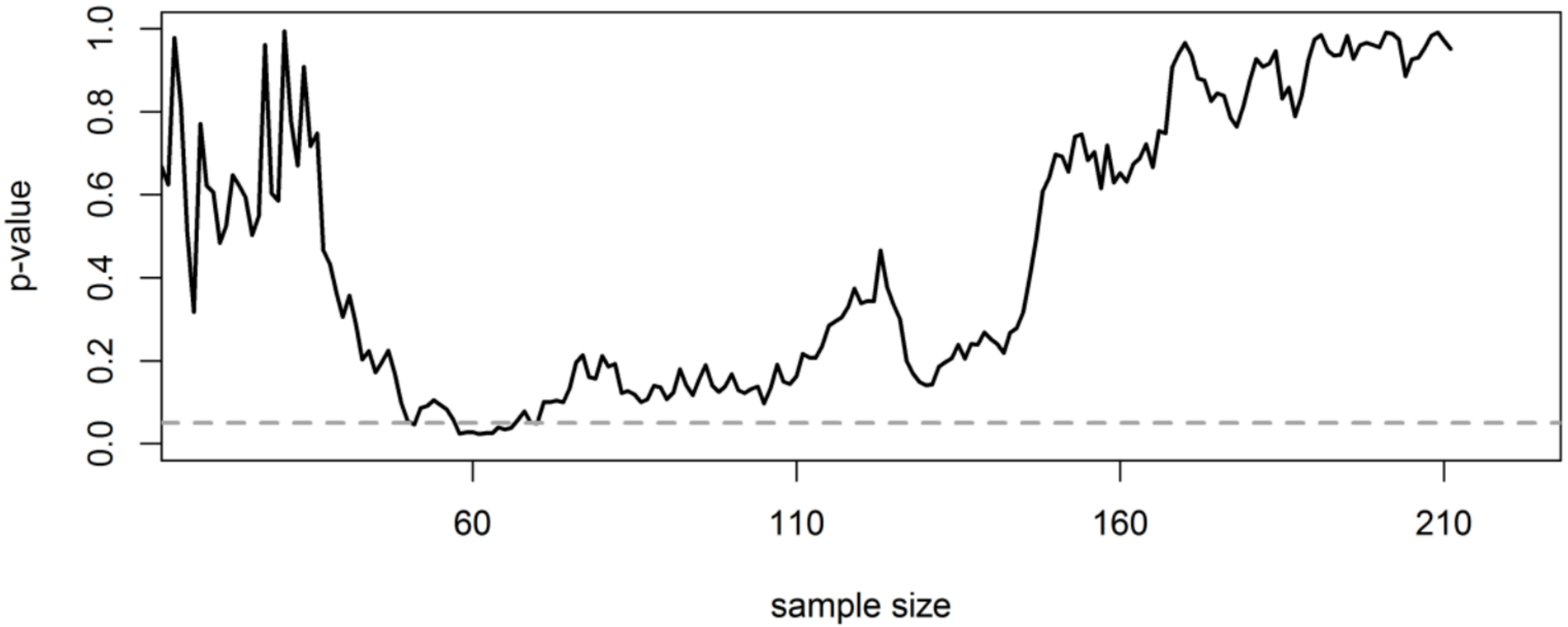
- This is called optional stopping, and invalidates p-values and their error guarantees

Type I error guarantee

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

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

Stopping rules and p-values



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

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)

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  Consider two weather forecasters A and B. On sunny days, P_A(RAIN) $\geq P_B$(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 $X := (X_1, X_2, \ldots)$.
- We wish to test a null hypothesis $H_0 : P^* \in \mathscr{P}$, where $\mathscr{P}$ is a set of probability distributions on some sample space.
- Often (but not always), we test H_0 in contrast with an alternative hypothesis $H_1 : P^* \in \mathscr{Q}$, where $\mathscr{Q}$ 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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- 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 $\mathfrak{F} := (\mathscr{F}_t)_{t \geq 0}$.
- 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 $\{\tau \leq t\} \in \mathscr{F}_t$ for each $t \geq 0$. Let $\mathscr{T}$ 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 $\tau \in \mathscr{T}$ and any $P \in \mathscr{P}$.

- (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 $\mathbb{F}$:
  $$\mathcal{G}_t = \sigma\left(\frac{X_1}{|X_1|}, \ldots, \frac{X_t}{|X_1|}\right), \forall t$$
- In $\mathbb{G}$, an (in a certain sense optimal) e-process $(\mathbf{e}_t)_{t \geq 0}$ for this problem can be derived.
- This process is not an e-process w.r.t. $\mathbb{F}$:

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

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

- **Ville's inequality**

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

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

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

What are good e-variables?

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

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

- 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

- The GROW e-value $E^*_{W_1}$ exists (for composite $\mathscr{H}_0$), and satisfies

$$\mathbb{E}_{Z\sim P_{W_1}}[\log E^*_{W_1}] = \sup_{E\in\mathscr{E}} \mathbb{E}_{Z\sim P_{W_1}}[\log E] = \inf_{W_0\in\mathscr{W}_0} D(P_{W_1} \,\|\, P_{W_0})$$

- 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 $E^*_{\mathscr{W}_1} = p_{W_1^*}(Z)/p_{W_0^*}(Z)$ can be found by a double KL-minimization problem $\min_{W_1\in\mathscr{W}_1} \min_{W_0\in\mathscr{W}_0} D(P_{W_1} \,\|\, P_{W_0})$ and they satisfy

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

Multiple testing: the problem

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- Examples:
  - testing whether some of 20.000 genes are linked to a disease
  - fMRI: 200.000 voxels
  - DNA methylation: 500.000 sites

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- If we test n true null hypotheses at level α, then on average we will (falsely) reject αn of them.
- 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 $\mathscr{R}$ 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	V	U	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 $\mathscr{R}$ 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

$$k_e^\star = \max \left\{ k \in [K] : \frac{k e_{[k]}}{K} \geq \frac{1}{\alpha} \right\}.$$

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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.

A problem

Testing a single hypothesis: no problem

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

$$\sup_{P \in \mathcal{P}} \left(\sup_{t \in \mathbb{N}} E_t \geq \frac{1}{\alpha} \right) \leq \alpha$$

Testing multiple hypotheses: a problem (1)

- Let's focus on e-BH for FDR control.
- Consider K parallel e-processes $E_t^1, \ldots, E_t^K$
- e-BH guarantees: $\sup_t \text{FDR}(E_t^1, \ldots, E_t^K) \leq \alpha$

Testing multiple hypotheses: a problem (2)

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

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

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

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

- 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: $\sup_t \text{FDR}\left(E_t^1, \ldots, E_t^K\right) \leq \alpha$
- But we would like to control:

  $$\text{FDR}\left(\sup_t E_t^1, \ldots, \sup_t E_t^K \right) \leq \alpha$$

- 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 $M_t^k := \max_{1 \le s \le t} E_s^k$, the running maximum processes,

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

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- 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

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

$$(X_0^1, X_0^2) \sim \begin{cases} (0,0), & \text{with probability } 1-2\alpha, \\ \left(\frac{1}{2\alpha}, \frac{1}{2\alpha}\right), & \text{with probability } 2\alpha, \end{cases}$$

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

$$E_t^1 \geq \frac{2}{\alpha}, \quad E_t^2 \geq \frac{2}{\alpha}, \quad \text{or both } E_t^1, E_t^2 \geq \frac{1}{\alpha}$$

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

A solution

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 $M_t^k := \sup_{1\le s\le t} E_s^k$ is the running maximum of an e-process, then

  $(A(M_t^k))_{t\ge 0}$ is also an e-process.

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- If $M_t^k := \sup_{1\le s\le t} E_s^k$ is the running maximum of an e-process, then

  $(A(M_t^k))_{t\ge 0}$ 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 $\mathscr{R}^{\text{e-BH}}(\mathbf{e})$ denote the e-BH rejection set based on a set of e-values $\mathbf{e} = e^1_{t_1}, \ldots, e^K_{t_K}$, which can be obtained from different time points $t_1, \ldots, t_K$.

I.e., $j \in \mathscr{R}^{\text{e-BH}}(\mathbf{e})$ if and only if $e^j_{t_j} > m/(\alpha \,|\, \mathscr{R}^{\text{e-BH}}(\mathbf{e}) \,|\,)$. Let A be an adjuster, so that $A\left(\sup_{t \leq s}(e^j_t)\right)$ 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

$$\text{FDR-sup}_s = \sum_{j \in H_0} \frac{\mathbf{1}\left\{ A\left(\sup_{t \leq s}(e_t^j)\right) \geq \frac{K}{\alpha\, |\mathscr{R}^{\text{e-BH}(\mathbf{e})}|} \right\}}{|\mathscr{R}^{\text{e-BH}(\mathbf{e})}| \vee 1}$$

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

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)
- 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

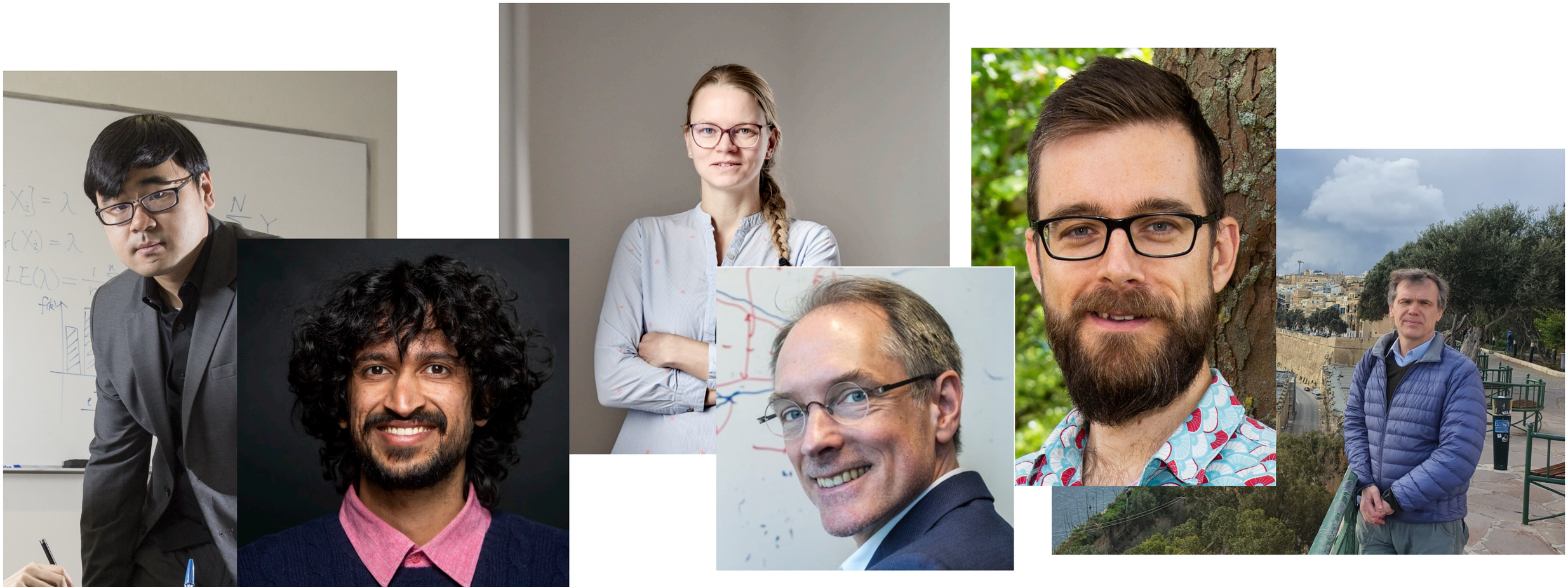
- Necessary and sufficient principle for multiple testing methods controlling an expected loss (think of FDR)
- Every such multiple testing method is a special case of a general closed testing procedure based on e-values.
- Uniform improvements of these methods
- Simultaneous error control
- Post-hoc 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?

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- A. Ramdas - Lecture: http://stat.cmu.edu/~aramdas/betting/Feb11-class.pdf