Combining p-Values

Permutation Closed Testing with Sum-Based Statistics

Combining p-Values via Averaging

Averaging Functions

$p_1, \ldots, p_K$ = p-values

r	$M_{r,K}(p_1, \ldots, p_K)$	special cases
$\mathbb{R} \setminus \{0\}$	$\left(\frac{p_1^r + \ldots + p_K^r}{K}\right)^{1/r}$	$r = -1$ harmonic, $r = 1$ arithmetic
0	$(p_1 \cdot \ldots \cdot p_K)^{1/K}$	geometric
$+\infty$	$\max\{p_1, \ldots, p_K\}$	maximum
$-\infty$	$\min\{p_1, \ldots, p_K\}$	Bonferroni

When multiplied by a positive constant $a_{r,K}$, the averaging function is a p-value.

Analysis

Tests for f variables and B data permutations:

$$\begin{pmatrix} p_1 & \dots & p_f \\ p_1^{(2)} & \dots & p_f^{(2)} \\ \vdots & & \vdots \\ p_1^{(B)} & \dots & p_f^{(B)} \end{pmatrix}$$

Average for $V \subseteq \{1, \dots, f\}$:

$$M_{r,|V|}(p_i,\ i \in V) = \left(\frac{g_V}{|V|}\right)^{1/r}$$

where

$$g_i^{(\pi)} = (p_i^{(\pi)})^r \qquad g_V^{\pi} = \sum_{i \in V} g_i^{(\pi)}$$

Extreme Values

The extreme values of

$$M_{r,|V|}(p_i,\ i \in V) = \left(\frac{g_V}{|V|}\right)^{1/r}$$

are the lowest. The corresponding extreme values of g_V are

- the lowest if $r \geq 0$
- the highest if $r < 0$

Simulations

Matrix of p-Values for f Variables and B Transformations (Sign-Flipping)

- f_1 variables have mean $\theta f / f_1$ and equi-correlation ρ_1
- the remaining variables have mean 0 and equi-correlation ρ_2
- the correlation between the two groups is fixed at 0
- n observations

$n \times f$ matrix: $\mathbf{X} = (\mathbf{X}_1, \ldots, \mathbf{X}_n)^\top$ with rows

$$\mathbf{X}_j = MVN_f(\boldsymbol{\mu}, \boldsymbol{\Sigma}) \qquad \boldsymbol{\mu} = \begin{pmatrix} \theta f / f_1 \\ \vdots \\ \theta f / f_1 \\ 0 \\ \vdots \\ 0 \end{pmatrix} \qquad \boldsymbol{\Sigma} = \begin{pmatrix} 1 & \ldots & \rho_1 & 0 & \ldots & 0 \\ \vdots & & \vdots & \vdots & & \vdots \\ \rho_1 & \ldots & 1 & 0 & \ldots & 0 \\ 0 & \ldots & 0 & 1 & \ldots & \rho_2 \\ \vdots & & \vdots & \vdots & & \vdots \\ 0 & \ldots & 0 & \rho_2 & \ldots & 1 \end{pmatrix}$$

Matrix of p-Values for f Variables and B Transformations (Sign-Flipping)

One-sample t-test on the i-th variable (column $\mathbf{X}_i$):
$H_0 : \mu_i = 0$ vs $H_1 : \mu_i > 0$

$$p_i = P\left(T_{n-1} \geq \frac{\text{mean}(\mathbf{X}_i)}{\text{sd}(\mathbf{X}_i)/\sqrt{n}}\right)$$

$B \times f$ matrix of p-values: repeat using B transformations (sign-flipping) of $\mathbf{X}$

Numerical Issues for $r < 0$

The algorithm defines the bounds by using sums of the form

$$\sum_{k=1}^{K} (p_k^{(\pi)})^r,$$

which is high when $p_k^{(\pi)} << 1$.

Smallest p-value: $p_{\text{min}} = \min\{p_i^{(\pi)} \,:\, i = 1, \ldots, f,\ \pi = 1, \ldots, B\}$

Every sum is smaller than $f \cdot p_{\text{min}}^r$.

Numerical Issues for $r < 0$

Let $M = .Machine\$double.xmax$.

If $f \cdot p_{\text{min}}^r < M$, then every sum will be finite.

Otherwise, we multiply all the p-values by

$$\lambda > \frac{1}{p}\left(\frac{M}{f}\right)^{1/r},$$

so that $f(p_{\text{min}}\lambda)^r < M$.

Simulations for 650 cases (441 scenarios, 13 r values)

S contains a percentage s_{size} of all variables

s_* and o_* are the percentages of false null hp within and outside S

- $r \in \{-100, -10, -2, -1, -0.5, -0.1, 0, 0.1, 0.5, 1, 2, 10, 100\}$
- $f = 50$, $n = 20$ and $B = 50$
- $\theta = 0.1$, $\rho_1 \in \{0, 0.99\}$ and $\rho_2 = 0$
- $s_{\text{size}} = 20$ (%)
- $s_*, o_* \in \{0, 10, 50, 90, 100\}$ (%)
- $\alpha = 0.20$
- maximum number of iterations: 10^4

Behavior of r: Percentage of Non-Rejections over 100 Simulations per Case

Non-rejections for $s_* = 0$

o_*	r												
	-100	-10	-2	-1	-0.5	-0.1	0	0.1	0.5	1	2	10	100
0	3	3	3	2	1	-	-	-	-	-	-	-	-
10	2	2	2	2	-	-	-	-	-	-	-	-	-
50	6	6	6	5	2	1	-	-	-	-	-	2	2
90	6	6	5	5	1	-	-	-	-	-	-	1	2
100	4	4	4	2	1	-	-	-	-	-	-	-	-

Non-rejections for $s_* = 10$

ρ_1	o_*	r												
		-100	-10	-2	-1	-0.5	-0.1	0	0.1	0.5	1	2	10	100
	0	**100**	**100**	**100**	**100**	**100**	**100**	96	-	-	-	-	-	-
	10	**93**	**93**	**93**	**93**	85	11	-	-	-	-	-	-	-
0	50	**13**	**13**	**13**	**13**	8	1	-	-	-	-	-	1	1
	90	**10**	**10**	9	7	2	-	-	-	-	-	-	-	-
	100	6	5	5	4	2	1	-	-	-	1	1	4	**8**
	0	**100**	**100**	**100**	**100**	**100**	**100**	96	1	-	-	-	-	-
	10	92	92	**93**	90	80	19	2	-	-	-	-	-	-
0.99	50	8	**9**	**9**	6	2	-	-	-	-	-	-	-	1
	90	**17**	**17**	16	13	9	9	8	7	9	7	5	10	9
	100	23	23	21	16	14	13	14	13	12	11	15	18	**24**

Non-rejections for $s_* = 50$

ρ_1	o_*	r												
		-100	-10	-2	-1	-0.5	-0.1	0	0.1	0.5	1	2	10	100
	0	**100**	**100**	**100**	**100**	**100**	**100**	**100**	96	-	-	-	-	-
	10	88	88	89	**92**	88	67	51	31	-	-	-	-	-
0	50	**16**	**16**	**16**	14	11	-	-	-	-	-	-	-	-
	90	**7**	**7**	**7**	**7**	5	-	-	-	-	-	-	2	2
	100	**5**	**5**	**5**	**5**	1	-	-	-	-	-	1	3	4
	0	90	91	92	**94**	93	88	84	78	-	-	-	-	-
	10	49	50	53	**58**	57	50	44	33	1	-	-	-	-
0.99	50	9	9	11	14	**16**	11	10	9	3	1	-	-	-
	90	18	18	19	26	27	29	**30**	29	25	18	15	11	11
	100	**28**	**28**	25	27	27	27	**28**	**28**	27	25	21	19	22

Non-rejections for $s_* = 90$

ρ_1	o_*	r												
		-100	-10	-2	-1	-0.5	-0.1	0	0.1	0.5	1	2	10	100
	0	99	99	**100**	**100**	**100**	99	98	94	18	-	-	-	1
	10	85	85	**88**	86	86	71	61	44	10	-	-	-	-
0	50	**30**	**30**	**30**	**30**	20	9	6	3	1	1	1	1	1
	90	**15**	**15**	**15**	13	9	4	1	1	-	-	-	2	5
	100	**9**	**9**	**9**	**9**	5	1	1	1	-	1	2	1	1
	0	46	46	58	65	71	**72**	71	69	8	-	-	-	-
	10	17	17	24	38	**42**	40	38	37	10	-	-	-	-
0.99	50	7	8	15	17	21	**23**	**23**	**23**	14	1	-	-	-
	90	16	16	22	25	25	**28**	**28**	**28**	**28**	26	16	1	1
	100	**30**	28	24	26	27	28	29	**30**	**30**	29	26	23	28

Non-rejections for $s_* = 100$

ρ_1	o_*	r												
		-100	-10	-2	-1	-0.5	-0.1	0	0.1	0.5	1	2	10	100
0	0	95	96	97	**99**	**99**	96	94	91	23	-	-	-	-
	10	83	83	84	**88**	**88**	72	56	47	7	-	-	-	-
	50	11	11	**12**	11	11	9	8	6	2	1	1	-	-
	90	**15**	**15**	**15**	13	5	3	1	1	1	-	-	3	3
	100	**15**	**15**	**15**	13	10	2	2	2	1	-	-	3	2
0.99	0	32	33	45	62	67	**68**	66	59	14	-	-	-	-
	10	19	19	25	33	40	**41**	**41**	38	15	-	-	-	-
	50	8	8	12	17	23	24	**25**	24	17	5	-	-	-
	90	12	12	14	22	25	**26**	**26**	**26**	**26**	24	13	3	-
	100	29	29	27	27	27	27	27	27	27	27	27	29	**30**

Non-rejections

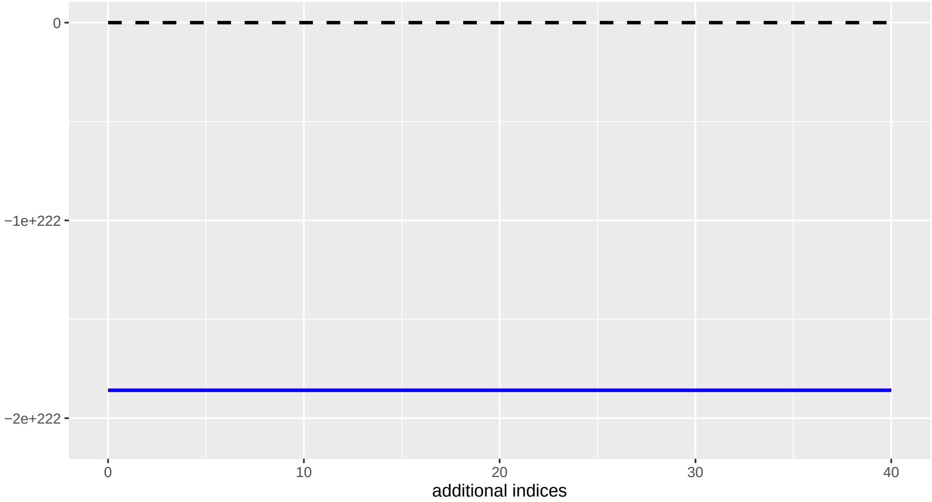
Small values of r tend to be more powerful in most cases

When the false null hp are highly correlated in a dense scenario (small signal spread across many variables), positive r values perform better

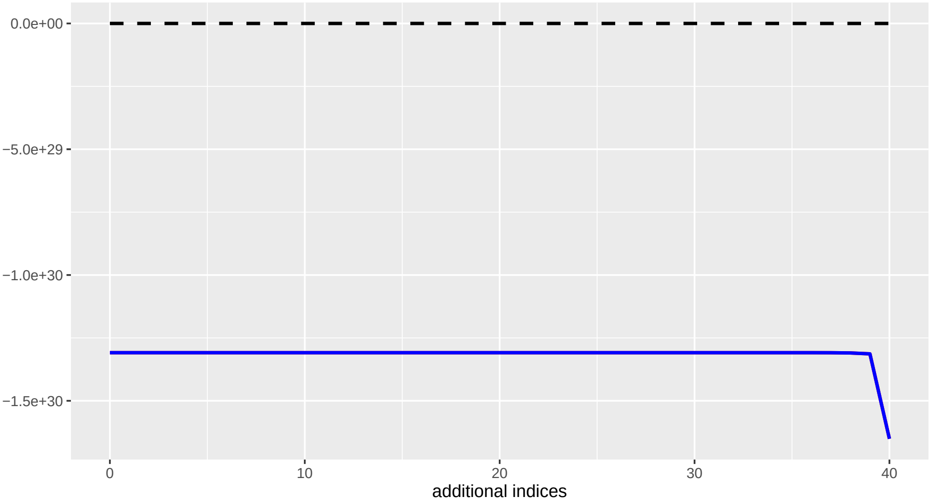
Behavior of r: Bounds for $s_* = 50$, $o_* = 10$, $\rho_1 = 0.99$

$r = -100$: rejection

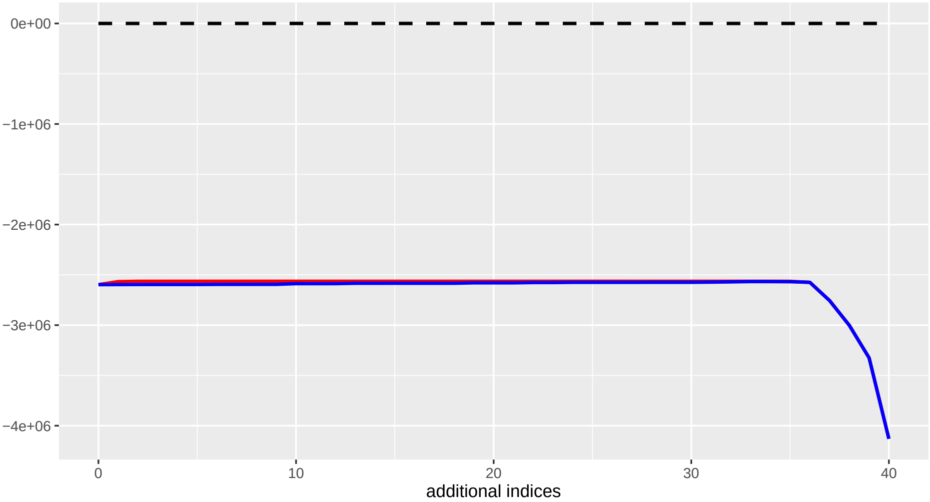
Correction for numerical issues using $\lambda = 6$



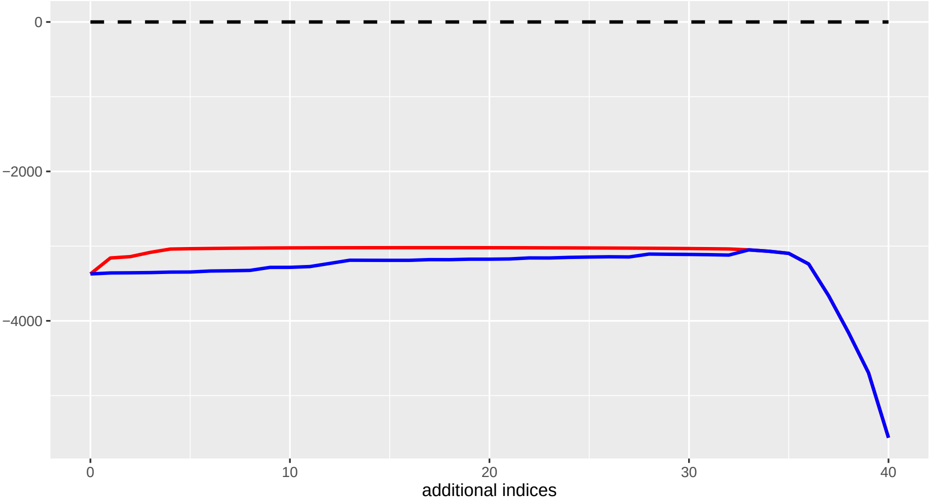
$r = -10$: rejection



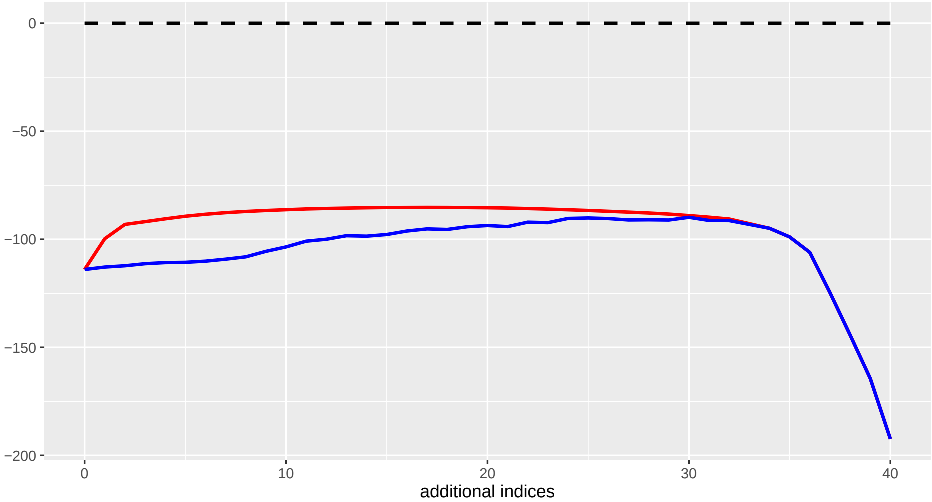
$r = -2$: rejection



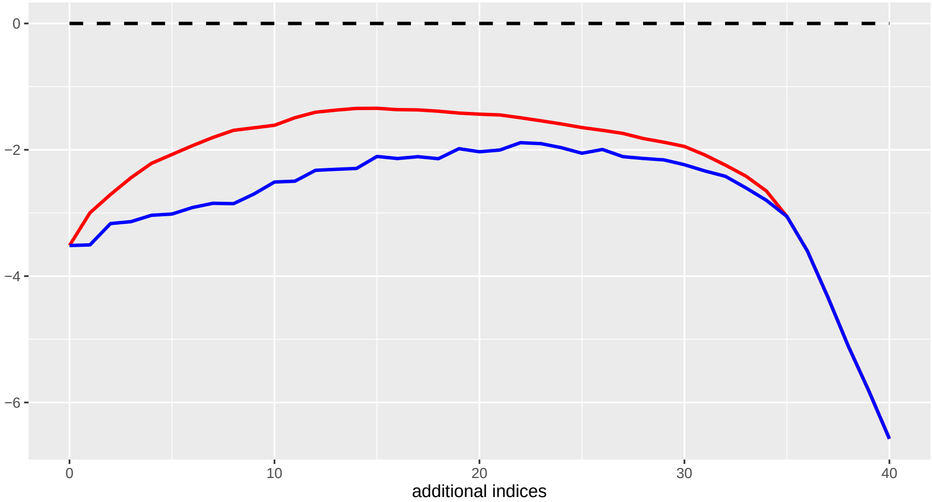
$r = -1$ (harmonic mean): rejection



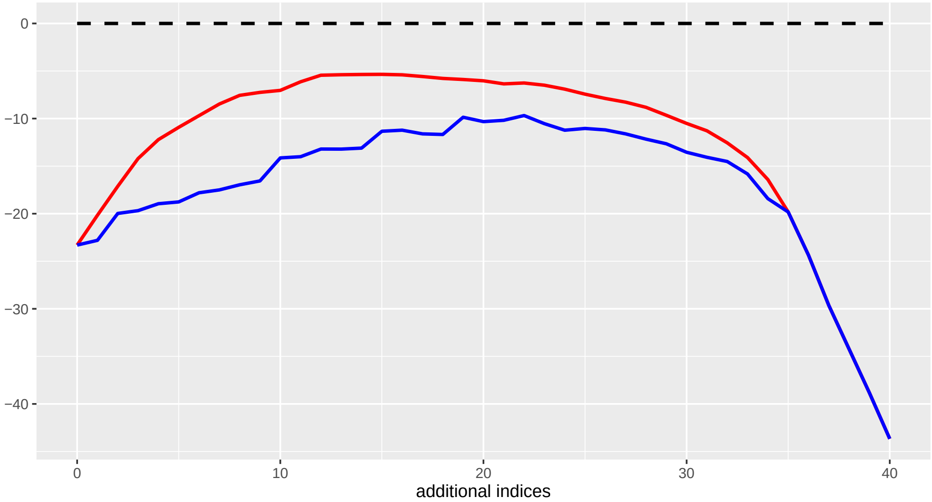
$r = -0.5$: rejection



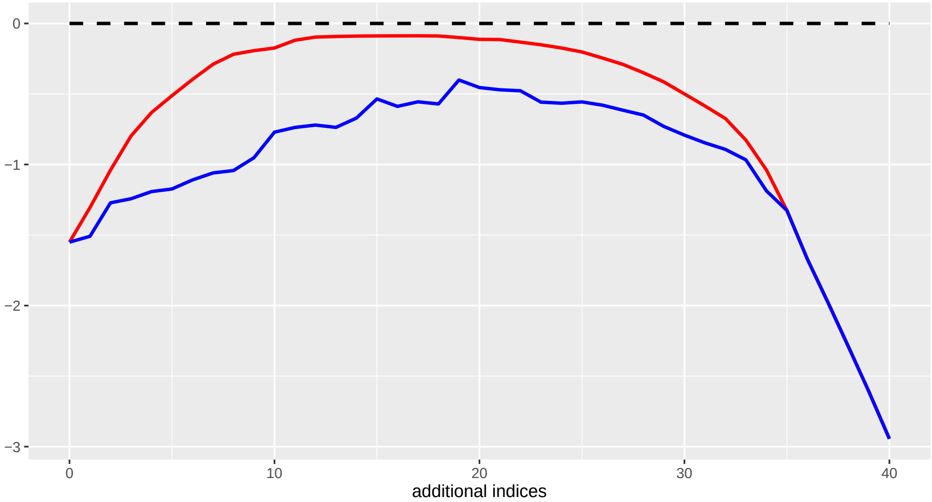
$r = -0.1$: rejection



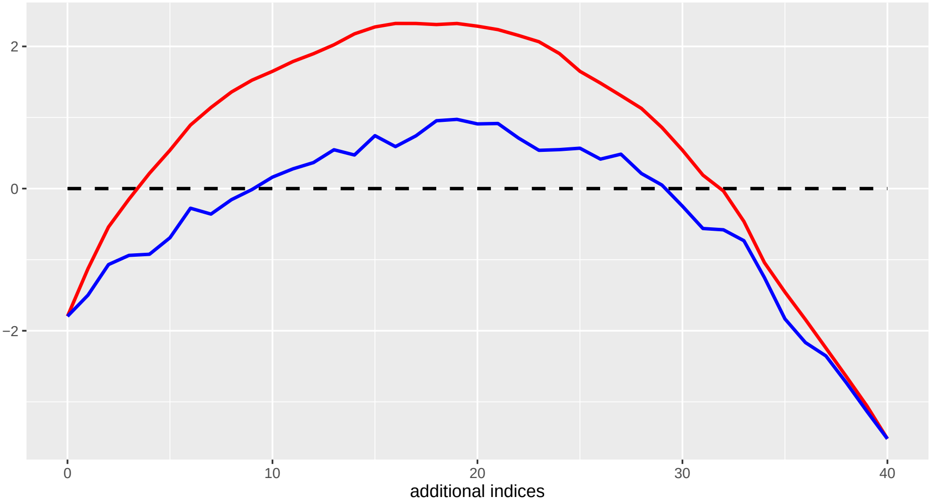
$r = 0$ (geometric mean): rejection



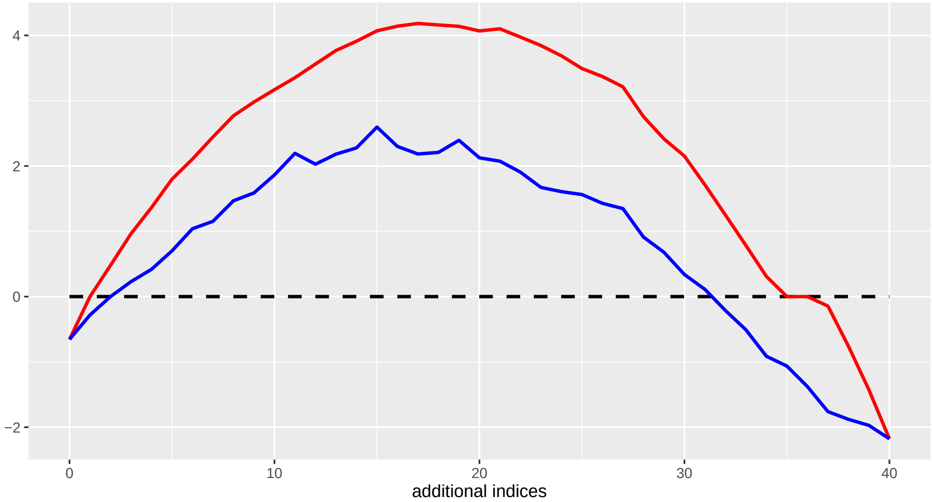
$r = 0.1$: rejection



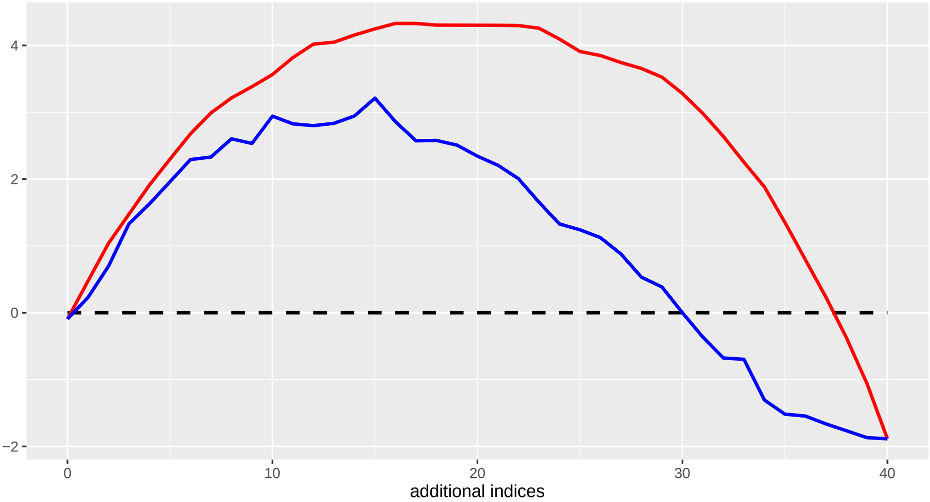
$r = 0.5$: non-rejection



$r = 1$ (arithmetic mean): non-rejection



$r = 2$: non-rejection



$r = 10$: non-rejection

$r = 100$ ($\approx$ maximum): non-rejection