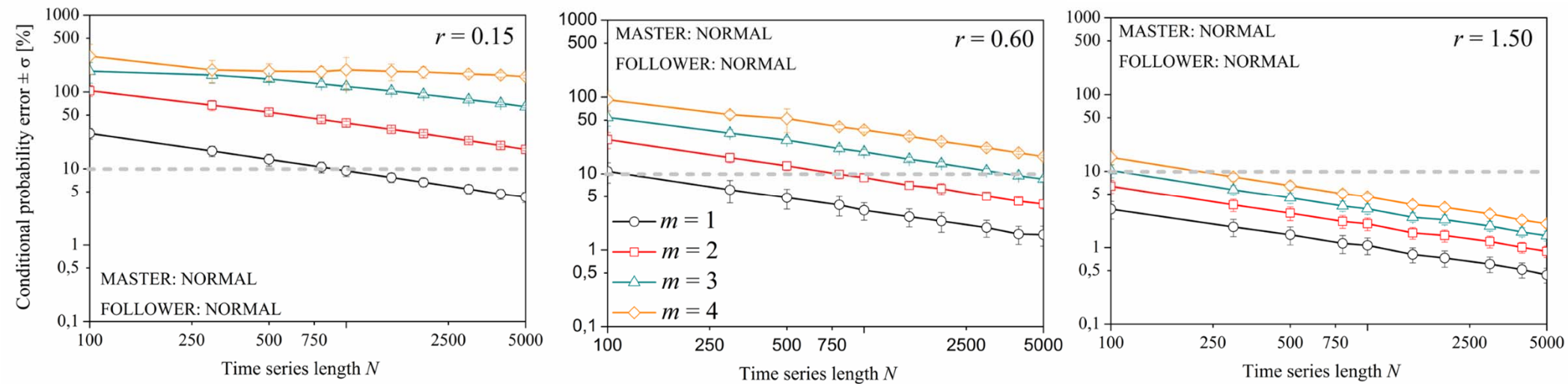


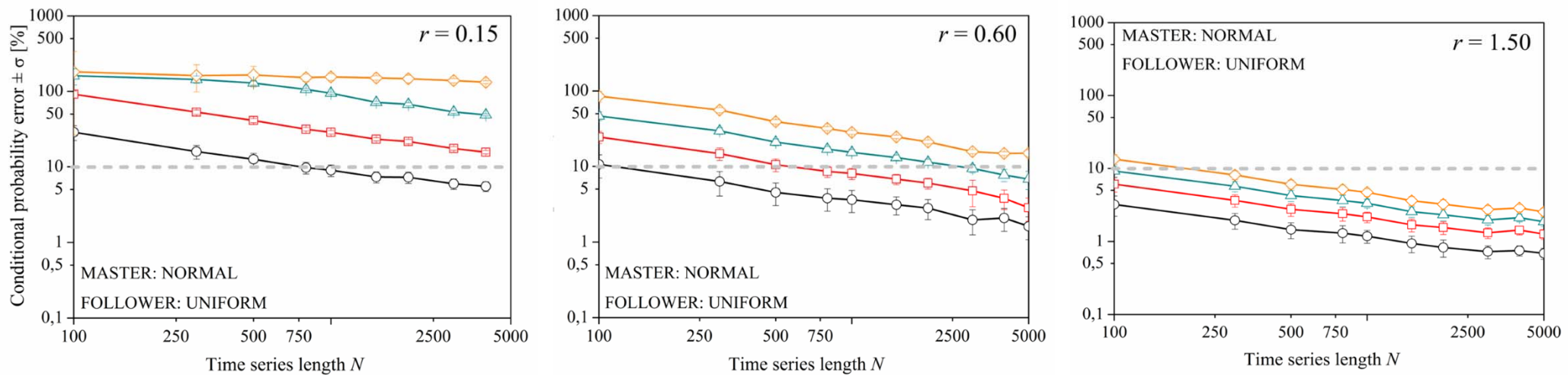
**Additional material for  
Figures 3, 4 and 5**

**Figure 3:**  
MASTER: normal  
FOLLOWER: normal



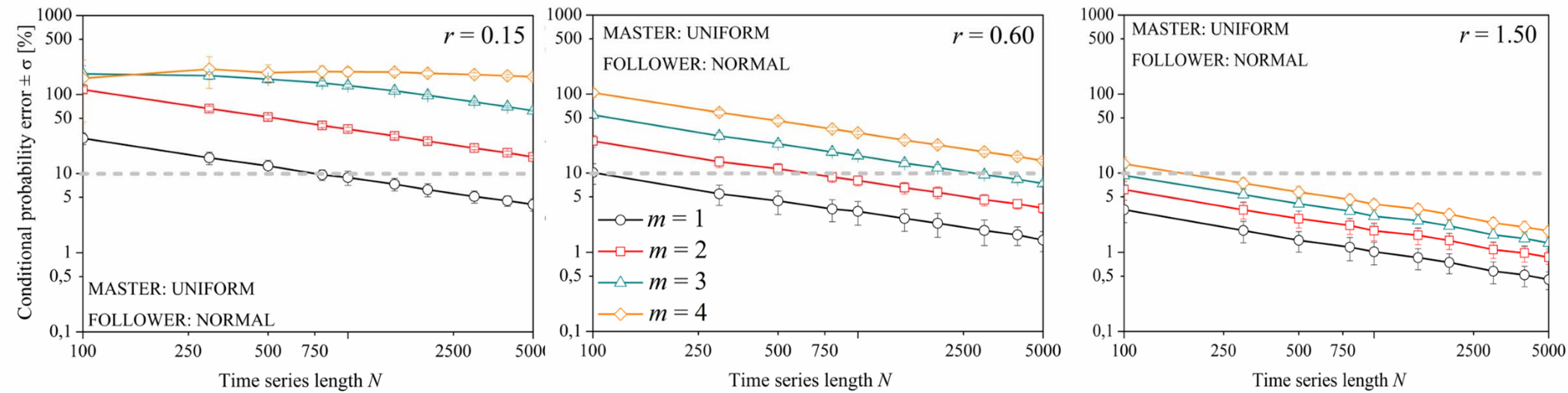
**Figure 3:** Conditional probability error [%] for a usual threshold value  $r = 0.15$  (left panel), higher threshold  $r=0.60$  (middle panel) and unusually high threshold  $r=1.50$  (right panel) ; gray dashed horizontal line marks 10% error; results are presented in a log-log plane as mean  $\pm \sigma$  (standard deviation).

**Figure 3:**  
MASTER: normal  
FOLLOWER: uniform



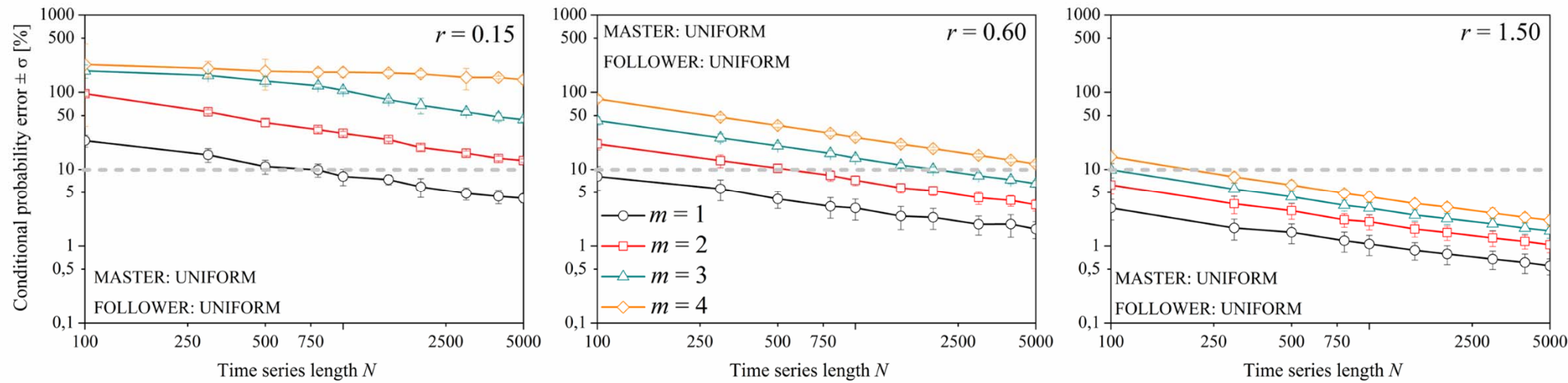
**Figure 3:** Conditional probability error [%] for a usual threshold value  $r = 0.15$  (left panel), higher threshold  $r=0.60$  (middle panel) and unusually high threshold  $r=1.50$  (right panel) ; gray dashed horizontal line marks 10% error; results are presented in a log-log plane as mean  $\pm \sigma$  (standard deviation).

**Figure 3:**  
MASTER: uniform  
FOLLOWER: normal



**Figure 3:** Conditional probability error [%] for a usual threshold value  $r = 0.15$  (left panel), higher threshold  $r=0.60$  (middle panel) and unusually high threshold  $r=1.50$  (right panel) ; gray dashed horizontal line marks 10% error; results are presented in a log-log plane as mean  $\pm \sigma$  (standard deviation).

**Figure 3:**  
MASTER: uniform  
FOLLOWER: uniform



**Figure 3:** Conditional probability error [%] for a usual threshold value  $r = 0.15$  (left panel), higher threshold  $r=0.60$  (middle panel) and unusually high threshold  $r=1.50$  (right panel) ; gray dashed horizontal line marks 10% error; results are presented in a log-log plane as mean  $\pm \sigma$  (standard deviation).

**X and Y normally distributed**

**Figure 4:** Percentage of probability estimates that fail to satisfy the criterion  $N-m+1 \geq 10/\text{probability [\%]}$ , presented in threshold-length ( $r$ - $N$ ) plane.

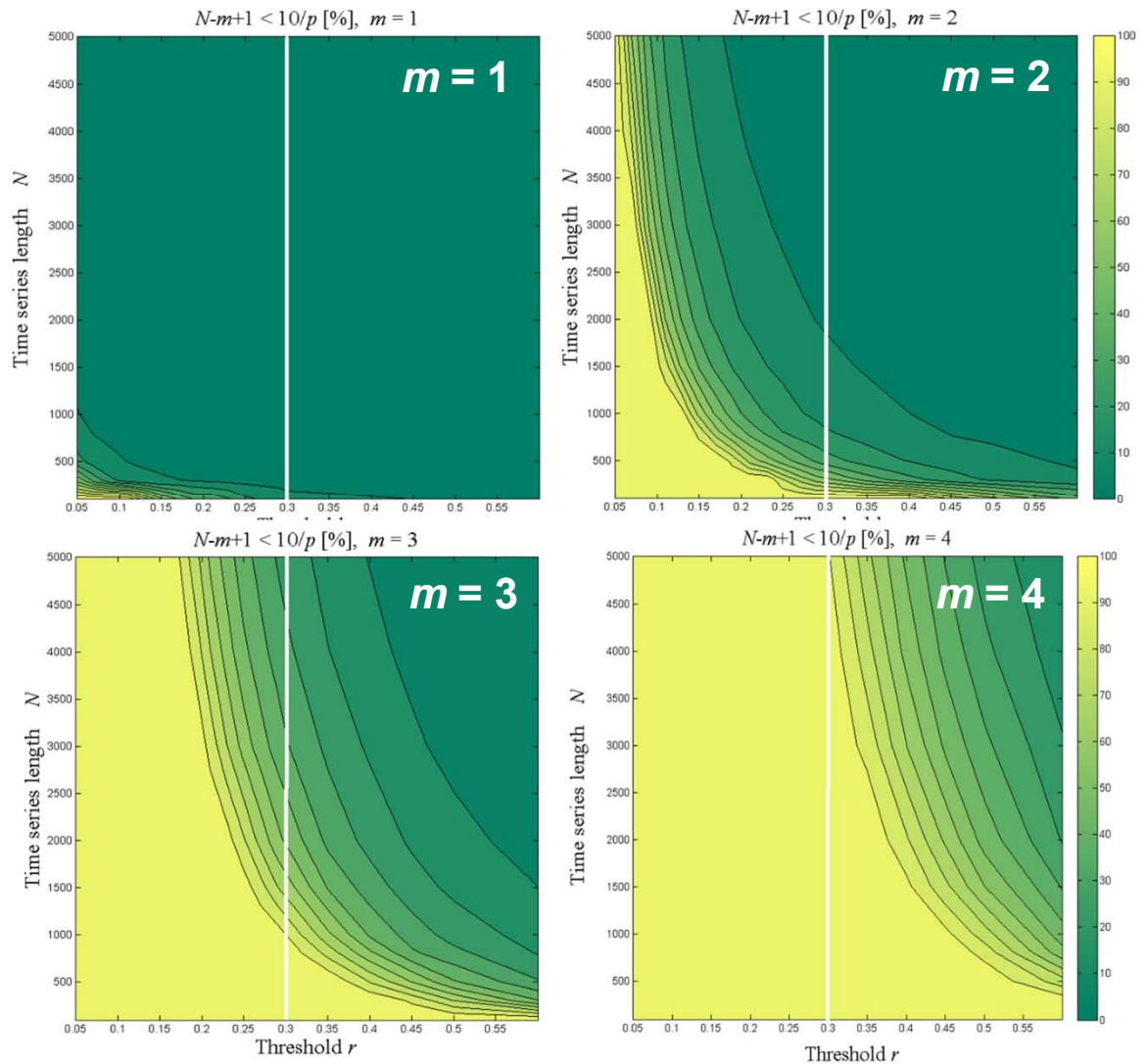
**X axis: threshold  $r$**

**Y axis: series length  $N$**

Panels correspond to  $m = 1, 2, 3, 4$

Failures are presented by color changes from green (0% failures) to yellow (100% failures);

White vertical line cuts each plane at threshold value  $r = 0.3$ .



X normally distributed, Y uniformly distributed

**Figure 4:** Percentage of probability estimates that fail to satisfy the criterion  $N-m+1 \geq 10/\text{probability} [\%]$ . presented in threshold-length ( $r$ - $N$ ) plane.

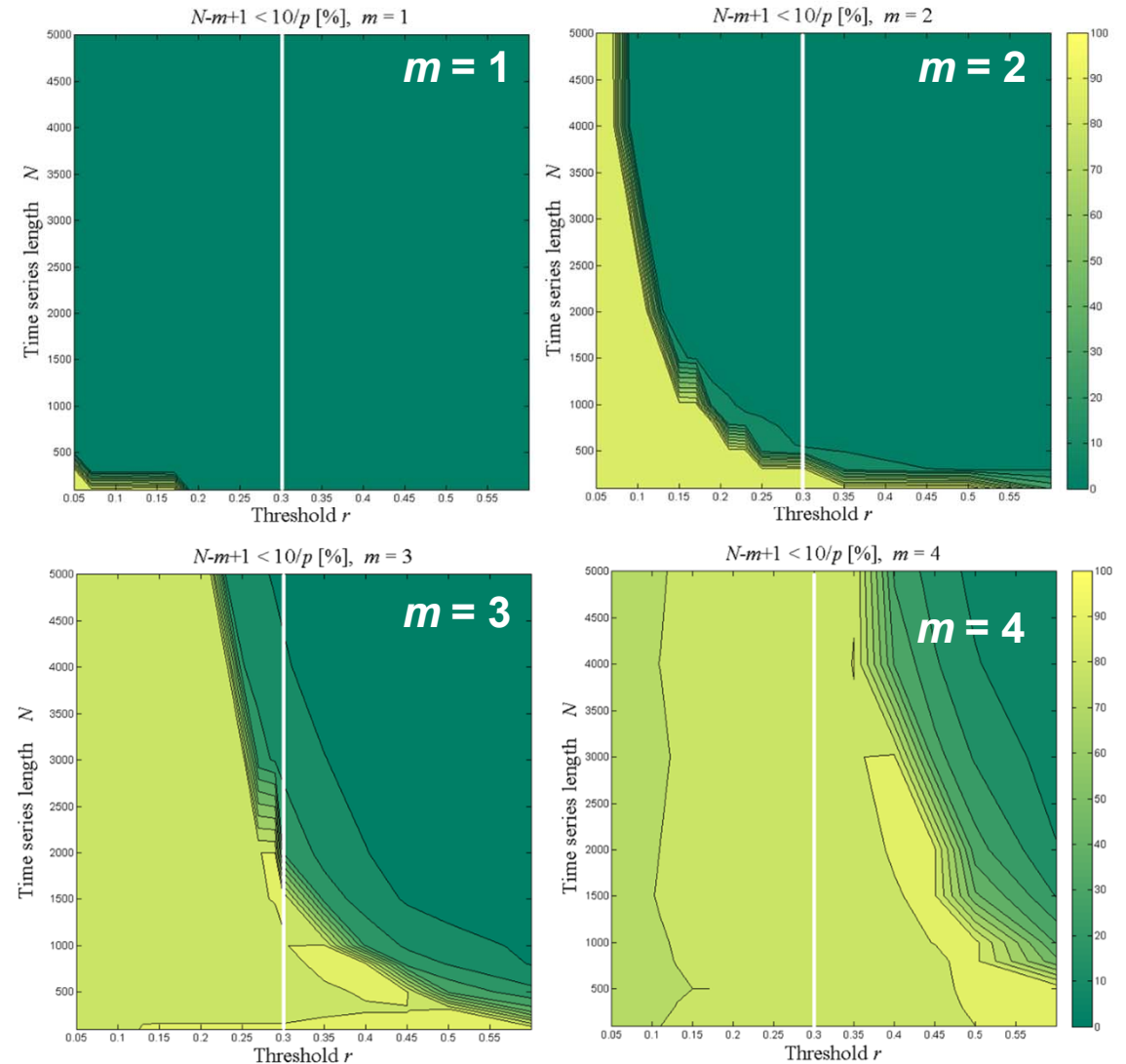
**X axis:** threshold  $r$

**Y axis:** series length  $N$

Panels correspond to  $m = 1, 2, 3, 4$

Failures are presented by color changes from green (0% failures) to yellow (100% failures);

White vertical line cuts each plane at threshold value  $r = 0.3$ .





X uniformly distributed, Y normally distributed

**Figure 4:** Percentage of probability estimates that fail to satisfy the criterion  $N-m+1 \geq 10/\text{probability [\%]}$ , presented in threshold-length ( $r$ - $N$ ) plane.

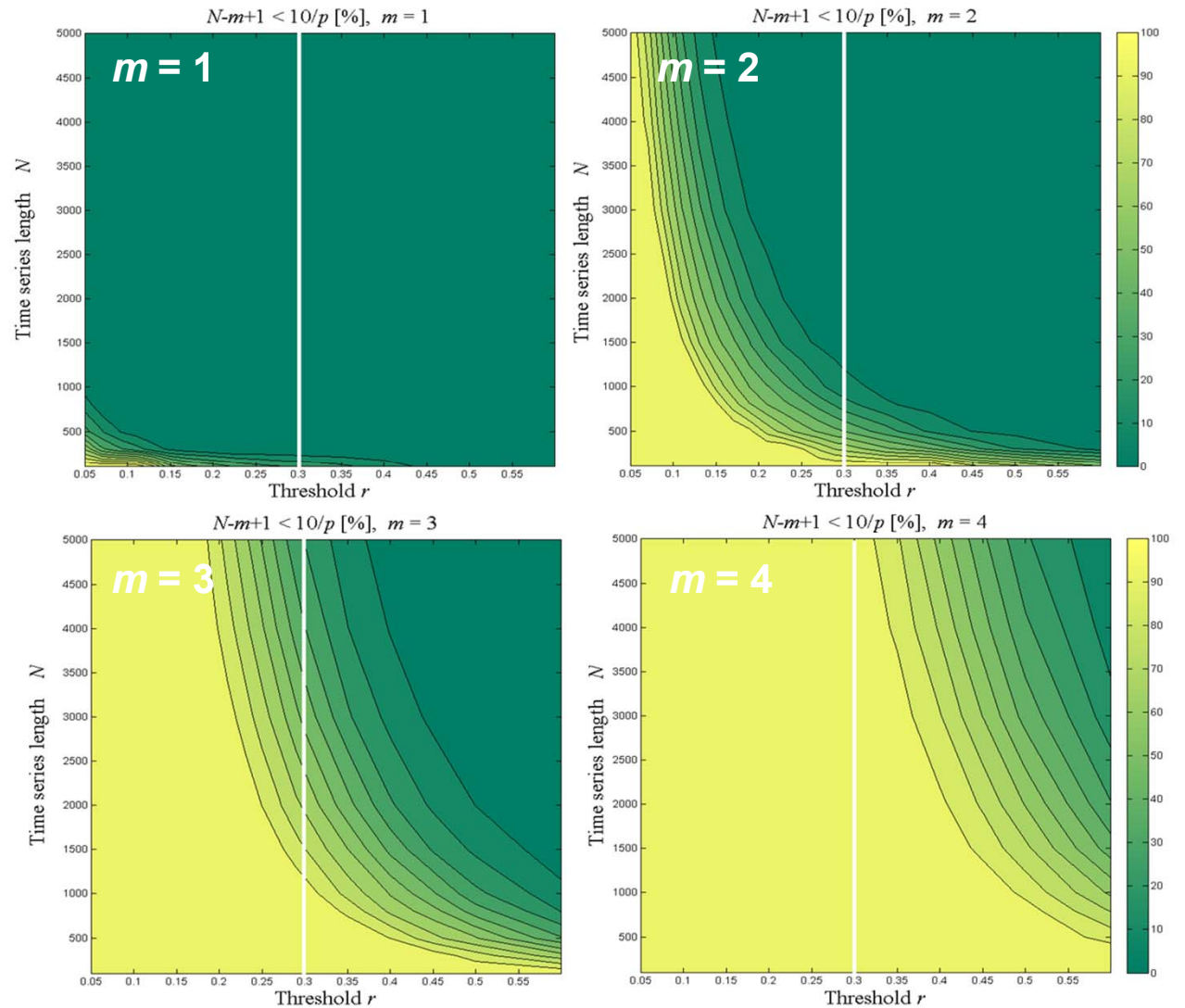
**X axis:** threshold  $r$

**Y axis:** series length  $N$

Panels correspond to  $m = 1, 2, 3, 4$

Failures are presented by color changes from green (0% failures) to yellow (100% failures);

White vertical line cuts each plane at threshold value  $r = 0.3$ .





**X and Y uniformly distributed**

**Figure 4:** Percentage of probability estimates that fail to satisfy the criterion  $N-m+1 \geq 10/\text{probability [\%]}$ . presented in threshold-length ( $r$ - $N$ ) plane.

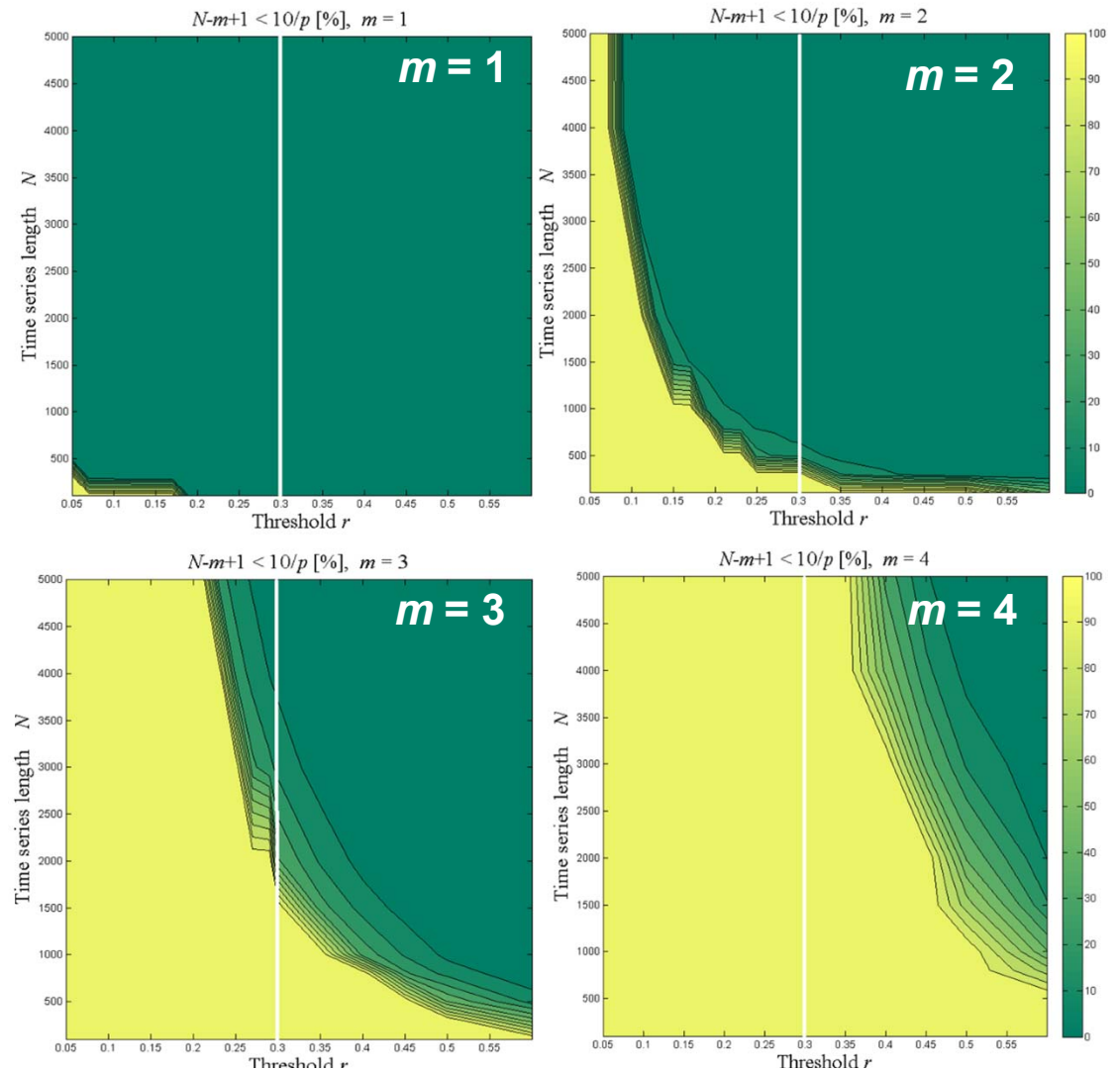
**X axis: threshold  $r$**

**Y axis: series length  $N$**

Panels correspond to  $m = 1, 2, 3, 4$

Failures are presented by color changes from green (0% failures) to yellow (100% failures);

White vertical line cuts each plane at threshold value  $r = 0.3$ .



**X and Y normally distributed**

**Figure 5:** Number of estimates for which probability = 0 in threshold-length ( $r$ - $N$ ) plane [%].

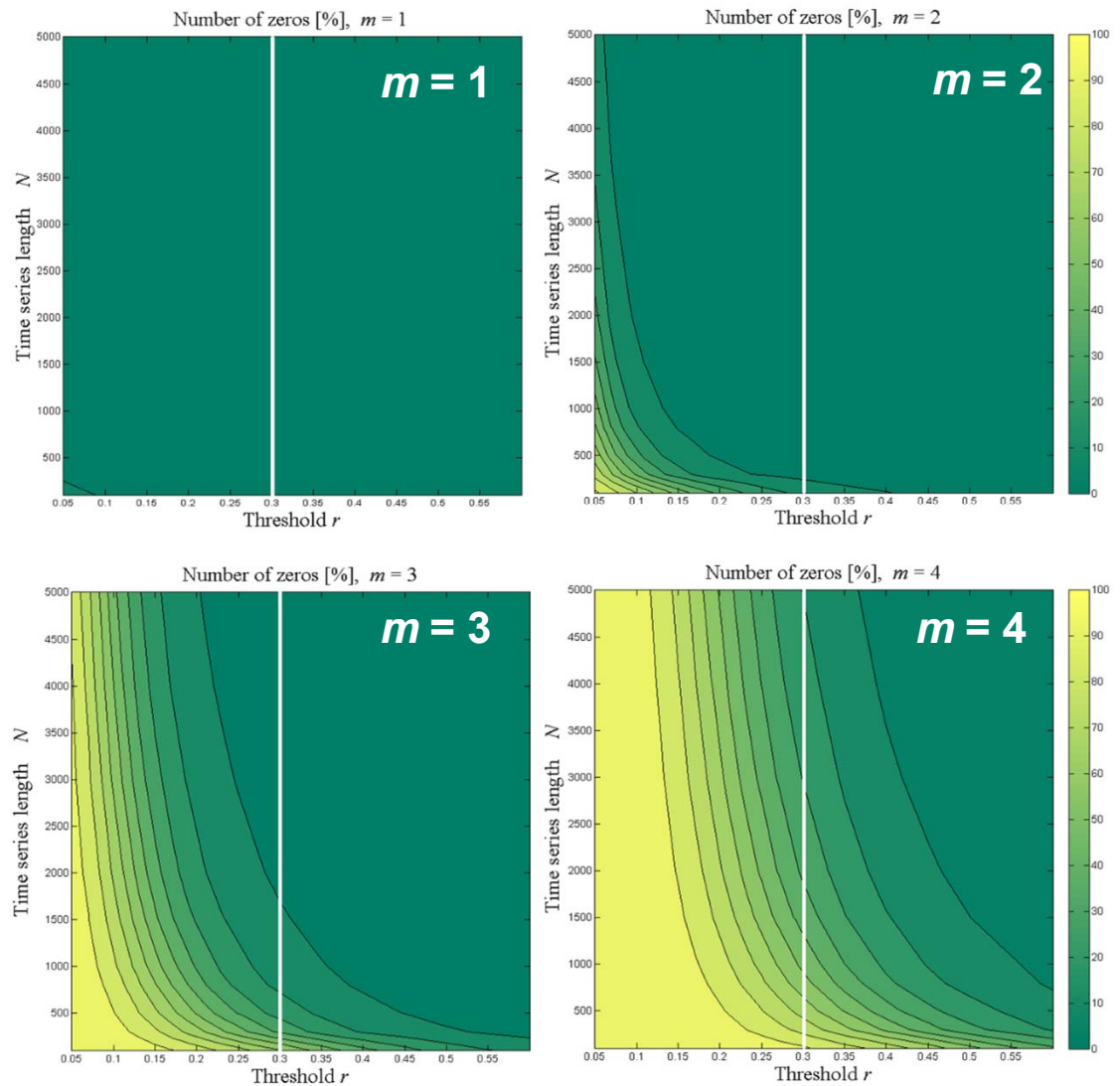
**X axis:** threshold  $r$

**Y axis:** series length  $N$

Panels correspond to  $m = 1, 2, 3, 4$

Number of zero estimates is presented by color changes from green (0% zero estimates) to yellow (100% zero estimates);

White vertical line cuts each plane at threshold value  $r = 0.3$ .



X normally distributed, Y uniformly distributed

**Figure 5:** Number of estimates for which probability = 0 in threshold-length ( $r$ - $N$ ) plane [%].

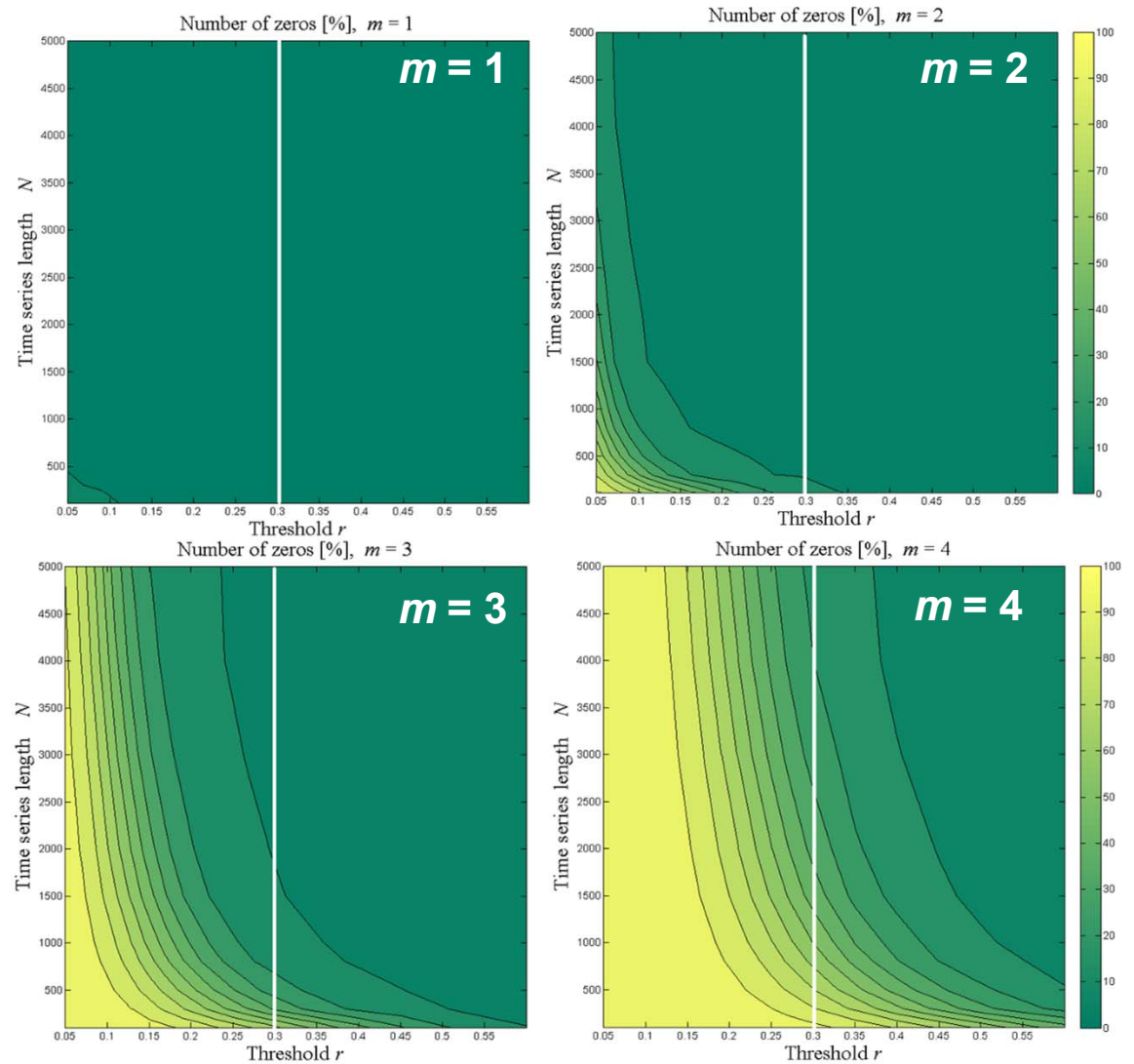
**X axis:** threshold  $r$

**Y axis:** series length  $N$

Panels correspond to  $m = 1, 2, 3, 4$

Number of zero estimates is presented by color changes from green (0% zero estimates) to yellow (100% zero estimates);

White vertical line cuts each plane at threshold value  $r = 0.3$ .



X uniformly distributed, Y normally distributed

**Figure 5:** Number of estimates for which probability = 0 in threshold-length ( $r$ - $N$ ) plane [%].

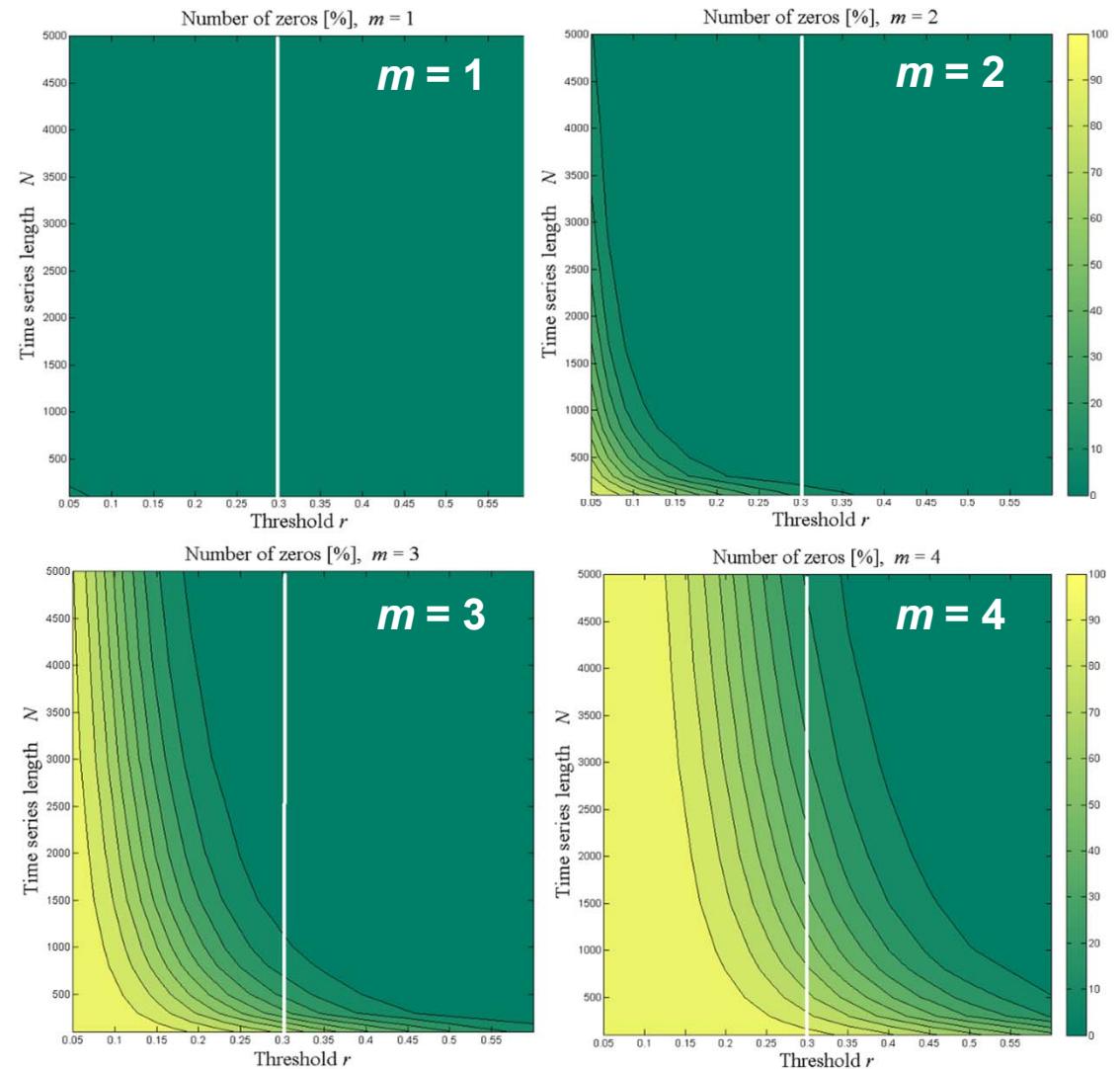
**X axis:** threshold  $r$

**Y axis:** series length  $N$

Panels correspond to  $m = 1, 2, 3, 4$

Number of zero estimates is presented by color changes from green (0% zero estimates) to yellow (100% zero estimates);

White vertical line cuts each plane at threshold value  $r = 0.3$ .



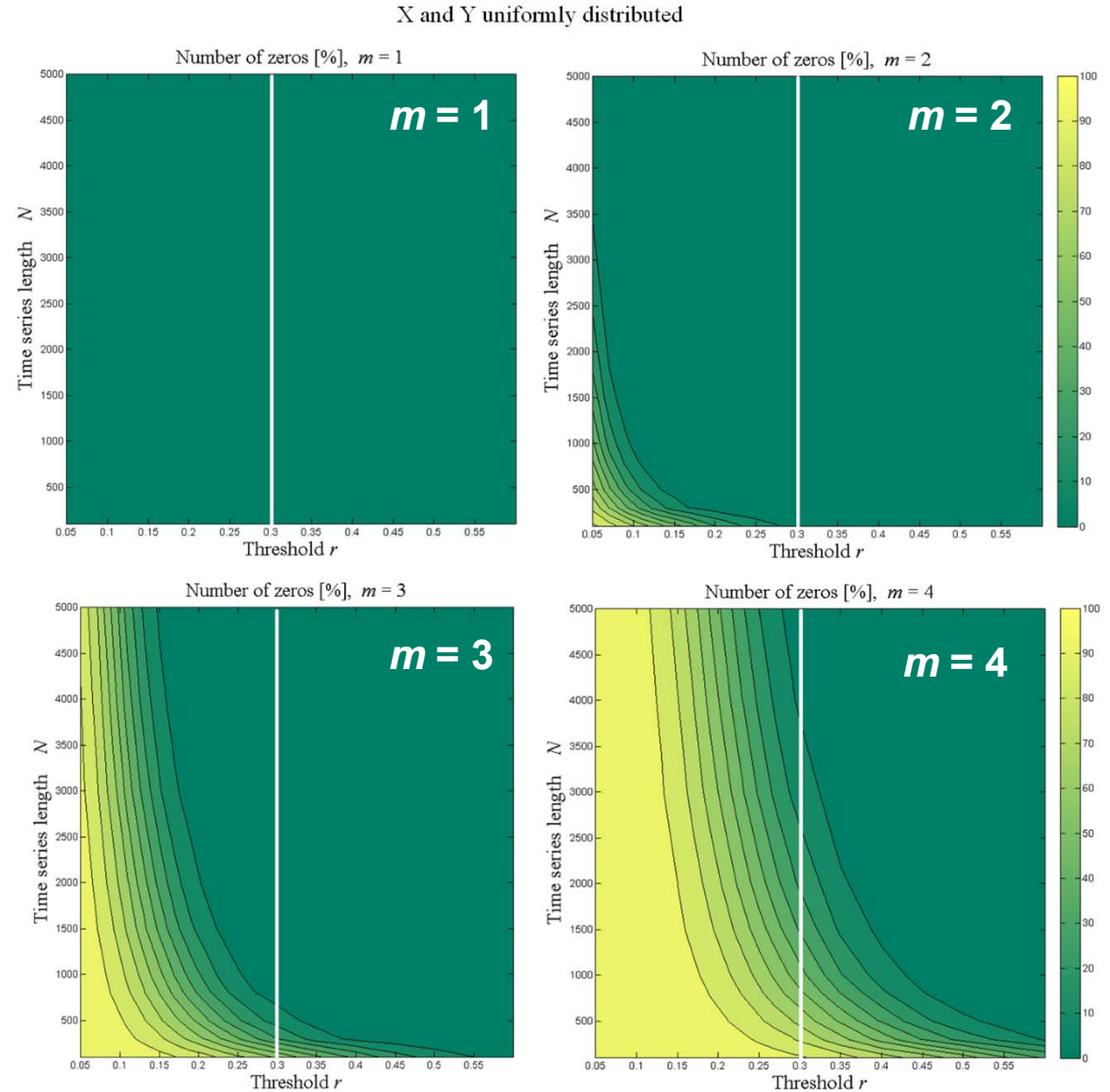
**Figure 5:** Number of estimates for which probability = 0 in threshold-length ( $r$ - $N$ ) plane [%].

**X axis:** threshold  $r$   
**Y axis:** series length  $N$

Panels correspond to  $m = 1, 2, 3, 4$

Number of zero estimates is presented by color changes from green (0% zero estimates) to yellow (100% zero estimates);

White vertical line cuts each plane at threshold value  $r = 0.3$ .



**Procedure for *XApEn* estimation**  
**- A BRIEF EXPLANATION -**



### ● STEP 1: Pre-processing

Each one of time series in study should comprise the same number of data points  $N$  ( $N < \text{length of the shortest recorded signal}$ ).

As for any analysis, all data series have to be examined in order to remove the artifacts.

Slow trend (occurring in moving patients and in freely moving laboratory animals) should be removed. We use a filter targeted for cardiovascular signals [25].

[25] M.P. Tarvainen, P.O. Ranta-aho, P.A. Karjalainen, "An advanced detrending approach with application to HRV analysis," *IEEE Trans. Biomed. Eng.*, vol. 42, no. 2, pp. 172–174, Feb., 2002.

After the detrendization, the time series have to be wide sense stationary. It can be checked by software or, as some researchers prefer, it can be checked visually.

### ● STEP 2: Standard scoring

Estimate mean and standard deviation of each time series (already of length  $N$  and without the trend and artifacts). For the  $i^{\text{th}}$  time series  $\mathbf{X}_i$ , with mean  $m_i$  and standard deviation  $\sigma_i$ , get the series with mean 0 and standard deviation 1 as follows:

$\mathbf{X}_{si} = (\mathbf{X}_i - m_i) / \sigma_i$ , meaning that from each sample its mean  $m_i$  should be subtracted, and the result divided by  $\sigma_i$ .

### ● STEP 3: Threshold calculation for maximal *ApEn*:

Chose which signal would be master (e.g.  $\mathbf{X}$  = SBP), and which signal would be its follower (e.g.  $\mathbf{Y}$  = PI). Form a differential time series of master signal,  $x_D(i) = x(i+1) - x(i)$ ,  $i = 1, \dots, N-1$ . Find a standard deviation  $\sigma_{DX}$  of differential time series  $\mathbf{X}_D$ . Chose a vector length  $m$  (2 or 3). Calculate theoretical threshold  $r_{\text{TH-A}}$  of **master** time series  $\mathbf{X}$  using equations (19).

$$r_{\text{TH-A}}(m) = \frac{e(m) + f(m) \cdot \sqrt{\sigma_{DX} / \sigma}}{\sqrt[4]{N/1000}}, \quad \sigma = 1, \quad (e, f) = \begin{cases} (-0.01, 0.05), & m = 1 \\ (-0.02, 0.23), & m = 2 \\ (-0.06, 0.43), & m = 3 \\ (-0.11, 0.65), & m = 4 \end{cases}$$



• **STEP 4: Threshold calculation for maximal *XApEn*:**

Form a differential time series of follower signal,  $y_D(i) = y(i+1) - y(i)$ ,  $i = 1, \dots, N-1$ . Find a standard deviation  $\sigma_{DY}$  of differential time series  $\mathbf{Y}_D$ . Calculate theoretical threshold  $r_{TH-X}$  of **master** time series  $\mathbf{X}$  using equations (18).

$$r_{TH-X}(m) = r_{TH-A}(m) + \left| a(m) + \frac{b(m) + c(m) \cdot \sqrt{(\sigma_{DX} + \sigma_{DY})/2}}{\sqrt[4]{N/1000}} \right|, \quad (a, b, c) = \begin{cases} (0, -0.015, 0.03), & m=1 \\ (-0.02, 0, 0.023), & m=2 \\ (0, -0.006, 0.043), & m=3 \\ (0, -0.11, 0.13), & m=4 \end{cases}$$

• **STEP 5: Thresholds calculation for reliable *XApEn* estimation:**

Calculate threshold  $r_{XW}$  that would be used as a parameter for *XApEn* estimation using Equation (20) that ensures a fulfillment of weak reliability criteria (preferred).

$$\begin{aligned} r_{XW}(m) &= 0.2 \cdot (m+1) + r_{TH-X}(m), & m \leq 4, N \leq 500, \\ r_{XW}(m) &= 0.17 \cdot (m+1) + r_{TH-X}(m), & m \leq 4, 500 < N \leq 2000, \\ r_{XW}(m) &= 0.15 \cdot (m+1) + r_{TH-X}(m), & m \leq 4, N > 2000 \end{aligned}$$

If signals are very long, strong reliability criteria might be used. Then the threshold should be calculated using Equation (21):

$$r_{XS}(m) = (m + 1 + 10^5 / N^2) \cdot (r_{TH-X}(m) + (5 - m)/10), \quad m \leq 4.$$

• **STEP 5: *XApEn* estimation:**

Estimate *XApEn* using  $N$  and  $m$  as chosen parameters, and threshold  $r_{XW}$  (or  $r_{XS}$  if applicable) as calculated parameter.