ARIbrain - Valid circular inference for fMRI analysis

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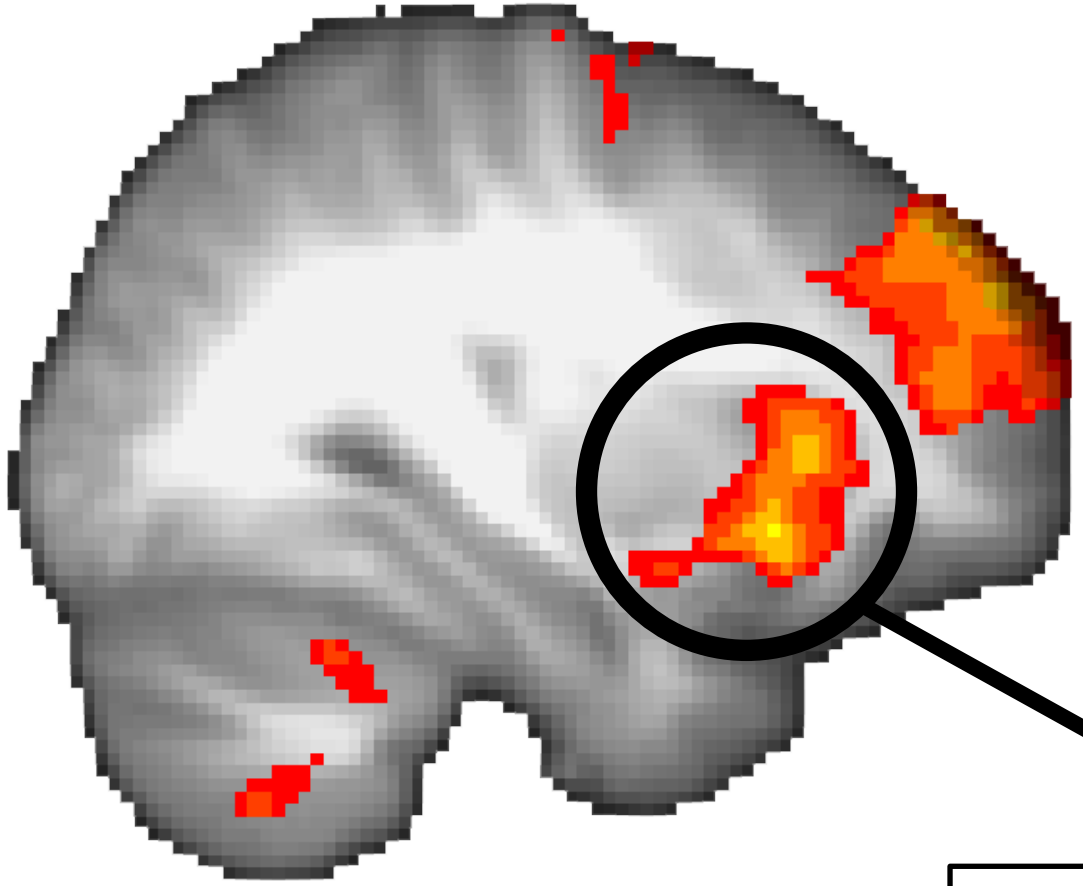
Thanks to:

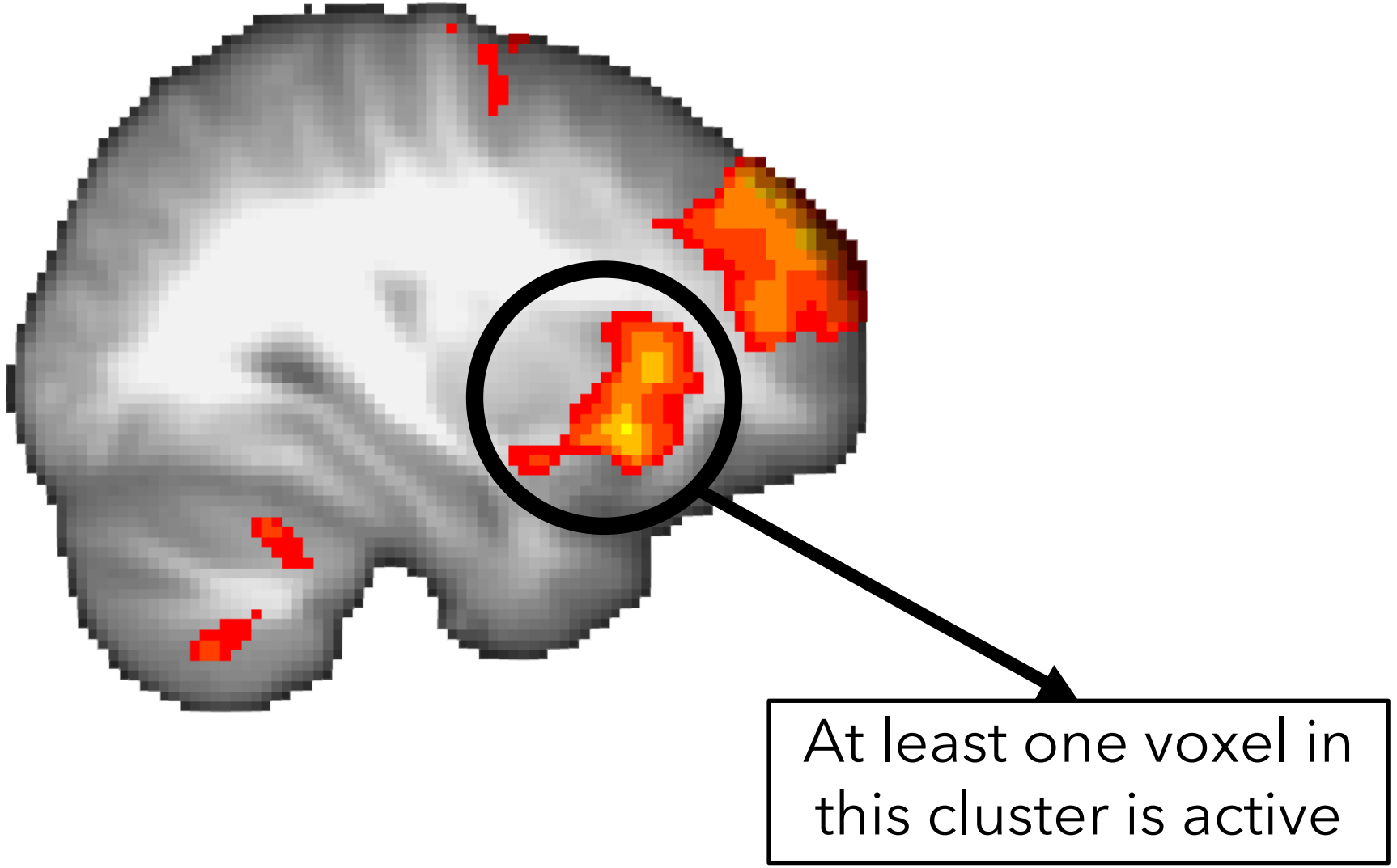
Xu Chen
Martha van Kempen
Jonathan Rosenblatt
Livio Finos
Aldo Solari
Jelle Goeman

fMRI cluster inference



~~All voxels in this cluster are active~~

fMRI cluster inference



Spatial specificity paradox

"The larger the cluster we find, the less we know about activity within that cluster."

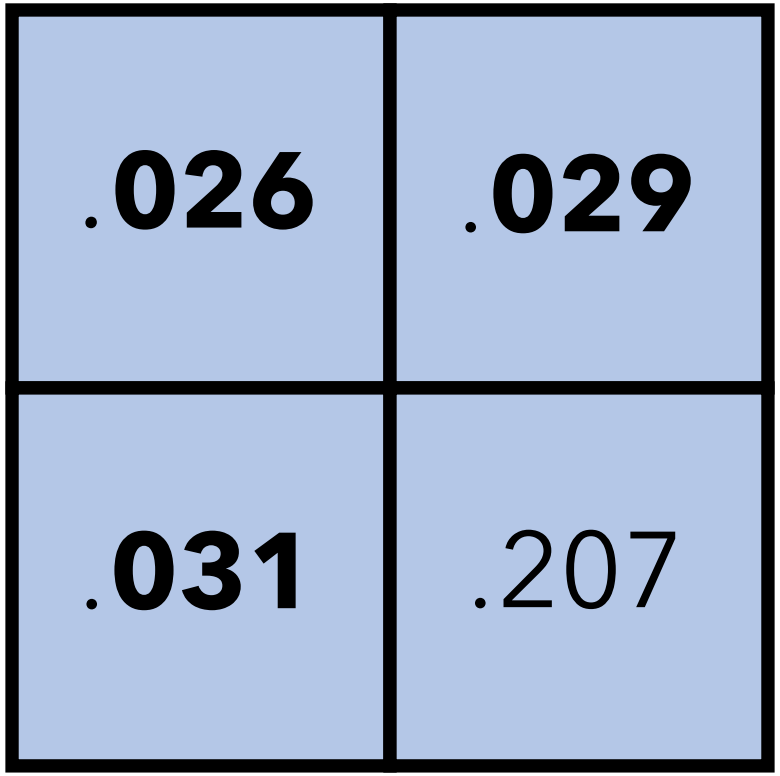
Goal

- Increase the spatial specificity of cluster inference by:
  - Estimating the number of truly active voxels of a cluster
  - For any cluster, as many times as you want.
  - With Familywise Error (FWE) control

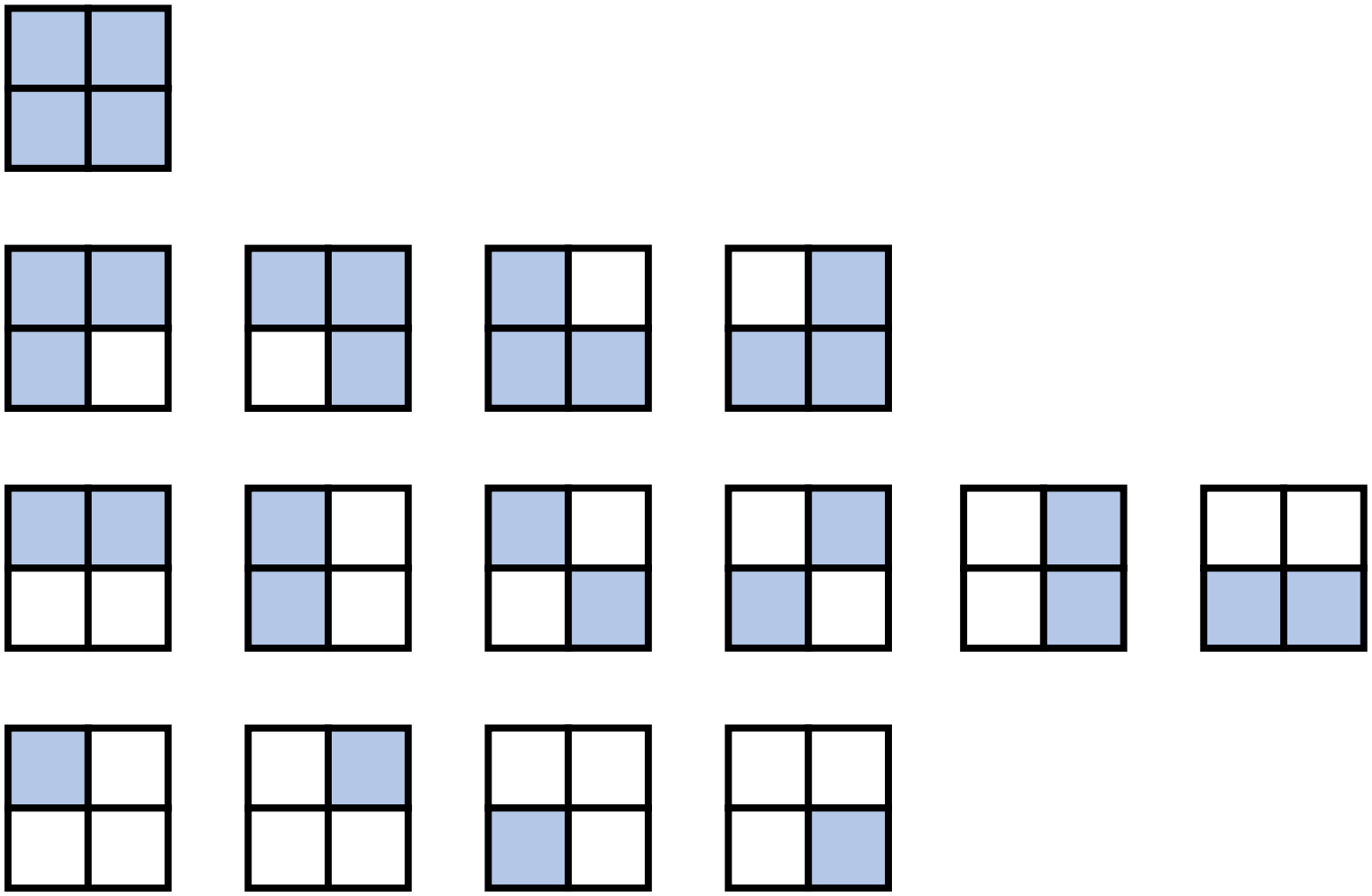
How?

- In of stead asking:
  - Give us a dataset, and we'll tell you which regions are active.
- We ask:
  - Give us a region, and we'll tell you how much activity is in there.

The four voxel brain



The four voxel brain - subsets



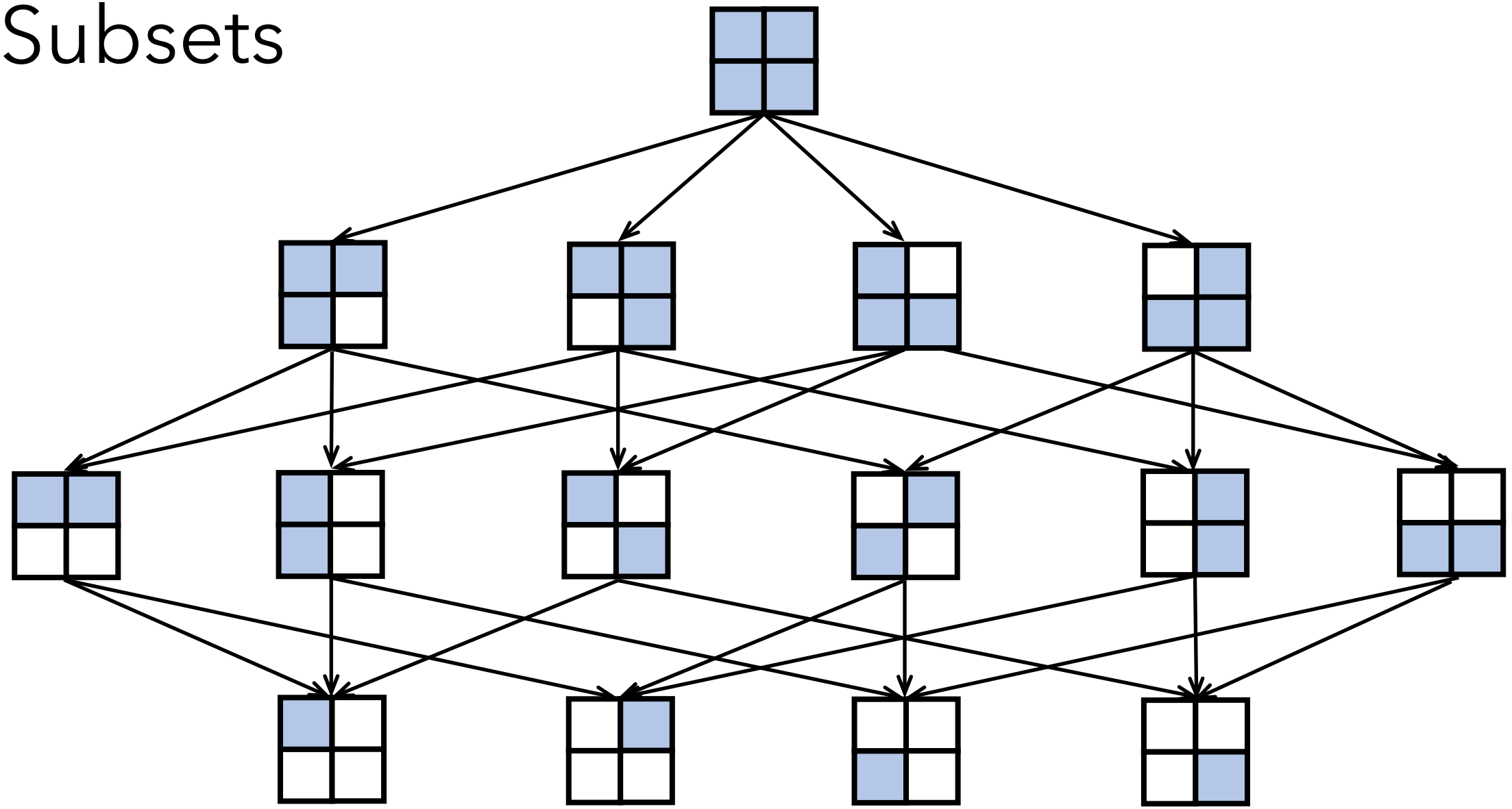
4 voxels set

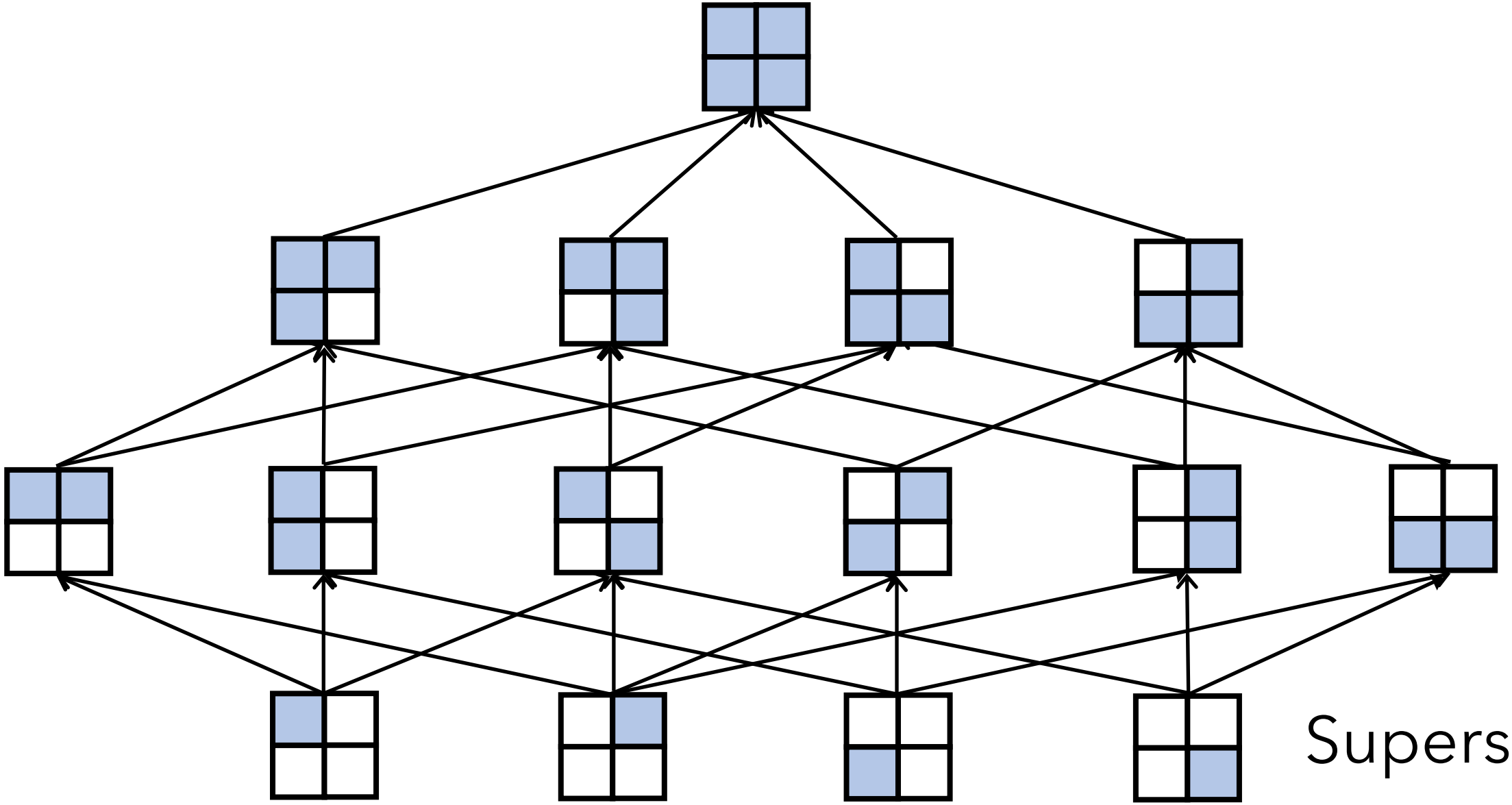
3 voxels sets

2 voxels sets

1 voxel sets

Subsets




Supersets

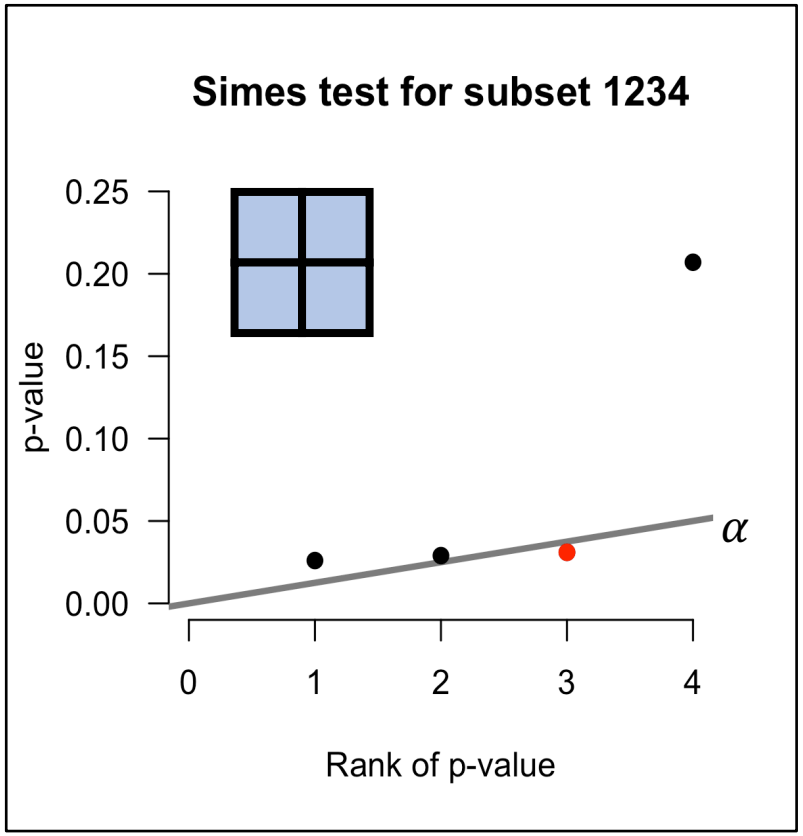
Simes test

Is there at least one active voxel in subset S?

$$H_s: a(S) = 0$$

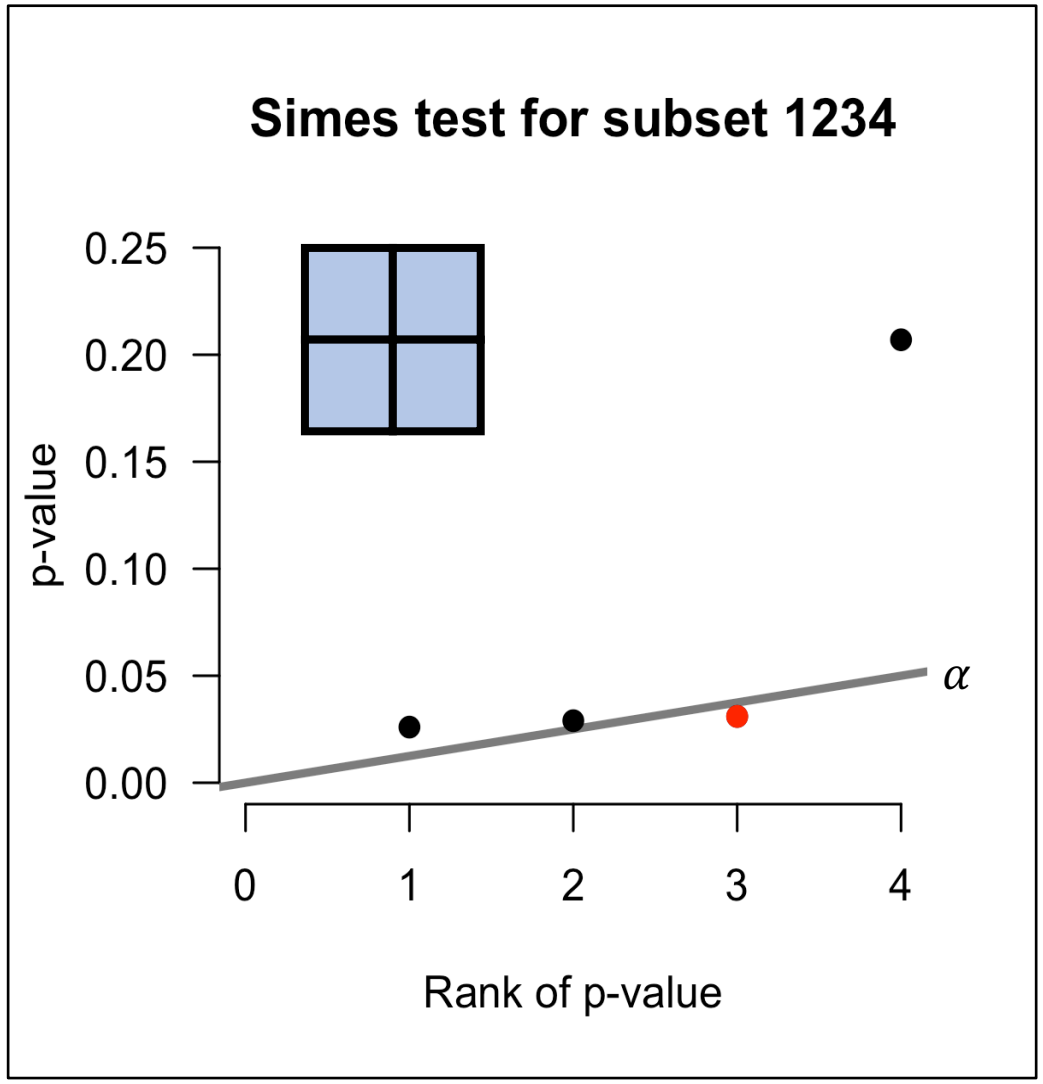
$$p_s = min\left\{\frac{|S|}{i} p(i:S), \text{with } 1 \leq i \leq |S|\right\}$$

Reject H_s if $p_s \leq \alpha$.

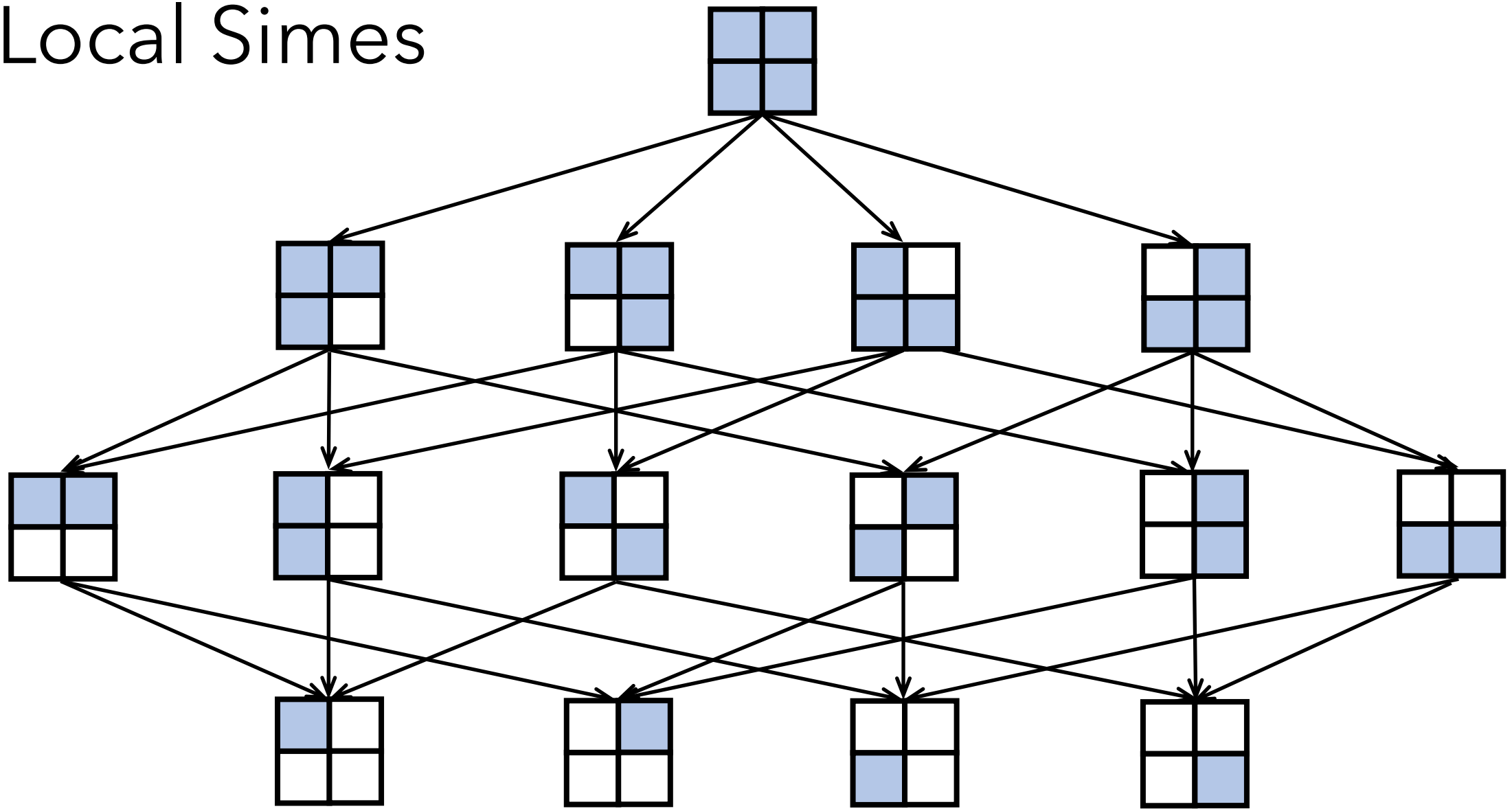


Simes test

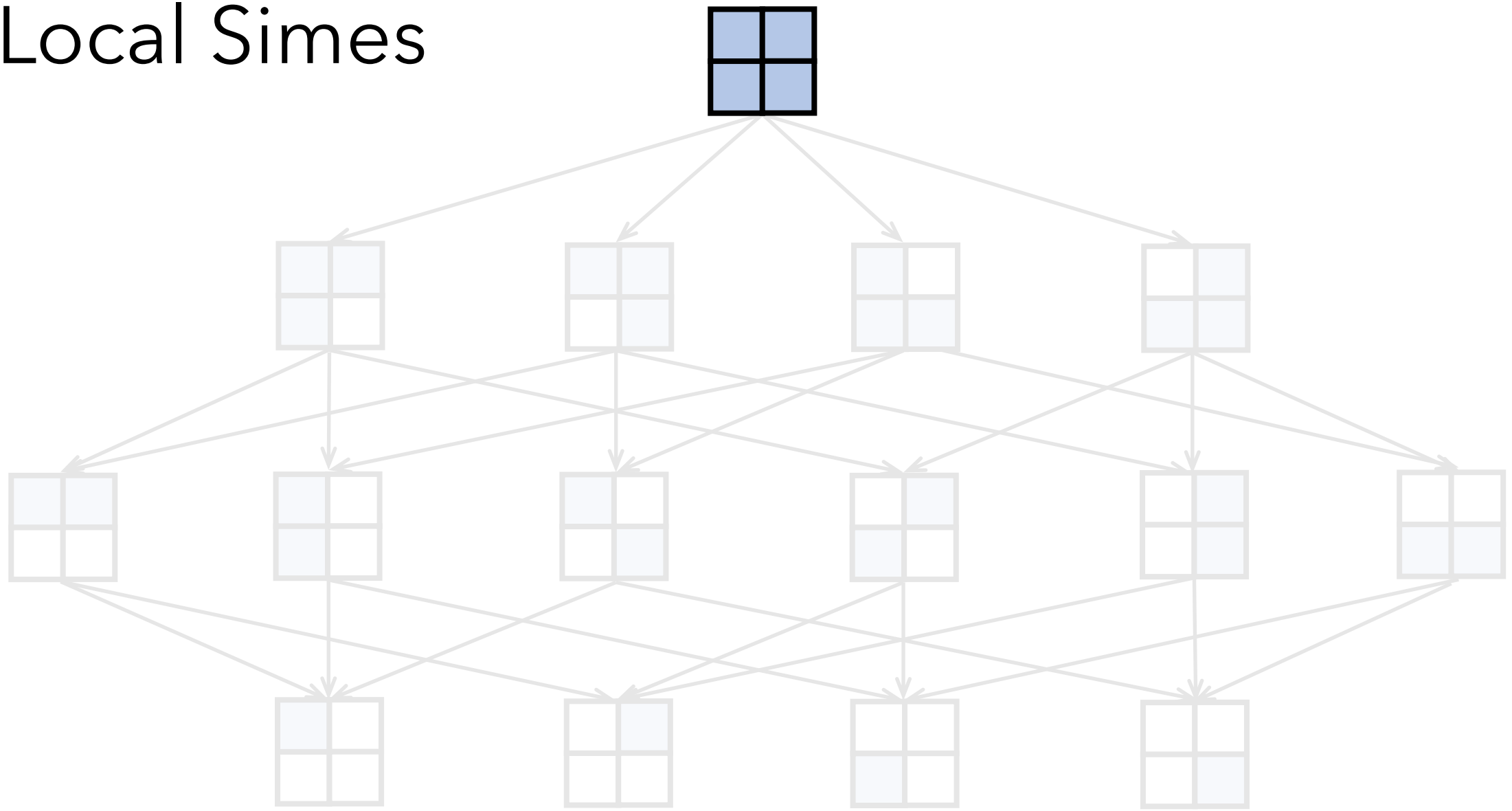
- Order p-values from smallest to largest.
- Draw a line from 0 to alpha.
- Is there any point below the line?



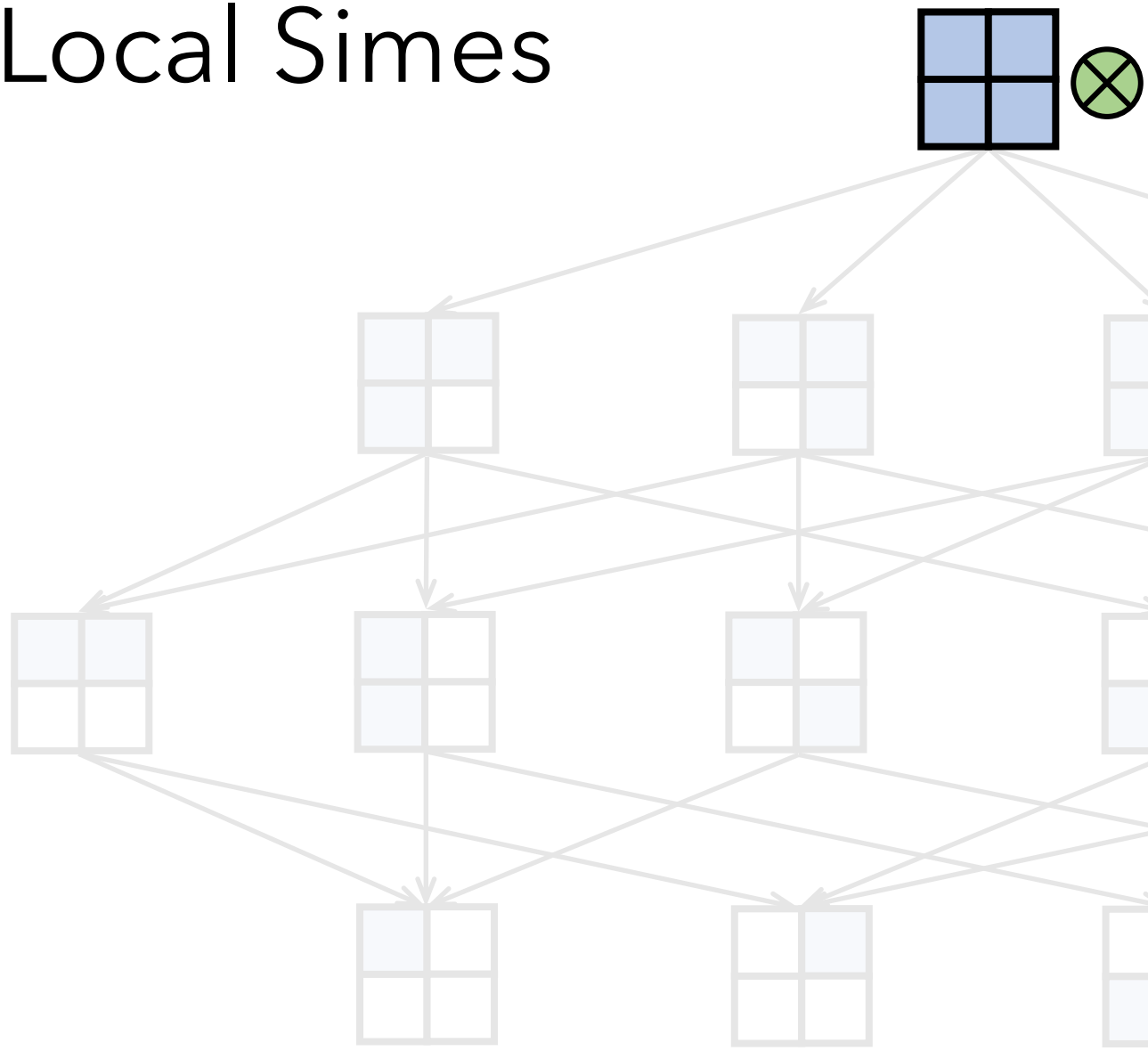
Local Simes

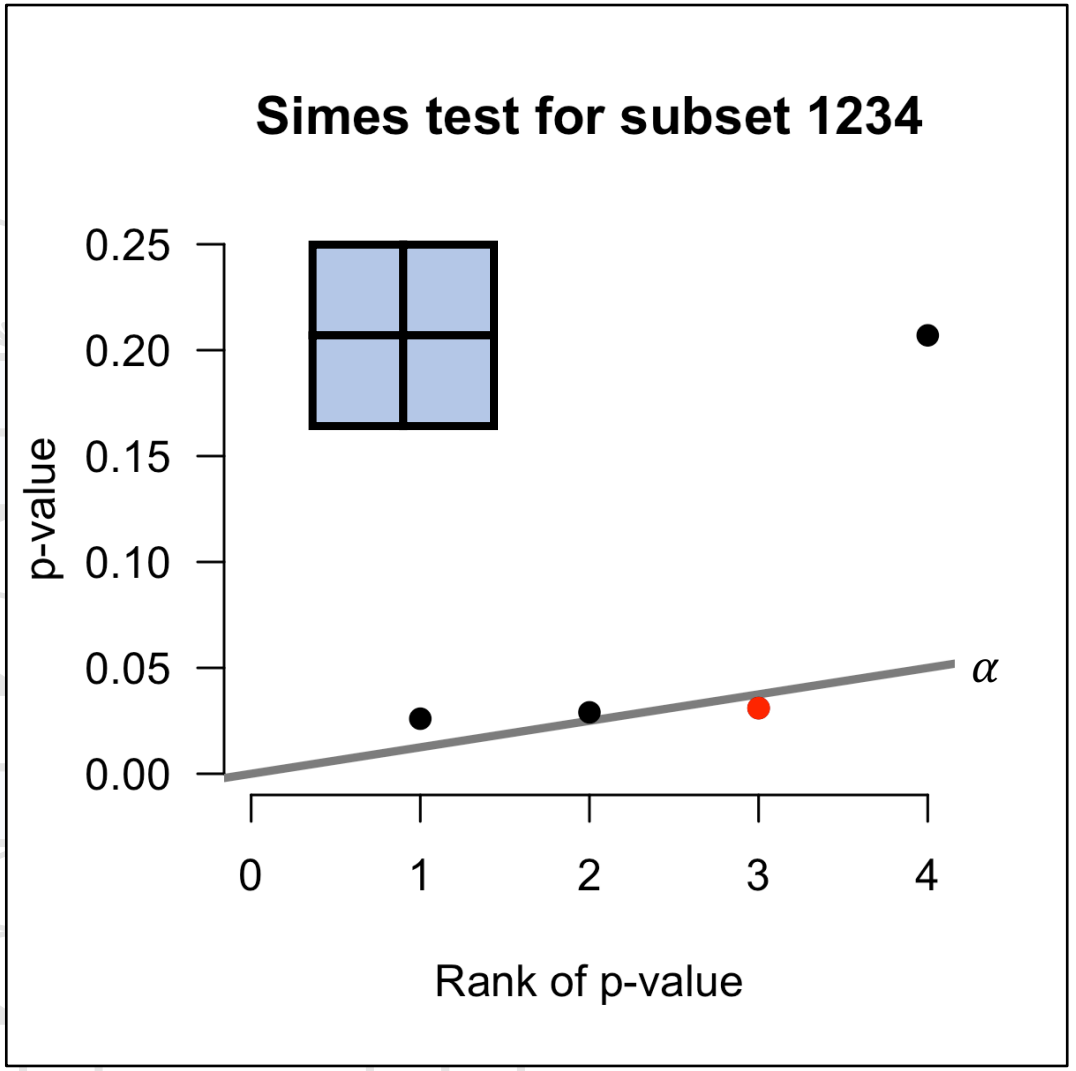


Local Simes

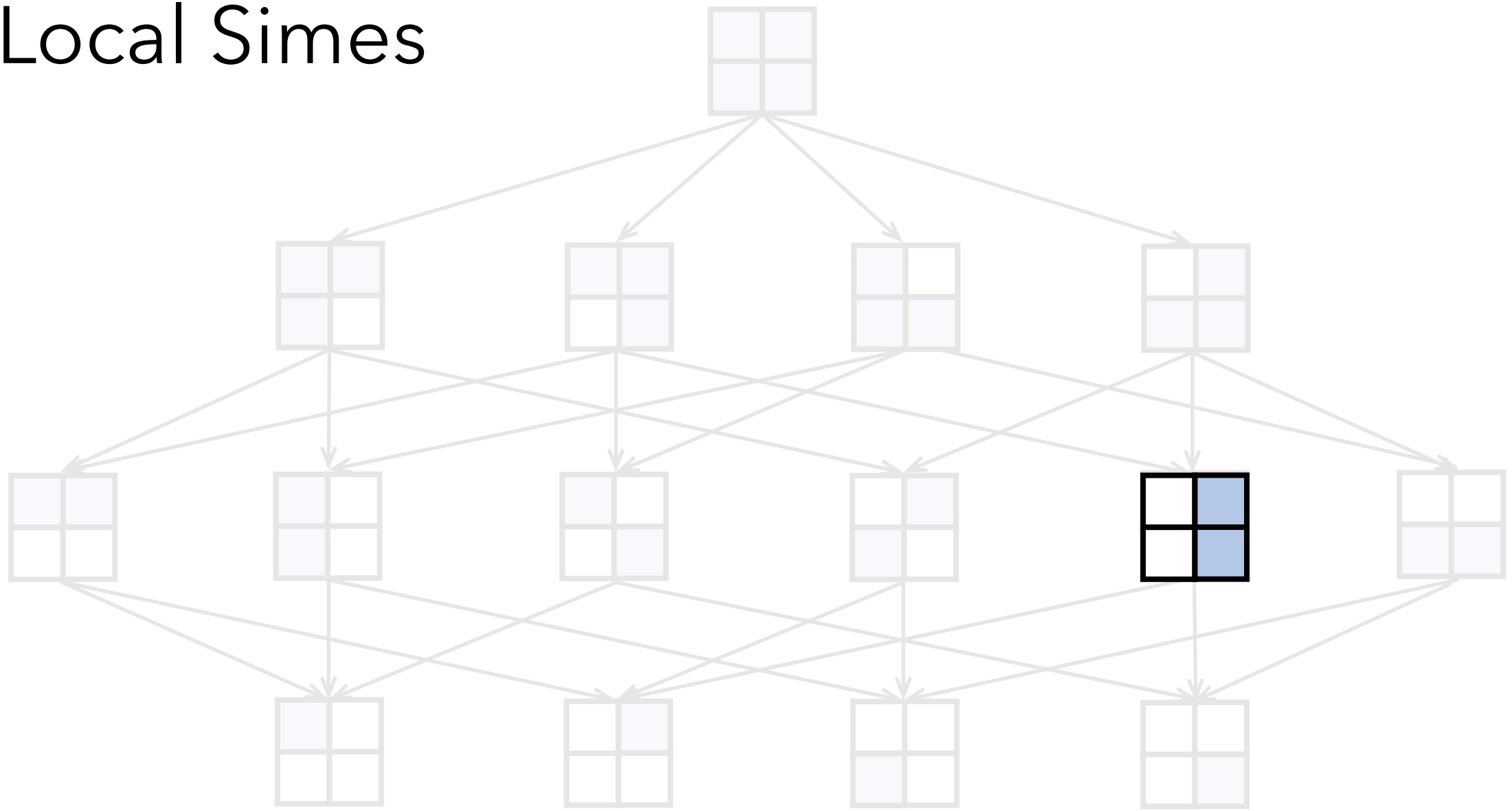


Local Simes

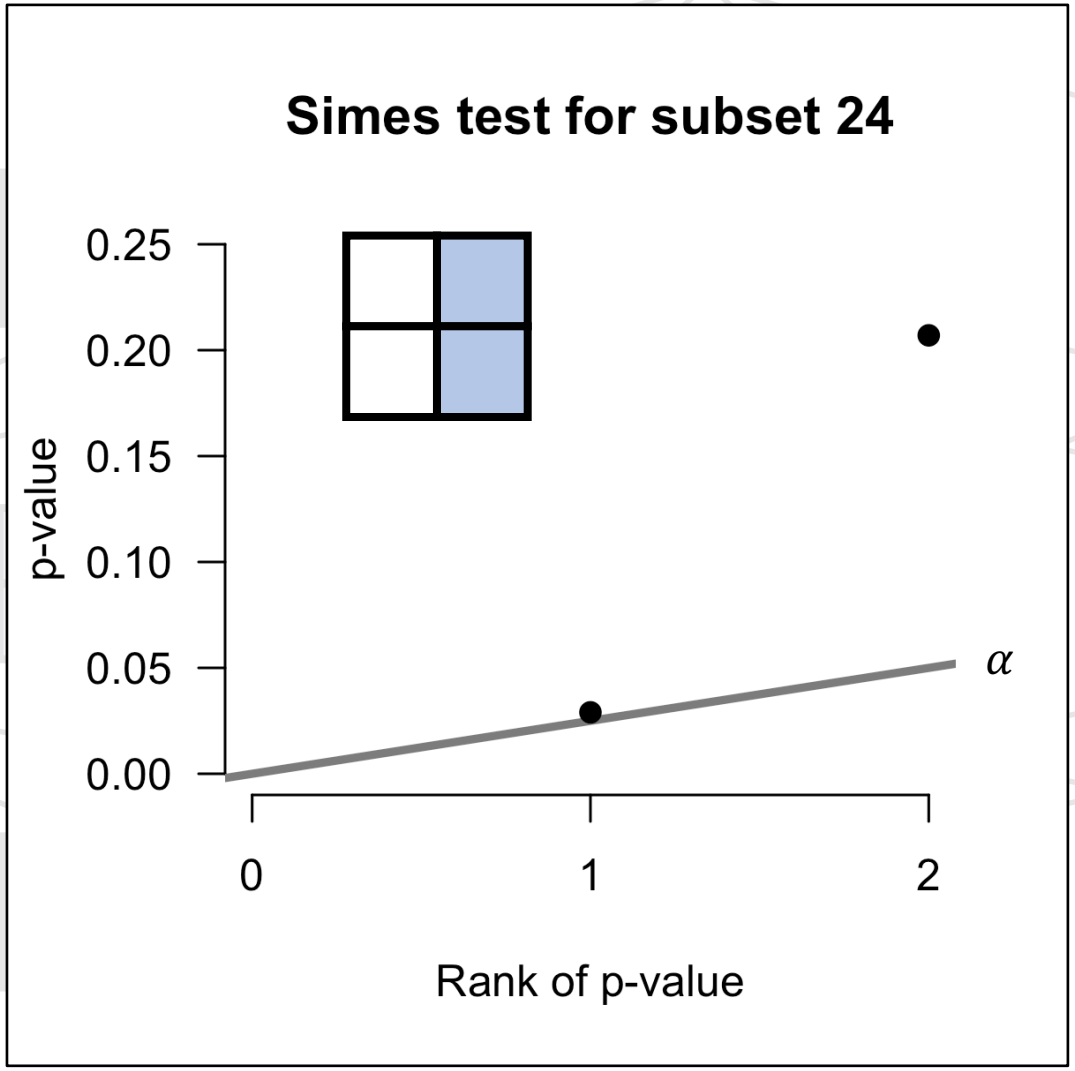



Simes test for subset 1234
0.25
0.20
0.15
0.10
0.05
0.00
p-value
α
0
1
2
3
4
Rank of p-value

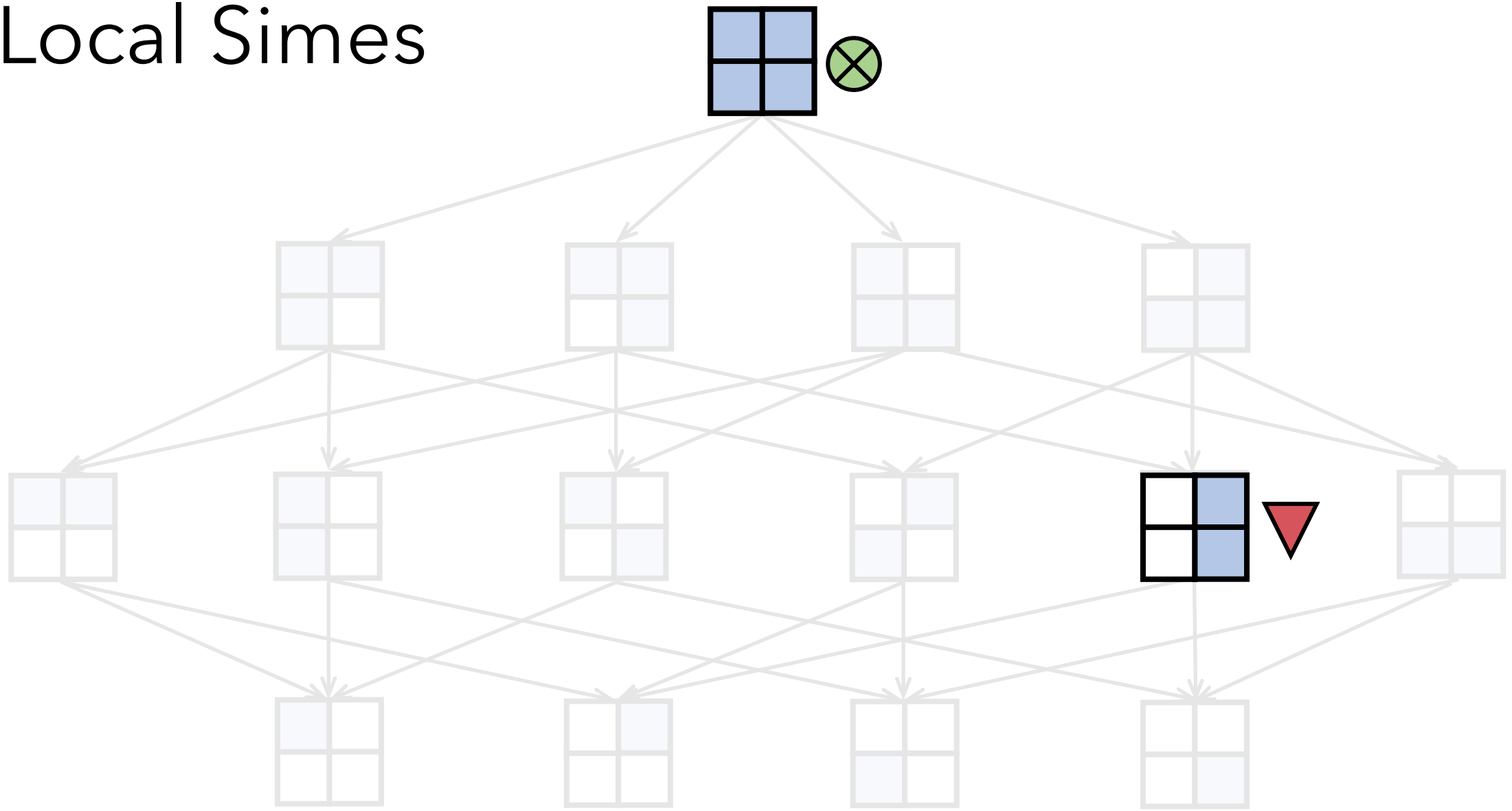
Local Simes



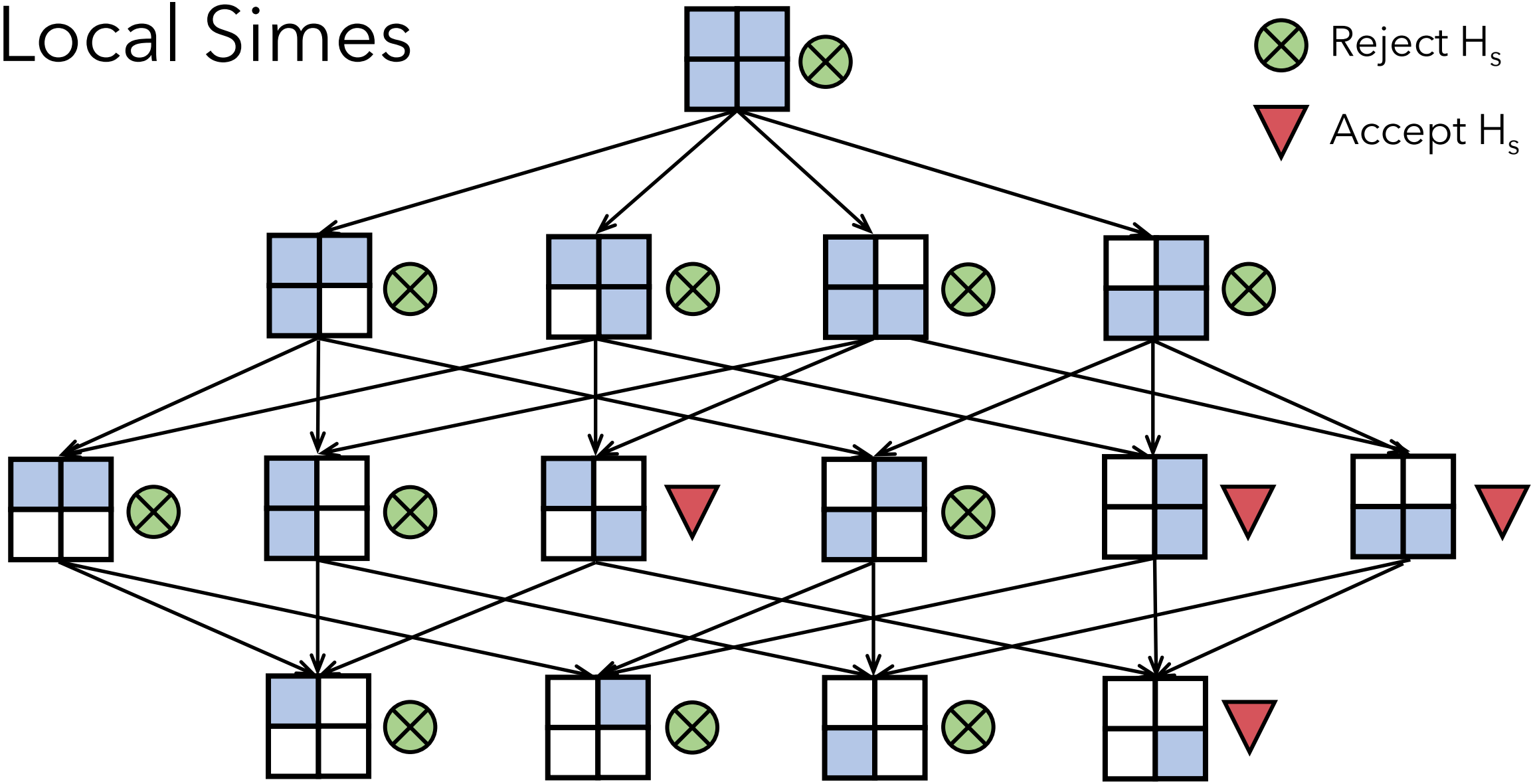
Local Simes


Simes test for subset 24
0.25
0.20
0.15
0.10
0.05
0.00
p-value
α
0
1
2
Rank of p-value

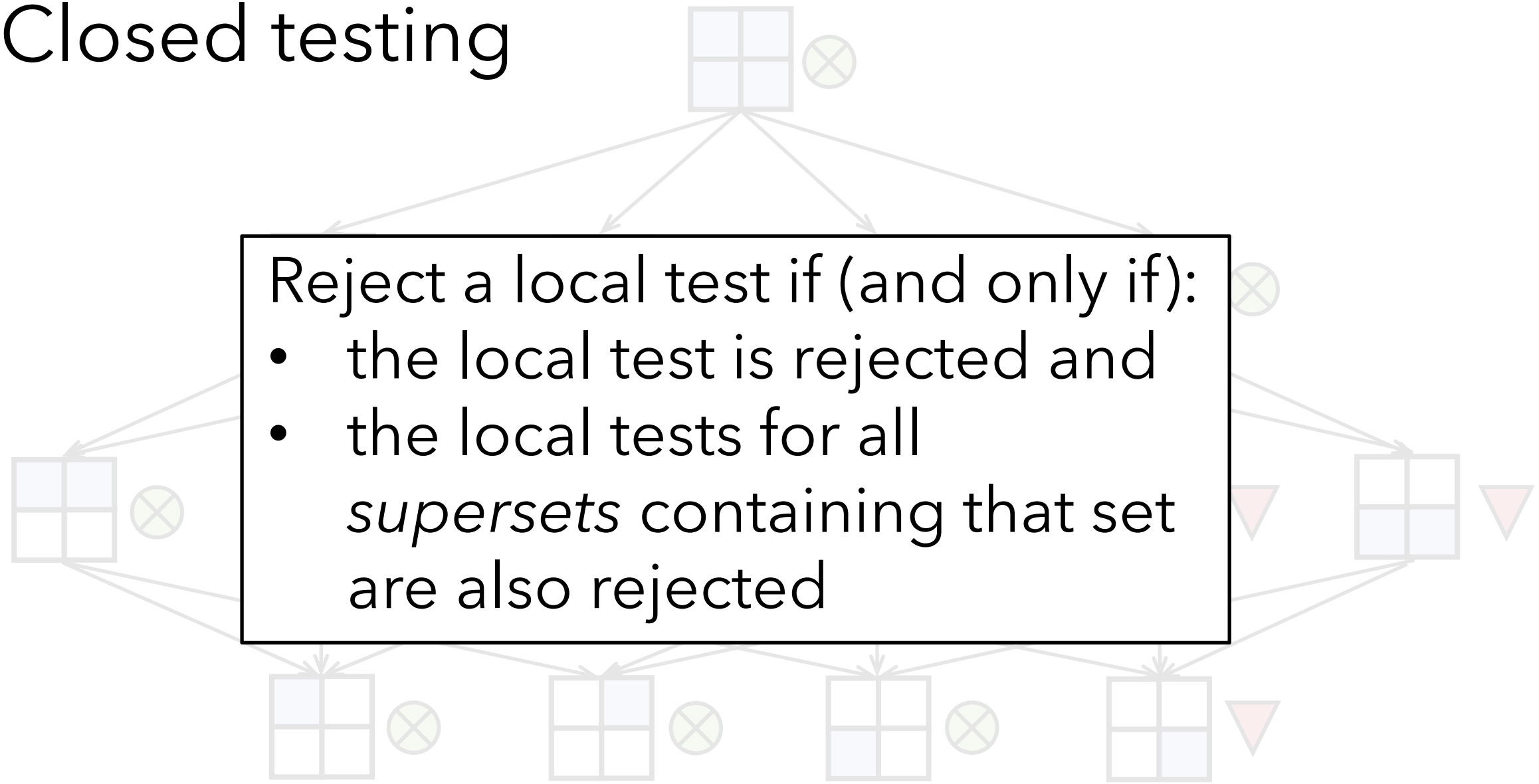
Local Simes



Local Simes



Closed testing

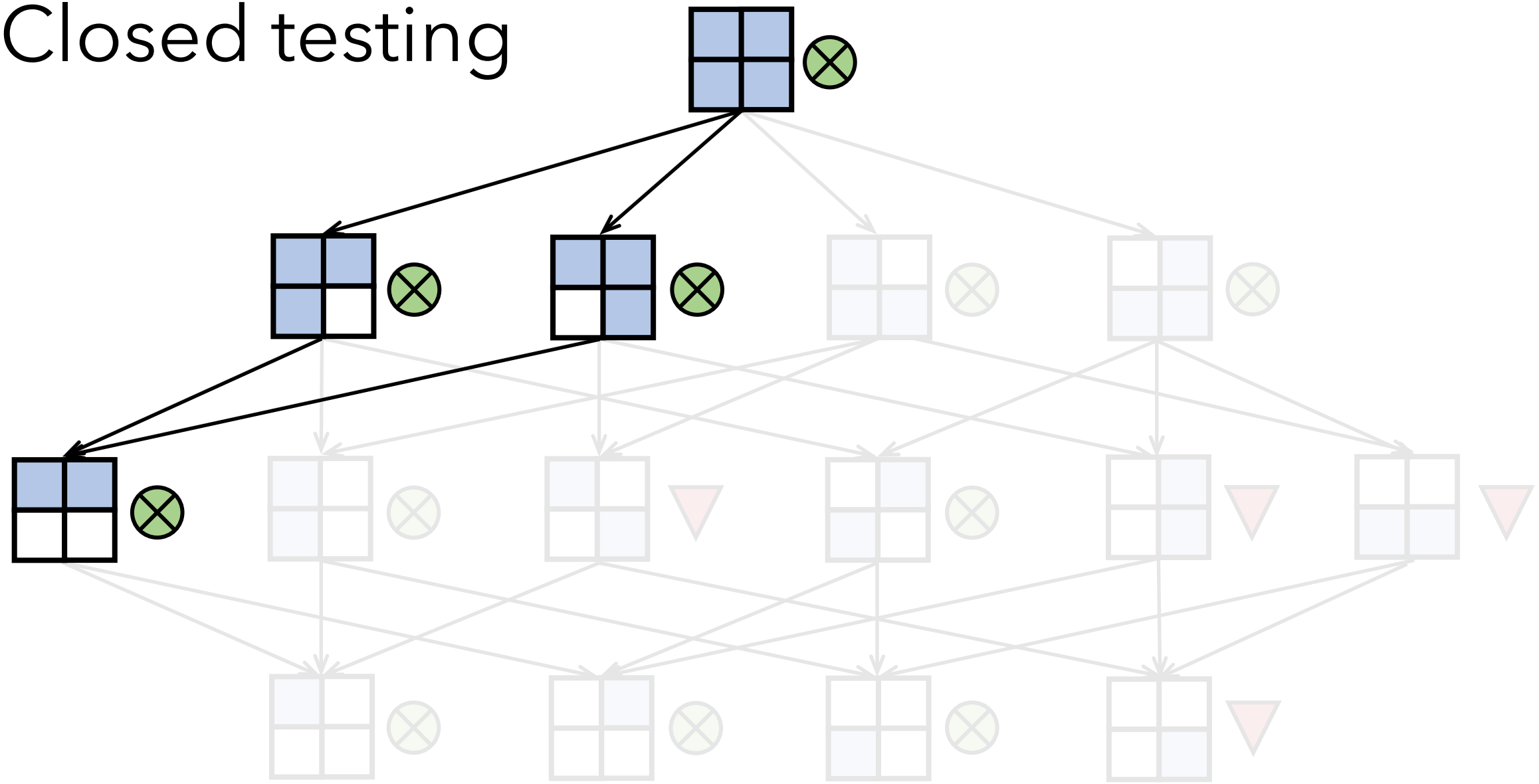


Reject a local test if (and only if):

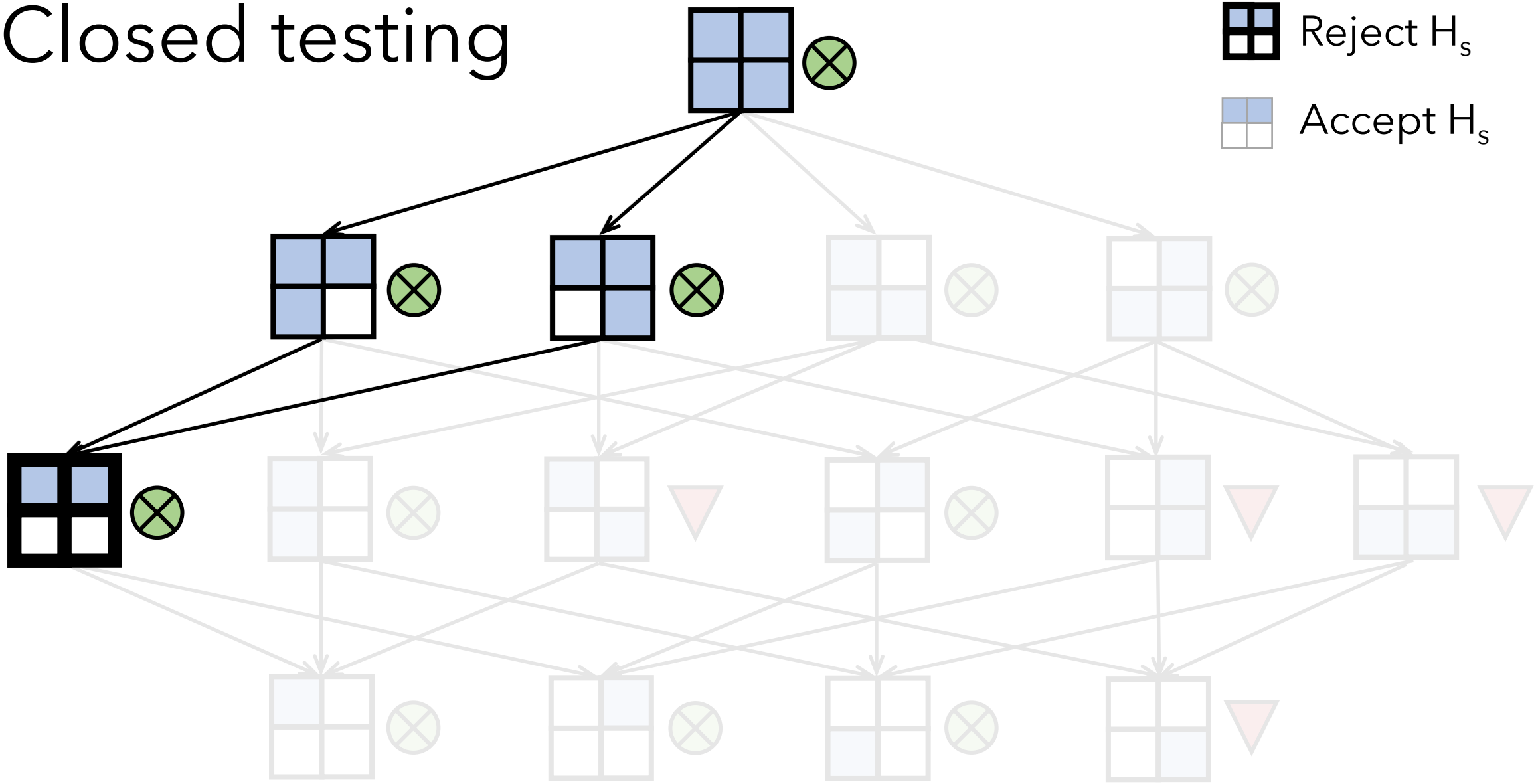
- the local test is rejected and
- the local tests for all *supersets* containing that set are also rejected

Closed testing

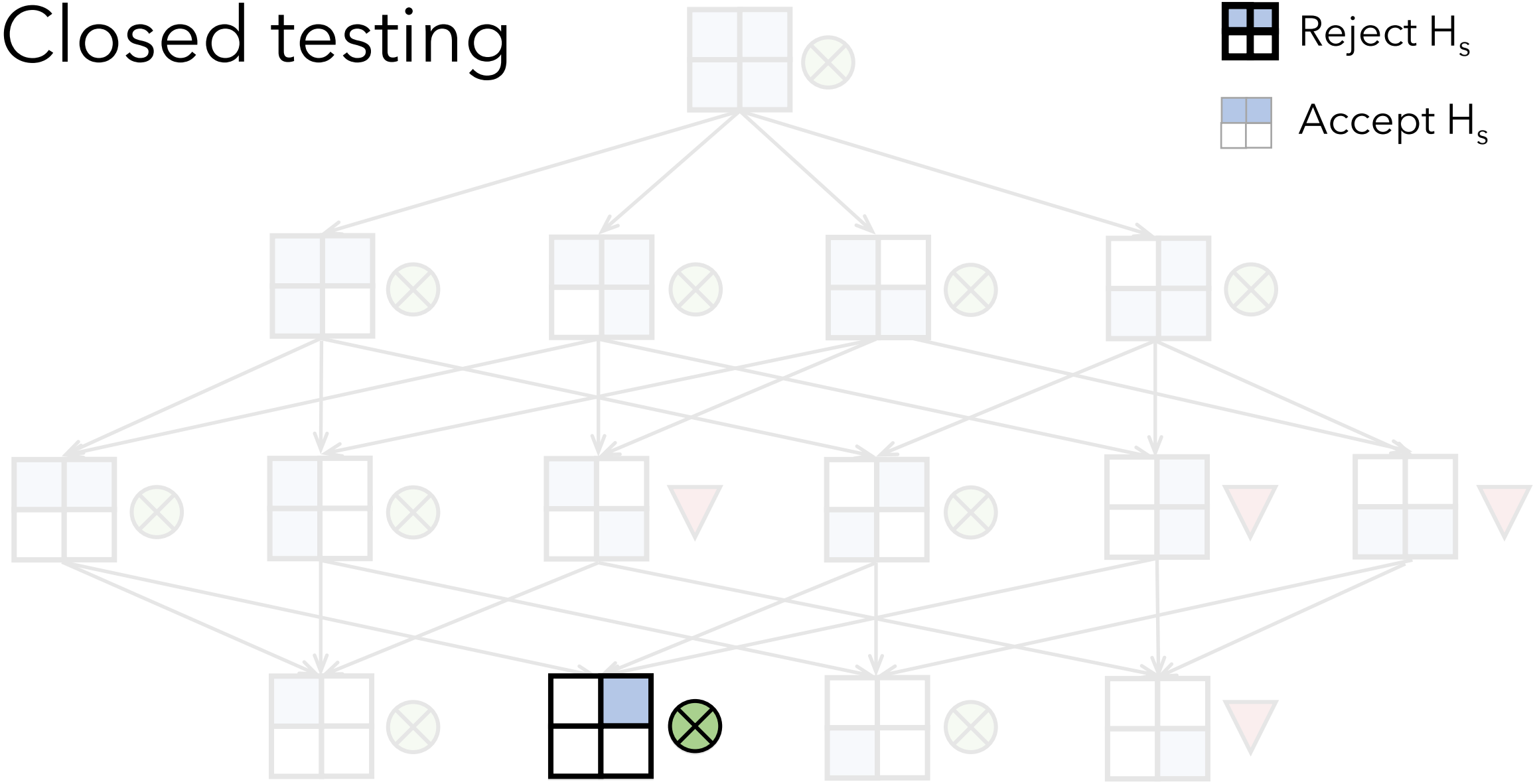
Closed testing



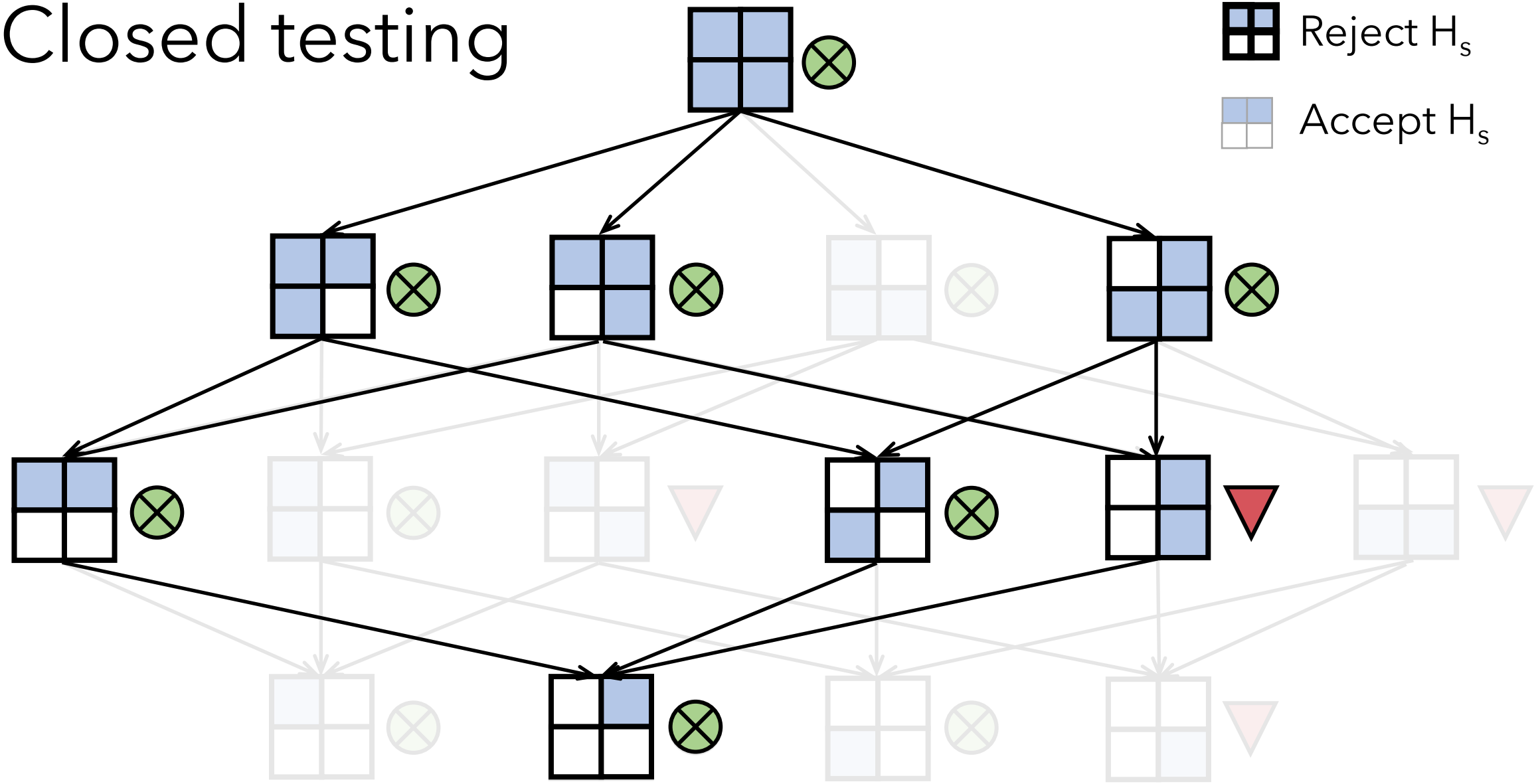
Closed testing



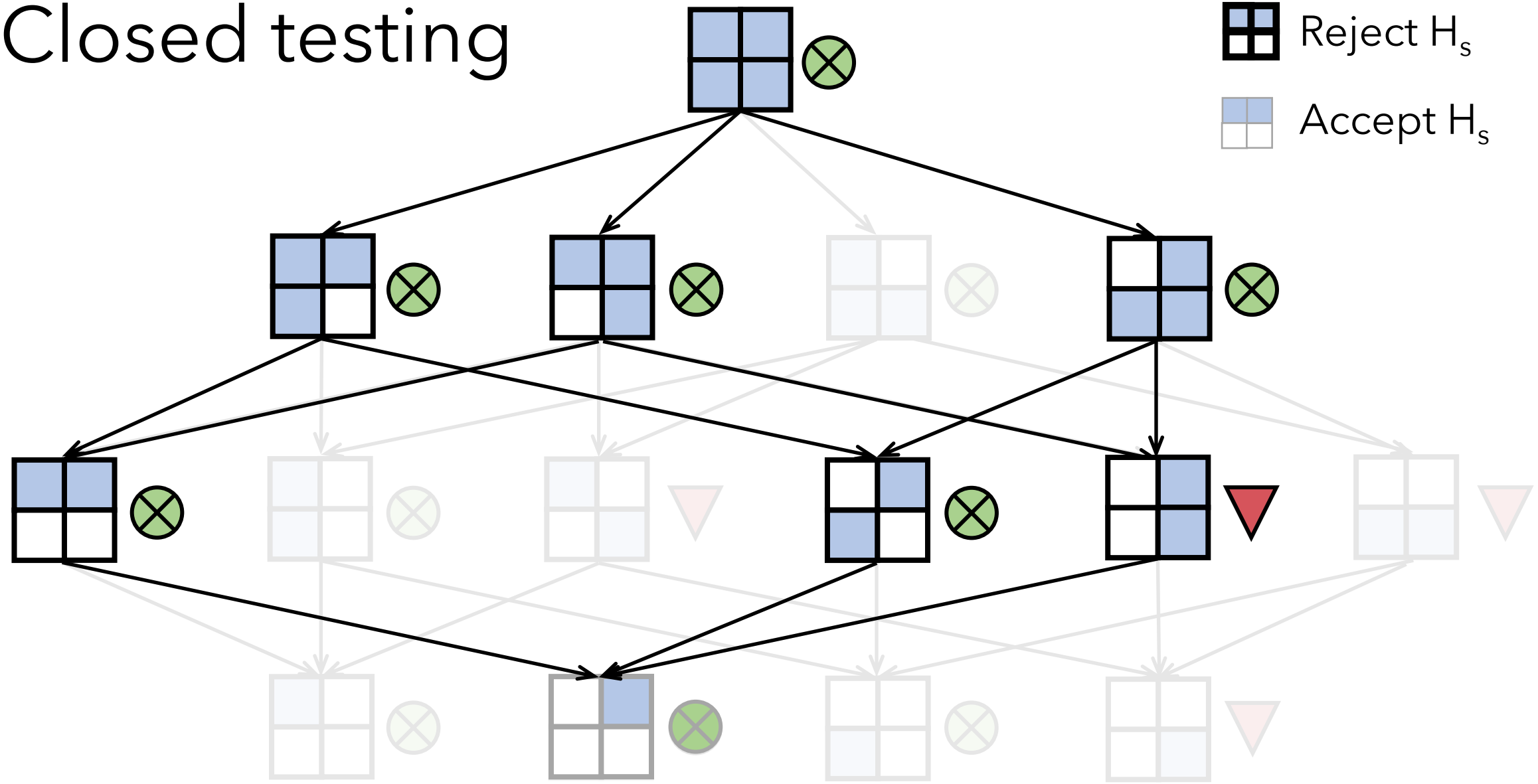
Closed testing



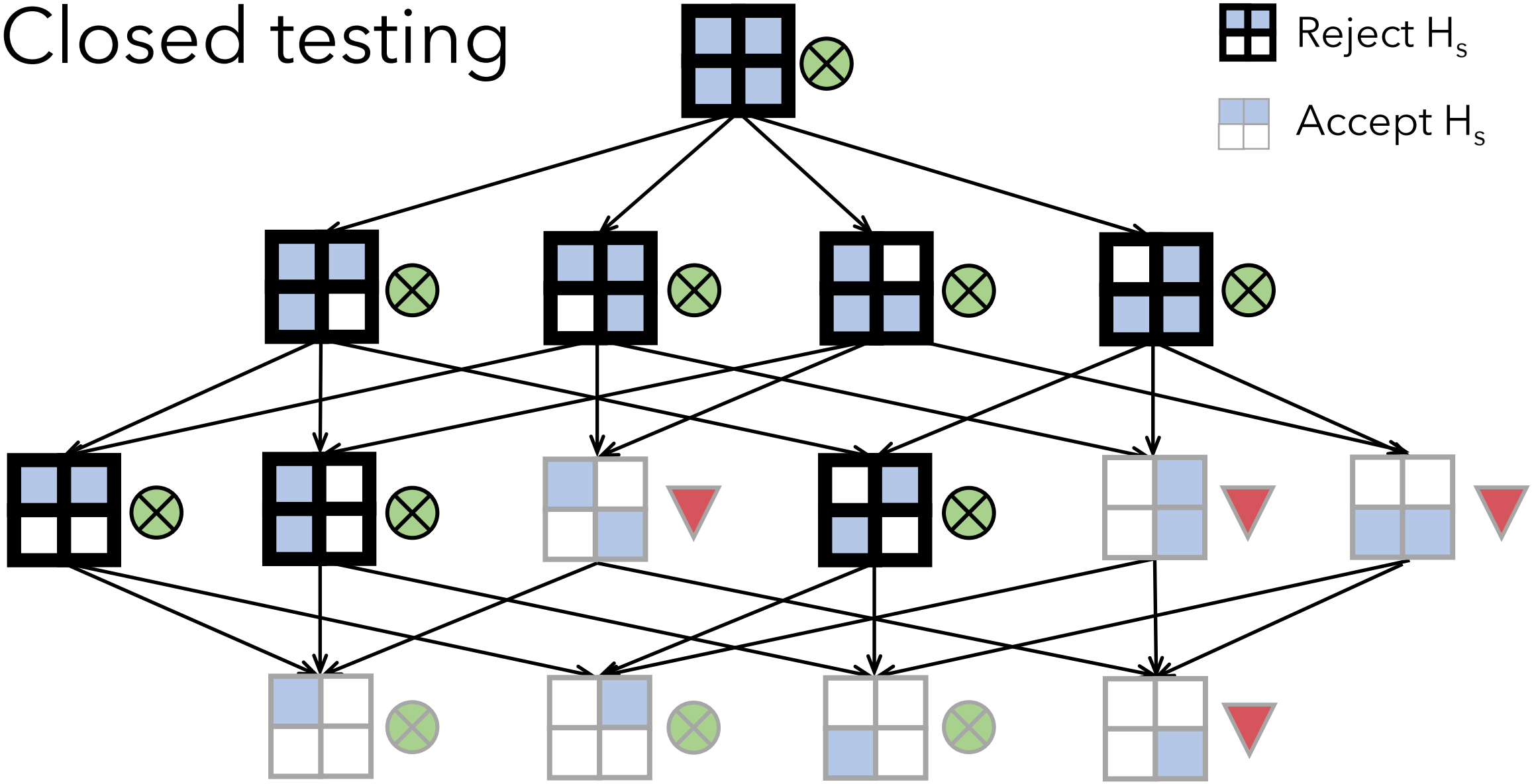
Closed testing



Closed testing



Closed testing

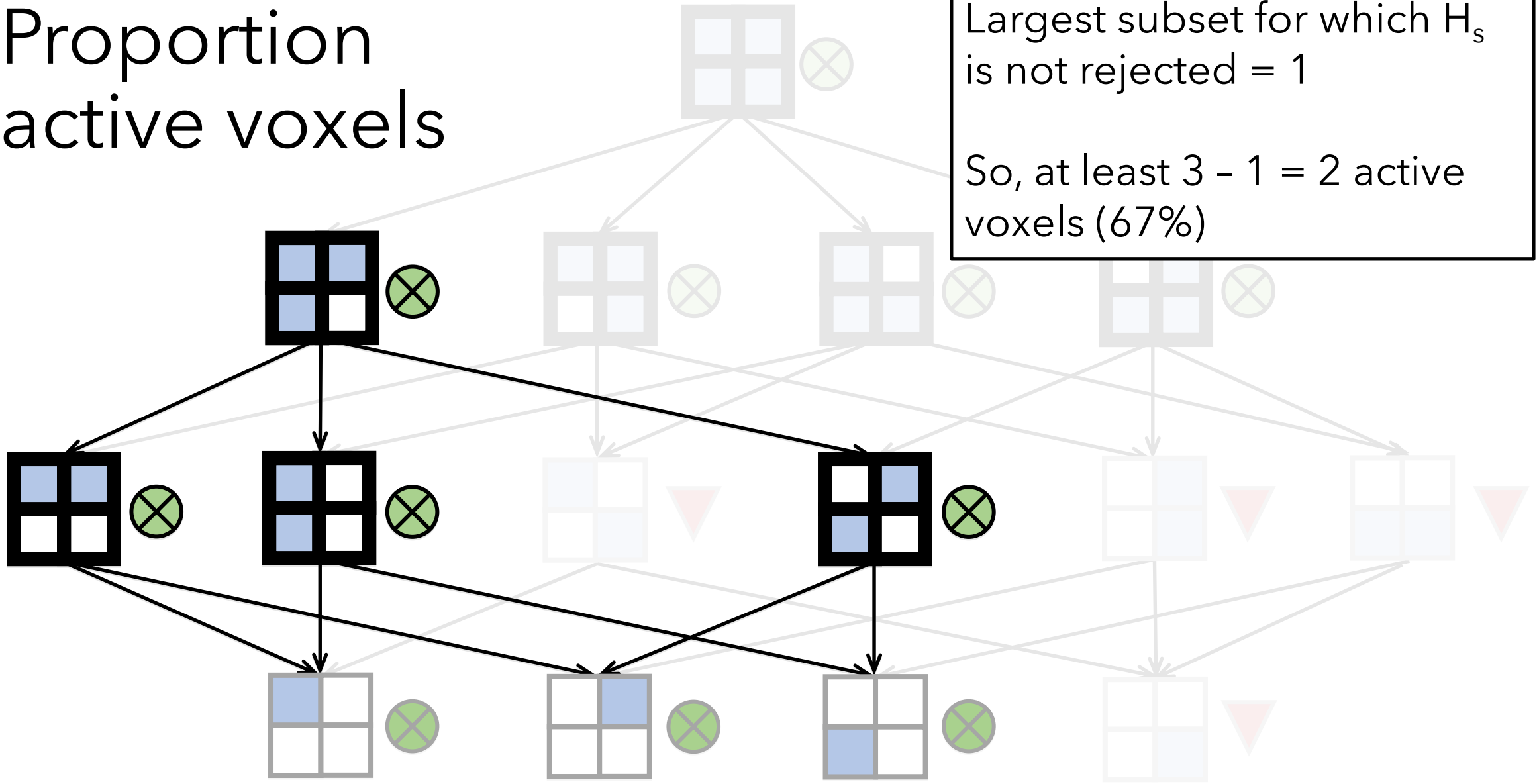


Proportion active voxels

Proportion active voxels

Largest subset for which H_s is not rejected = 1

So, at least 3 – 1 = 2 active voxels (67%)

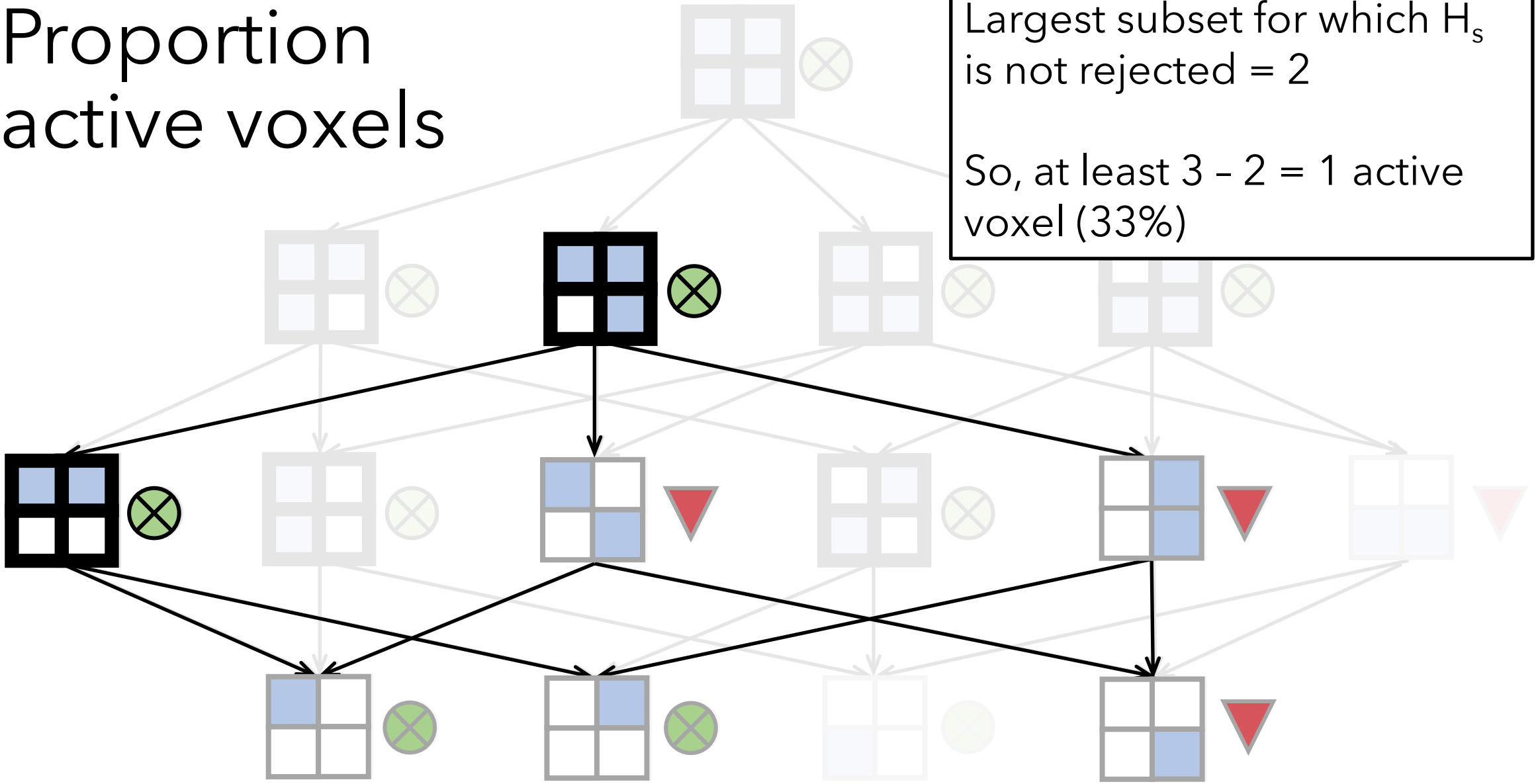


Proportion active voxels

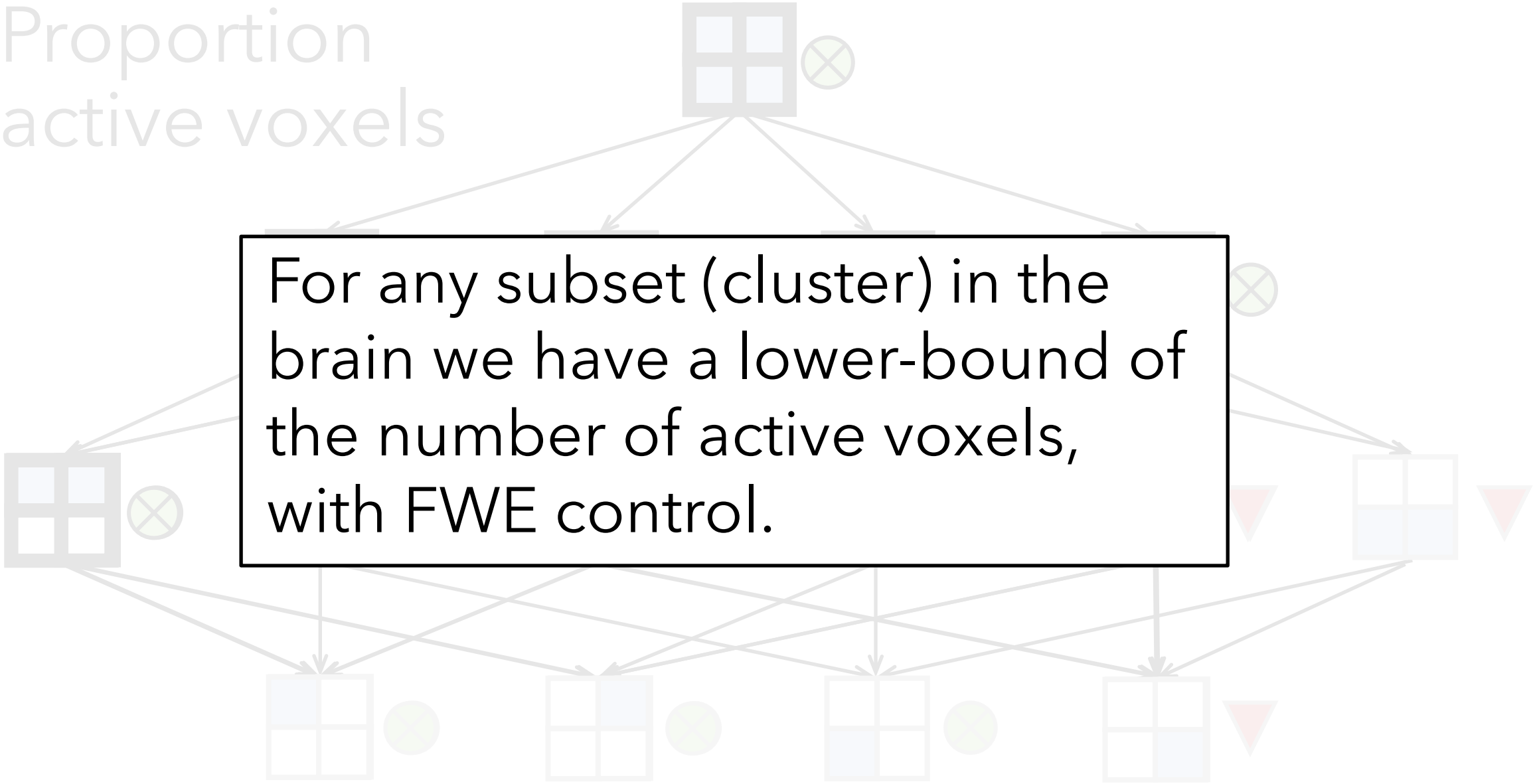
Proportion active voxels

Largest subset for which H_s is not rejected = 2

So, at least 3 – 2 = 1 active voxel (33%)



Proportion active voxels



For any subset (cluster) in the brain we have a lower-bound of the number of active voxels, with FWE control.

Ok, this works for 4 voxels, but how about 200,000 voxels?

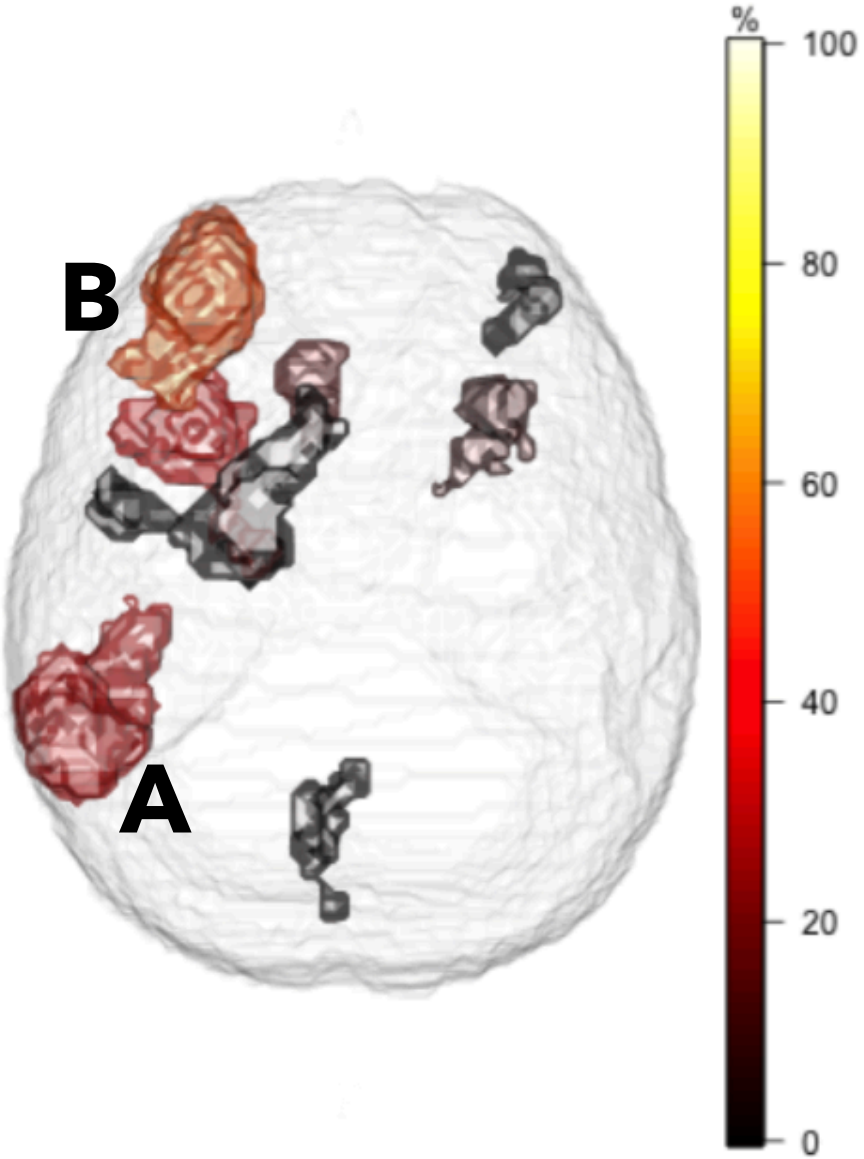
- For 200,000 voxels there are $2^{200,000}$ possible subsets (a lot).
- Due to the structure of the Simes test and the closed testing procedure we can do this very efficiently.
- For 200,000 voxels: computation time within seconds.

All-resolutions inference

- In exchange for your p-values and any region-of-interest you'll get:
  - Within seconds
  - A lower-bound of the number of truly active voxels of that region
  - For any region, as many times as you want.
  - With FWE control

Go / No-go data

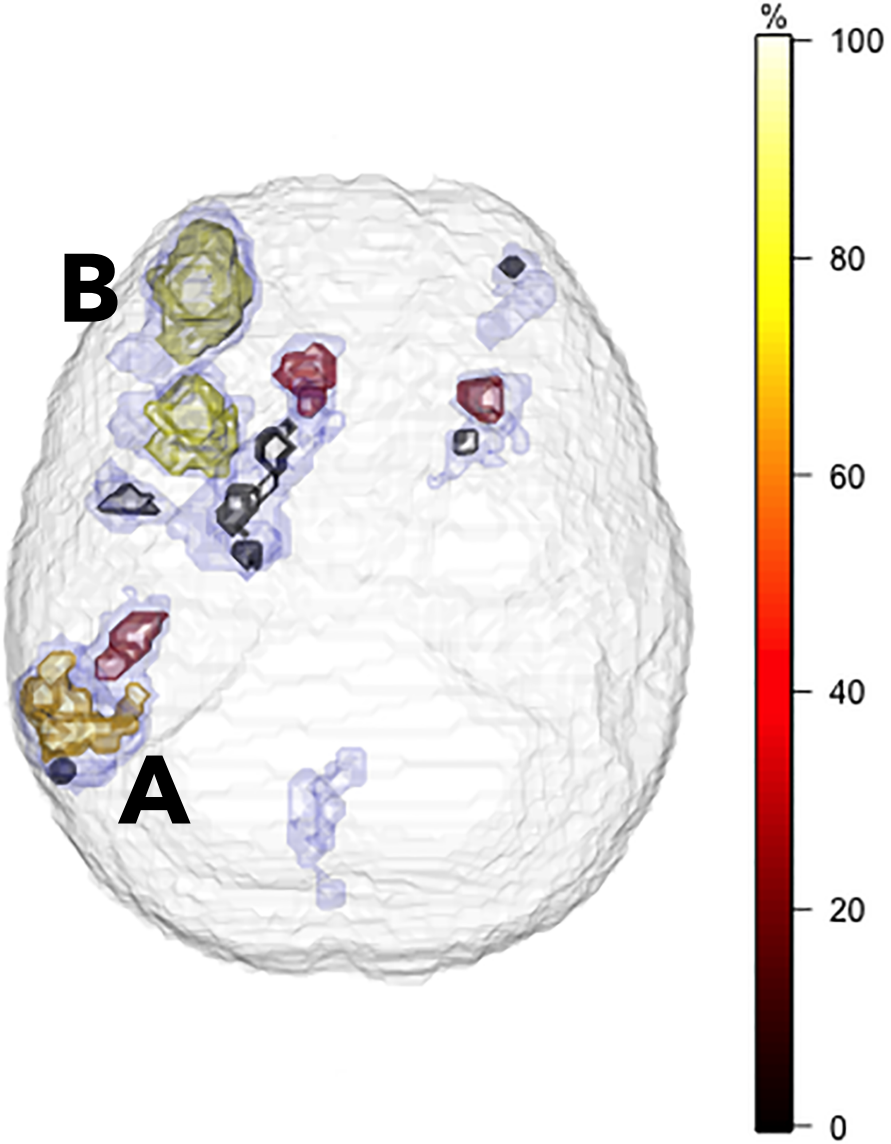
Cluster	Thres.	Size	# Active	% Active
A	Z > 3.2	2191	624	28.5 %
B	Z > 3.2	1835	847	46.2 %



Rosenblatt, Weeda, Finos, Solari & Goeman (2018). Neuroimage

Go / No-go data

Cluster	Thres.	Size	# Active	% Active
A	Z > 3.2	2191	624	28.5 %
1	Z > 4	405	267	65.9 %
2	Z > 4	133	31	23.3 %
3	Z > 4	6	0	0 %
B	Z > 3.2	1835	847	46.2 %
1	Z > 4	963	826	85.8 %



Rosenblatt, Weeda, Finos, Solari & Goeman (2018). Neuroimage

ARIbrain – R package

```
#load library
library(ARIbrain)

#run ARI
out <- ARI(Pmap = '/stats/pvalue1.nii.gz',
           clusters = '/cluster_zstat1.nii.gz',
           mask = '/mask.nii.gz',
           Statmap = '/stats/zstat1.nii.gz')


A hommel object for 166407 hypotheses.
Simes inequality is assumed.

With 0.95 confidence: at least 12938 discoveries.
9384 hypotheses with adjusted p-values below 0.05.

      Size FalseNull TrueNull TDP  dim1 dim2 dim3      Stat
cl4   7257      6257     1000 0.86   23   56   40 10.789868
cl3   6206      5313      893 0.86   69   56   39 10.640452
cl2    694       355      339 0.51   52   51   33  6.859994
cl1    340        27      313 0.08   25   70   50  4.746142
cl0 151910         0   151910 0.00   64   79   41  4.319296

>
```

ARIbrain – R Shiny app