Measuring neglect and realizing that many times it's not there

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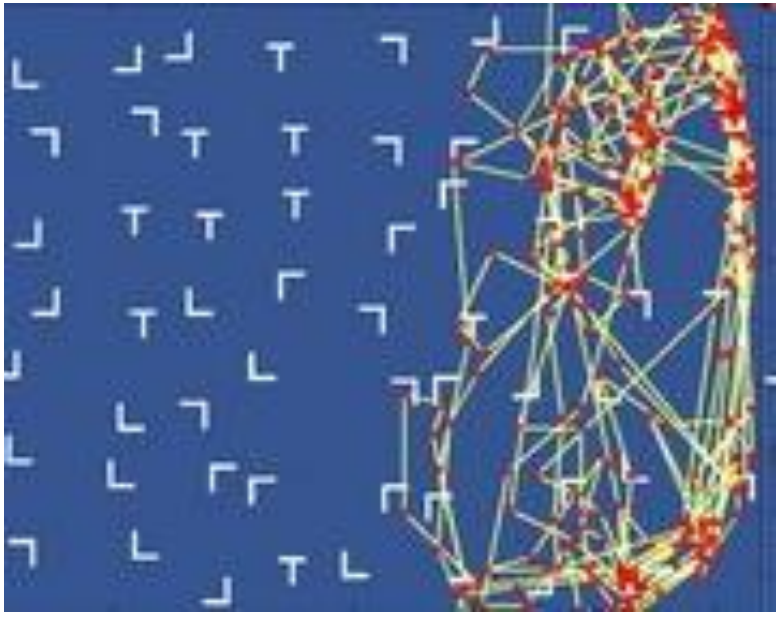
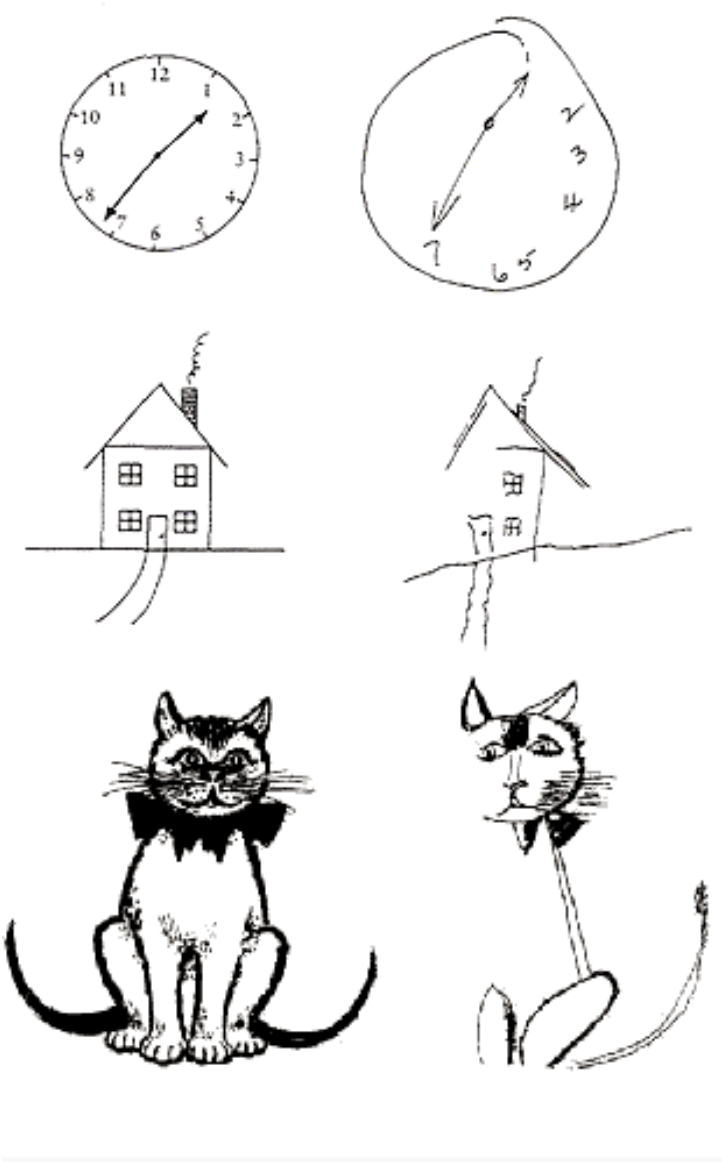
Unilateral neglect

Well-studied syndrome typically following right-hemisphere damage

-Patient fails to process and respond to contralesional stimuli





No standard (stat) diagnostic procedure

Huge variety of neglect tests, **one** data structure: *spatial position by hit-miss score*

DIFFERENT

(i) ***sensory modalities*** (visual, auditory, tactile, …)

(ii) ***types of response*** (verbal, reaching movement, eye movement, dichotomized response times, dichotomized physiological responses like ERP, fMRI, skin conductance, …)

(iii) ***extra cognitive operations*** (presence/absence of distractors, …)

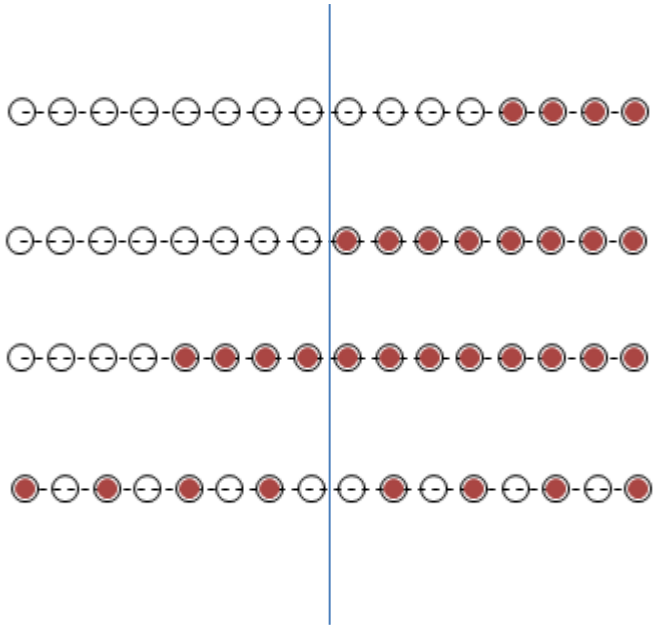
(iv) ***tasks*** (active search within a homogeneous field of simultaneously presented stimuli, like in visual or haptic cancellation, or explicit/implicit detection of single stimuli presented one at a time in different locations, like in Posner's paradigm, or short/long-term memory recall of previously inspected stimulus arrays, …)

However scoring procedures vary considerably (inconsistent results) and are generally suboptimal

Talk outline

- Inadequacy of many measures
- One good candidate: *Mean Position of Hits* (*MPH*)
- *MPH* hidden variability: False Positive Rate inflation problem – empirical data support
- Statistical model of *MPH* solves (?) the problem
- Software
- Conclusions

The simplest thought experiment

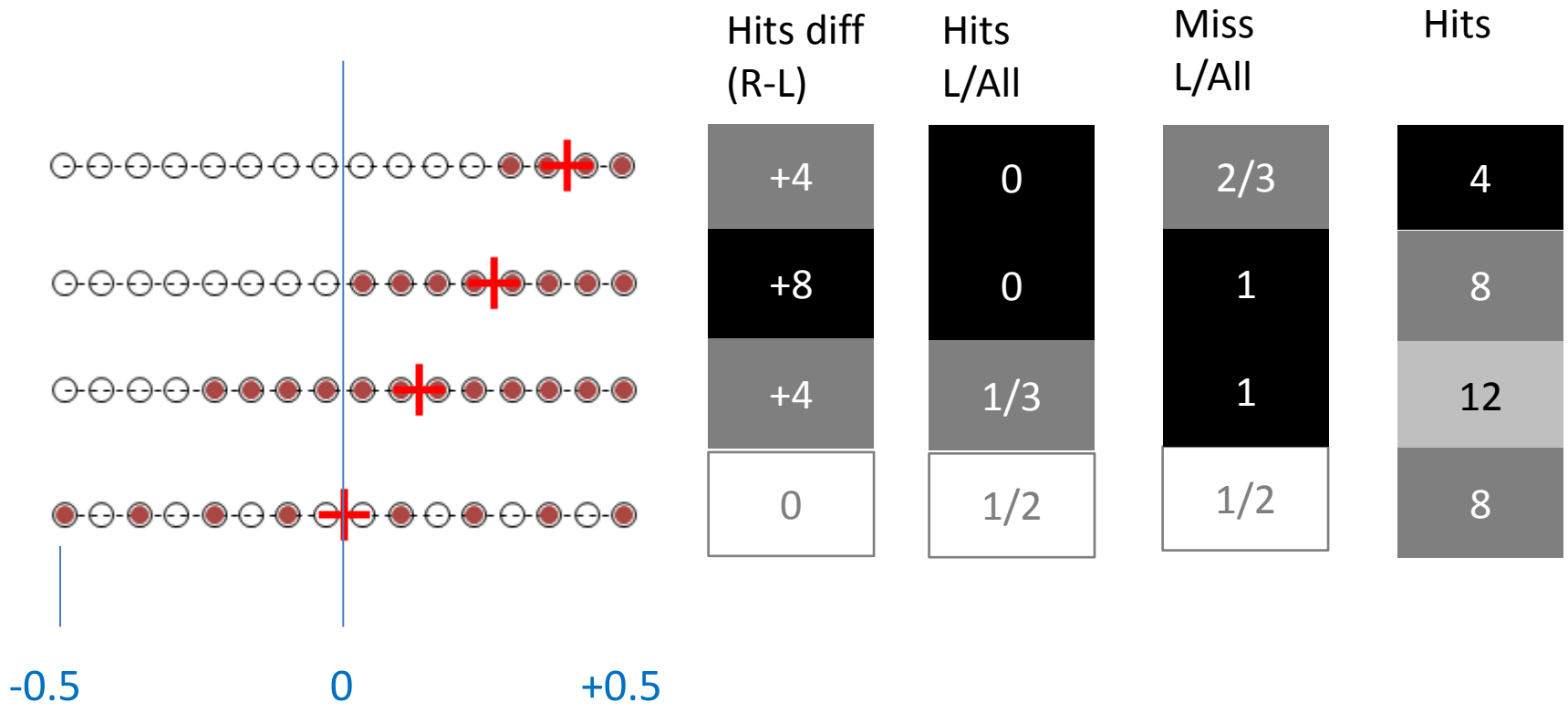


Hits diff (R-L)	Hits L/All	Miss L/All	Hits
+4	0	2/3	4
+8	0	1	8
+4	1/3	1	12
0	1/2	1/2	8
OR, S	S	OR, S	OR, S

Violations (Order Reversal, Separation)

Common neglect measures are inadequate

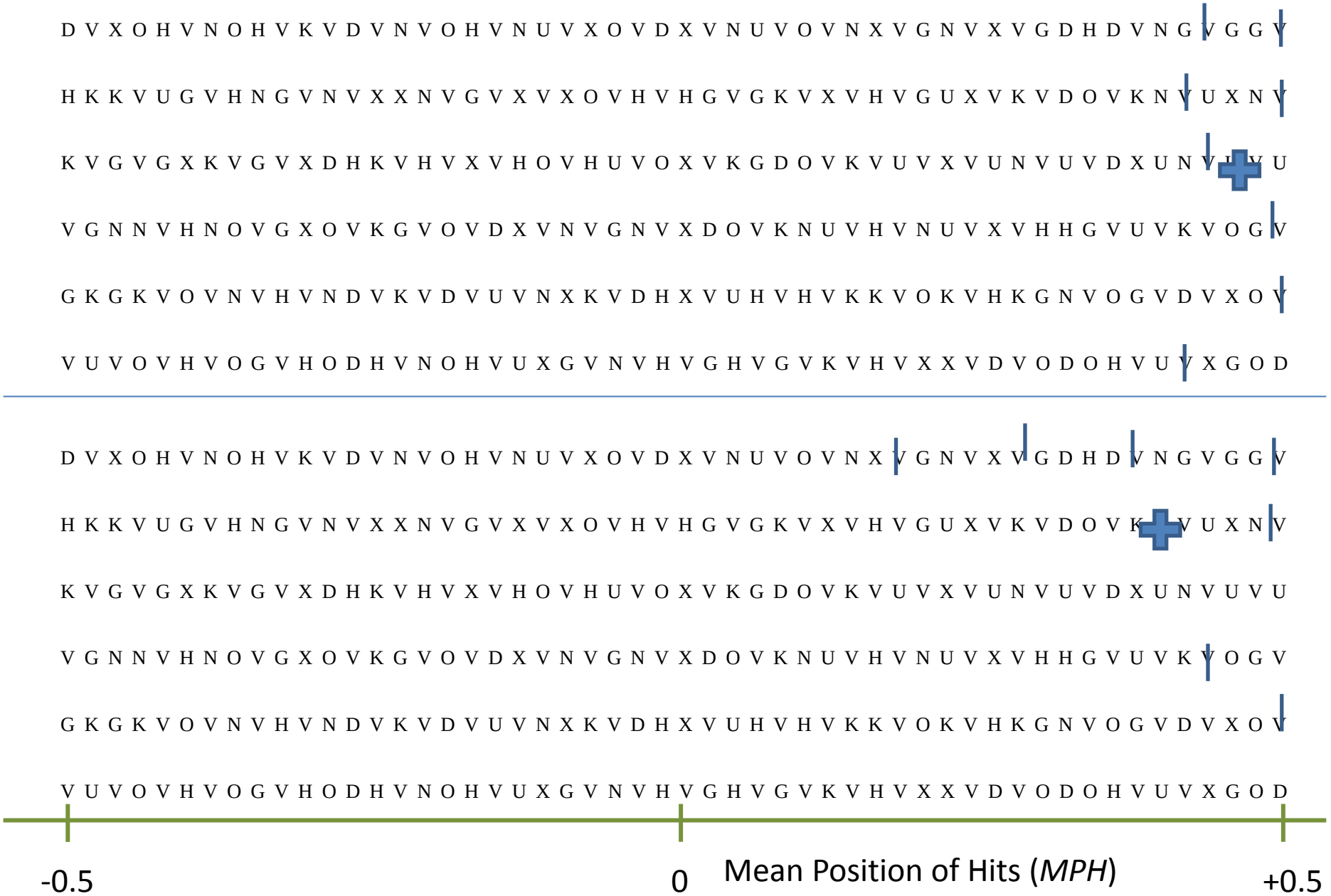
Mean Position of Hits (*MPH*)



-Optimal theoretical and statistical properties (over *variance* measures, the *median*, the *midrange*, the mean for *omissions*…).

-A very close mathematical object has already been used for cancellation tasks (Binder et al, 1992; Rorden & Karnath, 2010, «CoC»)

Cancellation tasks – e.g. «Diller-V»



MPH Graphic Editor

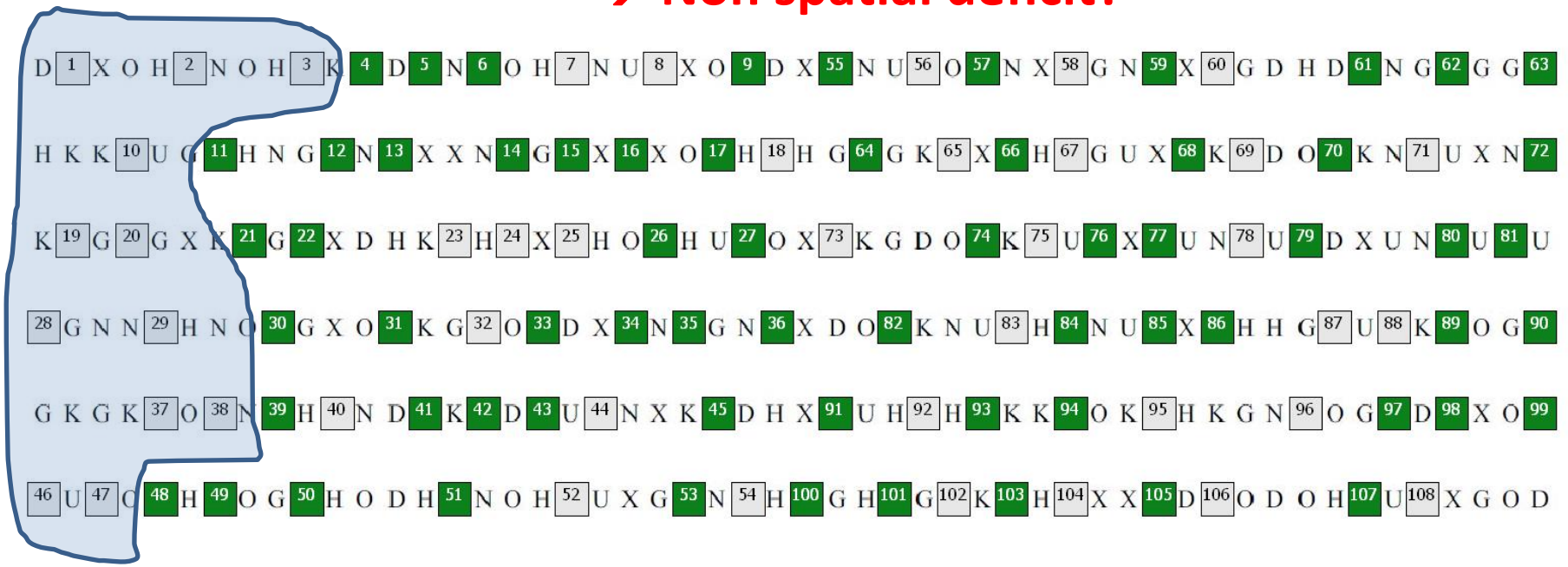
File | Edit | Advanced | Diagnosis

Edit boxes is: OFF | Size of Boxes | Size of Font | Color of boxes HIT | Color of boxes MISS

Positive or negative?

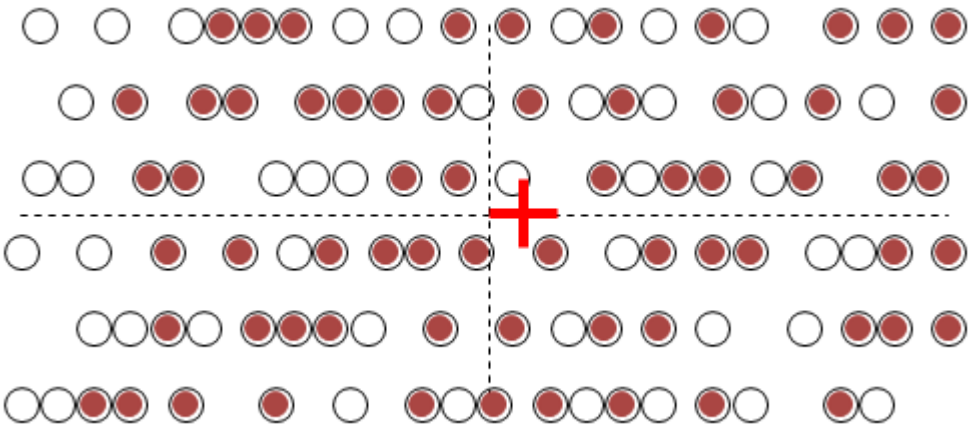
Many *other* omissions

→ Non spatial deficit?



MPH=0,0377 Z=1,5780 1-TAILED P=0,0573 2-TAILED P=0,1146

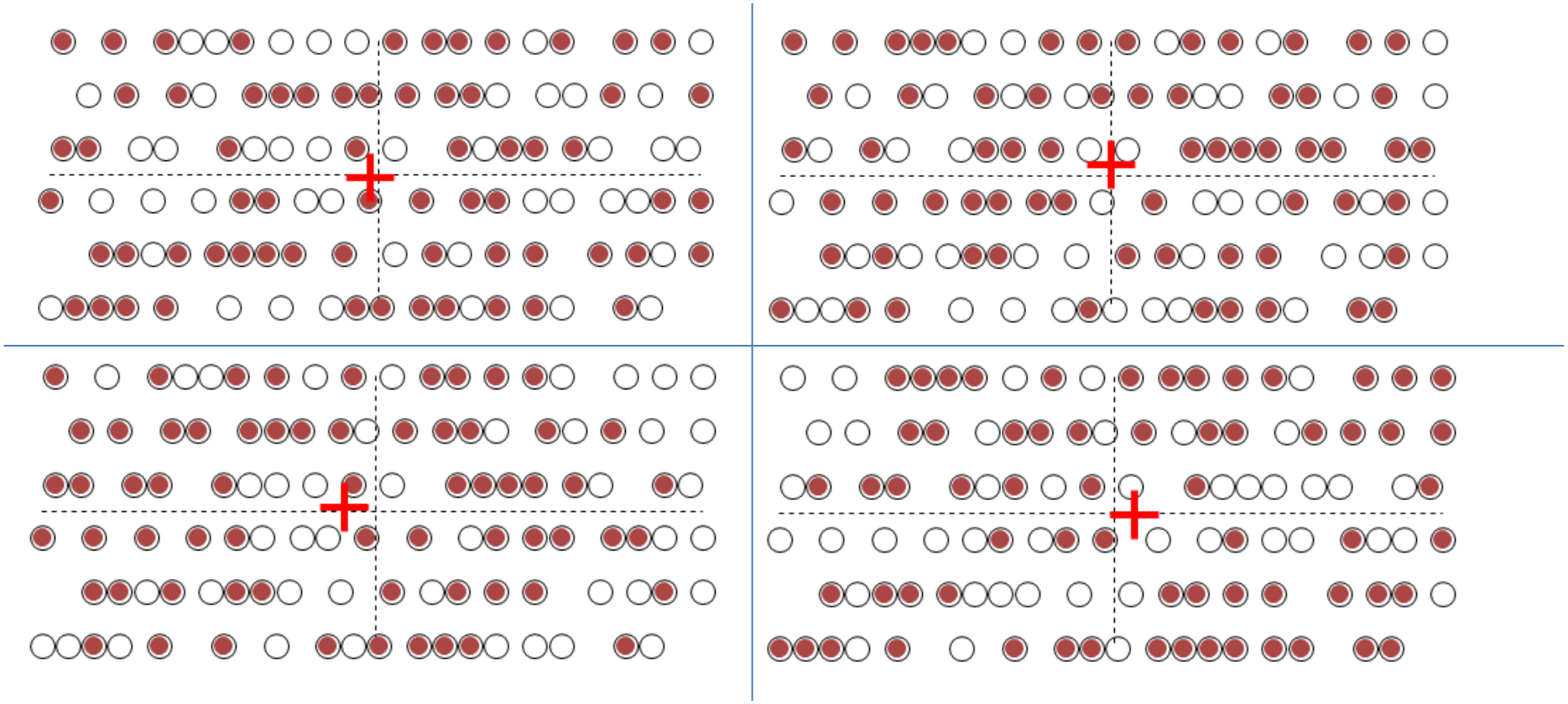
Horizontal ◉ Vertical ○



MPH = +0.038

Classical *z* = 6.39

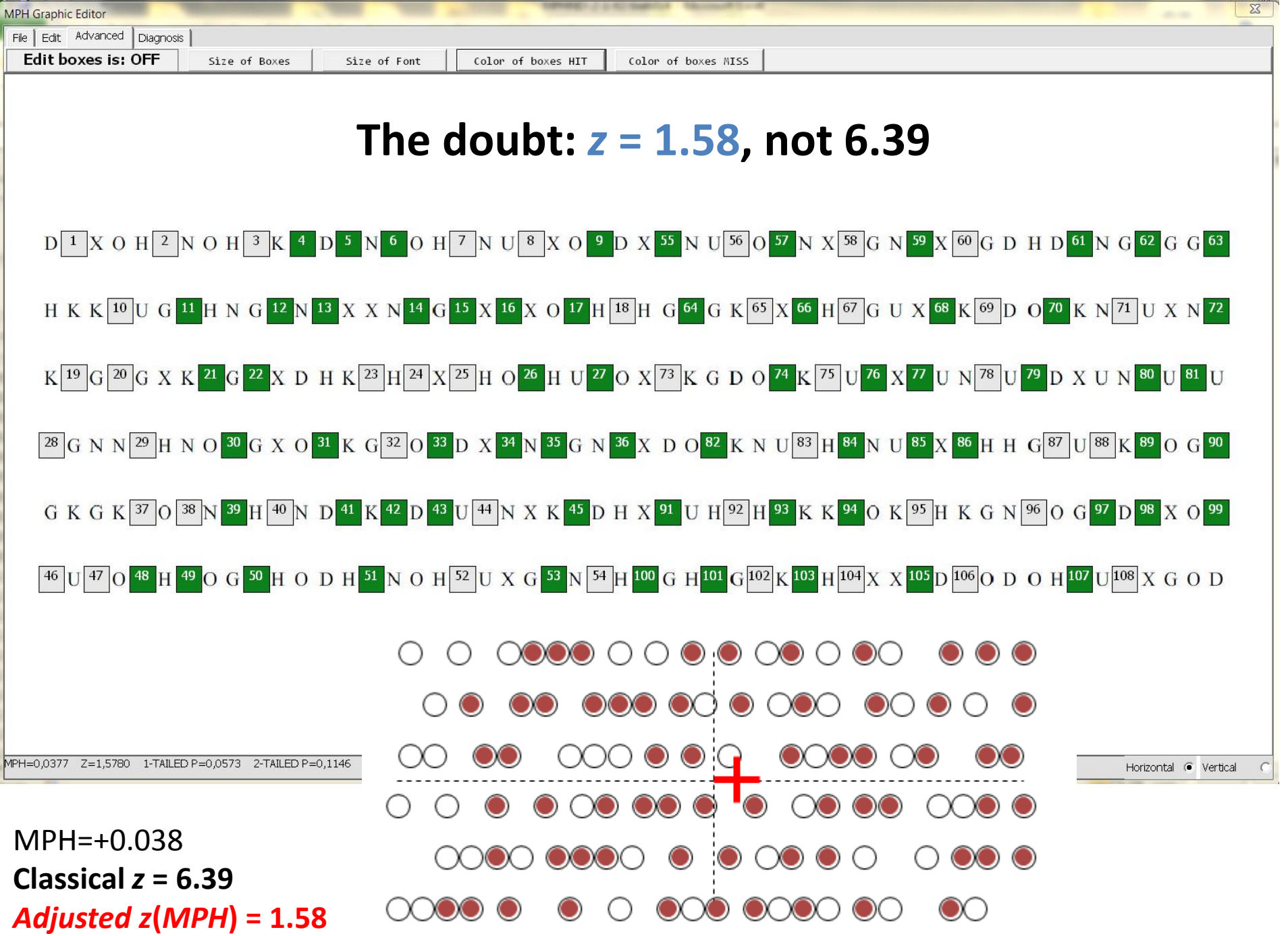
Shuffling the position of the 65 Hits…



Shuffling the Hits provides an estimate of what a patient with a non-spatial deficit is expected to do

MPH variation (dev.st= 2.36% of display width) is **much larger** than the normal range (0.57% of display width)

The doubt: $z = 1.58$, not 6.39



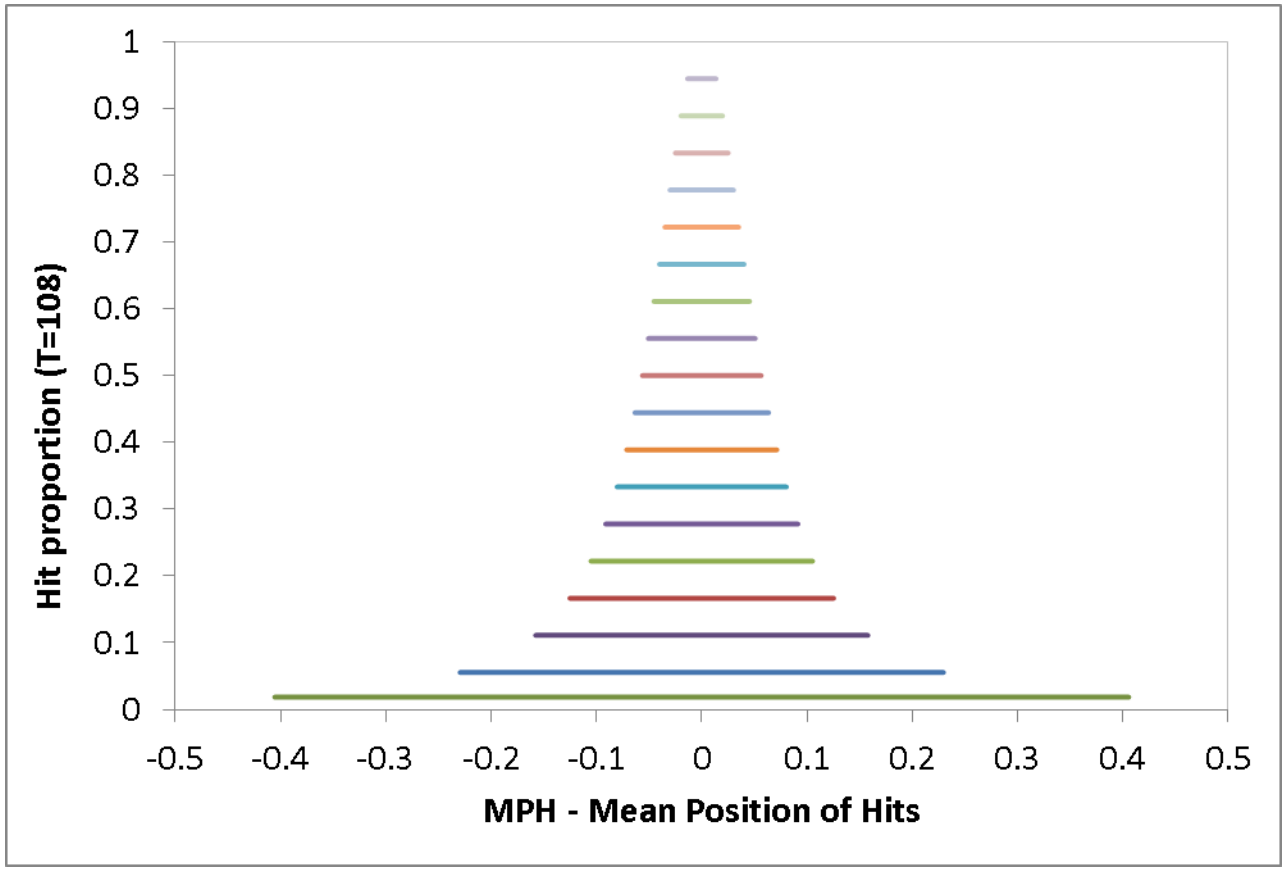
MPH=+0.038

Classical z = 6.39

Adjusted z(MPH) = 1.58

Instability of *MPH*

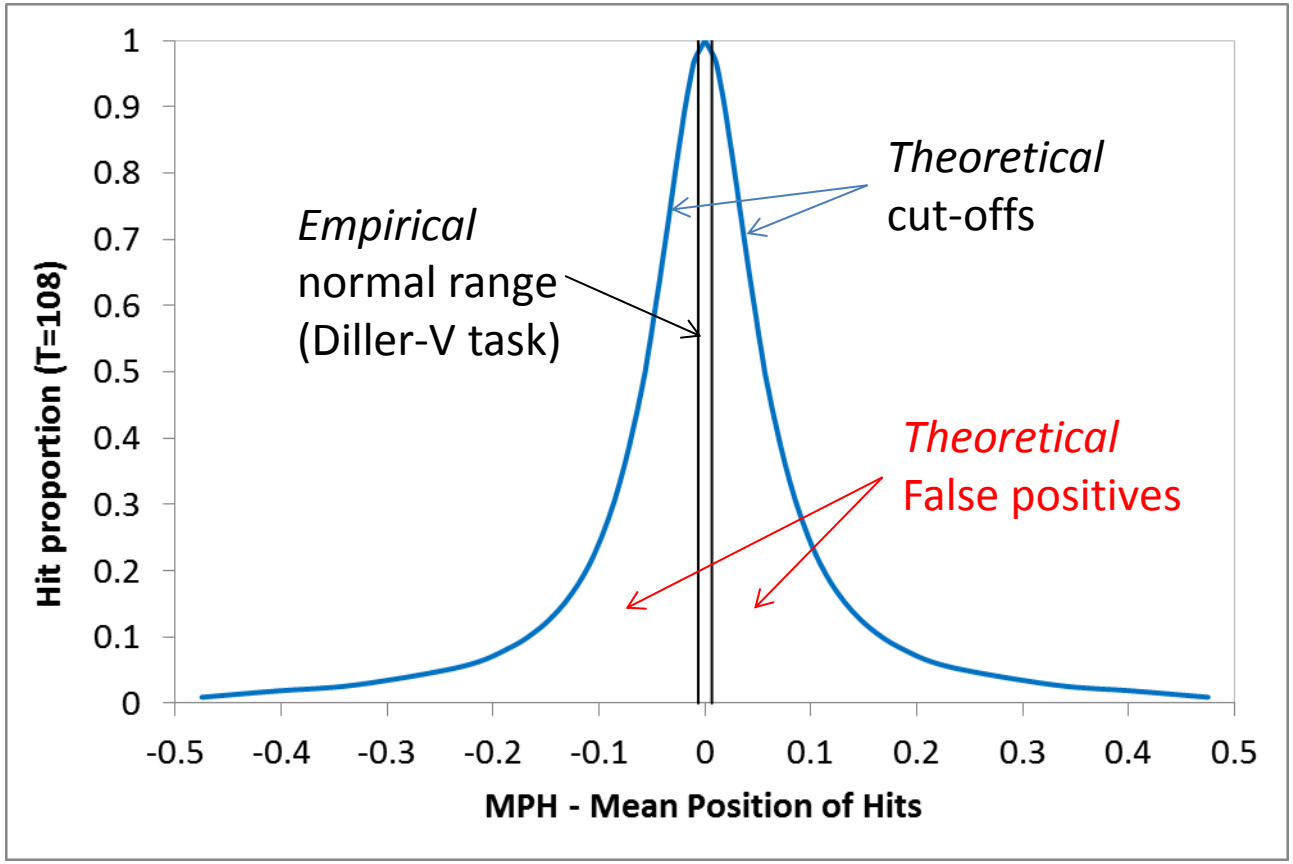
95% ranges (-1.96SD to +1.96SD)



As with *any* other neglect measure, *MPH*'s variation (under the null) massively depends on overall Hit rate

This is the expected effect when deficits *other* than neglect (non-spatial) are present

Many false positives predicted to be yielded by classical diagnostic procedures



Many patients *without* neglect and with any *other* deficit affecting stimulus processing should be mistaken for neglect patients

How many?

Aim: to estimate (the upper bound of) False Positive Rate (FPR) in a real RH population

Methods

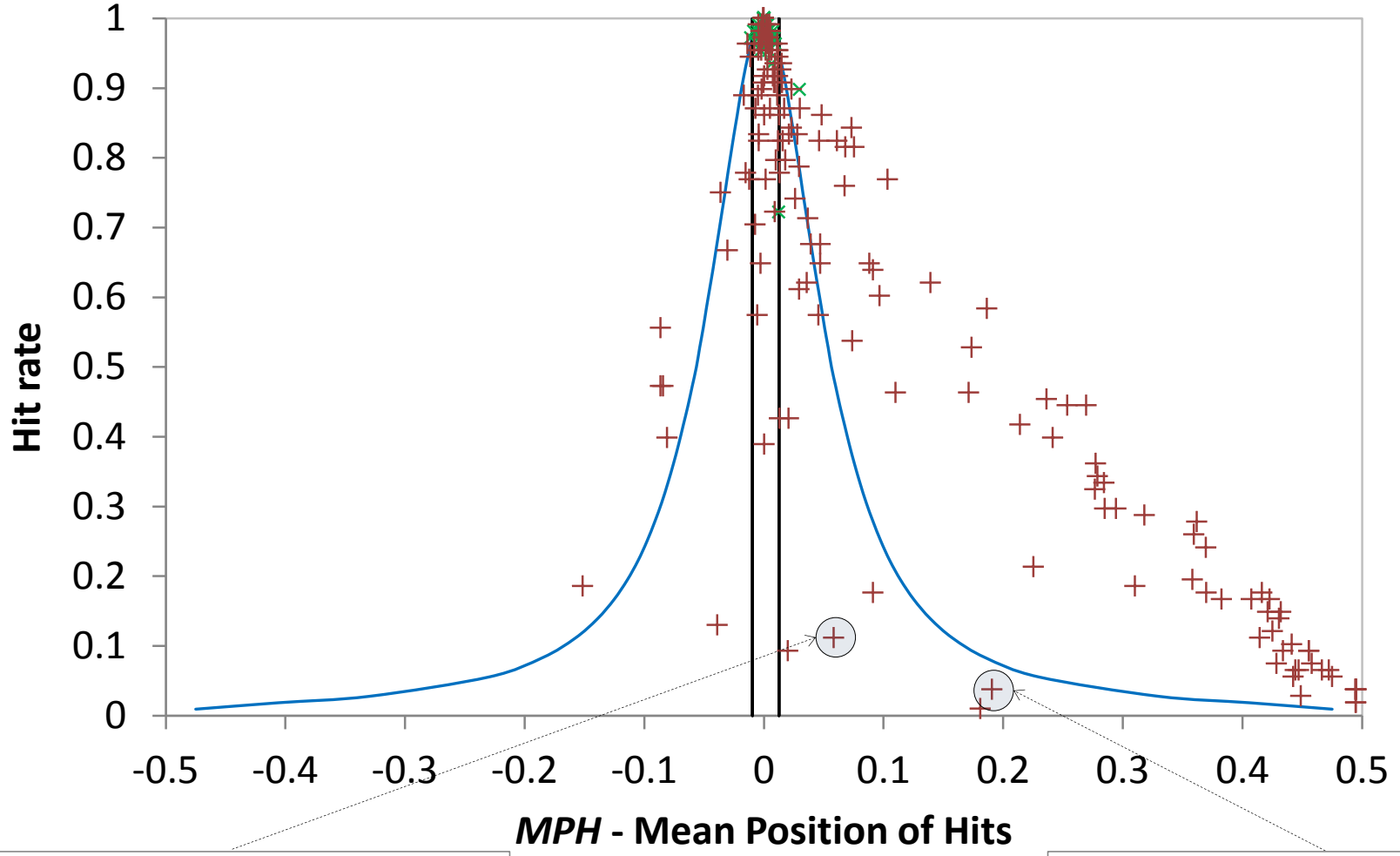
Subjects

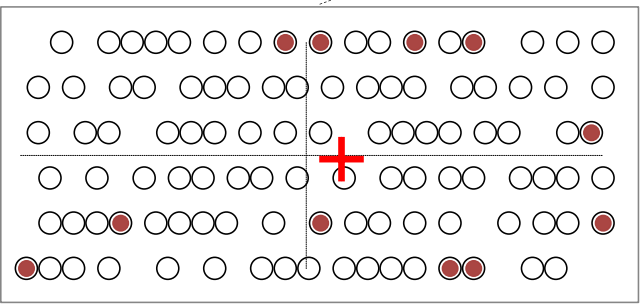
- 237 RH patients (retrospective data) from several institutions (Vimodrone, Trieste, Udine, Pavia, St Andrews…, years 1995-2013)
- 77 healthy controls

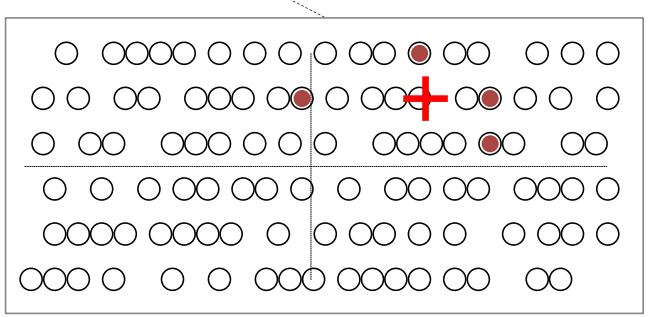
Tasks

Diller-V (170 RH + 52 C), Diller-H (67 RH + 25 C)

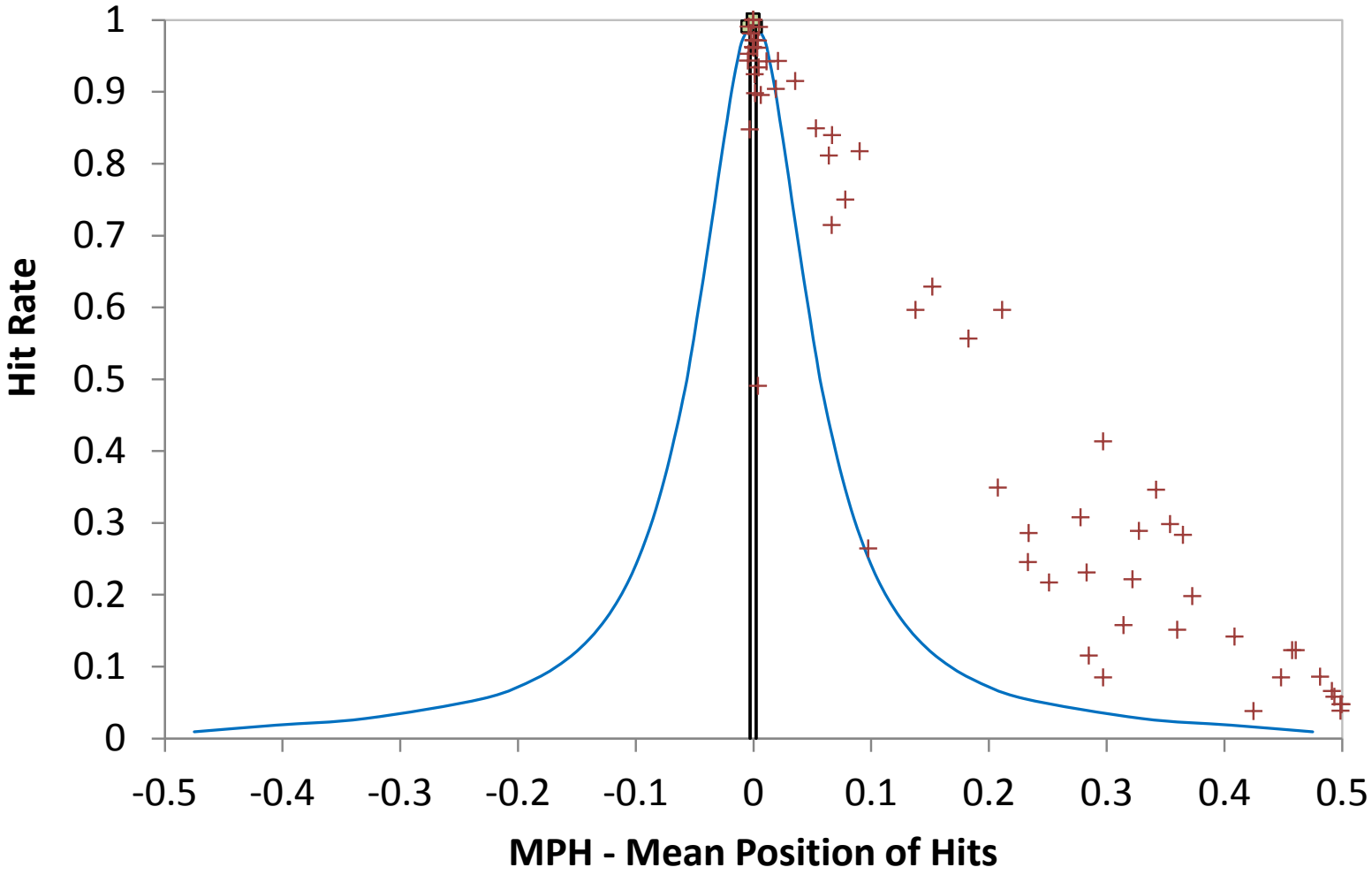
Diller-V results



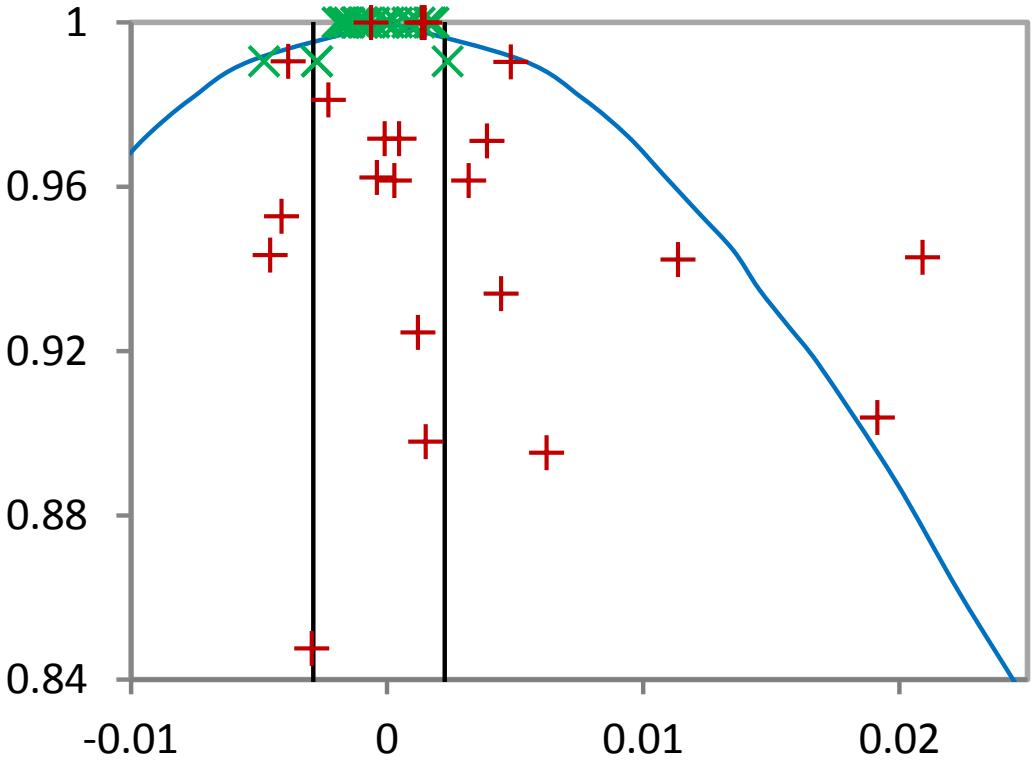




Diller-H results



Zooming in on the top



Upper-bound FPR estimates Rates (nominal: 5%)

Diller V	***Classical diagnostics***			
	neg	pos	tot	pos rate
All pts	61	109	170	0.641
Only *z* (*MPH*) neg	59	26	85	**0.306**
	z(MPH) diagnostics			
	neg	pos	tot	pos rate
All pts	85	85	170	0.5
Diller H	***Classical diagnostics***			
	neg	pos	tot	pos rate
All pts	10	57	67	0.851
Only *z* (*MPH*) neg	10	11	21	**0.524**
	z(MPH) diagnostics			
	neg	pos	tot	pos rate
All pts	21	46	67	0.687

Diller-V: 30.6%

Diller-H: 52.4%

[Upper-bound: it assumes that all true N+ patients are outside the zMPH range – a likely ***over***estimate]

Table 1 *Counts of Positive and Negative cases according to the classical and the z(MPH) diagnostic criteria, for both Diller tasks.* ***Upper-bound False Positive Rates*** *are reported in* ***red****.*

Solution

Use adjusted *z*(*MPH*) – the **blue cut-offs**, which bring FPR back to 5%

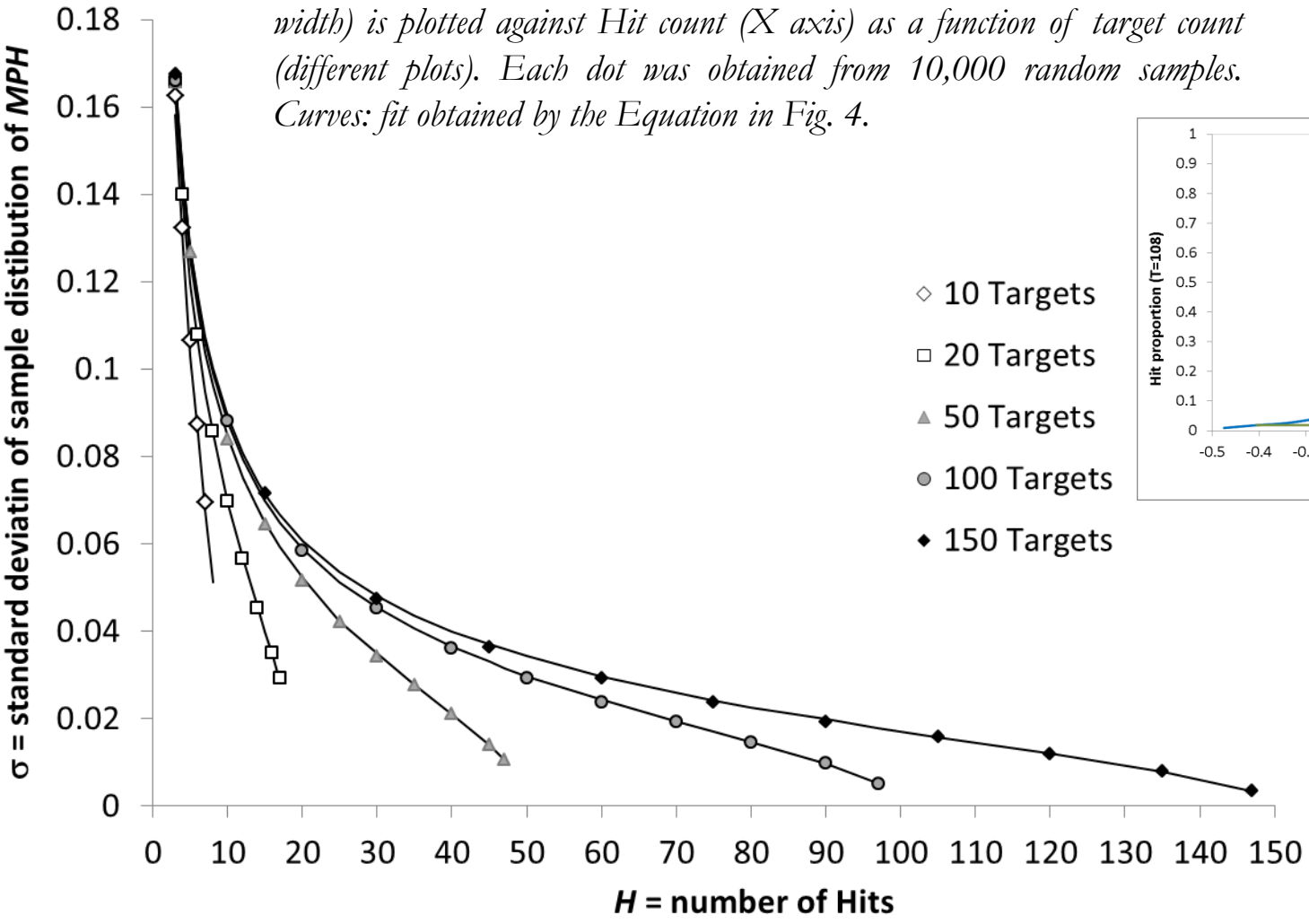
How to obtain the **blue cut-offs**

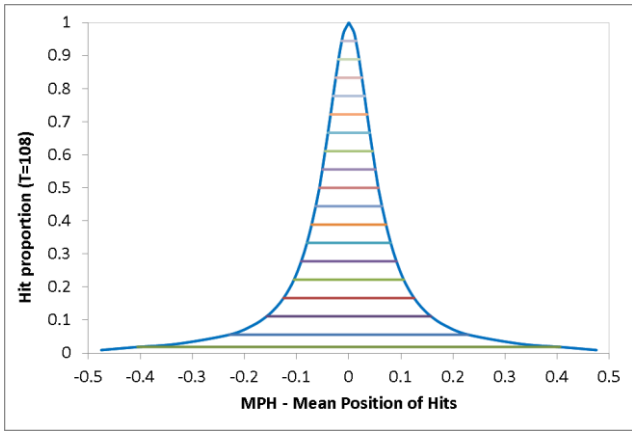
(i) Shuffling (e.g. in R) – clinicians will never use it!

(ii) Some general mathematical approximation – tests vary for N of targets, their exact distribution, etc., however targets are usually homogeneously distributed

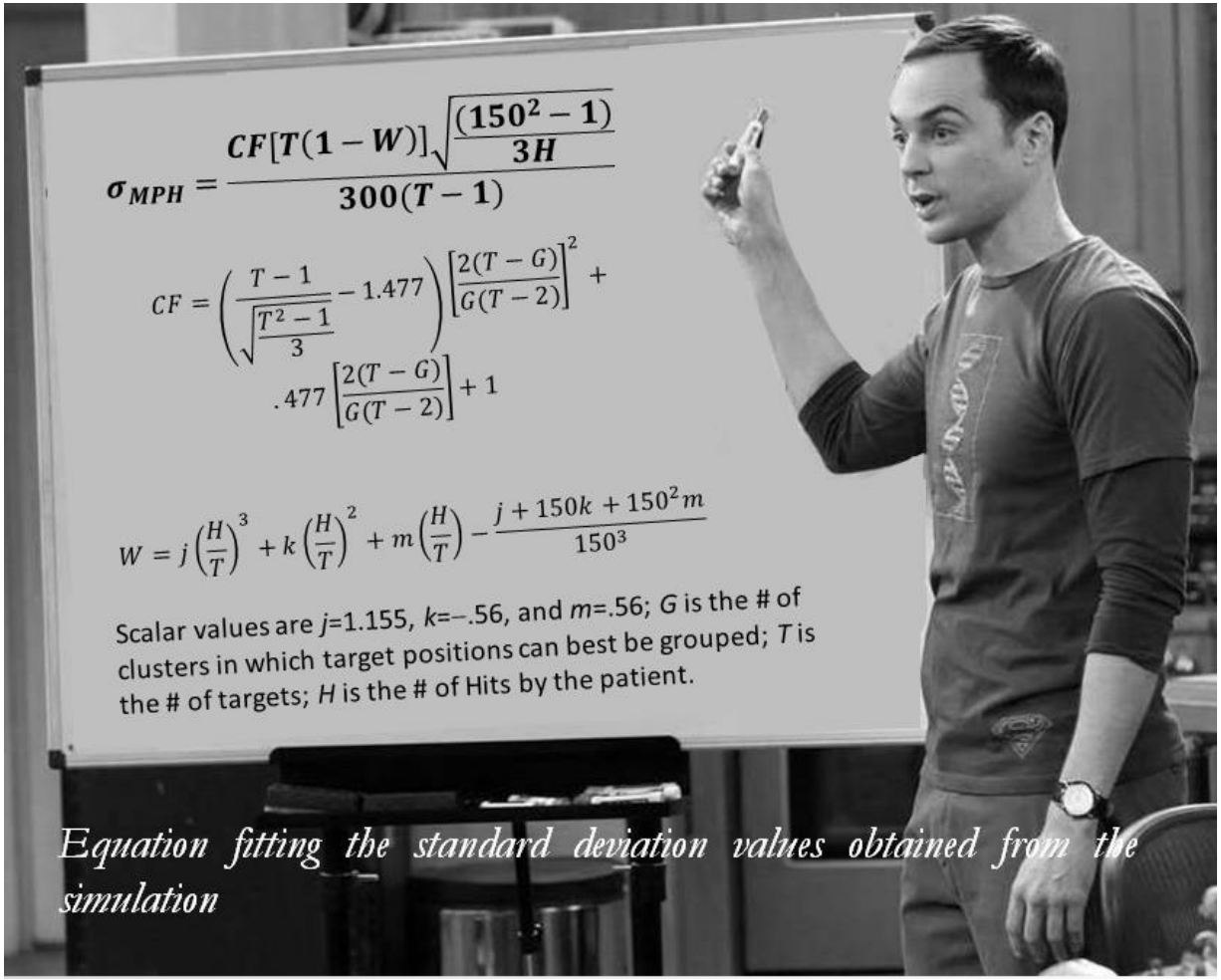
Simulation data fitting

Fig. 3 *The standard deviation of MPH (Y axis; 1 = overall display width) is plotted against Hit count (X axis) as a function of target count (different plots). Each dot was obtained from 10,000 random samples. Curves: fit obtained by the Equation in Fig. 4.*





Equation of the standard deviation (2017 paper)



Equation fitting the standard deviation values obtained from the simulation

The software

http://psicologia.unipv.it/toraldo/mean-position-of-hits.htm

INPUT	Min 10, max 256 targets		
	Horizontal	Vertical	Hit=1;
Target ID	*X*	*Y*	
1	188.4057	420.0843	0
2	419.0743	420.0843	1
3	592.0759	420.0843	0
4	765.0774	420.0843	0
5	880.4117	420.0843	0
6	995.7461	420.0843	0
7	1226.4148	420.0843	0

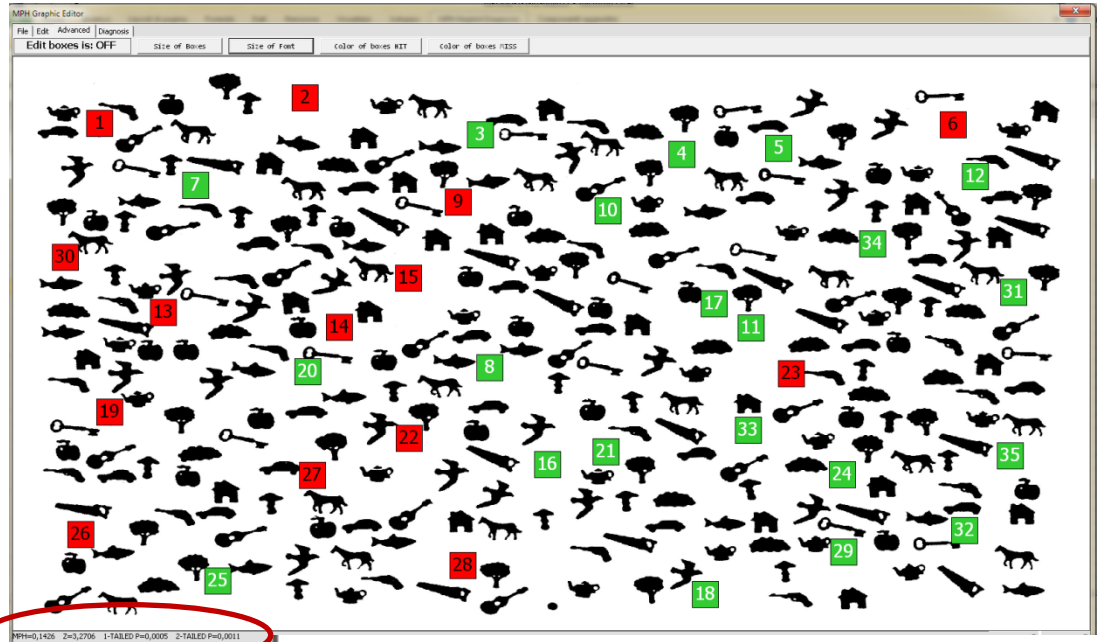
OUTPUT PREVIEW

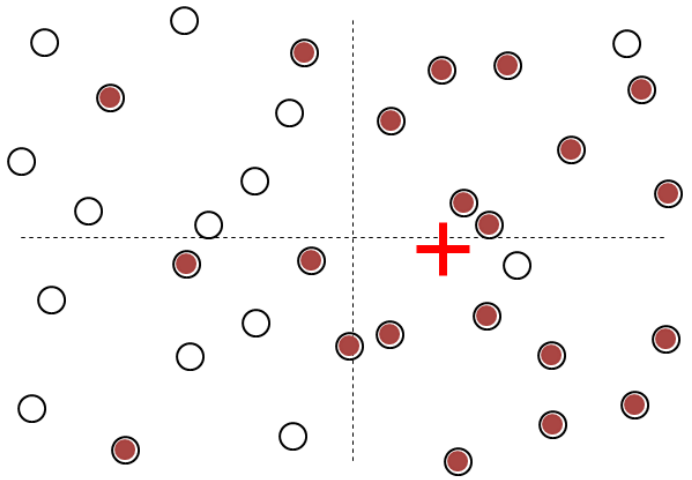
MPH in which dimension, Horizontal or Vertical? (H/V)

H

MPH=	-0.2485
Z=	-3.4293
1-tailed p=	0.0003
2-tailed p=	0.0006

Just google *Toraldo MPH* or *Toraldo neglect*





Almost universal

_z_(_MPH_) analysis applies to the vast majority of neglect tests, namely, all those sharing the _spatial position by hit-miss score_ data structure

Thus it holds for different…

(i) ***sensory modalities*** (visual, auditory, tactile, …)

(ii) ***types of response*** (verbal, reaching movement, eye movement, dichotomized response times, dichotomized physiological responses like ERP, fMRI, skin conductance, …)

(iii) ***extra cognitive operations*** (presence/absence of distractors, …)

(iv) ***tasks*** (active search within a homogeneous field of simultaneously presented stimuli, like in visual or haptic cancellation, or explicit/implicit detection of single stimuli presented one at a time in different locations, like in Posner's paradigm, or short/long-term memory recall of previously inspected stimulus arrays, …)

However it does NOT hold for other tasks

E.g. Bisection, Pointing Straight Ahead, Landmark, Piazza del Duomo (yet) …

Control sample not strictly necessary (if math model assumptions approximately hold: homogeneity of target distribution, isoprobability within subject and across space)

Conclusions

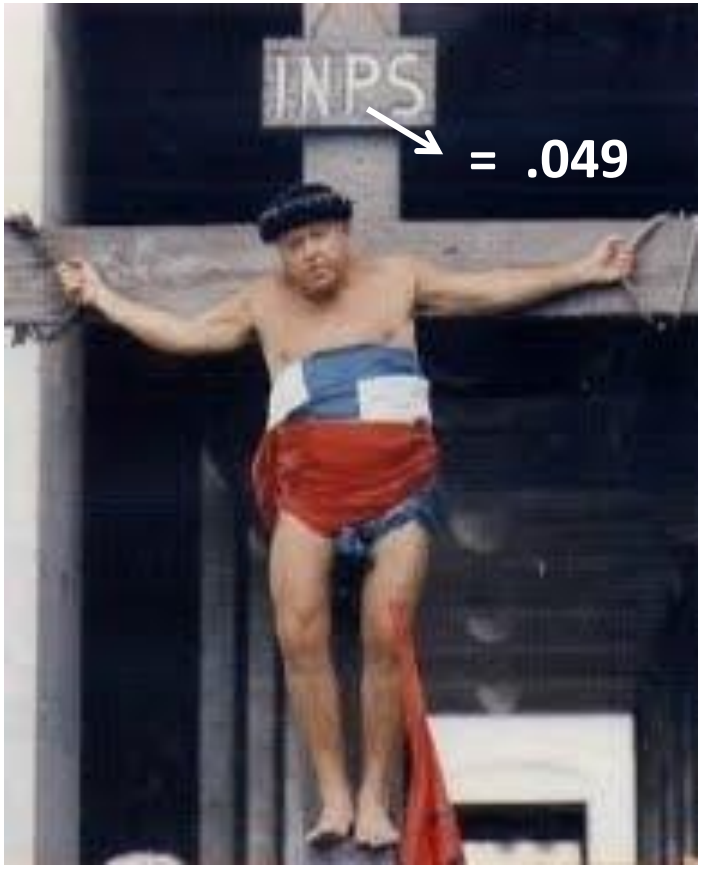
- General statistical method for diagnosing neglect, valid across several tasks – promoting uniformity
- Solves the problem of arbitrary cut-offs
- Avoids so-far-overlooked inflation of false positive rate
- Little likely to need a control sample (patient's data enough)
- Math implemented in an Excel Worksheet – raw data are sufficient

Crocifissione in sala mensa?

Capi d'accusa

Utilizzo dei *p*-value (!)

Assenza di calcolo della potenza (!)



Mitigating circumstances

-Lavoro pubblicato nel 2017 e svolto in buona parte nel 2016 quando avevo appena incontrato, sul sagrato fuori dall'Aula Magna di Pavia (la via di Damasco?), l'***Usciere*** (dell'ordine dei frati che anelano alla canonizzazione del reverendo Bayes)

-*p*-value (relatively) justified in clinical settings (diagnostic error risk is the target)

-Power is not straightforward to derive: we do not know what patients «really» have neglect (lacking a gold standard) – moreover the mathematics in the Bayesian implementation of the problem is far from trivial

Paolo Sommaruga

Cristian Romaniello

psicologia.unipv.it/toraldo/mean-position-of-hits.htm

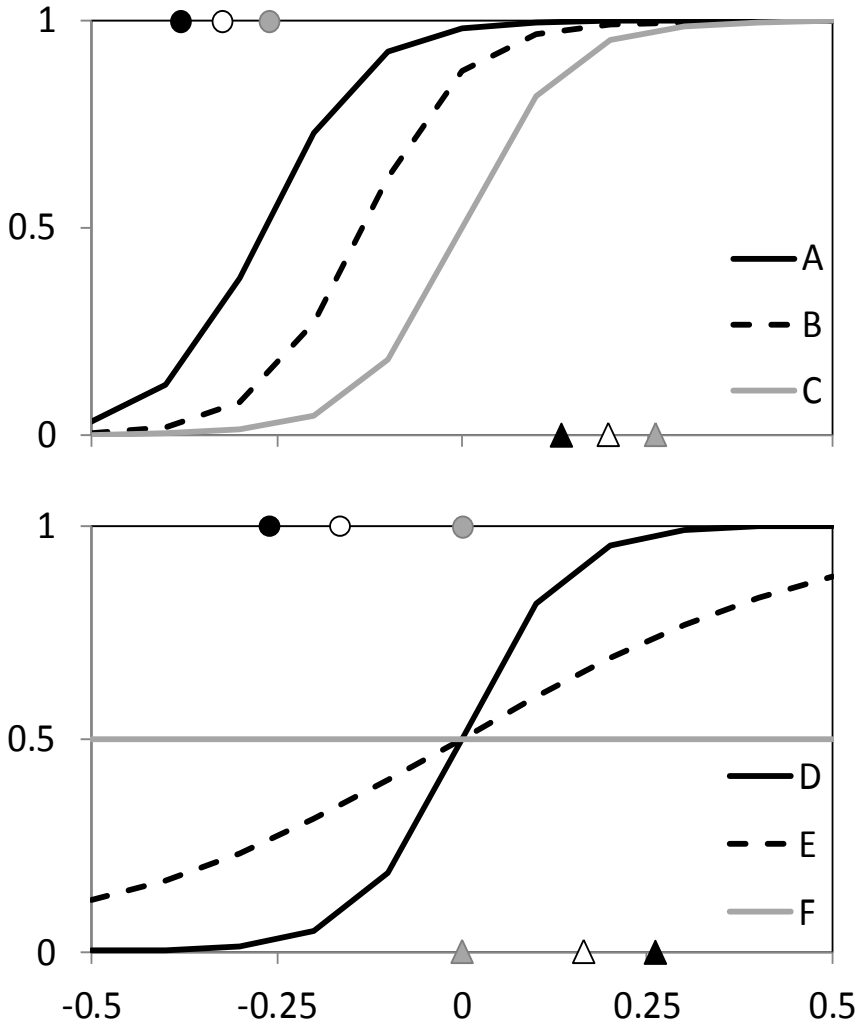
or Google search:

- Toraldo MPH
- Toraldo neglect

Usciere: Massimiliano Pastore

Backup Slides

Thought experiments



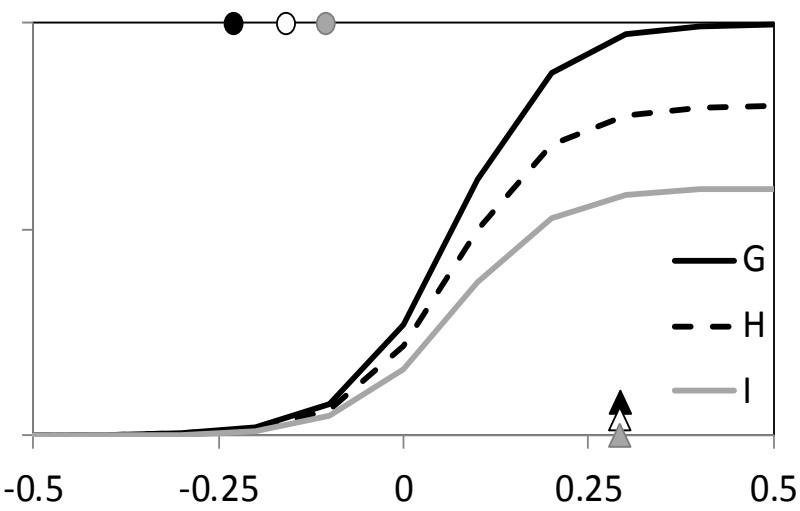
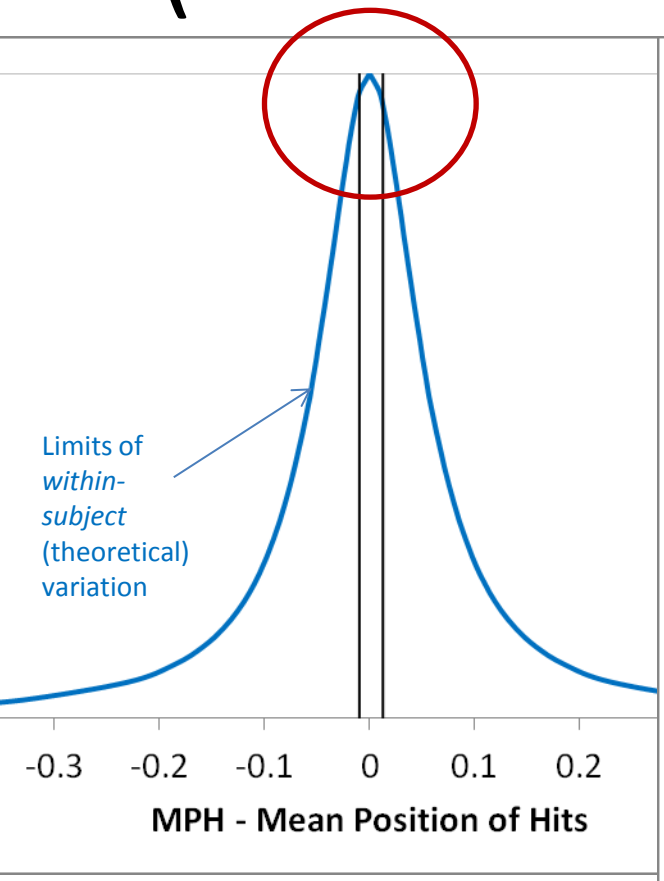
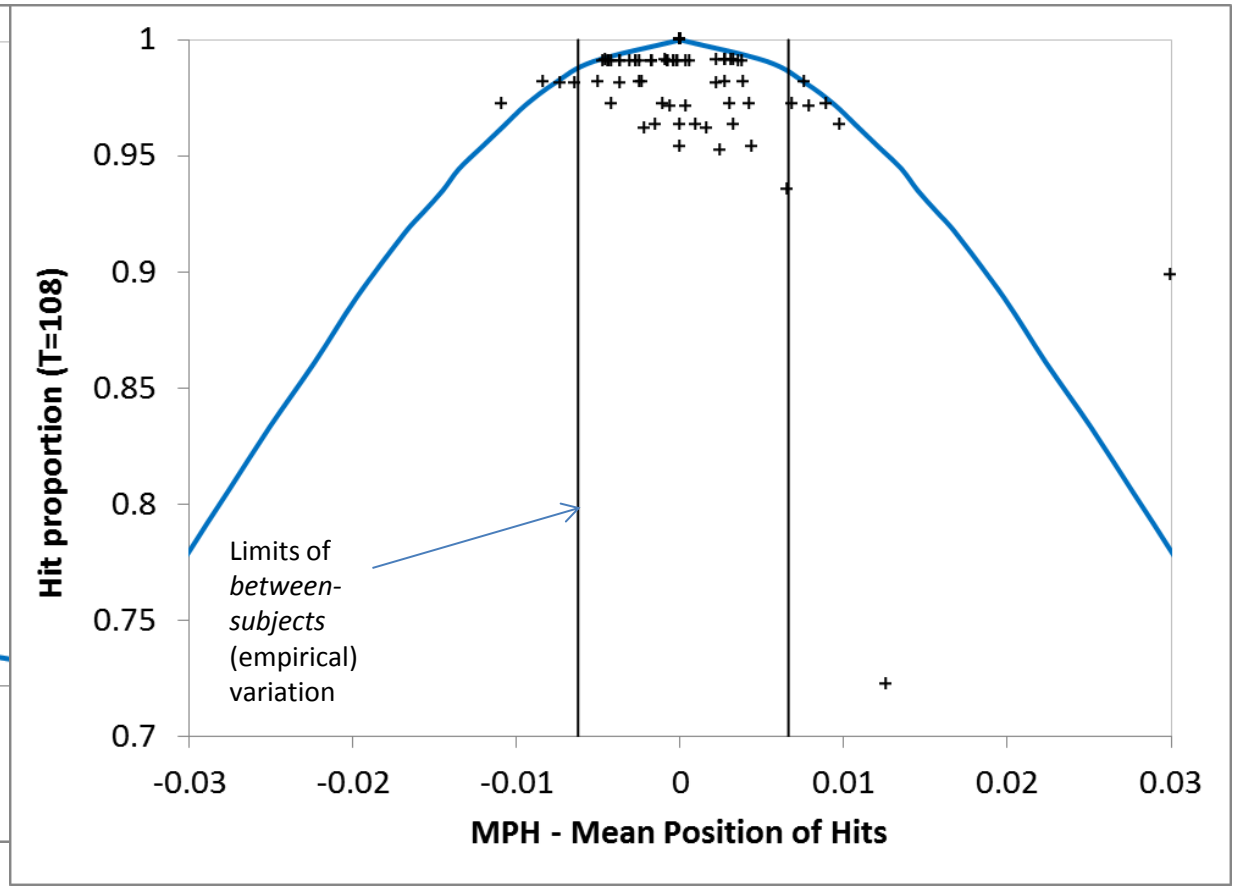


Fig. 2 *Hit rate (Y axis) is plotted against horizontal position (X axis, from the leftmost, –0.5, to the rightmost, +0.5, target) for nine imaginary patients. Curves of patients A-B-C vary only for the* ***Location*** *of the drop in performance, D-E-F only for the* ***Slope*** *of the drop, and G-H-I only for the* ***Ceiling****. Theoretical reasons [Ref. 1] suggest that neglect severity changes between patients A-B-C, and between patients D-E-F, but not between patients G-H-I. The MPH index (Mean Position of Hits) obeys this rule, while Mean Position of Omissions (MPO) violates it. MPHs are shown as triangles on the X axis of each panel (black, white and grey refer to the black, dashed and grey curves respectively); MPOs are shown as disks along the top edges of the panels.*

(2017 data) Zooming in on the top





199 controls (**black +**) performed nicely within the theoretical limits of within-subject variation (**blue**) [no difference between the SDs: *BF* = 18.7 favouring the null]

-Inference: *normal subjects do not have lateral biases at all* – they only vary for their space-independent probability of Hits

-***No need of control groups (for visual search tasks of the Diller type): knowing within-subject predicted variation is enough***

List of assumptions

"True" neglect severity is conceptualized as the unknown mean ν of the distribution whose probability density function is the Hit rate logistic curve in the space ranging from -.5 (leftmost target) to .5 (rightmost target). *MPH* is an asymptotically unbiased estimator of ν (i.e. the mean *MPH* equals ν when the number of target positions = +∞) if the following assumptions hold.

(1) The logistic curve is driven by three parameters: *slope*, *location* and *upper asymptote*, or '*ceiling*' (see above). The *lower asymptote*, or '*floor*' is assumed to be zero (3-parameter curve).

(2) Targets occupy positions that are equispaced along the studied spatial dimension ('**equispacing**').

(3) Each position hosts an equal number of targets ('**ties homogeneity**').

Moreover, the statistical model used to diagnose neglect holds if, also:

(4) In a given normal subject or brain-damaged patient without neglect, all targets have exactly the same probability of being detected, no matter their nature or position ('**isoprobability**' or '**no lateral bias**' assumption).