

ThermoFisher
SCIENTIFIC

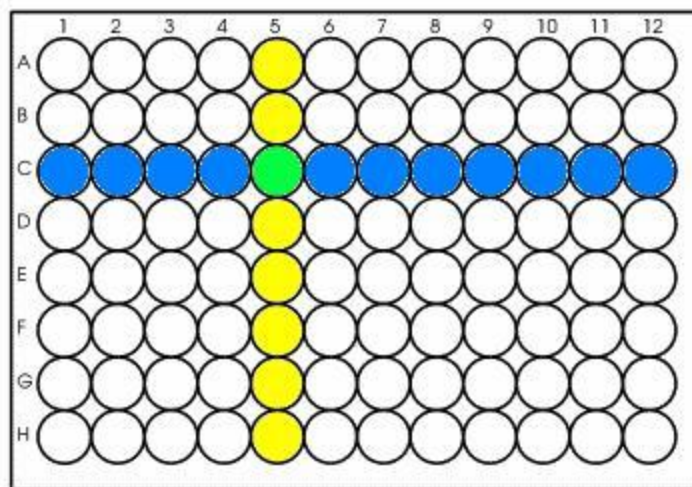
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Computational Assessment of Screening Statistics with NoiseMaker

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Background

- High-throughput screening (HTS) is often one of the early steps in a drug discovery process
- Systematic positional effects are common
- Brideau et al. 2003 say B score corrects positional effects well
- Makarenkov et al. 2007 question this assertion



- The magnitude of positional effects and the number of real hits are unknown in real high-throughput screening data

NoiseMaker

- An HTS data simulator
 - Written in C# for Windows
 - Freeware
- Randomly adds a specified number of “true” hits
- Adds systematic effects and random noise to the “true” data

NoiseMaker 0.9

Help

Hits Noise

True Data File: ? C:\projects\B score testing\plate map Browse

Plate Type: ? 8x12 (96 well)

of Replicates: ? 3

Output File: ? C:\projects\B score testing\noise data

Noise Makers: ?

	Element	Element Index	Mean Change	StandardDev
	Screen	1	0	1
	Row	3	2	0
	Column	5	0	1
▶	Plate	10	2	1

Apply Floor ? 0

Apply Ceiling ?

Make Noise

Performance of B Score

- Makarenkov et al. tested B score on data with increased *variance* in some rows and columns
 - 1% of the wells are real hits $\sim N(5, 1)$
 - All non-hit wells $\sim N(0, 1)$
 - Positional effect $\sim N(0, c)$ added to row C & column 5 on every plate
- True positive rate degrades quickly with increasing variance

c	0	1	2	3	4	5
True positive rate	83.67%	75.83%	64.50%	56.50%	51.25%	42.83%
False positive rate	0.17%	0.24%	0.36%	0.44%	0.49%	0.58%
False negative rate	16.33%	24.17%	35.50%	43.50%	48.75%	57.17%

Performance of B Score (cont.)

- Brideau et al. developed B score for data with altered *means* in some rows and columns
 - 1% of the wells are real hits $\sim N(5, 1)$
 - All non-hit wells $\sim N(0, 1)$
 - Positional effect $\sim N(c, 0)$ added to row C & column 5 on every plate
- True positive rate remains stable with altered means

c	0	1	2	3	4	5
True positive rate	83.67%	82.42%	82.83%	84.75%	83.58%	85.00%
False positive rate	0.17%	0.18%	0.17%	0.15%	0.17%	0.15%
False negative rate	16.33%	17.58%	17.17%	15.25%	16.42%	15.00%

Conclusion & Future Directions

- B score effectively compensates for positional effects that alter row or column means
- B score does not compensate well for positional effects that increase row or column variances
- Altered means are far more common in real HTS data
- Thus, B score remains a useful method for analyzing HTS data
- Future simulations will include:
 - Hits with varying strengths
 - Other types of positional effects
 - More scoring methods
- The NoiseMaker software is freely available
 - contact amanda.birmingham@thermofisher.com for an installer