

# Transcriptomic Signature of Obesity



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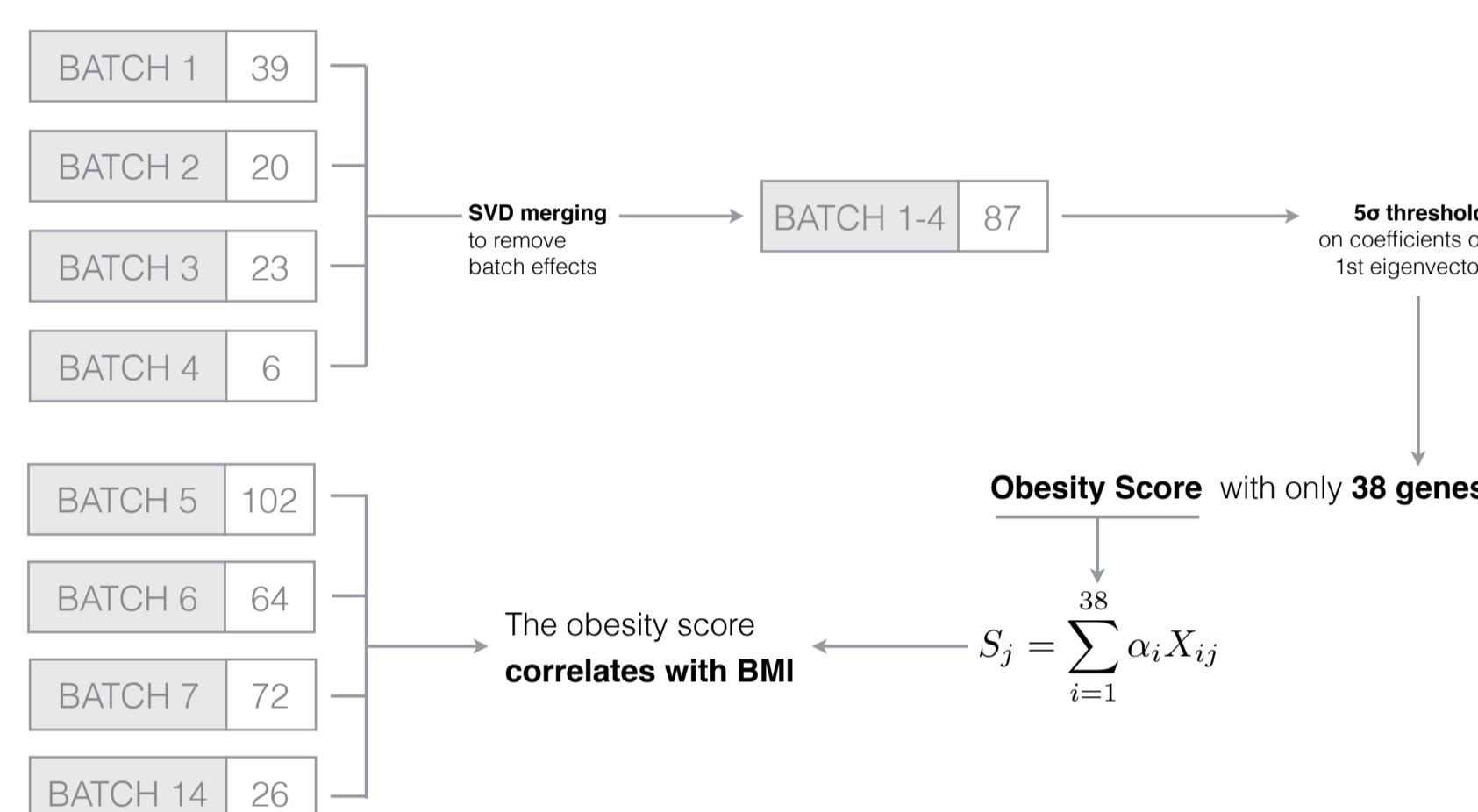
## Obesity: Genes or Environment?

Observational studies suggest that obesity might have a Mendelian origin, but it is not clear if gene expression patterns observed in obese subjects are secondary to genetic traits or not.

Well-established cases of Mendelian forms of obesity approximately account for only 5% of the severely obese cases.

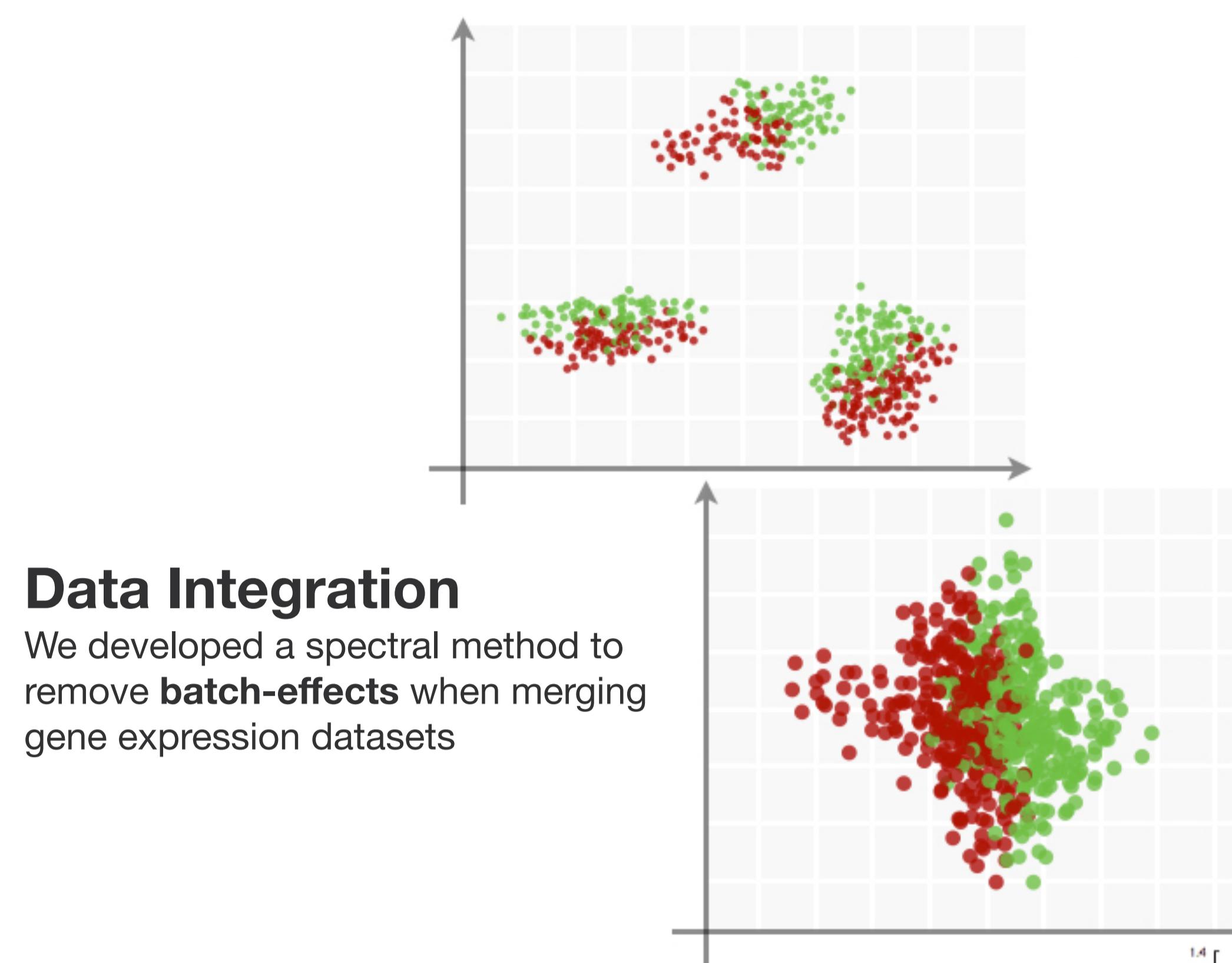
## Obesity Score

We merge four datasets (batches 1-4), totalling 87 samples, to construct a robust (5- $\sigma$ ) obesity signature.



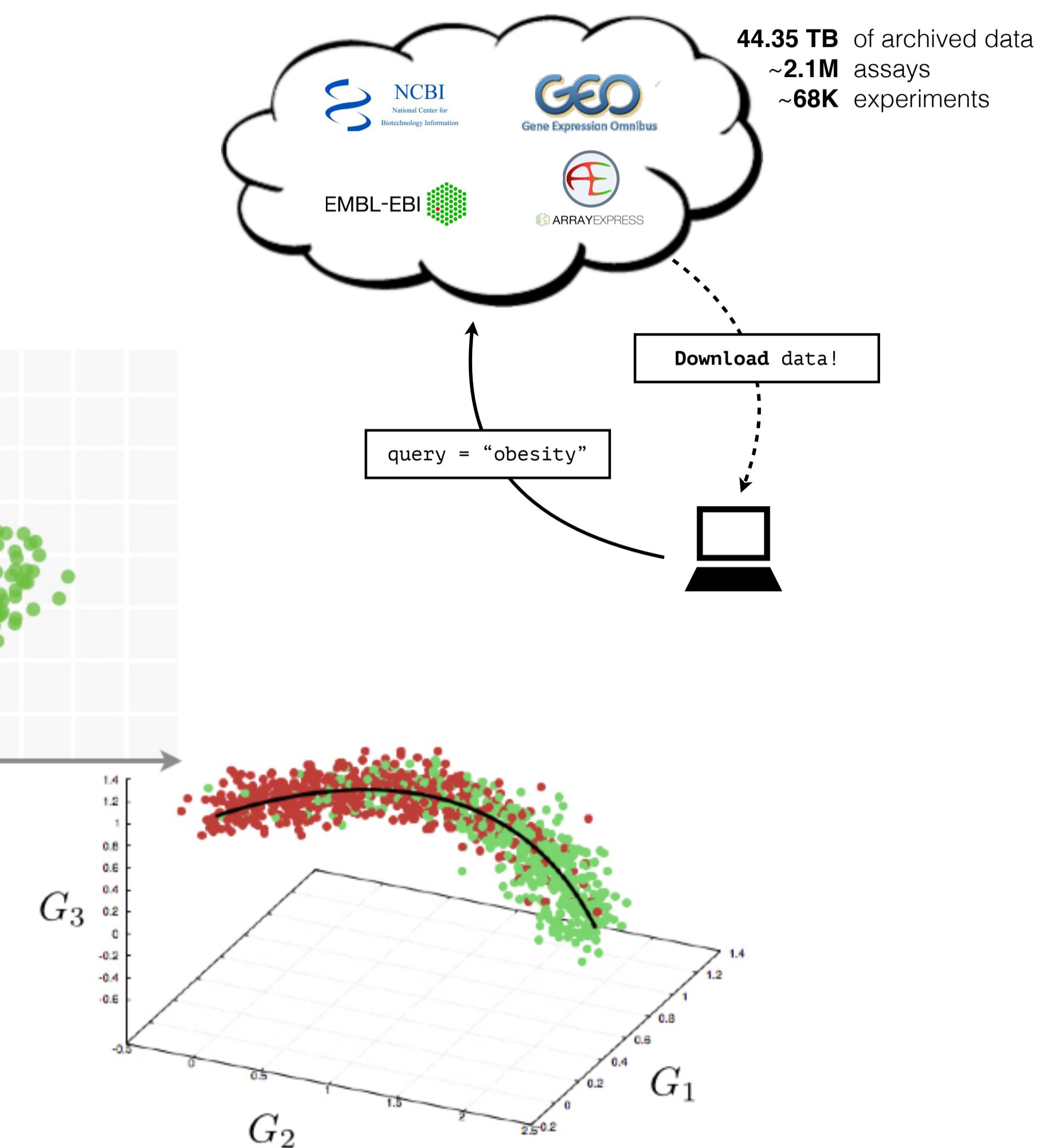
## Stefano Zapperi

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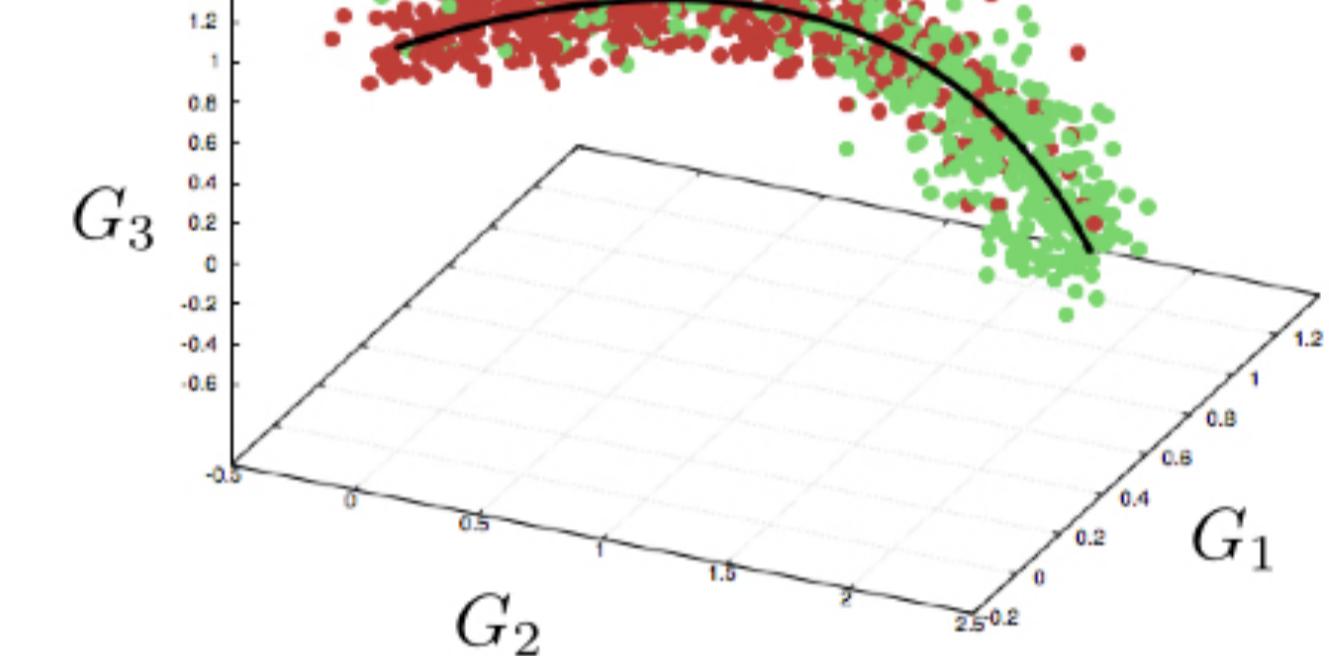
## Data Integration

We developed a spectral method to remove **batch-effects** when merging gene expression datasets



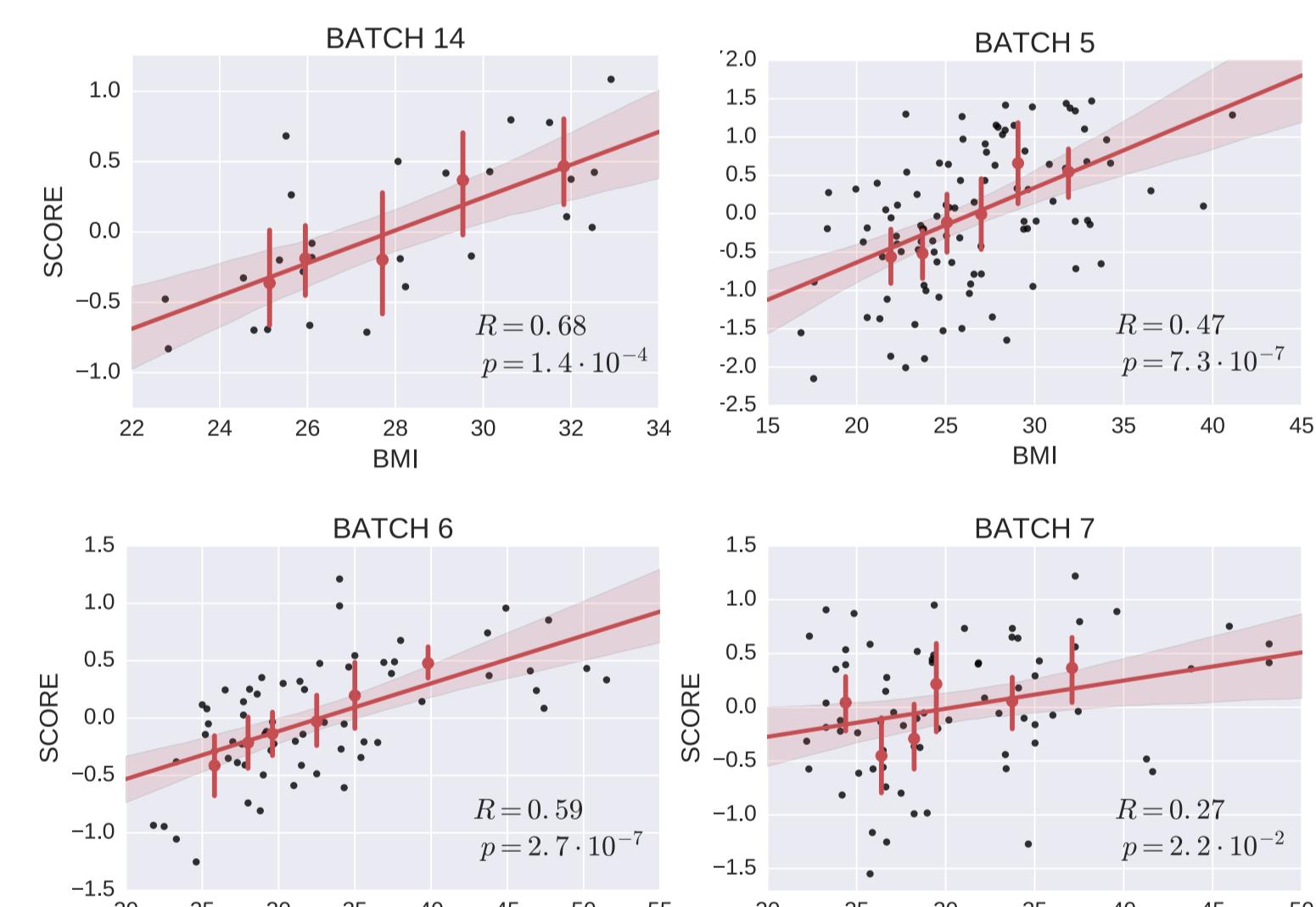
## Dimensionality Reduction

We use Pathway Deregulation Scores (PDS) to reduce the number of dimensions from tens of thousands of genes to just hundreds of pathways.



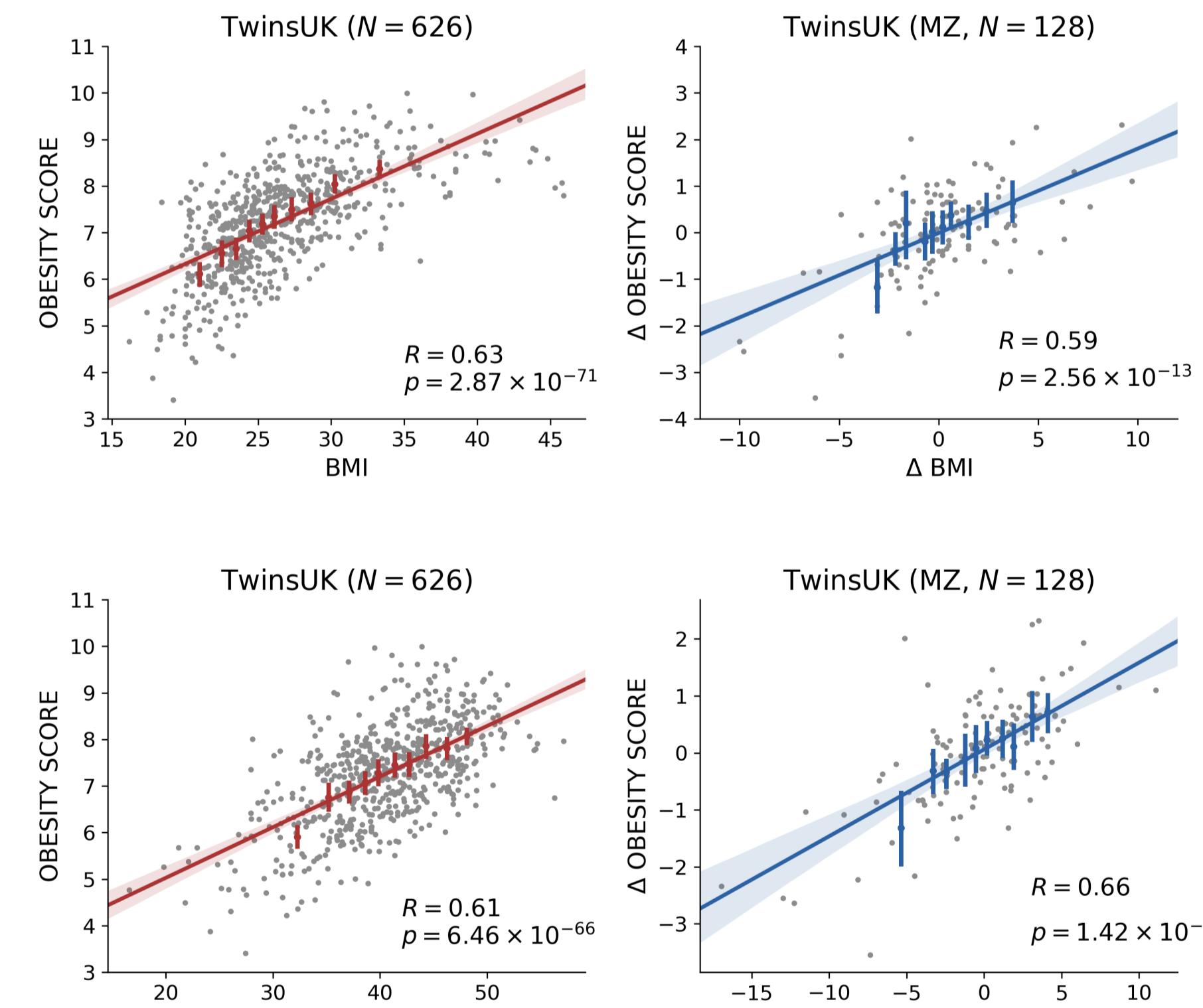
## Obesity Score and BMI

Our score correlates with BMI on four independent datasets (batches 5-7, 14).



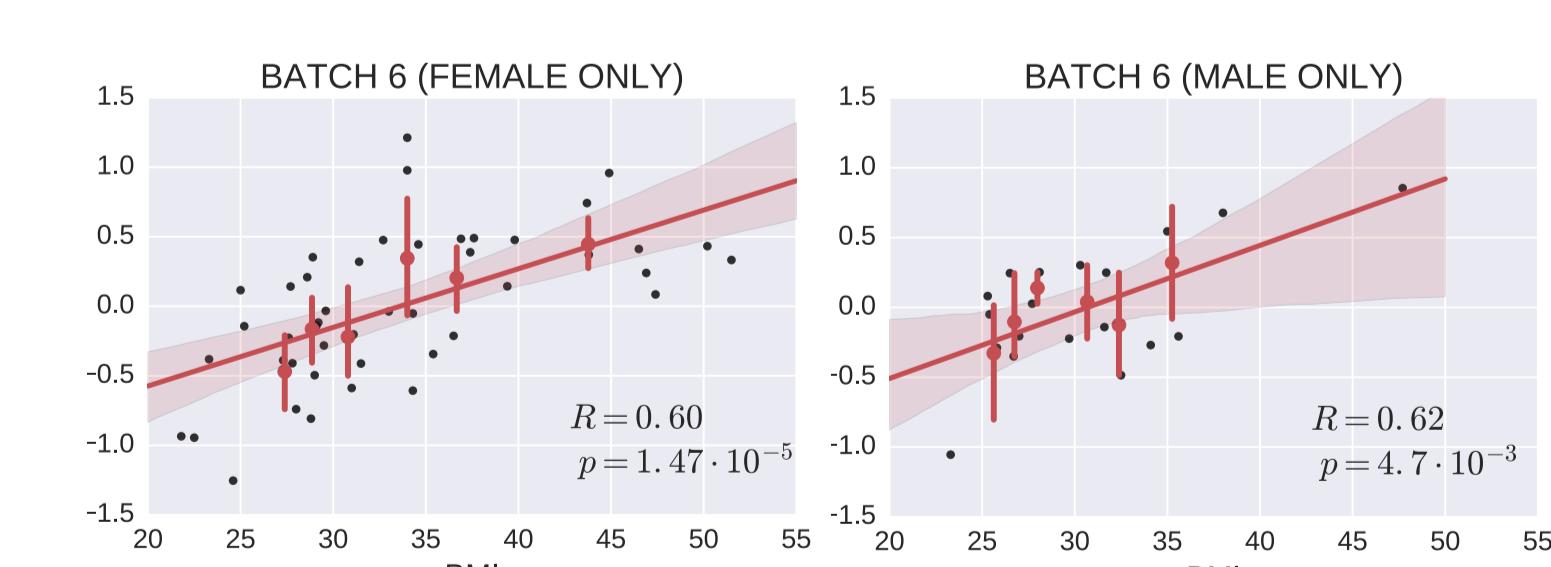
## Obesity Score and Twins

We further validate our results with the TwinsUK dataset (N=626). The obesity score correlates with BMI and %FAT.



## Obesity Score and Gender

Results do not depend on gender. The obesity score correlates with BMI both for F and M subjects.



## Datasets

Batch	Lean	Overweight	Obese	Total	Gender	BMI	Tissue	Accession code	Ref.
Batch 1	20	0	19	39	19 M / 20 F	categorical	Adipose	GSE2508	6
Batch 2	10	0	10	20	All F	categorical	Adipose	GSE16637	7
Batch 3	6	(10)	17	23	Unknown	numerical	Adipose	GSE27949	8
Batch 4	3	0	3	6	Unknown	categorical	Adipose	GSE48964	9
Batch 5	42	39	21	102	49 M / 53 F	numerical	Adipose	GSE62117	10
Batch 6	.5	24	35	64	19 M / 45 F	numerical	Adipose	GSE64567	11
Batch 7	14	28	30	72	All F	numerical	Normal breast	GSE33526	12
Batch 8	131	131	142	404	All F	categorical	Breast tumor	GSE78958	13
Batch 9	—	—	—	979	All F	none	Breast tumor	—	?
—	—	—	—	114	All F	none	Normal breast	—	?
Batch 10	0	0	18	18	All F	categorical	Adipose	GSE65540	28
Batch 11	—	—	—	275	Unknown	none	Monocytes	GSE66306	?
—	—	—	—	488	Unknown	none	Blood	—	?
Batch 12	12	0	36	48	All F	categorical	Monocytes	GSE32575	14
Batch 13	0	0	12	12	Unknown	categorical	Monocytes	GSE54350	30
Batch 14	4	14	8	26	16 M / 10 F	numerical	Adipose	E-MEXP-1425	23

## References

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- F. Font-Clos, S. Zapperi and C. A. M. La Porta. 2017. "Integrative Analysis of Pathway Deregulation in Obesity." *NPJ Systems Biology and Applications* 3 (June): 18.
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- A. Livshits, A. Git, G. Fuks, C. Caldas, and E. Domany. 2015. "Pathway-Based Personalized Analysis of Breast Cancer Expression Data." *Molecular Oncology* 9 (7): 1471–83.



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