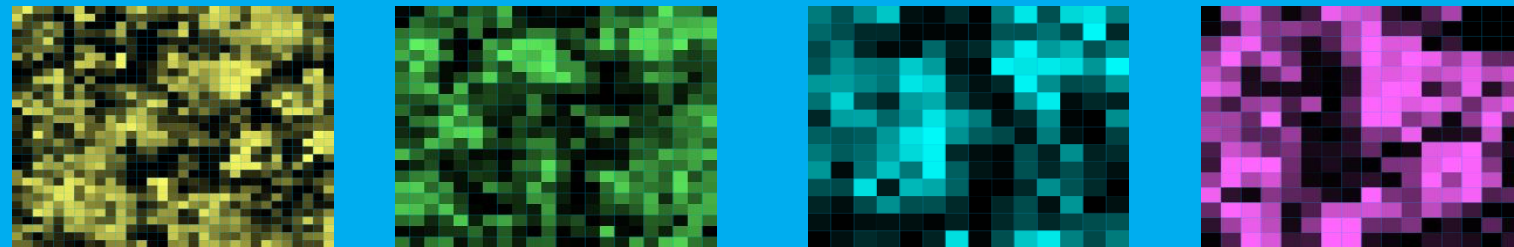


The Characteristic Direction: A Geometrical Approach to Differential Expression – Part Three



Network Analysis in Systems Biology

Neil Clark, PhD

Instructor, Ma'ayan Lab

Department of Pharmacology and Systems Therapeutics

Icahn School of Medicine at Mount Sinai, New York, NY 10029

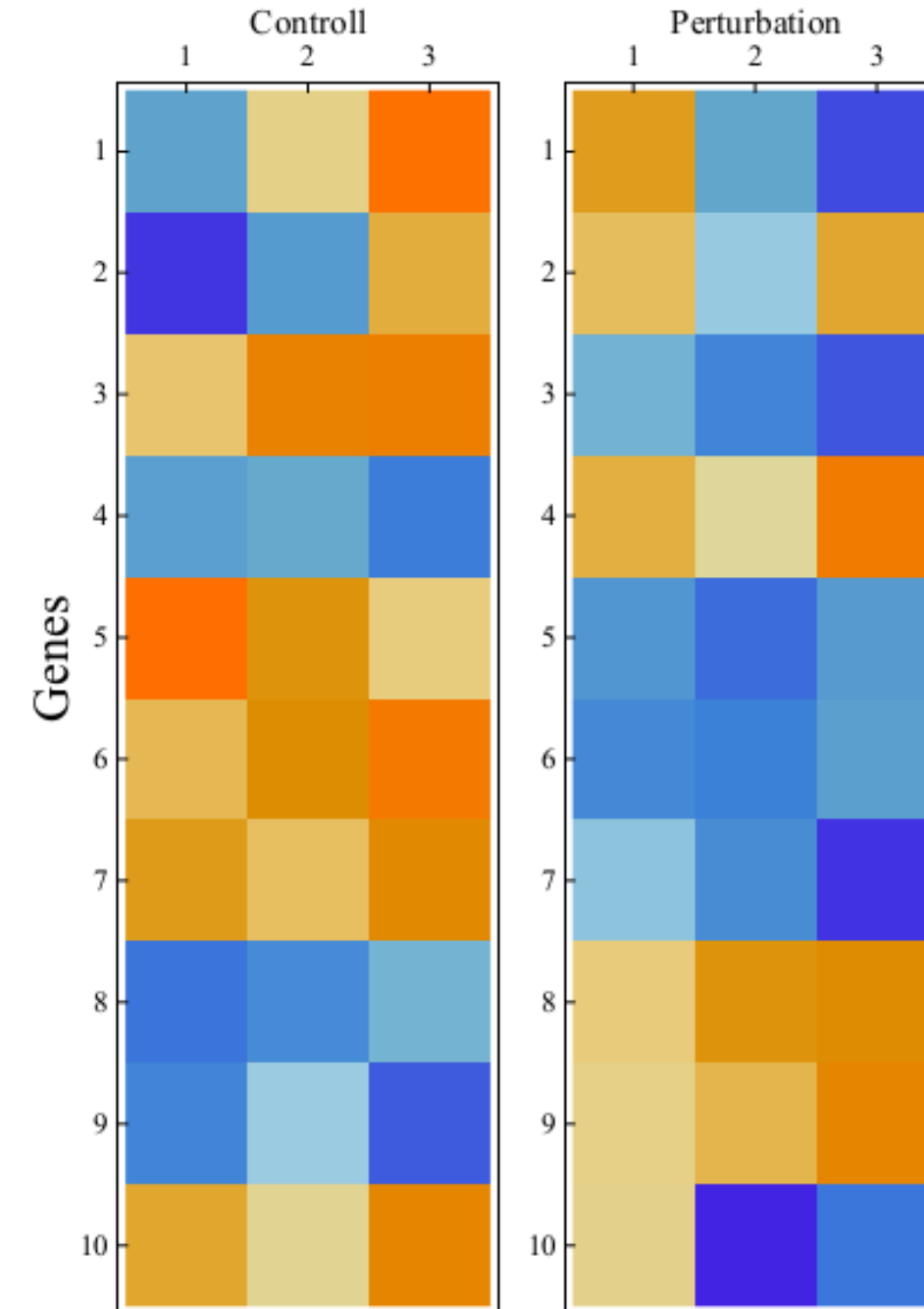


Some Commonly Used Approaches

- ▶ Fold change
 - Ratios of expression levels. No Account of variance.
- ▶ Welsh's t test
 - Assumes Gaussianity
- ▶ Significance Analysis of Microarrays (SAM)
 - A modification of the t test
- ▶ Limma
 - Apply a linear model to each individual gene

Validation using Independent ChIP-Seq Data for Perturbed TF

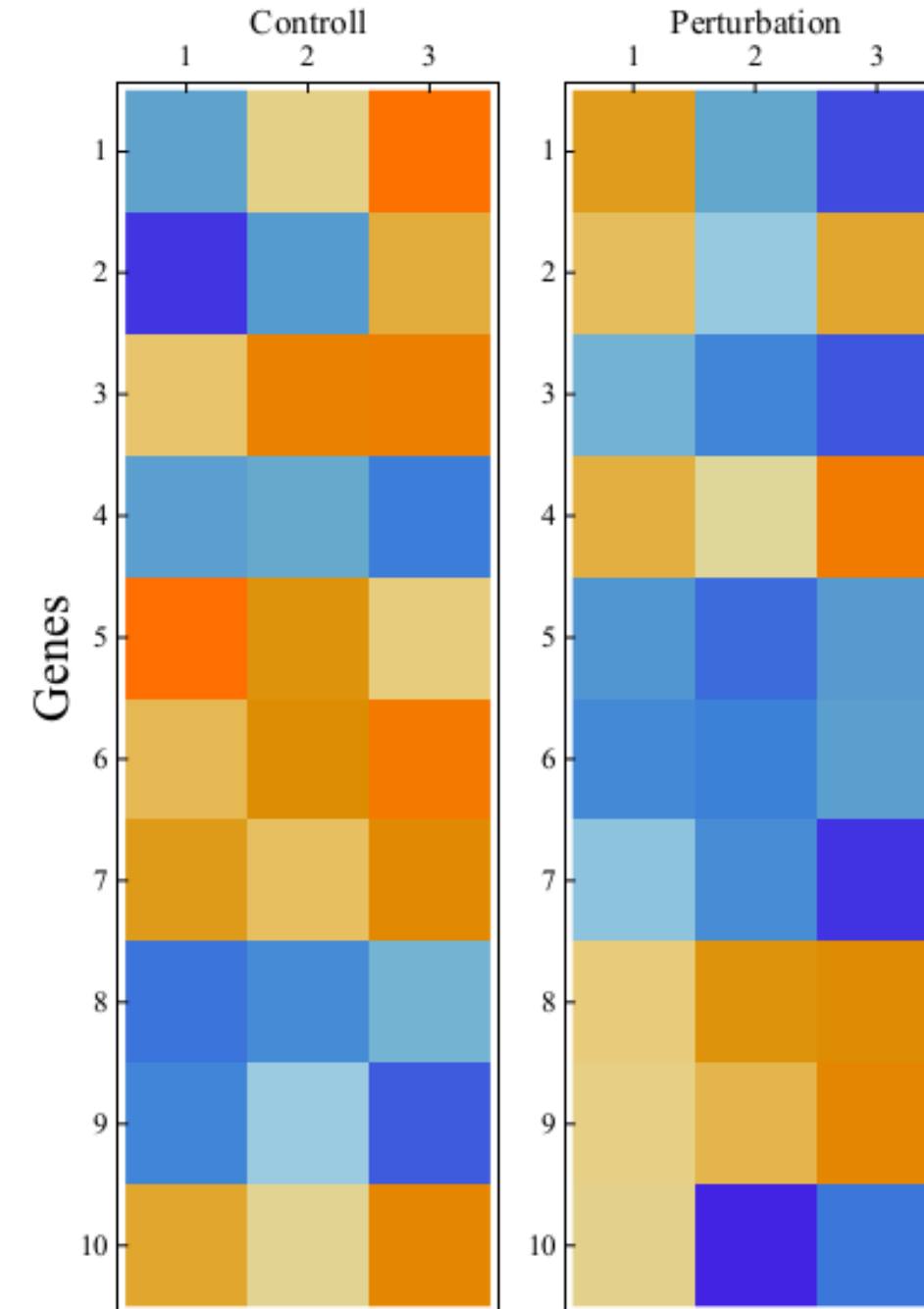
A schematic of one expression data set from the perturbation of a transcription factor.



Validation using Independent ChIP-Seq Data for Perturbed TF

Assess the significance of the genes according to the method being used (e.g. Characteristic direction, Limma, SAM, etc..)

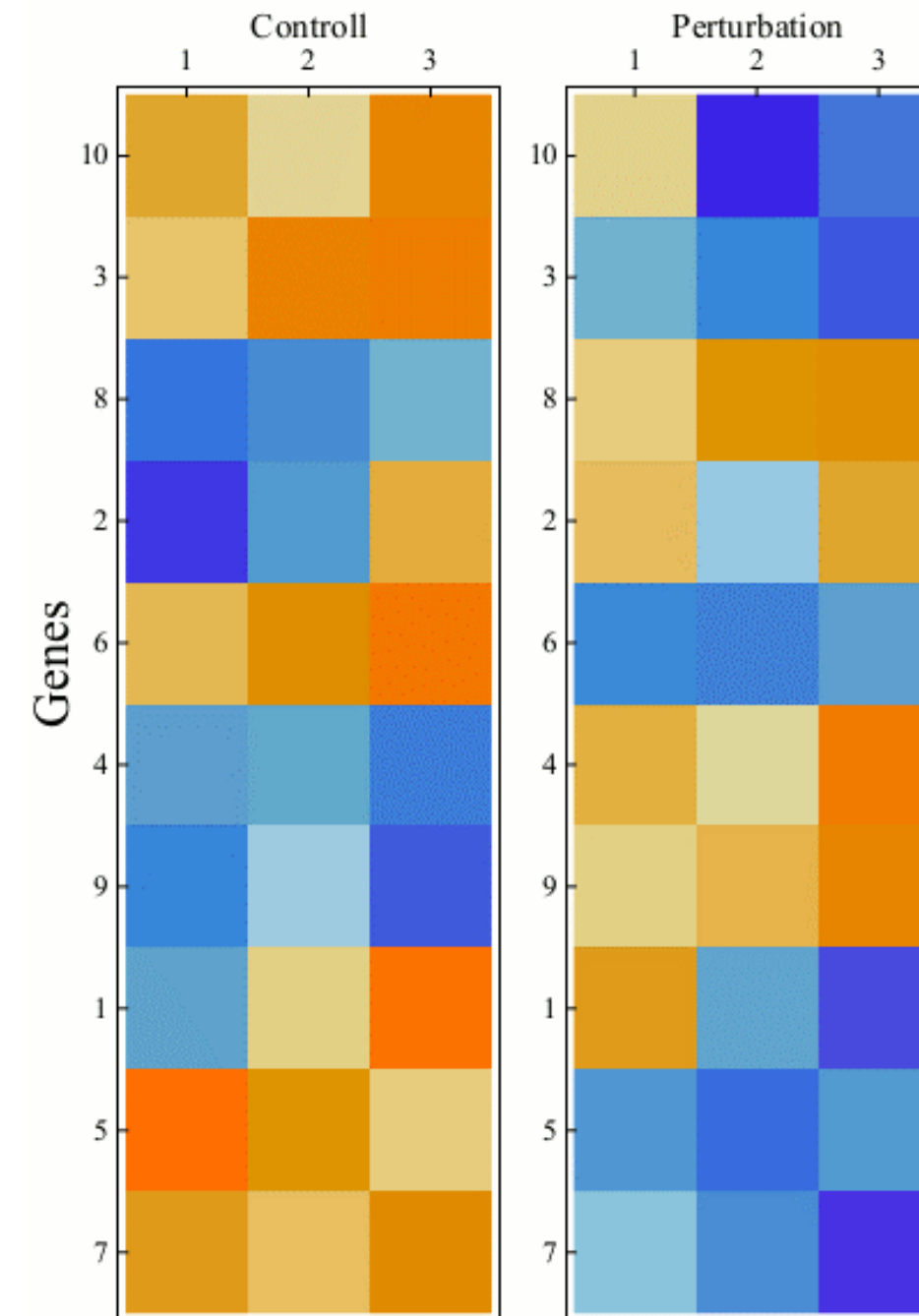
Rank the genes according to their significance



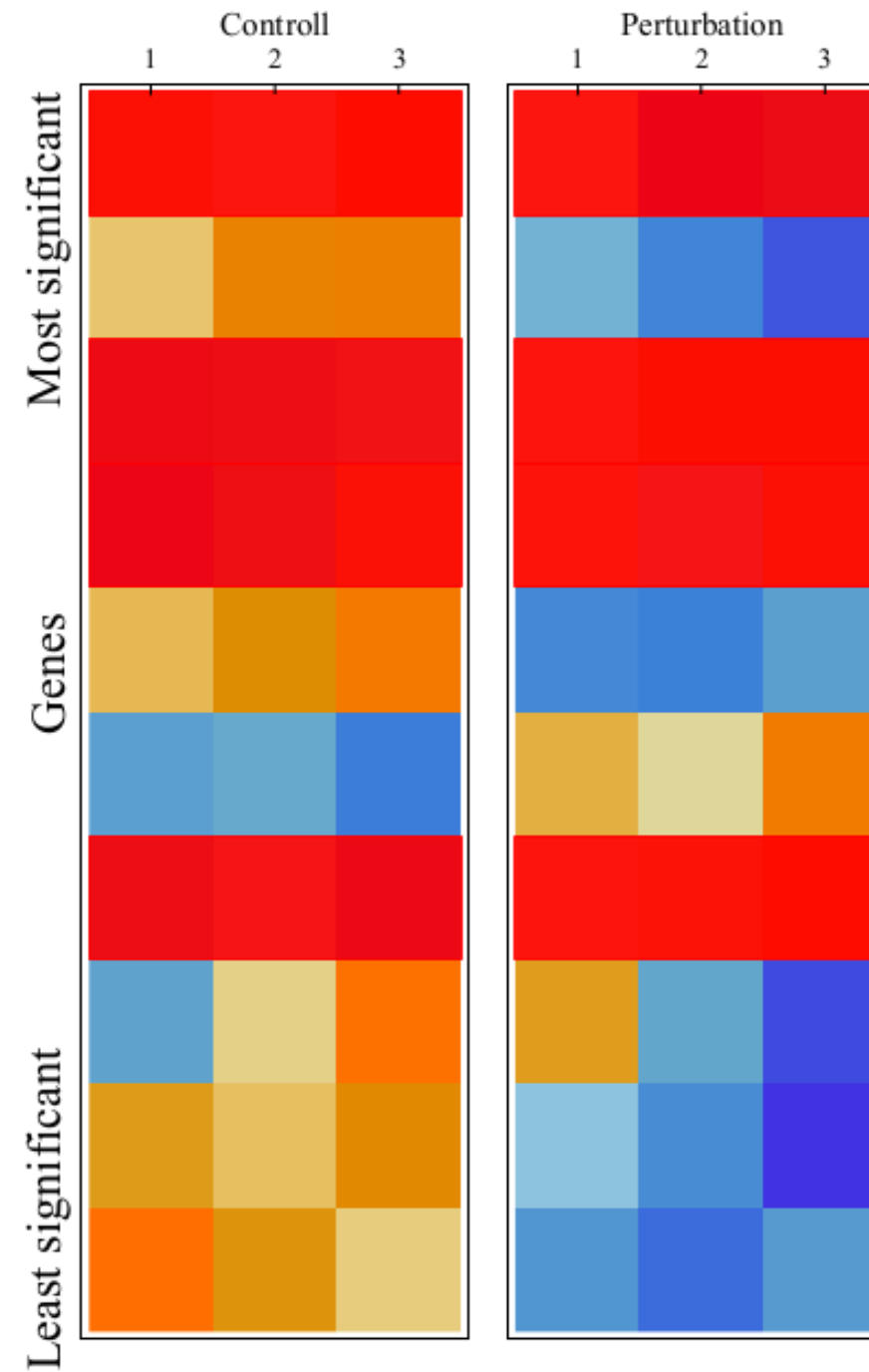
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Validation using Independent ChIP-Seq Data for Perturbed TF

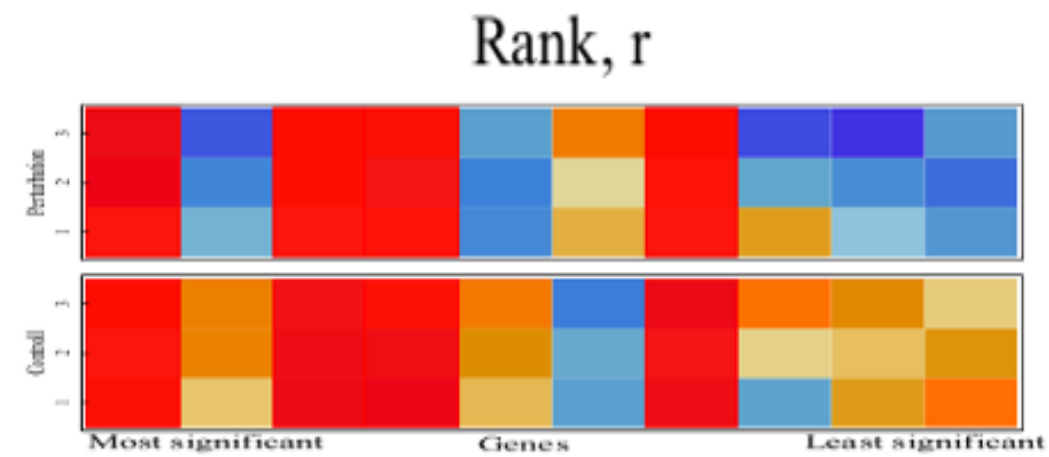


Genes associated with binding sites of the perturbed transcription factor

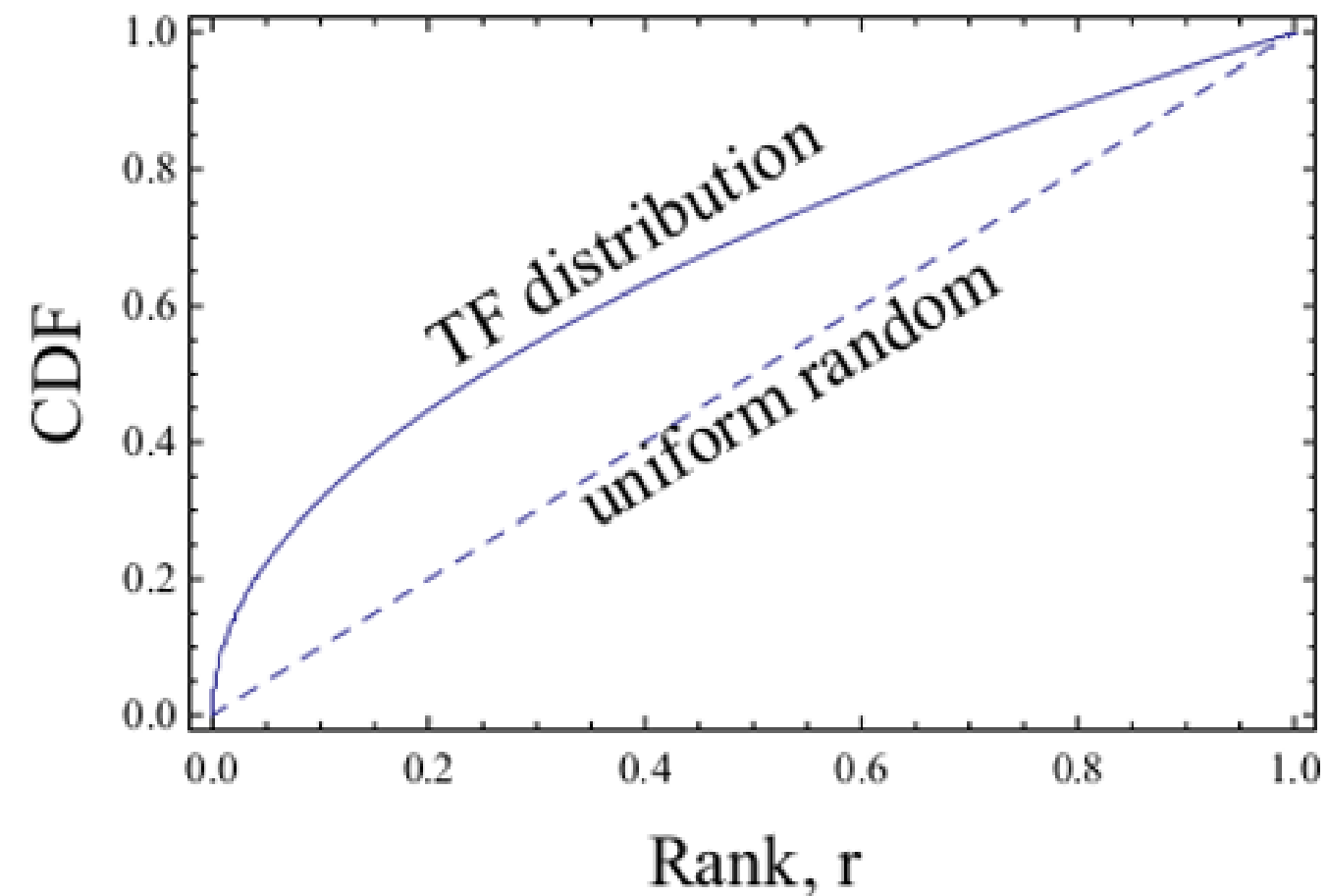
Validation using Independent ChIP-Seq Data for Perturbed TF



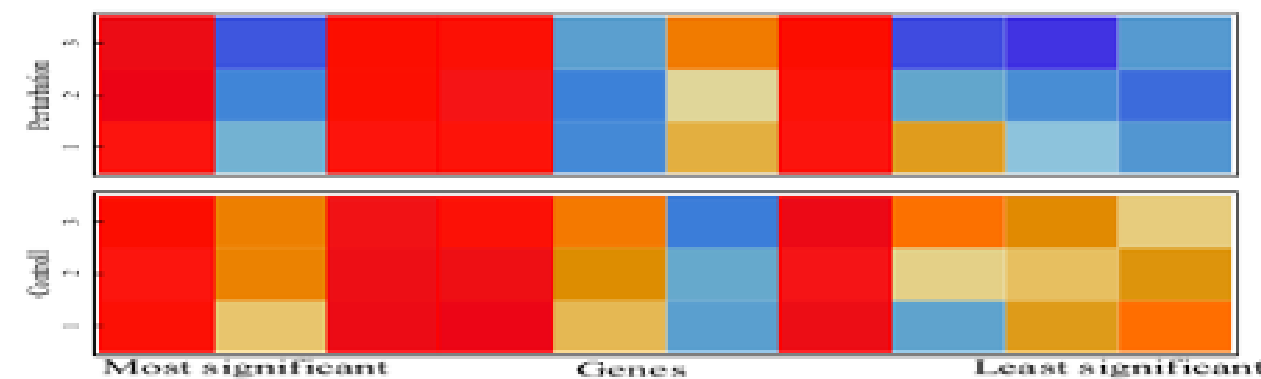
Validation using Independent ChIP-Seq Data for Perturbed TF



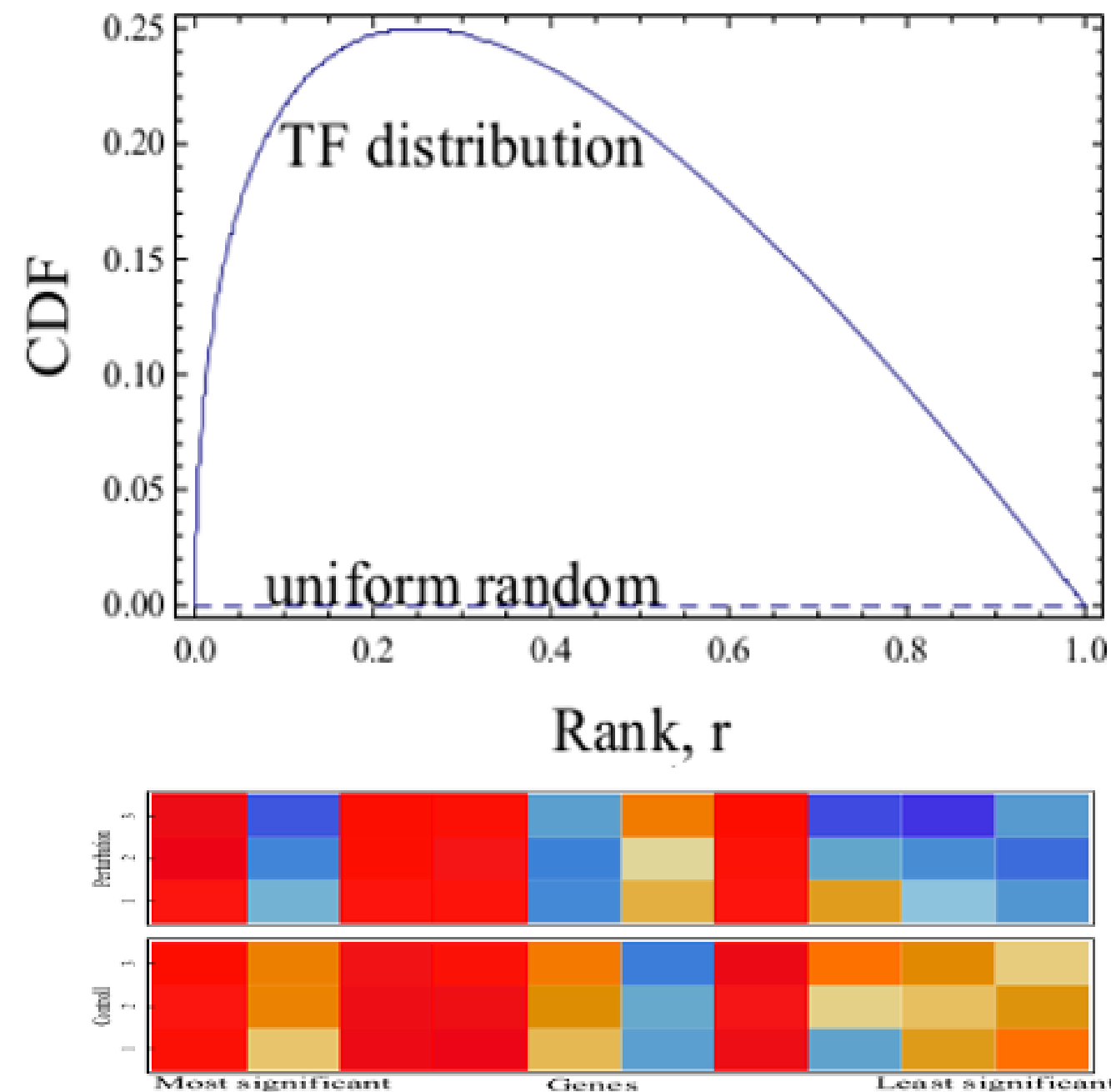
Validation using Independent ChIP-Seq Data for Perturbed TF



Examine the cumulative distribution of the genes associated with binding sites of the perturbed transcription factor.



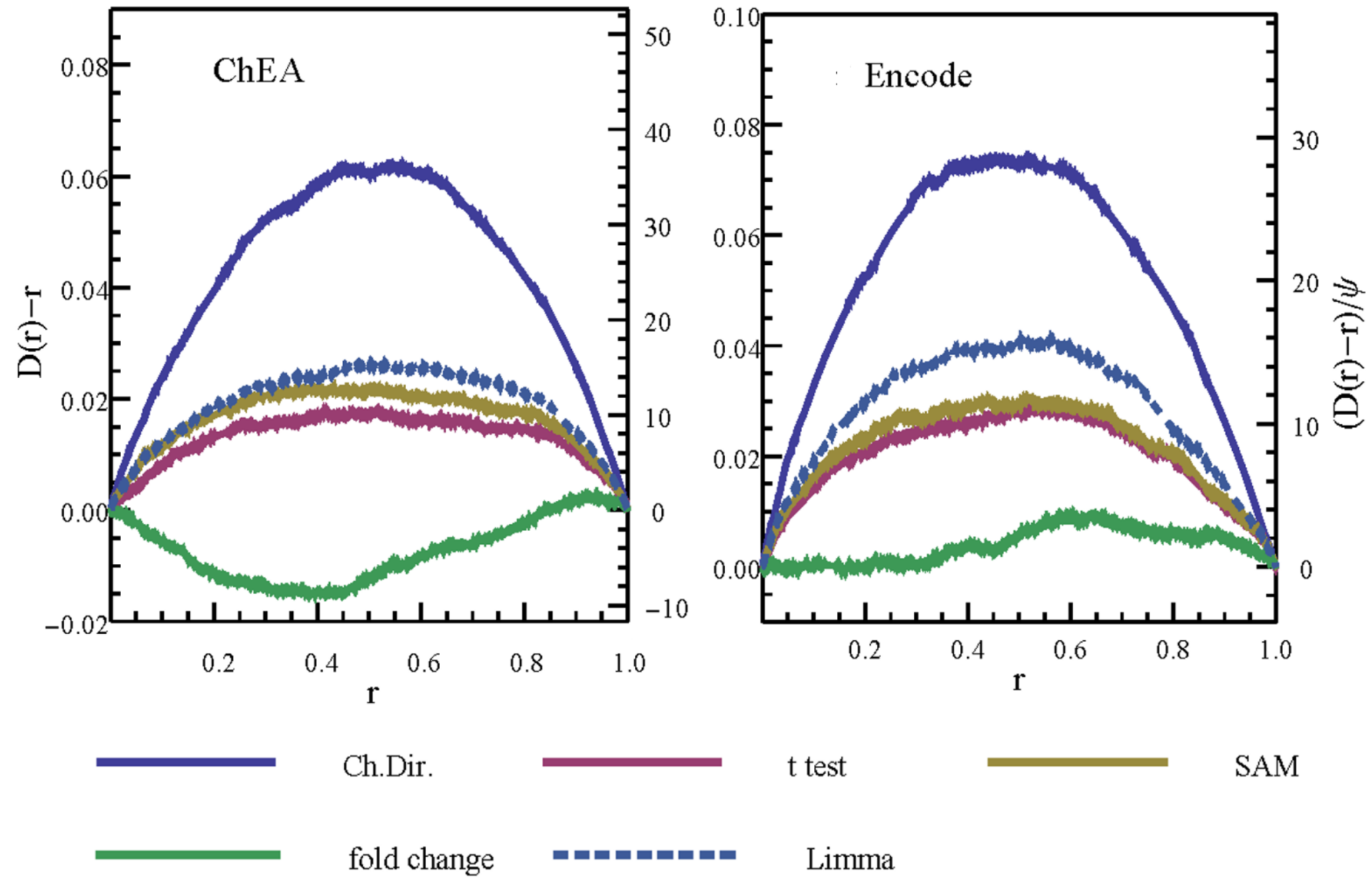
Validation using Independent ChIP-Seq Data for Perturbed TF



Compare the cumulative distribution to what would be expected if the gene rankings were essentially random.

The height of the resulting curve is an indication of the degree to which the ChIP-Seq genes are recovered in the expression profiling by the method used.

Results



Drug Perturbation Results

