

# CiteFuse enables multi-modal analysis of CITE-seq data

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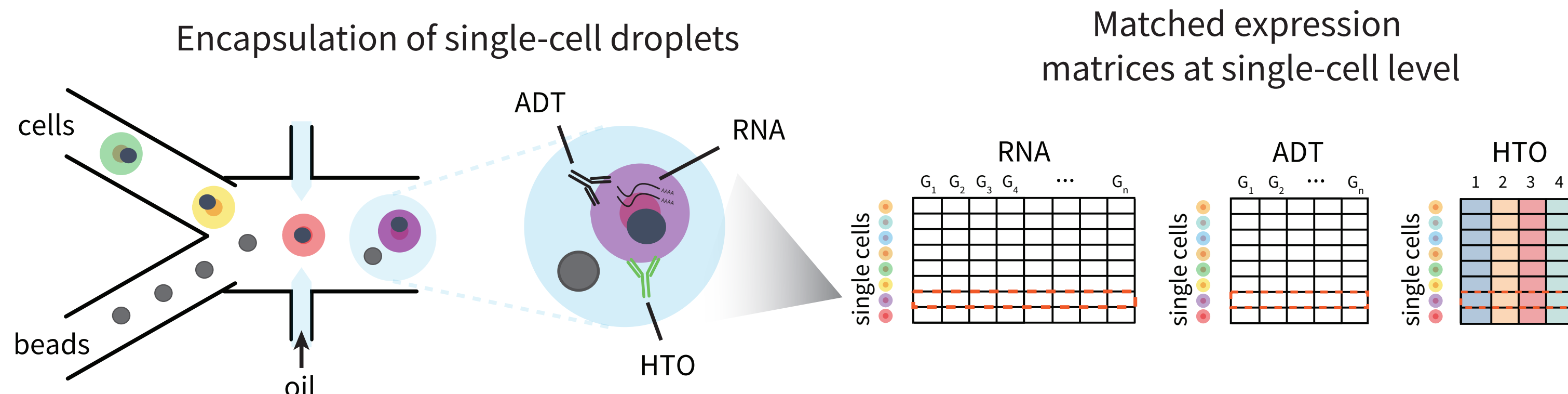
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## The dawn of single-cell multi-omics

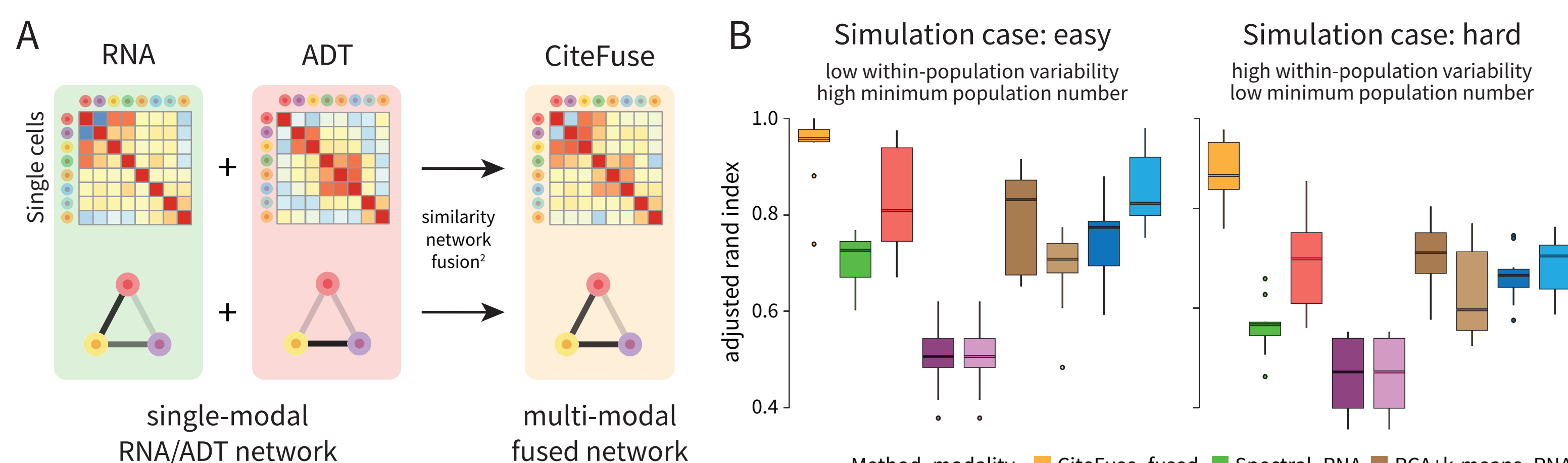
Single-cell technologies have transformed our understanding of cellular diversity and state by enabling high-throughput profiling of diverse information from individual cells [1]. Most of the technologies have focused on the measurement of a single modality. With fast-evolving technologies now measuring joint information from single cells, what more can we learn from multi-modal data?

## CITE-seq generates multi-modal data from the same cell

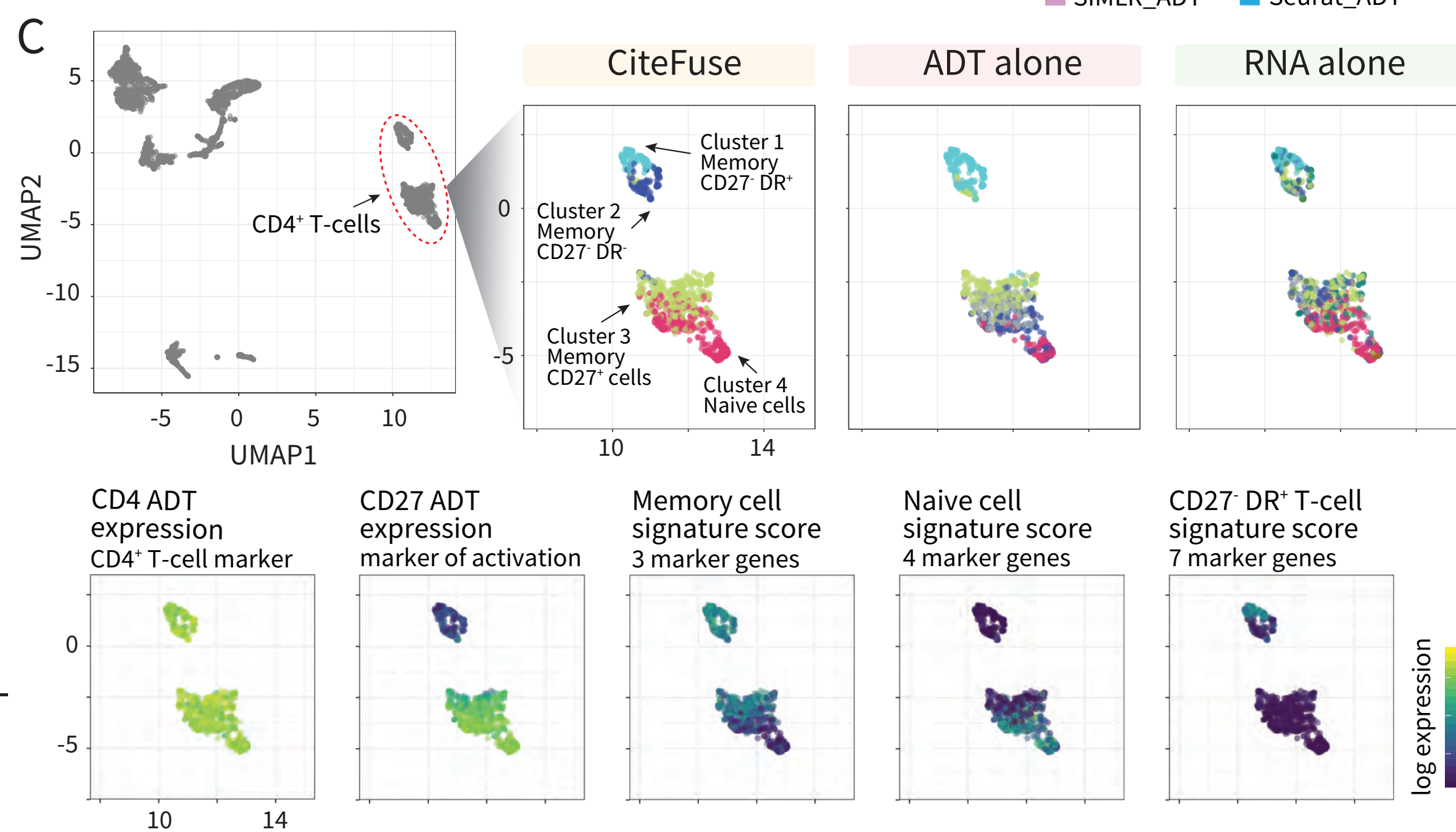


(A) A schematic of the micro-fluidic-based CITE-seq experiment [2] and the generation of matched RNA, antibody-derived tags (ADT), and hashtag oligonucleotide (HTO) expression matrices where rows indicate single cells and columns indicate RNA, ADTs, or HTOs, respectively.

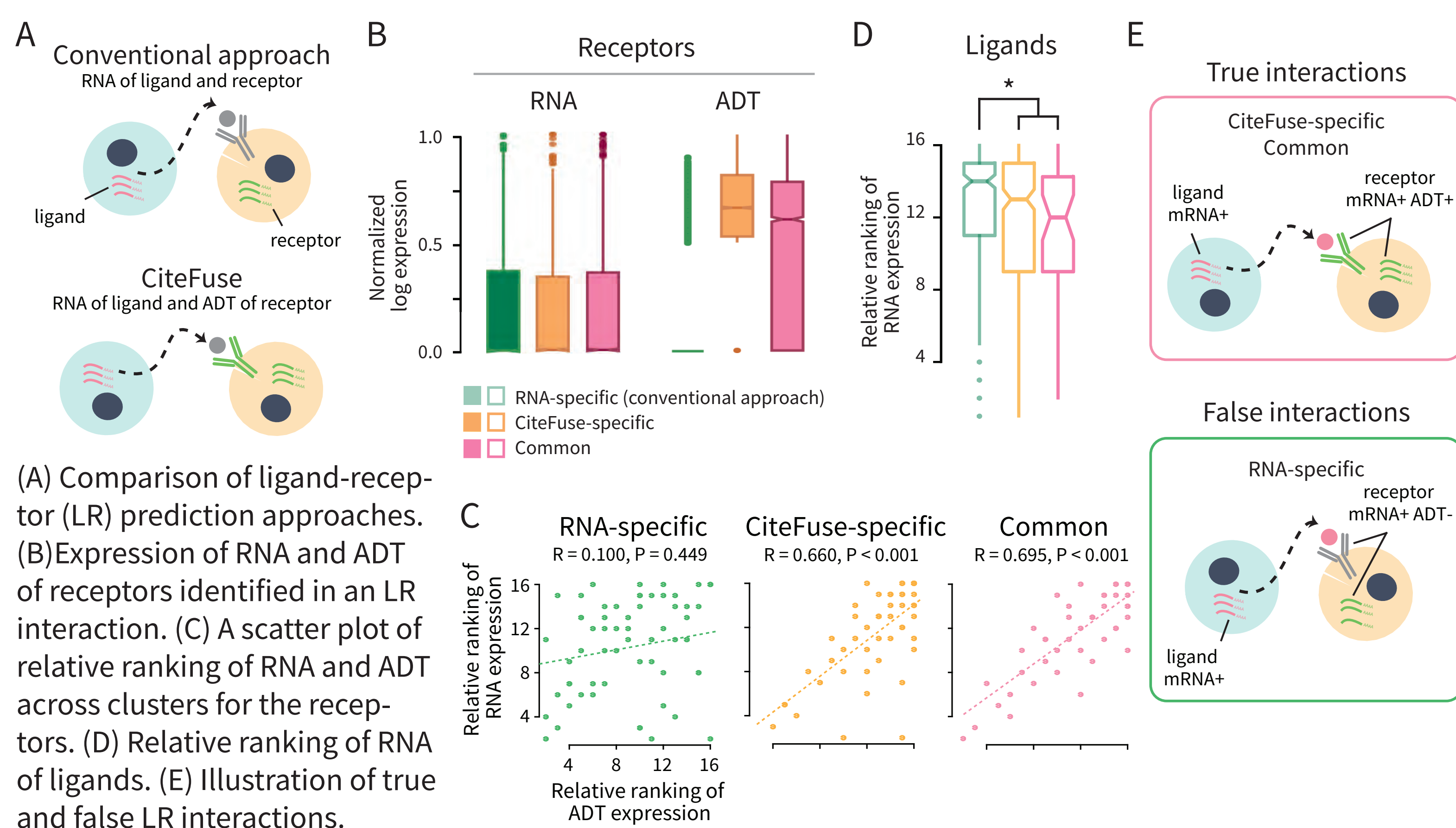
## CiteFuse gains information from multi-modal analysis



(A) Integration of multi-omic CITE-seq data with similarity network fusion [3]. (B) Evaluation of CiteFuse and other clustering algorithms on simulated CITE-seq data (n=10). (C) UMAPs of the complete human PBMC CITE-seq data [4] and CD4<sup>+</sup> T-cells (smaller panels). Clustering outputs are highlighted by data modality or expression of key markers of T-cell subpopulations.



## CiteFuse facilitates prediction of accurate ligand-receptor interactions



## Acknowledgements and References

[1] Stuart and Satija (2019) *Nature Review Genetics* [2] Stoekius et al. (2017) *Nature Methods* [3] Wang et al. (2014) *Nature Methods* [4] Mimitou et al. (2019) *Nature Methods* [5] Stoekius et al. (2019) *Genome Biology* [6] Wolock et al. (2019) *Cell Systems*

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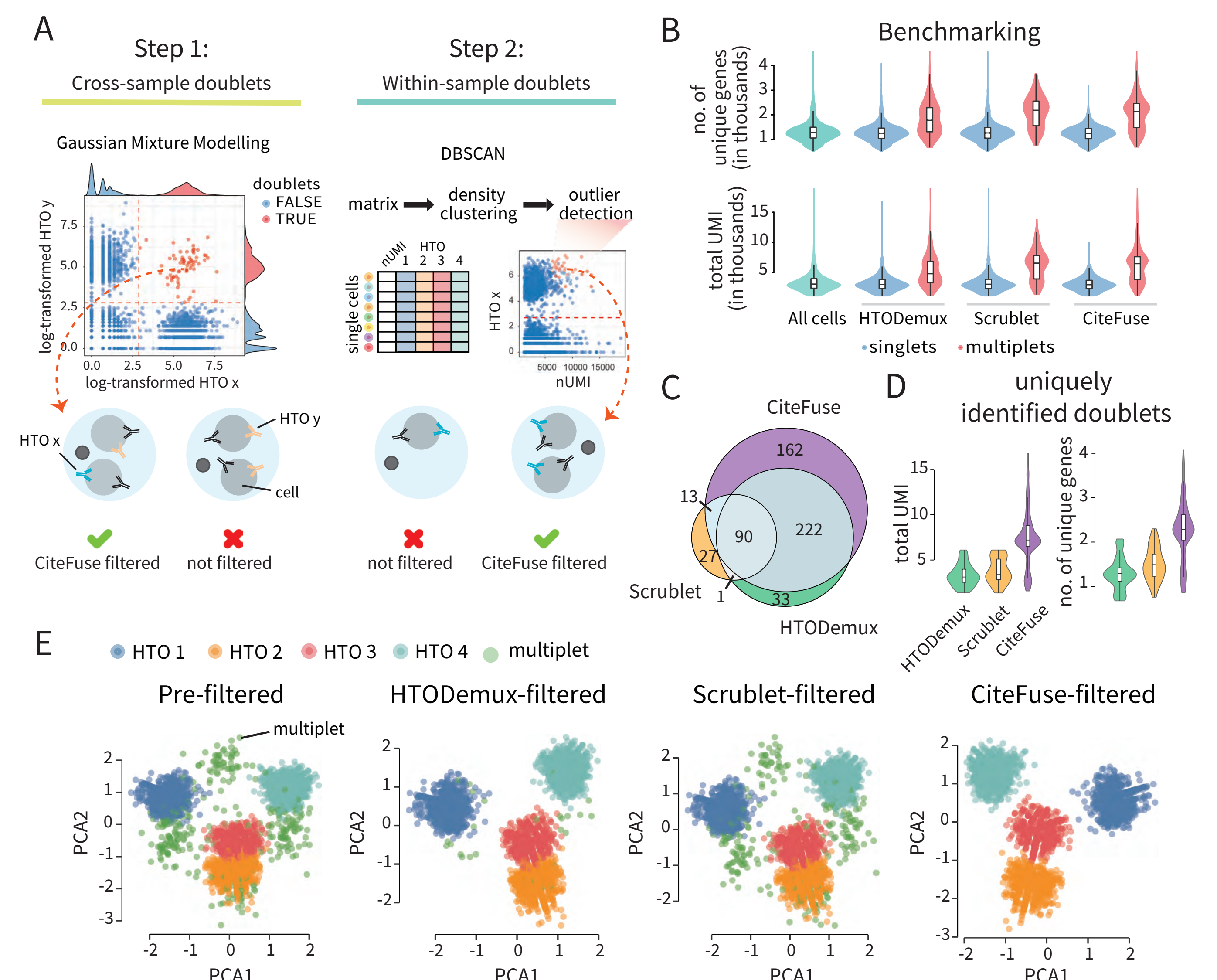


<https://doi.org/10.1101/2020.05.11.299911>



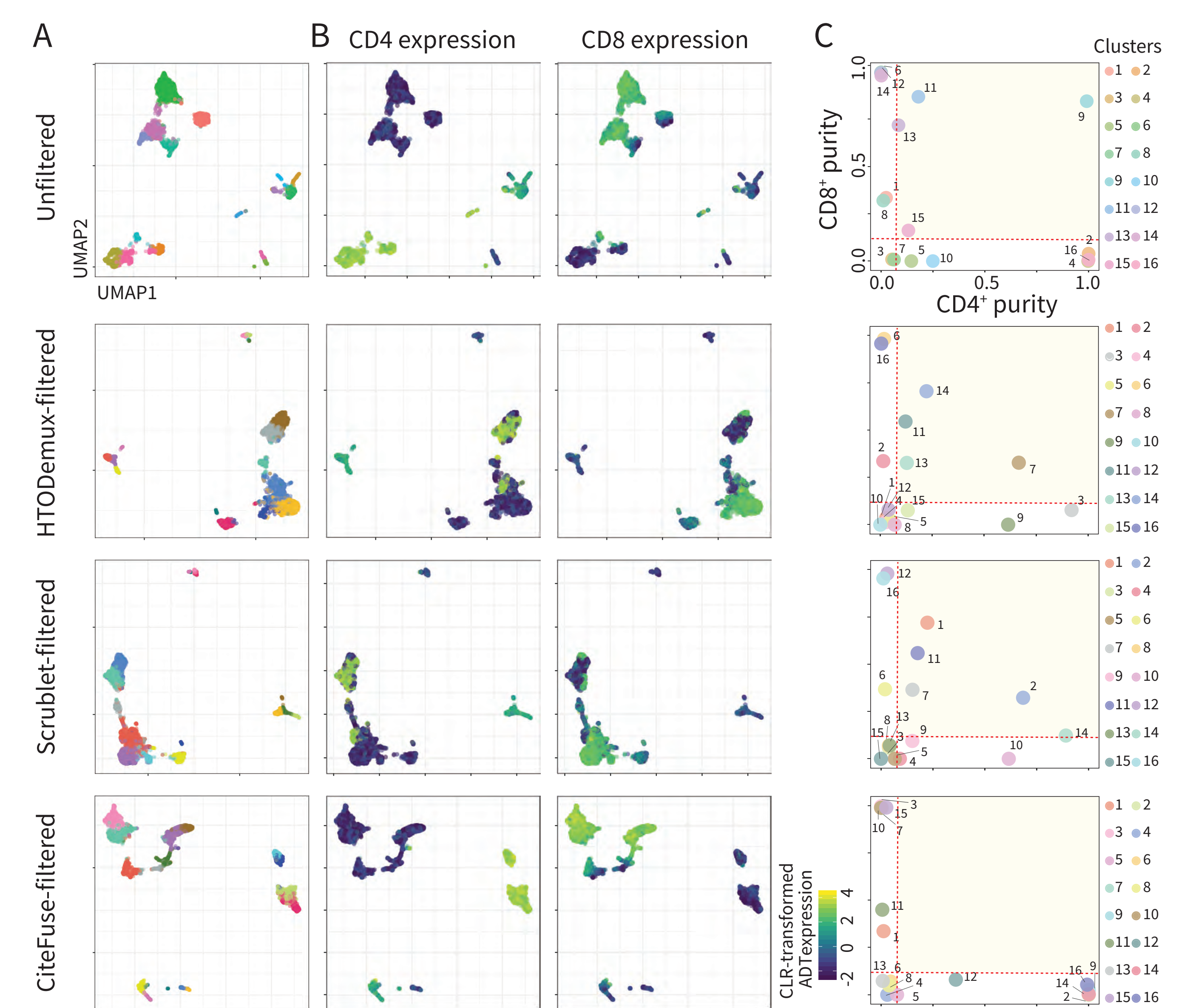
THE UNIVERSITY OF SYDNEY

## A stepwise doublet detection method filters both within- and cross-sample doublets



(A) An overview of the doublet detection approach in CiteFuse. (B) Total number of unique molecular identifiers (UMIs) and number of unique genes expressed in all cells and in HTODemux- [5], Scrublet- [6] and CiteFuse-identified singlets and doublets. (C) Venn diagram depicting the overlap in predicted doublets. (D) Evaluation of doublets uniquely identified by each method. (E) PCA visualization of HTO expression before and after filtering doublets.

## CiteFuse-filtered dataset best preserves the separation between CD4<sup>+</sup> and CD8<sup>+</sup> T-cells



(A) UMAPs of the unfiltered (4292 cells), HTODemux- (3753 cells), Scrublet- (3968 cells), and CiteFuse-filtered (3612 cells) human PBMC datasets. CLR-transformed ADT expression of (B) CD4 and CD8 expression. (C) Plots of purity scores of CD8<sup>+</sup> cells (y-axis) against CD4<sup>+</sup> cells (x-axis).

## Take home messages for CiteFuse

- CiteFuse gains information from multi-modal integration of CITE-seq data
- Doublet detection approach in CiteFuse effectively removes both within- and cross-sample doublets
- CiteFuse facilitates accurate ligand-receptor interaction prediction