Data Science Meets Biology

Boosting phenotypical profiles for early drug discovery: team Air

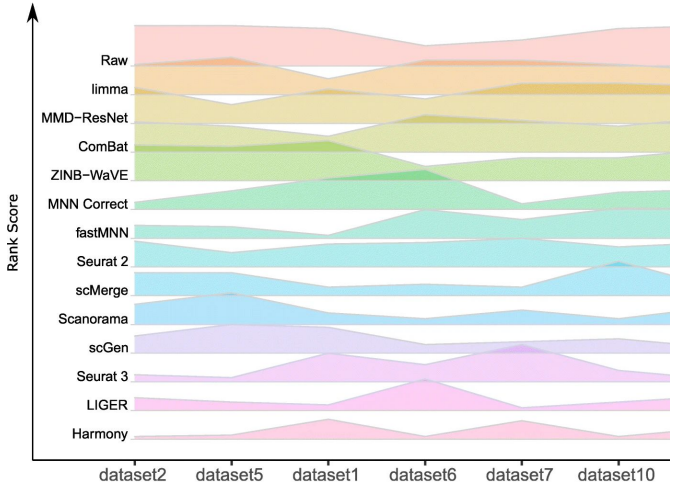
Berlin, 6-9.09.2024

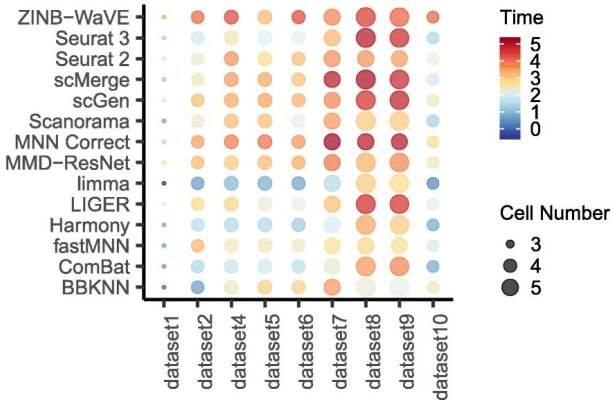
Batch effects correction: background

Batch effects are data variations due to unintended technical differences in reagents, processing times, equipment, or experimental platforms.

Batch effect correction is necessary to detect true biological differences.

- ➢ Linear methods (Combat and Sphering)
- ➢ Neural-network based methods (scVI and DESC)
- ➢ Mixture-model based method (Harmony)
- ➢ Nearest neighbor-based methods (MNN, fastMNN, Scanorama, Seurat-CCA, and Seurat-RPCA)
  (compared by Arevalo et al., 2024; Tran et al., 2020)

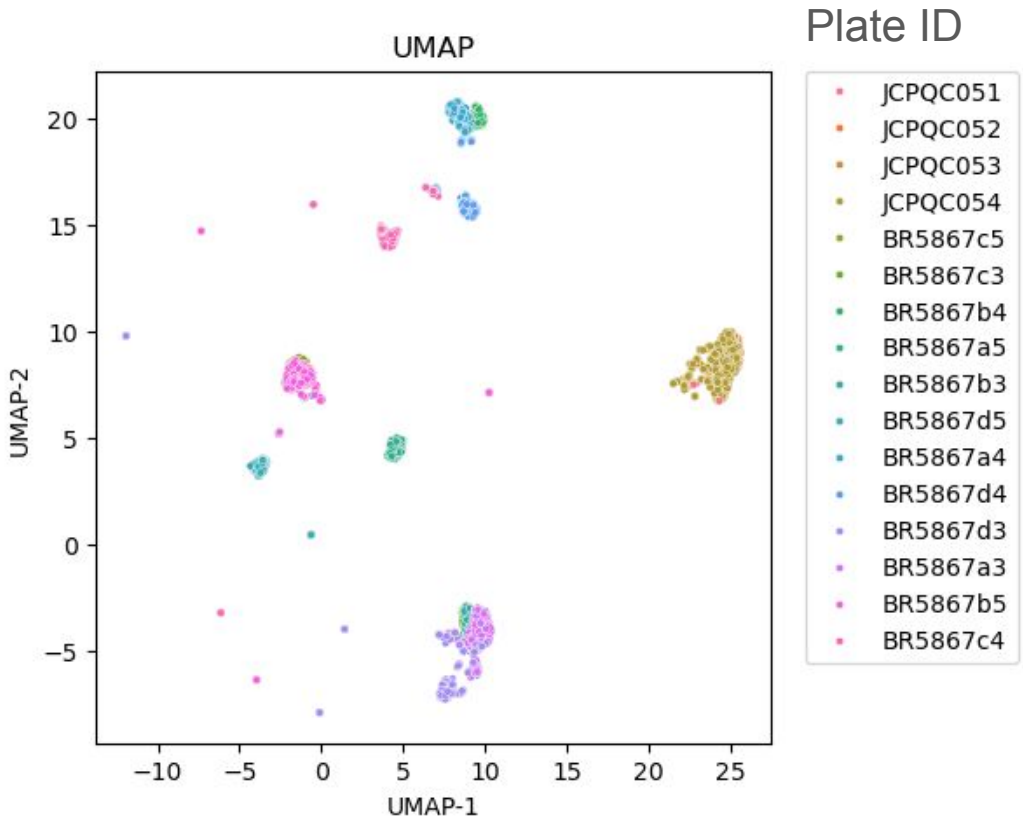




Tran et al., 2020

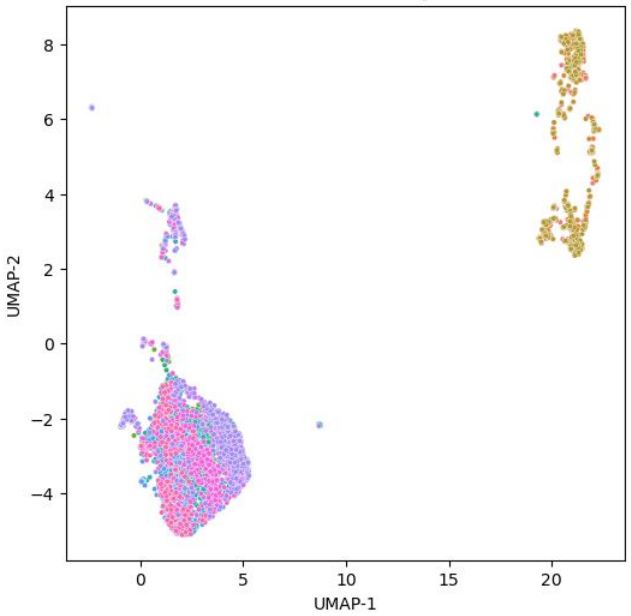
Batch effects correction

- Harmony
- Scanorama
- CombatPy



Performance comparison

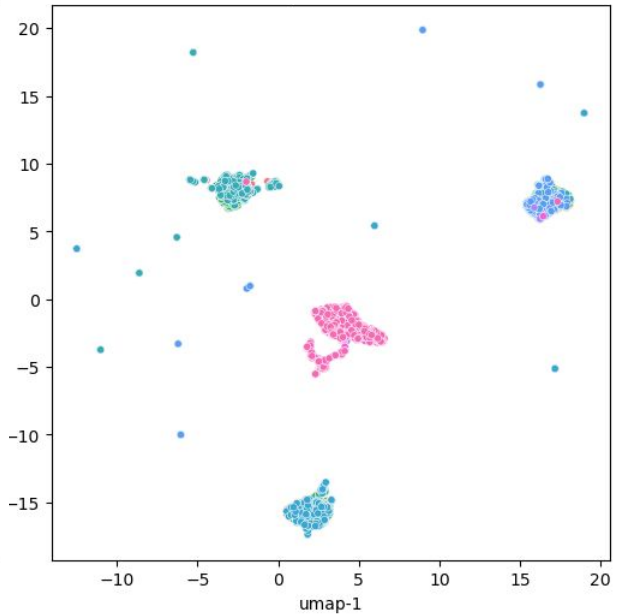
Harmony



Recommended for all types of batch effects, is faster and Python-based

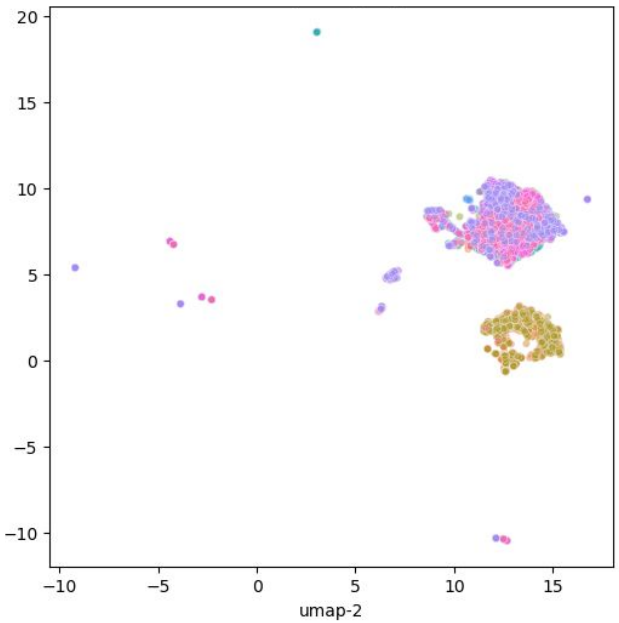
(Arevalo et al., 2024; Korsunsky, 2019; Tran et al., 2020)

Scanorama



Bad performance

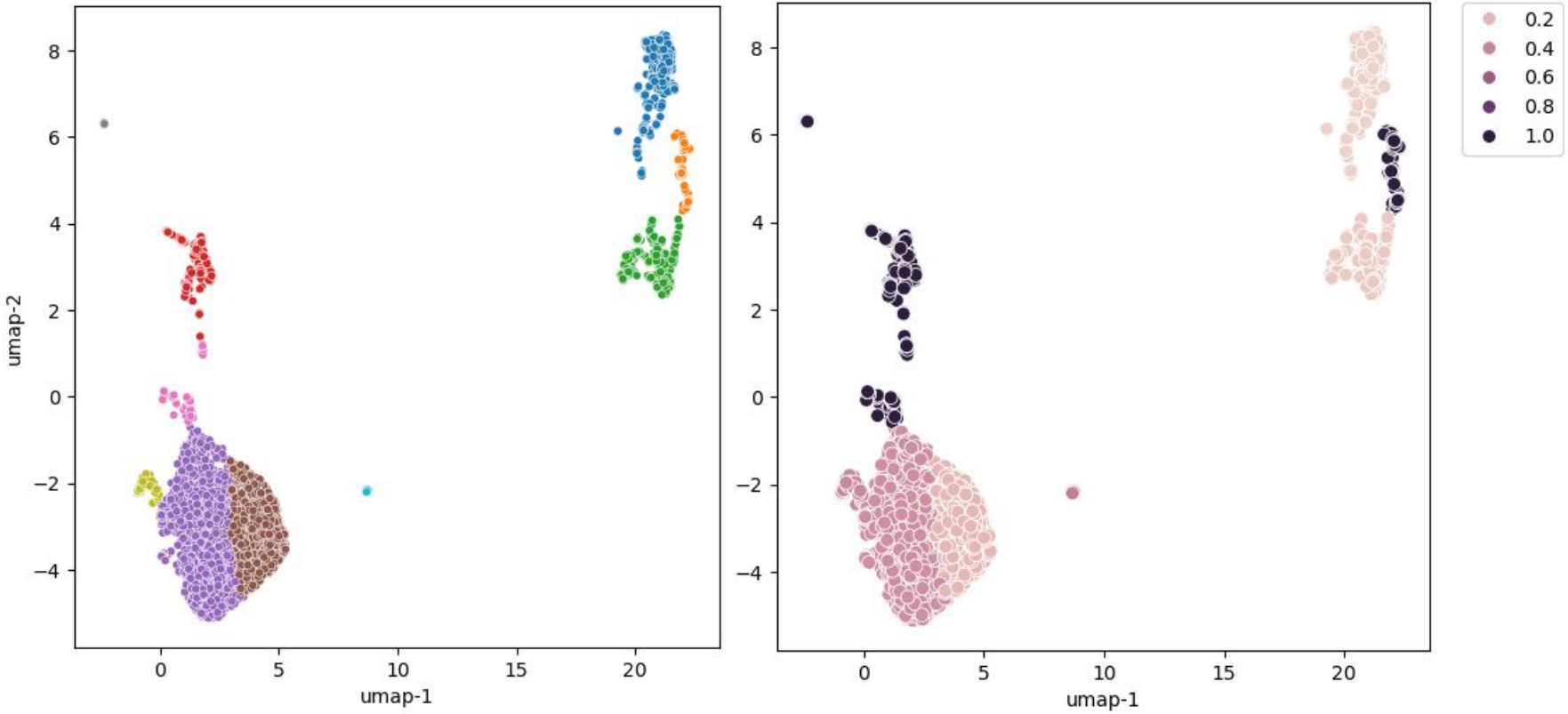
CombatPy



Positive controls did not cluster with any treatment

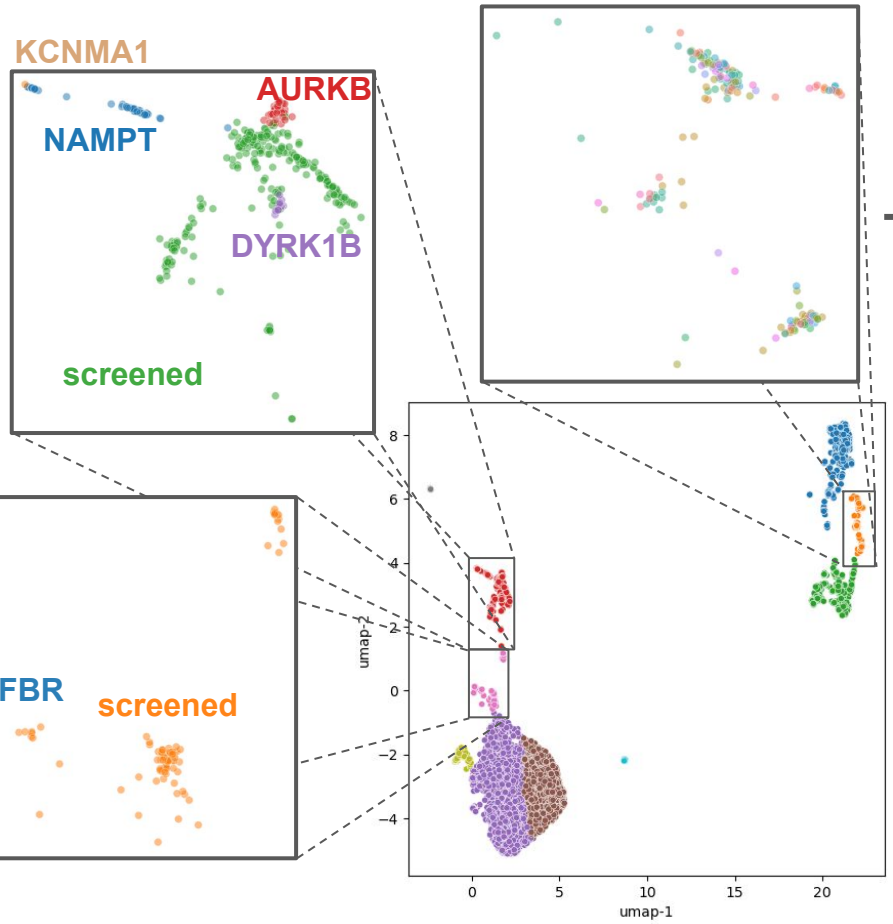
Spectral clustering

Cluster purity
(positive control / positive + negative)

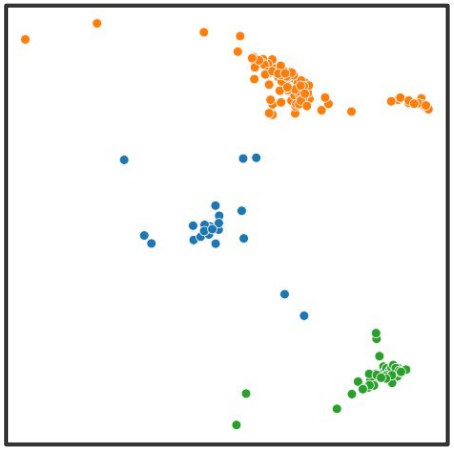


Which compounds show effects?

96 new unique drugs
similar activity to targets of
DYRK1B
AURKB
cell cycle and kinase activity



TGFBR1
role in cancer progression



Cell cycle regulation
mix of many targets

Potential therapeutic effects in cancer treatment

Activity of tested drugs

Group 1:

Effect similar to targets of:

2 important protein kinases

AURKB - key regulator of mitosis, inhibitors are known to suppress tumor growth
DYRK1B -promoting resistance to apoptosis

And less similar to:

(NAMPT) - overexpressed in cancer cells
regulating NAD+ levels → DNA repair, gene expression, and stress response.

Group 2:

Effect similar to targets of:

TGFBR1 - tumor suppression (early), promotion (late)

Potential therapeutic effects in cancer and immune disorders

Common pathways of target genes clustered together

Subgroup 1: cancer, signaling, apoptosis, development, and immune responses

1. Cell cycle regulation: ATM, BRD4, CCND1, CDK2, CDK7, CDK9

2. Apoptosis: BAX

3. Immune response: BTK, CSF1R, FPR1, HCK, FLT3, ITGB2, LCK, LYN

4. Signal transduction: BTK, DDR2, FPR1, KRAS, LCK, PAK4, PDPK1, PIK3CG, PLD1, PRKCE, RGS4, TGFBR1

5. Neurotransmission: GRIN2A, OPRM1, RGS4

6. Stress response: HSP90AA1, HSP90AB1

7. Calcium signaling: CATSPER4, TNNC1

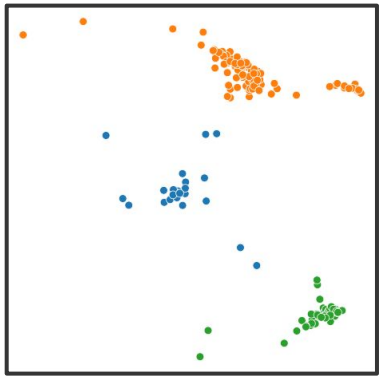
Subgroup 2: signaling, development, metabolism, and immune responses

1. Cell growth and differentiation: RET, CDK7

2. Inflammatory response: TNF

3. Vascular development and homeostasis: KDR, PTGIR, S1PR1

4. Sugar metabolism: AKR1B1



Subgroup 3: cell proliferation, differentiation, and responses to external stimuli

1. Cell cycle regulation: CCND1, FOXM1, PLK1

2. Signal transduction: CHRM2, FLT3, OPRL1, RGS4, S1PR1

3. Stress response and protein folding: HSP90AA1, HSP90AB1

4. Metabolic pathways: HSD11B1, PPARD, IMPDH1

5. Cytoskeletal dynamics: TUBB, TUBB3, TUBB4B

Thank you!

Organizers

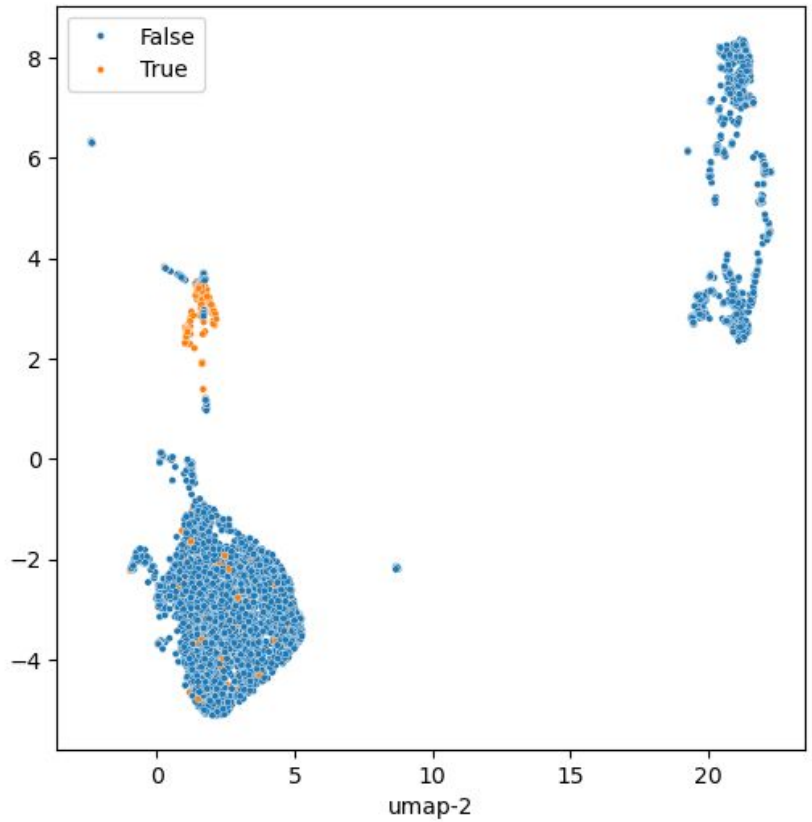
Bogdan Avanesy
Ekaterina Vasileva

Mentors

Bayer & MDC

Berlin, 6-9.09.2024

Class0 drug specificity



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