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EXCELENCIA SEVERO OCHOA

EVENFLOW

The Personalized Medicine Use Case of the EVENFLOW project

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October 1, 2024

Tackling a major challenge in biomedicine

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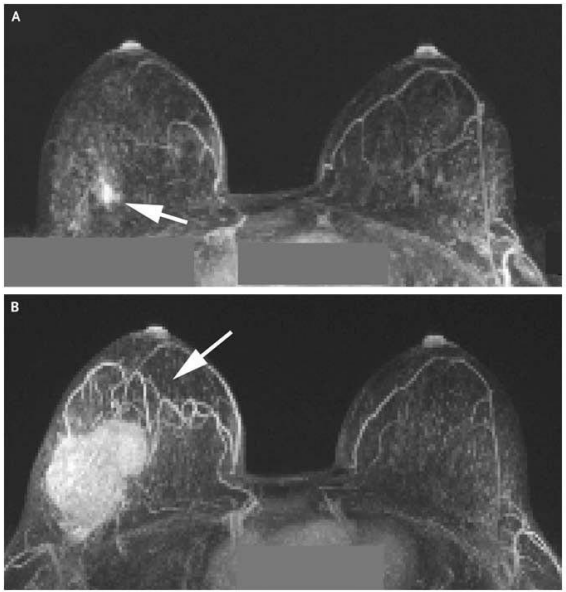
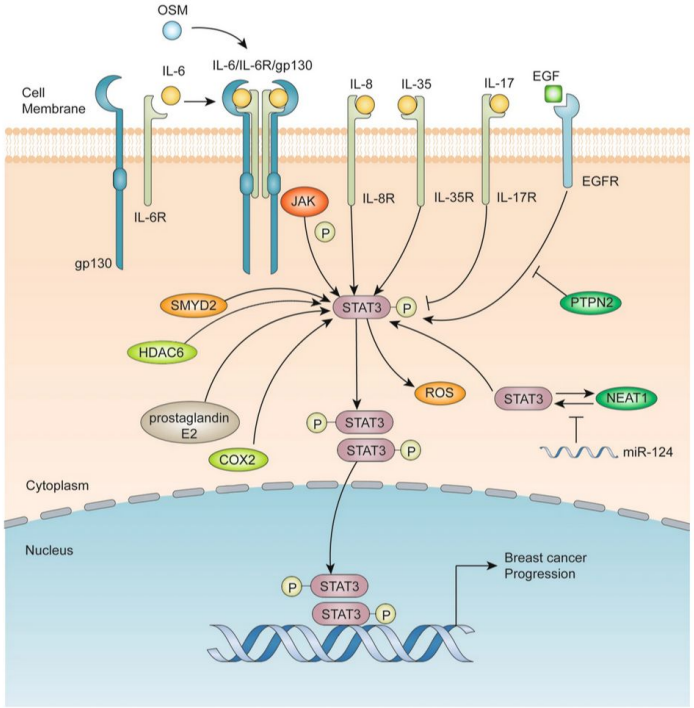
The role of time in biological processes



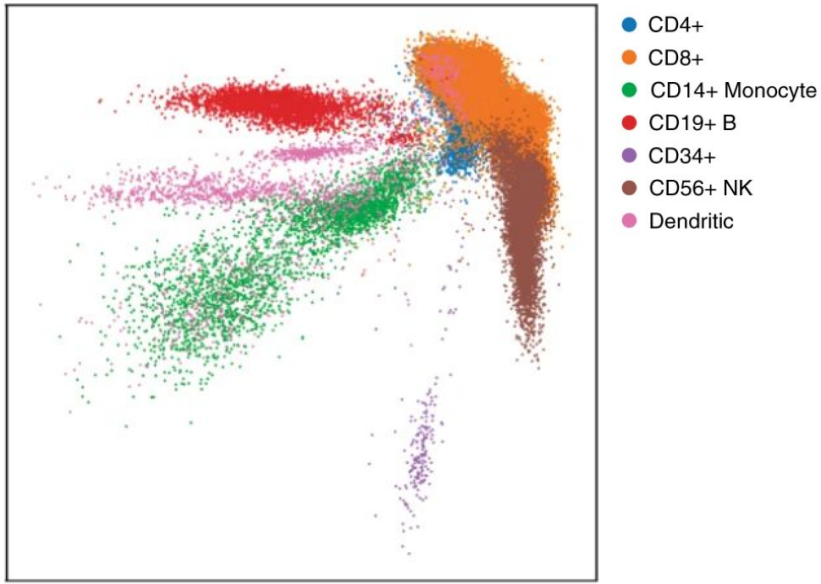
N Engl J Med. 2007;356(13):e12.
doi: 10.1056/NEJMicm063760.



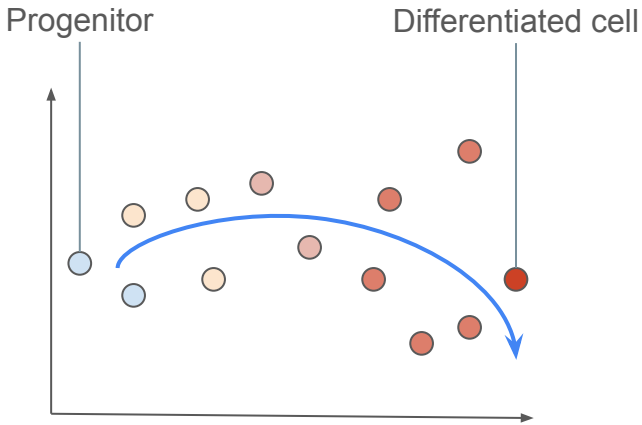
Cell Commun Signal. 2020;18(1):33.
doi: 10.1186/s12964-020-0527-z

How can we accurately reconstruct temporal processes from just a series of snapshots?

Lessons learnt from single cell dynamics



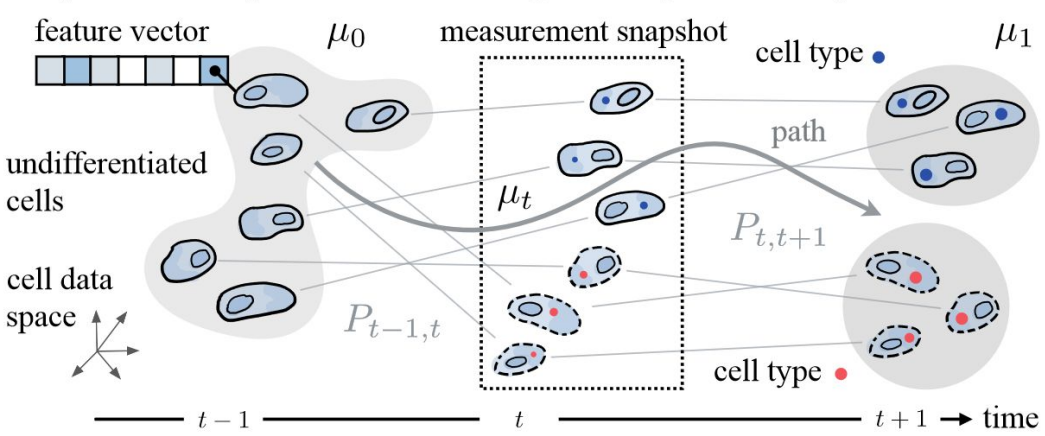
Eralsan & Simon et al. *Nat Comm* 2019



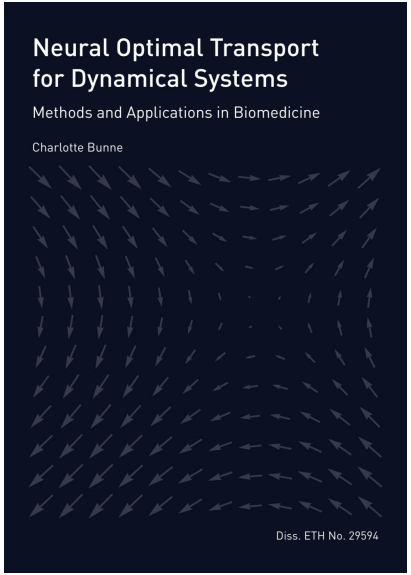
adapted from F. Thais (ECCB 2024)

Learning meaningful **data representations**
can elucidate underlying dynamic processes

Lessons learnt from single cell dynamics



adapted from Bunne (ETH Zurich, 2023)



Operations based on such data representations can aid in generating accurate predictions

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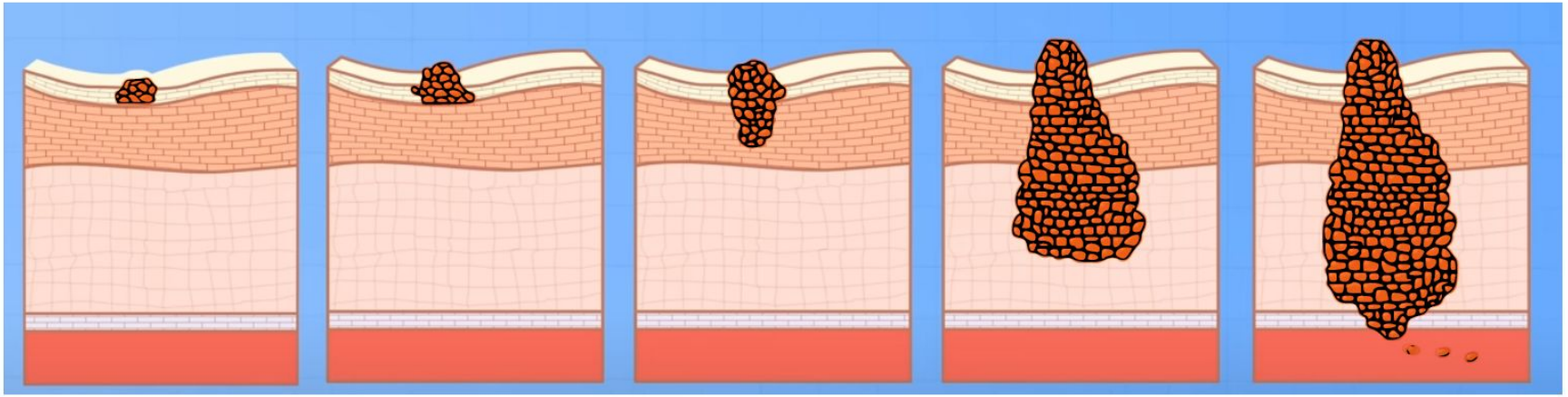
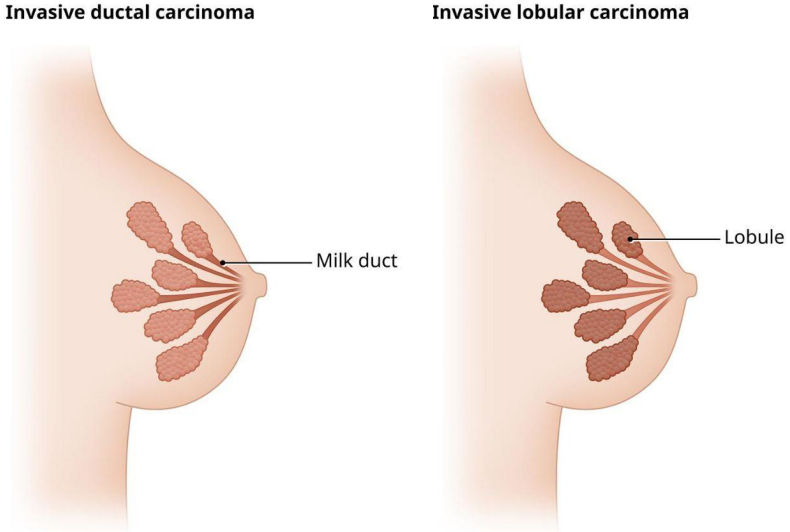
Identifying the molecular determinants of cancer staging

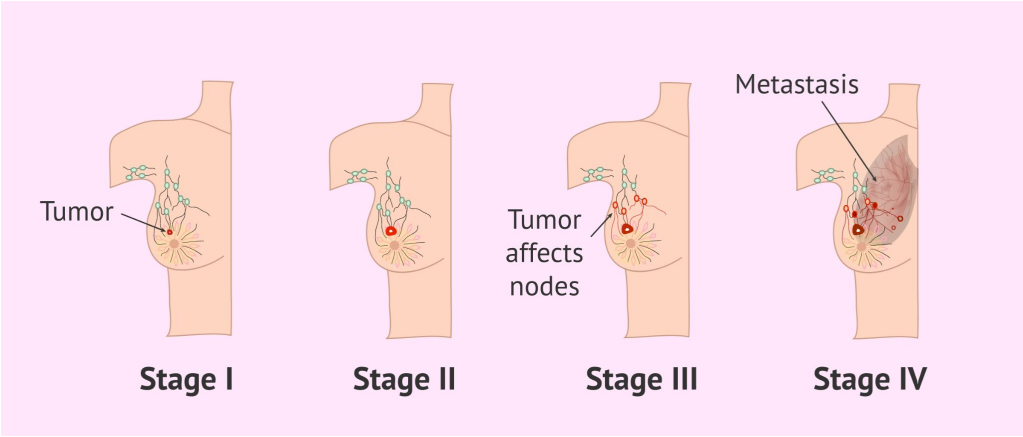
benign tumor

metastasis



Identifying the molecular determinants of cancer staging





100% 5-year survival

90% 5-year survival

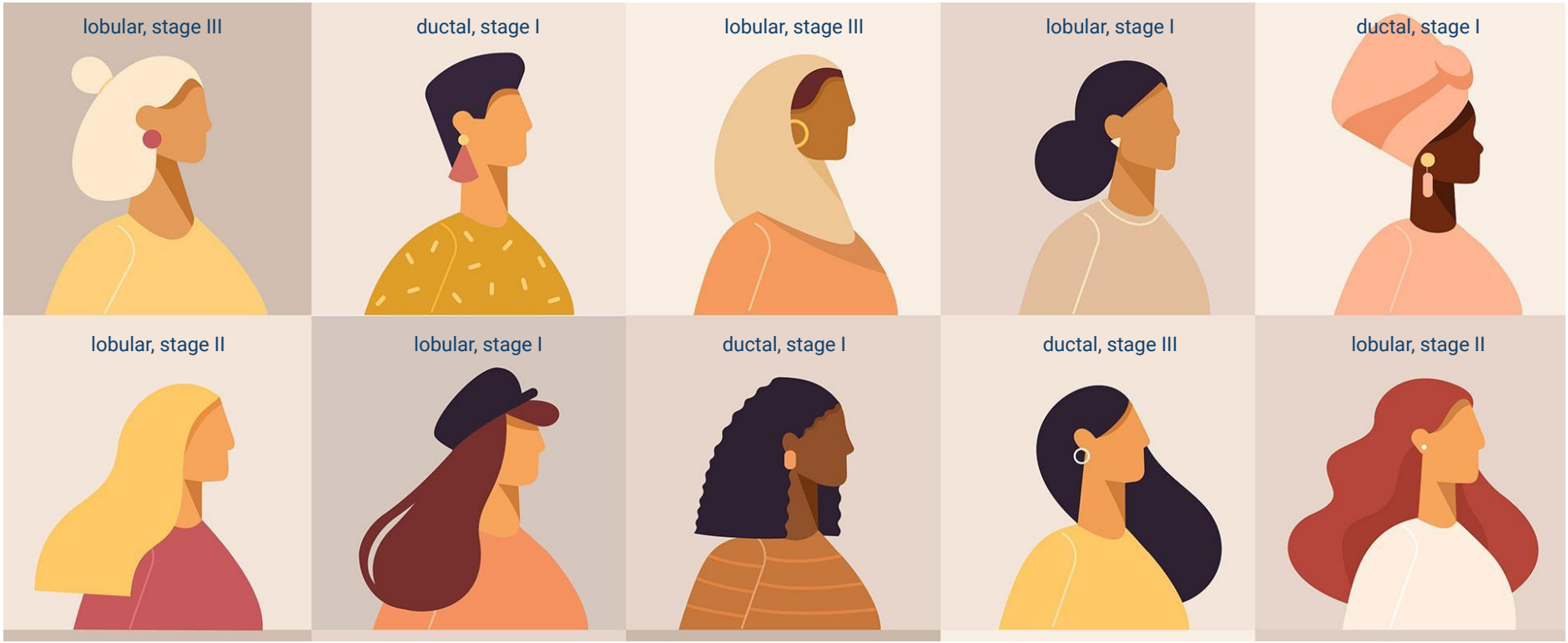
70% 5-year survival

25% 5-year survival

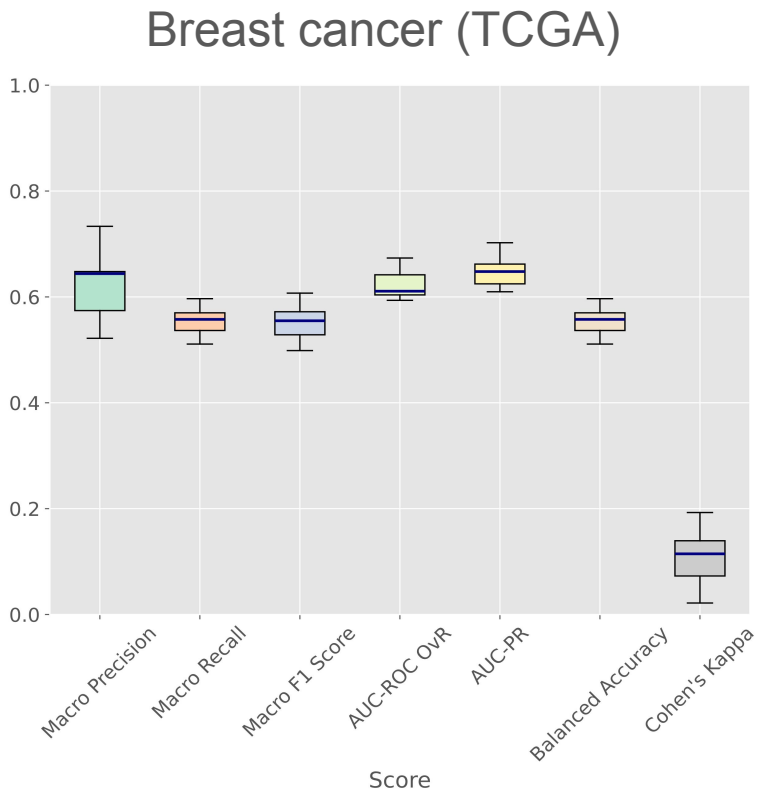
TCGA
The Cancer Genome Atlas

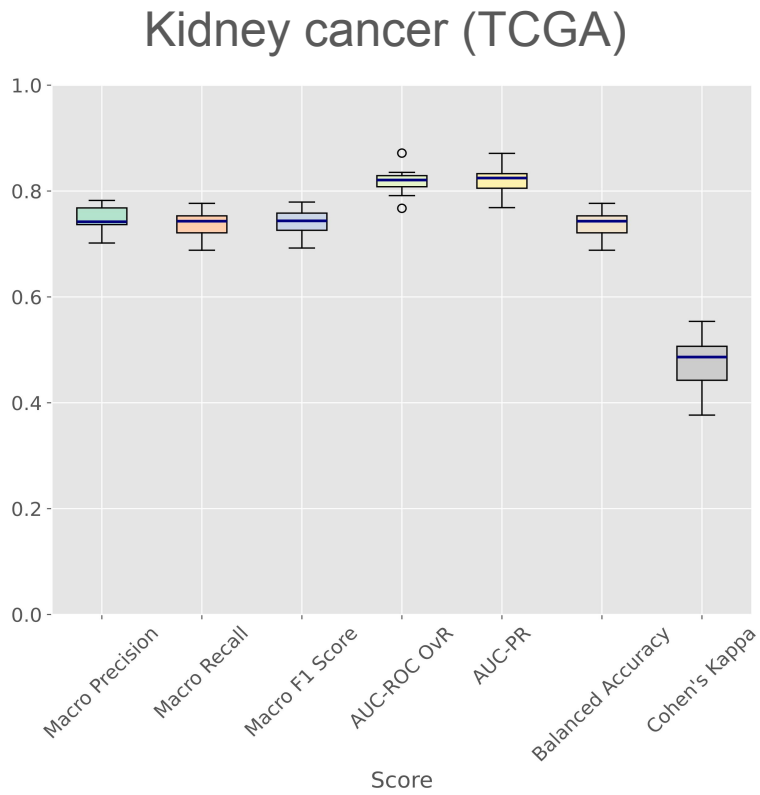
~900 women

gene expression data
(bulk RNA-sequencing)

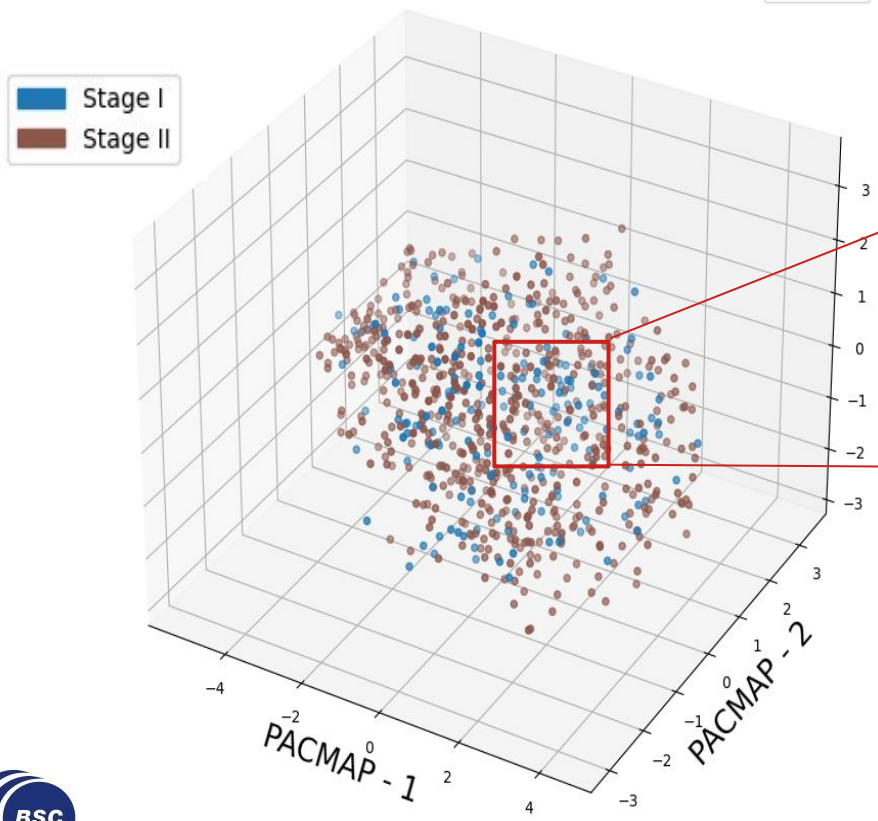


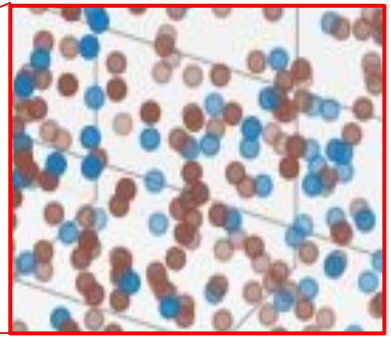
Predicting breast cancer staging is hard…





…due to cancer heterogeneity

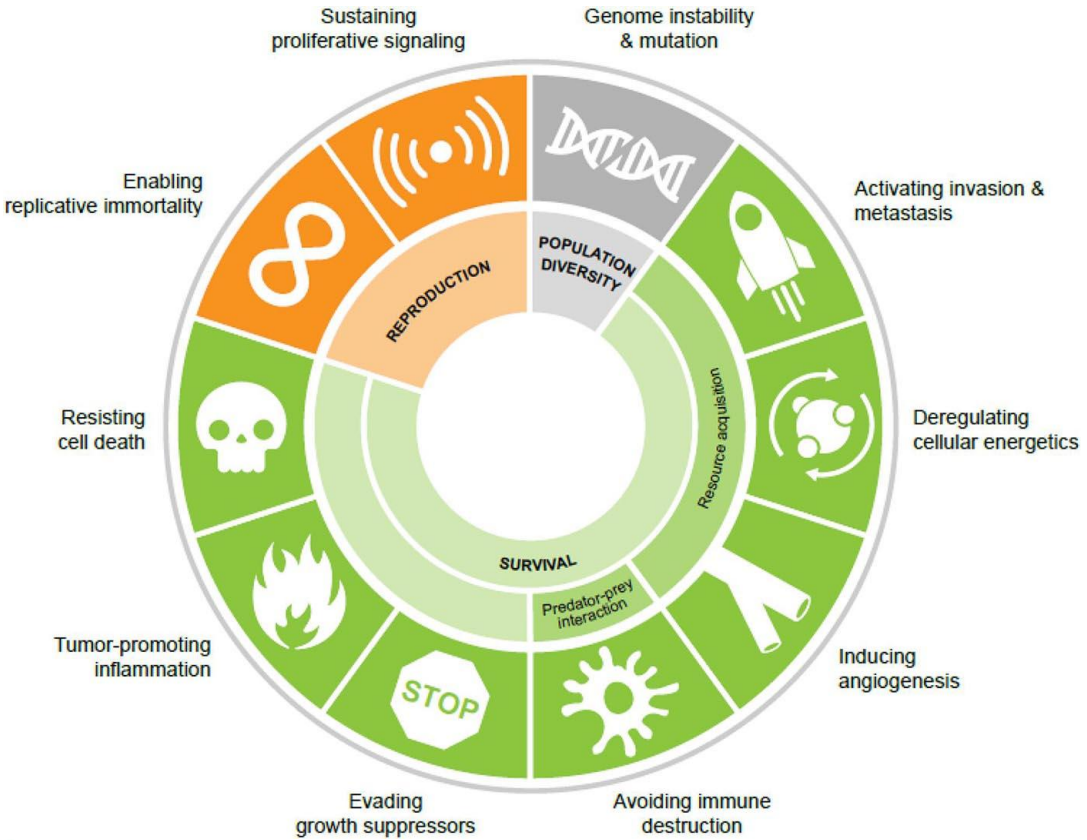




Global low separability

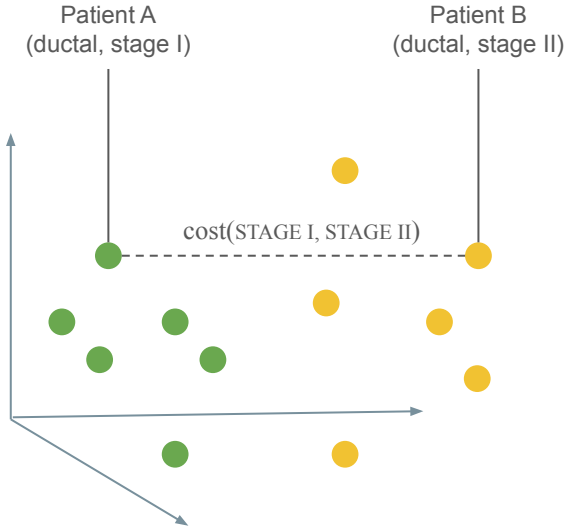
but local similarities between consecutive stages!

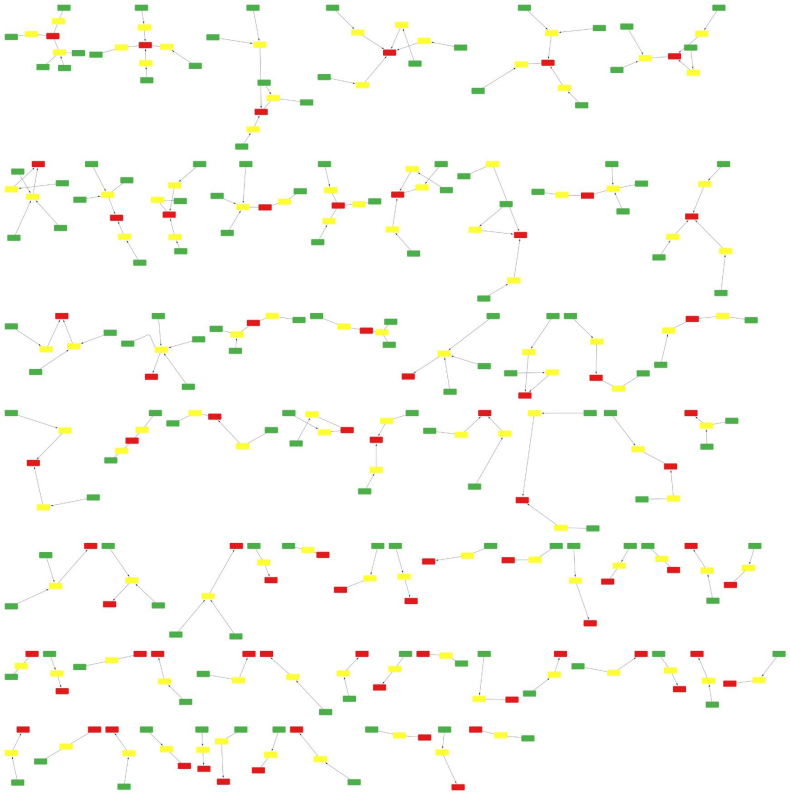
Hallmarks of cancer



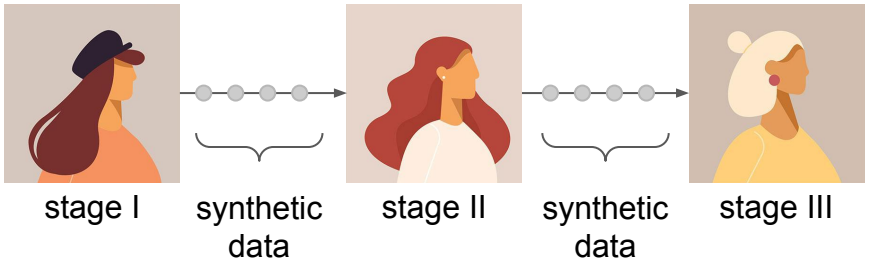
Somarelli *Front. Ecol. Evol.* 2021

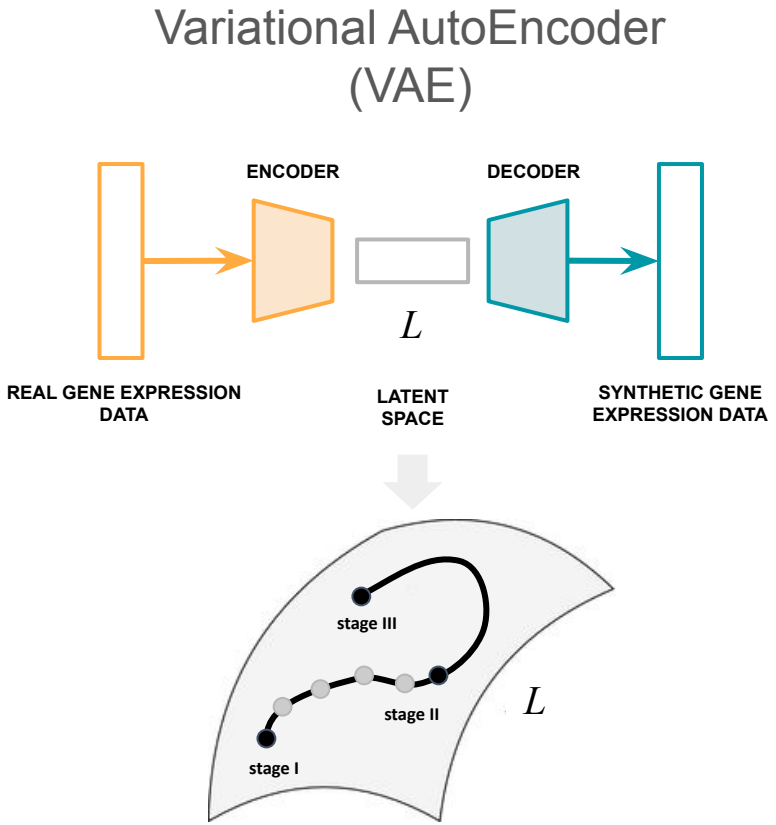
Pseudo-time stage trajectories as a Linear Assignment Problem



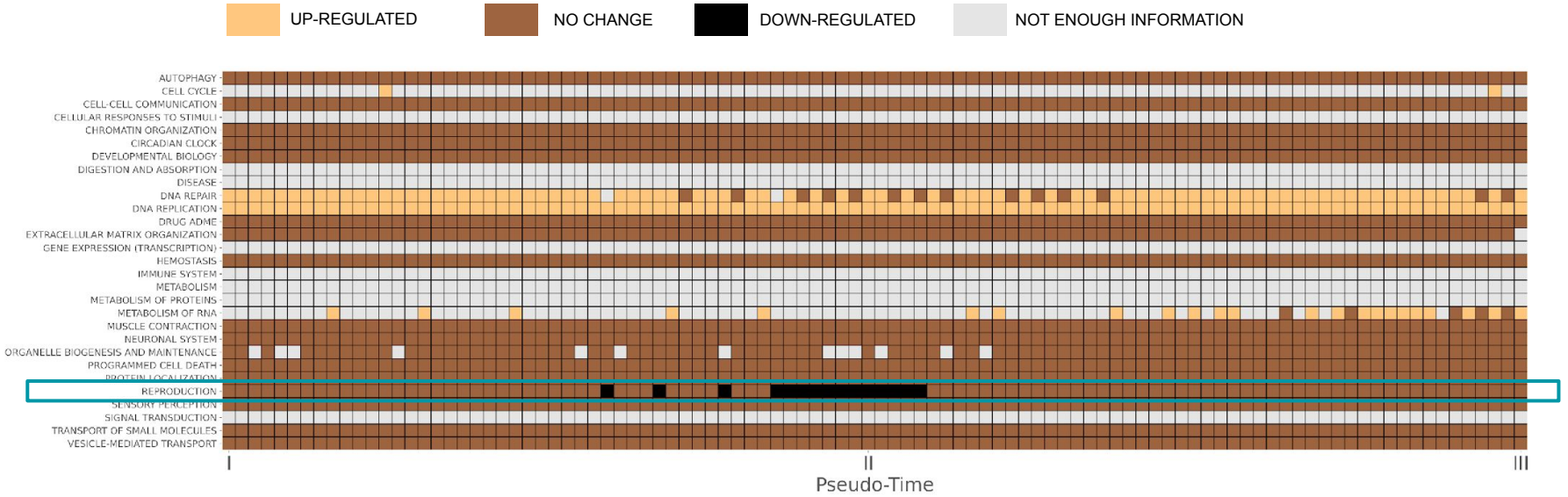


Leveraging Generative AI to reconstruct the stage transitions



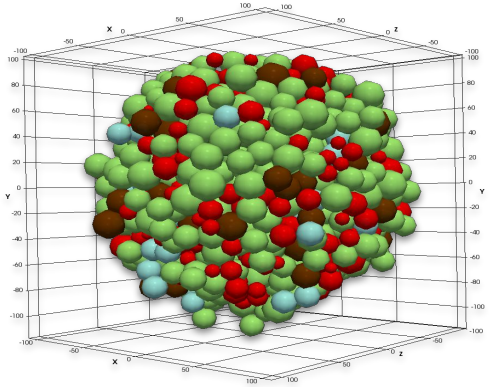


Pathway enrichment analysis across stage transitions

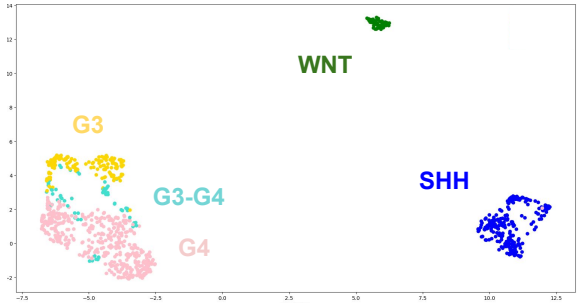


ACR, ADAM21, ATM, B4GALT1, BLM, BMP4, BRCA1, BRCA2, CATSPER1, CATSPER2, CATSPER3, CATSPERG, CXCR4, DMC1, EOMES, H2AFX, HSPA2, HVCN1, LMNA, LMNB1, MND1, MSH4, MSH5, NANOG, NANOS3, OVGP1, PDPN, POU5F1, PRDM1, PSMC3IP, RAD21, RAD51, RAD51C, RBBP8, REC8, SOX17, STAG1, STAG3, SUN2, SYCE2, SYCP2, SYNE1, SYNE2, TFAP2C, ZP1, ZP3

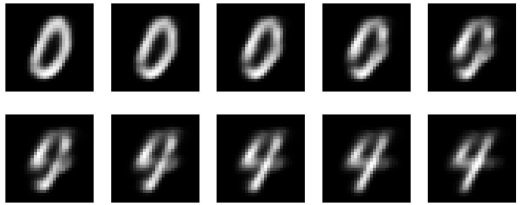
EVENFLOW beyond breast cancer



MULTI-SCALE CELLULAR SIMULATIONS OF TUMOR GROWTH



SYNTHETIC DATA AUGMENTATION IN MEDULLOBLASTOMA



CONDITIONAL PSEUDO-TIME TRAJECTORY GENERATION IN BREAST CANCER

Critical insights and takeaways

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Critical insights and takeaways

- The Personalized Medicine Use Case of the EVEFLOW project tackles the challenging problem of **reconstructing dynamical processes from snapshots**.
- The Use Case focuses on identifying the **molecular determinants of cancer staging** specifically in breast cancer characterized by data heterogeneity and sparsity.
- The applications of AI techniques based on **representation learning and generative models** can elucidate dynamic processes, identifying biomarkers of cancer staging and facilitate prediction and forecasting.

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Thanks!

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