The Onsager prominence model

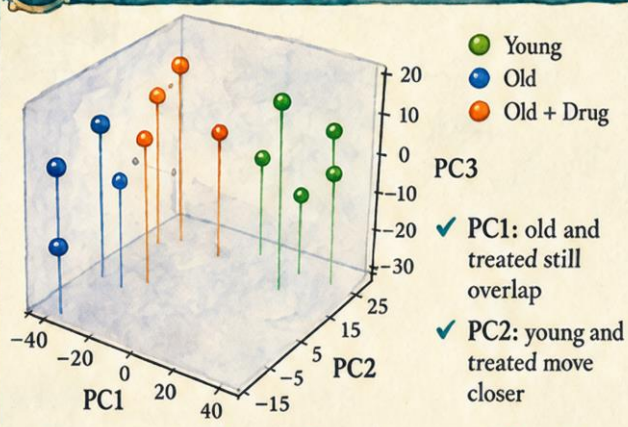
A pathway-level method for charting recovery and unintended worsening in RNA-seq experiments

alpha-stage model

1 Why was it needed?

- Many experiments have 3 states: control, perturbation, and perturbation + treatment.
- Pairwise GSEA or ORA compares two groups at a time, so recovery itself is hard to measure.
- A treatment may rescue some pathways while making others worse.

2 Partial recovery can hide in the data

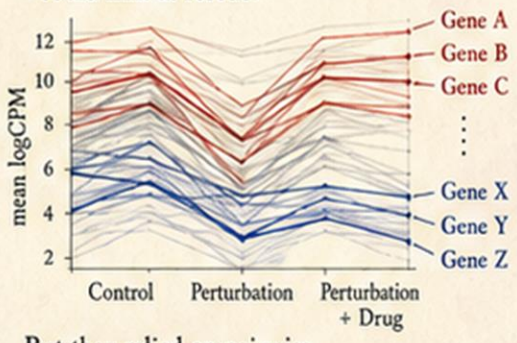


- ✓ PC1: old and treated still overlap
- ✓ PC2: young and treated move closer

Recovery may be real, but uneven and hard to read pathway by pathway.

3 Before Onsager

Earlier line-plot approaches could hint at rescue.



But they relied on pairwise enrichment and did not handle worsening well.

4 A compass for treatment direction

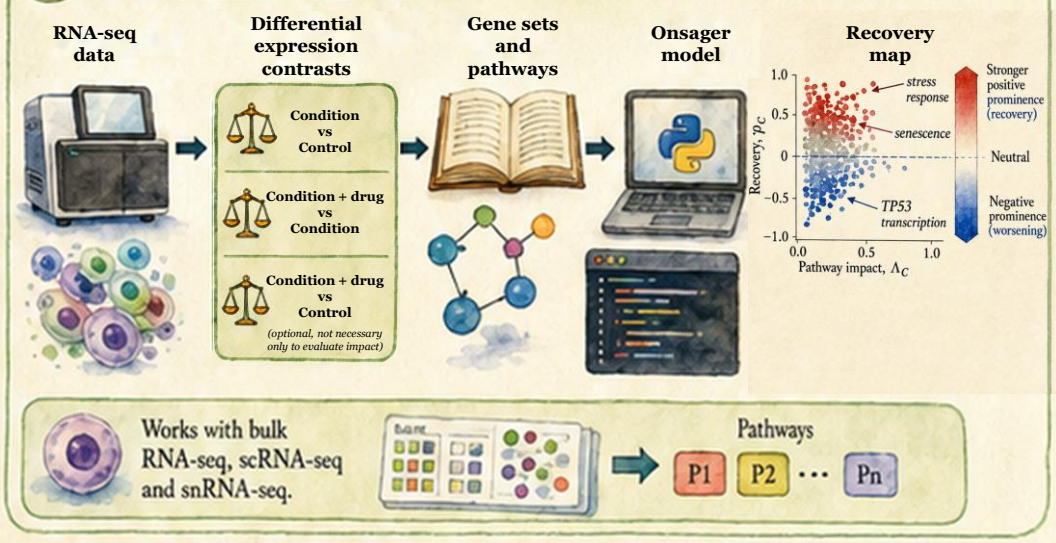
Towards control
recovery / rescue
Biology moves in a health-promoting direction.

Little shift
neutral / limited recovery
Changes are minimal—the system holds steady.

Away from control
worsening / unintended burden
Biology moves in a dysregulating direction.

A treatment can move biology toward control, hardly shift it, or push some pathways farther away.
The model helps reveal *direction*, not just change.

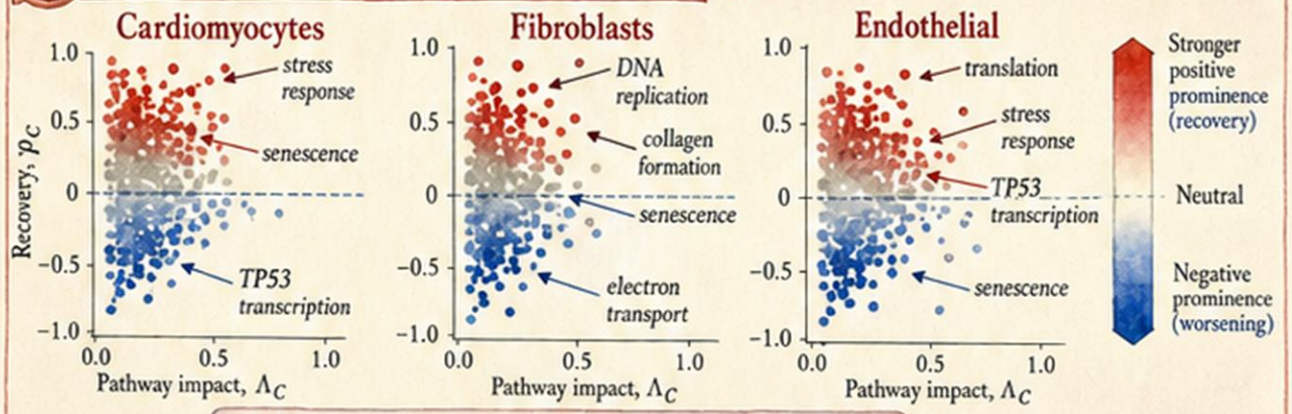
5 How it works



6 What makes it different?

- Detects both recovery and unintended worsening
- Shows partial recovery rather than forcing a yes/no answer
- Works at pathway level, not only gene by gene
- Keeps quality and uncertainty in view
- Useful wherever a treatment aims to restore a perturbed state

7 What does the output look like?



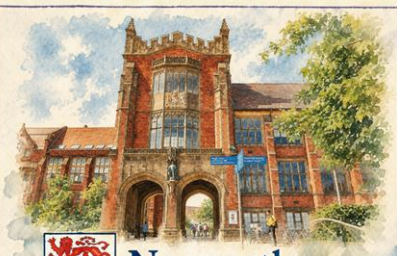
Top = recovered pathways. *Bottom = worsened pathways.*

8 The people behind the model

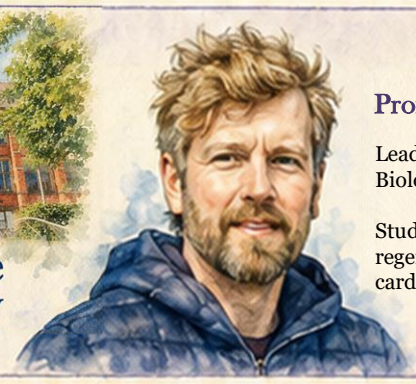
Dr Marco Trevisan-Herraz

Research Associate in bioinformatics and computational biology.

With a background in theoretical physics and biophysics, he develops computational and statistical tools for omics and single-cell data.



Newcastle University



Professor Gavin Richardson

Lead of the Vascular Medicine and Biology Theme.

Studies myocardial senescence, regeneration, and ageing in cardiovascular biology.

BIG TAKEAWAY

The Onsager model offers a new, still-evolving way to map both rescue and risk in RNA-seq experiments.

It helps researchers see not only what a treatment restores, but also what it may disturb.