

# Decoding the Mechano-Metabolic Landscape of Cell Migration Through Quantitative Analysis and Modelling



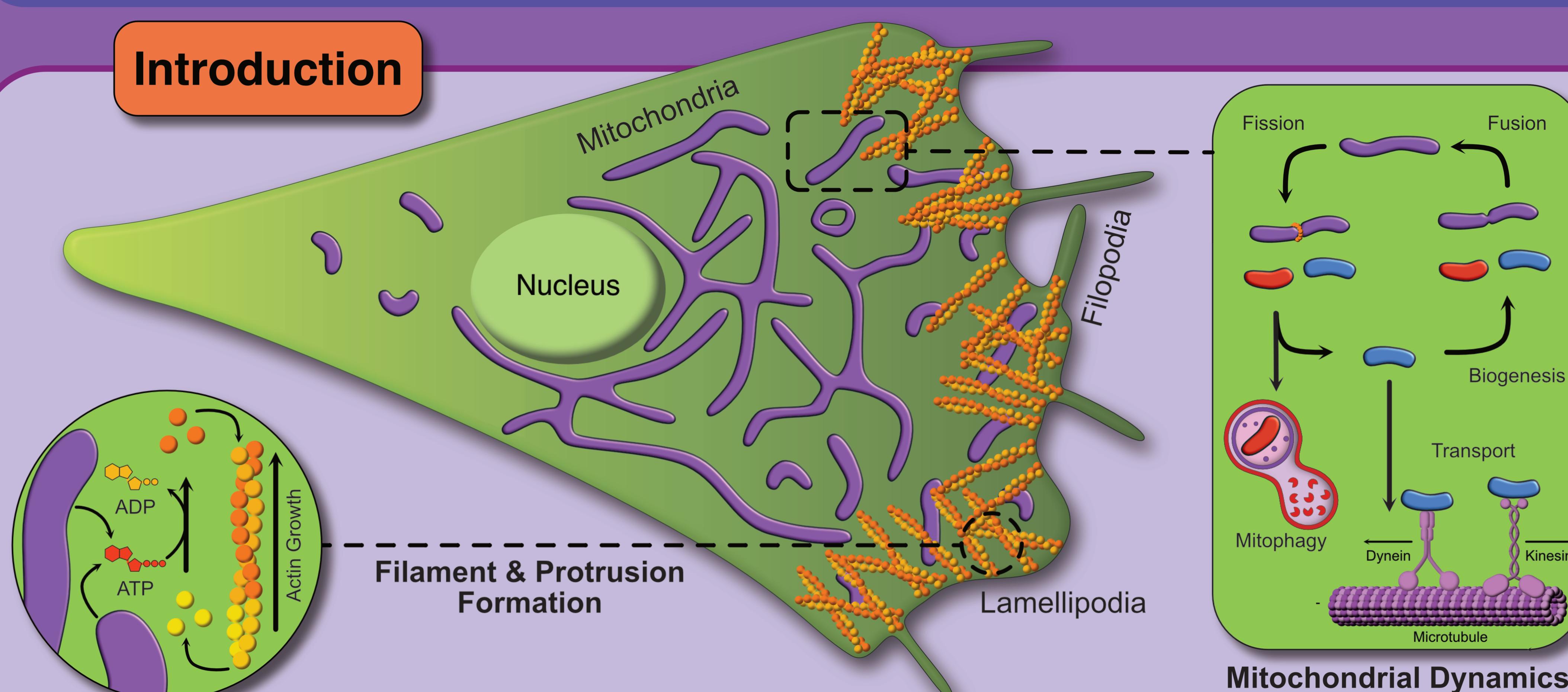
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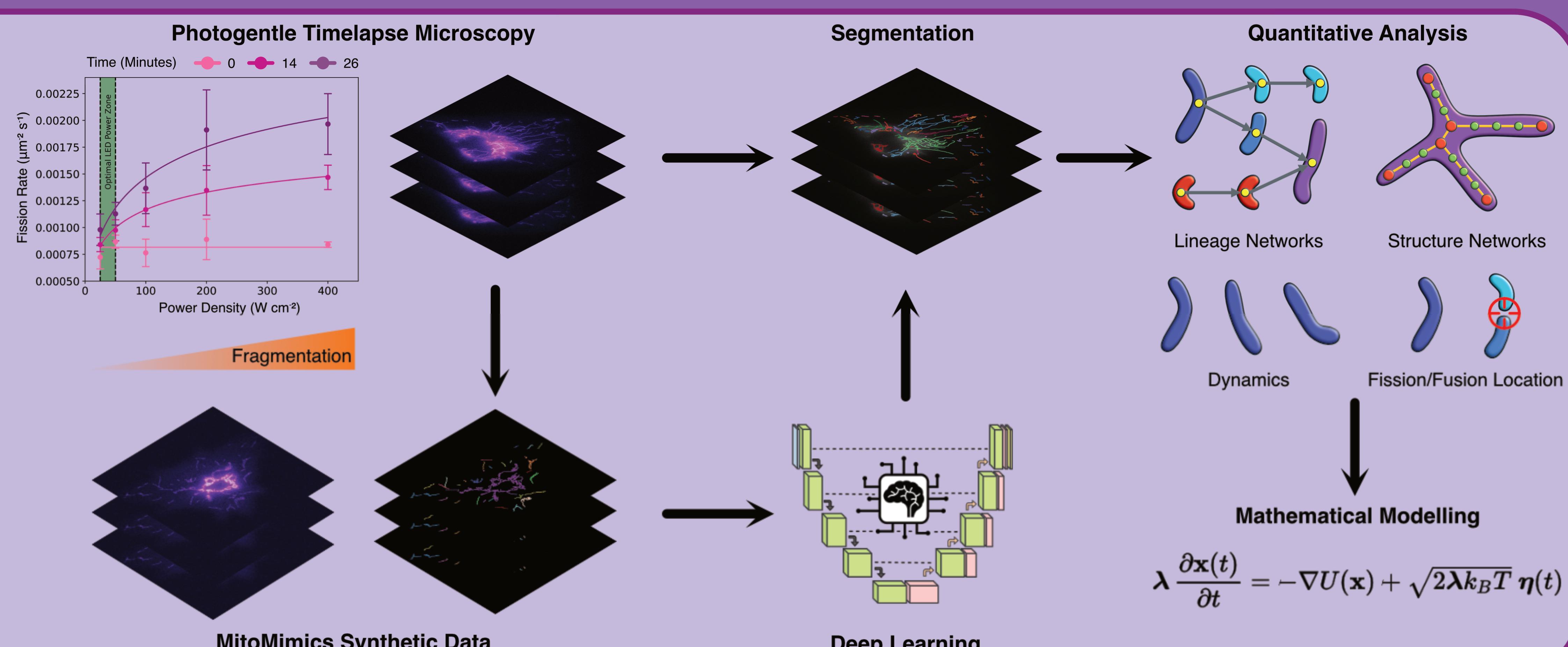
## Introduction



- Cell migration requires cytoskeletal remodelling and localised energy production
- Mitochondrial fission/fusion balance and positioning regulate energy distribution
- IRSp53 coordinates actin organisation, protrusions, and membrane curvature, for migration
- Emerging evidence links IRSp53 to mitochondrial morphology
- How does the absence of a cytoskeletal linked protein, IRSp53, alter mitochondrial dynamics?

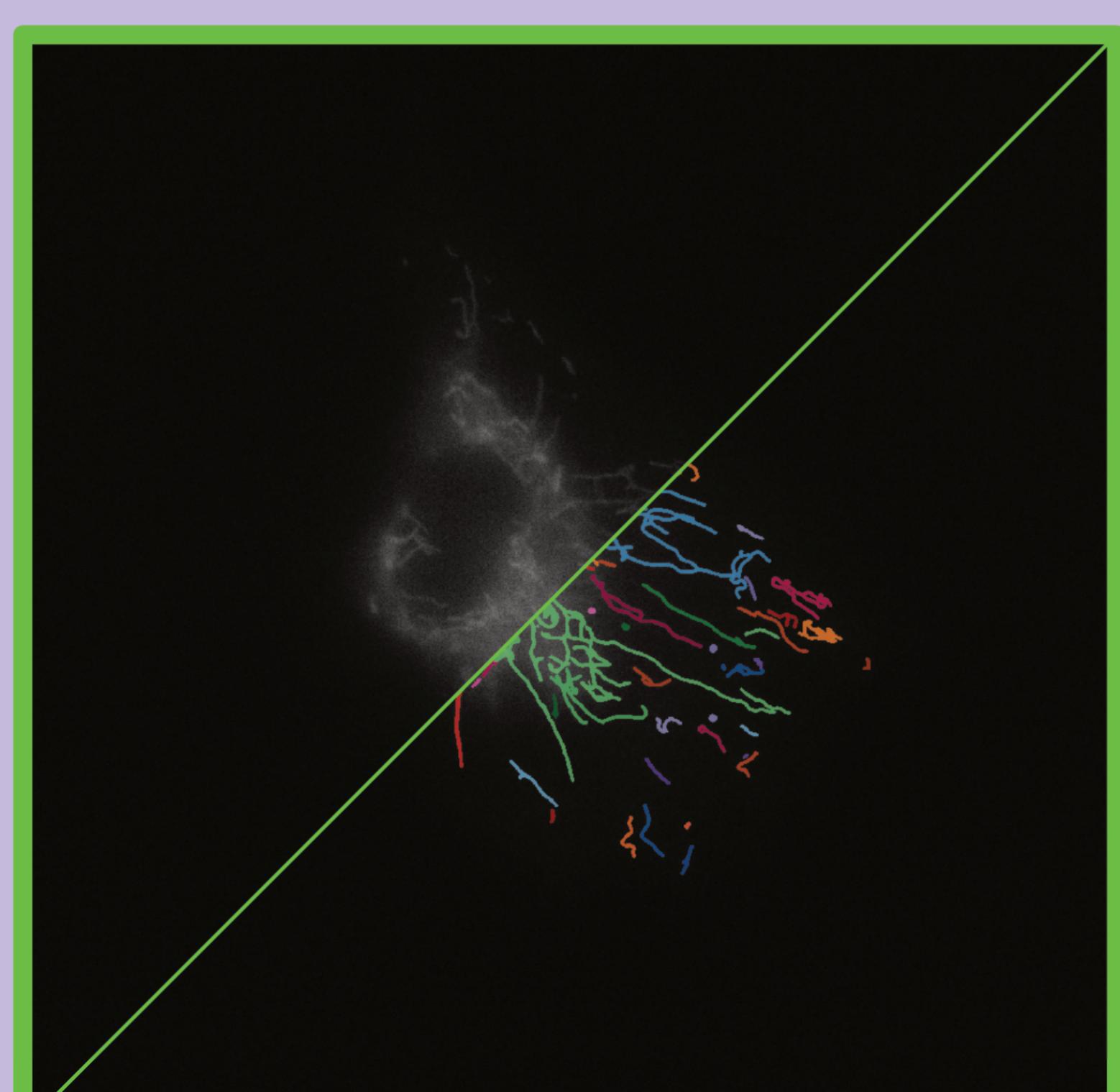
## Methods

1. Long-term mitochondrial dynamics imaged using photogentle microscopy
2. Synthetic timelapses generated via **MitoMimics** to train dual deep learning models (U-Mamba)
3. Model segments and tracks mitochondria in real data
4. Dynamics, fission/fusion, morphology, and network features are quantified
5. Extracted parameters inform mathematical modelling and hypothesis testing

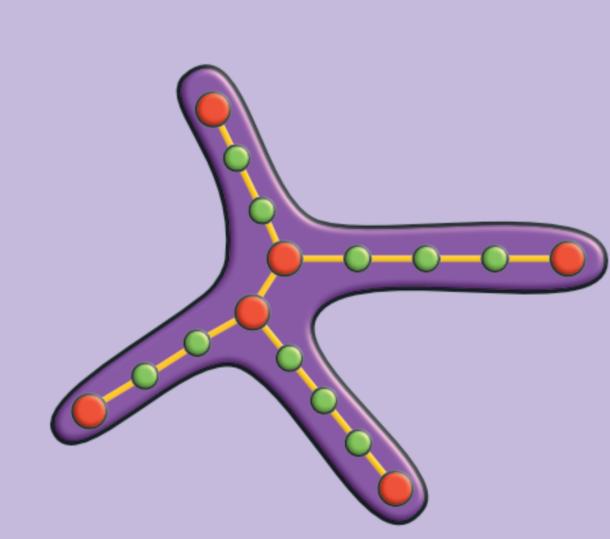


## Results & Discussion

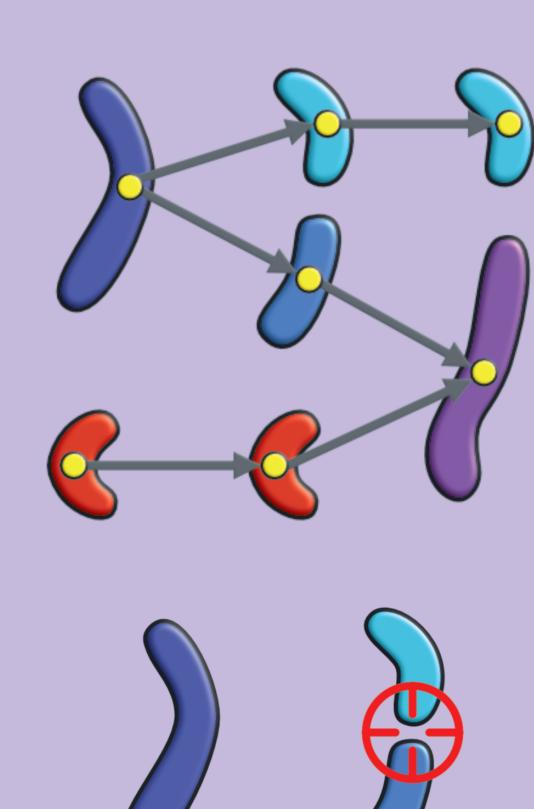
RPE1 WT



Levels of Organisation & Interaction



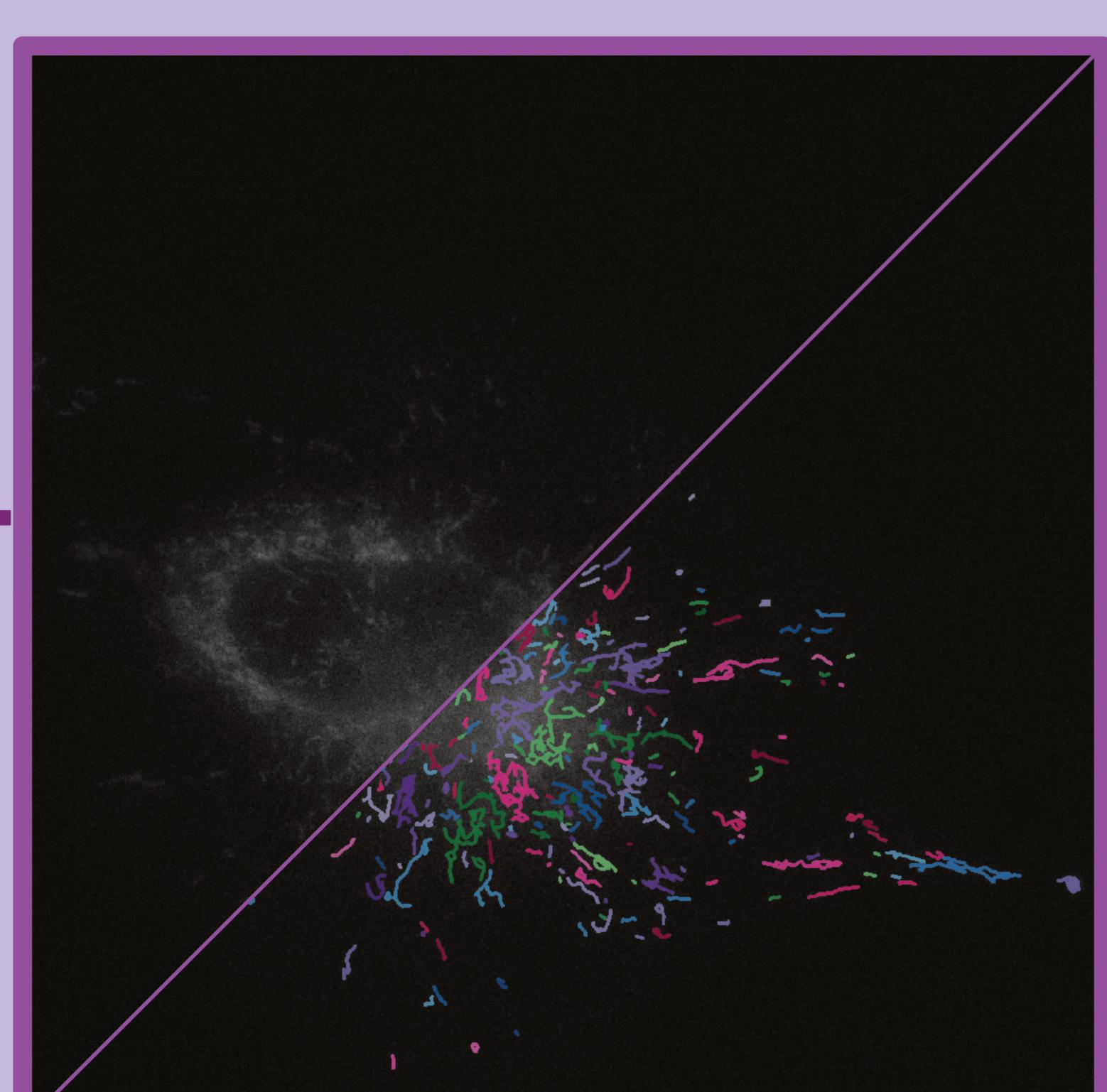
Branching highlights how well-connected mitochondria are, enhances energy distribution, and redistribution of proteins



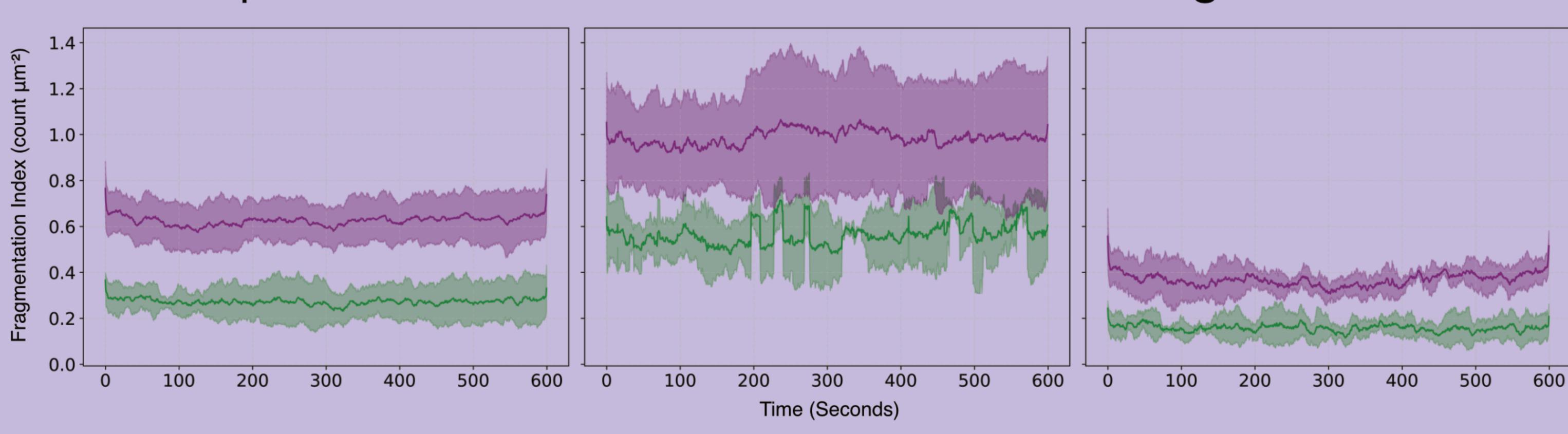
Fission/fusion are necessary for remodelling, quality control, and redistribution of mitochondria

- IRSp53 KO destabilises the mitochondrial network and disrupts mitochondrial homeostasis
- Fragmented, slower mitochondria may fail to supply ATP at areas of high energy demand
- This may lead to reduced migratory capacity

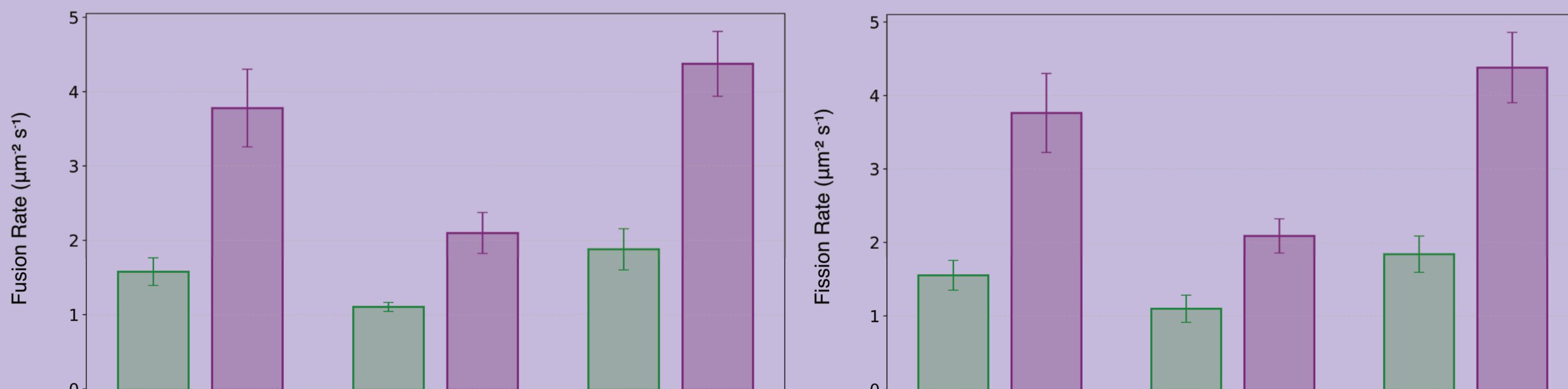
RPE1 IRSp53 KO



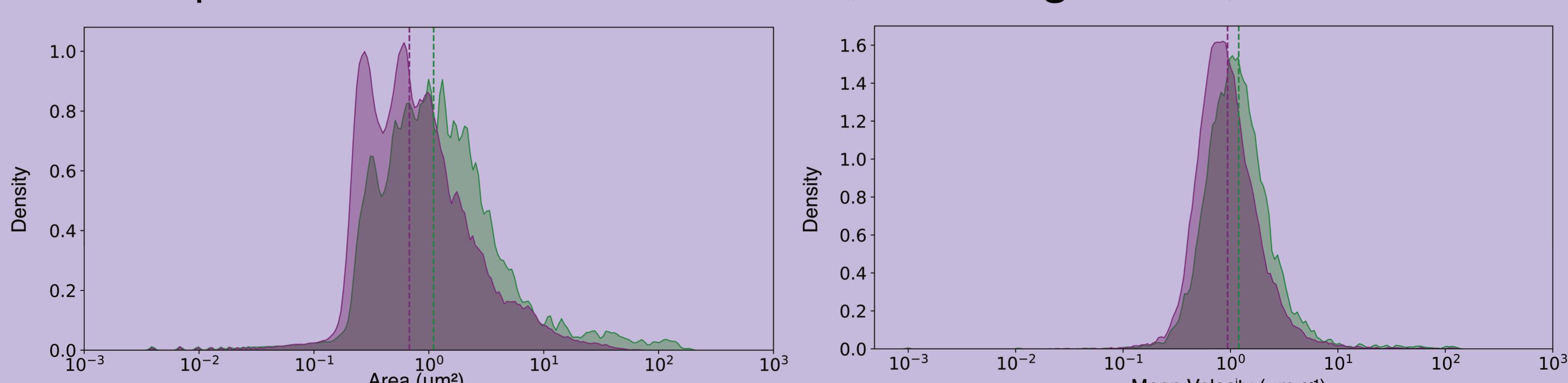
IRSp53 KO cells show increased mitochondrial fragmentation



Mechanical knockout increases mitochondrial fission and fusion



IRSp53 KO mitochondria are smaller, more fragmented, and slower



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