Modeling the Impact of Cellular Senescence on Wound Healing in Aging Lung Alveolar Epithelial Tissue

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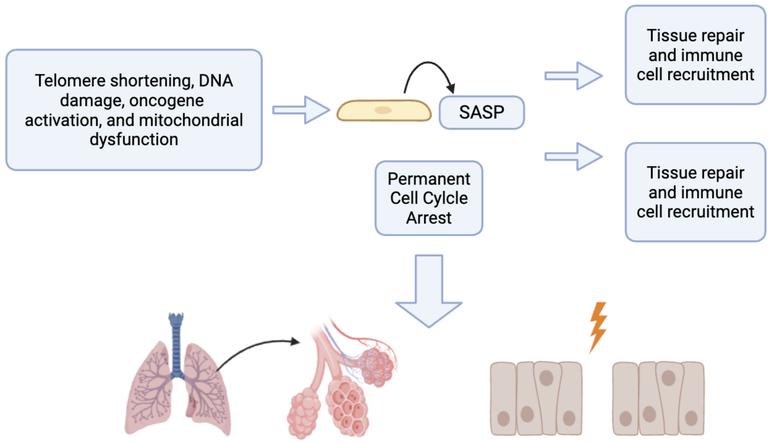
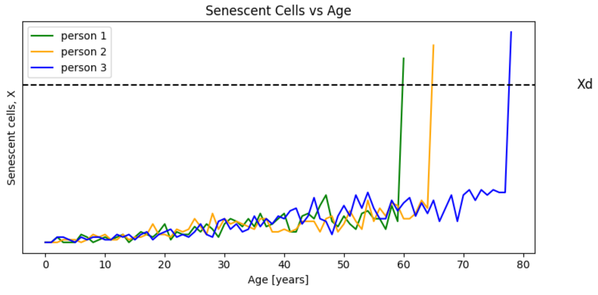
Aging and Cellular Senescence

- Advancements in healthcare, disease prevention, and medical technology have significantly increased human life expectancy over 20th century.
- However, biological aging is inevitable and aging causes age-related diseases.
- Cellular senescence is a significant hallmark of aging.



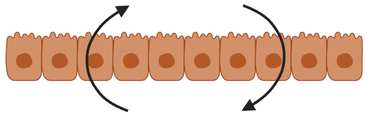
- As person ages, cellular senescence increases and there is a threshold of disease related to senescent cells.



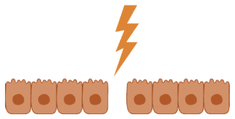
Xd

Threshold of Tissue Integrity

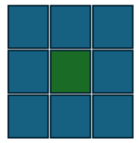
- In silico wound healing model, permeability is selected to be a threshold of tissue integrity.



- Epithelial barrier is disturbed as organism ages due to cellular senescence.



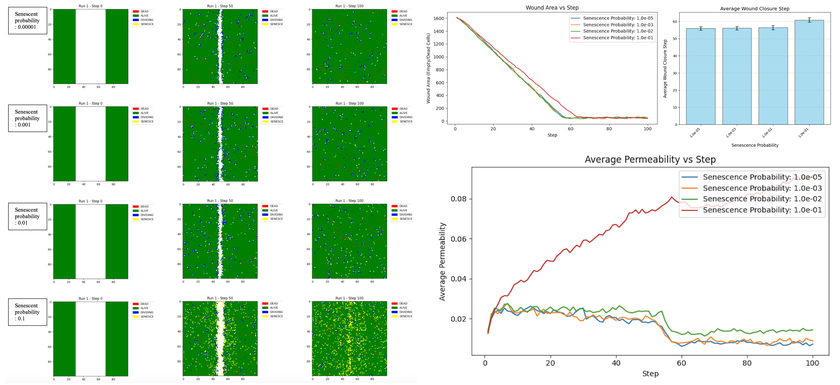
Agent Based Model (ABM)



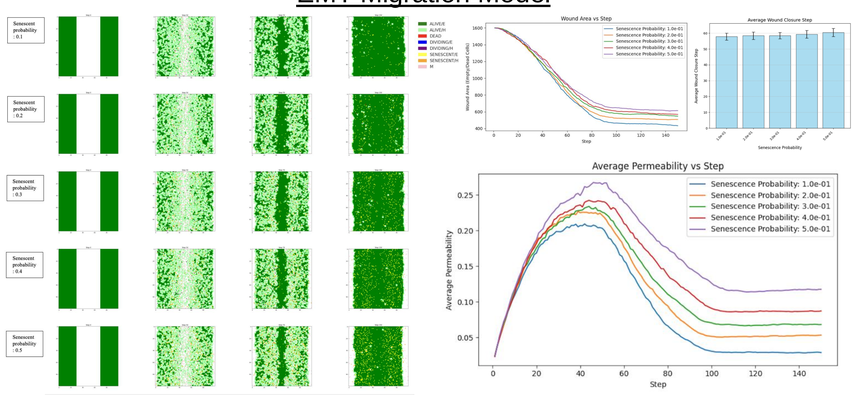
* Agent Based model is used in the wound healing simulation since each cell has its own fate and decisions on 100X100 grid

- Three wound healing models with rules of epithelial ABM

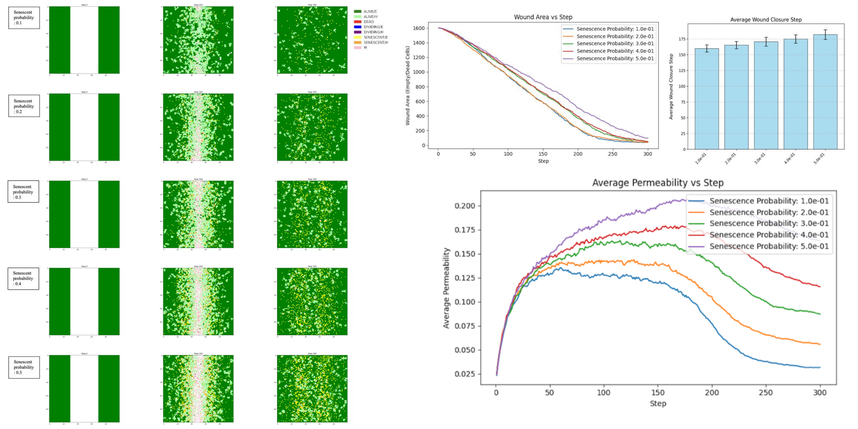
Proliferation-Driven Wound Healing Model



EMT Migration Model



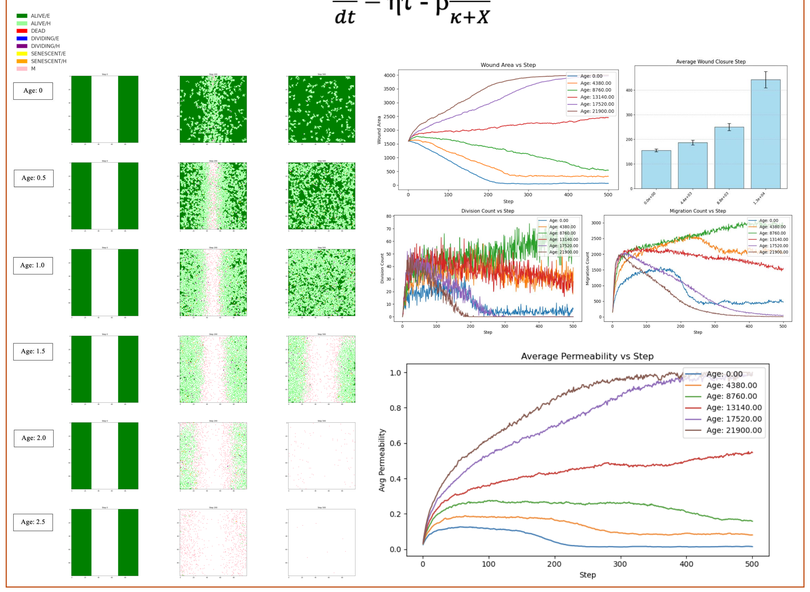
Density Directed Migration Model



Alon Senescent Cell Dynamics Model

Change in senescent cell in tissue = production – removal + noise

$$\frac{dX}{dt} = \eta\tau - \beta\frac{X}{\kappa+X}$$



Limitations in Models and Future Research

Limitations in simulation setup

- Cell composition of initial tissue is not accurately reflected in the simulation. This explains the aggressiveness of Alon Senescent Cell Dynamics Model.
  → Requires in depth research about the initial condition of aging lung epithelial tissue.
- Cell morphology and discontinuity of a tissue.
  → Requires different python tools to simulate the morphology of different cell type and tissue discontinuity can be solved by adding hidden simulation at each edge of the tissue.

Limitations in cell fate algorithms

- Discontinuity of simulation
  → The cellular phenomena that are faster than 1 hour cannot be simulated.
- Imprecise parameters (probability of cell decision)
  → Migration probability of hybrid senescent cells and mesenchymal senescent cells are uncertain and probability of epithelial to hybrid cell or mesenchymal cell to epithelial cell is unclear.

Reference

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