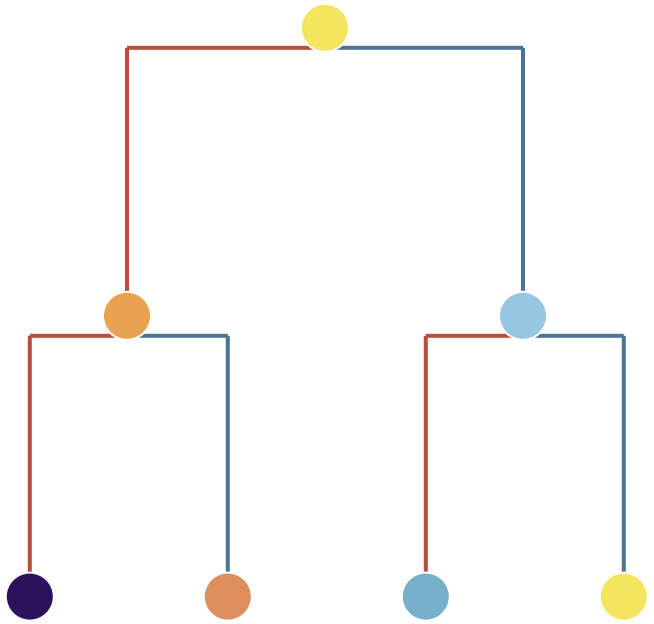
A minimal lineage model for damage accumulation

How damage is inherited, repaired, partitioned, amplified, and terminated across cell divisions.

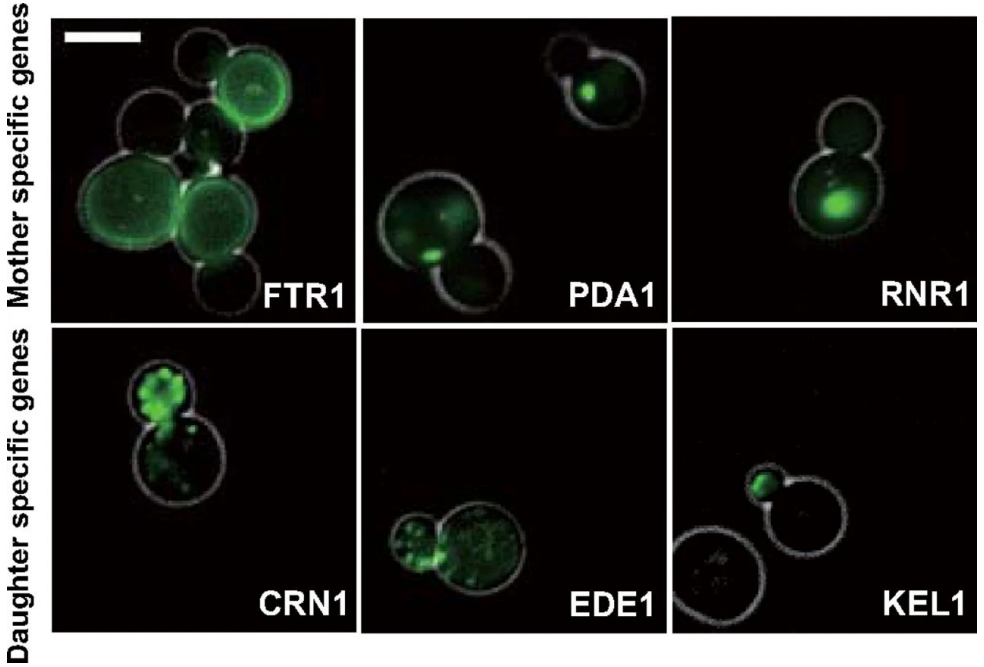
Hongying Lin

2026.7.28



Asymmetric inheritance is observed across cellular systems

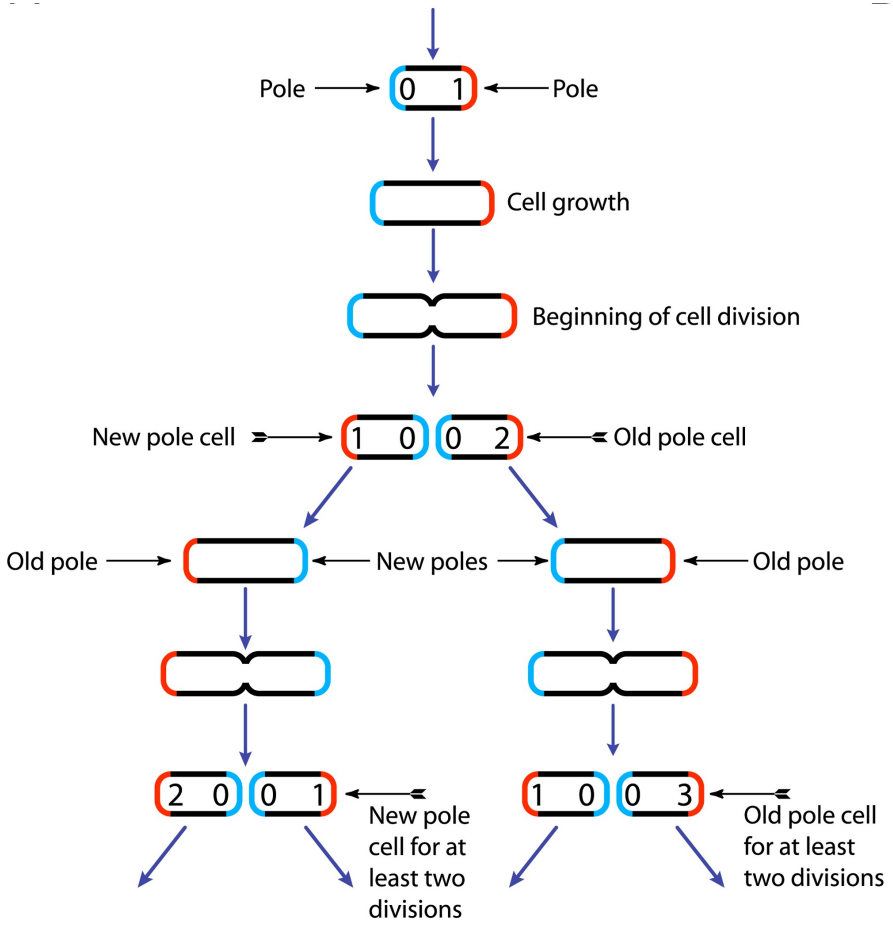
Budding yeast	Age-associated components can remain enriched in mother cells while buds are comparatively rejuvenated.

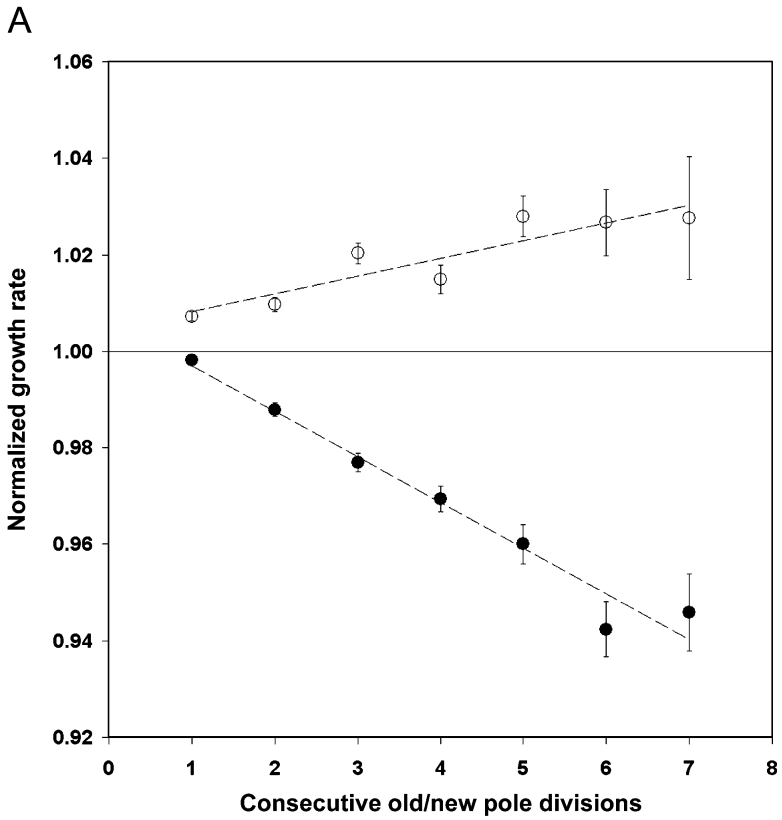


Sources: Yang et al., 2015

Asymmetric inheritance is observed across cellular systems

Escherichia coli Old-pole lineages can show slower growth and an elevated mortality risk.



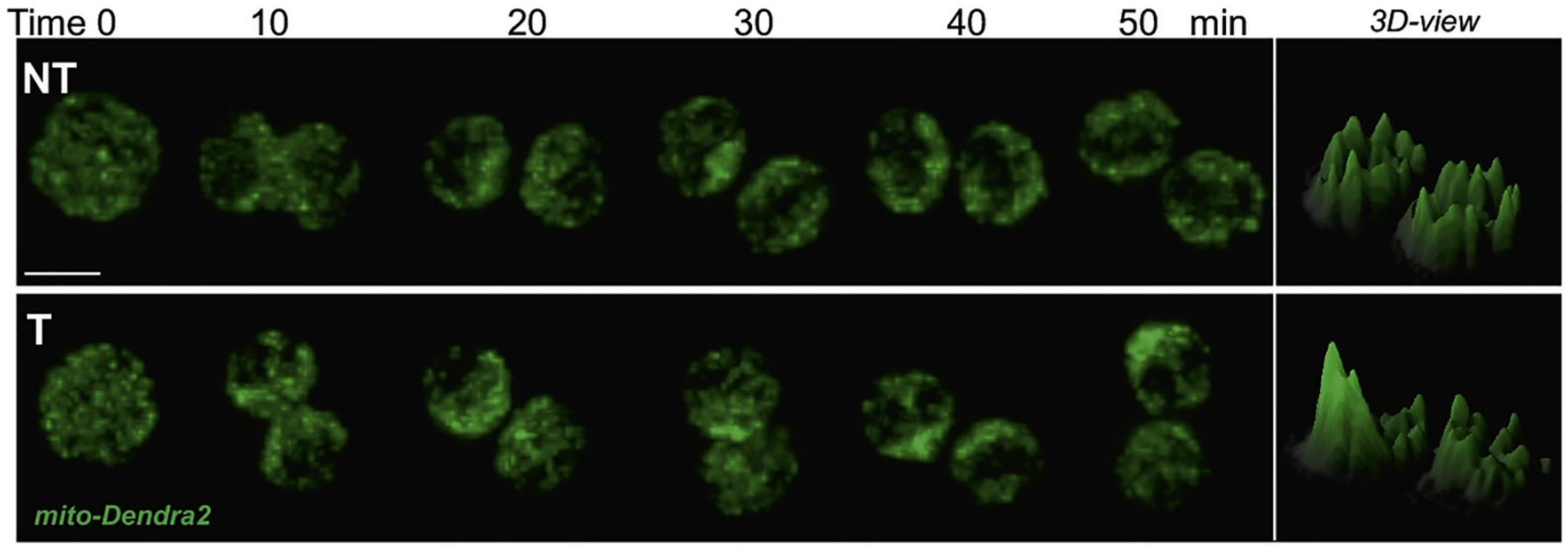


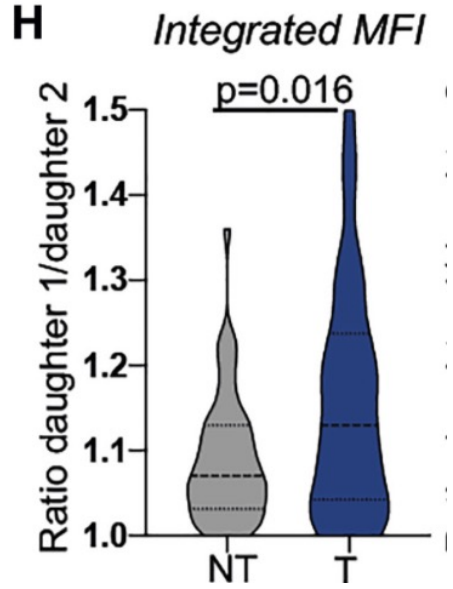
Sources: Stewart et al., 2005

Asymmetric inheritance is observed across cellular systems

Hematopoietic stem cells

Less functional mitochondria can be preferentially retained during active HSC division.





Sources: Hinge et al., 2020

Lineage information distinguishes cell state from cell history

A snapshot reports a cell's current state
A lineage model asks which sequence of ancestral events produced it.

Snapshot question

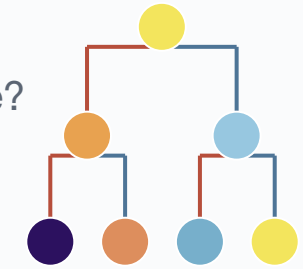
Which cells carry more damage?

Similar states can arise from different histories.

Lineage question

Which ancestral events generated the state?

Accumulation, repair, partitioning, noise, or selection?

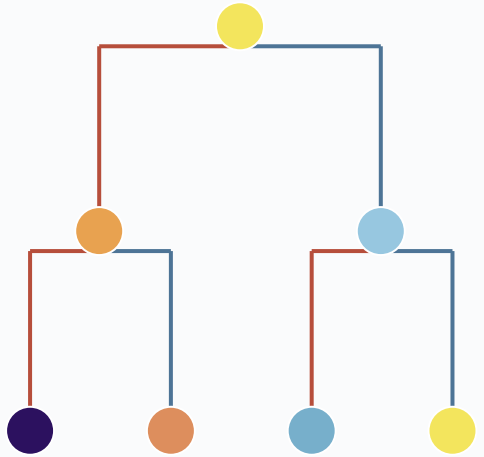


The model converts present-day cell states into explicit, testable hypotheses about cellular history.

Partitioning generates distinct lineage histories

s = 0
Symmetric partitioning

s > 0
Asymmetric partitioning



A discrete cell-cycle model tracks one damage state per cell

State

D_t

Update

P_t

Decision

$P_t < T?$

Daughters

D_O, D_N

$D_t \rightarrow P_t \rightarrow$ survive or die $\rightarrow D_{O,t+1}$ and $D_{N,t+1}$

- Time advances in division cycles.
- D_t is an abstract, non-negative damage burden carried by one cell at cycle t.

A discrete cell-cycle model tracks one damage state per cell

State

D_t

Update

P_t

Decision

$P_t < T$?

Daughters

D_O, D_N

$D_t \rightarrow P_t \rightarrow$ survive or die $\rightarrow D_{O,t+1}$ and $D_{N,t+1}$

$$P_t = \max(0, (1 - r)D_t + a + \varepsilon_t)$$

if $P_t < T$, $D_O = (0.5 + s)P_t$ and $D_N = (0.5 - s)P_t$.

Each parameter encodes an explicit biological hypothesis

Parameter	Mathematical role	Question for simulation
input a / repair r	Sets baseline accumulation per cycle.	Does damage stabilize or drift upward?
asymmetry s	Biases distribution of pre-division damage.	Do O and N histories diverge?
threshold T / noise epsilon	Sets termination and stochastic variation.	Which branches die, and how robust is the signal?

Task 1

How does a cell respond to the accumulated damage?

- Repair ability decline as cells accumulate more damage?
- Accumulated damage cause more new damage in the new cell division?

Try to modify the model to include the consideration

One update rule governs every division

1

Inherited damage

D_t

2

Repair and input

r, a, epsilon_t

3

Nonlinear scaling

f, q

4

Death threshold

P_t >= T?

5

Partition

0.5 +/- s

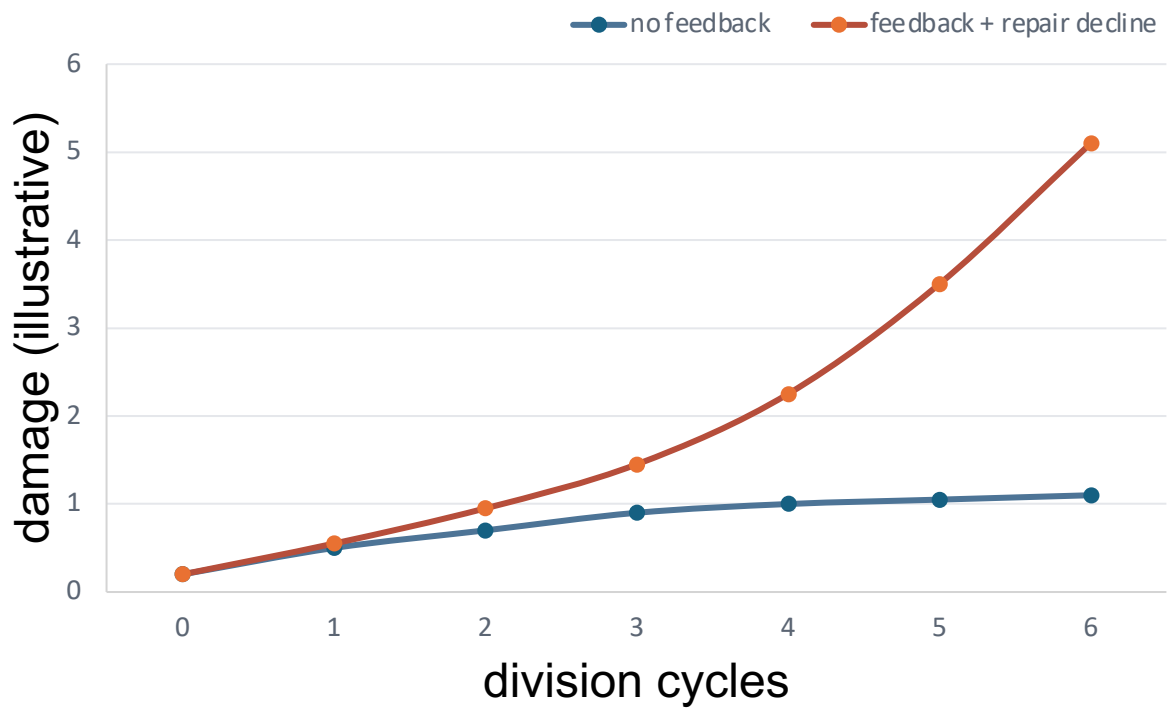
$$P_t = \max(0, (1 - r/(1 + qD_t))D_t + a(1 + fD_t) + \epsilon_t)$$

If $P_t \geq T$, the cell dies; otherwise damage is partitioned to daughters.

Each parameter encodes an explicit biological hypothesis

Parameter	Mathematical role	Question for simulation
input a / repair r	Sets baseline accumulation per cycle.	Does damage stabilize or drift upward?
asymmetry s	Biases distribution of pre-division damage.	Do O and N histories diverge?
feedback f / decline q	Makes accumulation damage dependent.	Does divergence accelerate?
threshold T / noise epsilon	Sets termination and stochastic variation.	Which branches die, and how robust is the signal?

Feedback and repair decline introduce nonlinear damage dynamics



Two phenomenological nonlinearities

Damage feedback, f
Existing damage raises new damage

Repair decline, q
Existing damage reduces effective repair

Question:
Is there a damage level beyond which return to a low-damage state becomes unlikely?

Illustrative curves from the tutorial model; biological motivation: Saarikangas et al., 2017; Henderson et al., 2014

Task 2

How do growth and maintenance trade-offs shape population fate?

- Does a faster-dividing population always persist better in the long term?
- How do division rate, repair ability, damage accumulation, and death together affect:
  - living population size?
  - cumulative cell deaths?

Try to construct and compare two population profiles:

- rapid growth / high damage
- slower growth / high repair

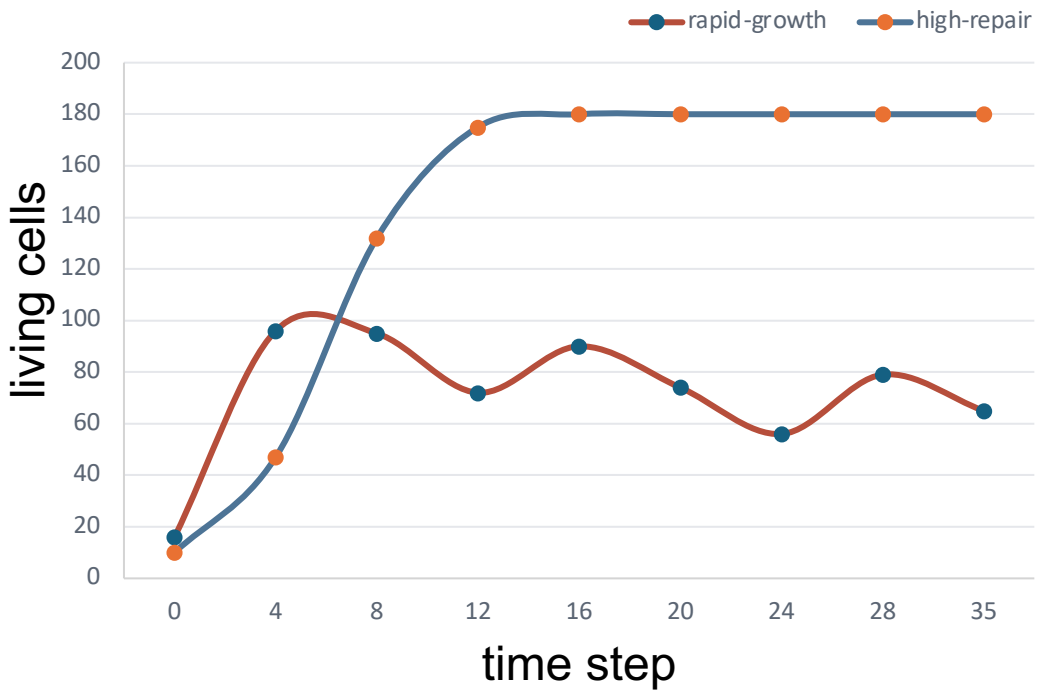
Population dynamics expose growth-maintenance trade-offs

A single lineage has no division probability, density dependence, or carrying capacity
population simulation adds these outcomes.

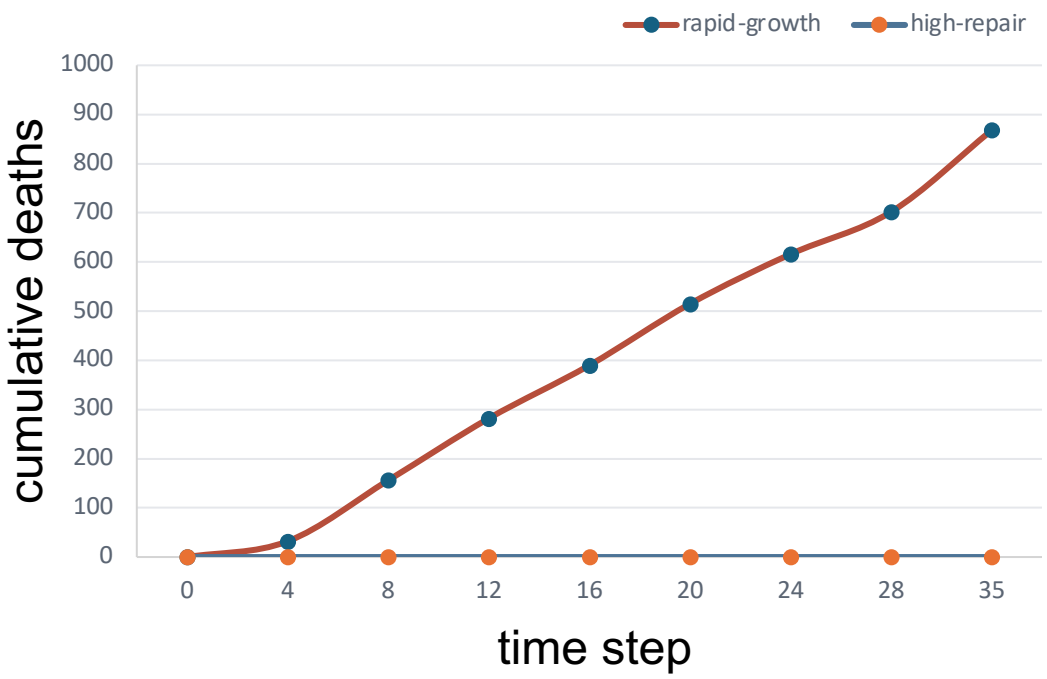
Rapid-growth profile (similar to r selection)	High division probability High damage / low repair	Early expansion is rapid, but damage and death are costly.
High-maintenance profile (similar to K selection)	Lower division probability Low damage / high repair	Early expansion is slower, but persistence can be greater.

Early proliferation can trade off against long-term persistence

Living population



Cumulative deaths



We can test more hypotheses with the model

A

Does death follow history?

Lower T: do deaths concentrate in high-O-history branches?

B

Can repair rescue a lineage?

Increase r or lower q: can an endangered lineage persist?

C

What should be measured next?

Track lineage-resolved damage, division timing, repair proxies, and death events.

The model is phenomenological, not fitted to one organism.
Use it to state which observable lineage pattern would support, weaken, or falsify a proposed mechanism.