AGING OF BIOFILMS USING A SINGLE-CELL GROWTH MODEL

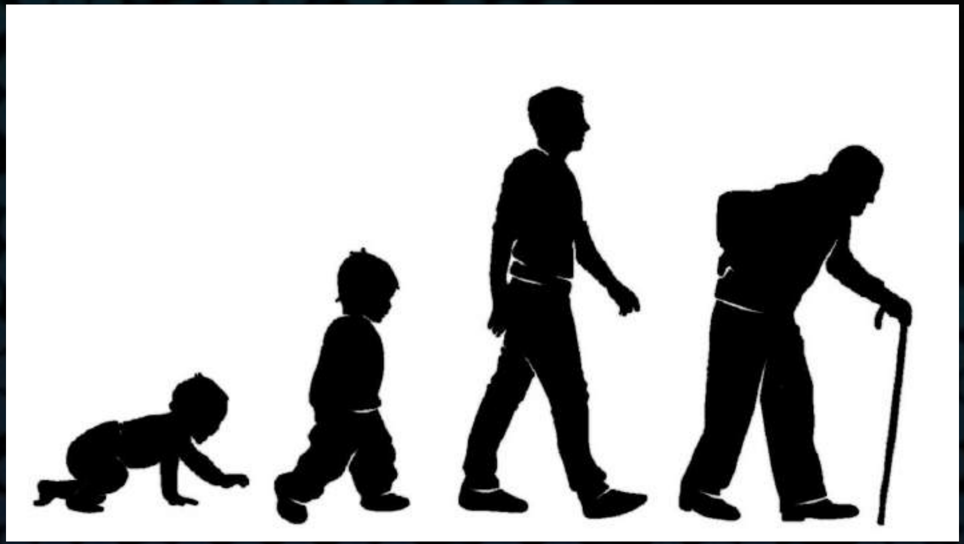
Robyn Wright [1,2], Robert Clegg [1], Timothy Coker [1,2] and Jan-Ulrich Kreft [1]

[1] University of Birmingham, UK

[2] University of Warwick, UK

AGING AND DAMAGE REPAIR

- **Aging:** a loss of function or an accumulation of damage with increasing age.
  - Bacteria are not traditionally thought of as exhibiting aging (Fredriksson & Nyström, 2006).
  - Aging has been demonstrated in single-celled organisms, but this is controversial (Barker & Walmsley, 1999; Ackermann *et al.*, 2003; Fredriksson & Nyström, 2006; Lindner *et al.*, 2008).
- Strategies for dealing with damage:
  1. Asymmetric damage segregation at division.
  2. Repair of damage.
- We wanted to investigate this from an evolutionary perspective using an individual-based model of single cell growth.



PREVIOUS AGING MODELS

Watve *et al.* (2006)	**Ackermann *et al.* (2007)**	**Erjavec *et al.* (2008)**
• Cells divide at certain time points. • Growth rate declines with age. • No cost to repair (oldest parts are converted to newest). • Cells die when they are in the oldest age class.	• Cells divide at certain time points. • Cells do not grow. • Damage decreases survival probability. • Damage is repaired at the cost of decreased survival probability. • External mortality.	• Cells divide once active protein reaches a threshold. • No repair, but decay of damage – no recycling back to active protein. • No cost of damage decay.

Clegg *et al.* (2014)

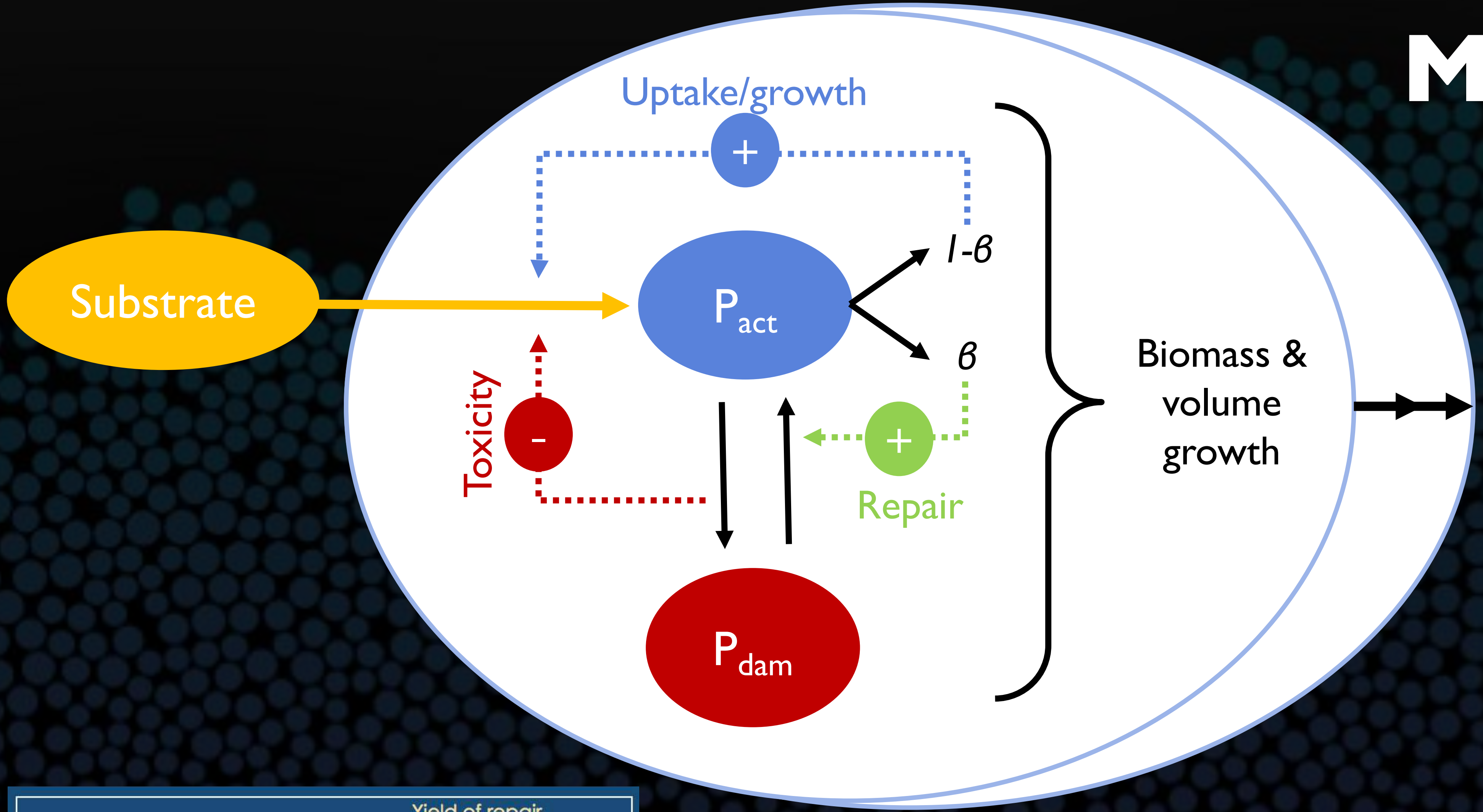
- Cells grow by consuming resource.
- Cells divide once total protein reaches a threshold.
- Repair is carried out by a separate class of protein.
- Protein is recycled with a certain efficiency.
- Damage may be either inert or toxic.
- Used constant and dynamic environments.
- Determined an optimal rate of repair in constant and dynamic environments.
- External mortality

OBJECTIVES

- Determine an optimal repair rate for a biofilm, as Clegg *et al.* (2014) did in the constant and dynamic environments.
- In order to do this we had to:
  - Develop an adaptive repair strategy.
  - Test this strategy in constant and dynamic environments.
  - Apply this to growth in biofilms.

METHOD

MODEL

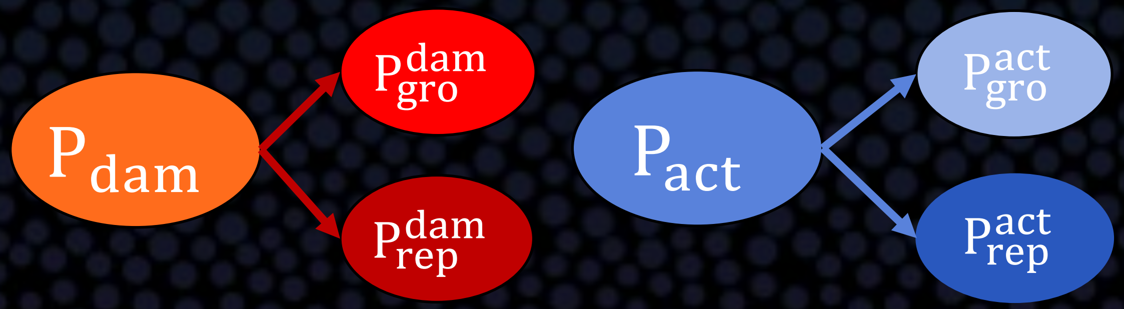


Yield of repair

$$\hat{\beta} = \left(\frac{Z}{1-Z}\right)\left(\pm\sqrt{\frac{Y_r}{\mu(S)}\frac{1}{1-Z}} - 1\right)$$

Cellular age

Specific growth rate



METHOD – ENVIRONMENTS AND STRATEGIES

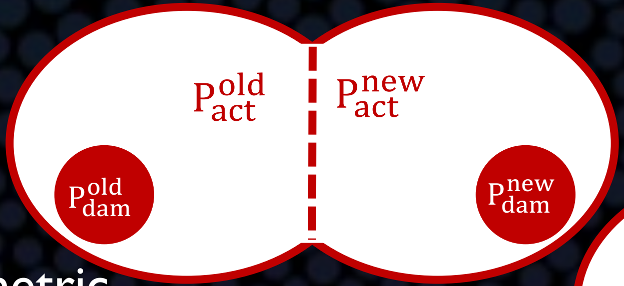
Environments:

- Constant environment
- Dynamic/chemostat environment
- Biofilms – alternating, side by side or random initial cell placement

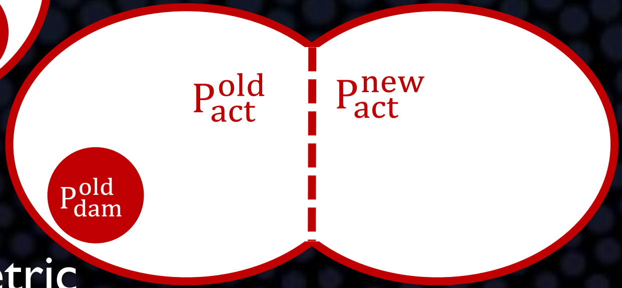
- Damage is toxic

Strategies:

- Symmetric, no repair
- Symmetric, fixed, optimal repair
- Symmetric, adaptive repair
- Asymmetric, no repair
- Asymmetric, fixed, optimal repair
- Asymmetric, adaptive repair



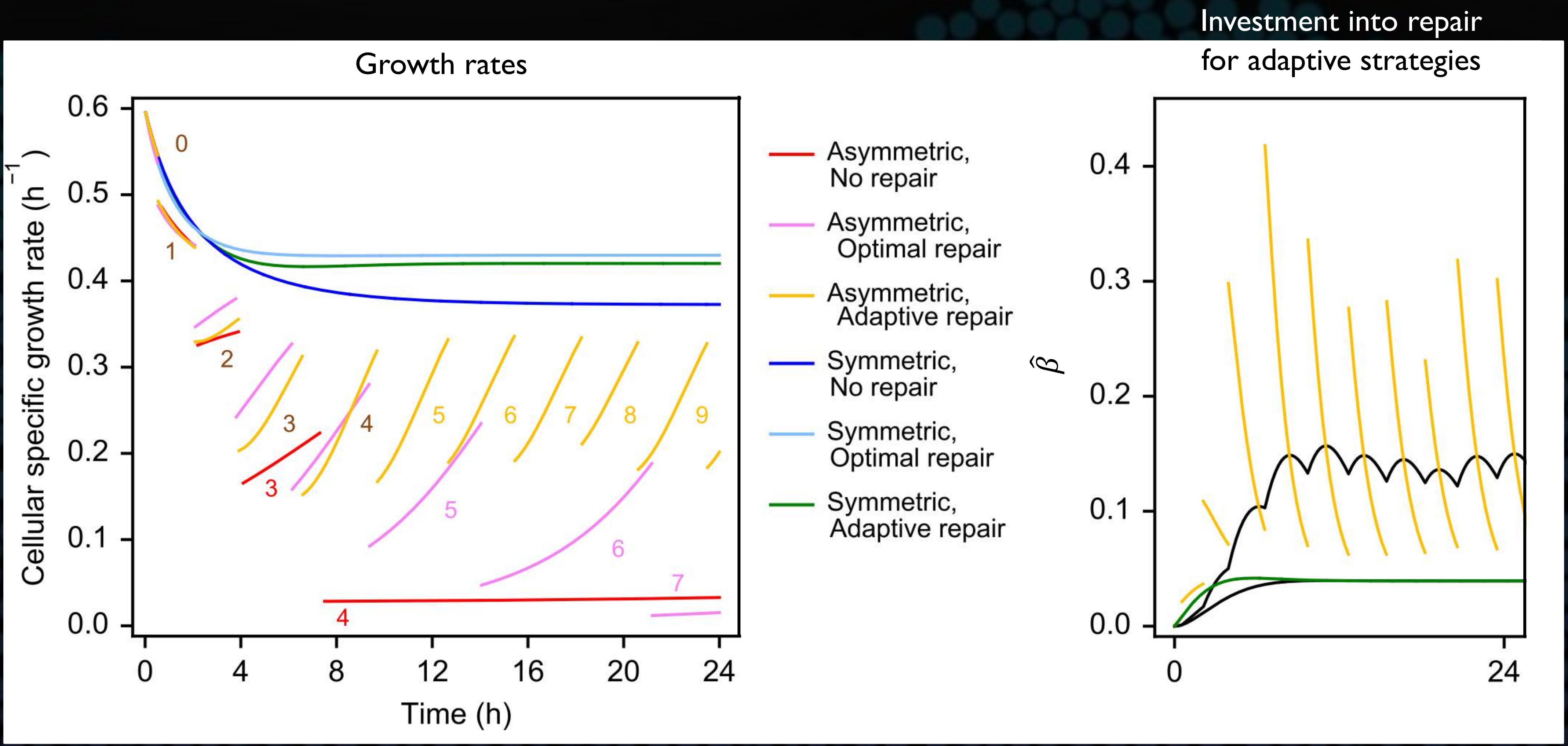
Symmetric



Asymmetric

INDIVIDUAL CELL

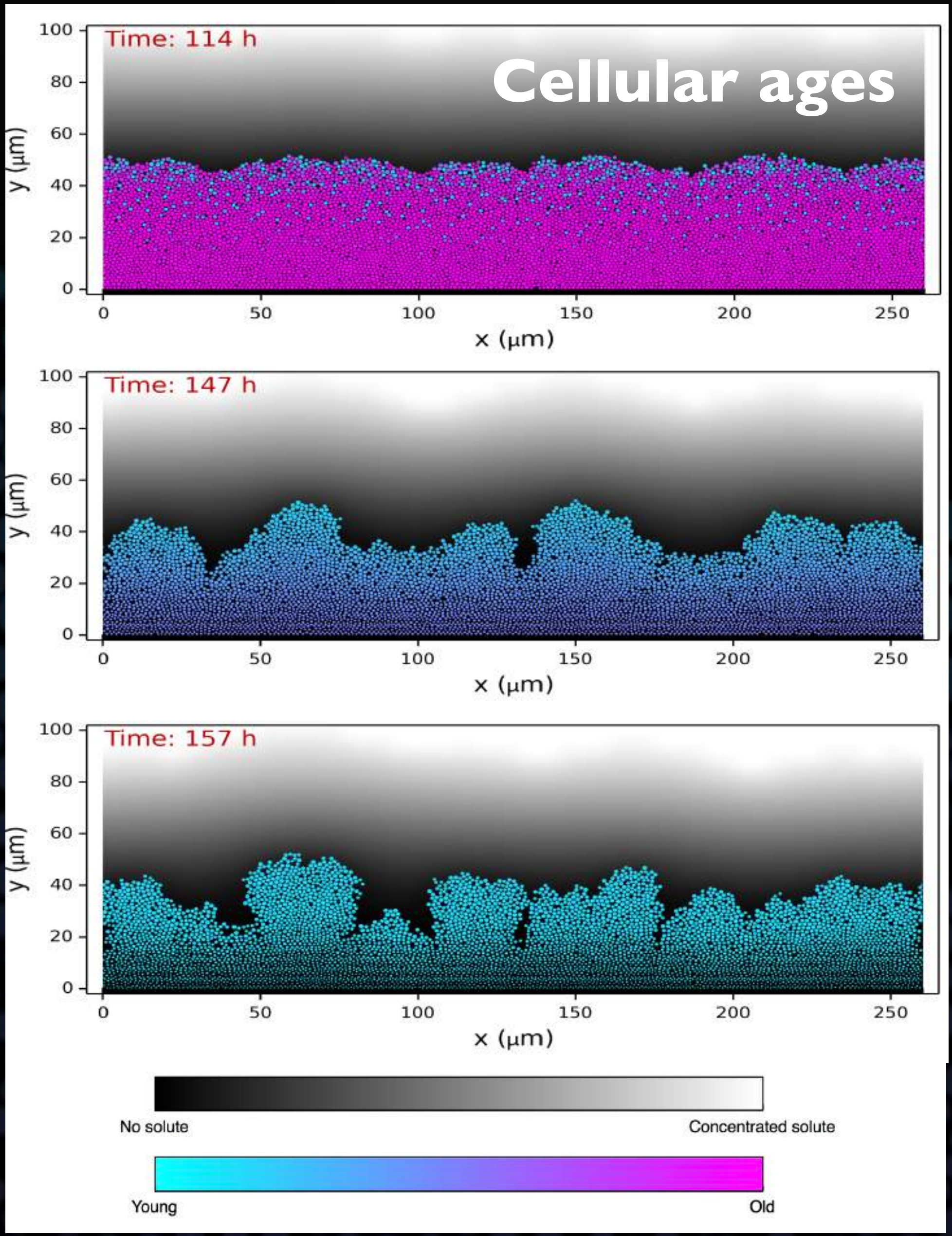
FOLLOWING OLD POLE CELL OVER TIME IN CONSTANT ENVIRONMENT



Constant – optimal fixed repair strategy is fittest

Dynamic – adaptive repair strategy is fittest

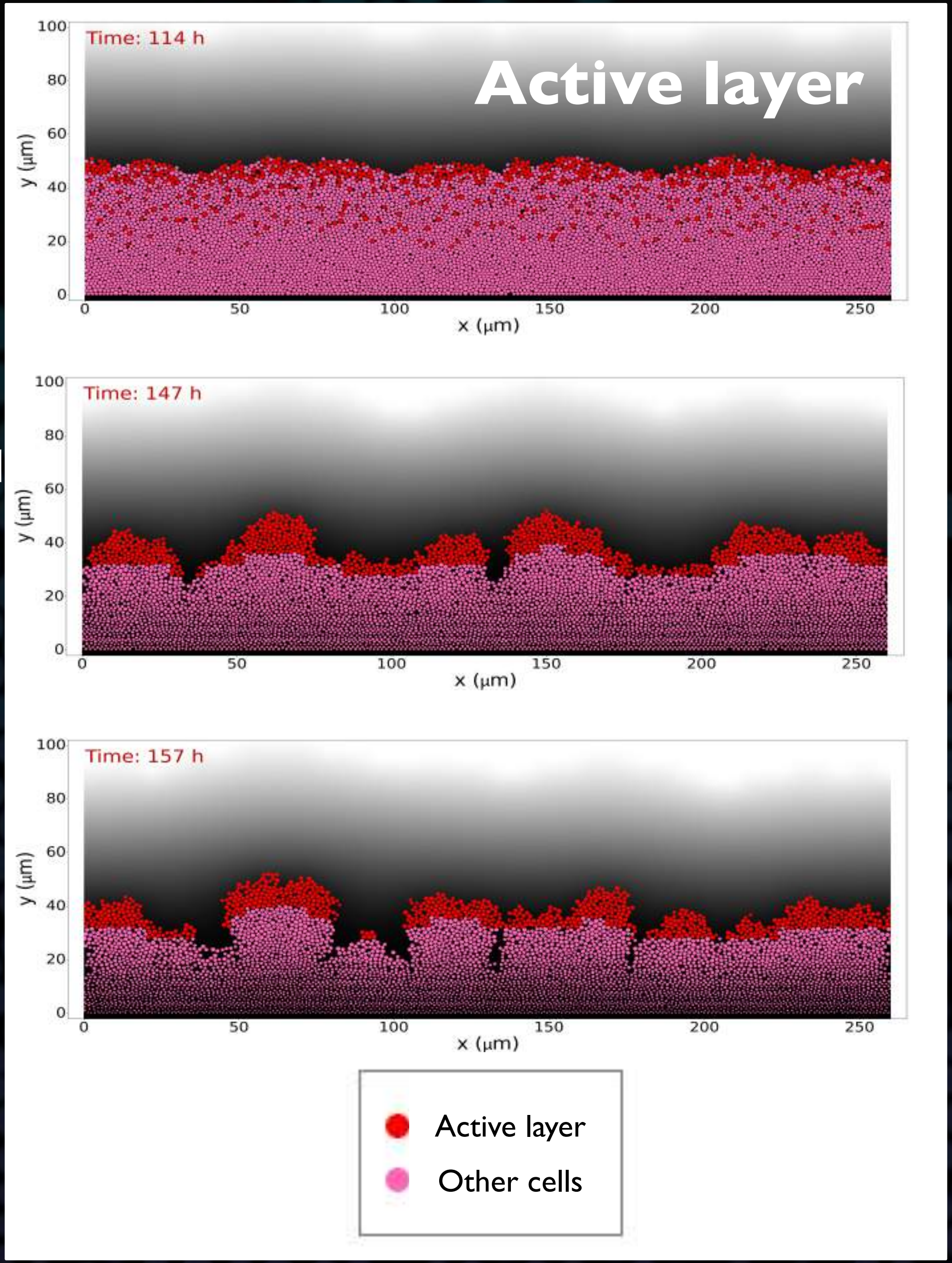
SINGLE SPECIES BIOFILMS



Asymmetric damage segregation

Optimal, fixed repair

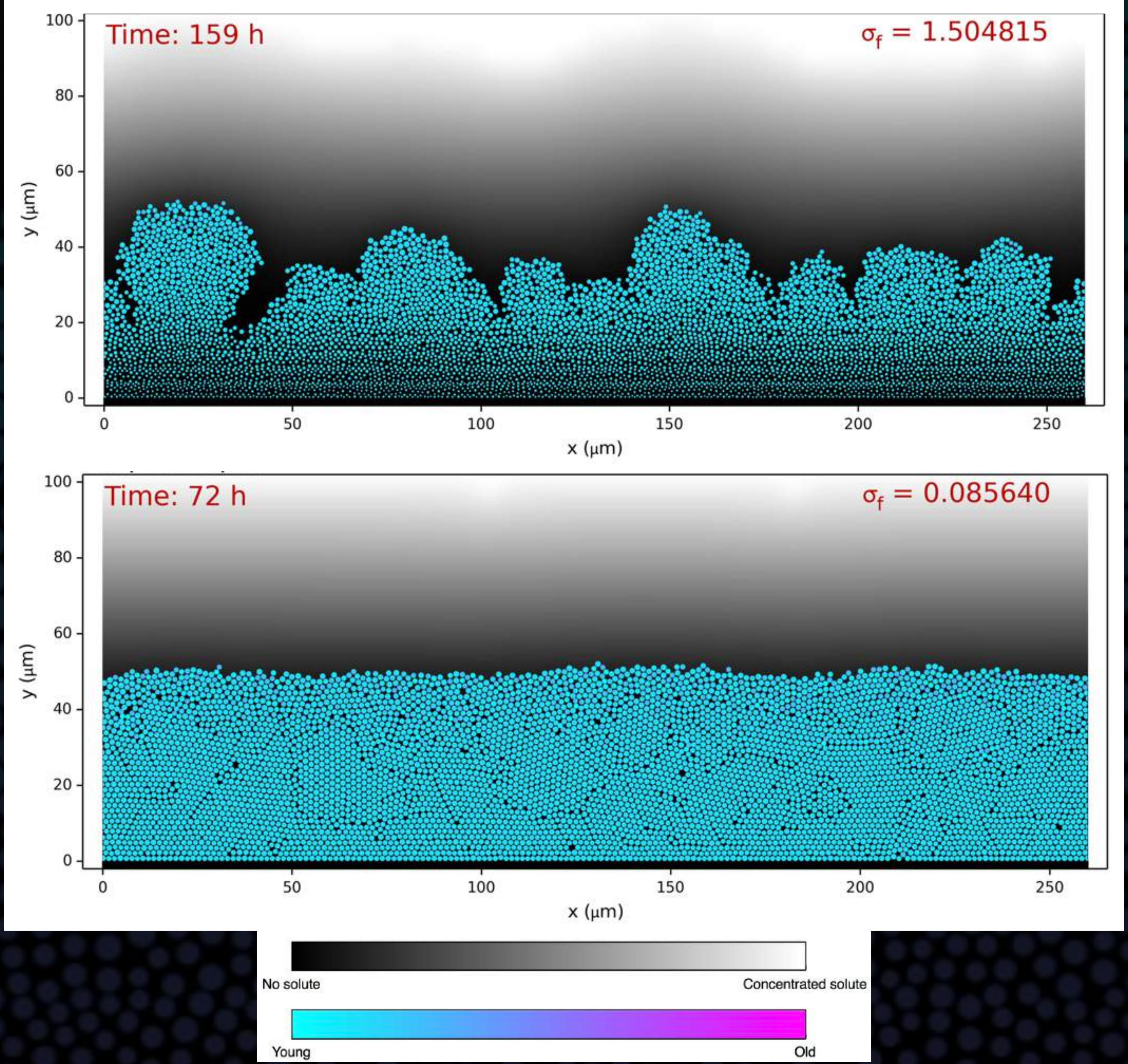
Adaptive repair



CELL SHRINKAGE

No ‘padding’

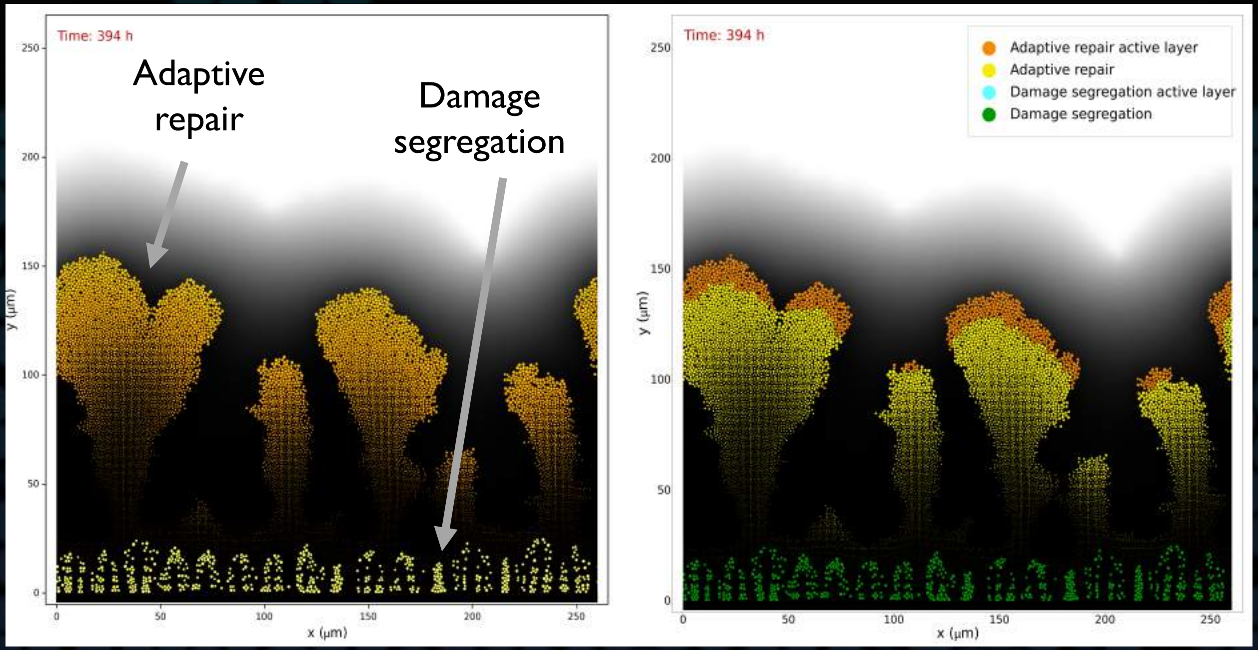
With ‘padding’



ALTERNATING INITIAL CELL PLACEMENT

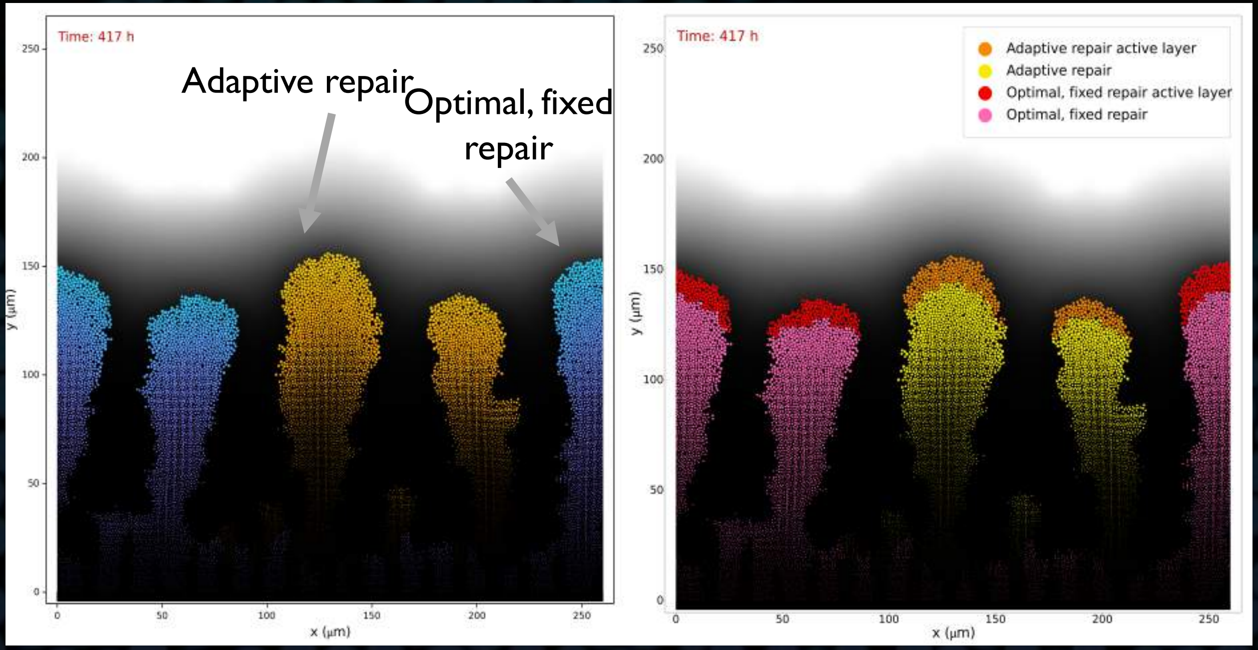
Adaptive repair vs. damage segregation

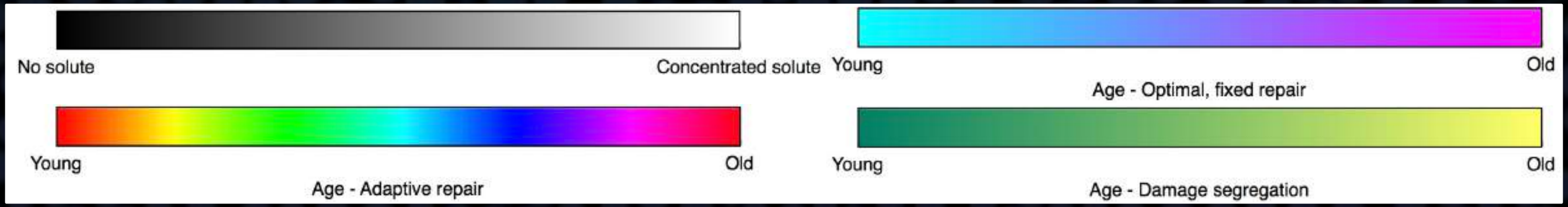
Cellular ages *Active layer*

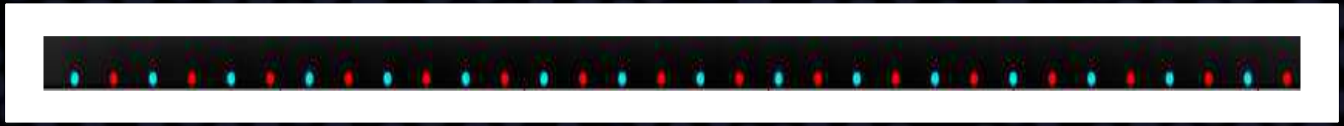


Adaptive repair vs. optimal, fixed repair

Cellular ages *Active layer*



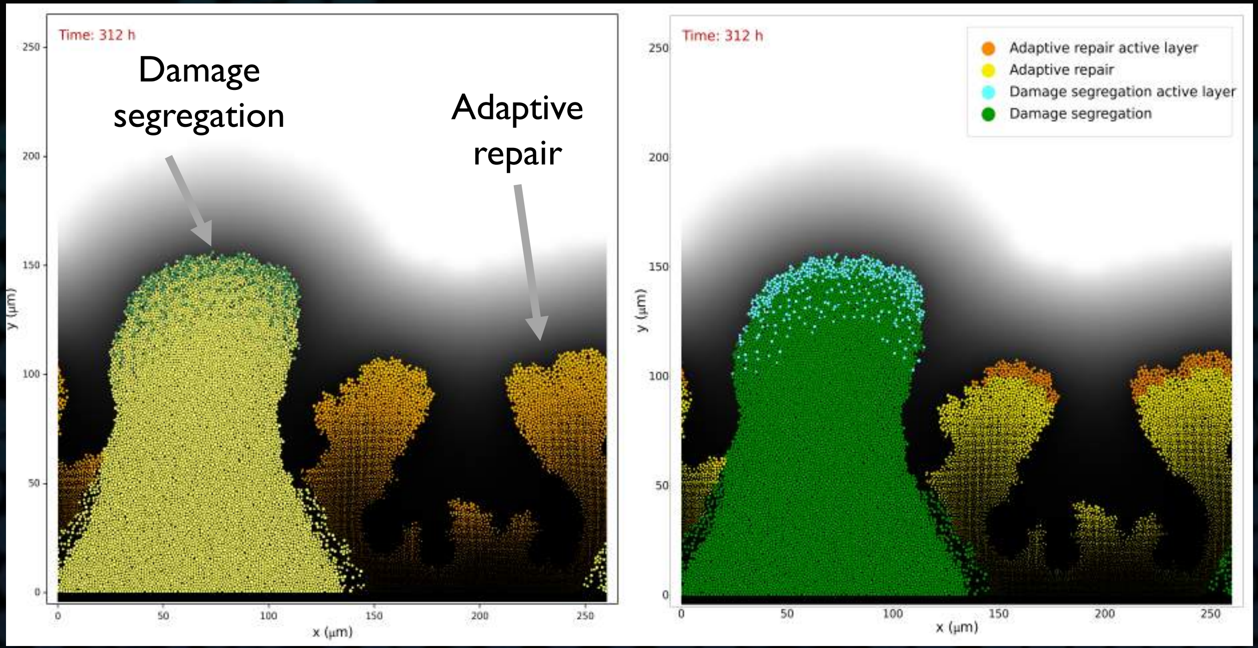




SIDE-BY-SIDE INITIAL CELL PLACEMENT

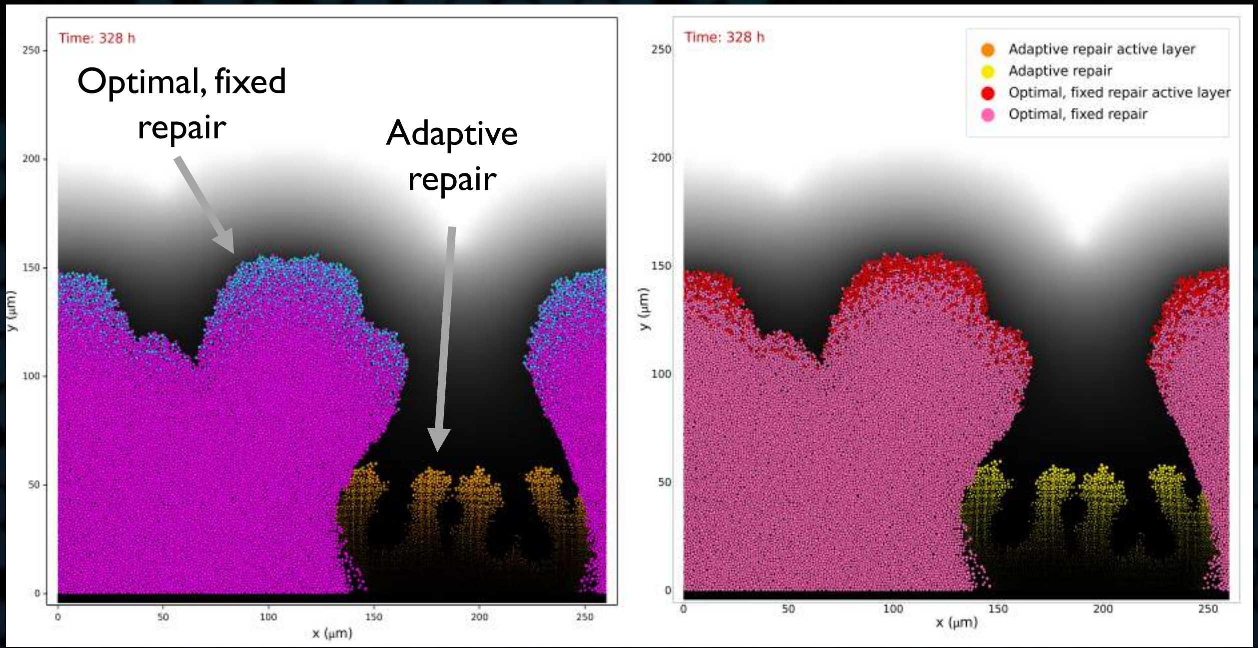
Adaptive repair vs. damage segregation

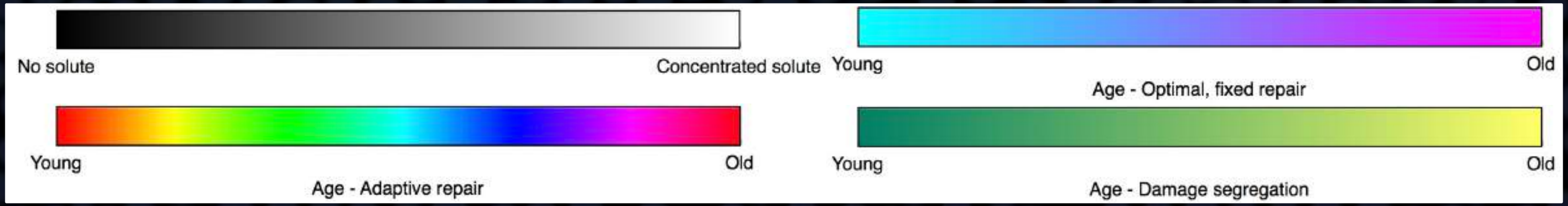
Cellular ages *Active layer*



Adaptive repair vs. optimal, fixed repair

Cellular ages *Active layer*

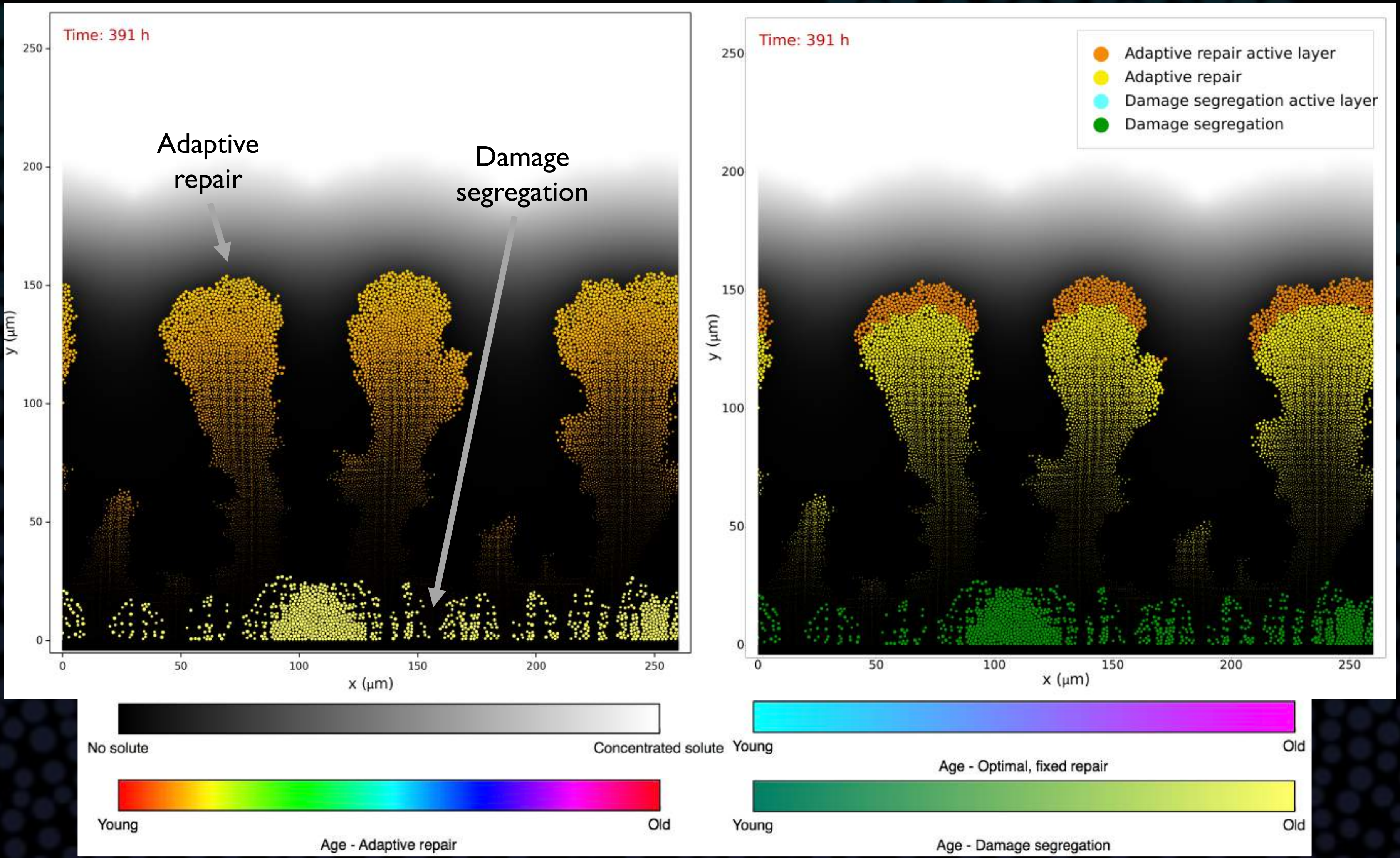




RANDOM INITIAL CELL PLACEMENT

Adaptive repair vs. damage segregation

Cellular ages *Active layer*



LIMITATIONS TO THE MODEL

- Repairing cells are shrinking and this causes changes in biofilm shape.
  - Needs conversion of protein from repair back into growth, when it is no longer needed.
- Variable damage rates needed.
  - Damage should realistically be dependent upon the cells' position in the biofilm.
  - Damage would not always occur at the same rate (different environments, presence of UV, etc.)

CONCLUSIONS

- Repair tends to be better than segregation of damage, but we need to add a way for this protein to be converted back to growth protein if it is no longer needed.
- We predicted that adaptive repair would be better than optimal, fixed repair, but this is not always the case.
- There is a conflict between what is best for the individual and what is best for the community.
  - The model determines only what is best for the individual cell.

THANKS TO...

Robert Clegg

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Timothy Coker

ANY QUESTIONS?

PER ARDUA AD ALTA
UNIVERSITY OF BIRMINGHAM

IMI
INSTITUTE OF MICROBIOLOGY AND INFECTION

MIBTP
Midlands Integrative Biosciences Training Partnership

BBSRC
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iDynoMiCS
iDynoMiCS - individual-based Dynamics of Microbial Communities Simulator