

Possible Origin of Division of Labor in Multicellular Organisms

An Agent-Based Model

Tianqin Ren
University of Missouri
trznz@missouri.edu
PaBST, 06/26/2025



BORDEAUX SUMMER SCHOOLS

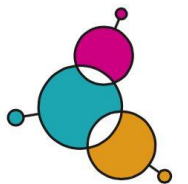
Coauthors

Claudia Gadaleta
Paris 1 Sorbonne Panthéon.

Sebastian Sander Oest
University of Oslo.

Jokubas Janusauskas
Karolinska Institute.

Claudio Davini
University of Bologna.



PhilInBioMed

Multicellularity and Division of Labor

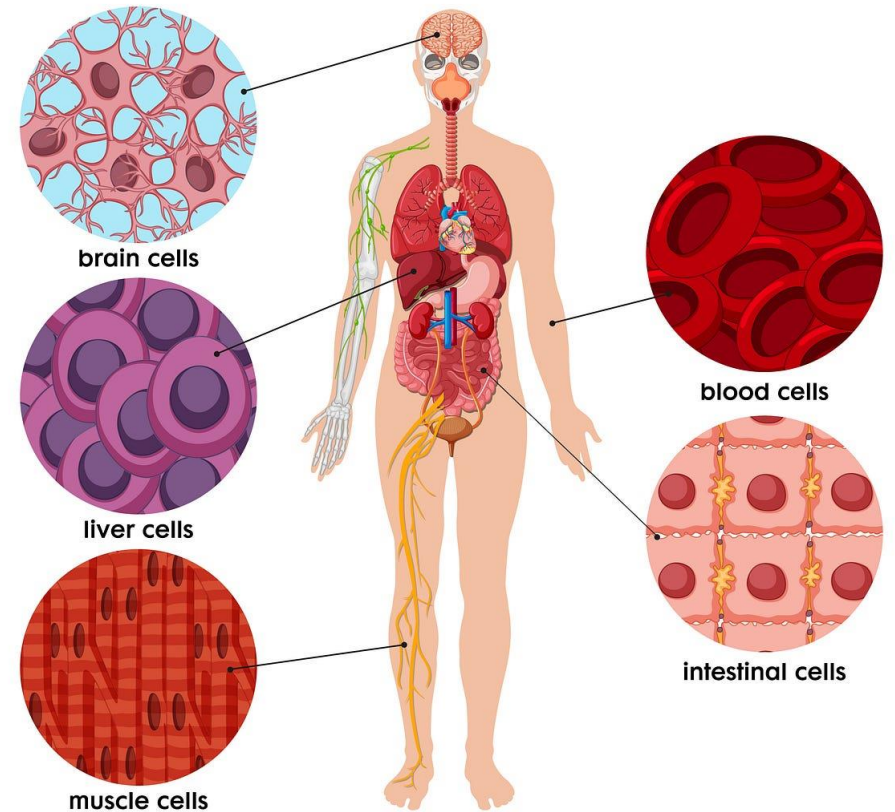


Paramecium



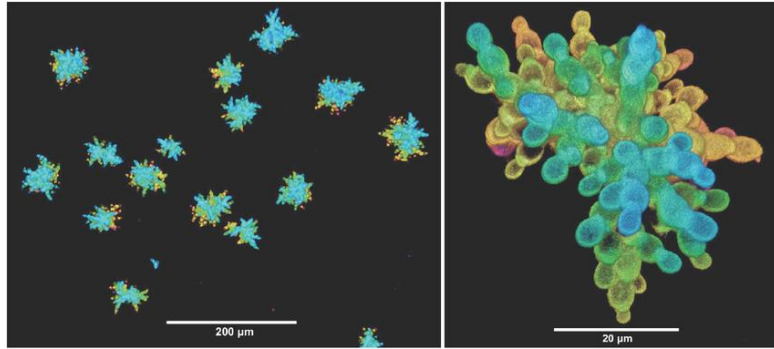
How?

Cells of The Human Body



Steps of The Transition

S. cerevisiae



Unicellular

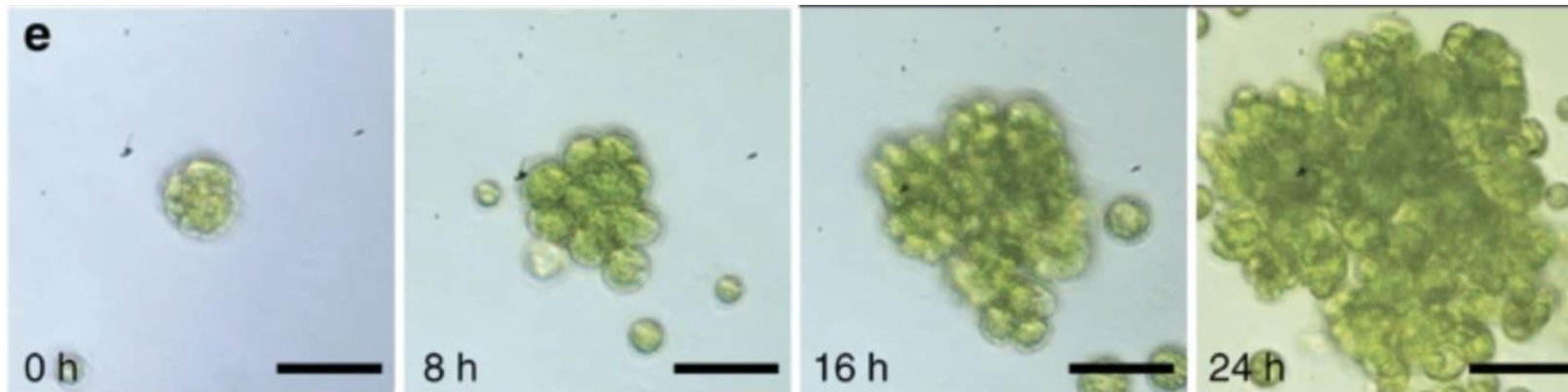


Multicellular,
undifferentiated

divide labor



Multicellular
with
division of labor



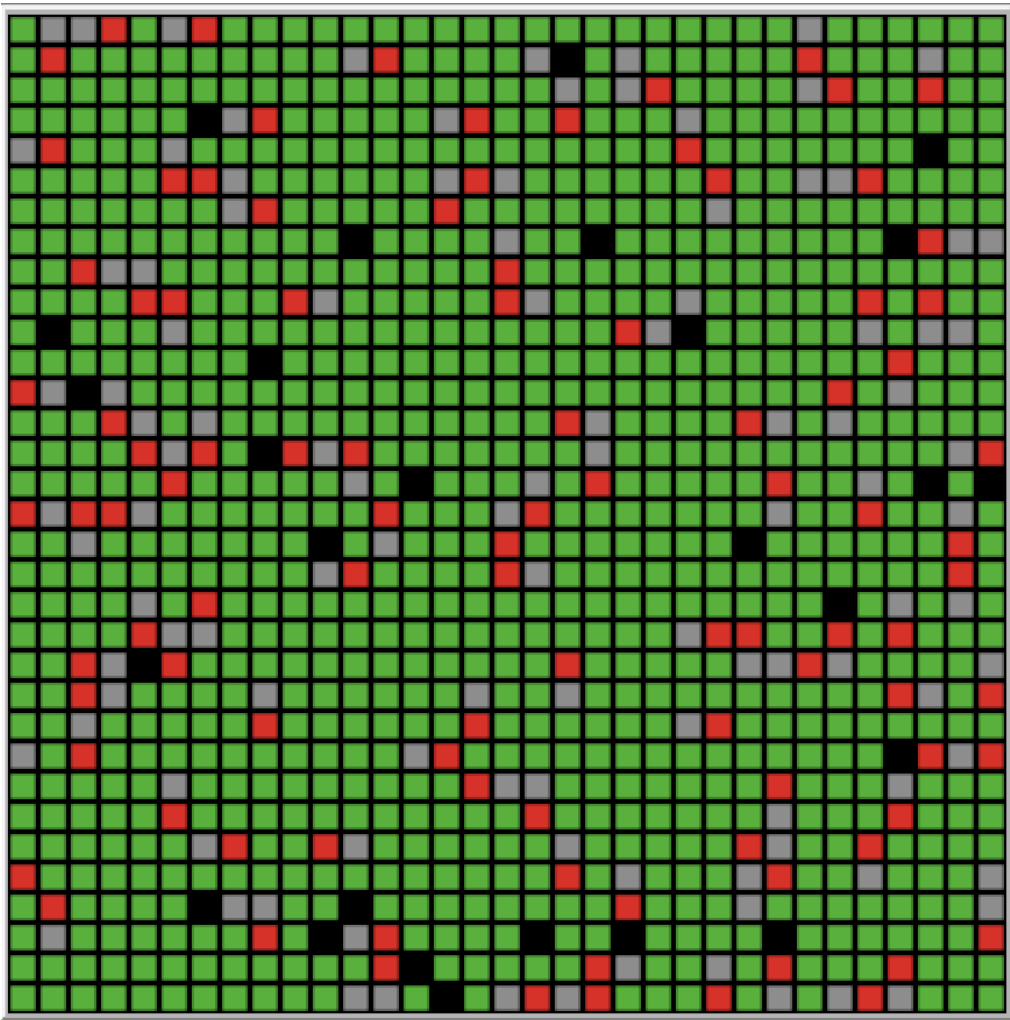
C. reinhardtii

Method: Agent-Based Model

- Agent: autonomous computational individual with particular properties and actions.
- A phenomenon is modeled in terms of agents and their interactions.
- **The global patterns spontaneously arise from the interaction of elements** without a centralized coordinator. Structure (or rules) at the micro-level leads to ordered pattern at the macro-level.

An Introduction to Agent-Based Modeling,

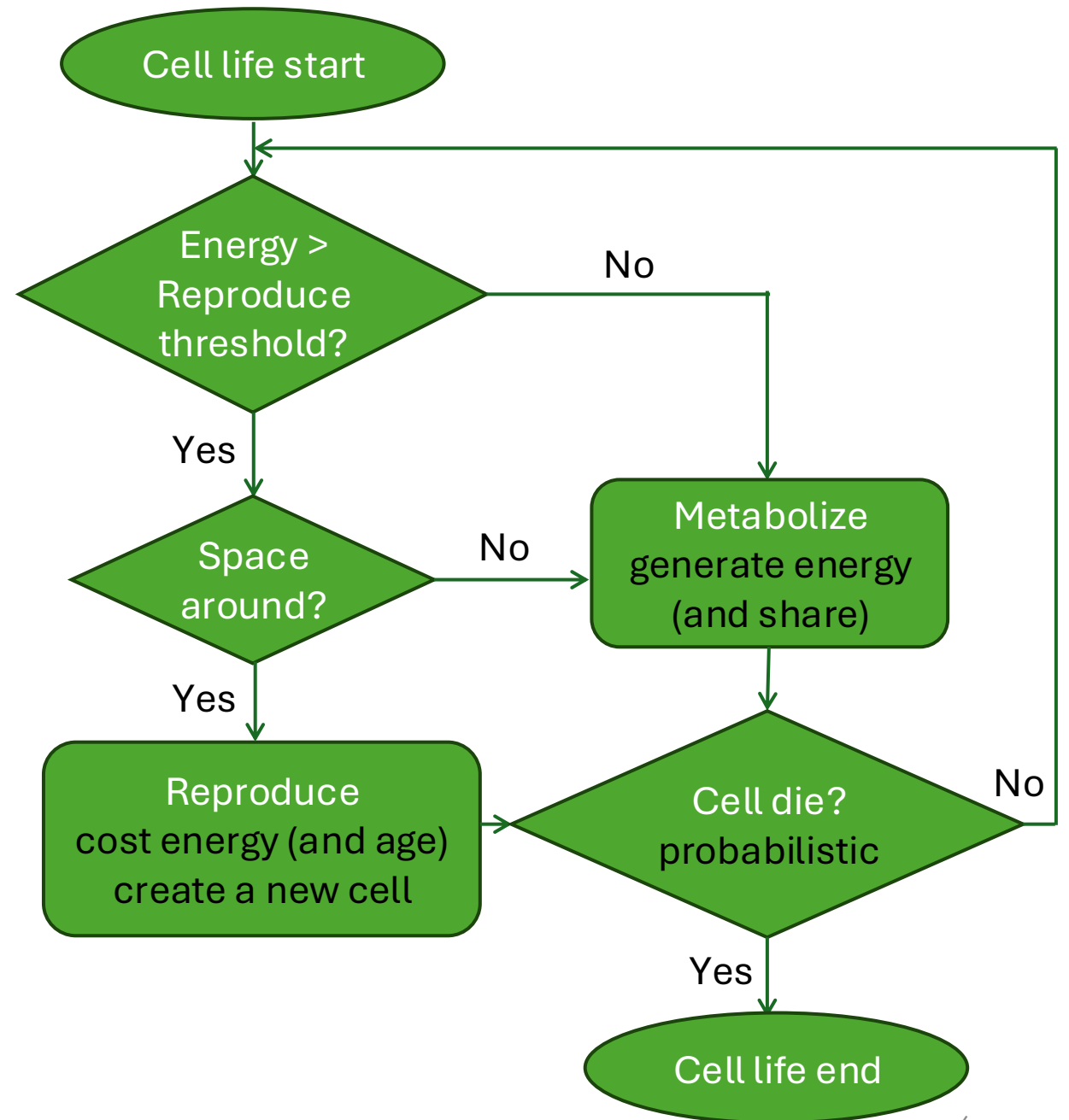
Uri Wilensky and William Rand (2015)



$33 \times 33 = 1089$ "cells"



← Play with the model!



Simulation Results

Each cell has both functions (reproduce/metabolize) and follows the exact same behavioral patterns.

Many cells perform both activities throughout life.

Two types of specialized cells occur:

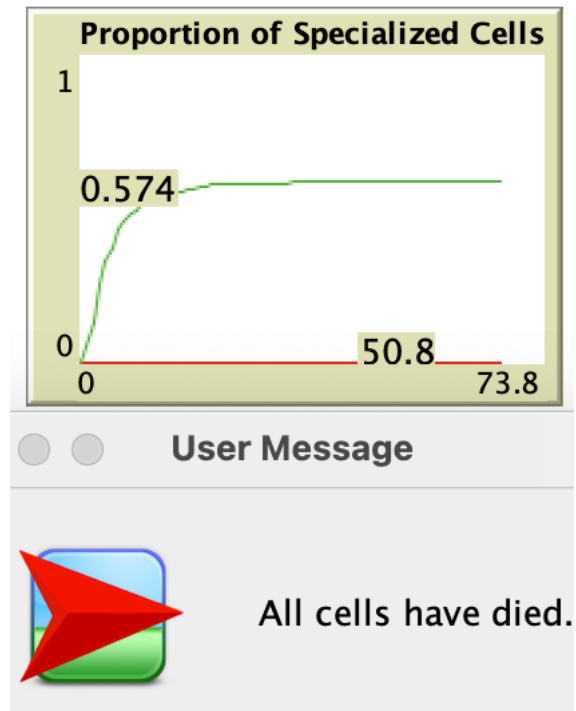
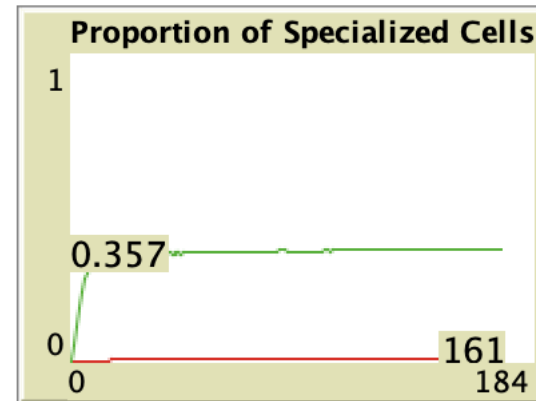
- **Reproducer:** Cells that solely reproduce throughout their life.
- **Metabolizer:** Cells that solely metabolize throughout their life.

Metabolizers

- As long as the organism can sustain itself, the proportion of metabolizers remains stable (around 0.35) across different energy parameters, regardless of whether energy is shared and the lifespan.
- The proportion of metabolizers is higher when the organism cannot sustain itself (when reproduction is too costly and cells die out).

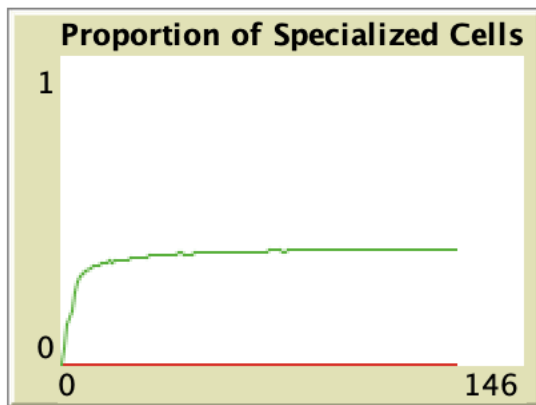
Explanation

- The space for new cells is limited. Some cells cannot reproduce even if energy is sufficient.
- When reproduction is too costly, cells can never have enough energy to reproduce.



Reproducers

- When energy is not shared, and reproduction has a non-zero energy cost, reproducers do not appear.
- When energy is shared, a small number of reproducers occur.

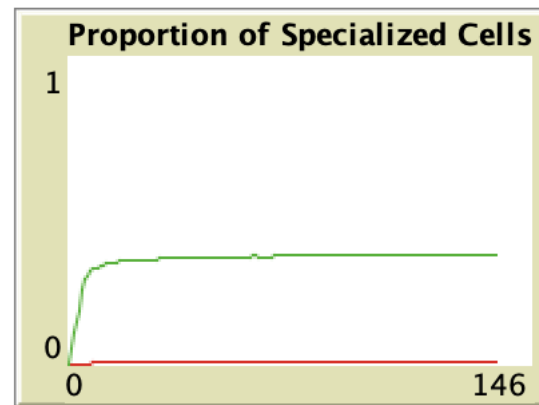


Alive Cells

1032

Reproducers

0



Alive Cells

1045

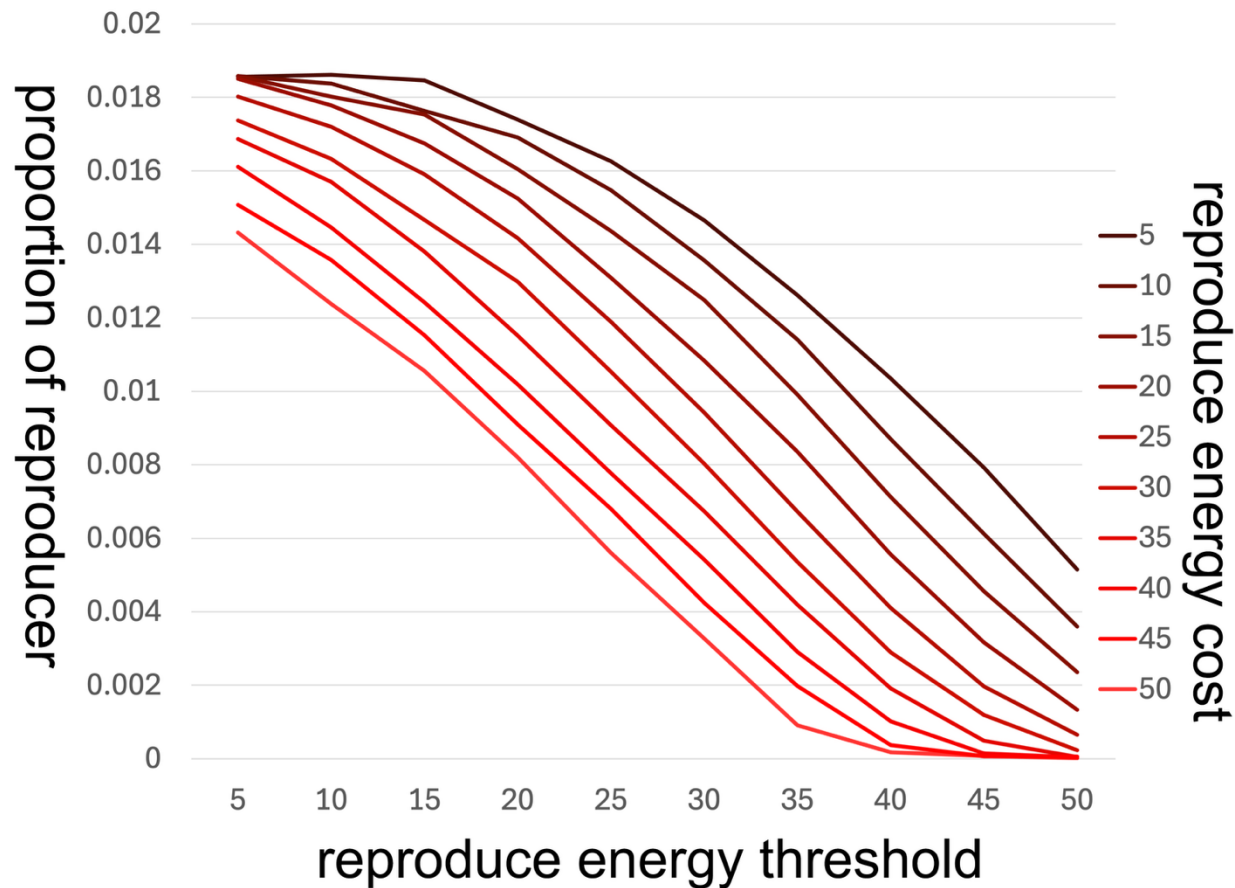
Reproducers

257

Explanation

- When energy is not shared, a newborn cell must metabolize at least once to reproduce.
- When energy is shared, some cells reproduce right after being born and then die after a few ticks.
 - The probability of death is non-zero at the start of life and increases as age grows.
 - Reproducers' death age is very young (usually 1-2).

Reproducers

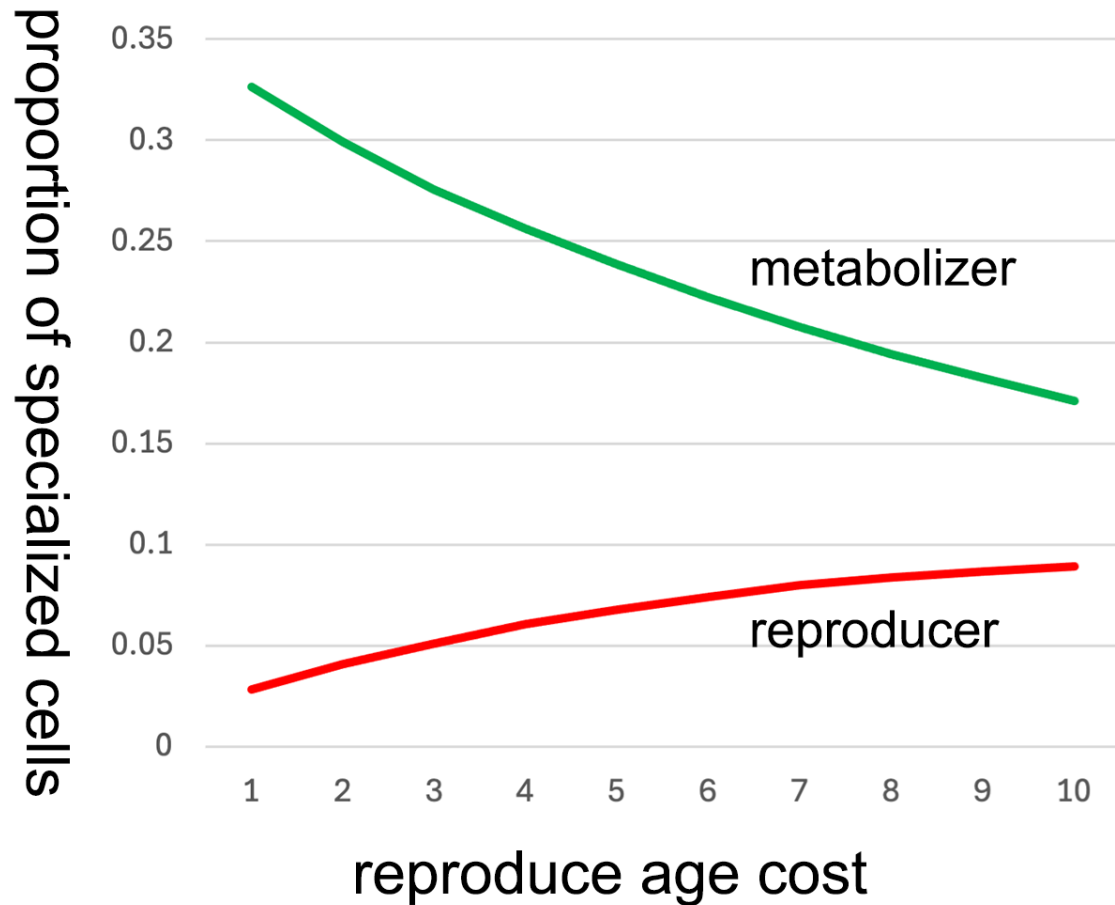


metabolize efficiency = 20; reproduce age cost = 0;
average lifespan = 15.

Explanation

- The lower the *reproduce energy threshold*, the more likely a cell is to reproduce right after it is born.
- The lower the *reproduce energy cost*, the more likely a cell is to continue reproducing before it first metabolizes.

Age Costs



reproduce threshold = 50; reproduce energy cost = 50;
metabolize efficiency = 50; average lifespan = 15.

Explanation

When reproduction has an age cost:

- More cells die early, creating more space for reproduction, making fewer metabolizers.
- Cells are more likely to die after a few rounds of reproduction, making more reproducers.

Assumptions and Justifications

1. Limited space for new cells

In yeast snowflakes, undifferentiated cells aggregate due to a failure in cell separation; thus, when a cell reproduces, the new cell must be located around the reproducing cell.

There are also trade-offs between size and fragility, limiting the size of multicellular organisms. (Ratcliff et al. 2012, 2015)

2. Shared energy among cells

Yeast cells share resources such as nutrients released by hydrolytic enzymes. (Koschwanez et al. 2011)

Assumptions and Justifications

3. Non-zero probability of early cell death

Studies on yeast have demonstrated that older cells are more prone to death due to accumulated damage. (Aguilaniu et al. 2003, Steinkraus et al. 2008)

There can also be external factors that cause the early death of cells.

4. Reproduction has energy and possible age costs

(Ratcliff et al. 2012)

Upshot

- With the assumptions as mentioned, cell specialization can occur spontaneously without mutation.
 - Some cells specialize in metabolism because of space limitations.
 - Some cells specialize in reproduction because of short lifespan.
- This mechanism is a possible origin of the division of labor in multicellular organisms.
- Some selective process may be needed for the division to stabilize.

Thank you!!

trznz@missouri.edu



Bibliography

- Aguilaniu, H., Gustafsson, L., Rigoulet, M., & Nyström, T. (2003). Asymmetric inheritance of oxidatively damaged proteins during cytokinesis. *Science (New York, N.Y.)*, 299(5613), 1751–1753. <https://doi.org/10.1126/science.1080418>
- Ispolatov, I., Ackermann, M., & Doebeli, M. (2012). Division of labour and the evolution of multicellularity. *Proceedings. Biological sciences*, 279(1734), 1768–1776. <https://doi.org/10.1098/rspb.2011.1999>
- Kirk D. L. (2005). A twelve-step program for evolving multicellularity and a division of labor. *BioEssays : news and reviews in molecular, cellular and developmental biology*, 27(3), 299–310. <https://doi.org/10.1002/bies.20197>
- Koschwanez, J. H., Foster, K. R., & Murray, A. W. (2011). Sucrose utilization in budding yeast as a model for the origin of undifferentiated multicellularity. *PLoS biology*, 9(8), e1001122. <https://doi.org/10.1371/journal.pbio.1001122>
- Ratcliff, W. C., Denison, R. F., Borrello, M., & Travisano, M. (2012). Experimental evolution of multicellularity. *Proceedings of the National Academy of Sciences of the United States of America*, 109(5), 1595–1600. <https://doi.org/10.1073/pnas.1115323109>
- Ratcliff, W. C., Fankhauser, J. D., Rogers, D. W., Greig, D., & Travisano, M. (2015). Origins of multicellular evolvability in snowflake yeast. *Nature communications*, 6, 6102. <https://doi.org/10.1038/ncomms7102>
- Steinkraus, K. A., Kaeberlein, M., & Kennedy, B. K. (2008). Replicative aging in yeast: the means to the end. *Annual review of cell and developmental biology*, 24, 29–54. <https://doi.org/10.1146/annurev.cellbio.23.090506.123509>
- Yanni, D., Jacobeen, S., Márquez-Zacarías, P., Weitz, J. S., Ratcliff, W. C., & Yunker, P. J. (2020). Topological constraints in early multicellularity favor reproductive division of labor. *eLife*, 9, e54348. <https://doi.org/10.7554/eLife.54348>