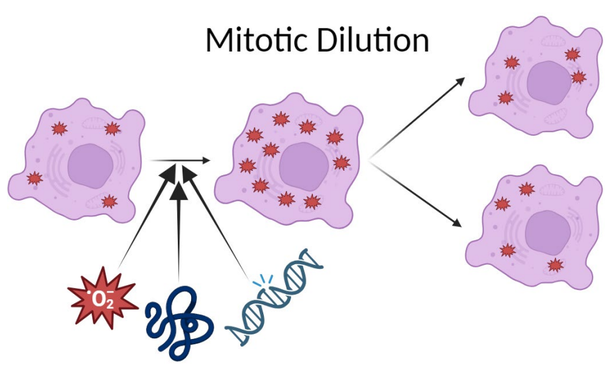
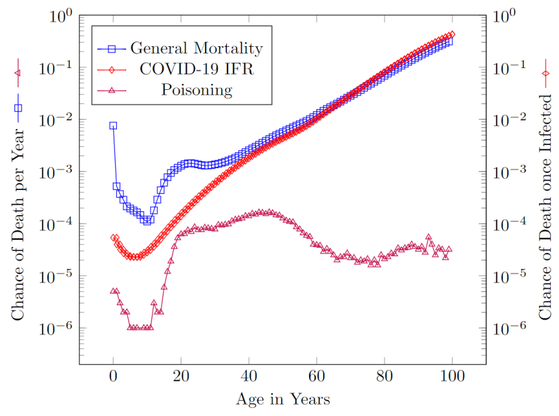
Binary Cellular Analysis: Understanding the Link Between Aging and Mortality Risk

Background

Our chance of death ***doubles*** with every eight years we age during adult life

- **Age-related diseases** account for more than **2/3** of all deaths worldwide
- Aging processes at the cellular level is a complex web of interconnected processes, but how it leads to **exponentially increasing** disease risks is unclear





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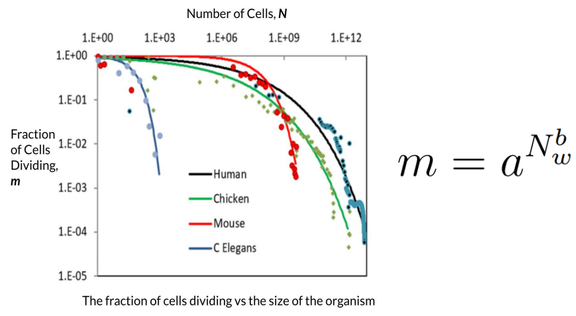
How do we link aging at the cellular level with observable mortality rates?

How do demographic factors like **gender, health conditions, or vaccination status** affect mortality risk?

Binary Cellular Analysis

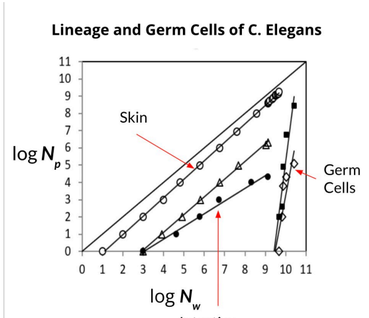
Binary Cellular Analysis considers the aggregate consequences of large numbers of **discrete** cellular events.



The fraction of cells dividing vs the size of the organism

$$m = a^{N_w^b}$$

*Citi et al

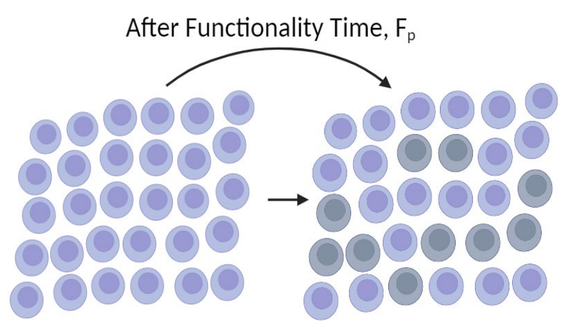


$$N_P = \left(\frac{N_w}{B_{N1}}\right)^{S_N}$$

*Citi et al

Two-Phase Model

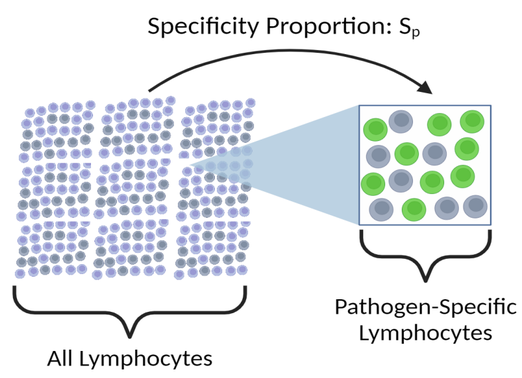
(1) Linking cellular aging to loss of function at cell population level



$$N_{PF} \approx 2F_P \cdot \frac{dN_P}{dt} = \frac{2\ln 2 * F_P}{c_P}\left(\frac{N_w}{B_{N1}}\right)^{\frac{c}{c_P}} a^{N_w^b}$$

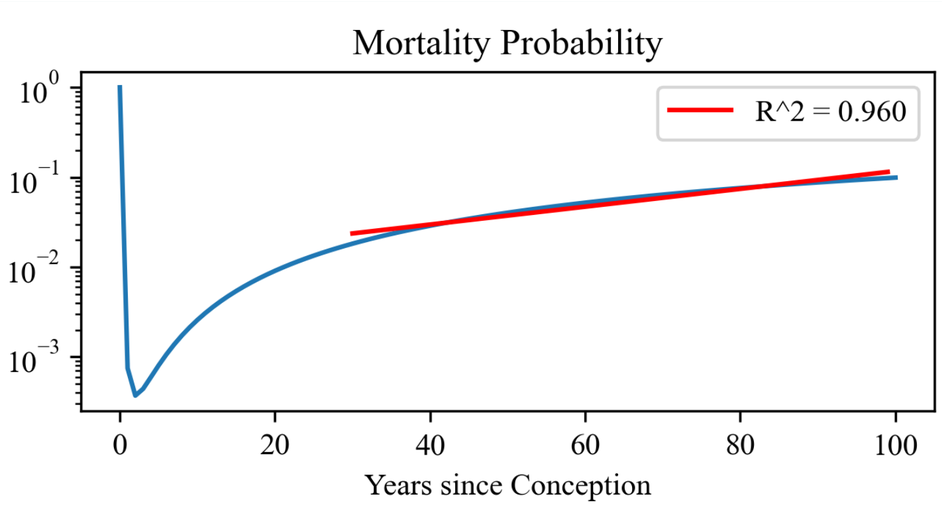
(2) Forecasting Chance of Mortality

Ex. Infection

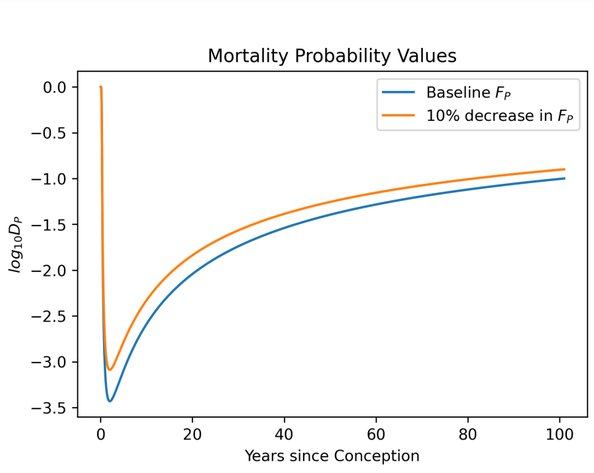


$$D_P(N_{PF}) = e^{\left(-\frac{S_p}{2(1-S_P)}N_{PF}\right)} = (1-S_{p^*})^{N_{PF}}$$

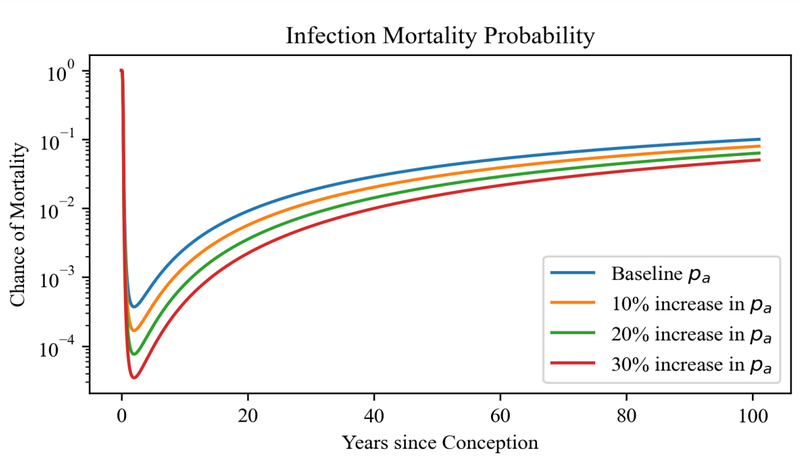
A Cellular Explanation of Infant and Adult Mortality



- **Exponentially increasing** adult mortality can be traced to **exponentially declining** mitotic fraction and frequency of damage repair
- **Infant and Adult** mortality can be traced back to the control of cell division
  - Supported by antagonistic pleiotropy theory of William and Hamilton and the disposable soma theory of Kirkwood



- **Sex chromosomes** may affect lifespan through cell functionality time (***F_p***). Females in most species may have higher ***F_p*** due to robust X-chromosome mechanisms.
- Suggests **health conditions** like diabetes significantly reduce cell functionality time (***F_p***), increasing mortality risk across various diseases, including COVID-19.



- Explains how each **vaccination/booster** reduces the risk of COVID-19 death by roughly 33% permanently
- Suggests specific, calculable increases in lymphocyte specificity linked to vaccination effectiveness

Project Significance and Application

These findings provide the ***first mechanistic explanation*** for the link between aging and mortality rates of age-related diseases.

1) Explains **demographic trends/relationships** between infant and adult mortality, and the impact of factors like gender and diabetes on mortality risk.
2) Identifies important underlying biological parameters to inform **anti-aging treatments/pharmaceutical** development
3) Informs **vaccine design** through a systematic approach to evaluating immune response based on reducing lethality
4) Informs **public health policy** through optimizing distribution and scheduling of treatments (e.g. vaccinations) across age groups

References:

Counting Cells by Age Tells Us About How, and Why, and When, We Grow, and Become Old and Ill
Luca Citi, Jessica Su, Luke Huang, James S Michaelson
medRxiv 2023.01.05.23284244; doi: https://doi.org/10.1101/2023.01.05.23284244