Economic Principles in Cell Biology

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Scaling Laws in Cell Evolution

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Contents

Goal: To showcase how major cellular features scale with size across cells

- 1. Cell size diversity across the tree of life
- 2. Scaling of cell composition
- 3. Scaling of energetic traits
- 4. Scaling of biosynthetic capacity
- 5. Summary
- 6. Open questions



The tree of life



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Phylogenetic diversity Cell volume



Schavemaker & Muñoz-Gómez (2022). Nat Ecol Evol 6:1307–1317



Phylogenetic diversity Prokaryotes



Ca. Thiomargarita magnifica

Phylogenetic diversity Eukaryotes



Micromonas spp.

Apusomonads

Acetabularia sp.

Gromia sp.



Power-law relationships

 $y = c \cdot M^{\alpha}$ $\log(y) = \alpha \cdot \log(M) + \log(c)$ y = mx + b



Metabolic Ecology: A Scaling Approach (Wiley-Blackwell, 2012)

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Developmental & evolutionary scaling laws

Within species

Across species





Developmental & evolutionary scaling laws How do they relate to each other?



Fenchel & Finlay (1983) *Microb Ecol* 9, 99–122



Cell density

$$M = 0.00057 \cdot V^{0.92}$$

$$N_{tot,p} = (2.0 \times 10^6) \cdot V^{0.95}$$

$$N_{tot,mRNA} = 6760 \cdot V^{0.42}$$



Lynch (2024) Evolutionary Cell Biology (Oxford University Press)

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Cell density

$$V_{v} = 8.36 \cdot V_{a}^{1.4}$$





Nucleoid and nucleus size, and DNA fraction

 $N: C \propto V^{-0.3}$



 $f_{DNA,prok} = 0.0072 \cdot V^{-0.77}$ $f_{DNA,euk} = 0.014 \cdot V^{-0.62}$



Cell shape Shape-shifting



Fenchel (2014) Protist 165, 485–492



Metabolic rate

- "Pace (or speed) of living and interacting with the environment"
- The rate at which energy and matter are transformed within a cell
- Energy consumed or produced per unit of time
 - Joules per time (seconds or hours)
 - nL O_2 per time
 - ATP hydrolyses per time
- Controversy on the scaling exponent with body mass/volume



Metabolic rate Fenchel & Finlay

 $R = 0.123 \cdot V^{0.75}$





Metabolic rate DeLong *et al.*



DeLong et al. (2010) Proc Natl Acad Sci USA 107, 12941-12945



Metabolic rate

 $R = 23.3 \cdot M^{1.01}$





Metabolic rate Hatton *et al.* $R = 0.001 \cdot M^{0.96}$



Hatton et al. (2019) Proc Natl Acad Sci USA 116, 21616–21622

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Metabolic rate Glazier





Lifetime ATP requirements



Lynch & Marinov (2015) Proc Natl Acad Sci USA 112, 15690–15695



Mitochondrial volume

 $V_{mt} \propto \sim 0.1 \cdot V^{\approx 1.0}$





Mitochondrial membranes and ATP synthases

$$N_{MOM} = 0.4 \cdot SA^{1.30}$$





Lynch & Marinov (2017) *eLife* 6, e20437

Growth rate



Lynch, Trickovic, & Kempes (2022) Sci Rep 12, 22586



Biosynthetic capacity

 $N_{ribo} = 8810 \cdot V^{0.8}$ 10⁹ 10⁸ 107 Ribosomes / Cell 10⁶ 10⁵ 10⁴ 10³ 10²

 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} **Cell Volume (\mu m^{3})**

10⁶

10¹

Lynch & Marinov (2017) *eLife* 6, e20437



Effective population size

 $N_e \propto M^{\sim -0.2}$



Lynch (2024) Evolutionary Cell Biology (Oxford University Press)



Summary

- Cells become less dense as they increase in size in evolution
- Cells evolve adaptations to overcome biophysical and physiological constraints
- Evolutionary innovations can alter scaling relationships
- Energetic features scale linearly but biosynthetic capabilities scale sublinearly with cell size
- Size is a major factor in cell evolution
- The efficiency of natural selection decreases as cells get larger



Open questions

- What are the causes of the scaling laws?
- How do they emerge from developmental scaling laws?
- How do evolutionary and developmental scaling laws interact with each other?
- Are scaling laws the result of biophysical constraints?
- Are scaling laws the outcome of optimal adaptive strategies?