

The background features a series of concentric, hand-drawn blue lines that resemble a topographical map or a series of orbits. These lines are centered around a bright yellow, heart-shaped area on the right side of the image. The overall aesthetic is soft and artistic, with a white background.

*The crosslinked extracellular matrix:
thermodynamic implications for longevity*

First principles fallacy

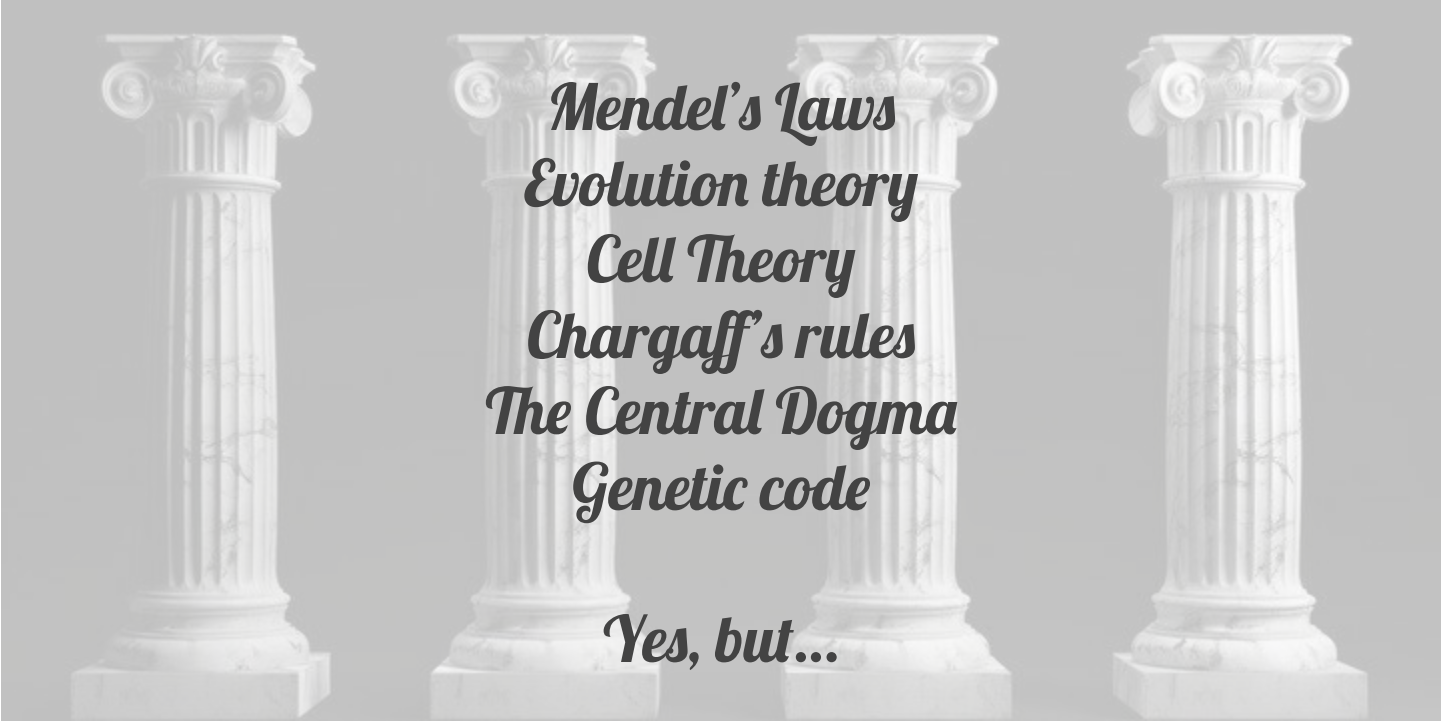


Discourse on the Method



What is life?

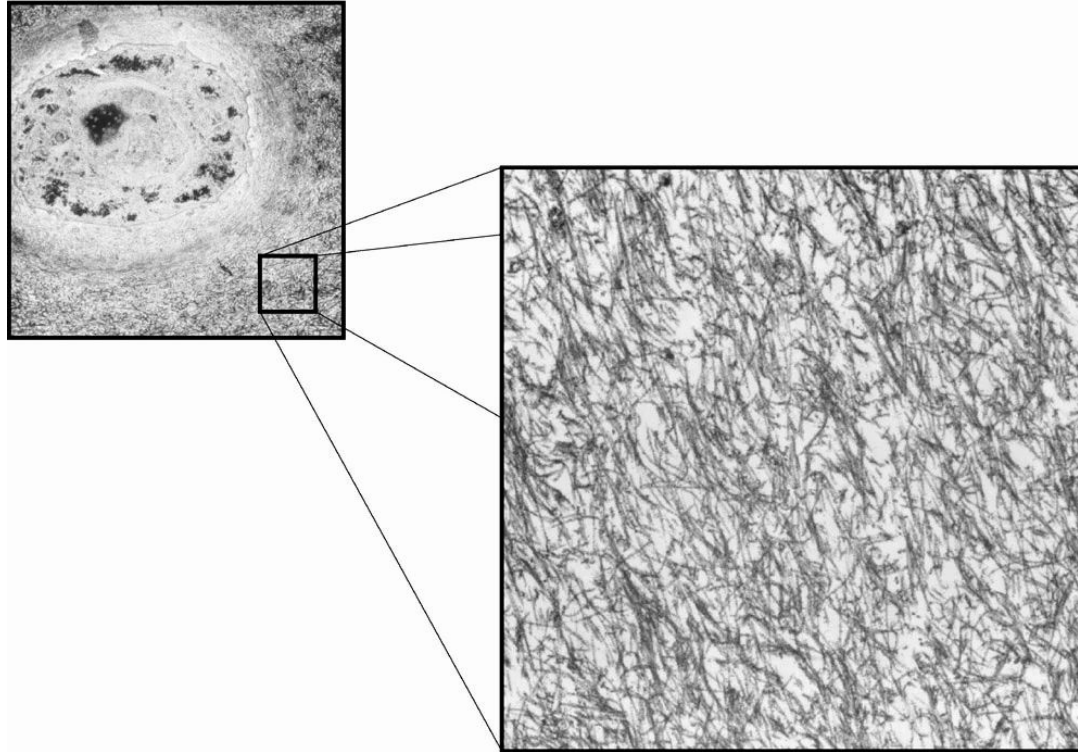
Biological first principles



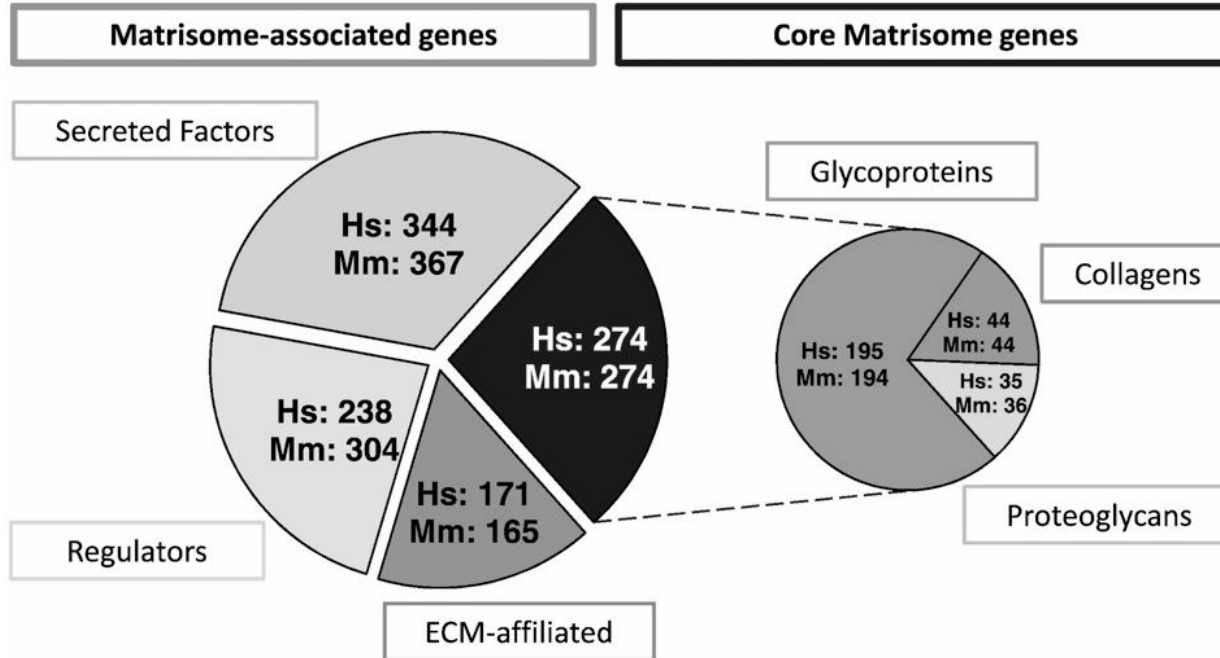
Mendel's Laws
Evolution theory
Cell Theory
Chargaff's rules
The Central Dogma
Genetic code

Yes, but...

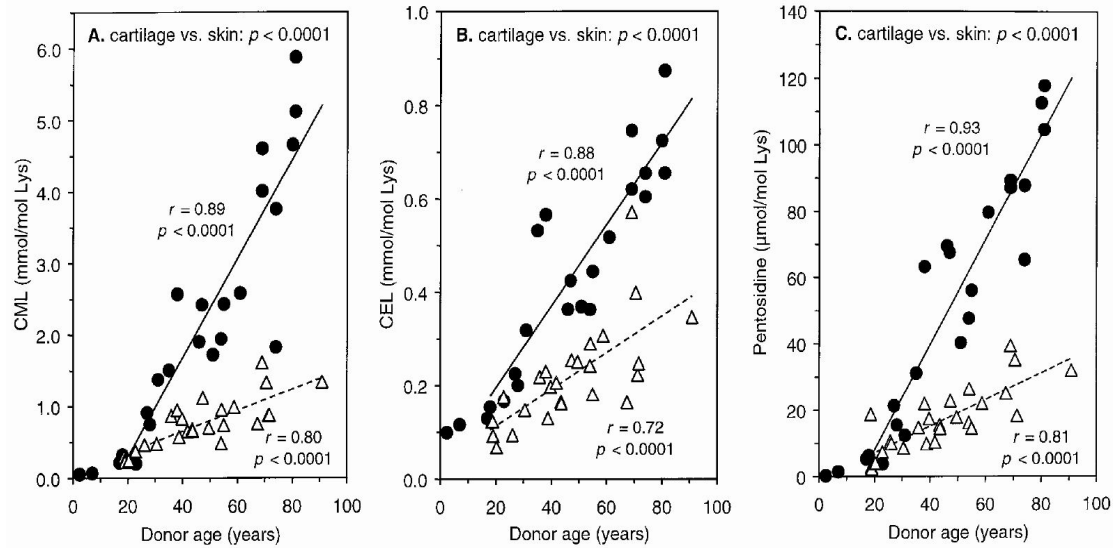
Ground substance



Extracellular matrix

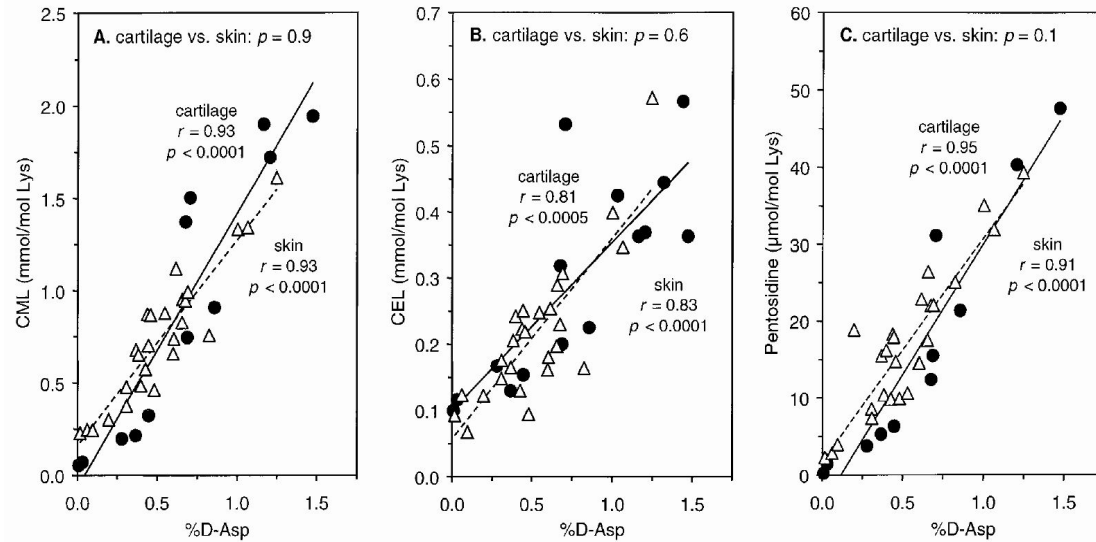


Extracellular matrix crosslinks



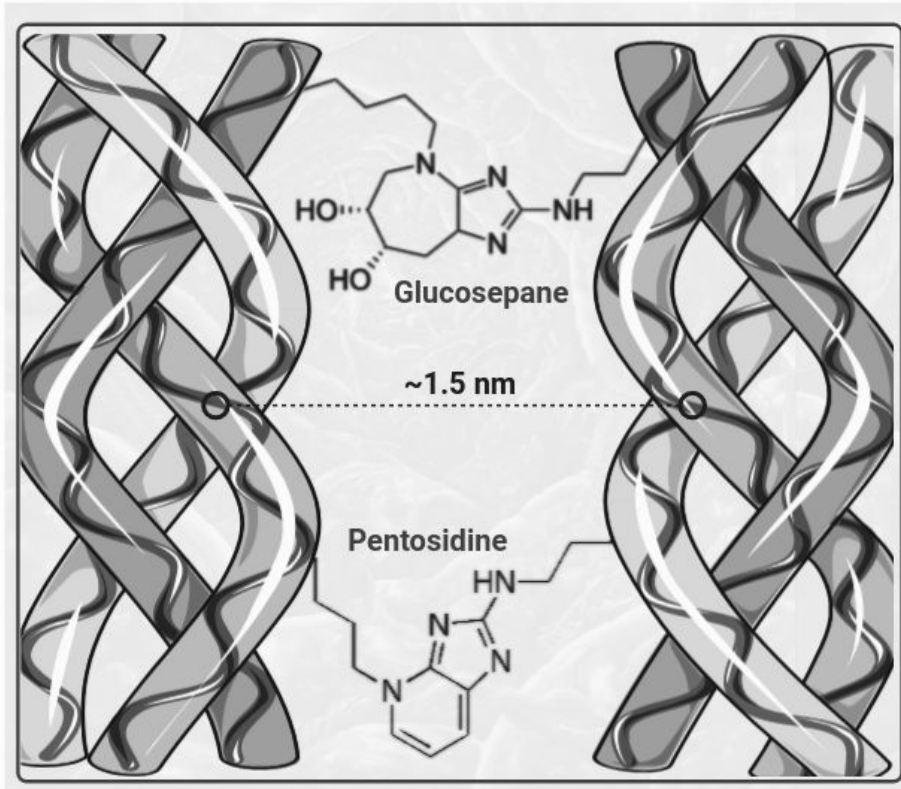
Glycation vs. age

Extracellular matrix crosslinks



Glycation vs. turnover

Arrow of time

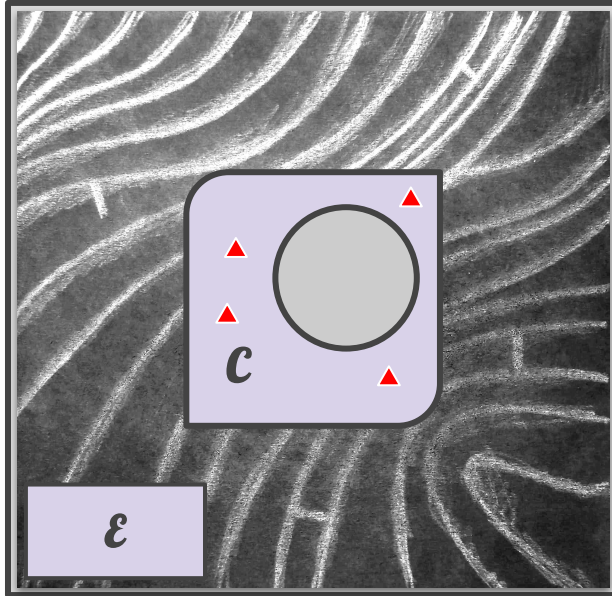


Crosslink accumulation:

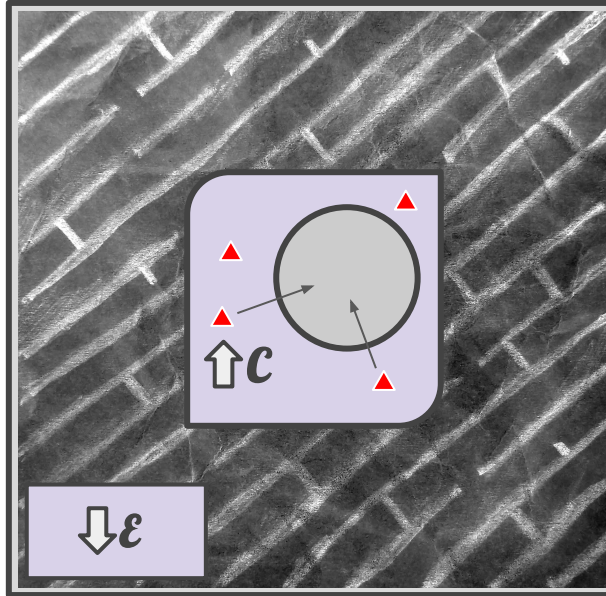
- (1) stochastic,
i.e. pervasive*
- (2) irreversible,
i.e. unidirectional*
- (3) vitally linked to metabolism,
i.e. universal*

At t_0 , $\varphi(C, \mathcal{E}) = \text{constant}$

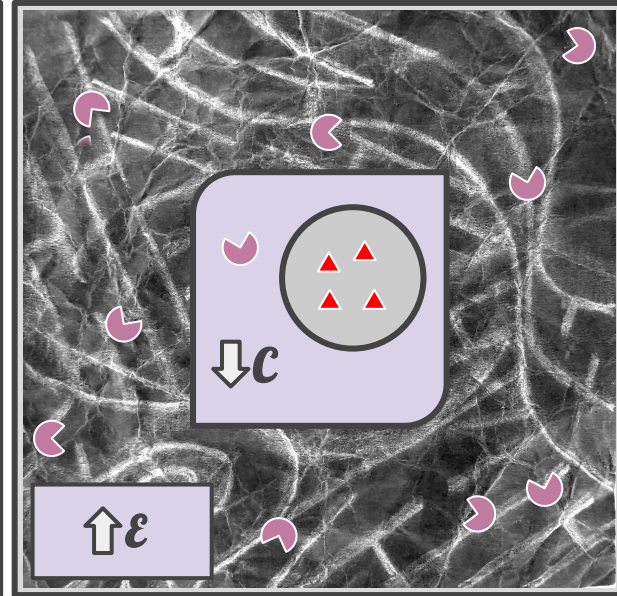
At $t > t_0$, $dC/dt \times d\mathcal{E}/dt < 0$



Young



Old



Pathological

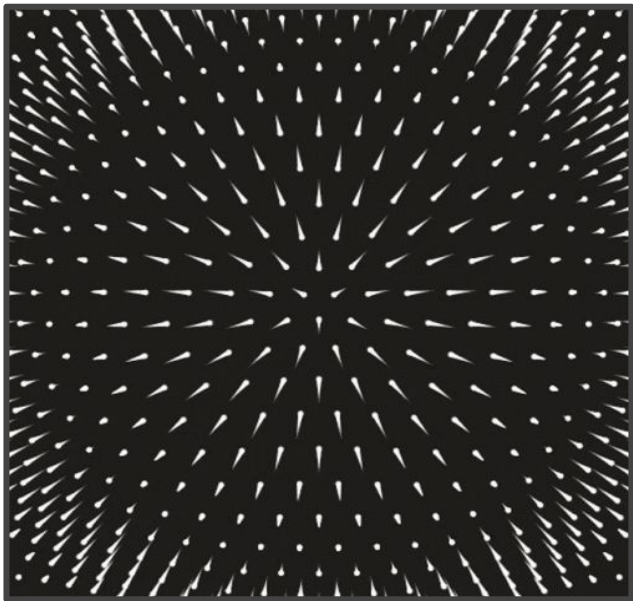
C - Intracellular entropy

E - Extracellular entropy

 - Matrix remodeling enzyme

 - YFP transcription factor

Delocalized Entropy Aging Theorem (DEATh)



i. $t_0: \phi(C, E) = \text{constant}$

ii. $t > t_0: \frac{dC}{dt} \cdot \frac{dE}{dt} < 0$

iii. $\frac{dC}{dt} = f(C, E)$

$$\frac{dE}{dt} = -g(C, E)$$

f, g - positive

***“Truly, what is stiff and hard is a companion of death;
what is soft and weak is a companion of life.”***

-- Tao Teh Ching, 76.

