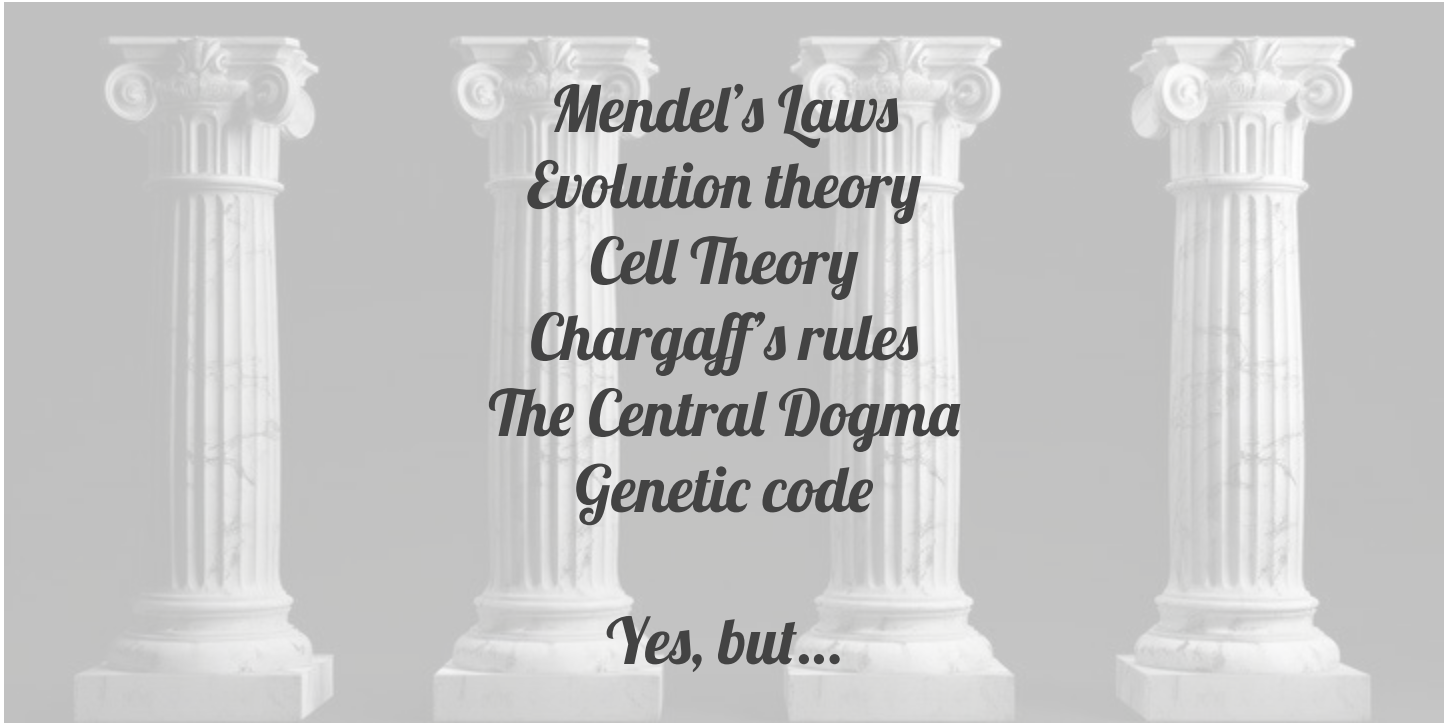
The crosslinked extracellular matrix: thermodynamic implications for longevity

First principles fallacy

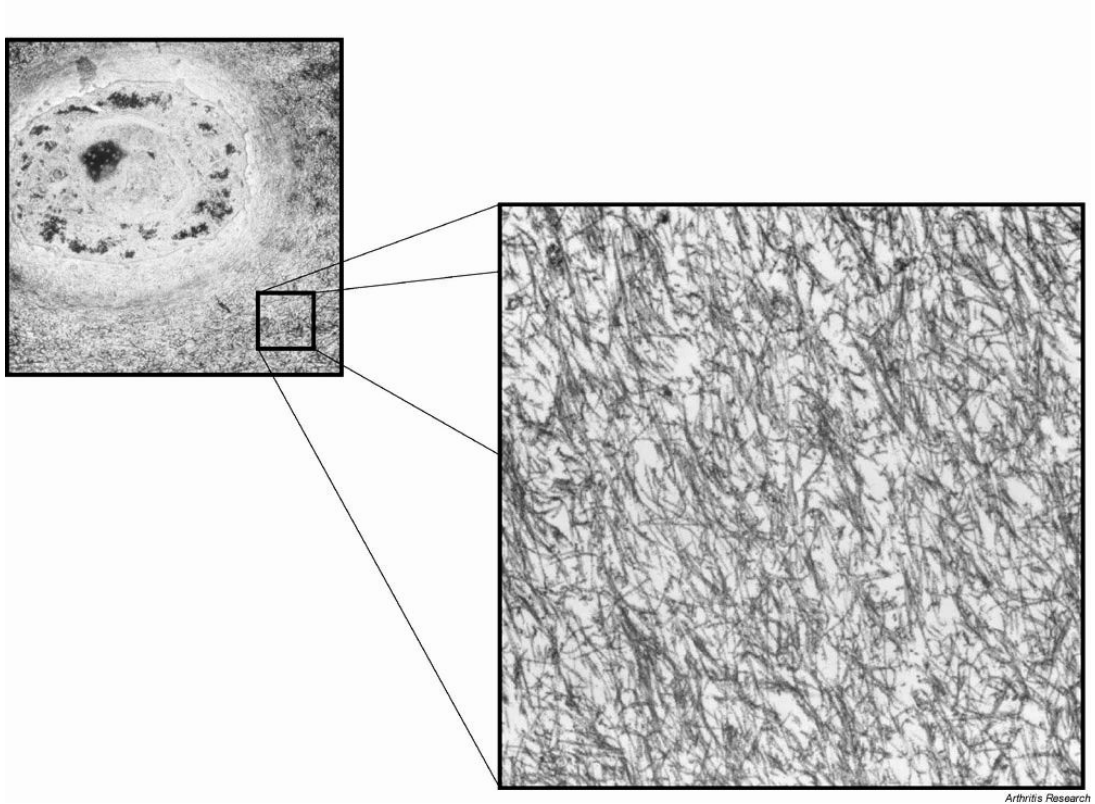
Discourse on the Method

What is life?

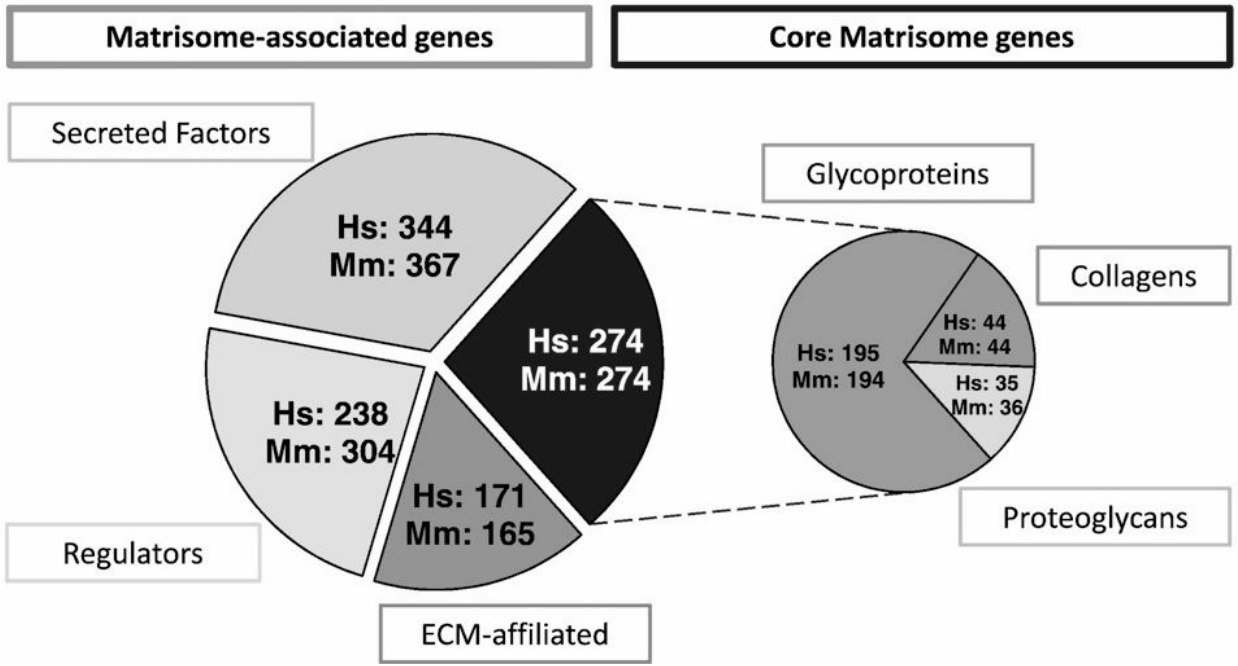
Biological first principles



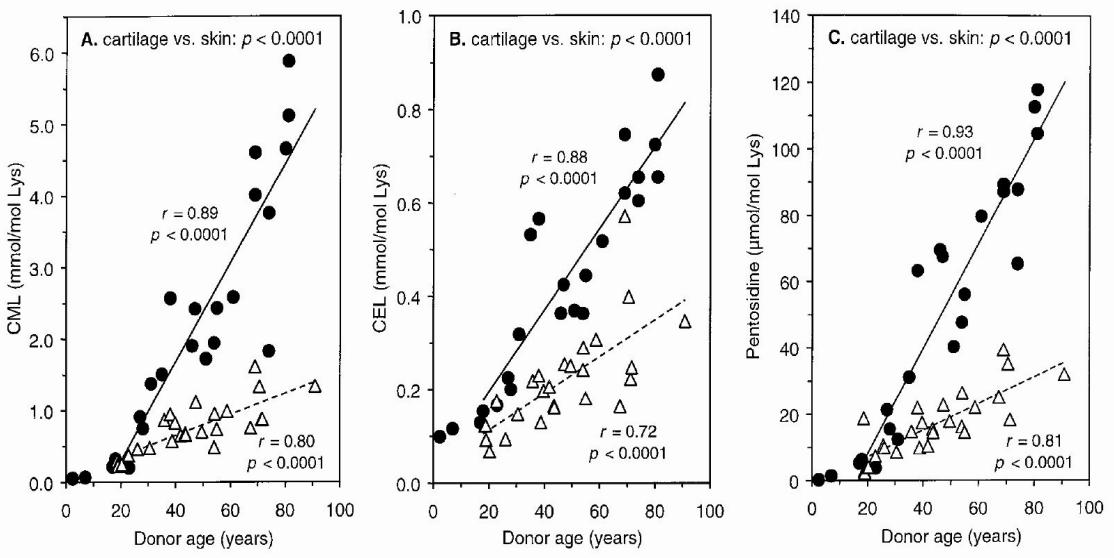
Ground substance



Extracellular matrix

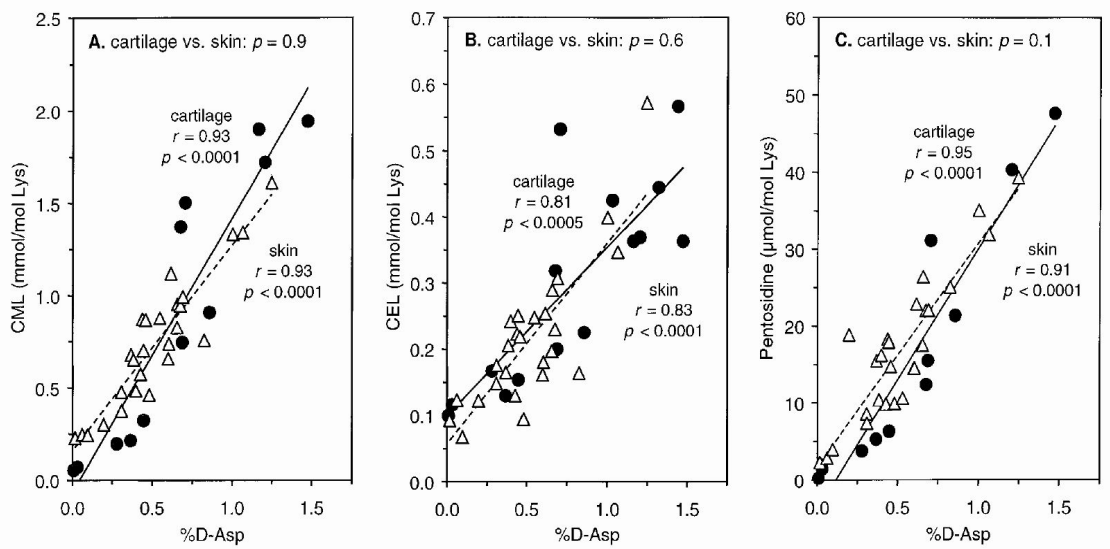


Extracellular matrix crosslinks



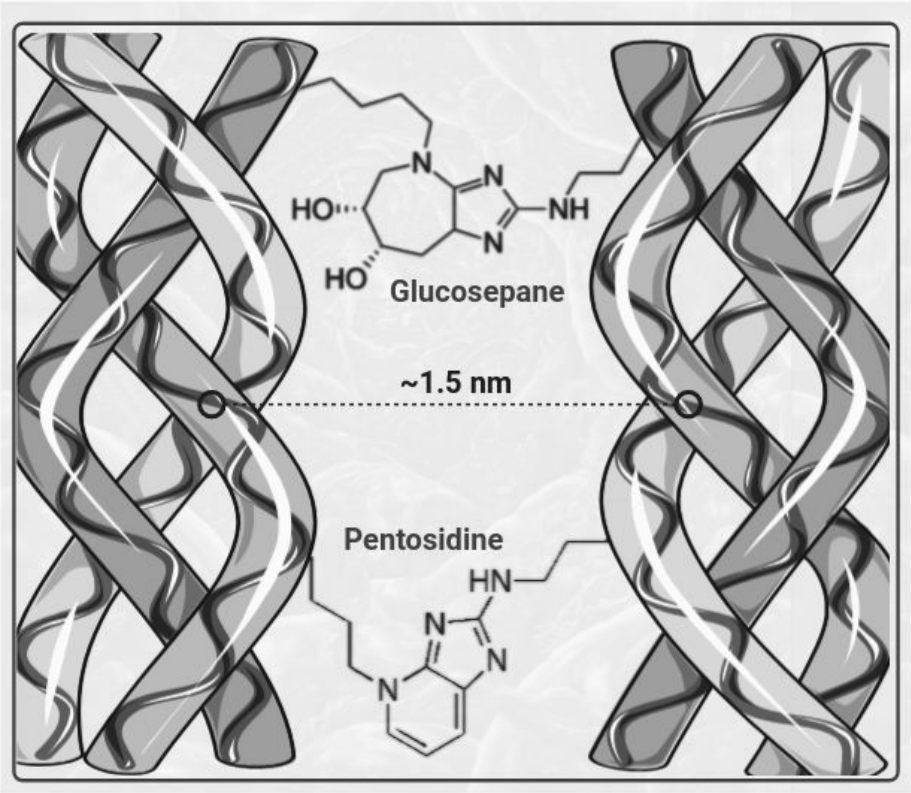
Glycation vs. age

Extracellular matrix crosslinks



Glycation vs. turnover

Arrow of time



Crosslink accumulation:

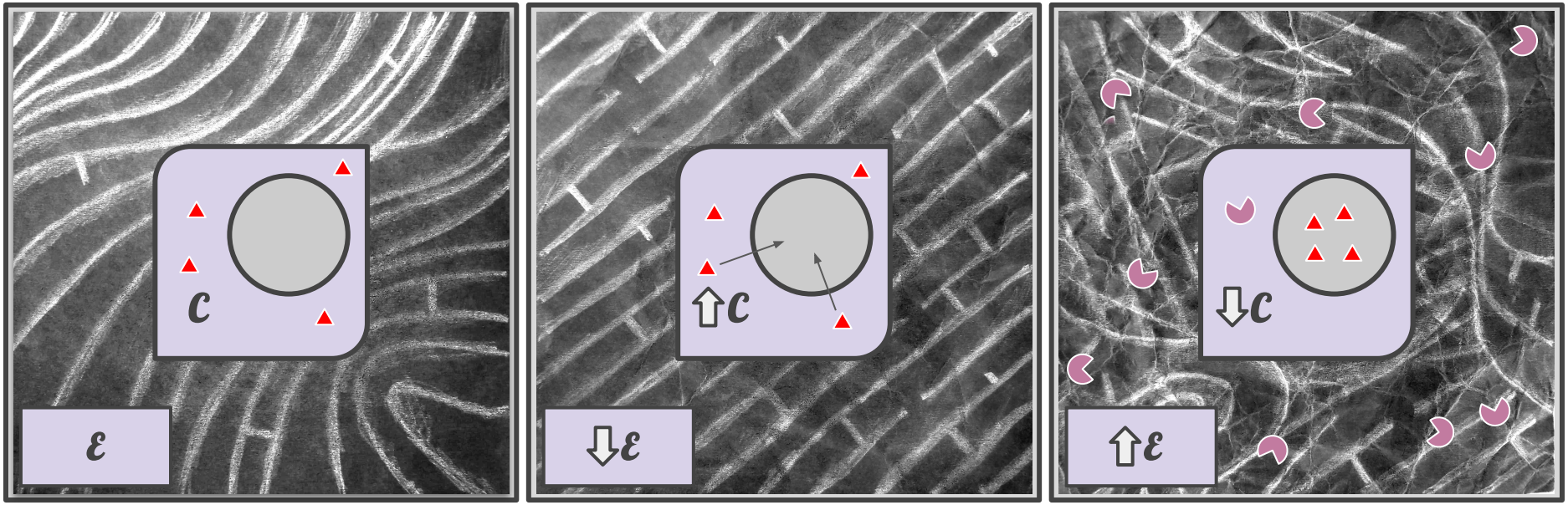
(1) stochastic,
i.e. pervasive

(2) irreversible,
i.e. unidirectional

(3) vitally linked to metabolism,
i.e. universal

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

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



Young

Old

Pathological

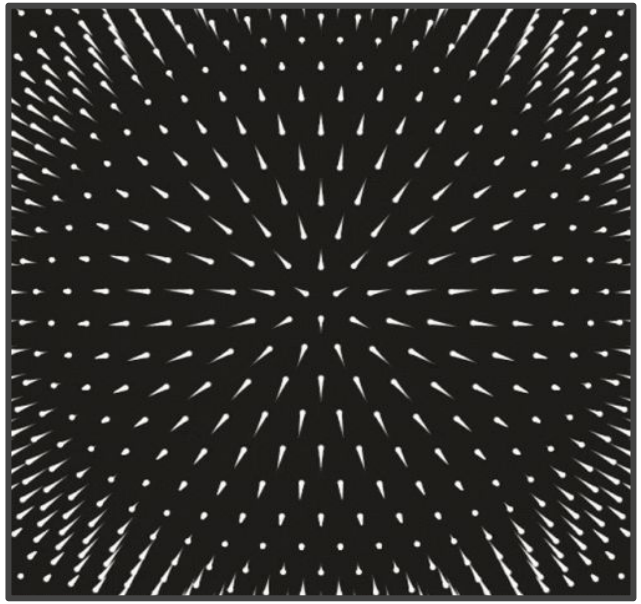
C - Intracellular entropy

ε - Extracellular entropy

- Matrix remodeling enzyme

- YAP 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.