

Prospects for defeating aging altogether

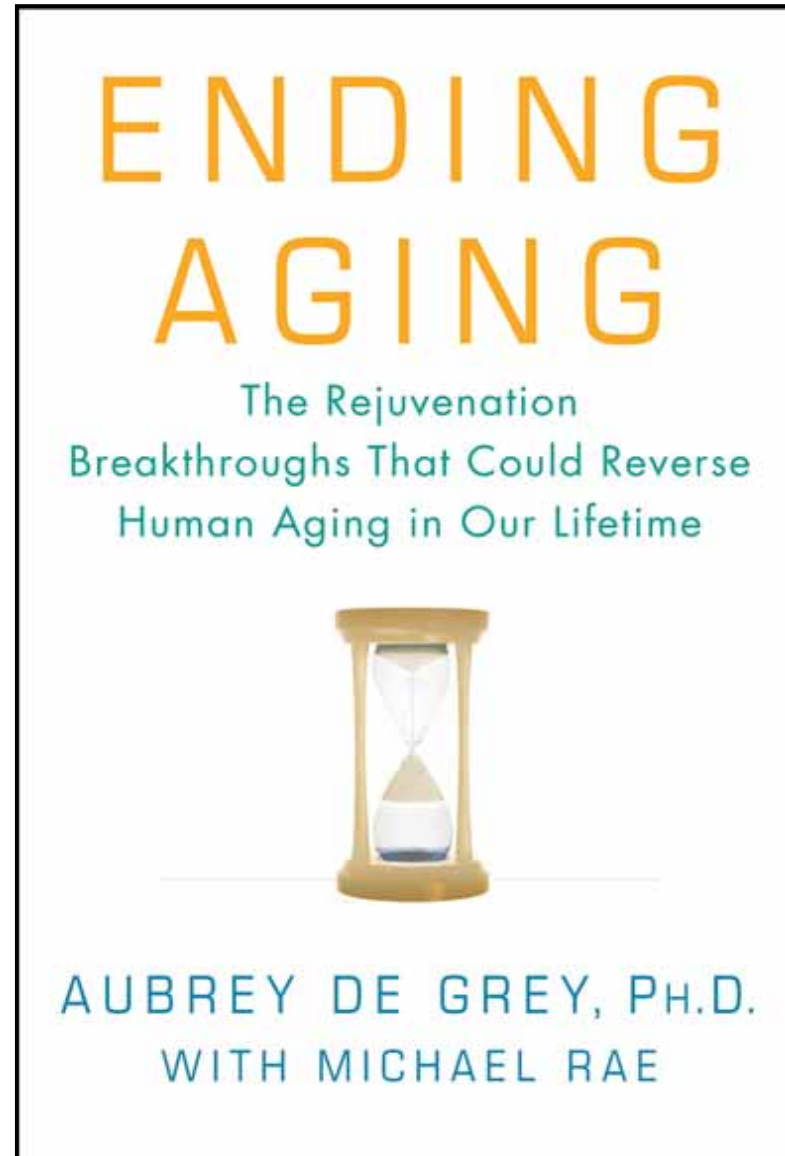
Aubrey D.N.J. de Grey, Ph.D.

**Chairman and CSO, Methuselah Foundation
Lorton, VA, USA and Cambridge, UK**

Email: aubrey@sens.org

Website: <http://www.mfoundation.org/>

Semi-technical book



**Out now:
\$17.79 at
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Why do this?

Why I am doing this



Fun



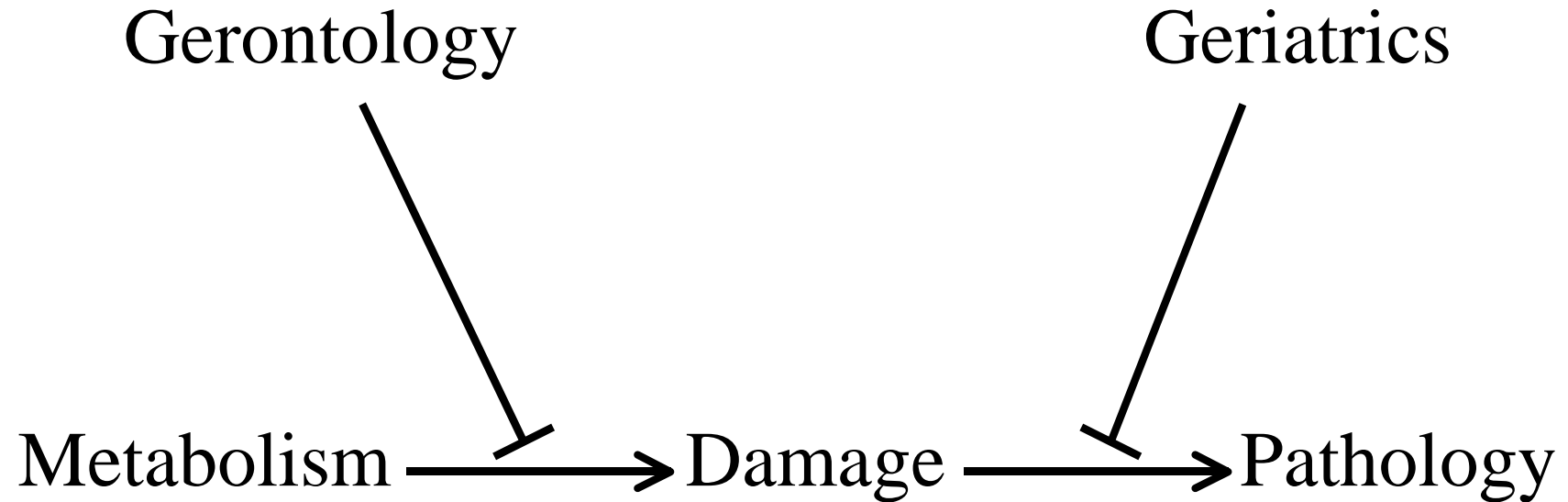
Not fun

What is aging?

Metabolism *always* causes “**damage**”

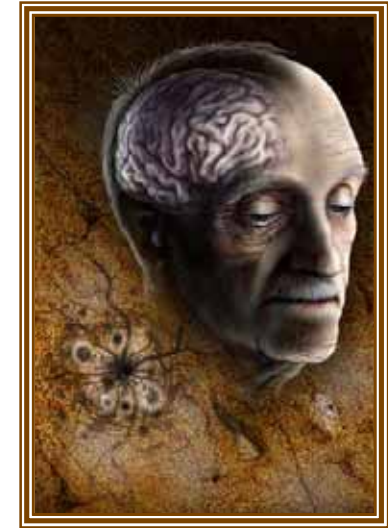
Damage *eventually* causes pathology

Strategies for intervention



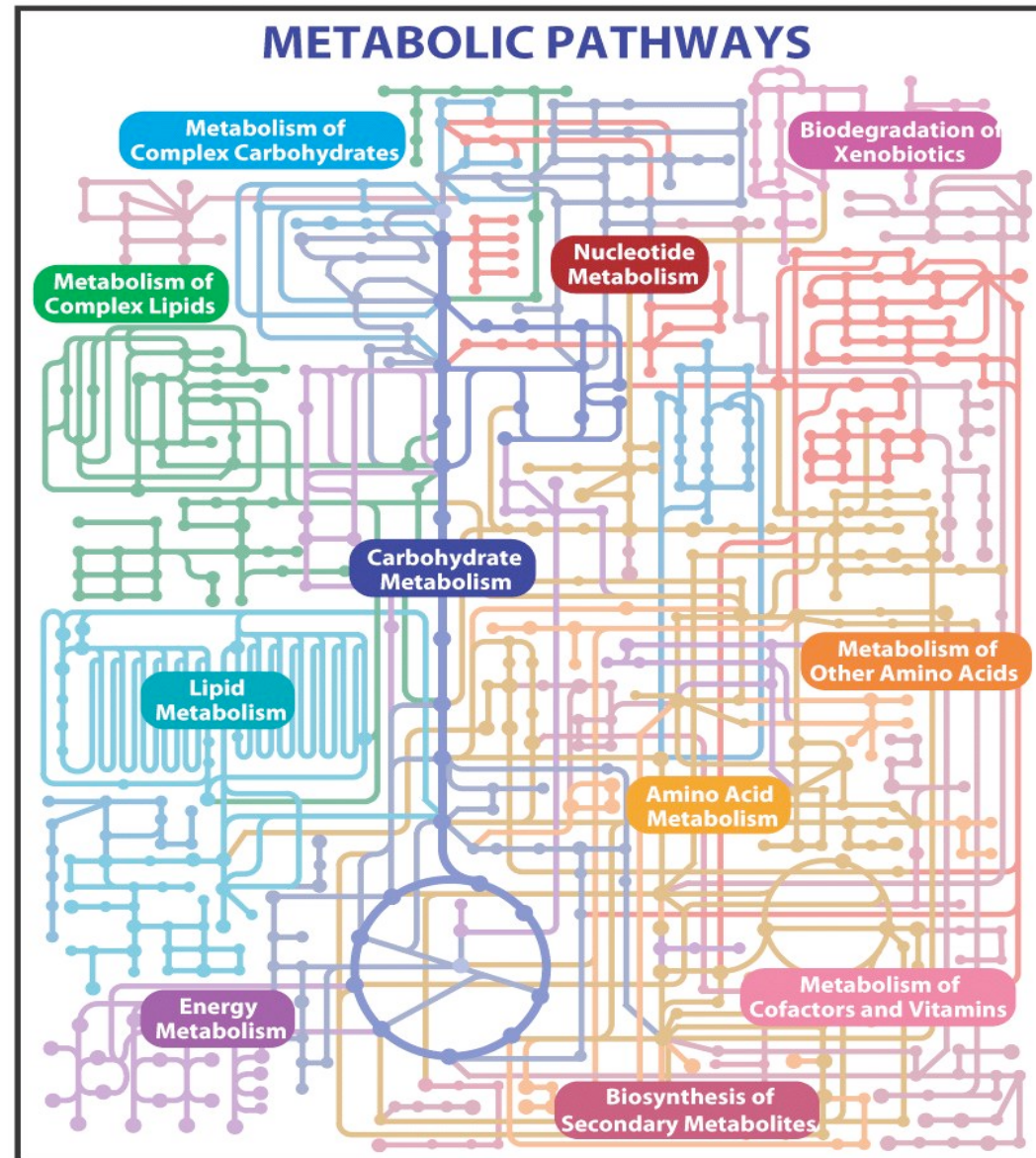
Problem 1: this is the pathology

- **Cancer**
- **Heart Disease**
- **Diabetes**
- **Incontinence**
- **Osteoporosis**
- **Macular Degeneration**
- **Alzheimer's**
- **Stroke**
- **Sarcopenia**
- **Osteoarthritis**
- **Hormonal Imbalance**
- **Kidney Failure**
- **Parkinson's**
- **Pneumonia**
- **Emphysema**
- **Sex Drive**



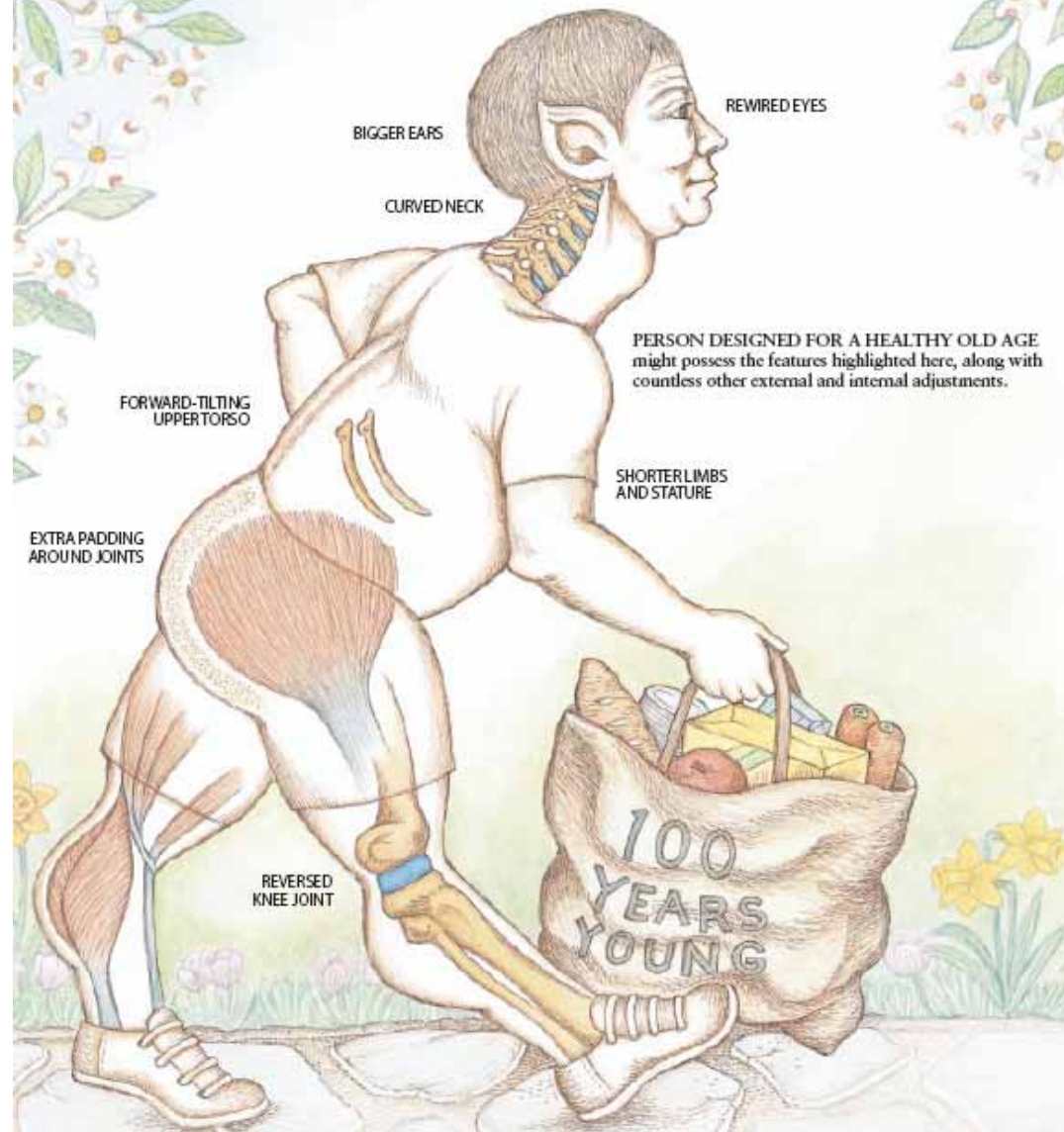
*... and
LOTS
more*

Problem 2: this is metabolism



If Humans Were **Built to Last**

by S. Jay Olshansky, Bruce A. Carnes and Robert N. Butler



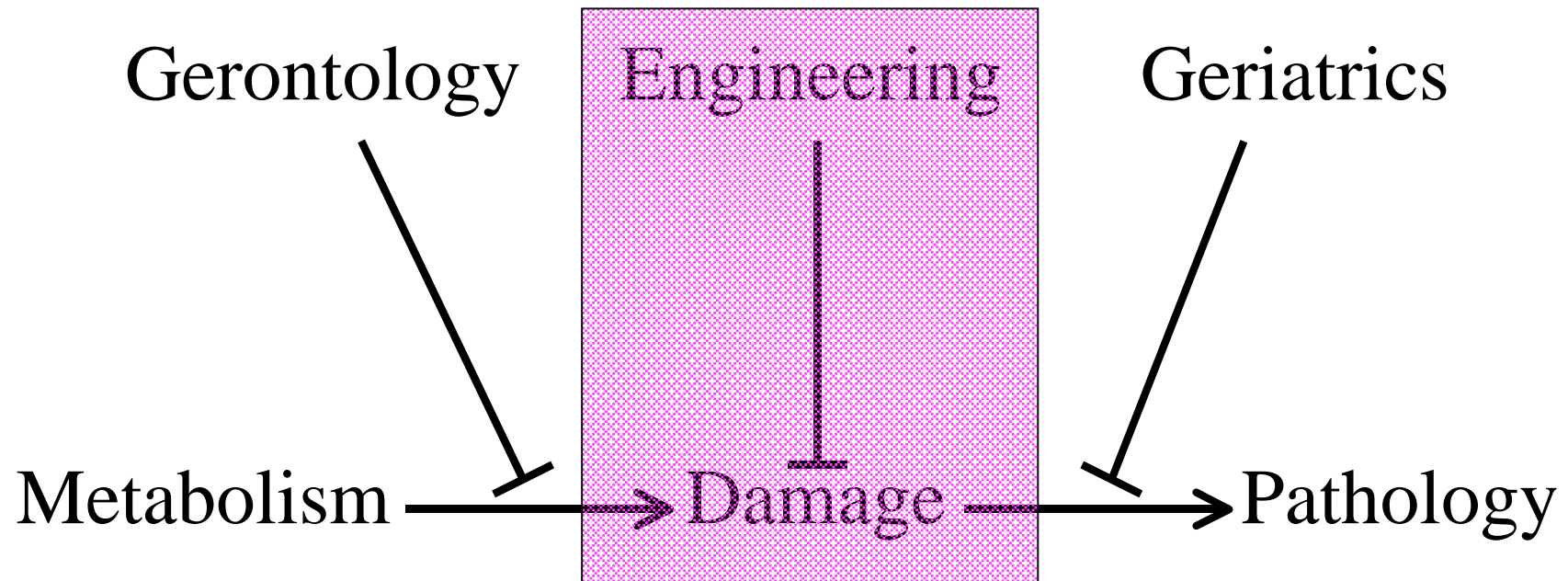
If VW Bugs were built to last



Maintained to last



Strategies for intervention



Claim: unlike the others, the engineering approach may achieve a large extension of human healthy lifespan quite soon

Reasons for the engineering approach

- it targets initially inert intermediates (“damage”)

Reasons for the engineering approach

- *it targets initially inert intermediates (“damage”)*
- *damage is simpler than metabolism or pathology*

This is the damage

Seven Deadly Things

- | |
|------------------------------------|
| 1. Junk - Inside Cells |
| 2. Junk - Outside Cells |
| 3. Cells - Too Few |
| 4. Cells - Too Many |
| 5. Mutations - Chromosomes |
| 6. Mutations - Mitochondria |
| 7. Protein Crosslinks |

No new type of damage identified since 1982!

Giving the middle-aged **30 years** of extra healthy life: **Robust Human Rejuvenation**

<i>Damage rising with age</i>	<i>It or its effects reversible by</i>
Cell loss, cell atrophy	Cell therapy, mainly
Extracellular junk	Phagocytosis by immune stimulation
Extracellular crosslinks	AGE-breaking molecules/enzymes
Death-resistant cells	Suicide genes, immune stimulation
Mitochondrial mutations	Allotopic expression of 13 proteins
Intracellular junk	Transgenic microbial hydrolases
Nuclear [epi]mutations (only cancer matters)	Telomerase/ALT gene deletion plus periodic stem cell reseedling

Only 30 years?!

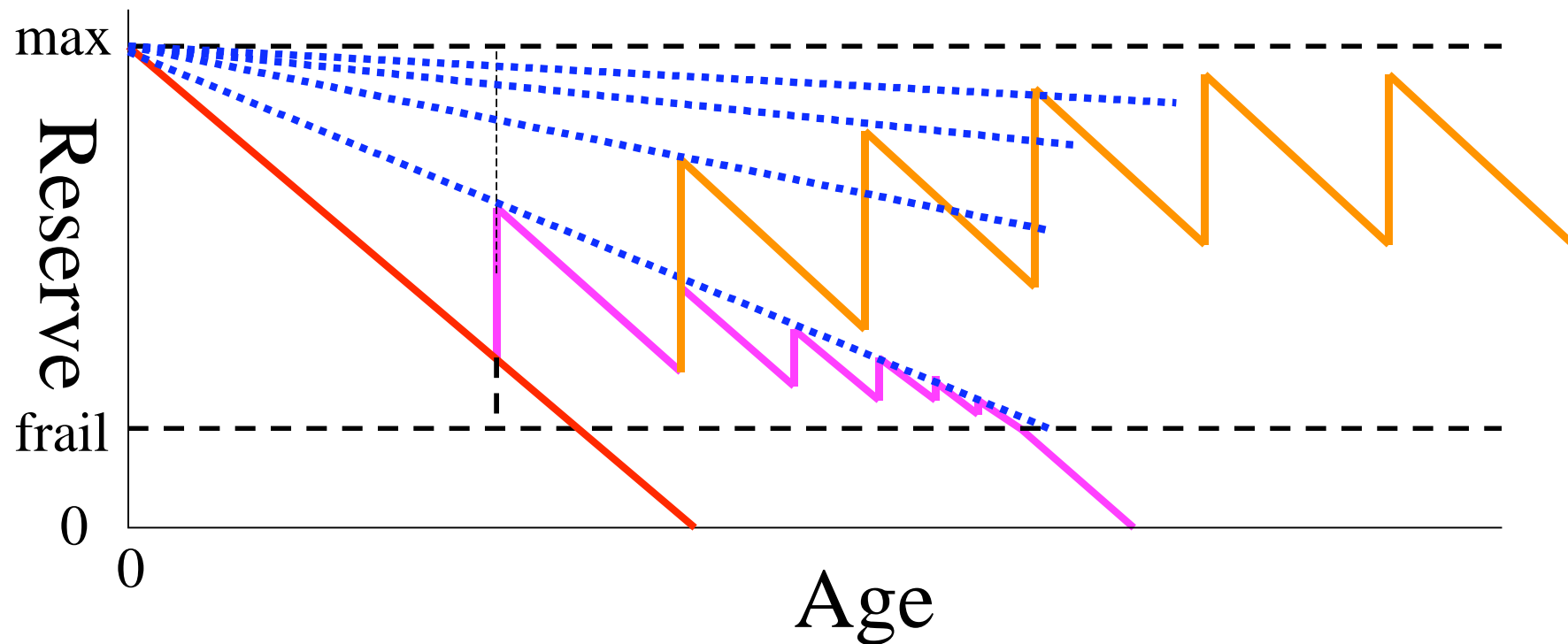
Hardly “defeating aging”...

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Mitochondrial mutations	Allotopic expression of 13 proteins
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Reasons for the engineering approach

- it targets initially inert intermediates (“damage”)
- damage is simpler than metabolism or pathology
- *repairing damage buys time*

Progress avoids diminishing returns



Fixing half the damage, then 3/4, then 7/8....

- outpaces the so-far-unfixable damage...
- **maintains healthspan indefinitely**

Longevity escape velocity (LEV)

The rate at which rejuvenation therapies must improve (following the achievement of RHR) in order to outpace the accumulation of so-far-irreparable damage

What rate of progress is realistic?

Data

1903



1927



1949



1969



Simulating aging

(Phoenix & de Grey, AGE 2007; 29:133)

Metabolism *ongoingly* causes “**damage**”

and

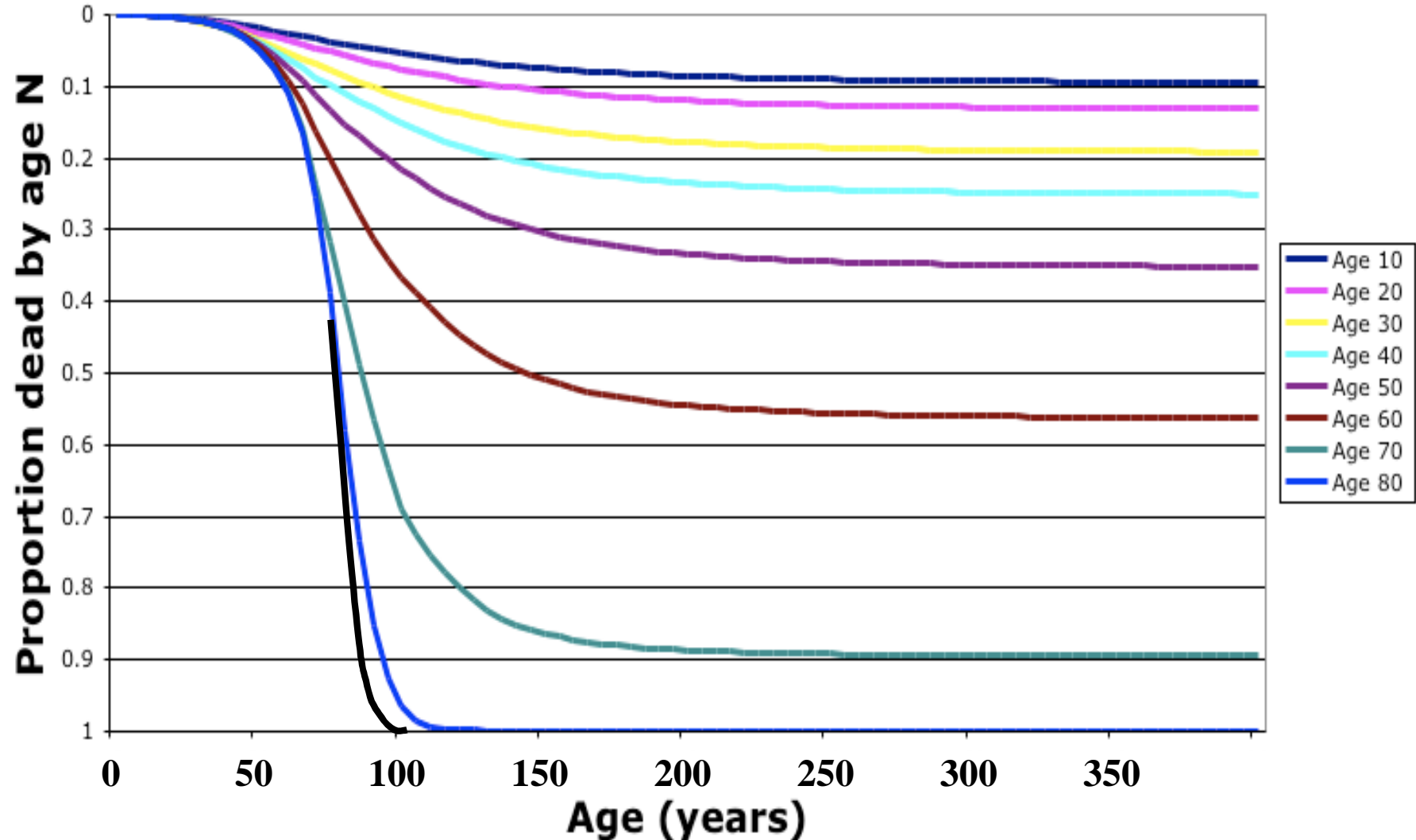
Damage *eventually* causes pathology

So....

*Simulations of aging (and intervention)
should simulate damage accumulation*

Results: LEV is very easy

Therapies double efficacy only every 42y



Data



What this means:

*The first 1000-year-old
is probably less than
20 years younger than
the first 150-year-old*

Optimistic or realistic?

The usual view

50% chance of Robust Mouse Rejuvenation in 10y:
rather optimistic, but not unreasonable

50% chance of Robust Human Rejuvenation in 25y:
very optimistic

Longevity Escape Velocity maintained thereafter:
complete fantasy

Optimistic or realistic?

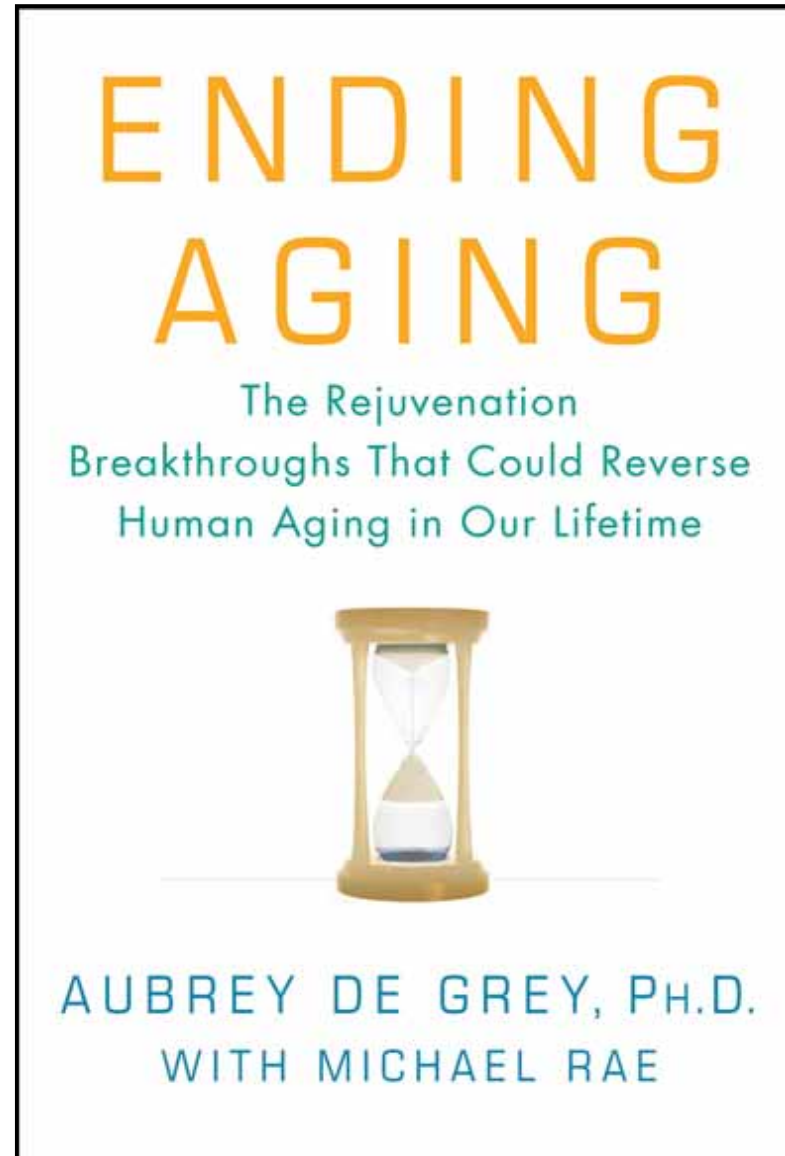
The rational view

50% chance of Robust Mouse Rejuvenation in 10y:
rather optimistic, but not unreasonable

50% chance of Robust Human Rejuvenation in 25y:
rather optimistic, but long-term that's OK

Longevity Escape Velocity maintained thereafter:
almost certain given pace of past technologies

Semi-technical book



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