The Evolution of Aging

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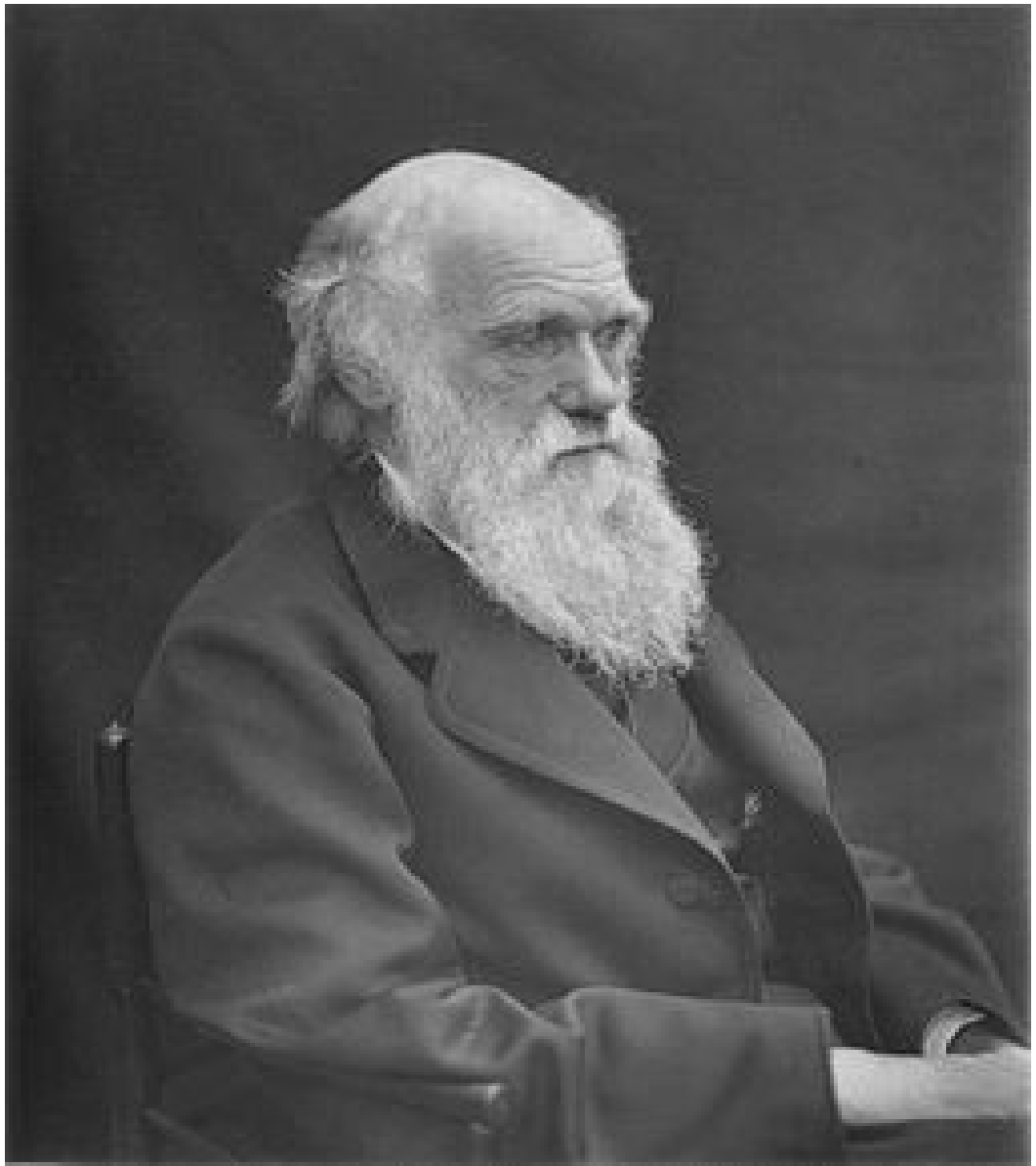
Sources of information:

The internet, and Steven Austad “Why we age”

Charles Darwin (circa 1878)



Darwin's definition of evolution:

"The process by which organisms change over time as a result of changes in heritable physical or behavioral traits."
Origin of Species,1859

Darwin thought that aging evolved so that elders could pass survival information and wisdom along to younger generations.

More definitions

- ***Aging***: Post-maturational modifications in the structure and function of organisms.
- ***Life span***: The outer limit for life of an organism
- ***Life Expectancy***: The average age a person is expected to live
- ***Longevity***: A *synonym* for life expectancy

Synonym – a word used in place of the one you can't spell!

If aging evolved then it would have changed over time?

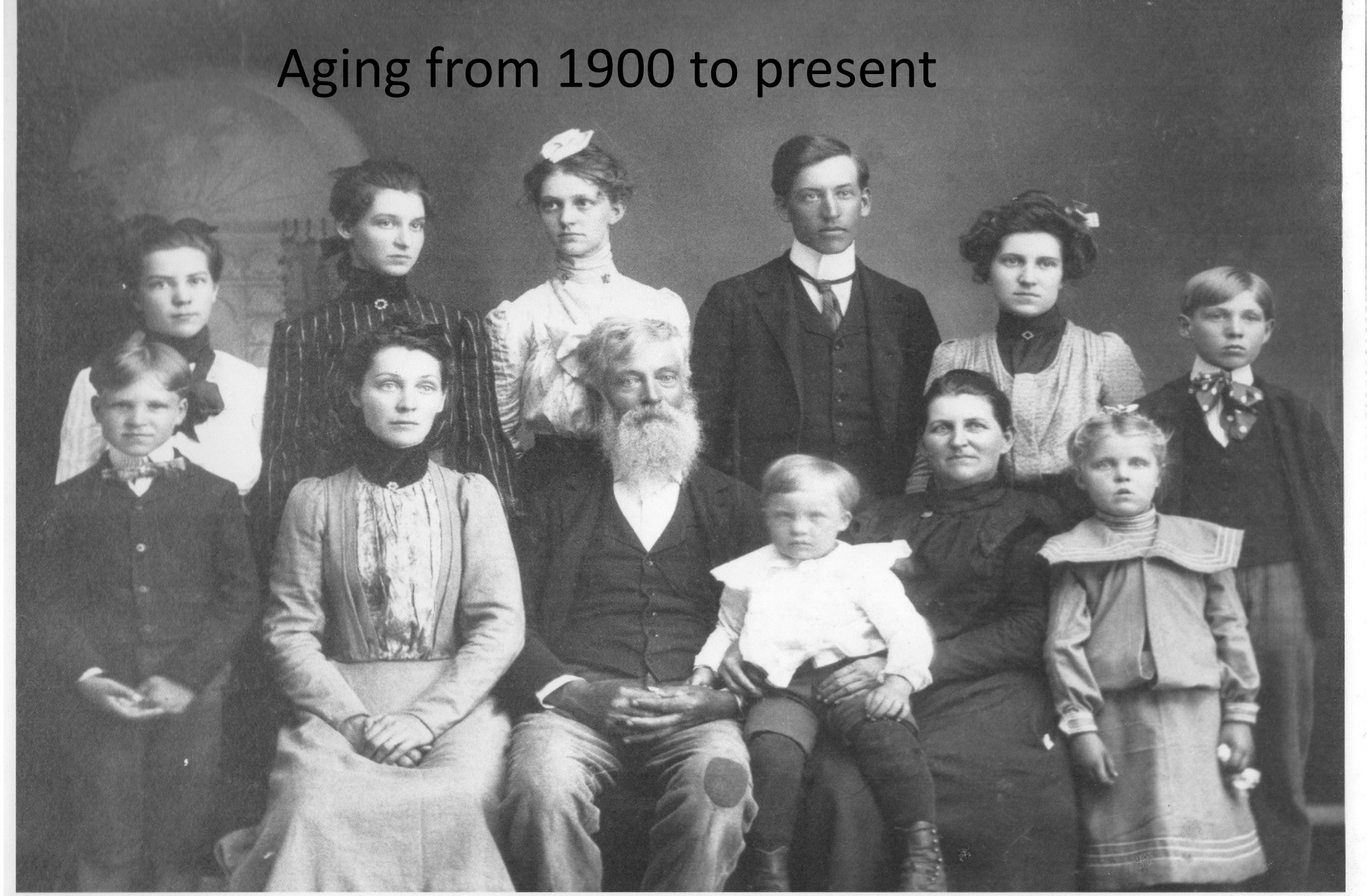
Humans migrated from Africa to Europe about 120,000 years ago.

Were hunter-gathers until the dawn of agriculture 10,000 years ago.

92% of our specie's existence was pre-civilization.

Hunter-gathers in general were taller and sturdier than modern humans. However:

Little or no evidence that our basic biology of aging has changed in the past 10,000 years.



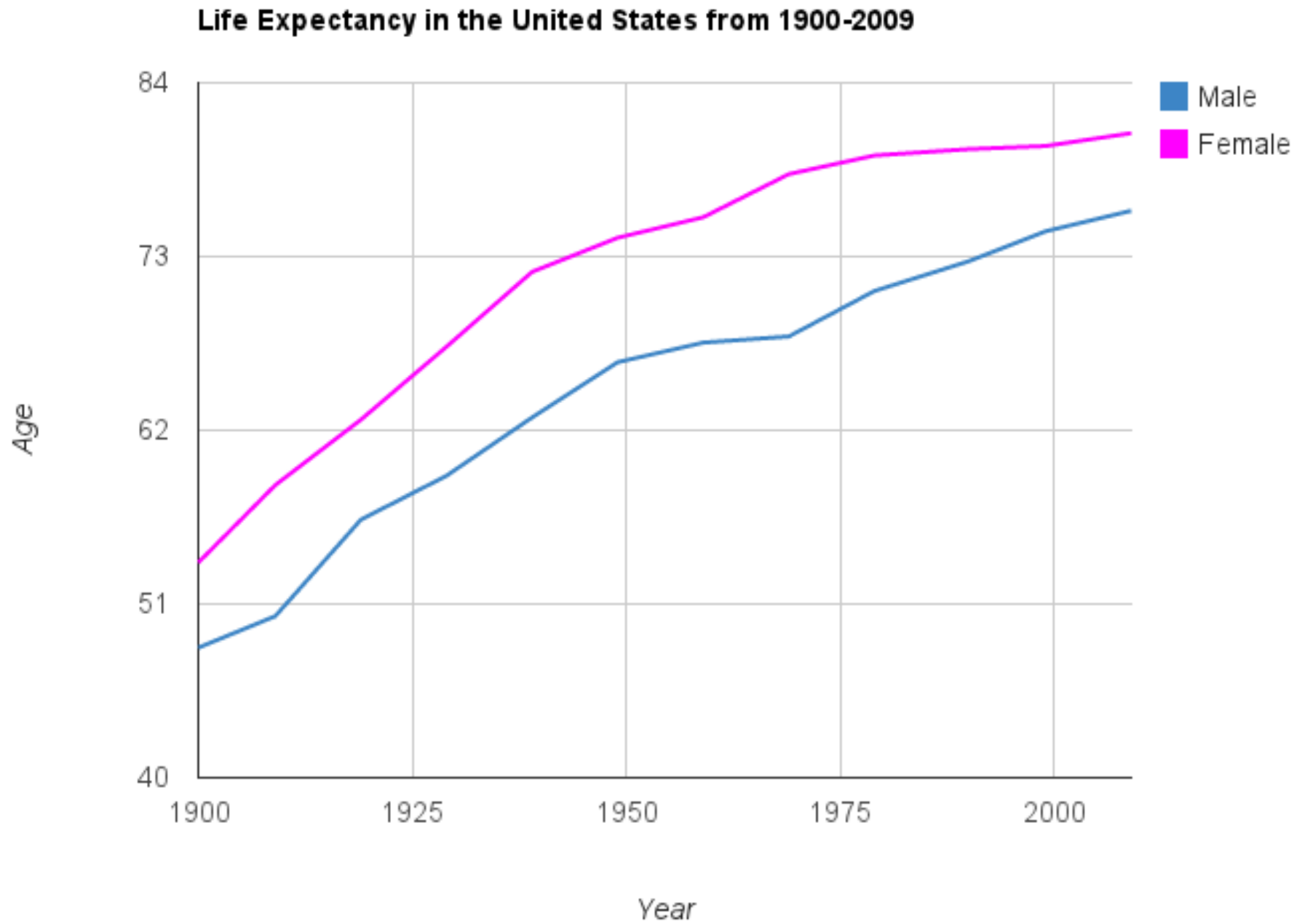
John and Mary Brandon-Bain and family, Morgan Co. Indiana, circa 1902

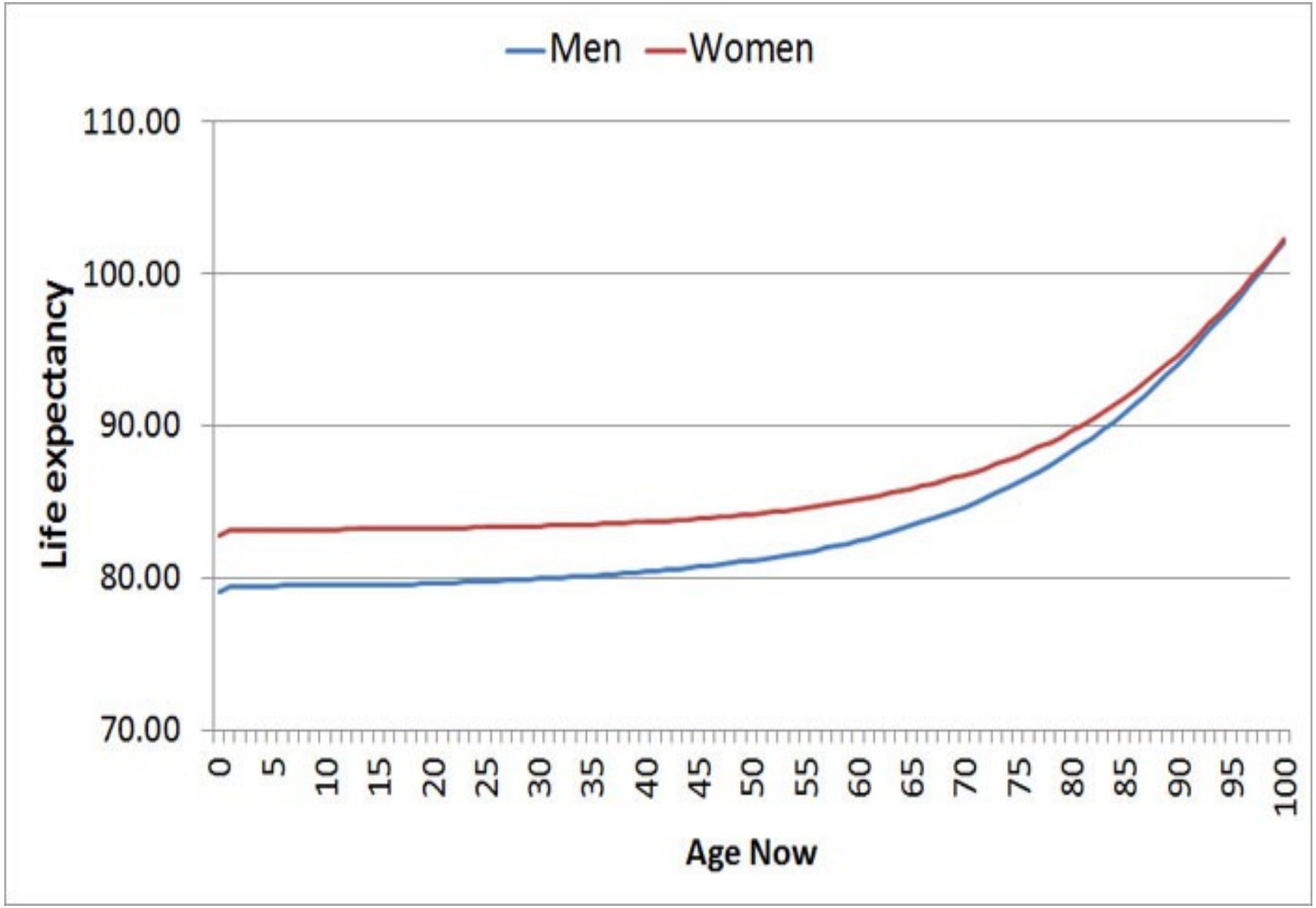
Max Planck, father of quantum physics, at about age 60, circa 1920

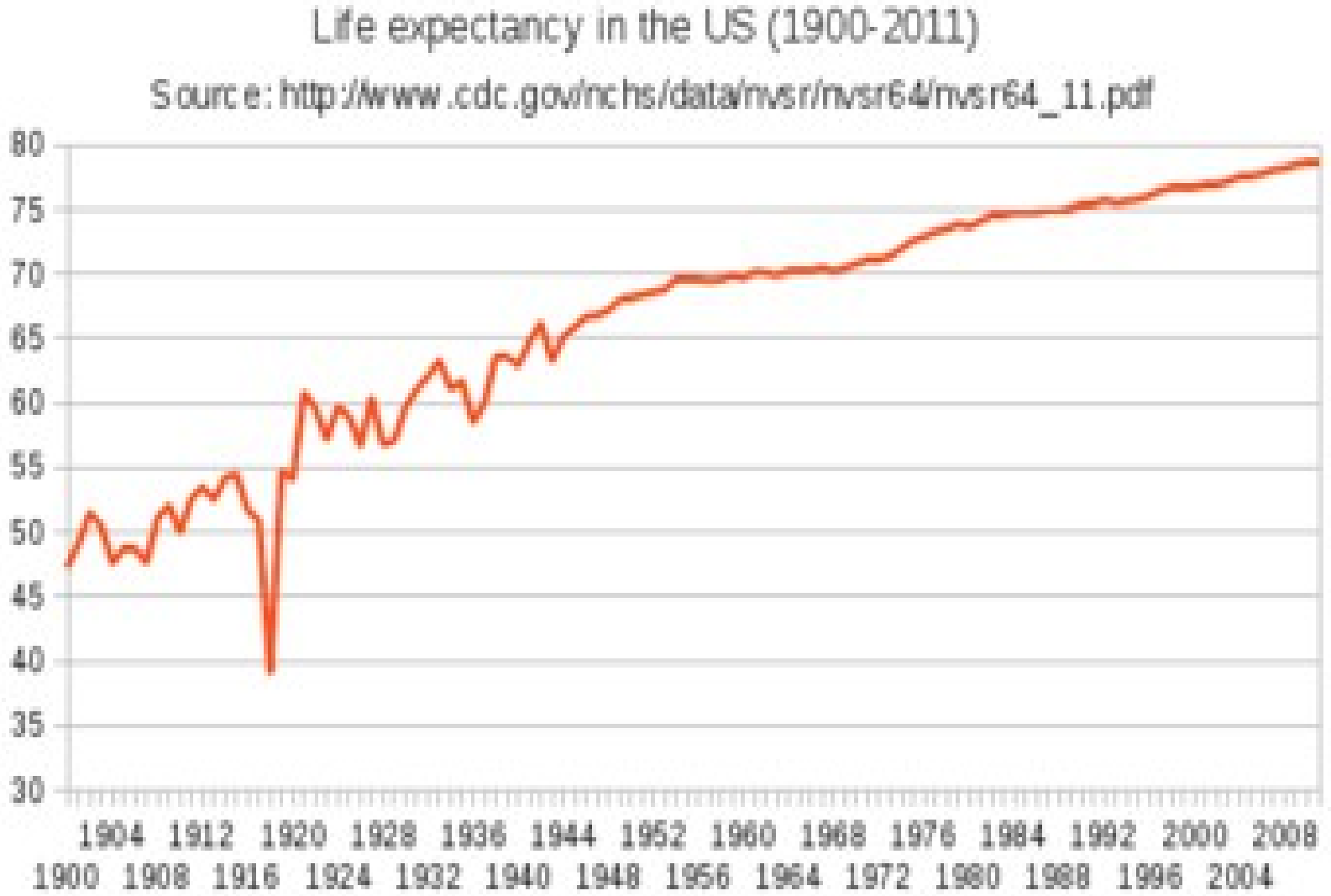
60 to 70 year old folks circa 1950

60 to 70 year old couple circa 2018

Betty Goedhart, 86 year old trapeze performer


Life Expectancy in the United States from 1900-2009
84
73
62
51
40
Age
1900
1925
1950
1975
2000
Year
Male
Female

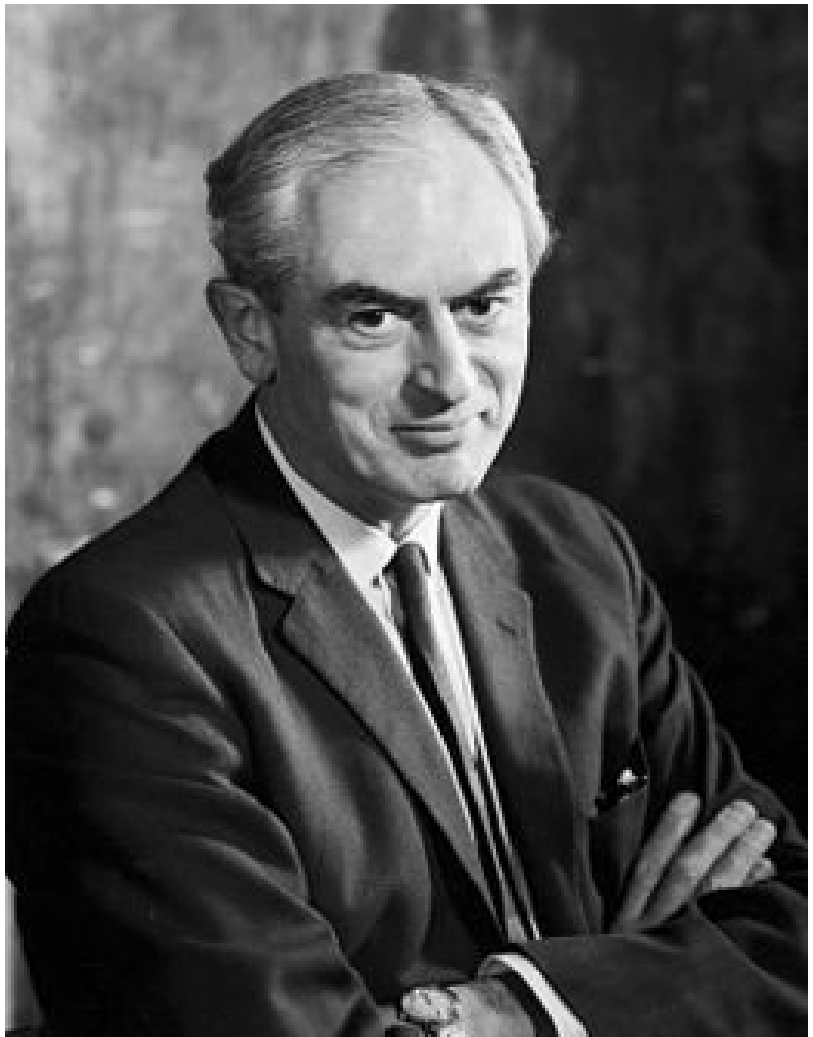

Men
Women
110.00
100.00
90.00
80.00
70.00
Life expectancy
0
5
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
Age Now


Life expectancy in the US (1900-2011)
Source: http://www.cdc.gov/nchs/data/nvsr/nvsr64/nvsr64_11.pdf
80
75
70
65
60
55
50
45
40
35
30
1900
1904
1908
1912
1916
1920
1924
1928
1932
1936
1940
1944
1948
1952
1956
1960
1964
1968
1972
1976
1980
1984
1988
1992
1996
2000
2004
2008

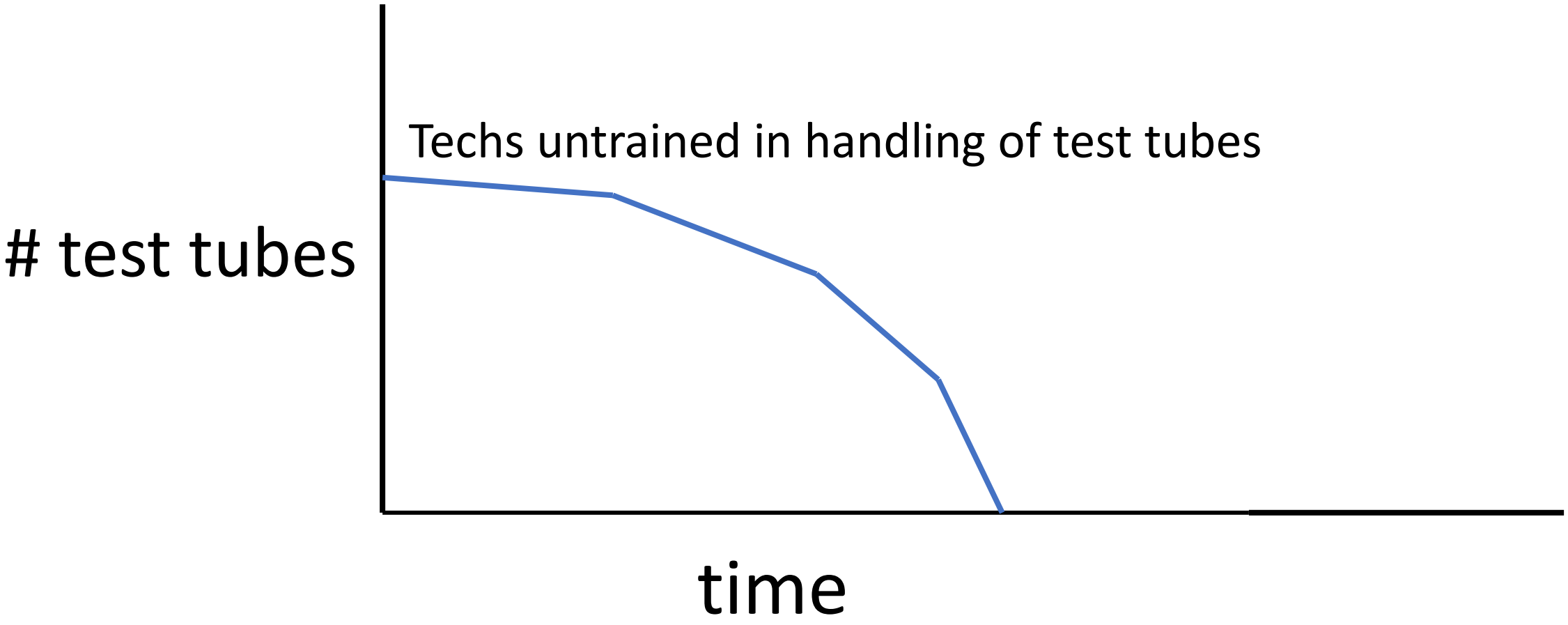
While there is no evidence that the biology of aging has changed over the past 100 years, longevity has Increased over the same time period. Accordingly:

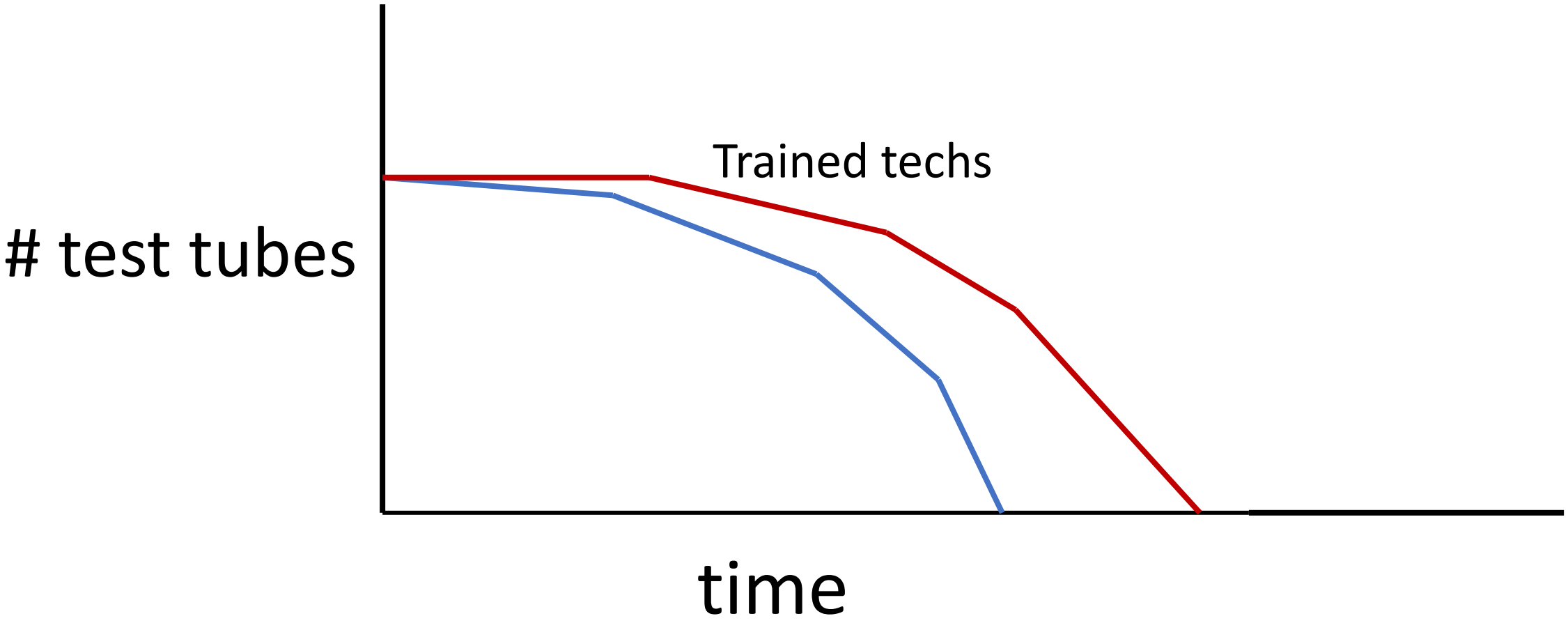
Aging and longevity seem to be separate phenomena

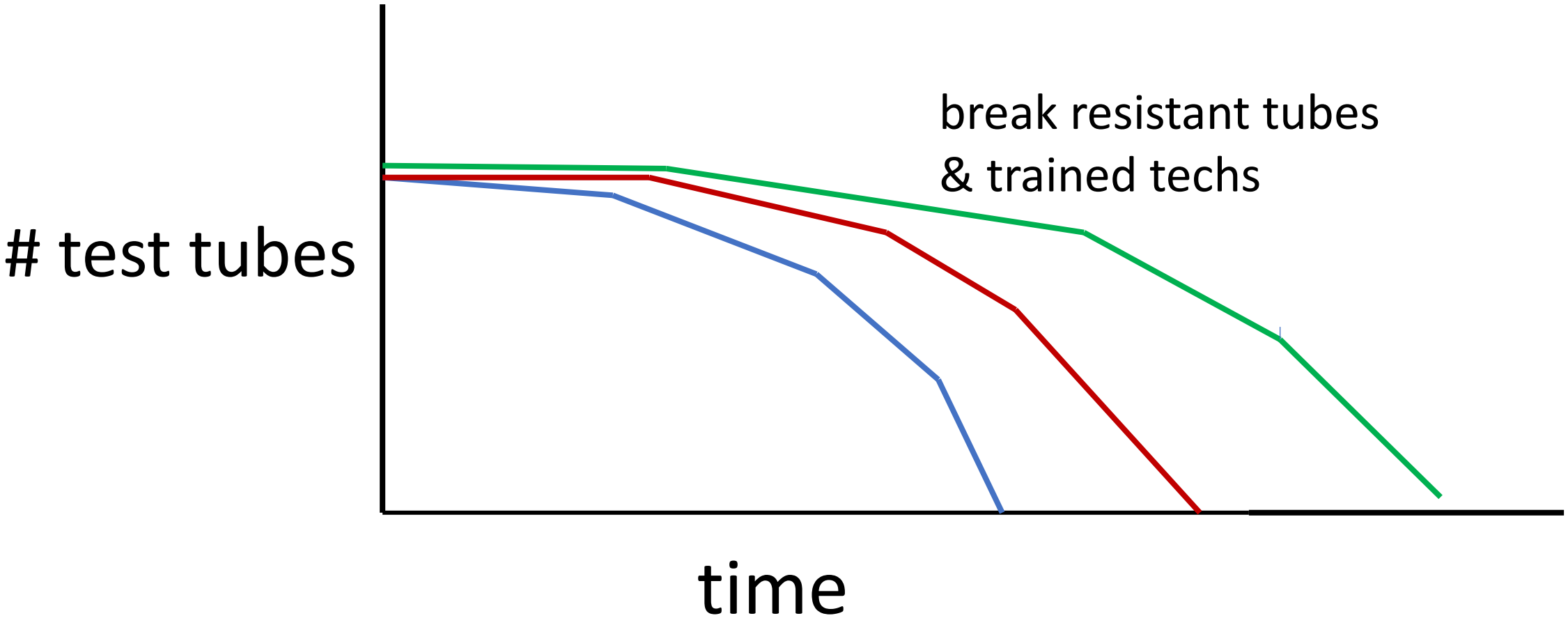
Peter Medawar, 1960 Nobel Prize Physiology and Medicine for discovery of acquired immune tolerance which explained organ transplant rejection.

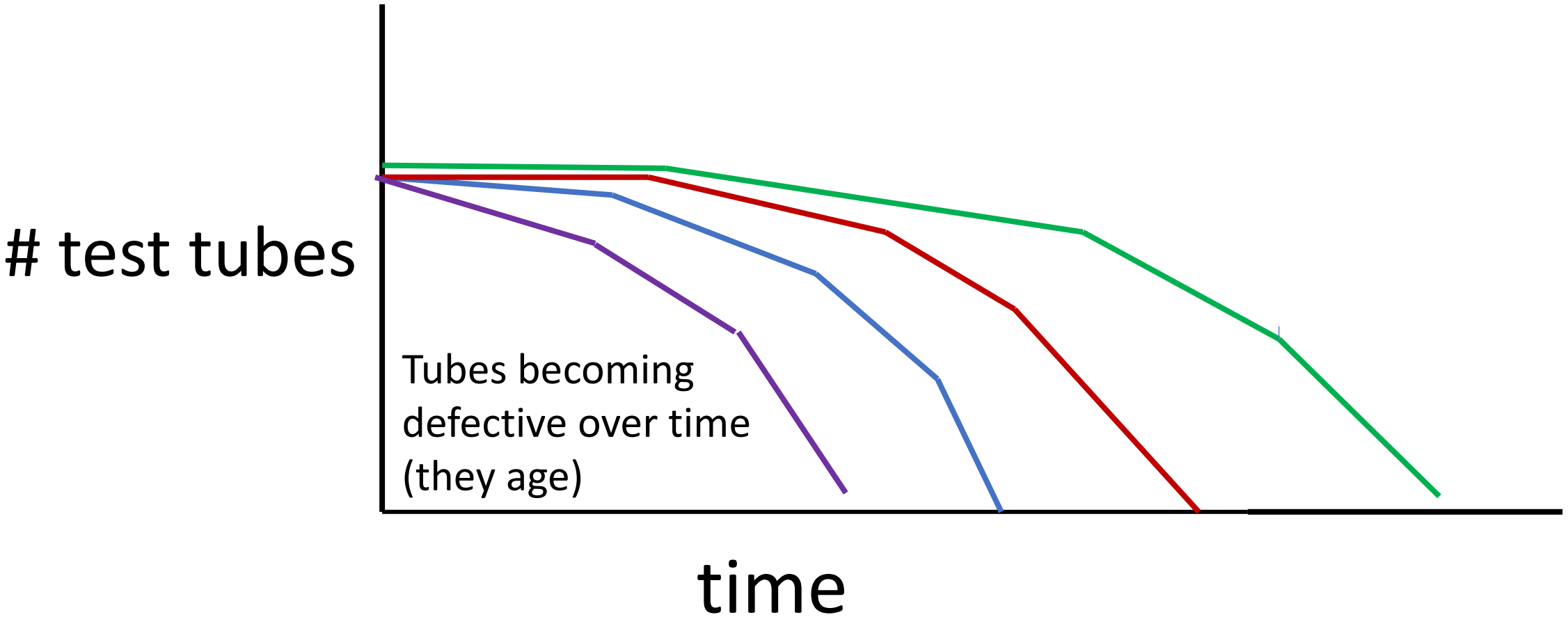


Most noted for his test tube breakage analogy of aging vs longevity.


Techs untrained in handling of test tubes
test tubes
time

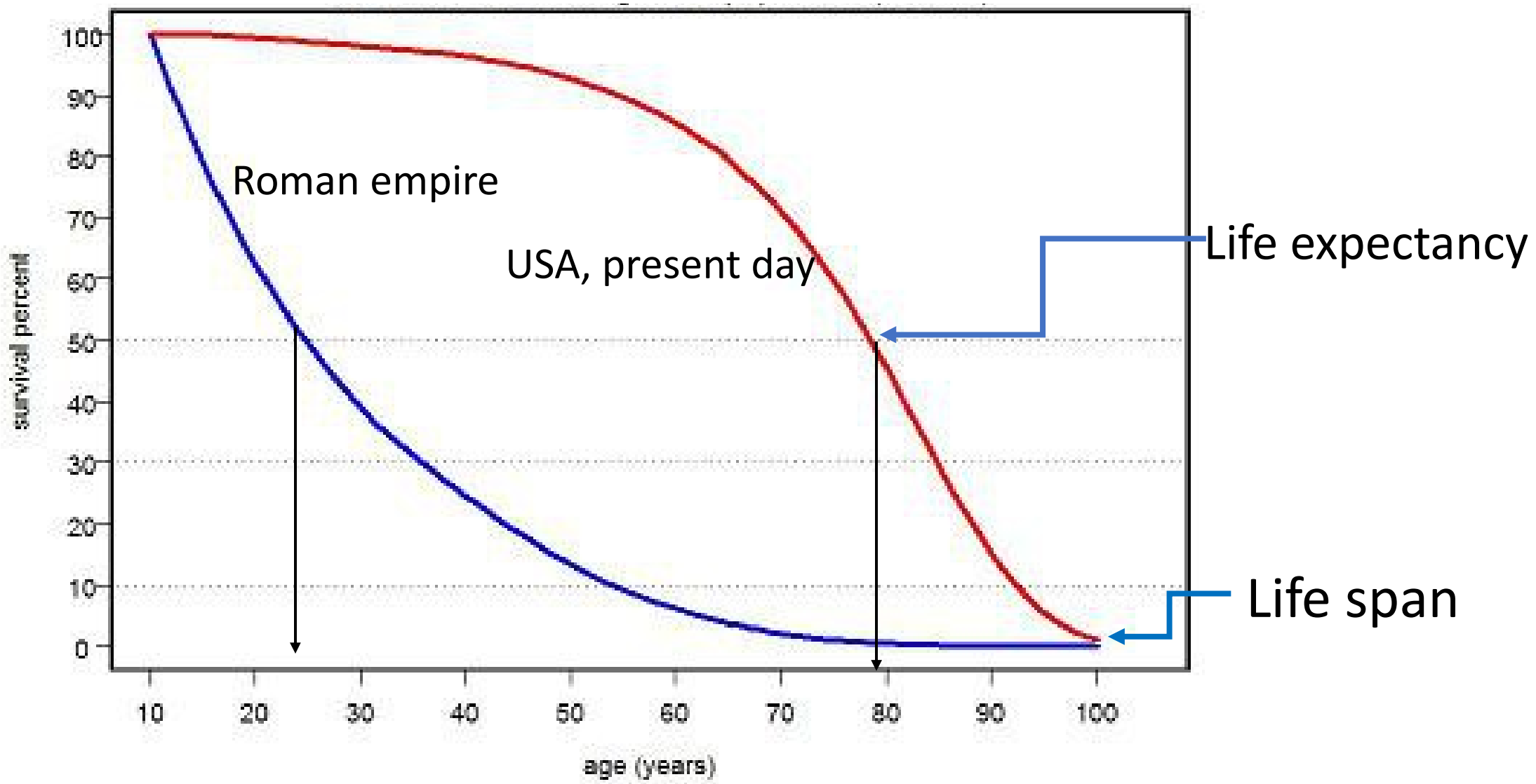

test tubes
Trained techs
time


test tubes
break resistant tubes
& trained techs
time

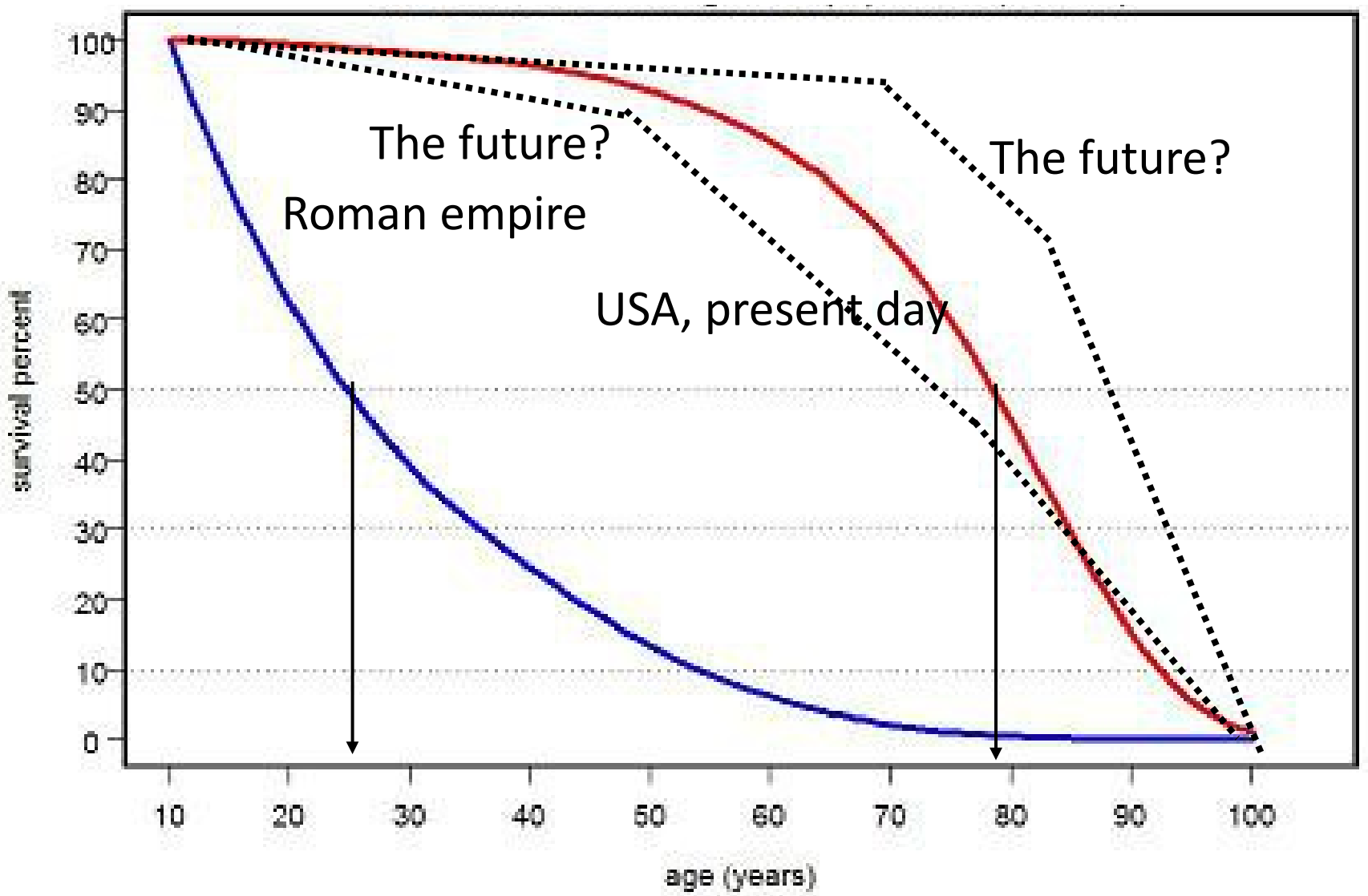

test tubes
Tubes becoming
defective over time
(they age)
time

Life expectancy (longevity) at historical epics

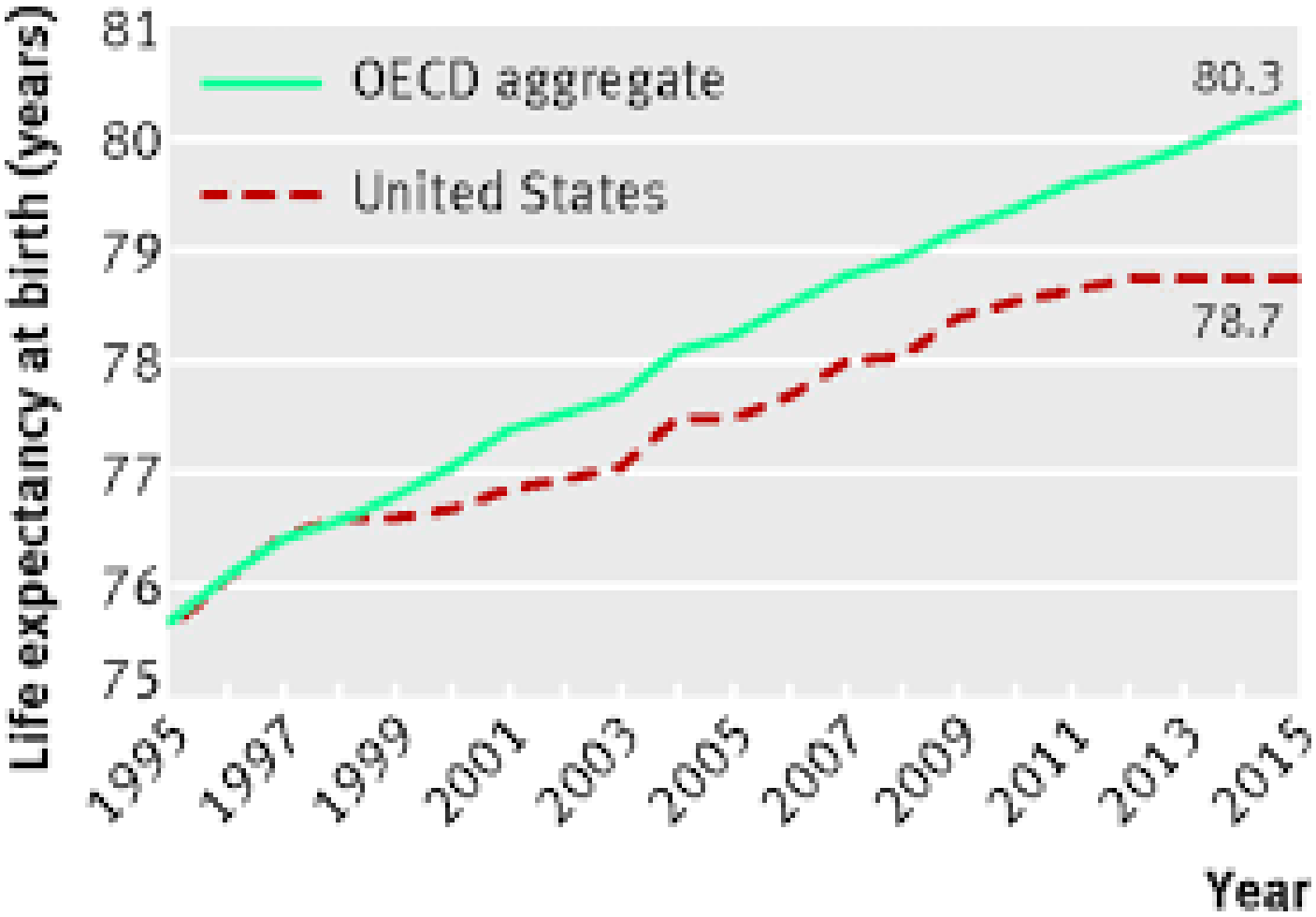
Longevity = the average age a person is expected to live



What is future life expectancy?



Life Expectancy data



OECD, Organization for Economic Cooperation and Development:
(Canada, Germany, Mexico, France, Japan and the UK)

Why the US has fallen behind other developed nations in life expectancy

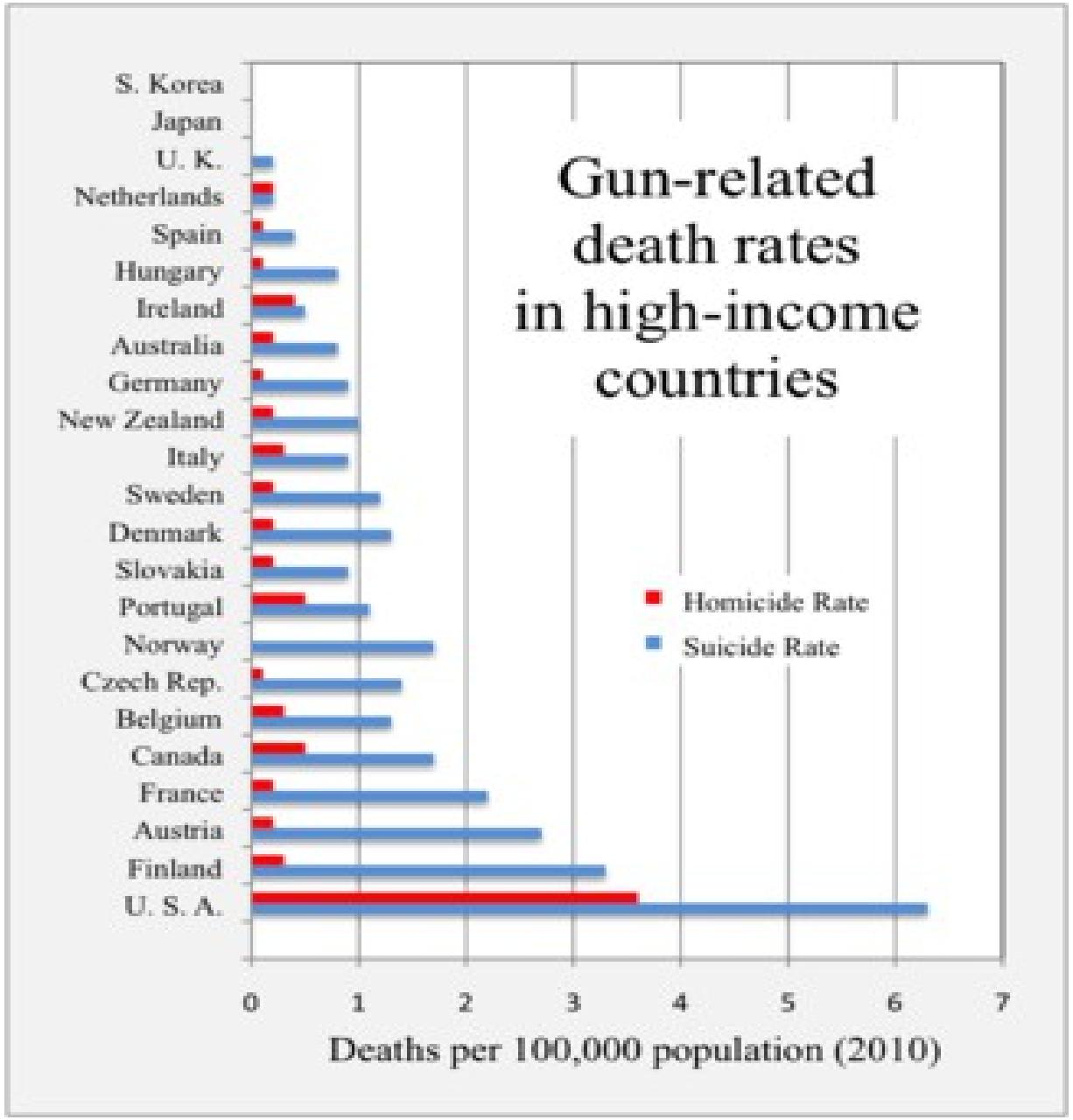
Substance abuse (Opioid epidemic)

Inadequate access to health care

Despair (hopelessness, desperation)

Gun violence

Steven Woolf, Center for Society and Health, Virginia Commonwealth University
Journal source (BMJ 2018; 362: k3096)
Web source <https://www.bmj.com/content/362/bmj.3096>


Gun-related death rates in high-income countries
S. Korea
Japan
U. K.
Netherlands
Spain
Hungary
Ireland
Australia
Germany
New Zealand
Italy
Sweden
Denmark
Slovakia
Portugal
Norway
Czech Rep.
Belgium
Canada
France
Austria
Finland
U. S. A.
Homicide Rate
Suicide Rate
0
1
2
3
4
5
6
7
Deaths per 100,000 population (2010)

Aging may be more environmental than genetic
Identical twins at age 97

Steve Austad , Chair Dept. Biology Univ. Alabama
The Methuselah Opossum Project: Role of environment in Aging

This project compared opossums living in a hazardous environment of mainland Georgia with opossums living in a hazard free environment on Sapelo island off the coast of Georgia for multiple generations.

Hypothesis: Animals living in a hazard free environment will age slower and live longer than those living in a hazardous environment.

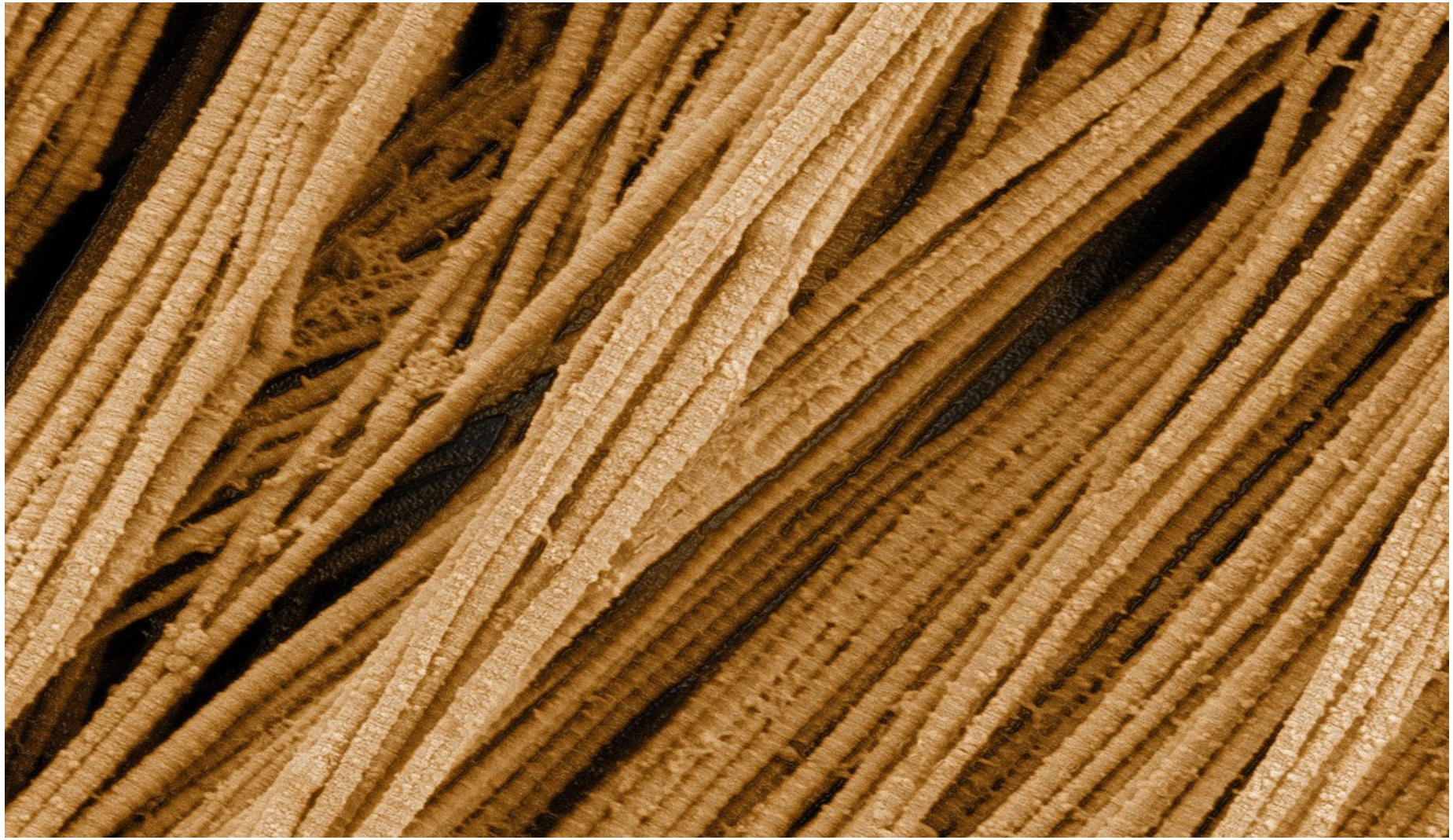
Opossums in the predator free environment of Sapelo island, Georgia age slower and live longer than mainland opossums. Why?

Methuselah Opossum Project: Results

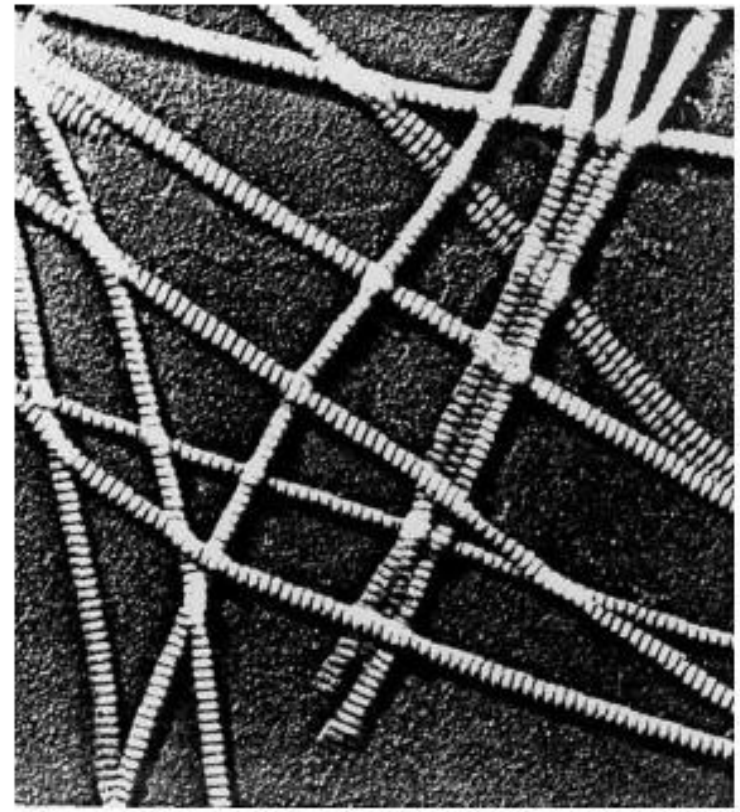
Compared to mainland opossums, Sapelo opossums:

- Spent more time above ground (reduced fear of predators)
- Lived longer (25% greater longevity)
- Lower mortality rate
- Reproduction? Fewer pups per liter, but more liters.
- Age more slowly
    - Evidenced by younger collagen fibers in tail tendons.
        - Greater flexibility at a given age

Electron micrograph of collagen fibers



Collagen Fibers



Methuselah Opossum Project: General Conclusion

Hazardous environments accelerate aging and reduce longevity

The commonality of the people previously shown (my great-grandad, etc) is that they lived in relatively hazard free environments!

Genes and Aging

The Darwinian process of genetic modification (evolution)

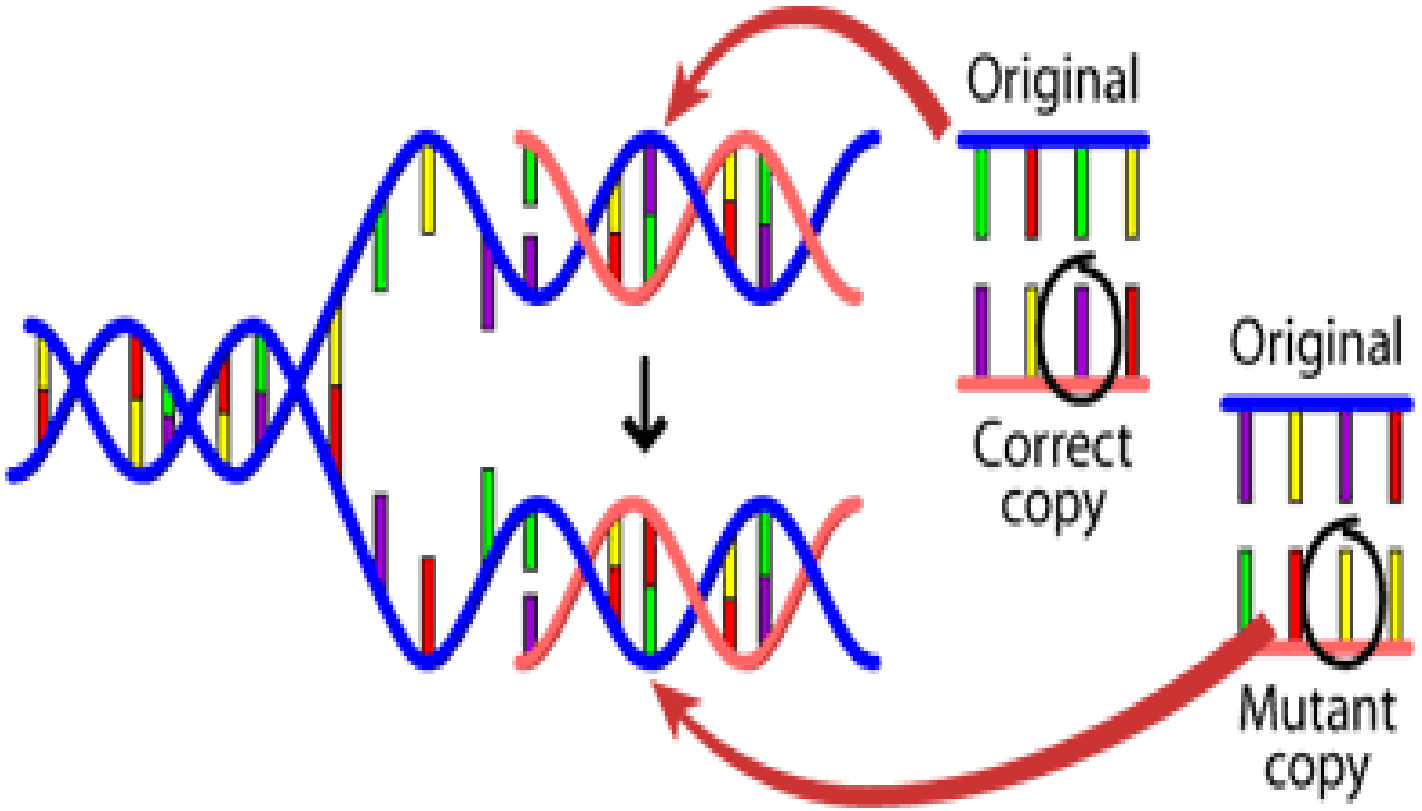
- Genes undergo random mutations.
  - Mutations that provide survival advantage are more likely to be passed onto the next generation.

Present understanding of genetic modification

- Genes undergo mutations in response to environmental stress.
  - Modified (mutated) gene benefits the individual.
    - May or may not be passed to next generation.

Mutations

Mutations are changes in base sequence of DNA



Genes and aging: Continued

Inherited (if your parents didn't have children, chances are you won't either)

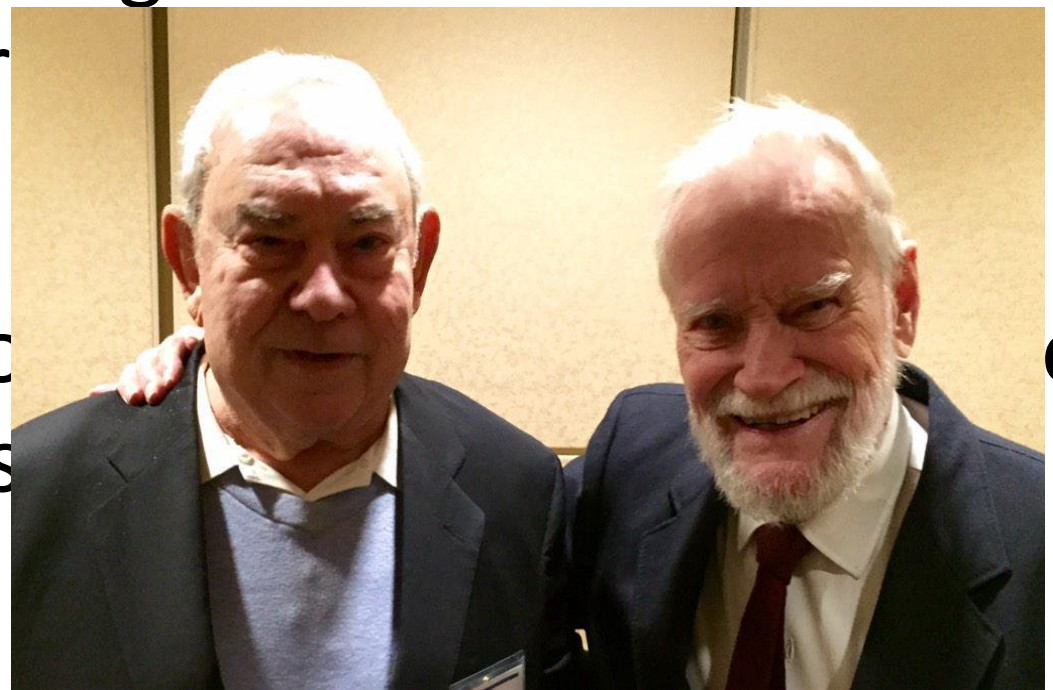
- Direct expression of a specific aging gene.
- Indirect genetic programming.

Genes developed or modified in response to environmental stress

- Uncertain to what, if any, role inheritance plays

- **Direct Expression of specific genes**: Holds that biological aging results from expression of a purposeful sequence of events written into the genome.

- Stimulated by the classic study of Hayflick and Moorhead (1961) showing that cells divide in the range of 50-70 times befor



Leonard Hayflick Paul Moorhead

  - Found to of telomeres, the end caps the expression of a gene.

Indirect Genetic Programing: Detrimental to Aging

- The tenet of this idea is that aging is an indirect consequence of genes whose detrimental effects are not manifested until later in life.

  - Genes that lead to ill health later in life (e.g., Alzheimer's disease) tend not to be selected out and

Genes that indirectly affect aging by extending lifespan (perhaps this is the gene Darwin had in mind)

CETP = cholesterol transfer protein

Sofiya Milman, American endocrinologist:
Discovered CETP gene (circa 2014)

CETP gene expresses CEPT which transfers cholesterol to high density lipoproteins (HDL).

HDL = the “good” cholesterol.
Removes cholesterol from blood vessels
Reduces atherosclerosis
Extends life expectancy (longevity)

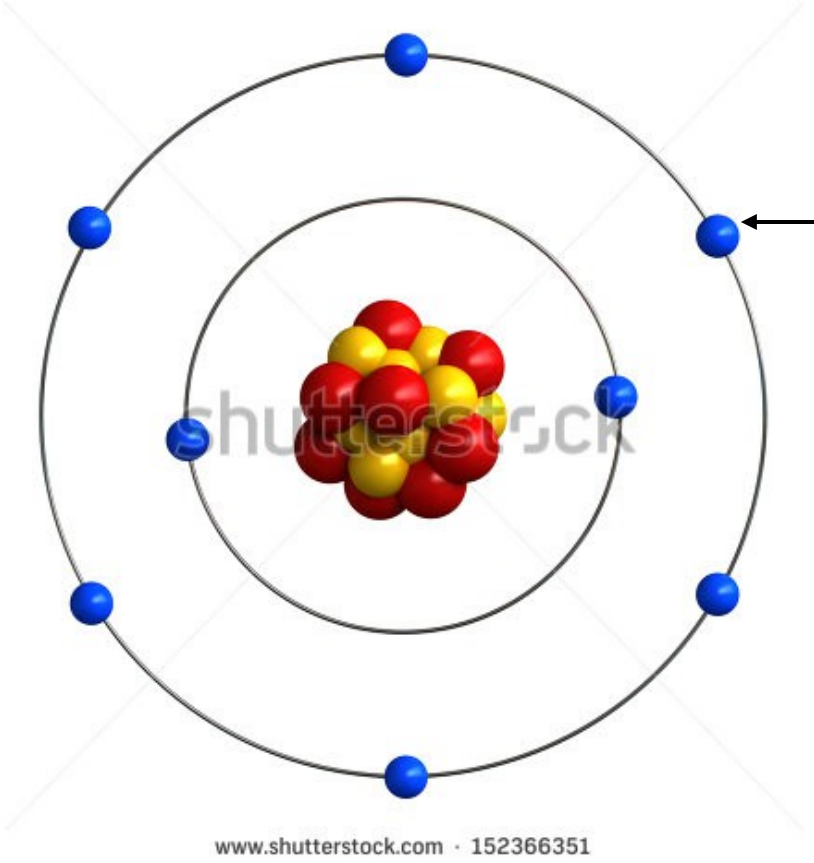
Genes Elicited in Response to Environmental Stress: Retard Aging

Collectively called “longevity assurance genes”

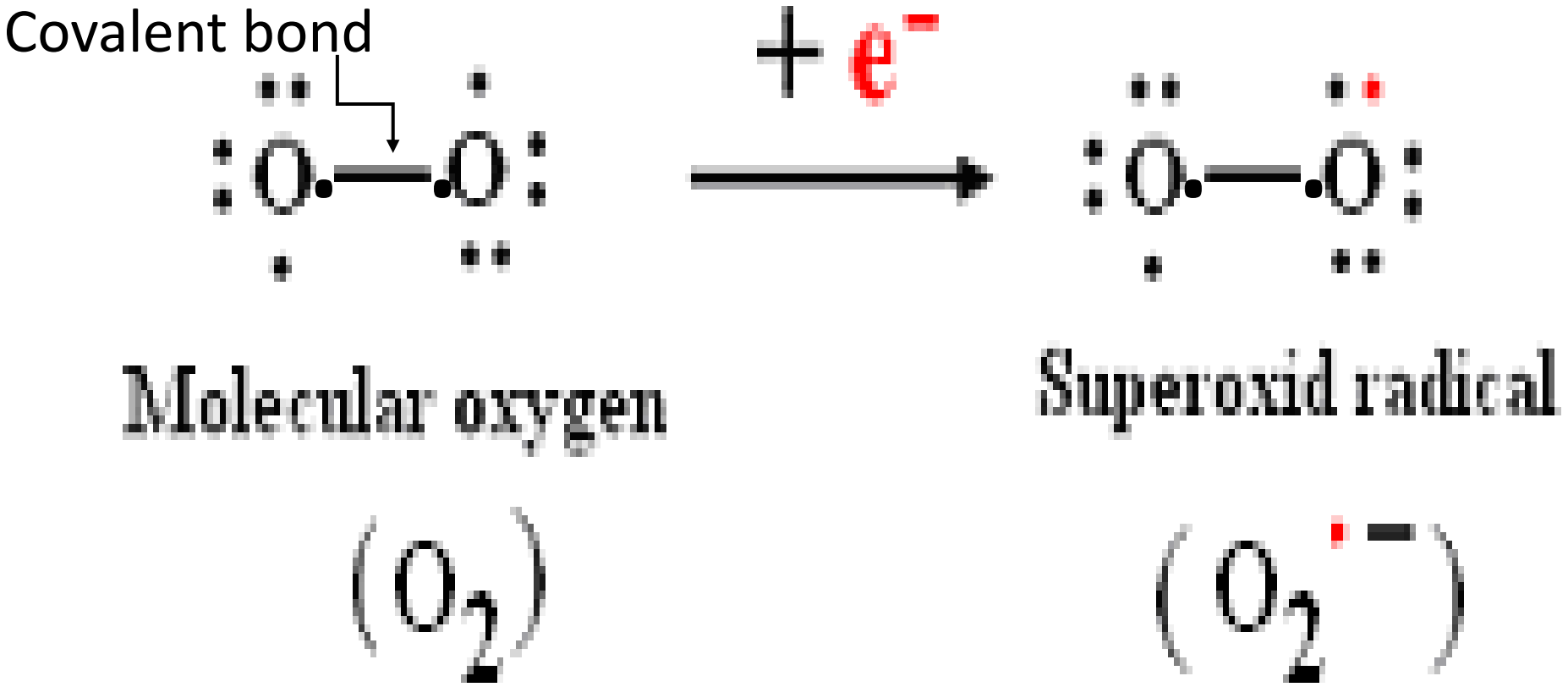
Basically protect against cell damage due to oxidative stress

Oxygen “free radicals”: Side effects of a cell’s metabolism

structure of the oxygen atom



Superoxide occurs by picking up an extra electron



Denham Harmon: Biogerontologist
Developed free radical theory of aging, Univ Calif Berkley (circa 1960)

Oxidative stress: A unifying theory

Oxygen consumption by cells

Free radical production

Cell damage: Any cell component including DNA

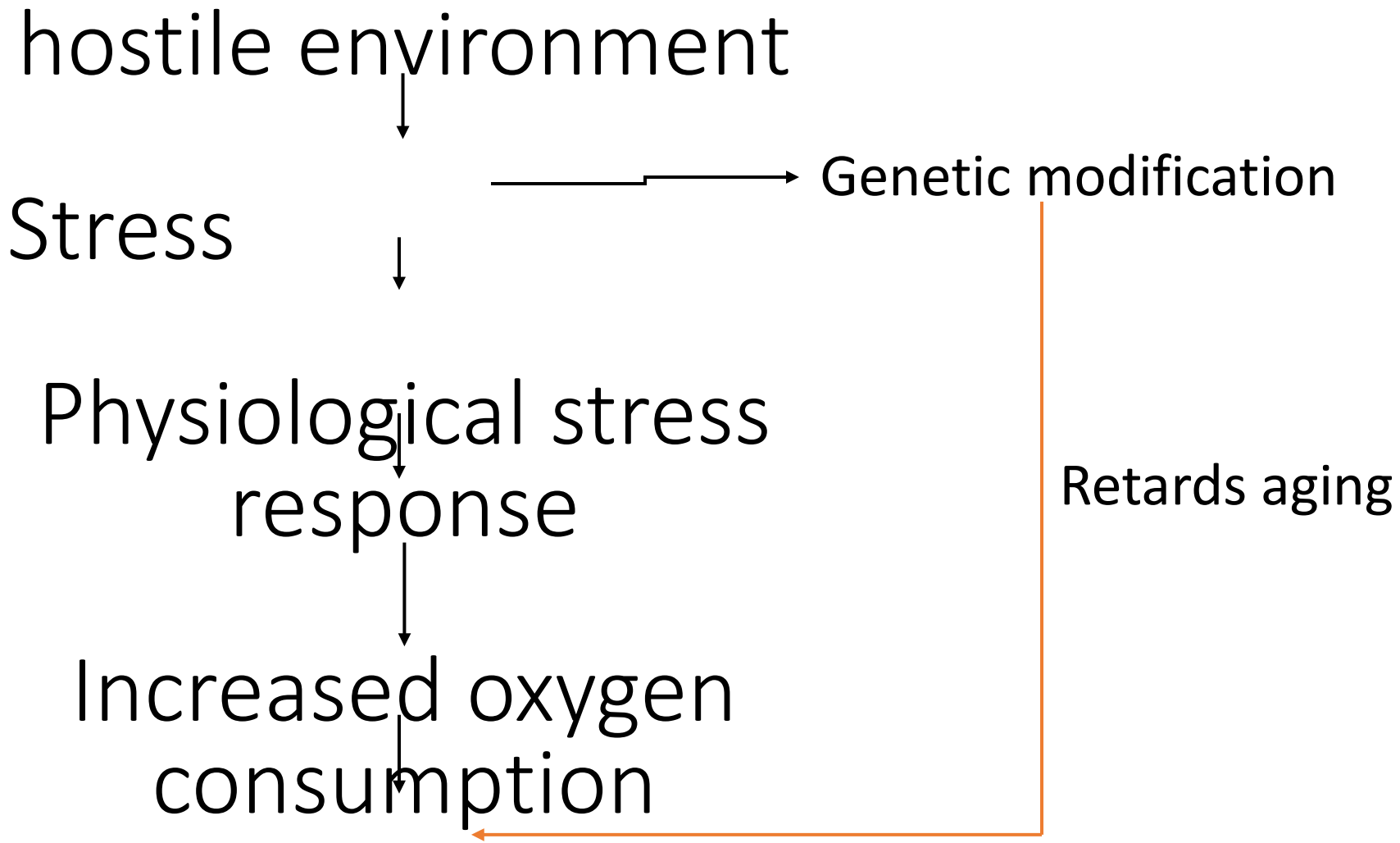
Tissue damage

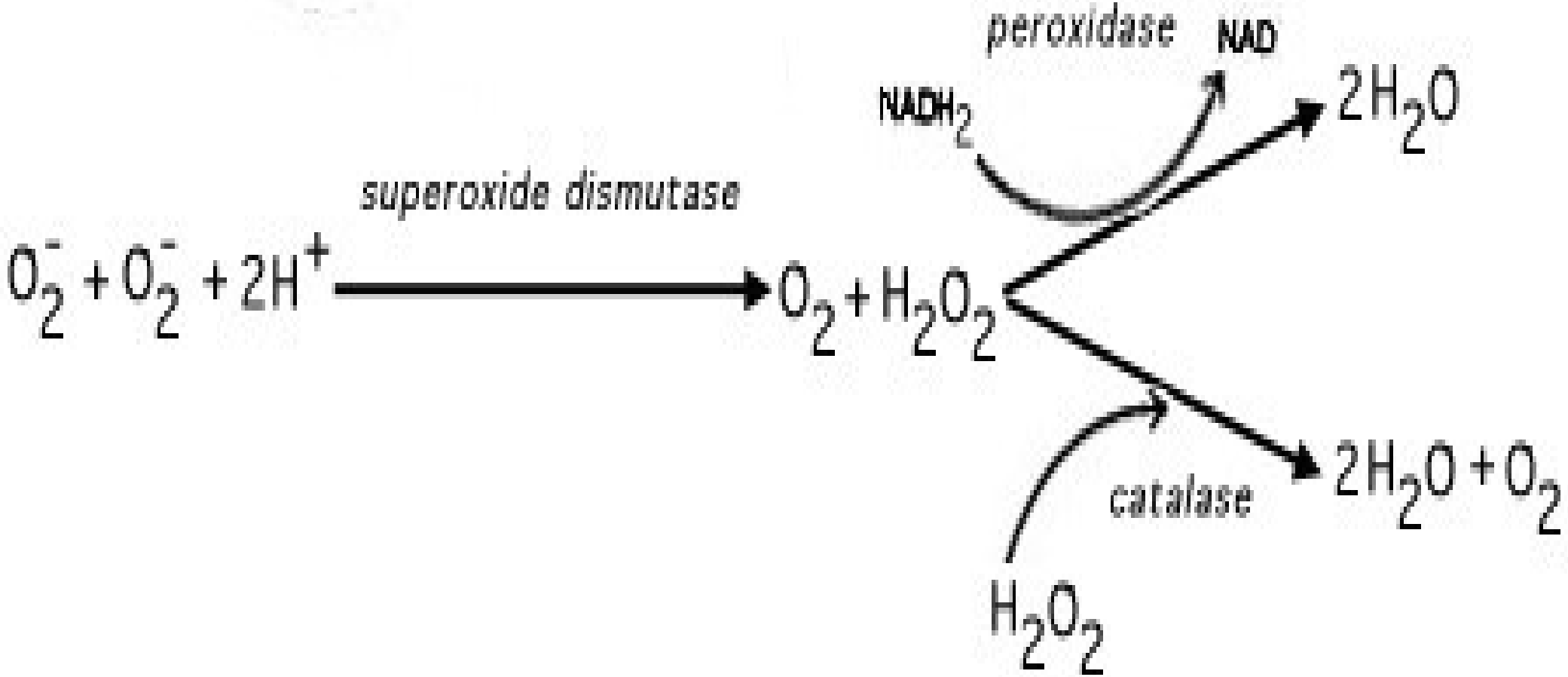
Organ and organ system damage

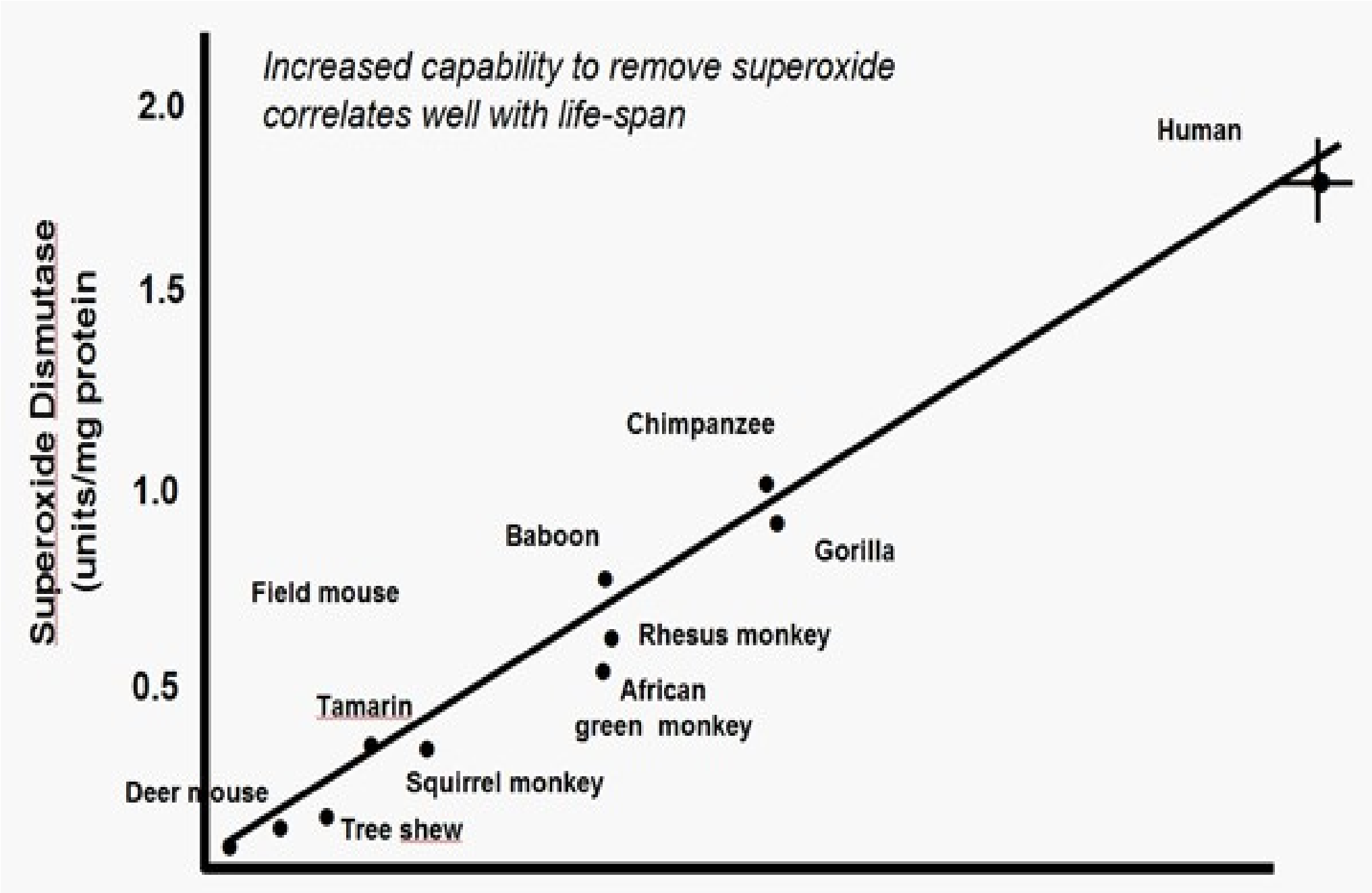
Organism damage

Aging occurs in a cell to organism direction

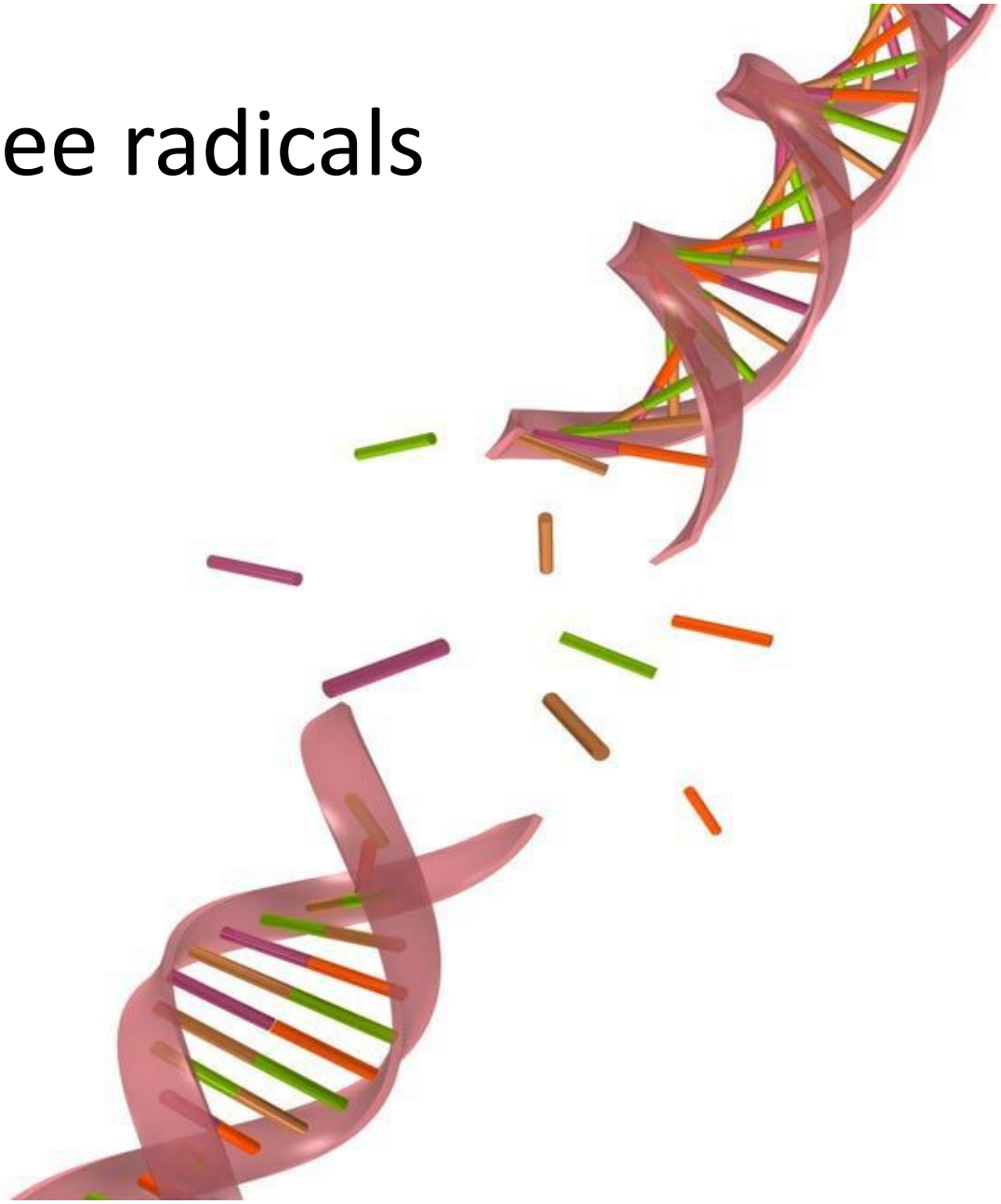
Stress, oxidative damaging and aging



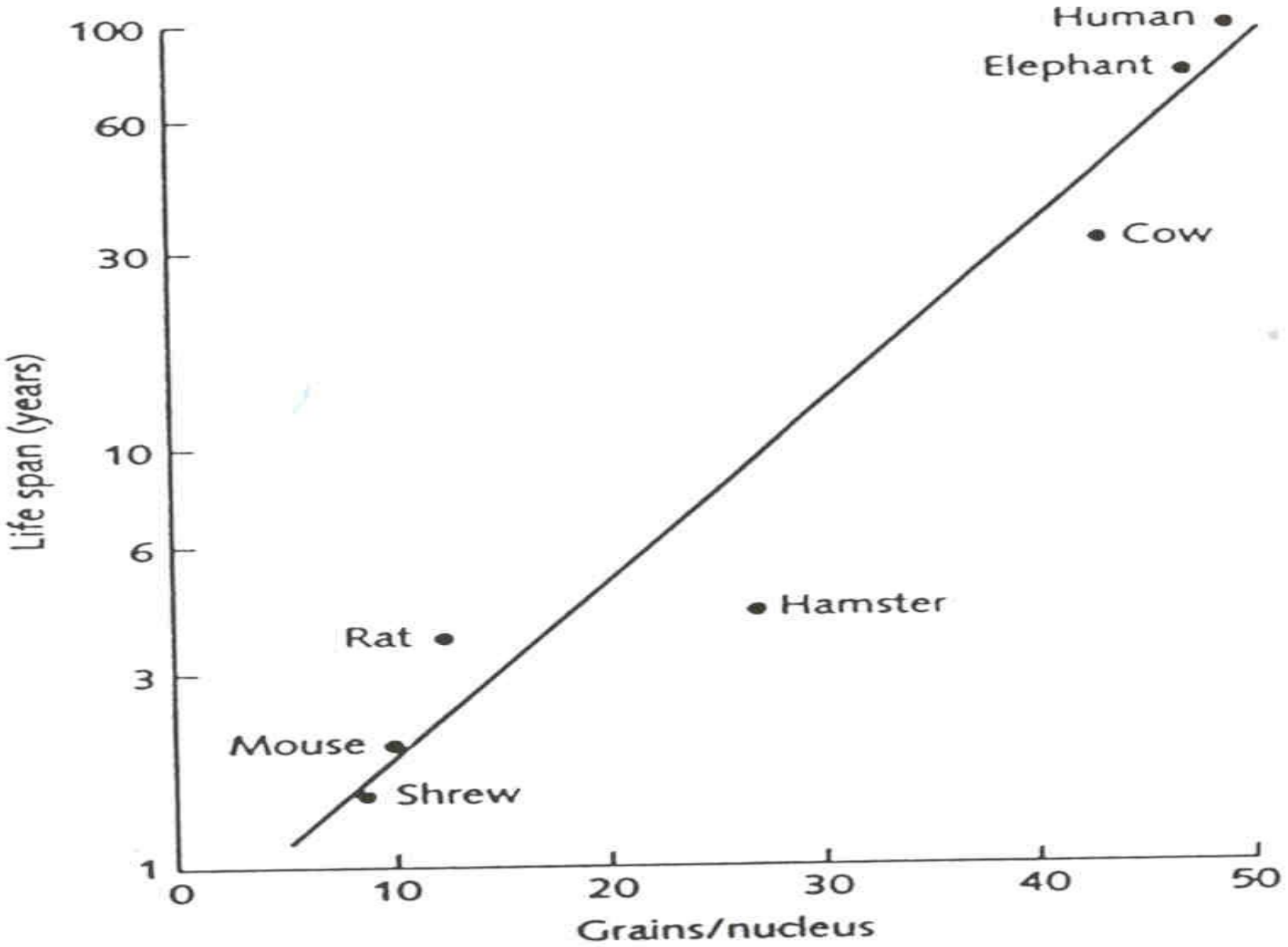

peroxidase
NAD
NADH2
2H2O
superoxide dismutase
O2- + O2- + 2H+
O2 + H2O2
2H2O + O2
catalase
H2O2


Increased capability to remove superoxide correlates well with life-span
Superoxide Dismutase (units/mg protein
2.0
1.5
1.0
0.5
Human
Chimpanzee
Baboon
Gorilla
Field mouse
Rhesus monkey
African green monkey
Tamarin
Squirrel monkey
Deer mouse
Tree shew

DNA damage by free radicals



DNA Repair proteins



How do genes respond to the environment?

A gene is a section of DNA on a chromosome which codes for the manufacture of a specific protein.

Each cell of our body contains 46 inherited chromosomes which collectively hold about 20,000 genes.

How big are chromosomes and genes

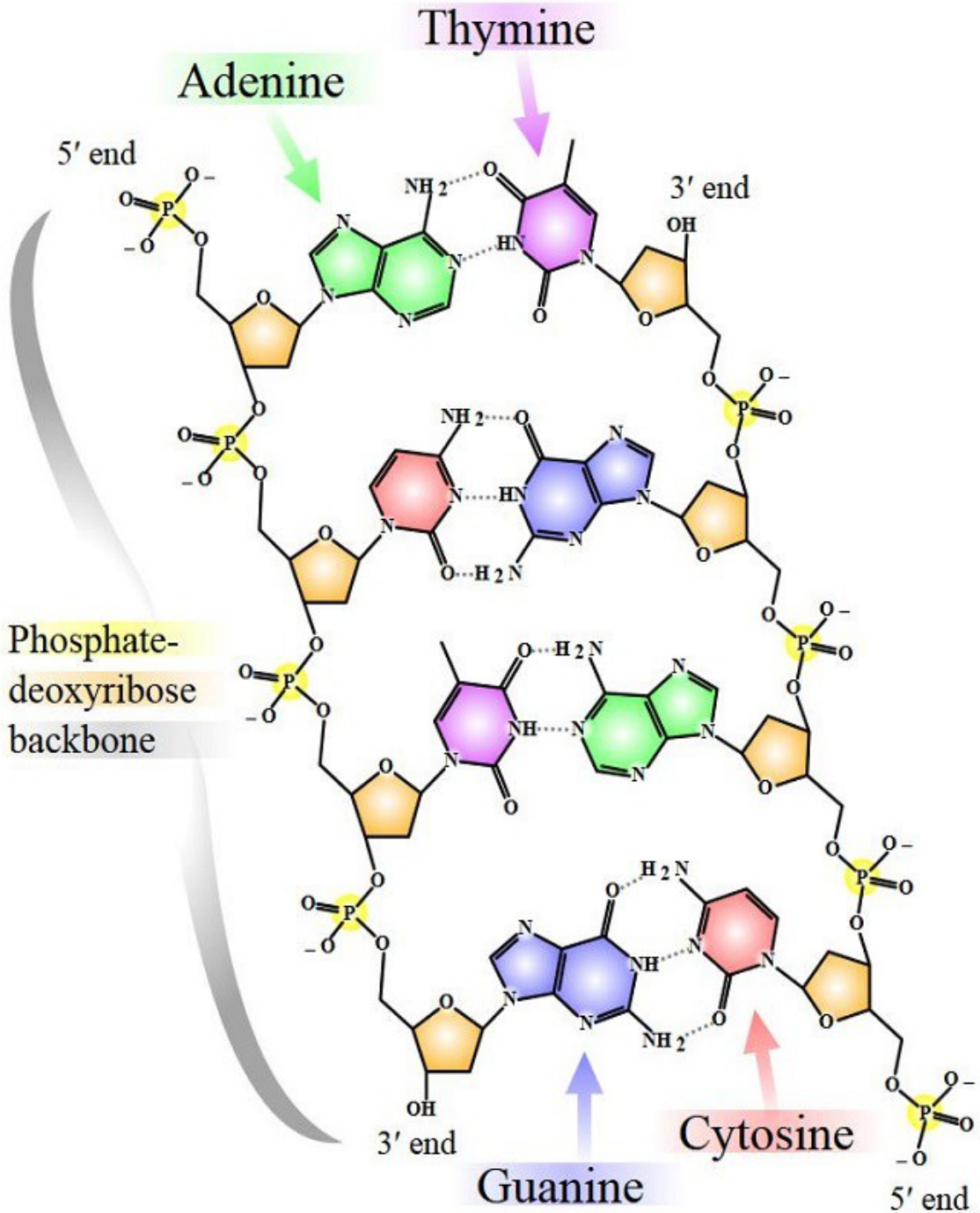
If we were to increase the size of chromosomes a million times, the diameter of a chromosome would be the size of a ramen noodle.

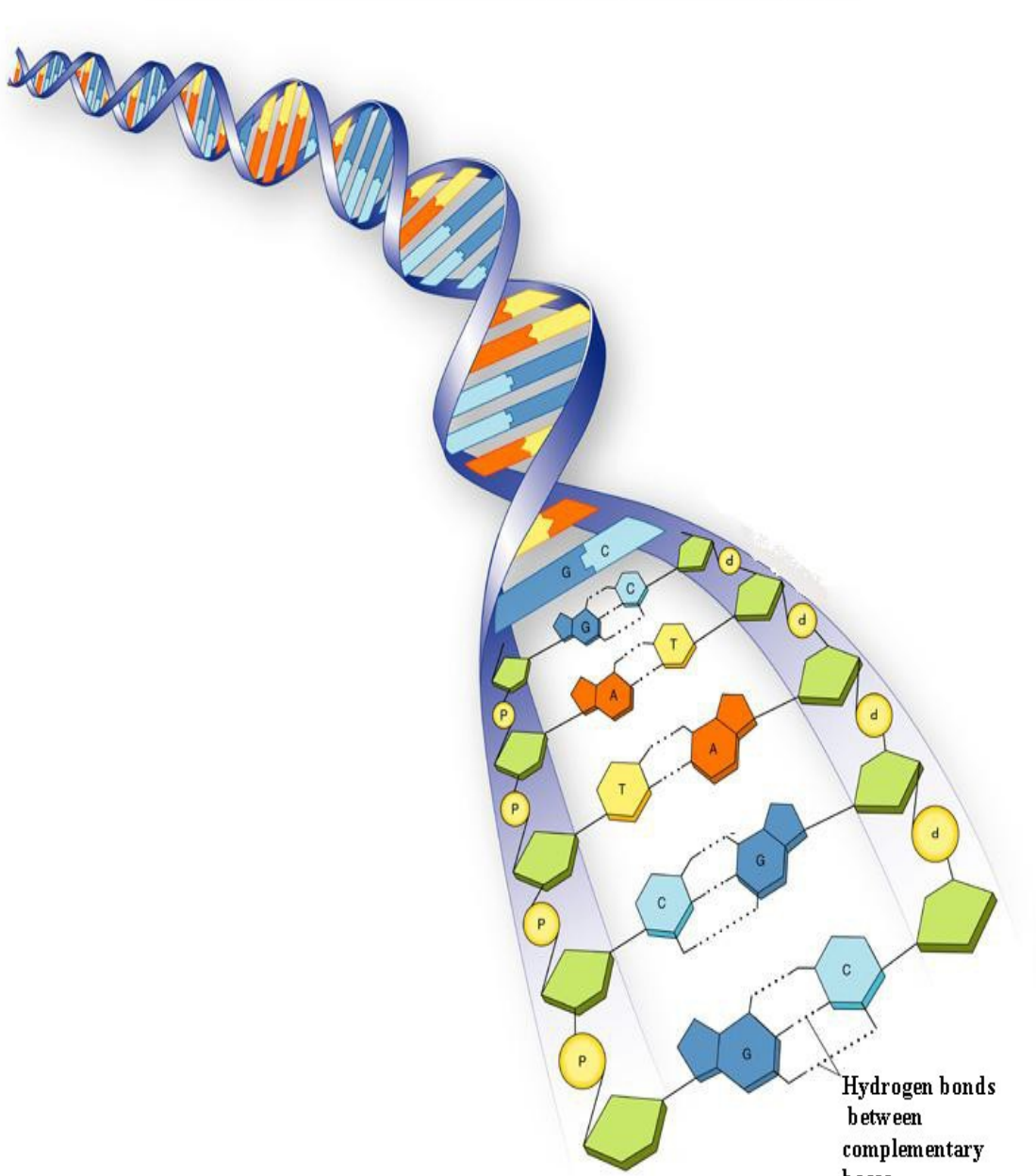
If all 46 chromosomes were then placed end to end they would stretch from New York City to Kansas City.

A single gene on a chromosome strand would be about the size of an automobile.

If all the chromosomes are then wound up into balls they would fit into a 3 BR house.

ramen noodles





T

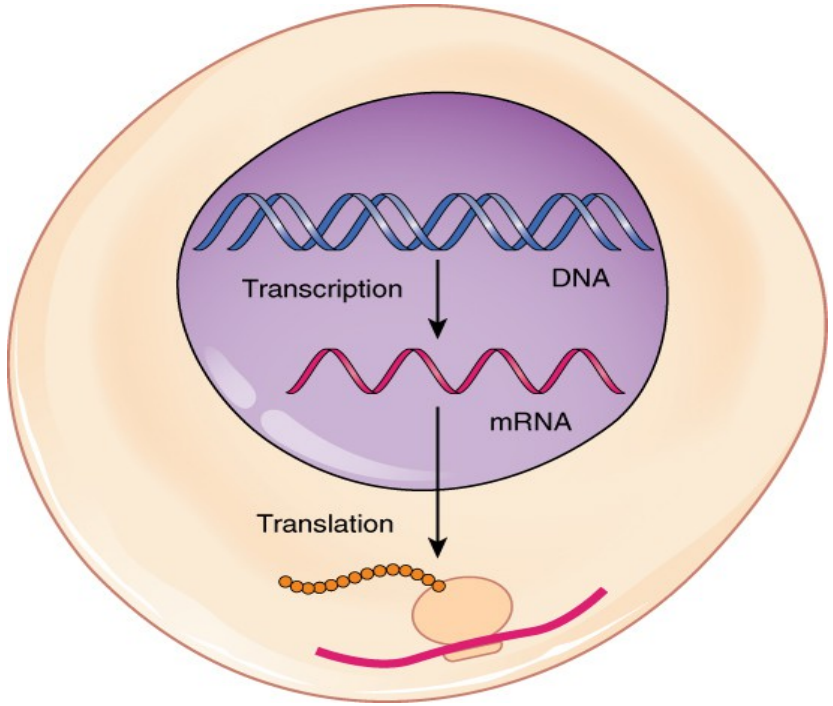
Genes code for the manufacture of proteins in two steps:

Transcription – the sequence of nucleotide bases on DNA that specify a particular protein (aka, a gene) are duplicated onto a similar molecule called messenger RNA (mRNA).

Translation – mRNA exits the nucleus of a cell and enters the cytoplasm where its base sequence codes for sequence of amino acids that comprise the primary structure of the protein coded for in DNA

Genetic expression - the sum of all steps from the activation of a gene to the manufacture of a functional protein.

The two basic steps in genetic expression

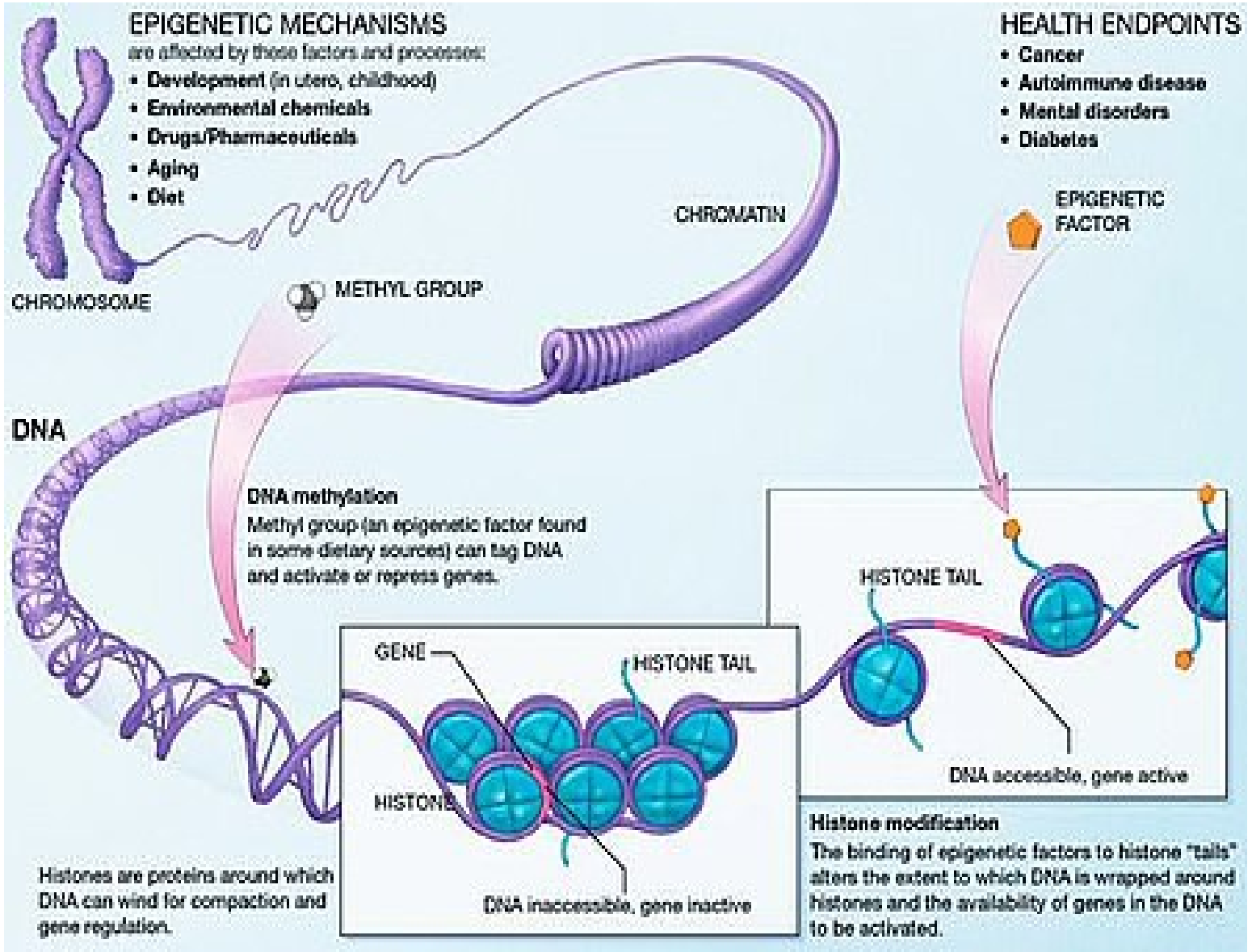


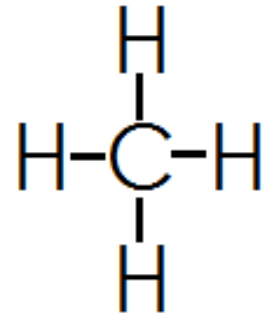
Transcription

Translation

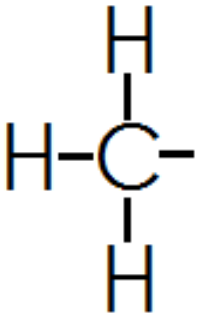
Epigenetics: Study of the structure and function of surface molecules on DNA

Alterations in gene functions that do not *directly* involve DNA sequences





methane



methyl group

Conrad Waddington, British biologist coined the term epigenetics in 1942 (before structure of DNA was known) to refer to how genes might interact with the environment.

We now know that the environment does affect genes through the actions of epigenetic molecules.

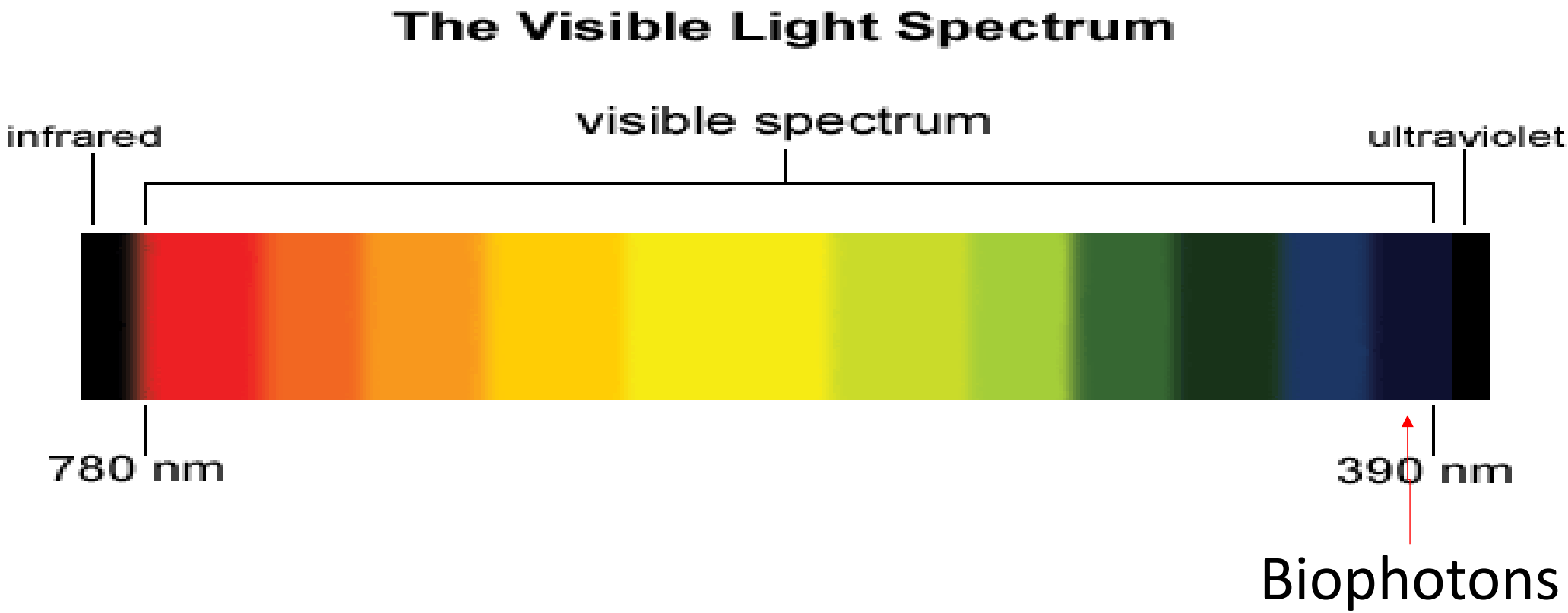
Biophotons – Photons within the light range of the electromagnetic spectrum emitted from and absorbed into living beings (Fritz-Albert Popp, 1974)

Possible mediators of:

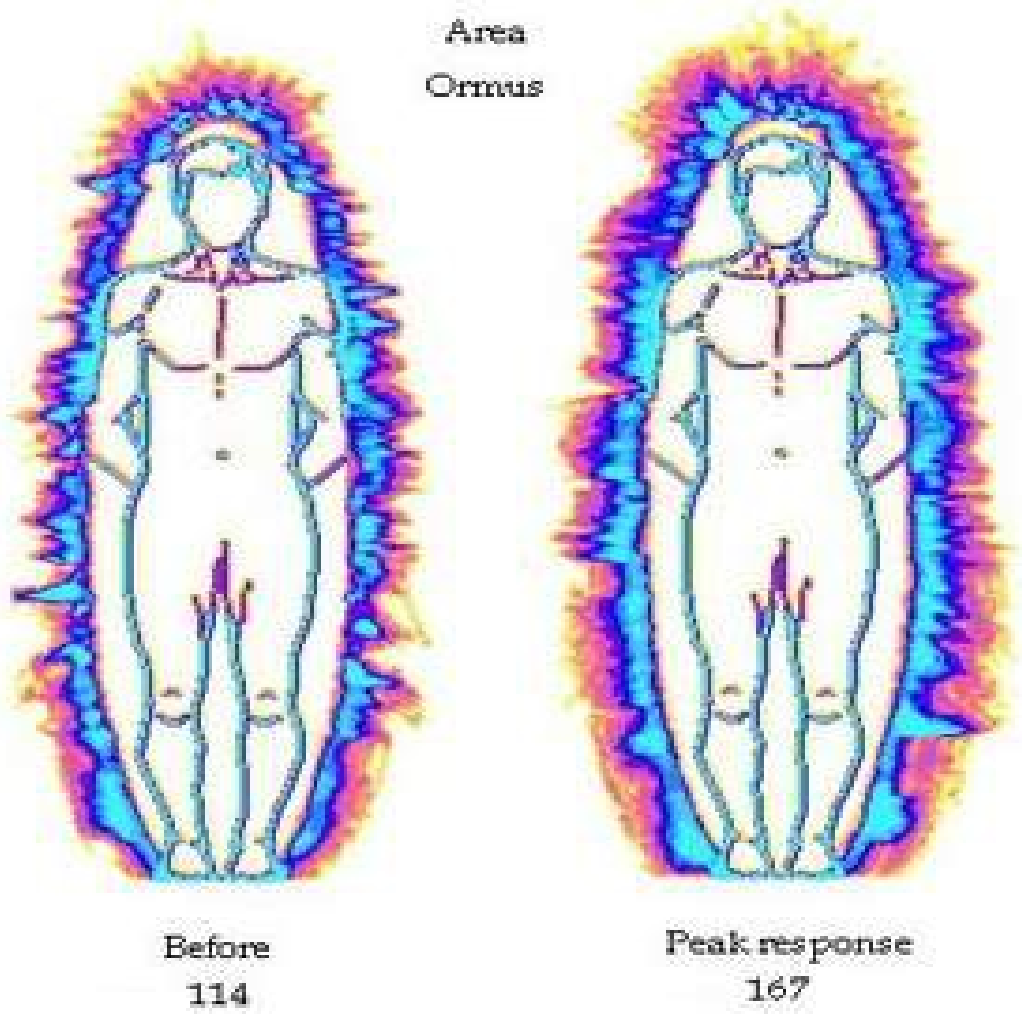
Inter-organism communication

telepathy, clairvoyance

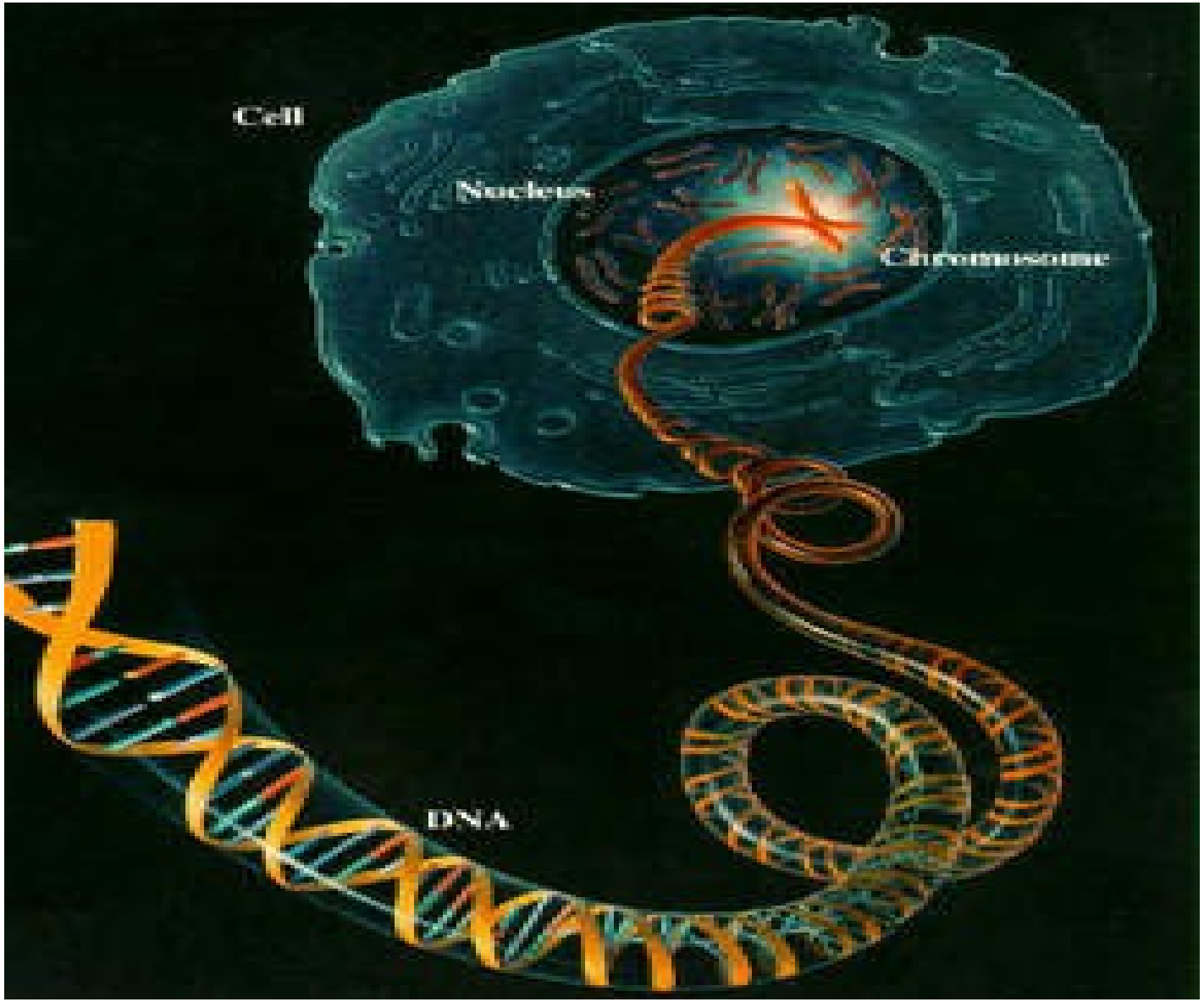
Environmental influences on genes


The Visible Light Spectrum
visible spectrum
infrared
ultraviolet
780 nm
390 nm
Biophotons

Popp's studies showed that people emit photons in the violet-ultraviolet range!



Photons are located within the DNA of cells



Biophoton mechanism of DNA response to the environment

DNA unwinds
Emits photons
Photons interact with environment
Photons from environment absorbed into an organism
Modify DNA via epigenetic molecules (eg, methyl groups)

Organisms sample and respond to the environment through photons.

Steve Horvath, UCLA biostatics developed DNA methylation analysis as a predictor of age: An epigenetic aging clock, 2013

Summary

No evidence that a specific gene evolved to promote aging

Several types of genes are involved in aging

- Genes that foster aging but don't become manifest until later in life
- Genes that retard aging by protecting against oxidative stress
  - Collectively termed longevity assurance genes
- Genes that may extend longevity by inhibiting age related disorders, such as atherosclerosis

Genetic mutations, whether they retard or promote aging, occur in response to environmental change