Aging and Mortality 0000 000000 00000000000 Evolutionary Theory of Aging

Bit String Model

Conclusion

Aging and Evolution

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1 de agosto de 2007

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Evolutionary Theory of Aging

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Aging and Mortality

- Definitions
- Facts
- Gompertz Law

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Evolutionary Theory of Aging

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Aging and Mortality

- Definitions
- Facts
- Gompertz Law
- 2 Evolutionary Theory of Aging
 - Theories
 - Special Cases of Aging

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 - Results

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Definitions				

Aging

- Ageing or aging is the process of systems' deterioration with time.
- Senescence is the combination of processes of deterioration which follow the period of development of an organism. It is a biological concept.
- **Organismal senescence** is the **aging** of whole organisms. We will use both.
- Cellular senescence, or Hayflick limit, is when normal cells lose the ability to divide.
- Why do we age? Is aging the result of fundamental limitations that apply to all living things, or because a limited life span conveys some advantage?

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Aging and Mortality

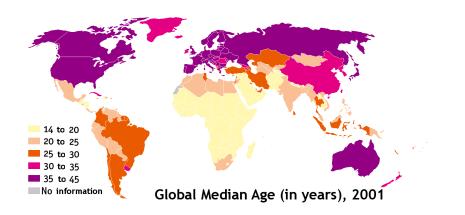
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Definitions

Median Age



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Evolutionary Theory of Aging

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Definitions

How to Measure Aging

Mortality rate, or **death rate**, is a measure of the number of deaths (in general, or due to a specific cause) in some population, scaled to the size of that population, per unit time.

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Aging and Mortality

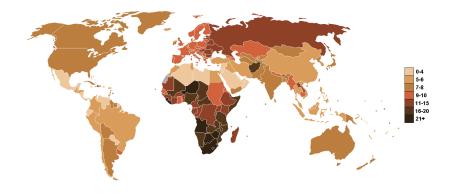
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Death Rate (deaths for 1,000)



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Summary	Aging and Mortality	Evolutionary Theory of Aging	Bit String Model	Conclusion
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Facts

Many Causes

Rank	Cause	Total deaths	%
1.	Ischaemic heart	7,208	12.6
2.	Cerebrovascular	5,509	9.7
3.	Lower respiratory infections	3,884	6.8
4.	HIV/AIDS	2,777	4.9
5.	Chronic obstructive pulmonary	2,748	4.8
6.	Diarrheal diseases	1,798	3.2
7.	Tuberculosis	1,566	2.7
8.	Malaria	1,272	2.2
9.	Cancer of trachea/bronchus/lung	1,243	2.2
10.	Road traffic accidents	1,192	2.1

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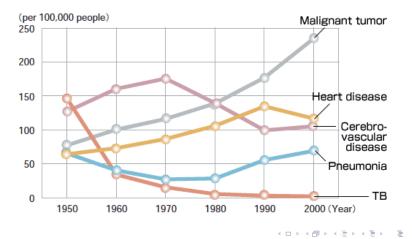
Facts

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Transition of Mortality Rates by main causes in Japan



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Facts

Aging and Mortality

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Time Evolution of Mortality Rates by Age

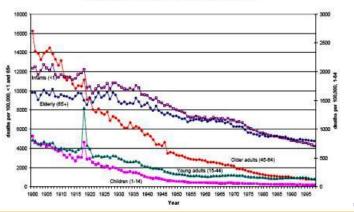


Fig. 4: All Cause Mortality by Age

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Facts

Aging and Mortality

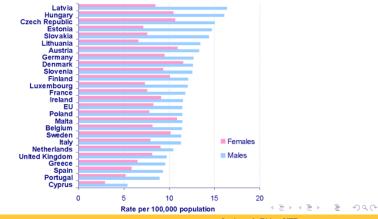
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Conclusion

Pancreatic Cancer in EU by Country and Sex

Figure 2.2: European age-standardised mortality rates, pancreatic cancer, by sex, EU, 2002



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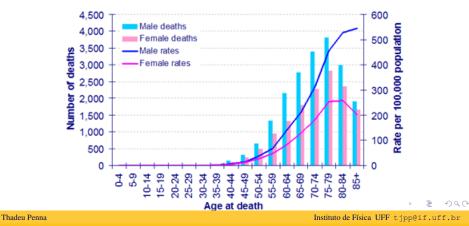
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Conclusion

Facts

Lung Cancer by Age and Sex

Figure 2.2: Number of deaths and age-specific mortality rates, lung cancer, by sex, UK, 2005



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Bit String Model

Conclusion

Facts

Aging and Physics

- Physicists do not die. We reach a maximum entropy state.
- Aging of Materials (glasses, mostly).
- We refer to biological aging.
- Aging depends on so many factors and causes.
- More a complicated system rather than a Complex system.
- So, what is the link ?

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Evolutionary Theory of Aging

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Gompertz Law

Gompertz law



Benjamin Gompertz

Gompertz - 1779, 1865

$$N(t+dt) = rN(t)\log\left(\frac{K}{N(t)}\right)$$

- *r*, growth rate
- *K*, equilibrium size
- tested on populations since 1825.

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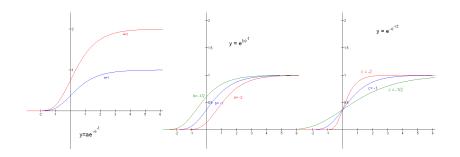
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Gompertz Curves



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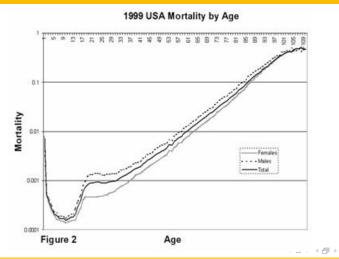
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Gompertz Law

USA mortality by age 1999



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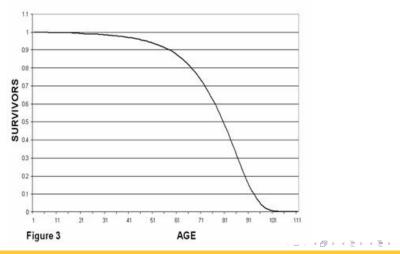
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 Evolutionary Theory of Aging

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Gompertz Law

USA survival rates by age 1999



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Evolutionary Theory of Aging

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USA mortality by age from 1901 to 1991



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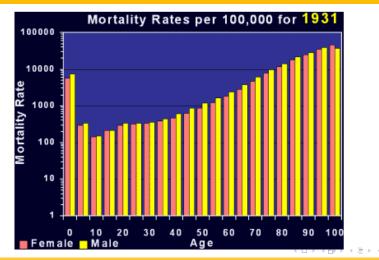
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USA mortality by age from 1901 to 1991



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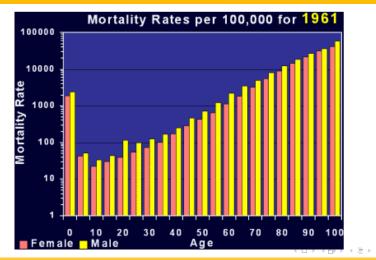
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USA mortality by age from 1901 to 1991



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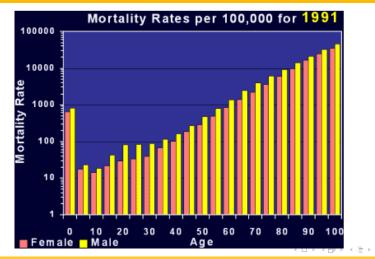
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USA mortality by age from 1901 to 1991



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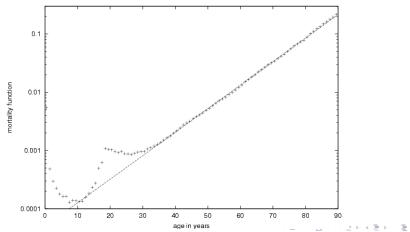
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 Evolutionary Theory of Aging

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Gompertz Law

German Mortality



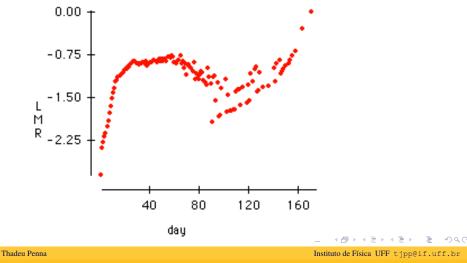
In[S(age -0.5)/S(age +0.5)] and 0.00005*exp(0.093*age)

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Summary	Aging and Mortality 0000 000000 000000000000000000000000	Evolutionary Theory of Aging 0000 000000	Bit String Model 0000 00000	
Gompertz Law				

Medflies Mortality (10⁶, 80000, 70000), days (1,35,36).

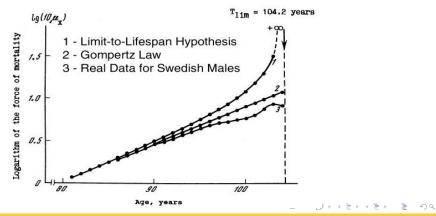


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Gompertz Law				

The Oldest Old

Mortality at Advanced Ages



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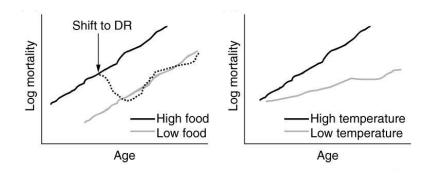
Gompertz Law

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Dietary restrictions and Temperature variations



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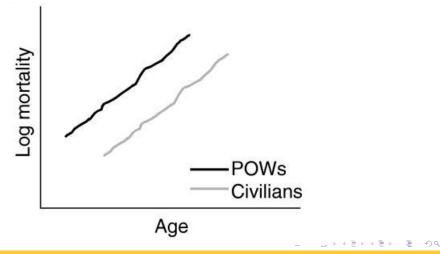
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Australian on the 2nd War



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Gompertz Law				

Universality ?

- Lifespan is dependent on the species but is roughly the same on similar species.
- More important, the exponential behavior of the mortalities is quite robust. Although mortalities rates depend on the time, cultural aspects (including nutrition), sex, races, etc.; under very different circumstances, the mortality grows exponentially with age
- Notable exceptions are the "oldest old" survivors (humans and flies). There is no reliable statistics of other species.
- Evolution is a clue. Physicists know how to do it.

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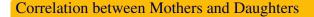
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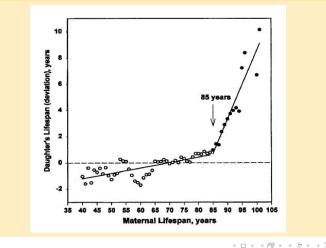
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Theories

Programmed Death

- **Programmed Death**, *Weismann* (1834 1914) : removing older members by programmed death provided more resources for the youngers (assumedly more evolved).
- Pro: it explained the inter-species differences in life span.
- Con: a trait has to be expressed in such a way that it affects survival or reproduction.
- if an individual die before the programmed death, it will not affect natural selection.

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Theories

Damage Accumulation

- damage to DNA
- poisonous byproduct of life processes
- limit on the number of divisions
- Aging is a defect

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An Unsolved Problem on Biology



Mutation Accumulation Theory

- the force of natural selection decreases once an organism reaches an age where it has had some opportunity to reproduce.
- random mutations causing adverse aging characteristics.
- ties aging to sexual maturity and reproduction

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Antagonistic Pleiotropy Theory



- Pleiotropy, Natural Selection, and the Evolution of Senescence
- Pleiotropy: a single allele or form of a gene (see Genetics) may affect more than one trait.
- combined effect of many pleiotropic genes that each had a beneficial effect in an animal's youth but had an adverse side effect in older

age.

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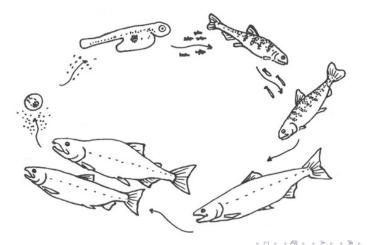
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Special Cases of Aging

Salmon Catastrophic Senescence



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Babys



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Special Cases of	Aging			

Other questions

• Humans have 2 sets of teeths. Elephants have six. What no more? Programmed death?

- Benefitial mutations are difficult.
- Canine longevity: wild animals tend to have both longer times to develop to sexual maturity and longer life spans. Larger dogs have shorter lifespan than the smaller breeds.
- Progeria: individuals usually die by age 14.
- Im summary, is aging a bug or a feature ?

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Definition				

Journal of Statistical Physics, Vol. 78, Nos. 5/6, 1995

A Bit-String Model for Biological Aging

T. J. P. Penna¹

Received September 14, 1994

We present a simple model for biological aging. We study it through computer simulations and fint it to reflect some features of real populations.

KEY WORDS: Aging, Monte Carlo simulations.

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Aging and Mortality 0000 000000 0000000000000000 Evolutionary Theory of Aging

Bit String Model

Conclusion

Definition



- Time is discrete.
- Each individual will be represented by a string of bits
- The string is not the genotype but a temporal reading of it.
- It matters **when** a mutation become active and not if it is present on the genotype.
- There is a limit on the number of active mutations (individuals will die)
- Individuals will reproduce at age *R*, newborns will have the same temporal genotype and additional mutations.

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Evolutionary Theory of Aging

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Bit String Model

Conclusion

Definition



- We start with a population with random genotypes.
- We test if the individual survives with a few active mutations
- We test if survives to a food and space limitation
- Can it reproduce ?
- Its age is then increased
- Repeat for many steps

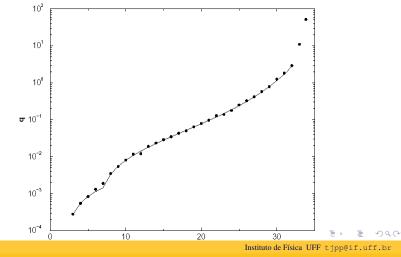
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Results				

Mortality

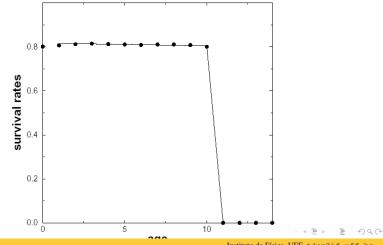


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Results				

Salmon



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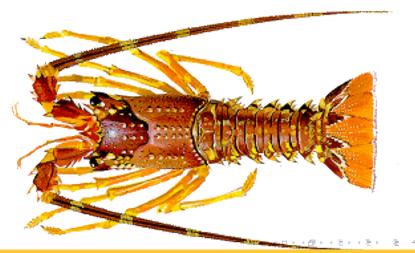
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Lobsters



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Results				
Lobste	rs			

• Fertility (cabo-verde "Panulirus laevicaudas"):

$$b(i) \sim 1 - \exp(-0.171 \, i)^{2.86}$$

- Fertility is proportional to its weight
- Only 3 eggs reach maturity age
- Fishing is $\approx 65\%$ of the stock.
- We proposed a new rule for lobster catching: save the older ones

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Simulation



T.J.P. Penna et al. | Physica A 295 (2001) 31-37

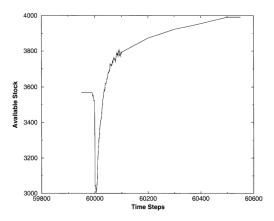


Fig. 1. Stock of lobsters at function of the time ("years"). After 60000 time steps, a maximum age for catching equal to 12 is imposed. The stock decreases at the very first years of regulation but it fastly

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Results				

- Optimal limit: 12 years old (to save 5%)
- The lifespan of the lobsters is increased (22 yrs)
- They are genetically fitter.
- It is hard to convince the fishmen
- Huge lobsters are not the tastier ones.

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What next?

- The model is extremely simple and easily extensible
- Should be use for any problem where age plays a role.
- 200 papers using it, but
- ... a few analytical ones (Coe and Mao, PRL)
- ... a few papers on predictions and ecological situation
- speciation ?
- why sex ?
- AIDS and therapy
- space reserved for your contribution

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