Getting Older
Monte Carlo Simulations of Biological Aging

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Overview

Purpose:
Discussion on the Mutation Accumulation theory of biological aging, based on the accumulation of random mutations and evolutionary population dynamics

- Simple Mutation Model

- Penna Bit-string Model

- Other Applications of the Penna Model

Introduction

"Out of chaos comes order" - Nietzsche

- Darwinistic selection produces *order*

- Biological mutations due to copying errors during DNA replication produce *disorder*

- Consider a living system where

  – Selection of the fittest eliminates many mutations

  – Newly generated mutations are random

Introduction - cont'd

- Three Cases:

  1. A mutation kills us *before* child-bearing age; no mutation is passed to any offspring

  2. A mutation kills us *during* child-bearing age; selection pressure eliminates most mutations from population

  3. A mutation kills us *after* child-bearing age; mutation stays in the population

- Even though new mutations occur randomly for all ages, accumulated mutations predominantly affect us in old age

Biological aging is organized.

Background

- There are many theories of biological aging
- Many theories previously assumed a priori that time-independent population exists
- Problem: Previous theories could not explain how mutational meltdown is avoided by nature
- Solution: Use Monte Carlo simulation to look at changing populations and their time decay to zero

Mutation Accumulation Theory

After many generations, the mutations at old age will be much more numerous that those active at young age.

Key Assumption:
All mutations are bad and hereditary

- Rare, good mutations are neglected

- No somatic mutations

A Basic Mutation Model - *mutation.f*

Purpose: To explore the effects of hereditary mutations

Variables:

npop	:	population
mchild	:	no. of children of ea. survivor
s	:	individual yearly survival probability
surviv	:	array of *s*
eps	:	percentage decrease of *s*
asp	:	average survival probability

Assumptions:

1. Bad mutation reduces *s* by *eps*

2. Deterministic birth

3. All individuals start at unity

4. Effects of aging ignored

A Basic Mutation Model - cont'd

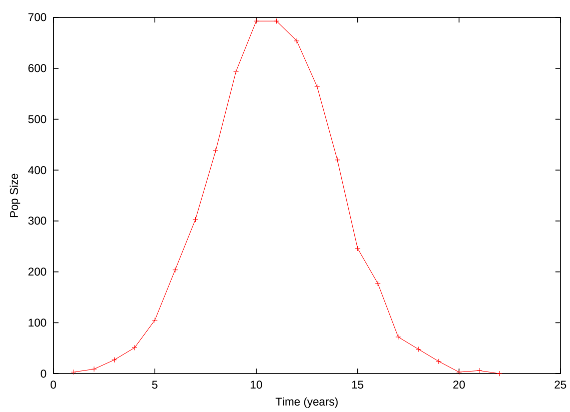
Algorithm:

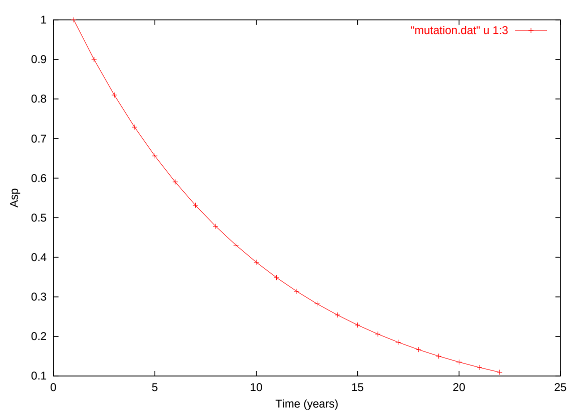
```
while(npop < maxpop && npop > 0) {
   asp = 0.0;
   icount = 0;
   for(i = 1; i <= npop; i++) {
       s = surviv[i];
       asp = asp + s;
       if(rand(0) < s) {
           icount++;
           surviv[icount] = s * (1.0 - eps);
       }
   }
   asp = asp / npop;
   npop = icount;
   for(i = npop; i >= 1; i--)
       for(j = mchild; j >= 1; j--)
           surviv[i+mchild+j-mchild] = surviv[i];
   npop = npop * mchild;
}
```

A Basic Mutation Model - cont'd

Case 1: Entire population subject to mutation each year

`init pop`	$= 1$	`mchild`	$= 3$
`eps`	$= 0.10$	`seed`	$= 123456789$



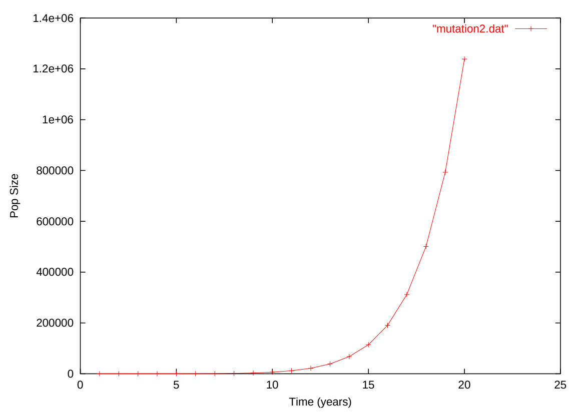


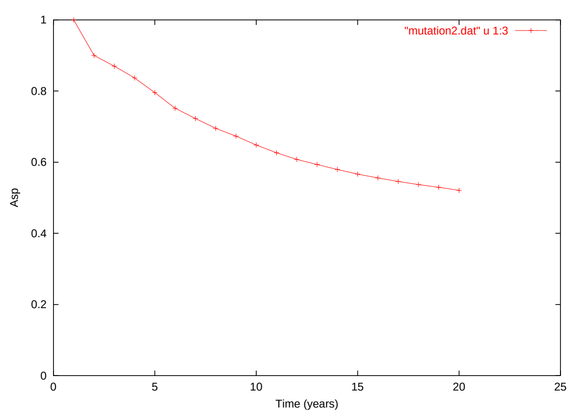
Population decays to 0 because $asp < 1/mchild$

A Basic Mutation Model - *mutation.f*

Case 2: Half the population escapes mutation

`init pop`	= 1	`mchild`	= 3
`eps`	= 0.10	`seed`	= 123456789





A Basic Mutation Model - cont'd

We can avoid mutational meltdown by:

1. Allowing a finite fraction of population to escape completely

2. Use Poisson distribution for the number of mutations instead of assuming that each individual has 0 or 1 mutation with equal probability

Penna Bit-string Model - *penna.f*

Purpose: To provide a mechanism that avoids mutational meltdown

- First model to reproduce Gompertz's law, which states that adult mortality increases exponentially with age

- Most widespread model used to simulate biological aging

Ways an individual can die:

1. Hereditary disease

2. Hunger

3. Lack of space

Penna Bit-string Model - cont'd

Reproduction: step-by-step

- 1 year = 1 bit in a 32-bit string
- A bit set to 1 = disease
- A bit set to 0 = good health
- The individual dies after the third bit is set
- At each time interval (one year), every surviving individual beyond reproductive age (*minage*) gives birth to one child with probability *pbirth*
- The child does not necessarily have more mutations than the parent

Penna Bit-string Model - cont'd

Results:

- Bits for old age were set
- Bits for young age were mostly 0
- After 1000 yrs, dangerous mutations occur everywhere

Two ways to escape mutational meltdown:

1. Mutations take effect *after* inidividuals have already reproduced
2. If the randomly selected bit in a child has already been set, another bit to set is not searched for

Other Applications of Penna

1. Medflies become healthier at old age; (only about 1% of the medflies survive to the age where healthy effects showed up

2. Northern cod drop in population in Canada possibly due to overfishing

3. Pacific Salmon

Conclusions

- Sex is difficult
  - Sexual reproduction involves the recombination of a random fraction of the genes from the father and mother
  - There are cases where the population dies out asexually and flourishes sexually

Conclusions - cont'd

- The Penna model is pretty good
  - Conforms to the exponential increase corresponding to Gempertz's law of human populations
  - Provides a loophole for escaping bad mutations and thus avoiding mutational meltdown
  - Has many applications
  - Helps us avoid unrealistic assumptions, such as constant populations
  - Supports the Mutation Accumulation theory, but does not claim that mutation accumulation is the main reason for aging