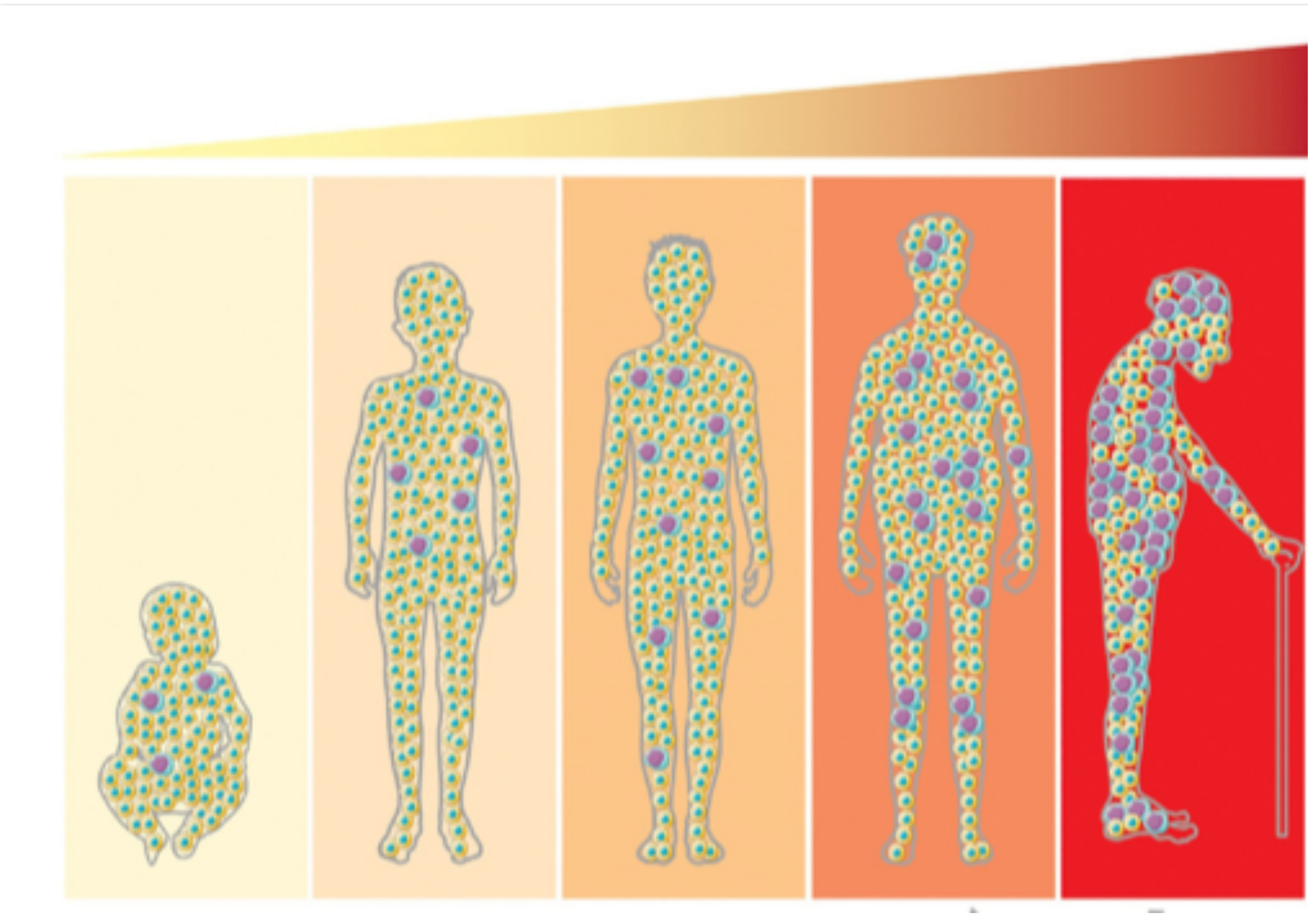
Part I - Ageing

What is ageing?
aka senescence

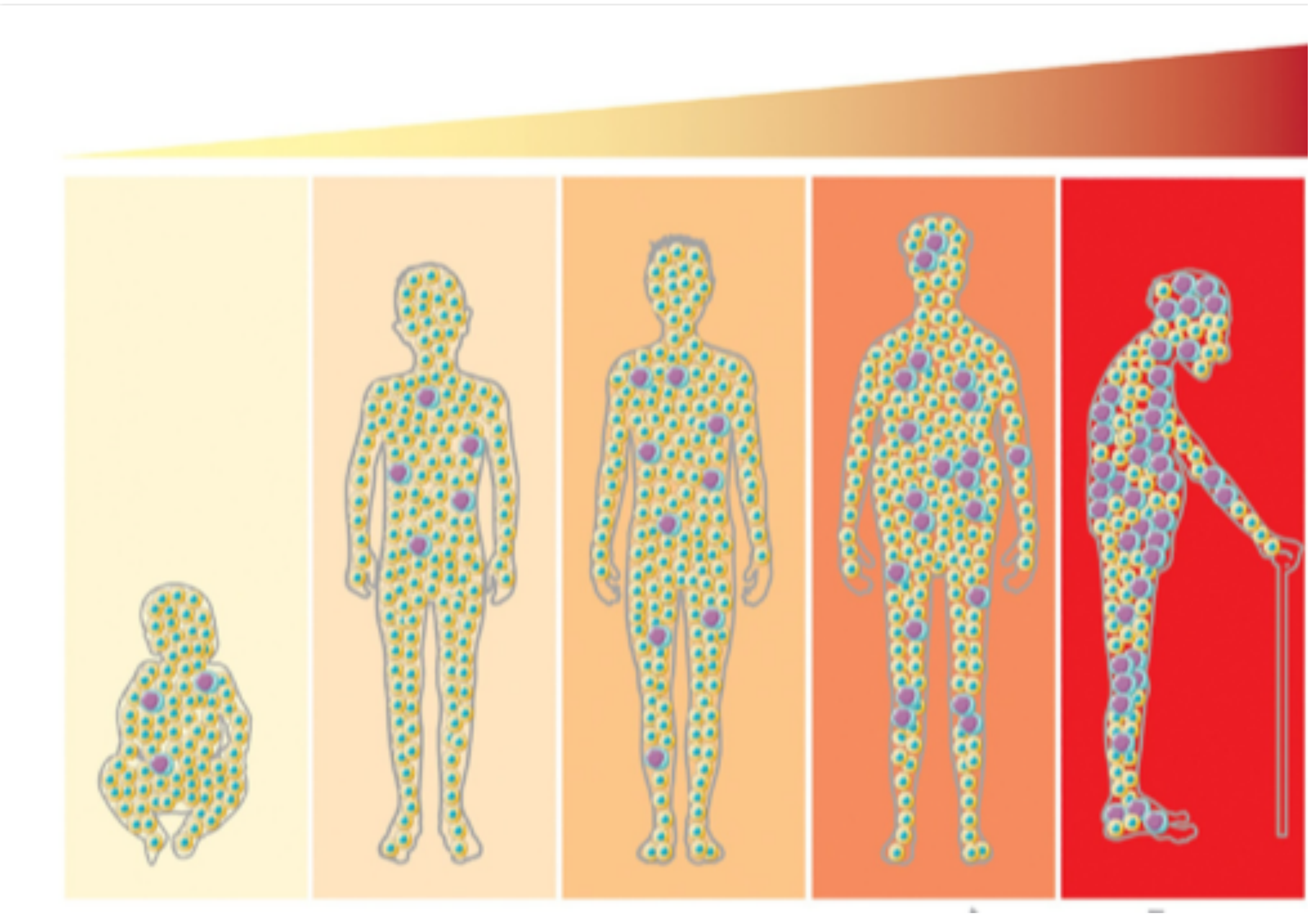
- Gradual deterioration of function.



Trends in Cell Biology 2020 30777-791DOI: (10.1016/j.tcb.2020.07.002)

What is ageing?
aka senescence

- Gradual deterioration of function.
- Decrease in survival rate and/or fecundity with age.



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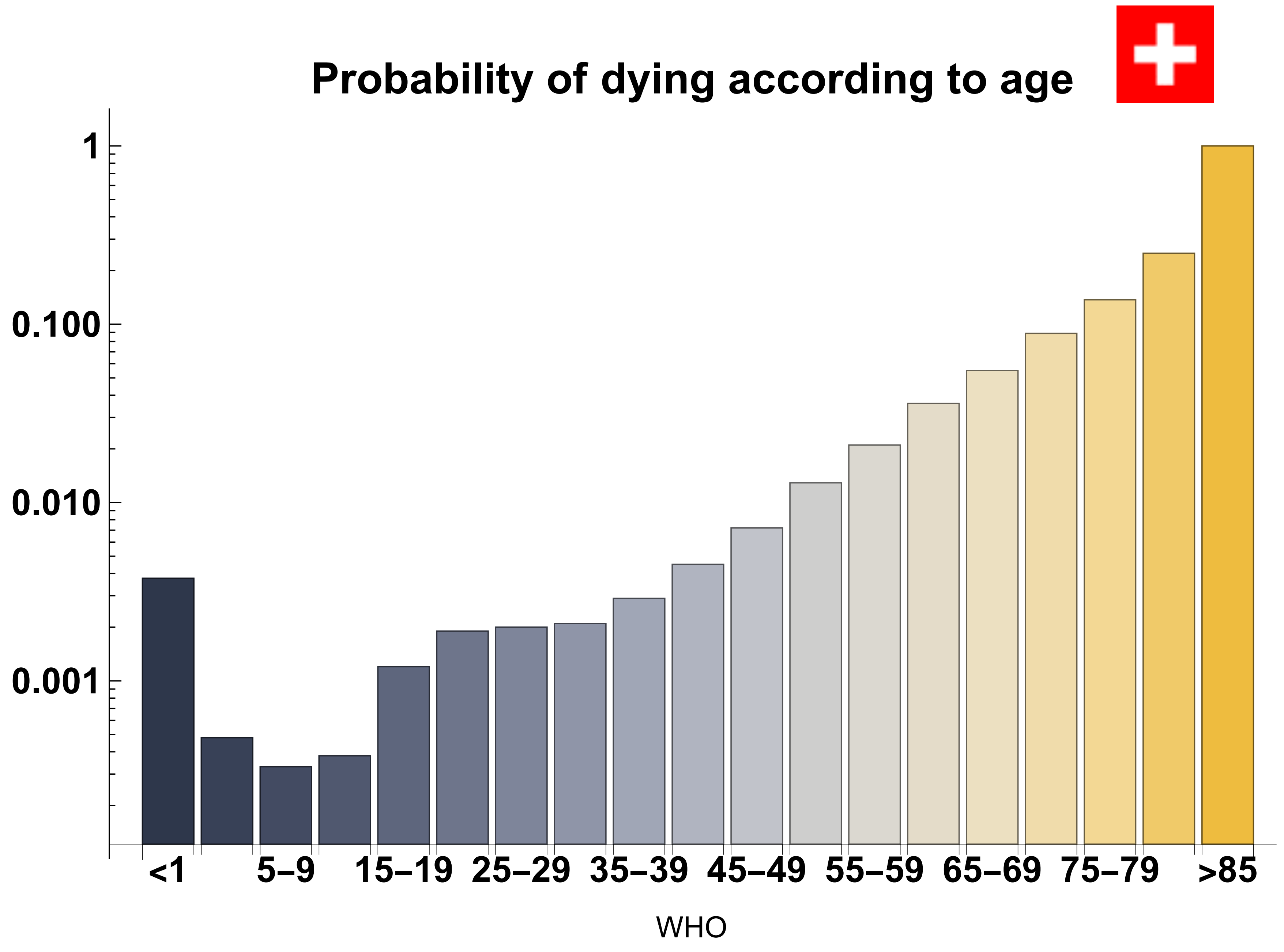
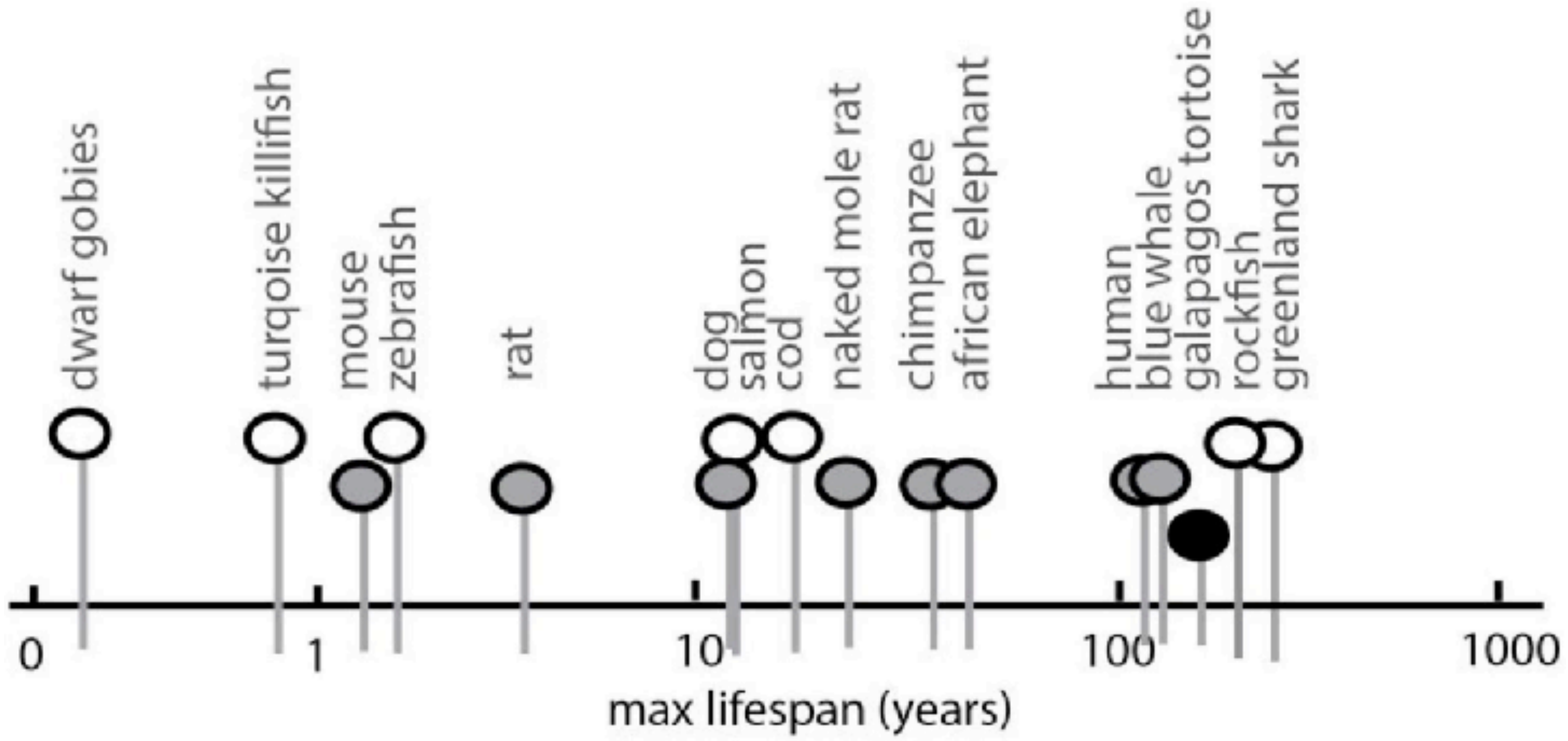


Natural variation in ageing

and lifespan



Treaster S, Karasik D andHarris MP (2021 Front. Genet. 12:678073.doi: 10.3389/
fgene.2021.678073

Natural variation in ageing

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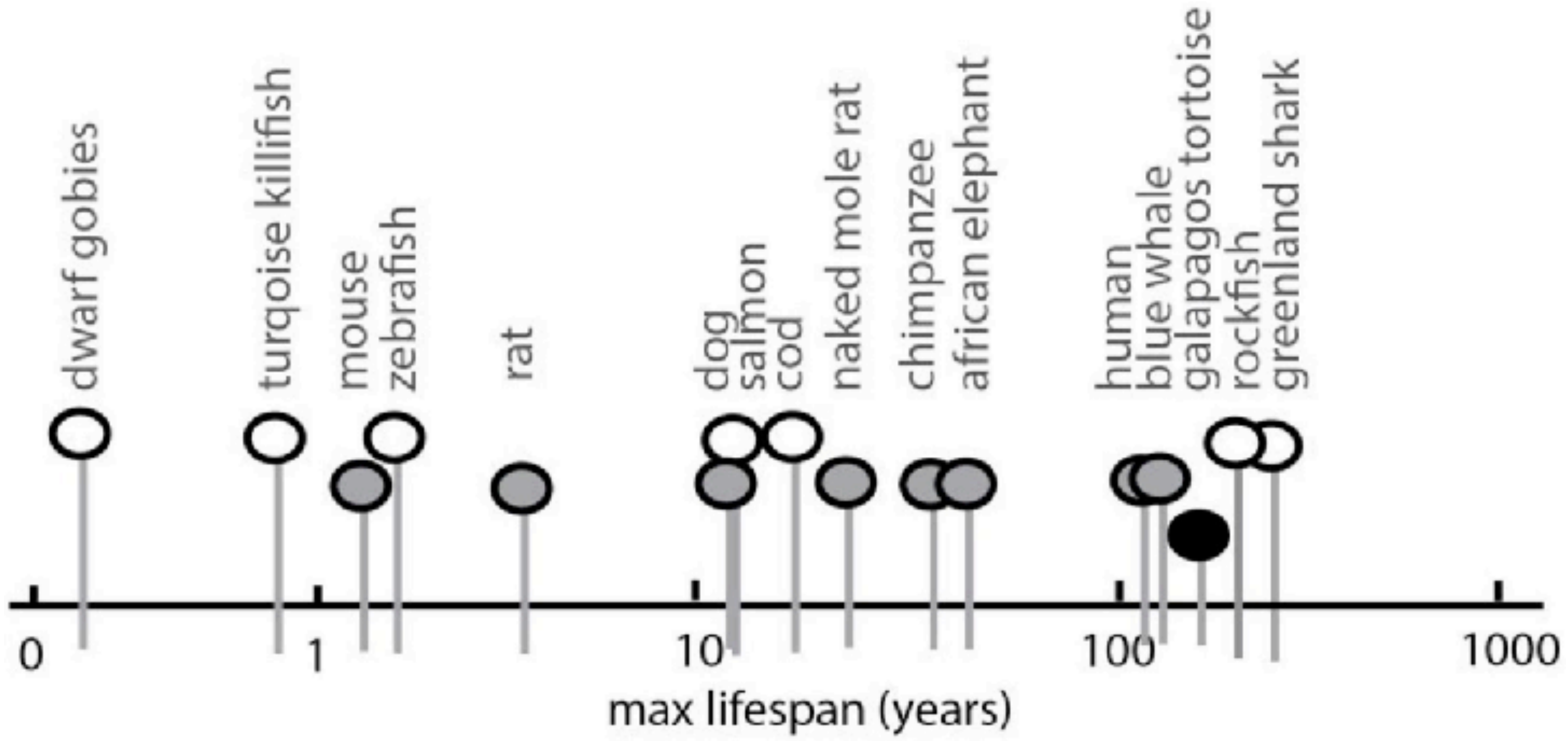

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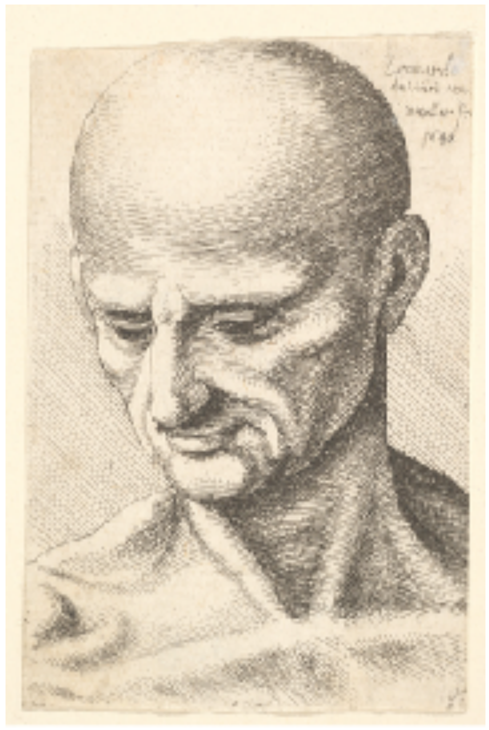
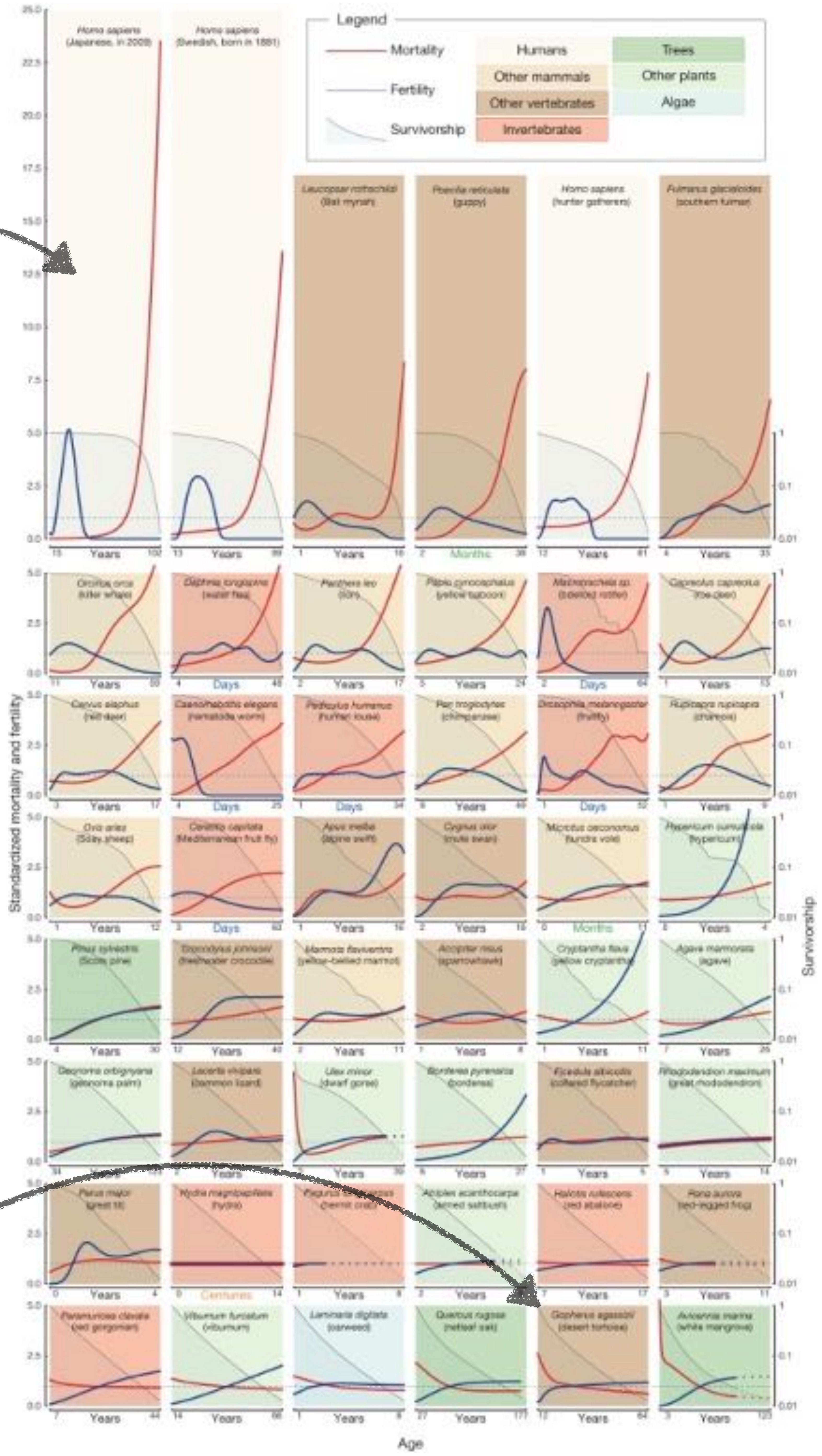


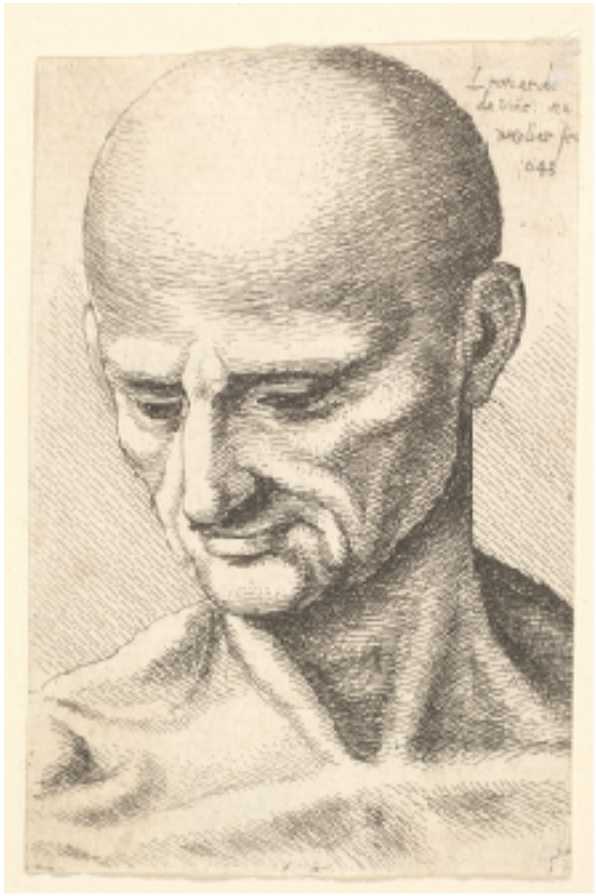
Homo sapiens

Gopherus agassizii
(desert tortoise)



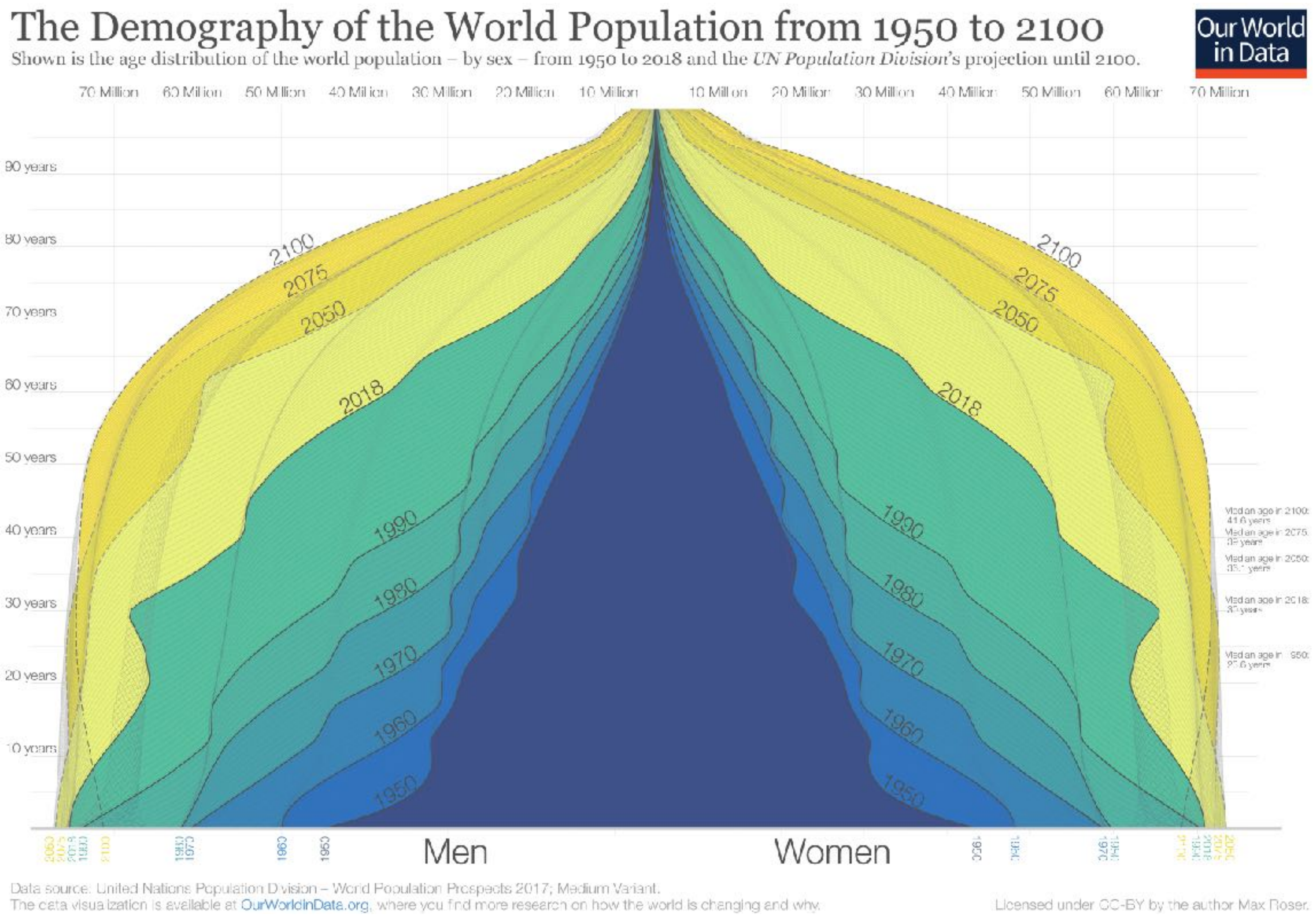
Jones *et al. Nature* **000**, 1-5 (2013) doi:10.1038/nature12789

Why do some species age while others seem not to?



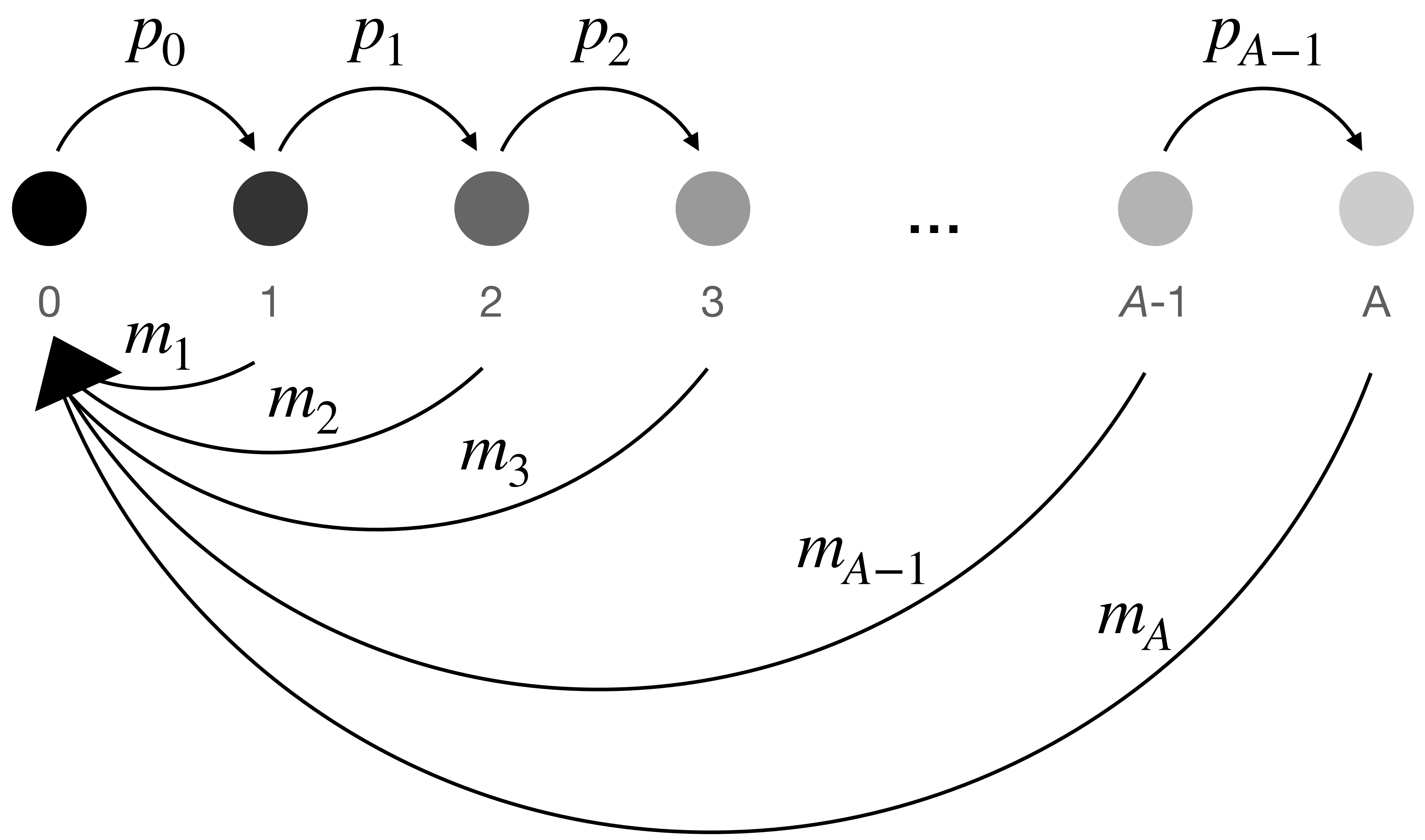
Modelling age structure

Dynamics of an age-structured population



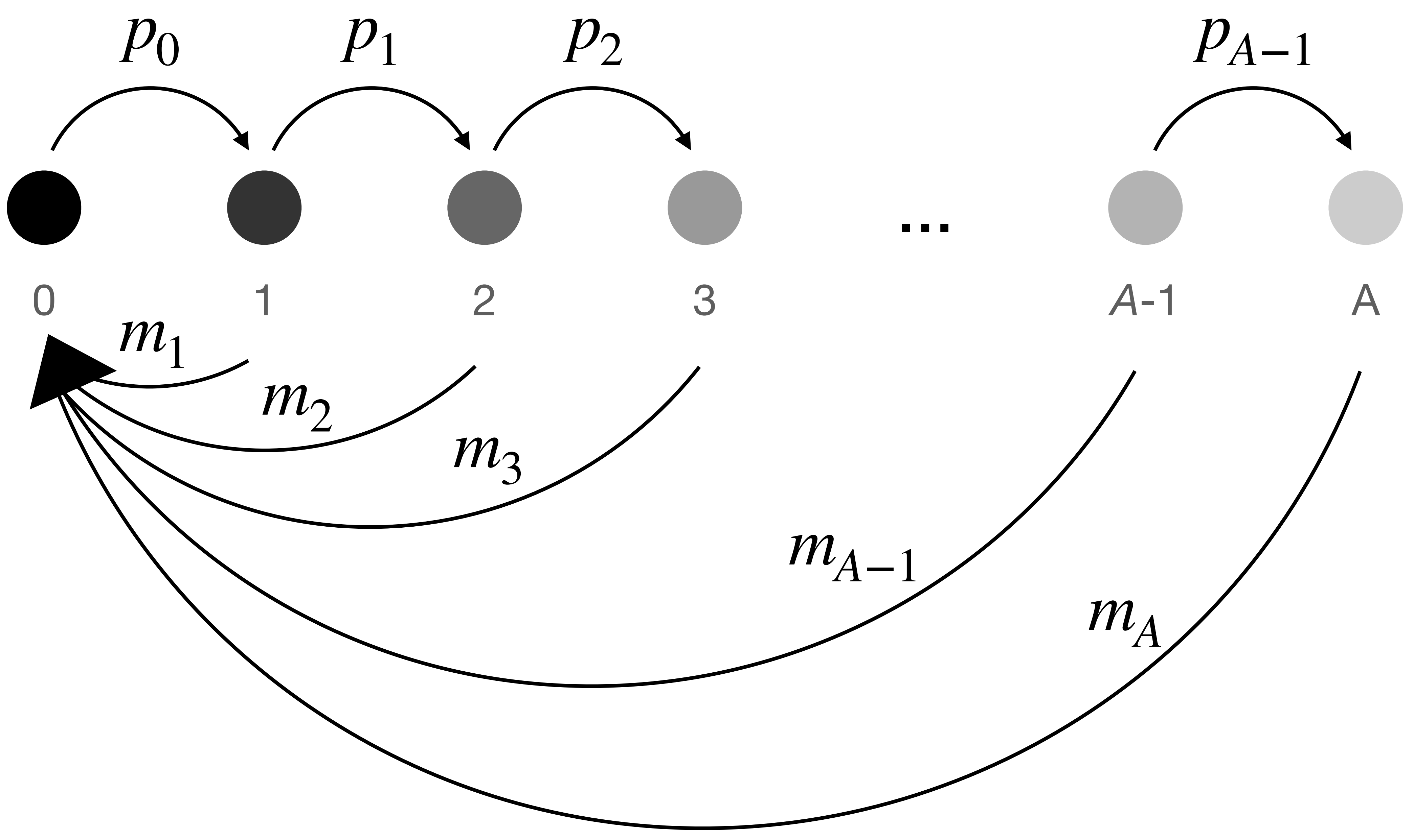
Dynamics of an age-structured population

- $n_{a,t}$ = n. of individuals of age *a* at time *t*
- p_a = probability of survival from age *a* to *a*+1
- m_a = fecundity at age *a* (i.e. number of newborns)
- $f_a = p_0 m_a$ = effective fecundity at age *a* (i.e. number newborns that survive to age 1, with probability p_0)



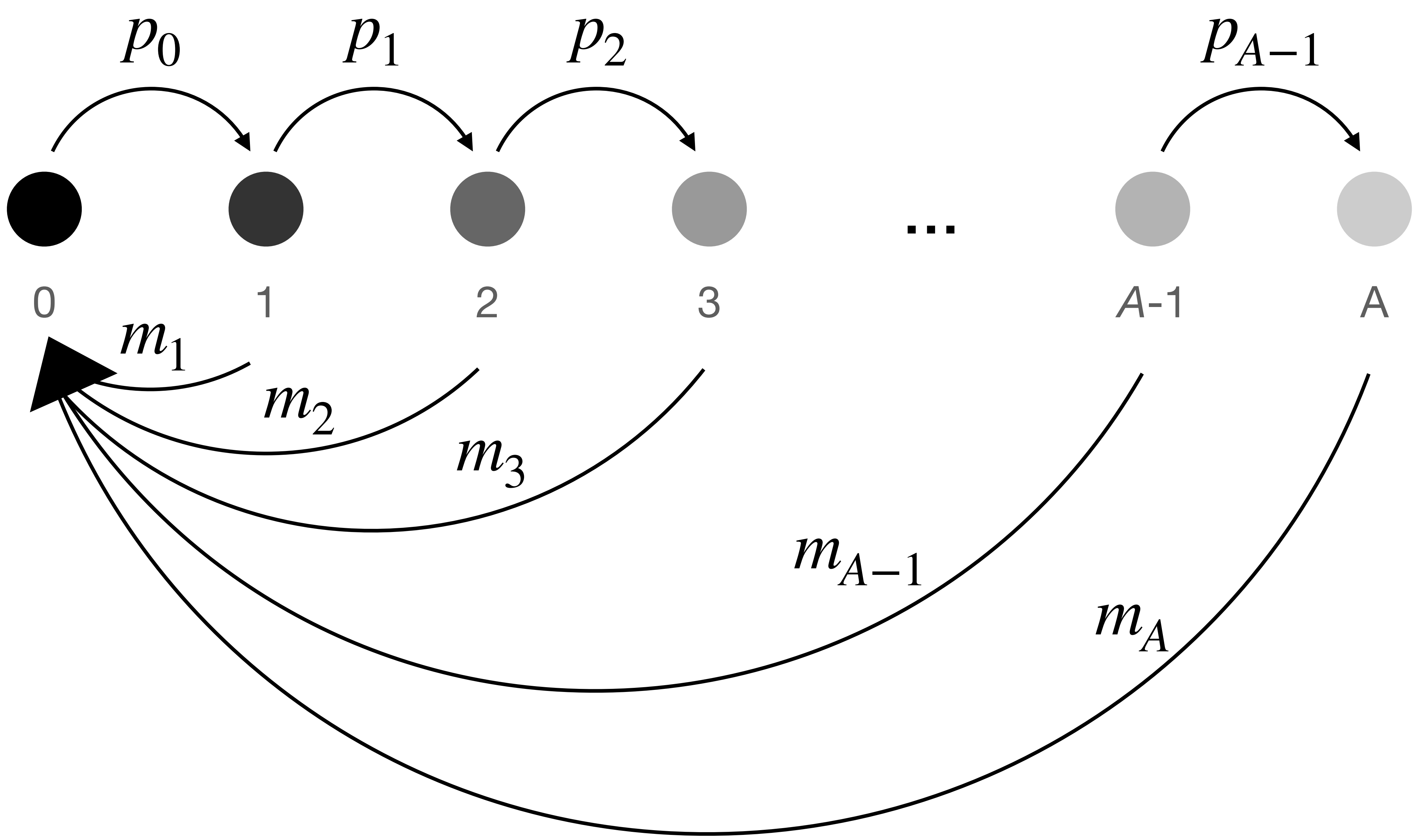
Dynamics of an age-structured population

$$n_{1,t+1} =$$



Dynamics of an age-structured population

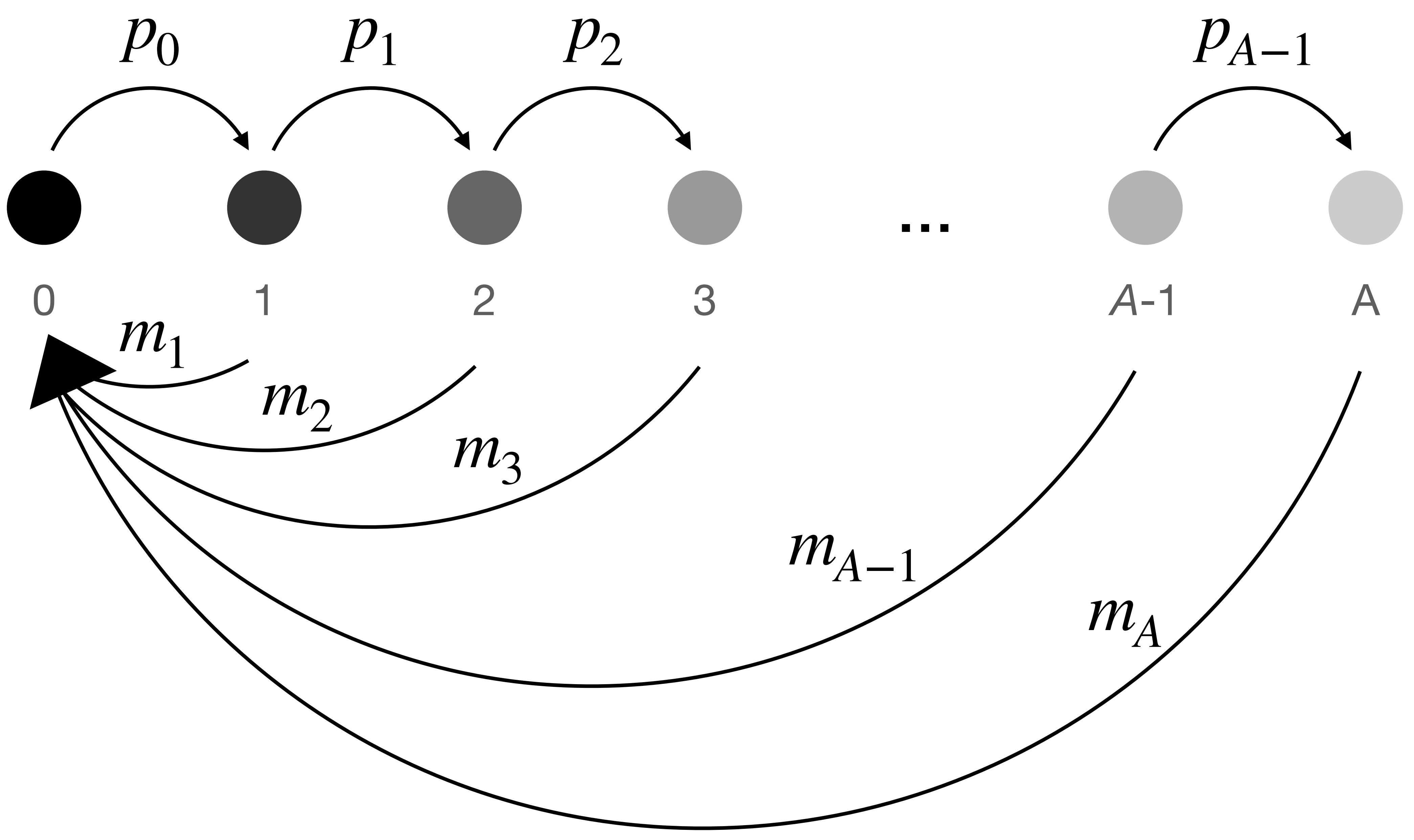
$$n_{1,t+1} = \sum_{a=1}^{A} \overset{p_0 m_a}{f_a} n_{a,t}$$



Dynamics of an age-structured population

$$n_{1,t+1} = \sum_{a=1}^{A} \overset{p_0 m_a}{f_a} n_{a,t}$$

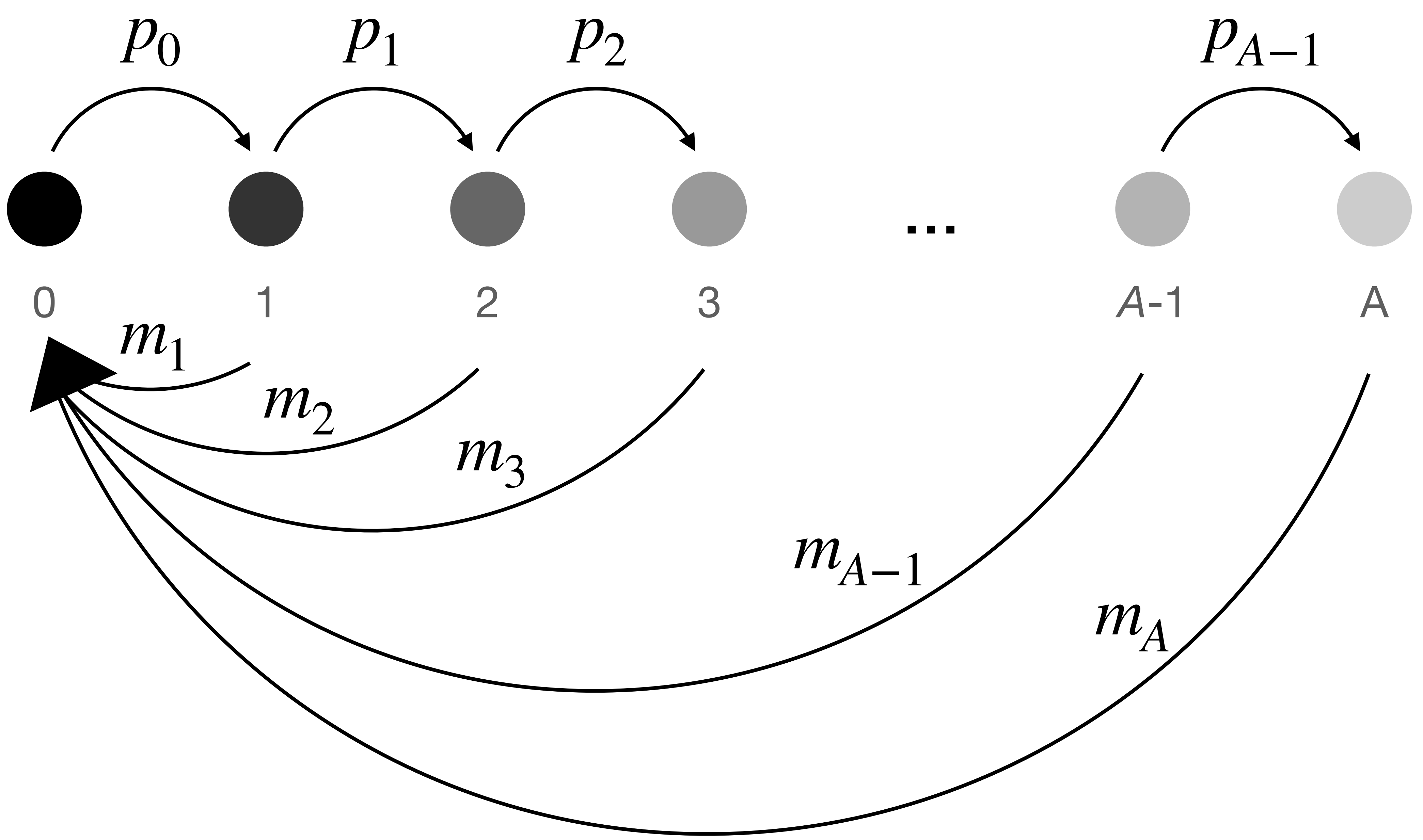
$$n_{a+1,t+1} =$$



Dynamics of an age-structured population

$$n_{1,t+1} = \sum_{a=1}^{A} \underbrace{f_a}_{p_0 m_a} n_{a,t}$$

$$n_{a+1,t+1} = p_a n_{a,t} \text{ for } a = 1, 2, \ldots, A\text{-}1$$



$$(A\boldsymbol{v})_j = \sum_i a_{ij} v_i$$

$$(AB)_{ik} = \sum_j a_{ij} b_{jk}$$

Leslie Matrix

$p_0 m_a$

$$n_{1,t+1} = \sum_{a=1}^{A} f_a n_{a,t}$$

$n_{a+1,t+1} = p_a n_{a,t}$ for a = 1, 2, ..., A-1

$$\boldsymbol{n}_t = \begin{pmatrix} n_{1,t} \\ n_{2,t} \\ n_{3,t} \\ \vdots \\ n_{A-1,t} \\ n_{A,t} \end{pmatrix} \qquad \boldsymbol{L} = \begin{pmatrix} f_1 & f_2 & f_3 & \dots & f_{A-1} & f_A \\ p_1 & 0 & 0 & \dots & 0 & 0 \\ 0 & p_2 & 0 & \dots & 0 & 0 \\ 0 & 0 & p_3 & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \dots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & p_{A-1} & 0 \end{pmatrix}$$

$$\boldsymbol{n}_{t+1} = \boldsymbol{L}\boldsymbol{n}_t$$

Asymptotic behaviour

$$\boldsymbol{n}_{t+1} = L\boldsymbol{n}_t$$

$$\boldsymbol{n}_1 = L\boldsymbol{n}_0$$

$$\boldsymbol{n}_2 = L\boldsymbol{n}_1 = L^2\boldsymbol{n}_0$$

$$\boldsymbol{n}_3 = L\boldsymbol{n}_2 = L^3\boldsymbol{n}_0$$

$$\vdots$$

$$\boldsymbol{n}_t = L^t\boldsymbol{n}_0$$

Asymptotic behaviour

$$
L = \begin{pmatrix}
0.32 & 0.57 & 0.57 & 0.57 & 0.57 & 0.57 & 0.57 \\
0.46 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0.77 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0.65 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0.67 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0.64 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0.88 & 0
\end{pmatrix}
$$

$$\boldsymbol{n}_{t+1} = L\boldsymbol{n}_t$$

$$\boldsymbol{n}_1 = L\boldsymbol{n}_0$$

$$\boldsymbol{n}_2 = L\boldsymbol{n}_1 = L^2\boldsymbol{n}_0$$

$$\boldsymbol{n}_3 = L\boldsymbol{n}_2 = L^3\boldsymbol{n}_0$$

$$\vdots$$

$$\boldsymbol{n}_t = L^t\boldsymbol{n}_0$$

Age *a* (years)	p_a	m_a	f_a
0	0.25		
1	0.46	1.28	0.32
2	0.77	2.28	0.57
3	0.65	2.28	0.57
4	0.67	2.28	0.57
5	0.64	2.28	0.57
6	0.88	2.28	0.57
7		2.28	0.57

Exponential increase

$$L = \begin{pmatrix} 0.32 & 0.57 & 0.57 & 0.57 & 0.57 & 0.57 & 0.57 \\ 0.46 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0.77 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0.65 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0.67 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0.64 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0.88 & 0 \end{pmatrix}$$

$$\boldsymbol{n}_{t+1} = L\,\boldsymbol{n}_t$$

$$\boldsymbol{n}_1 = L\boldsymbol{n}_0$$

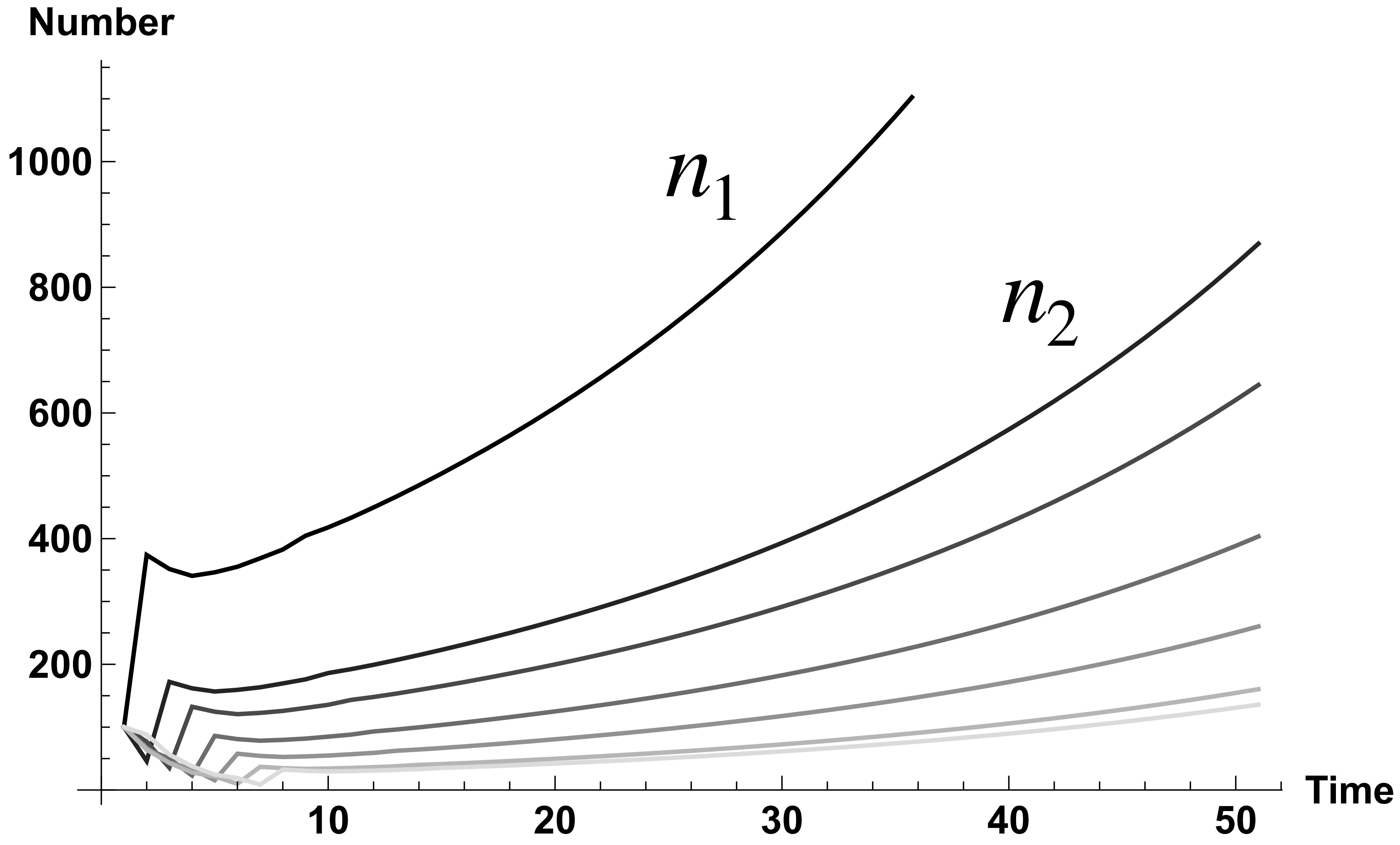
$$\boldsymbol{n}_2 = L\boldsymbol{n}_1 = L^2\boldsymbol{n}_0$$

$$\boldsymbol{n}_3 = L\boldsymbol{n}_2 = L^3\boldsymbol{n}_0$$

$$\vdots$$

$$\boldsymbol{n}_t = L^t\boldsymbol{n}_0$$

Age *a* (years)	p_a	m_a	f_a
0	0.25		
1	0.46	1.28	0.32
2	0.77	2.28	0.57
3	0.65	2.28	0.57
4	0.67	2.28	0.57
5	0.64	2.28	0.57
6	0.88	2.28	0.57
7		2.28	0.57



Extinction

$$\boldsymbol{n}_{t+1} = L\,\boldsymbol{n}_t$$

$$\boldsymbol{n}_1 = L\boldsymbol{n}_0$$

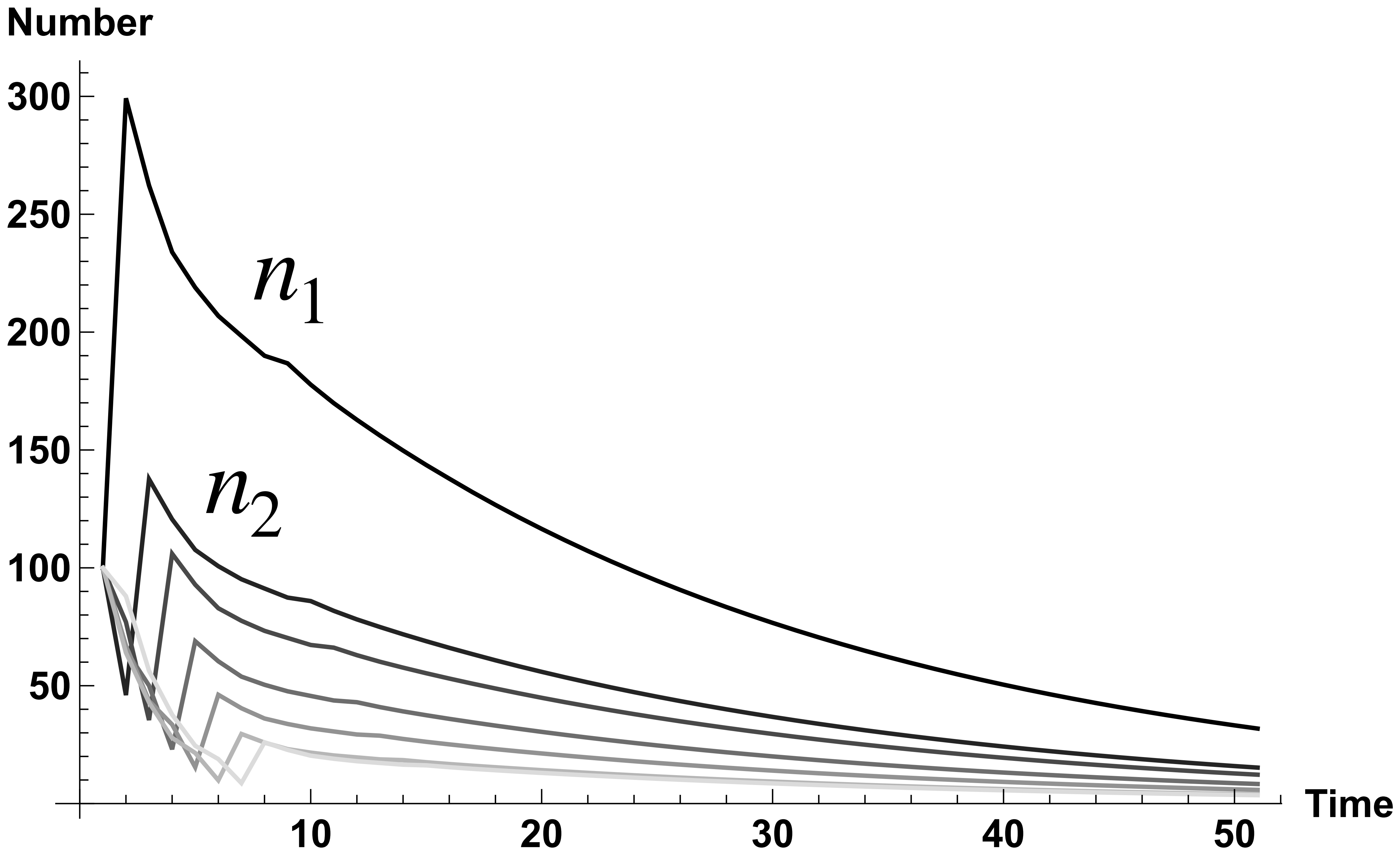
$$\boldsymbol{n}_2 = L\boldsymbol{n}_1 = L^2\boldsymbol{n}_0$$

$$\boldsymbol{n}_3 = L\boldsymbol{n}_2 = L^3\boldsymbol{n}_0$$

$$\vdots$$

$$\boldsymbol{n}_t = L^t\boldsymbol{n}_0$$

Age a (years)	p_a	m_a	f_a
0	~~0.25~~ 0.2		
1	0.46	1.28	0.256
2	0.77	2.28	0.456
3	0.65	2.28	0.456
4	0.67	2.28	0.456
5	0.64	2.28	0.456
6	0.88	2.28	0.456
7		2.28	0.456



Stable age distribution

$$\boldsymbol{n}_{t+1} = L\boldsymbol{n}_t$$

$$\boldsymbol{n}_1 = L\boldsymbol{n}_0$$

$$\boldsymbol{n}_2 = L\boldsymbol{n}_1 = L^2\boldsymbol{n}_0$$

$$\boldsymbol{n}_3 = L\boldsymbol{n}_2 = L^3\boldsymbol{n}_0$$

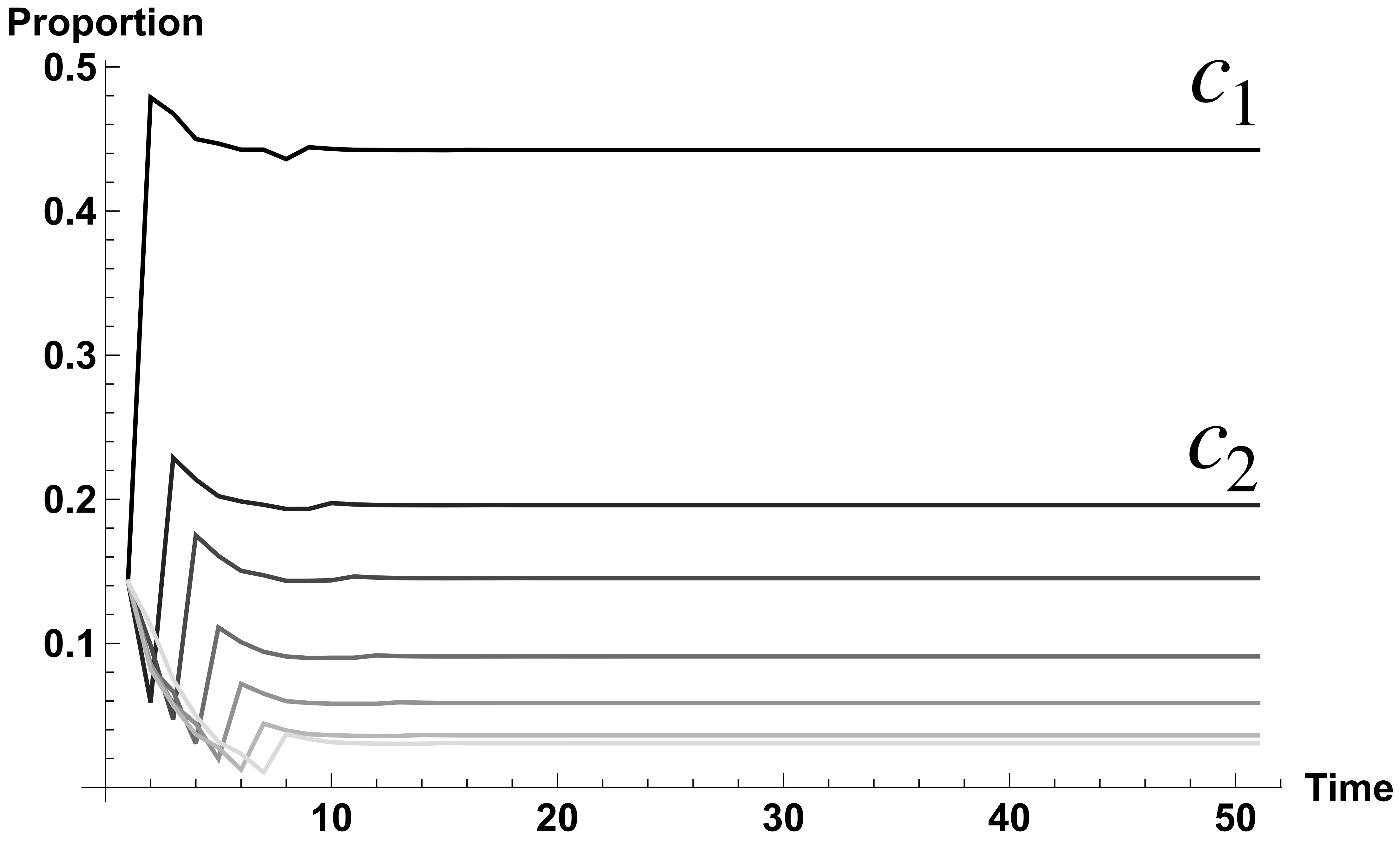
$$\vdots$$

$$\boldsymbol{n}_t = L^t\boldsymbol{n}_0$$

Age a (years)	p_a	m_a	f_a
0	0.25		
1	0.46	1.28	0.32
2	0.77	2.28	0.57
3	0.65	2.28	0.57
4	0.67	2.28	0.57
5	0.64	2.28	0.57
6	0.88	2.28	0.57
7		2.28	0.57

$$c_{a,t} = \frac{n_{a,t}}{\sum_{a=1}^{A} n_{a,t}}$$

= proportion of individuals of age *a* at time *t*



Growth rate

In the long run (large *t*),

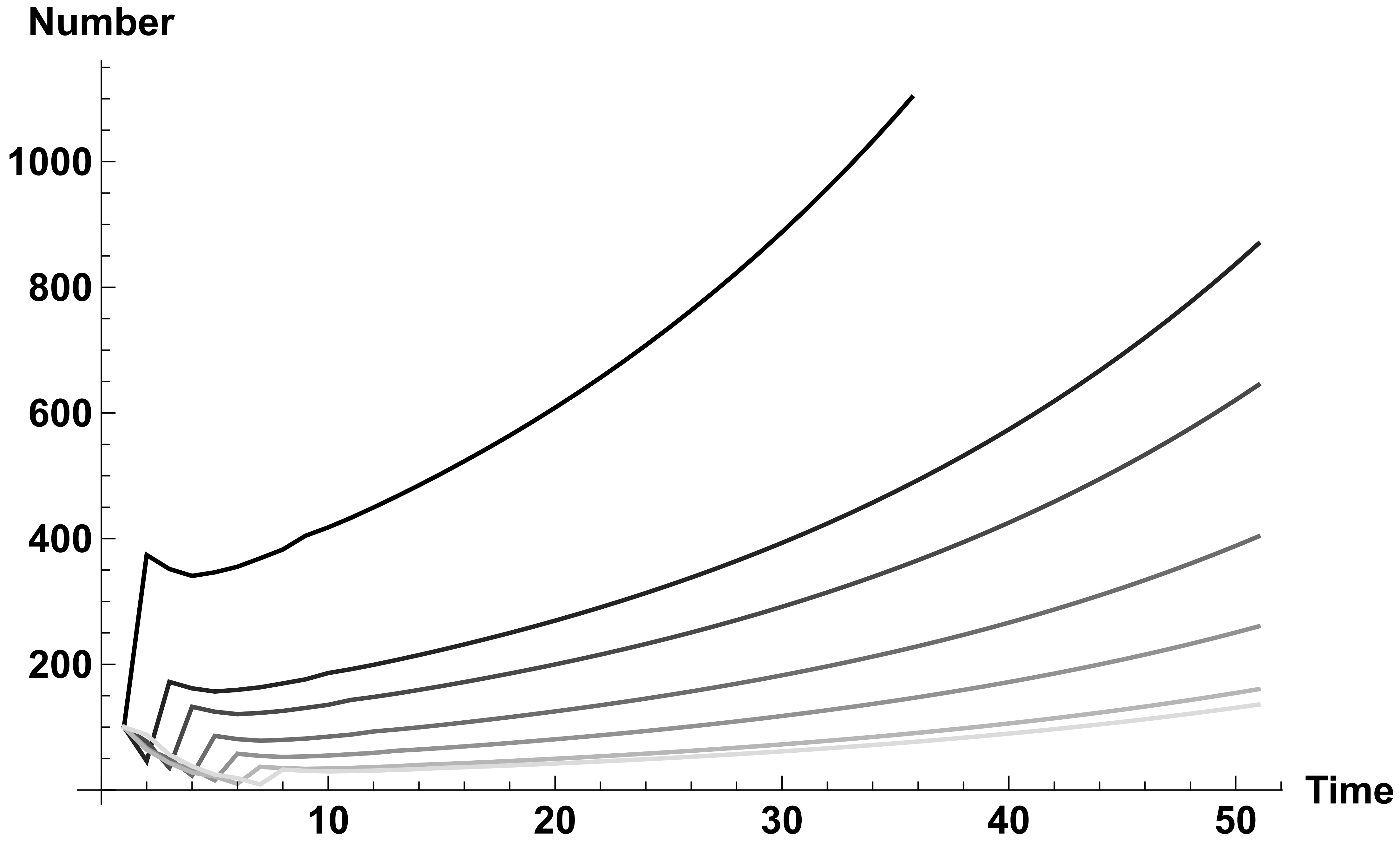
$$\boldsymbol{n}_t \to c_0 \lambda^t \boldsymbol{u}$$

where:

- λ is the growth rate (and leading eigenvalue of the Leslie matrix L);

- $\boldsymbol{u}$ is the stable age distribution (associated right eigenvector, i.e. $L\boldsymbol{u} = \lambda \boldsymbol{u}$, with entries summing to one);

- $c_0 = \boldsymbol{v} \cdot \boldsymbol{n}_0 > 0$ is a positive constant, where $\boldsymbol{v}$ is vector of reproductive values (given by $\boldsymbol{v}^{\mathrm{T}} L = \lambda \boldsymbol{v}$, such that $\boldsymbol{v}^{\mathrm{T}} \boldsymbol{u} = 1$).



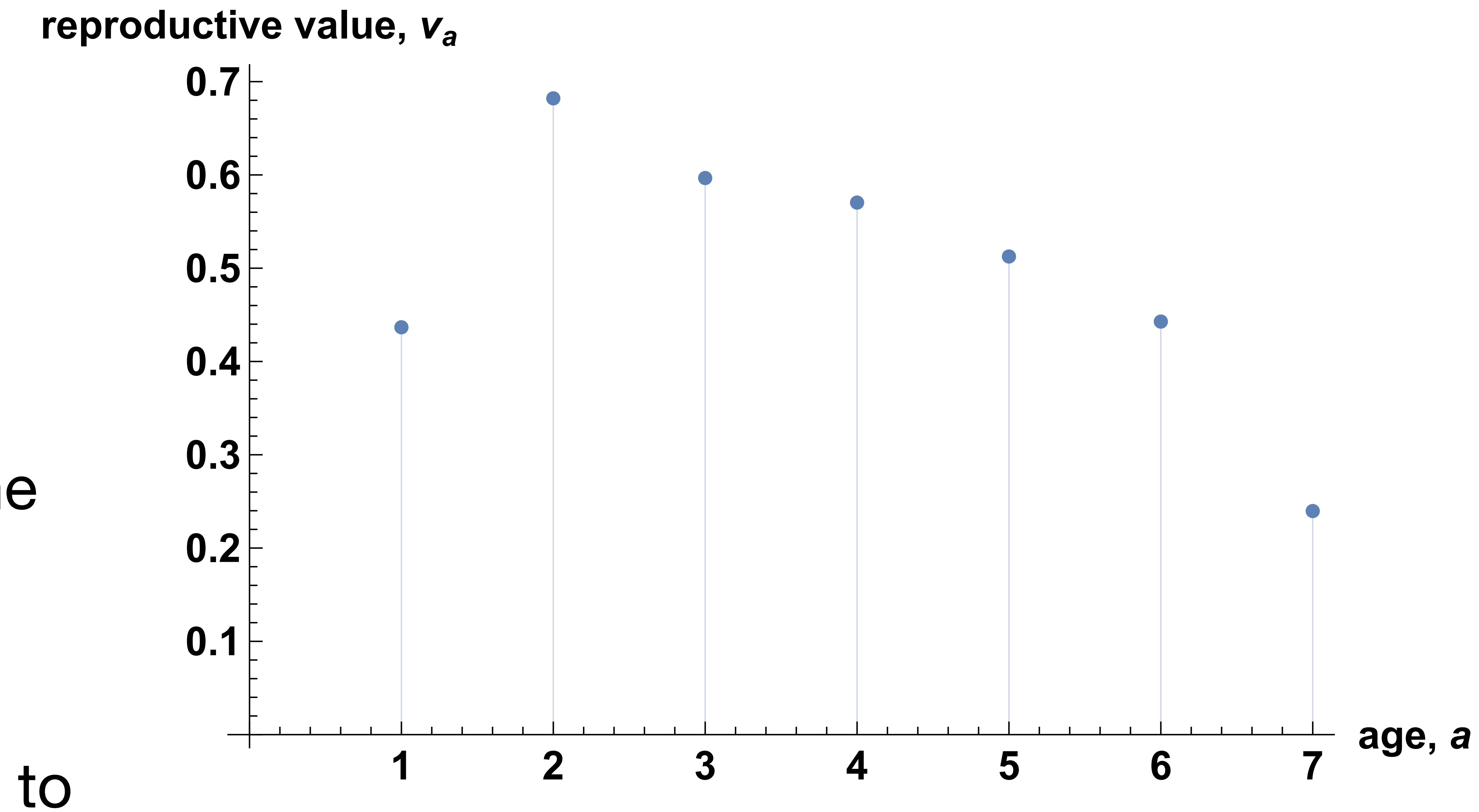
Reproductive values

In the long run (large t),

$$\boldsymbol{n}_t \to c_0 \lambda^t \boldsymbol{u}$$

where:

- λ is the growth rate (and leading eigenvalue of the Leslie matrix L);
- $\boldsymbol{u}$ is the stable age distribution (associated right eigenvector, i.e. $L\boldsymbol{u} = \lambda \boldsymbol{u}$, with entries summing to one);
- $c_0 = \boldsymbol{v} \cdot \boldsymbol{n}_0 > 0$ is a positive constant, where $\boldsymbol{v}$ is vector of reproductive values (given by $\boldsymbol{v}^{\mathrm{T}} L = \lambda \boldsymbol{v}$, such that $\boldsymbol{v}^{\mathrm{T}} \boldsymbol{u} = 1$).



reproductive value ~ relative importance of individuals of different ages in the initial population in determining the total population size in the distant future

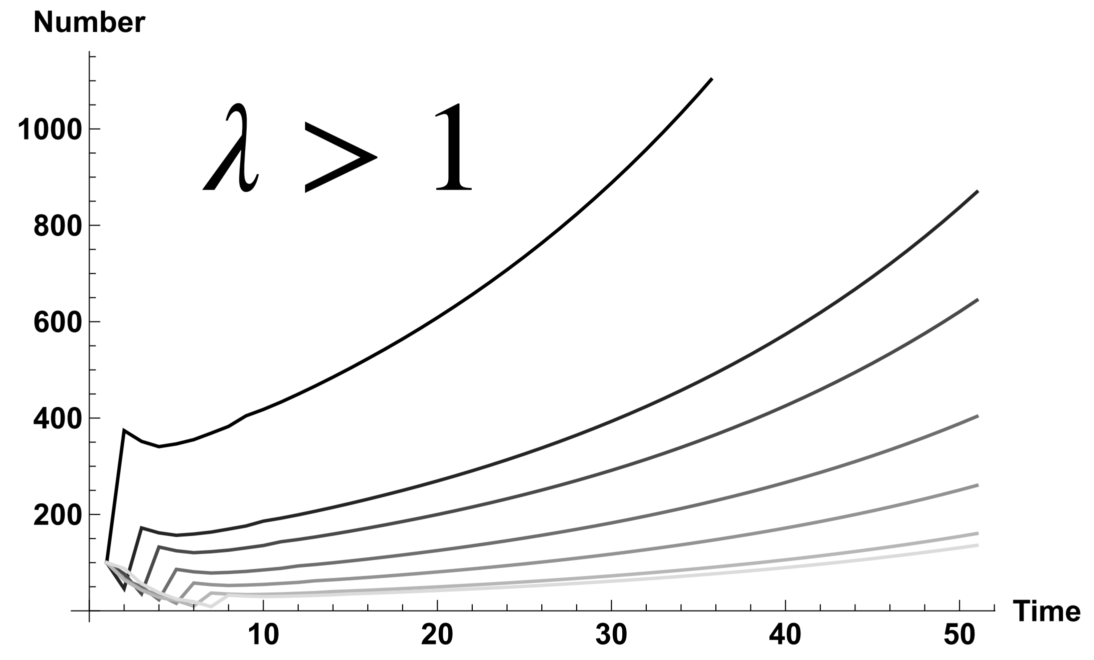
Explosion *vs.* Extinction

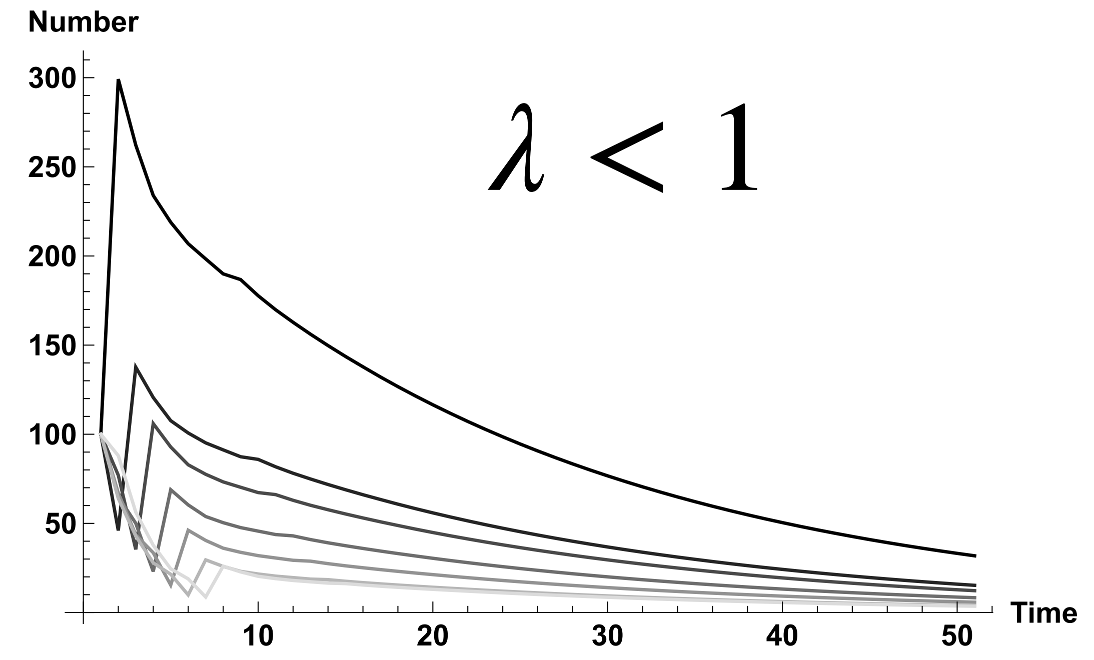
In the long run (large *t*),

$$\boldsymbol{n}_t \to c_0 \lambda^t \boldsymbol{u}$$

where:

- λ is the growth rate (and leading eigenvalue of the Leslie matrix L);
- $\boldsymbol{u}$ is the stable age distribution (associated right eigenvector, i.e. $L\boldsymbol{u} = \lambda \boldsymbol{u}$, with entries summing to one);
- $c_0 = \boldsymbol{v} \cdot \boldsymbol{n}_0 > 0$ is a positive constant, where $\boldsymbol{v}$ is vector of reproductive values (given by $\boldsymbol{v}^{\mathrm{T}} L = \lambda \boldsymbol{v}$, such that $\boldsymbol{v}^{\mathrm{T}} \boldsymbol{u} = 1$).





Population grows exponentially at rate λ when $\lambda > 1$ (otherwise goes extinct when $\lambda < 1$).

Age distribution stabilises to $\boldsymbol{u}$.

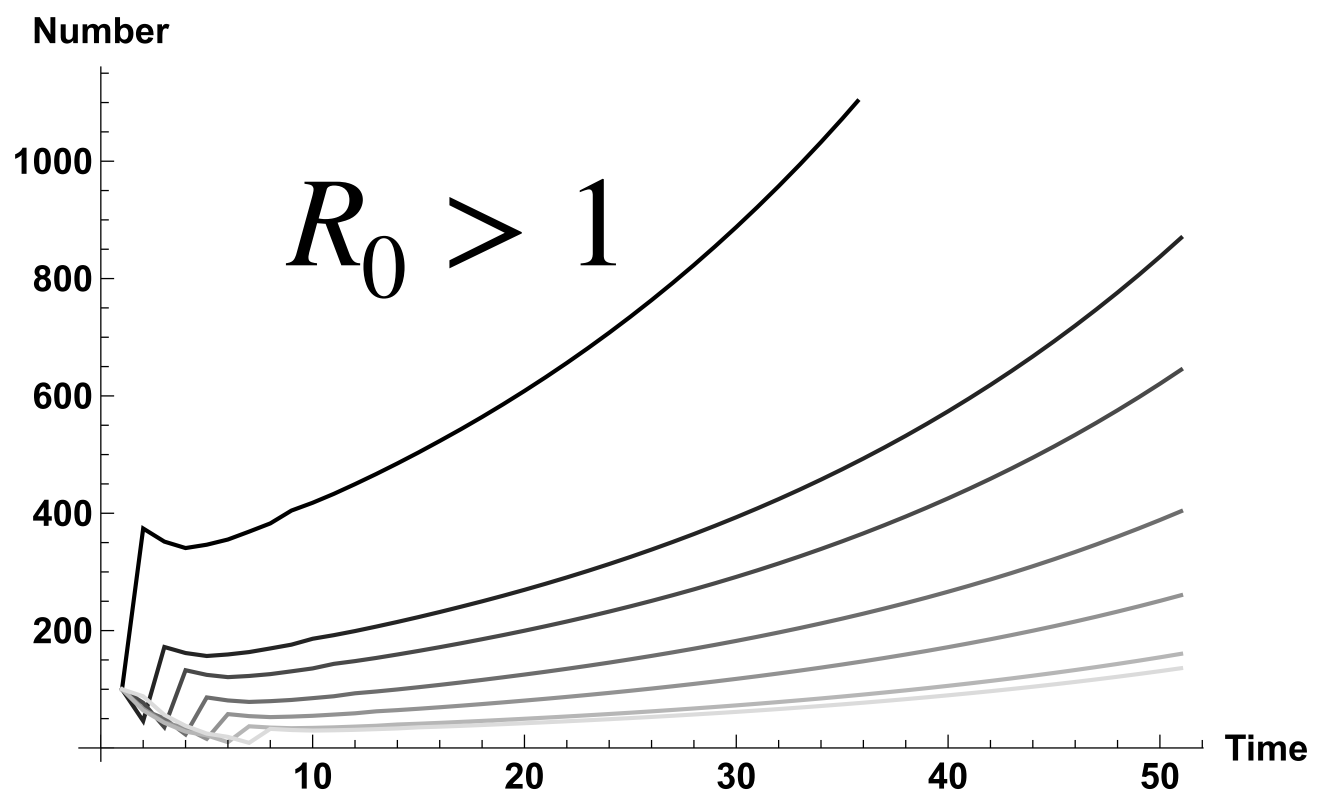
Lifetime reproductive success

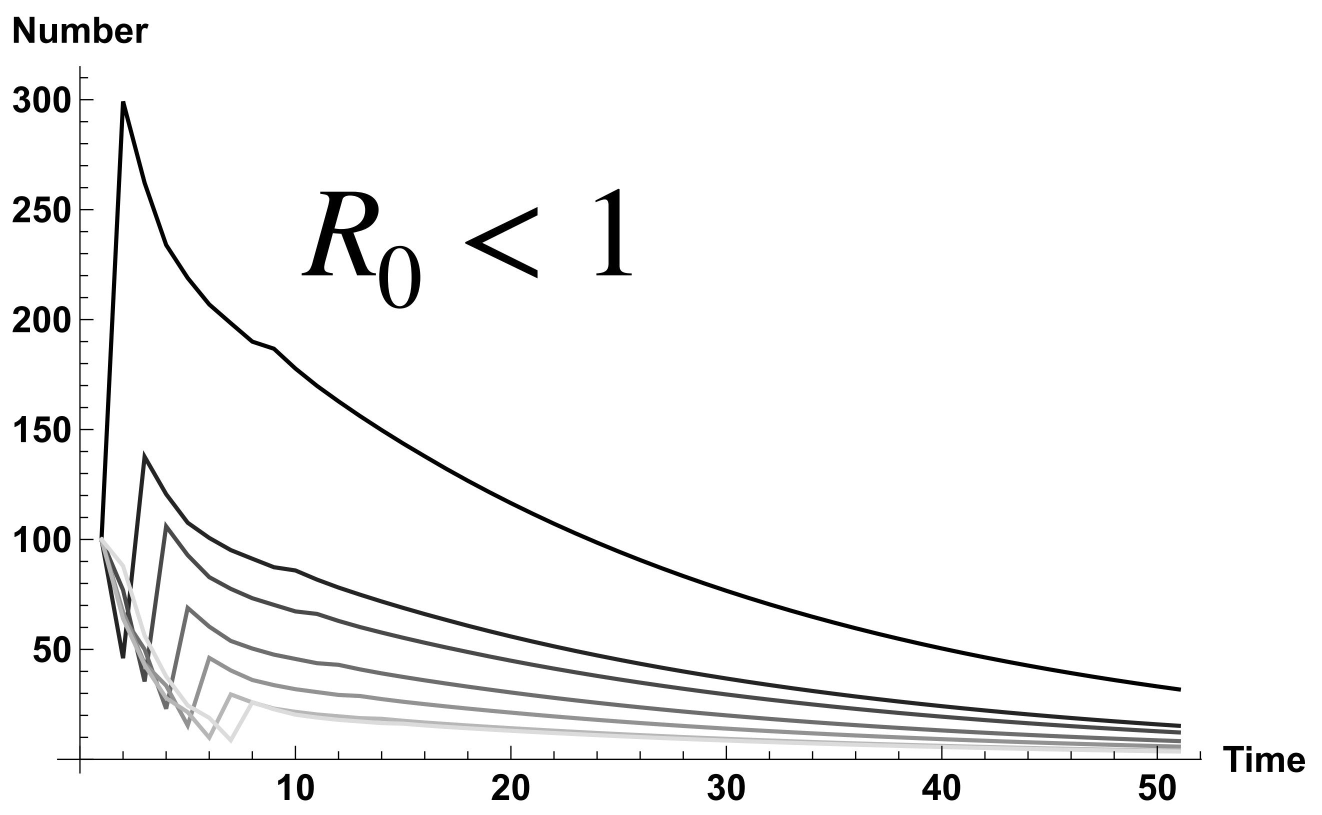
$l_a = p_0 p_1 p_2 \ldots p_{a-1}$ = probability of survival until age *a*

$$R_0 = \sum_{a=1}^{A} l_a m_a$$

= lifetime reproductive success

= expected number of offspring during one's lifetime.

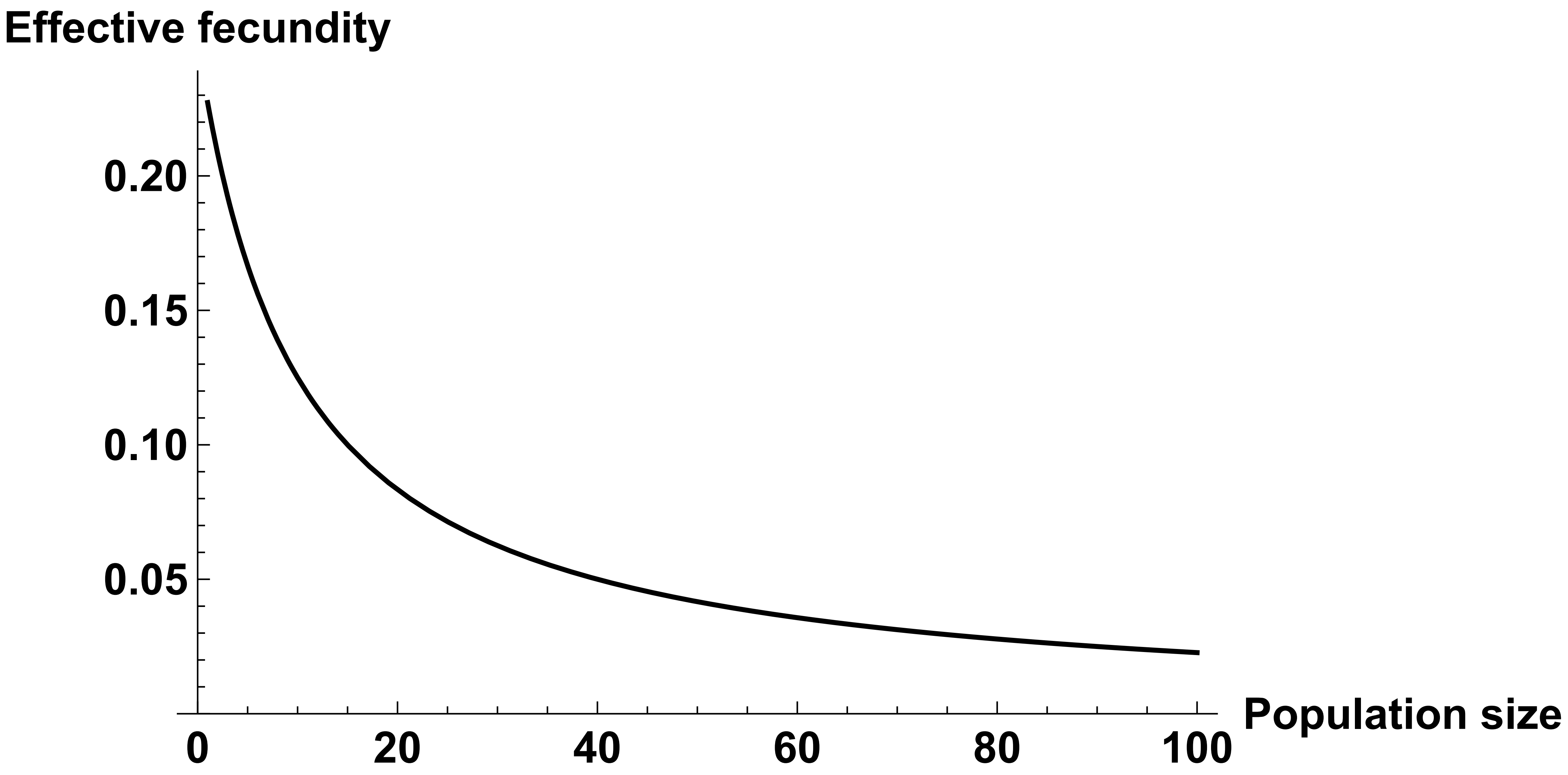




$\lambda > 1$ if and only if $R > 1$

Density-dependence

- Competition for resources —> density regulation
- i.e. survival and/or reproduction decreases with population size
- Leslie matrix now depends on $\boldsymbol{n}_t$, $L(\boldsymbol{n}_t)$
- Population size converges to equilibrium where $R_0 = 1$



Convergence to demographic equilibrium

- Competition for resources —> density regulation
- i.e. survival and/or reproduction decreases with population size
- Leslie matrix now depends on $\boldsymbol{n}_t$, $L(\boldsymbol{n}_t)$
- Population size converges to equilibrium where $R_0 = 1$

$0.25 \Big/ \left(1 + \gamma \sum_{a=1}^{A} n_{a,t}\right)$

Age a (years)	p_a	m_a	f_a
0	~~0.25~~		
1	0.46	1.28	0.32
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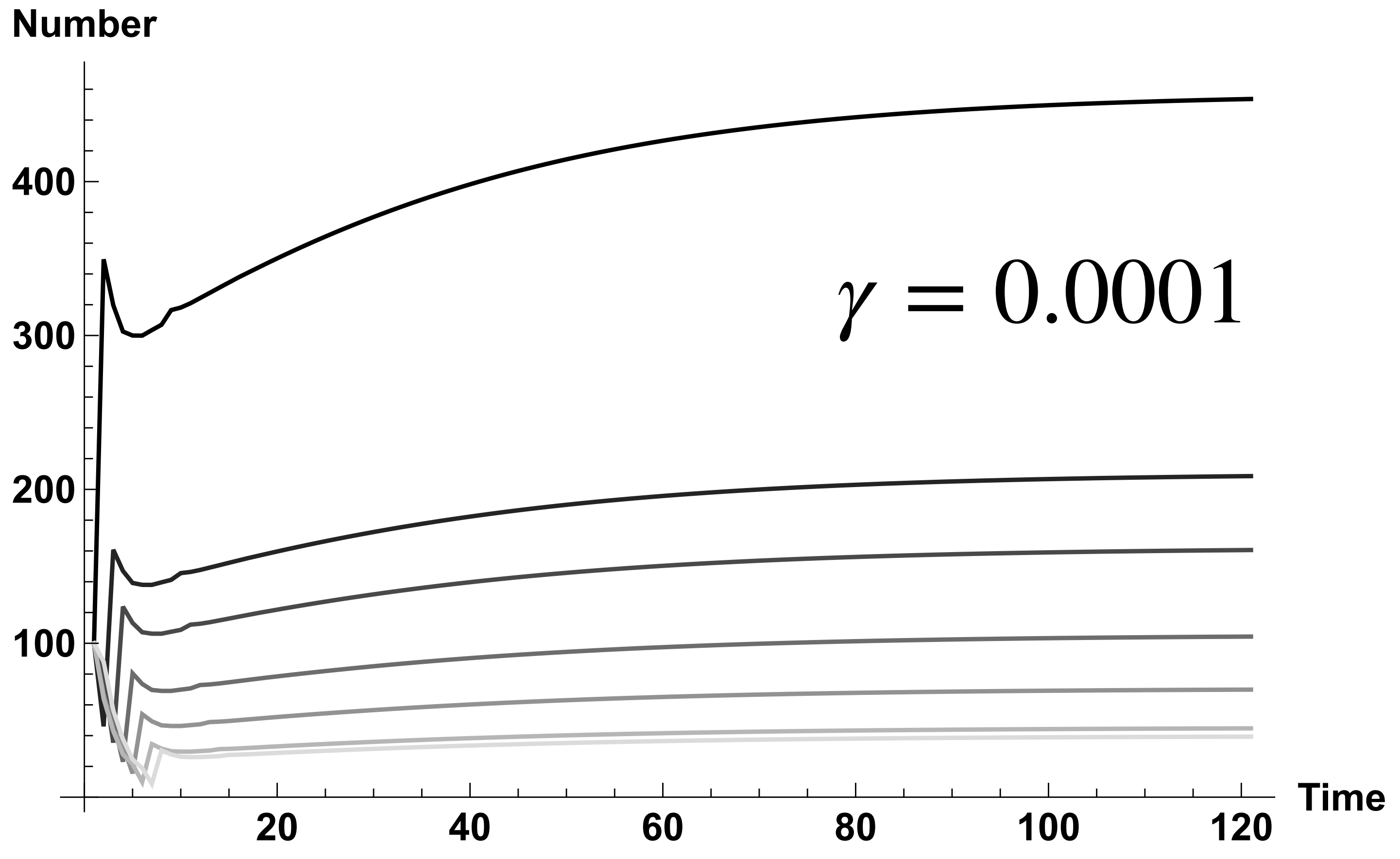
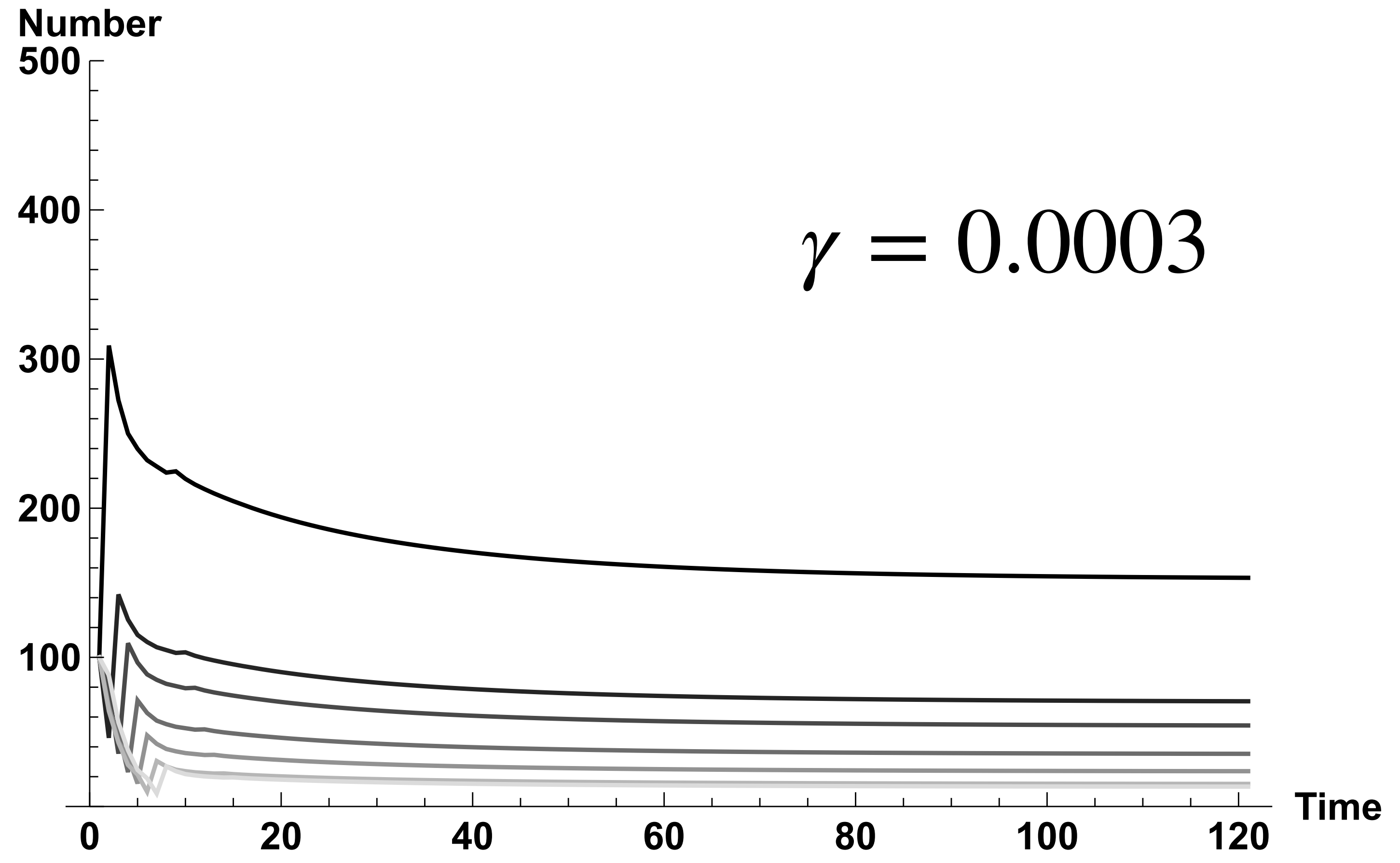
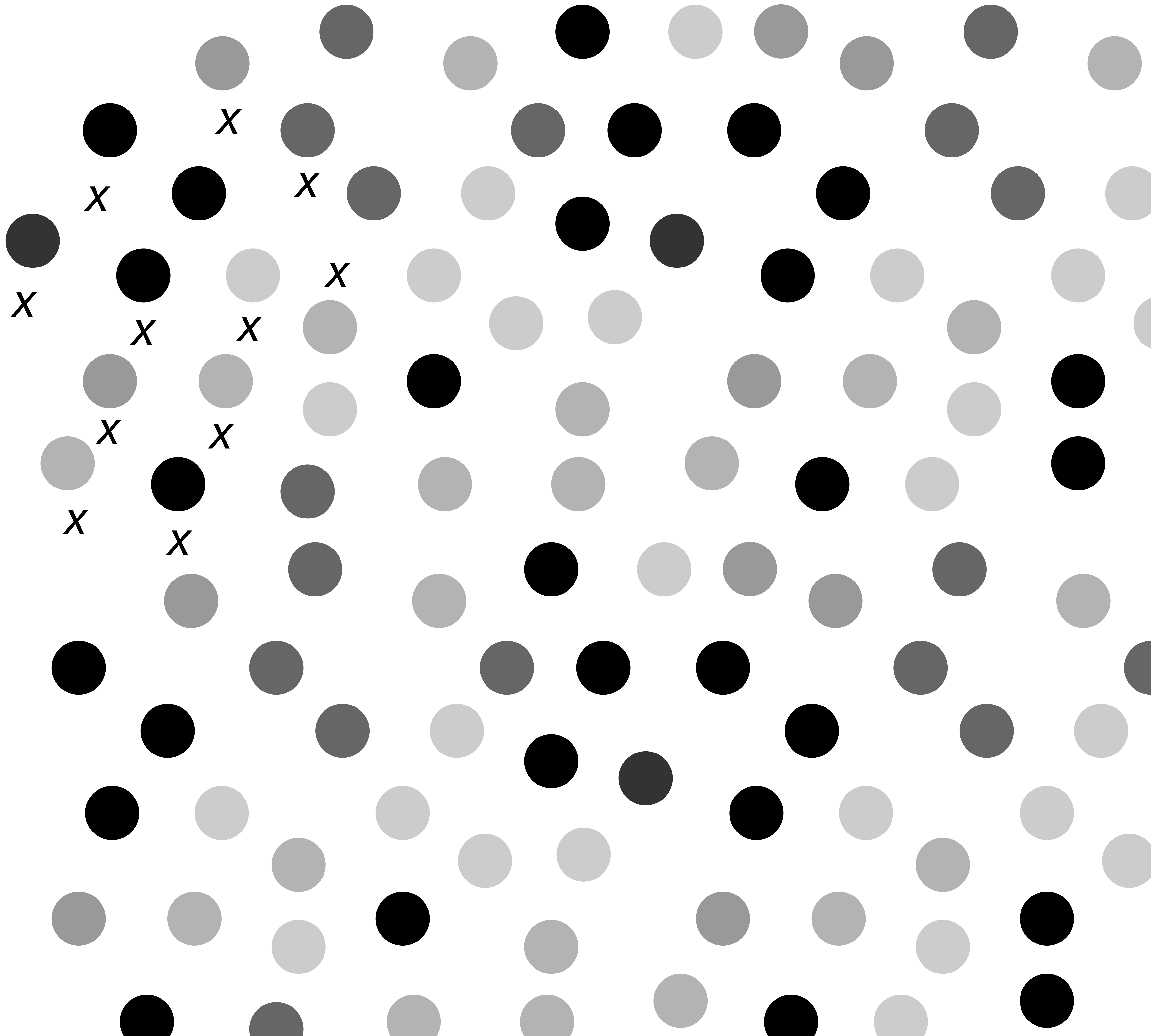




Evolution in age-structured population

Mutant fitness and reproductive success

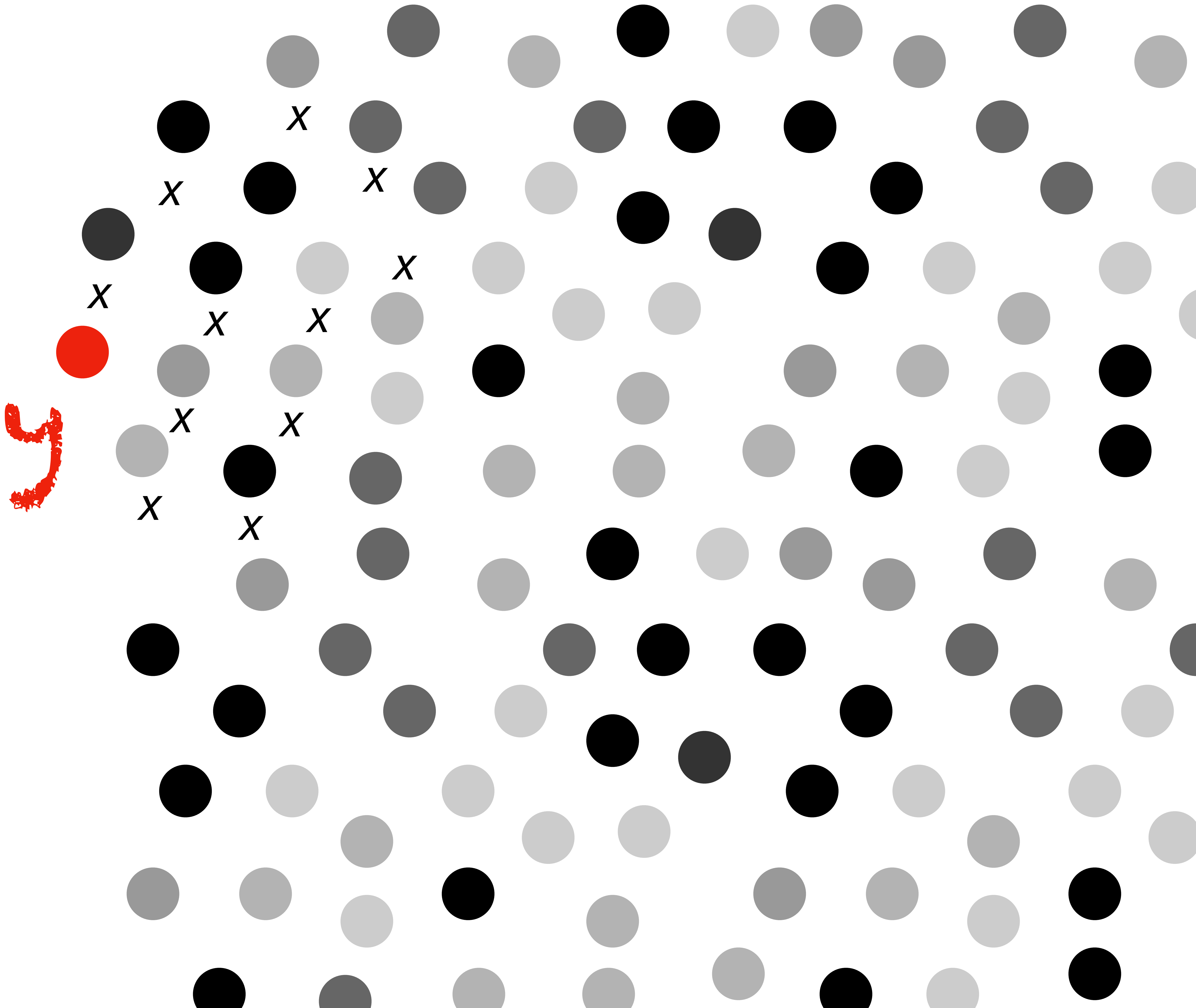
- Consider a population monomorphic for trait x (e.g. bill size, neck length) at demographic equilibrium (under density-dependent regulation).



Mutant fitness and reproductive success

- Consider a population monomorphic for trait *x* (e.g. bill size, neck length) at demographic equilibrium (under density-dependent regulation).

- Suppose a mutant appears with alternative trait *y*.



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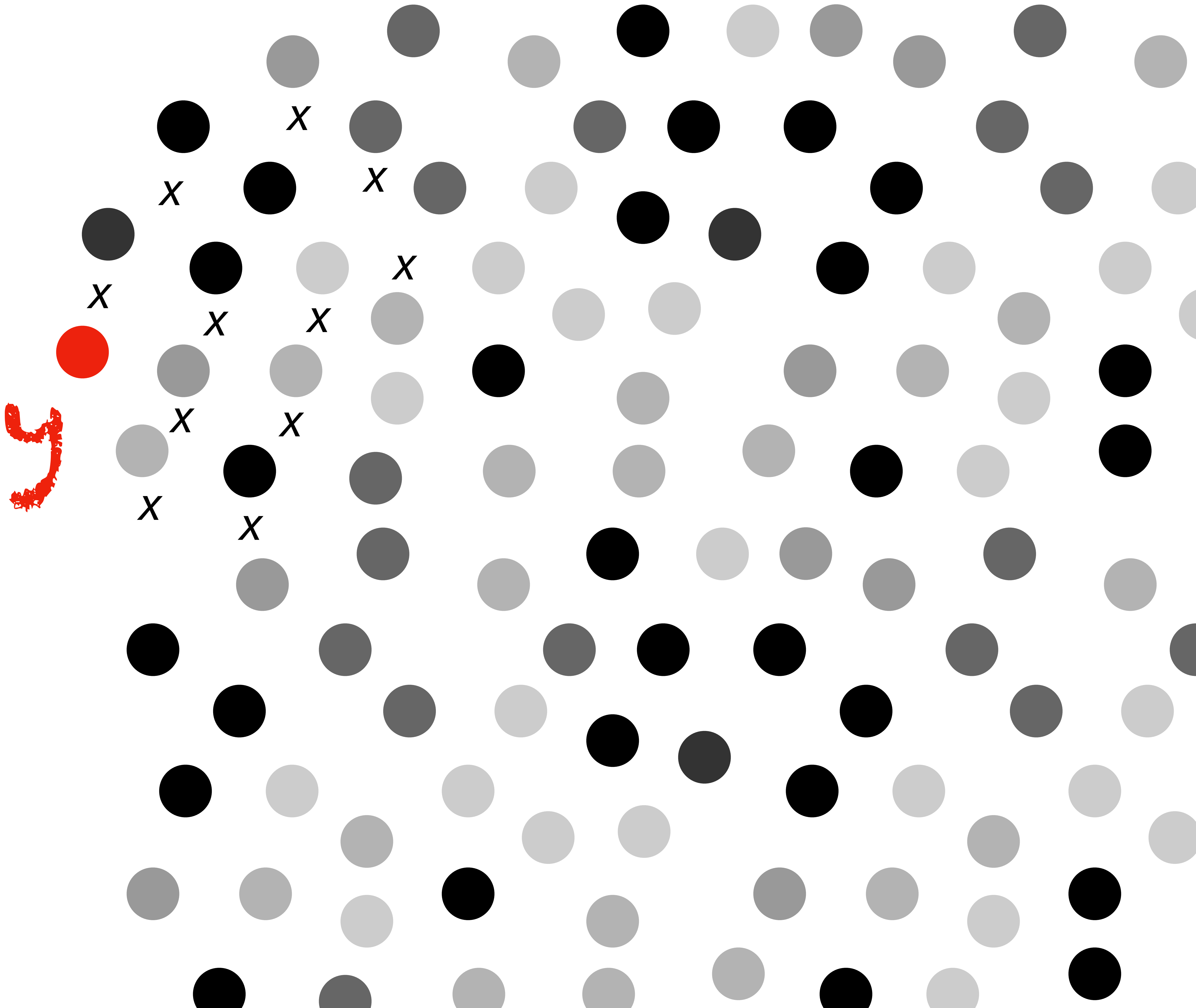


Is the mutant going to invade and replace the resident ?

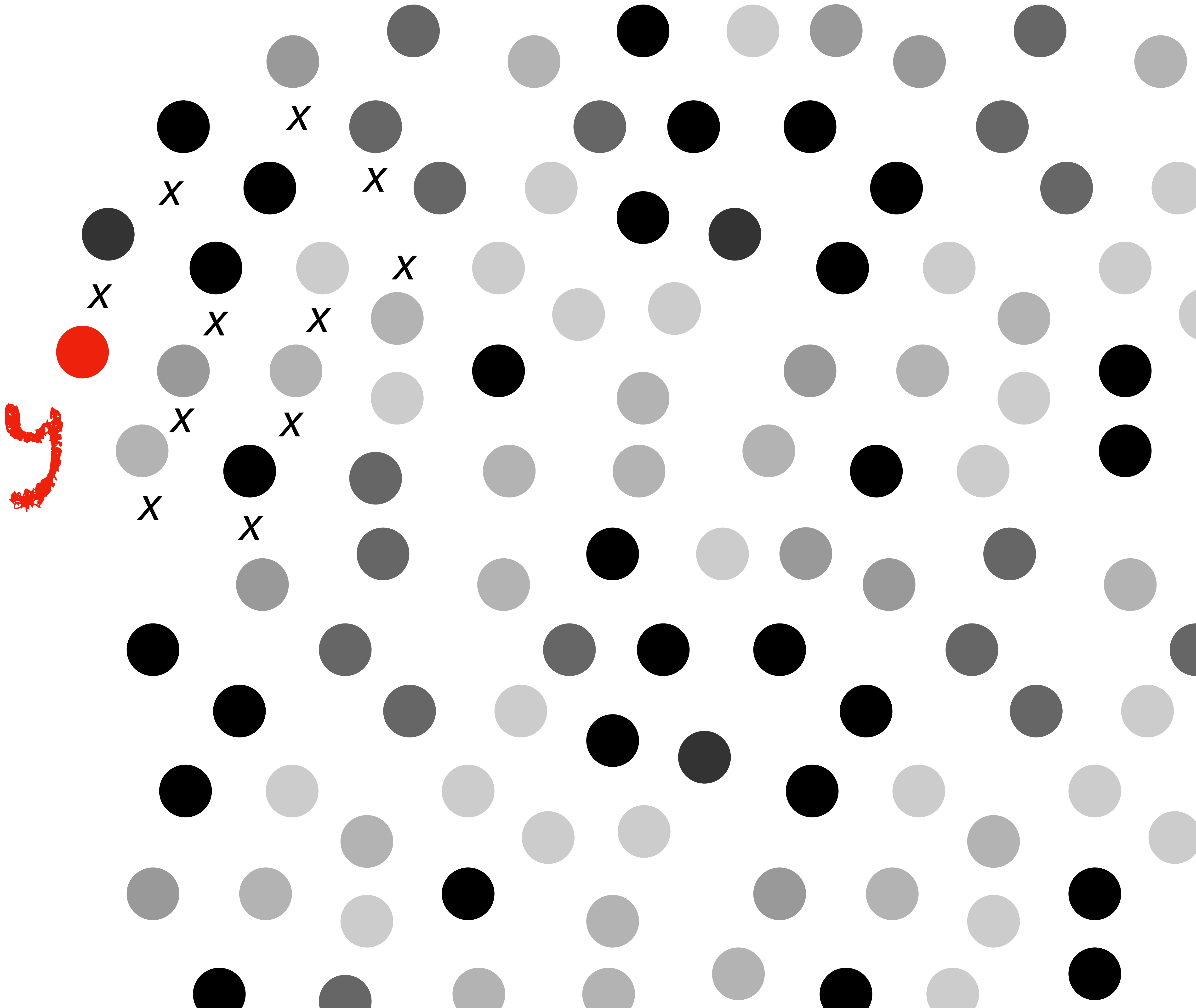
Mutant fitness and reproductive success

- Consider a population monomorphic for trait *x* (e.g. bill size, neck length) at demographic equilibrium (under density-dependent regulation).
- Suppose a mutant appears with alternative trait *y*.
- In a large well mixed population, mutant invades only if

$$R_0(y,x) = \sum_{a=1}^{A} l_a(y,x)m_a(y,x) > 1$$

Pr of survival to age *a* of a rare *y* mutant in a population of *x*

Fecundity of a rare *y* mutant of age *a* in a population of *x*



Mutant fitness and reproductive success

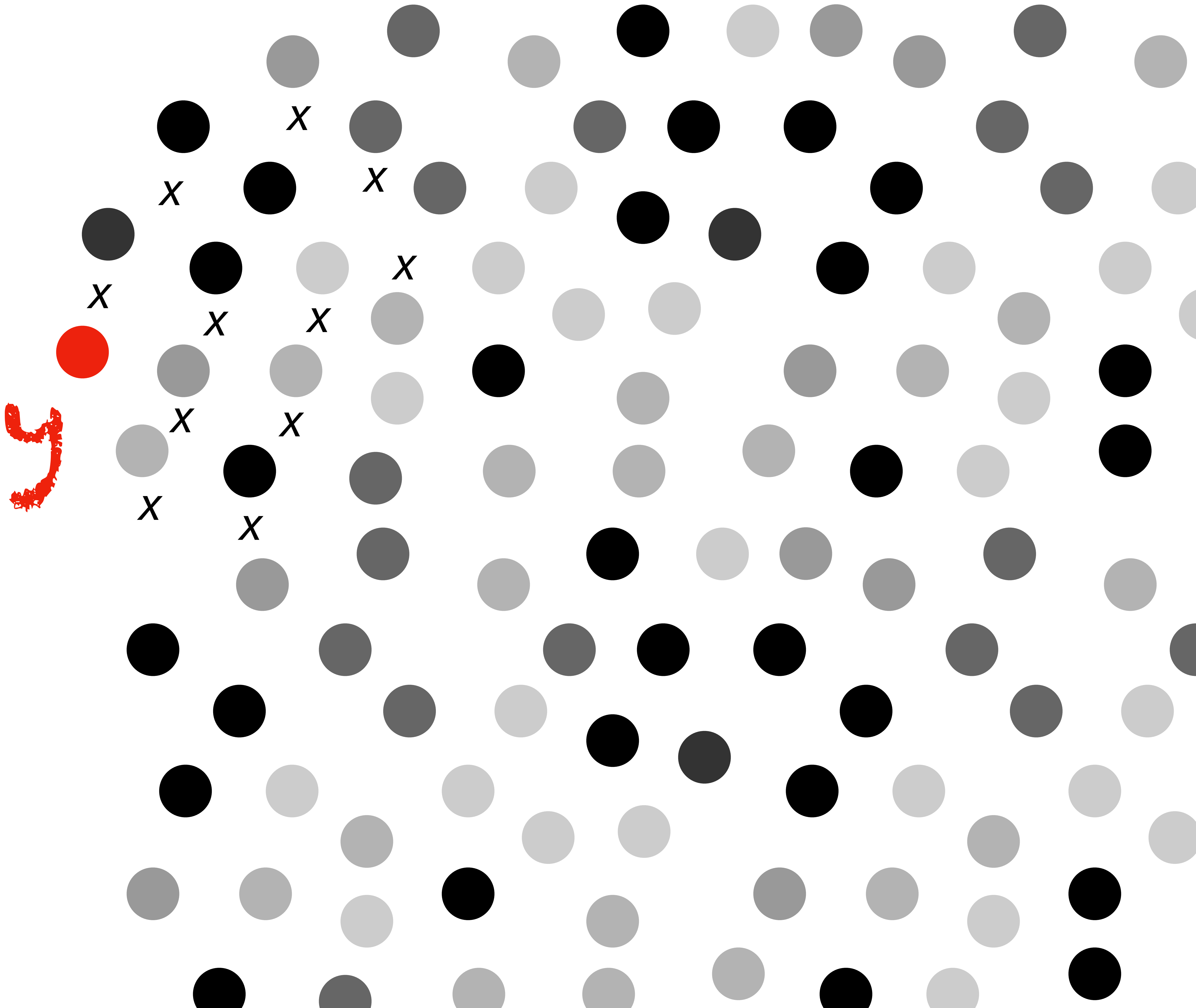
- Consider a population monomorphic for trait *x* (e.g. bill size, neck length) at demographic equilibrium (under density-dependent regulation).

- Suppose a mutant appears with alternative trait *y*.

- In a large well mixed population, mutant invades only if

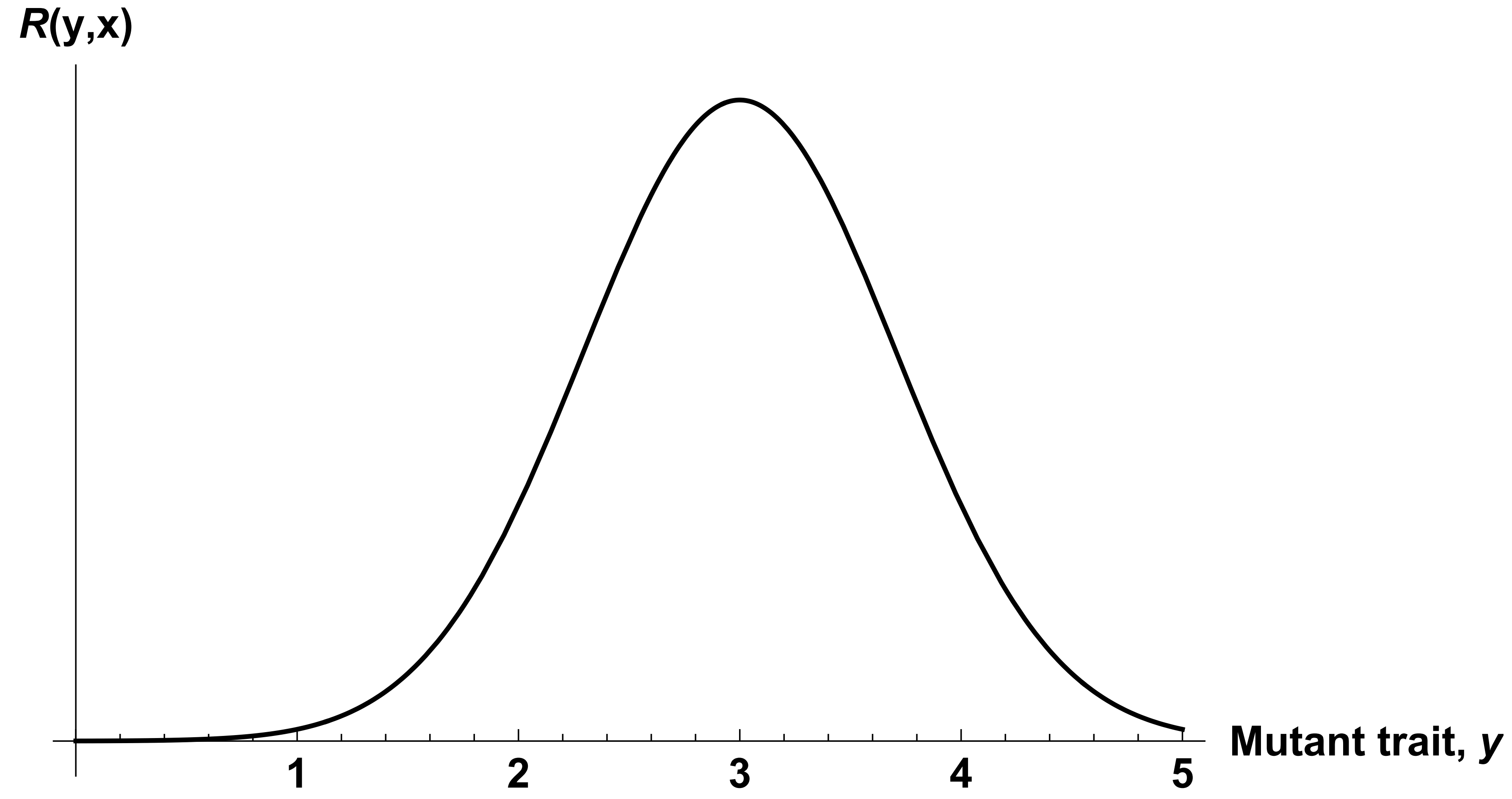
$$R_0(y,x) = \sum_{a=1}^{A} l_a(y,x)m_a(y,x) > 1$$

i.e. if a mutant on average has more than one offspring over its lifetime.



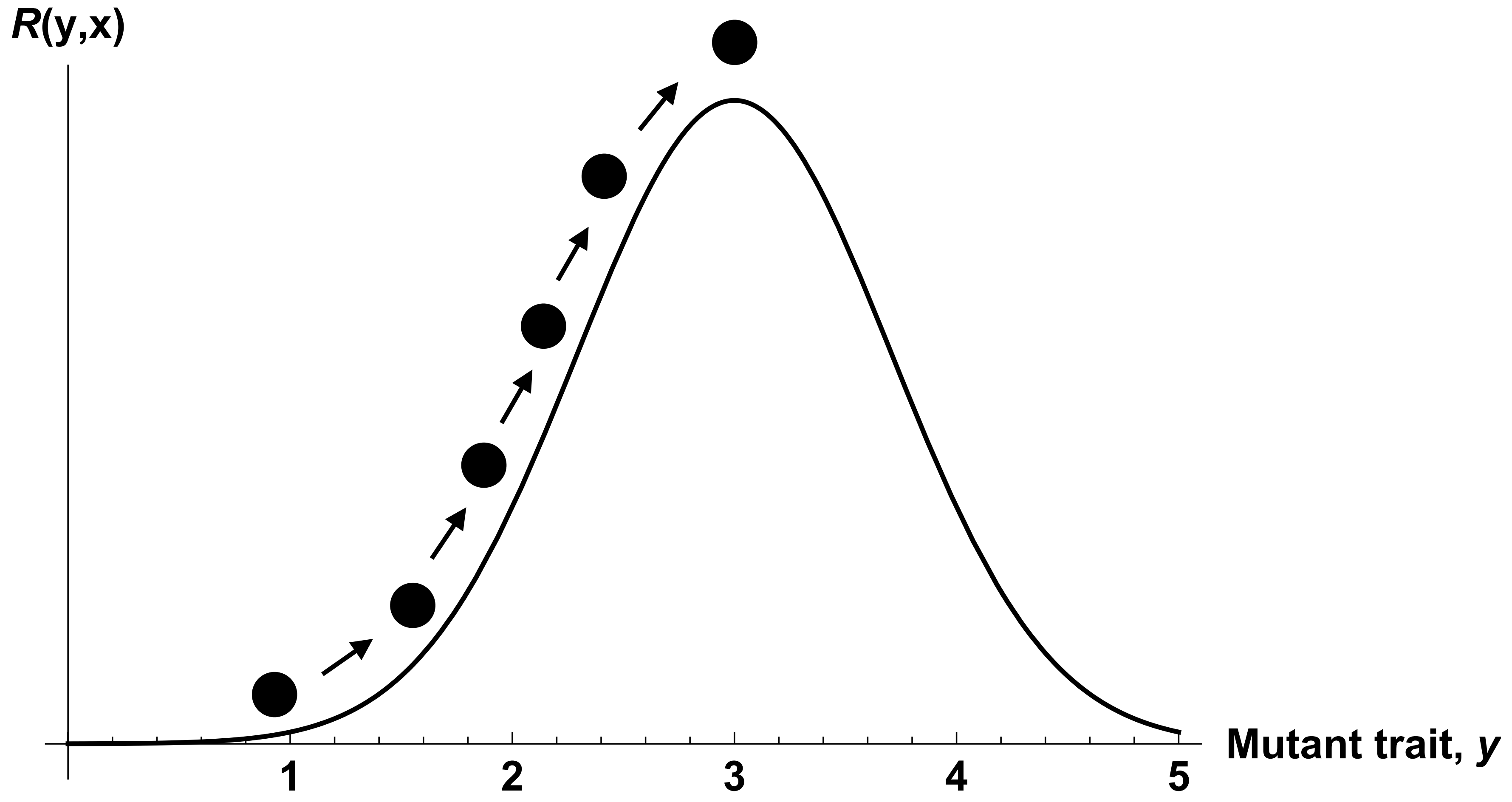
Evolutionary analysis

- For quantitative traits, mutant lifetime reproductive success $R_0(y, x)$ defines a **fitness landscape.**



Evolutionary analysis

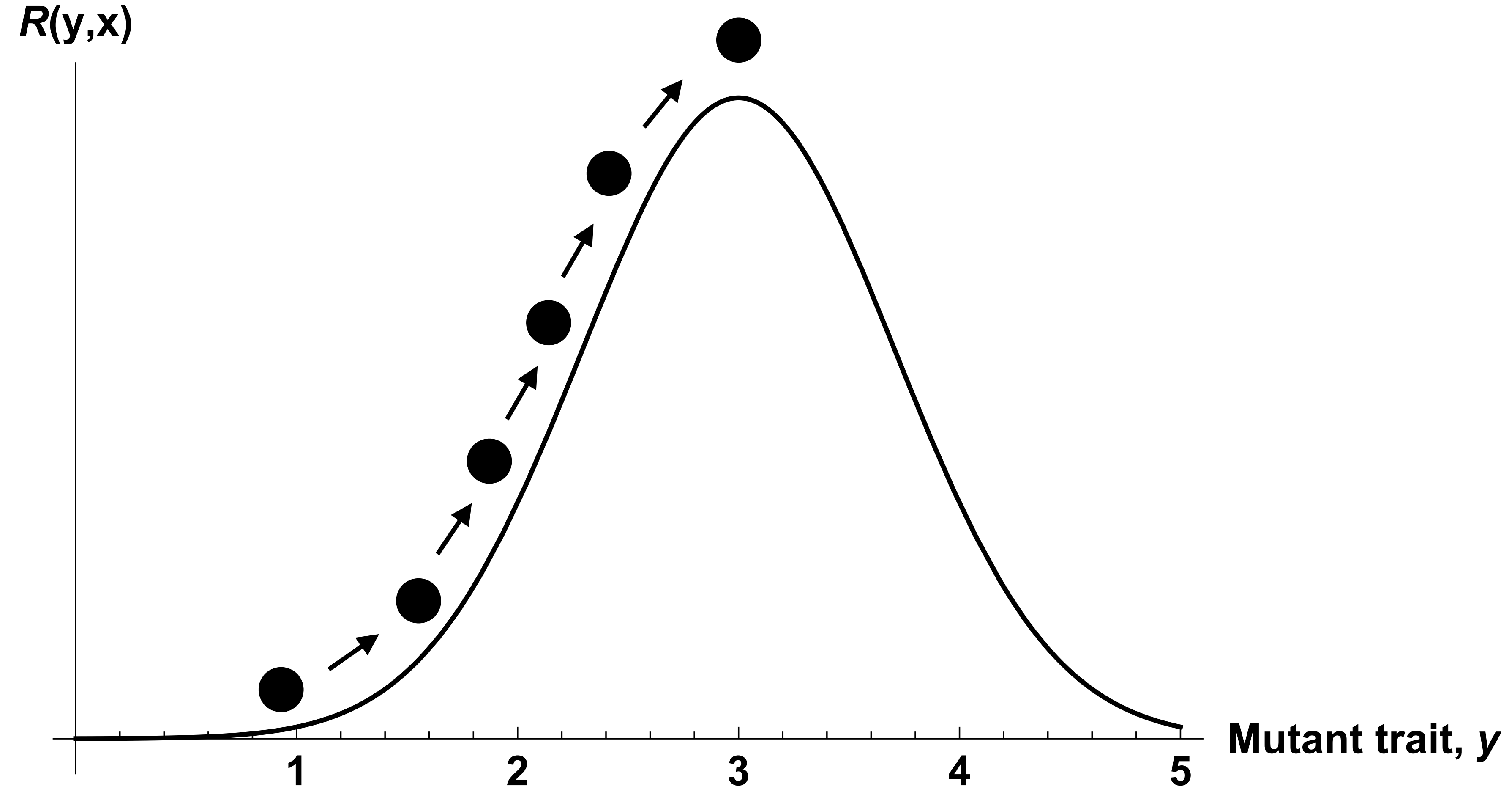
- For quantitative traits, mutant lifetime reproductive success $R_0(y, x)$ defines a **fitness landscape.**
- An evolving population **climbs** this landscape to arrive to a maximum.

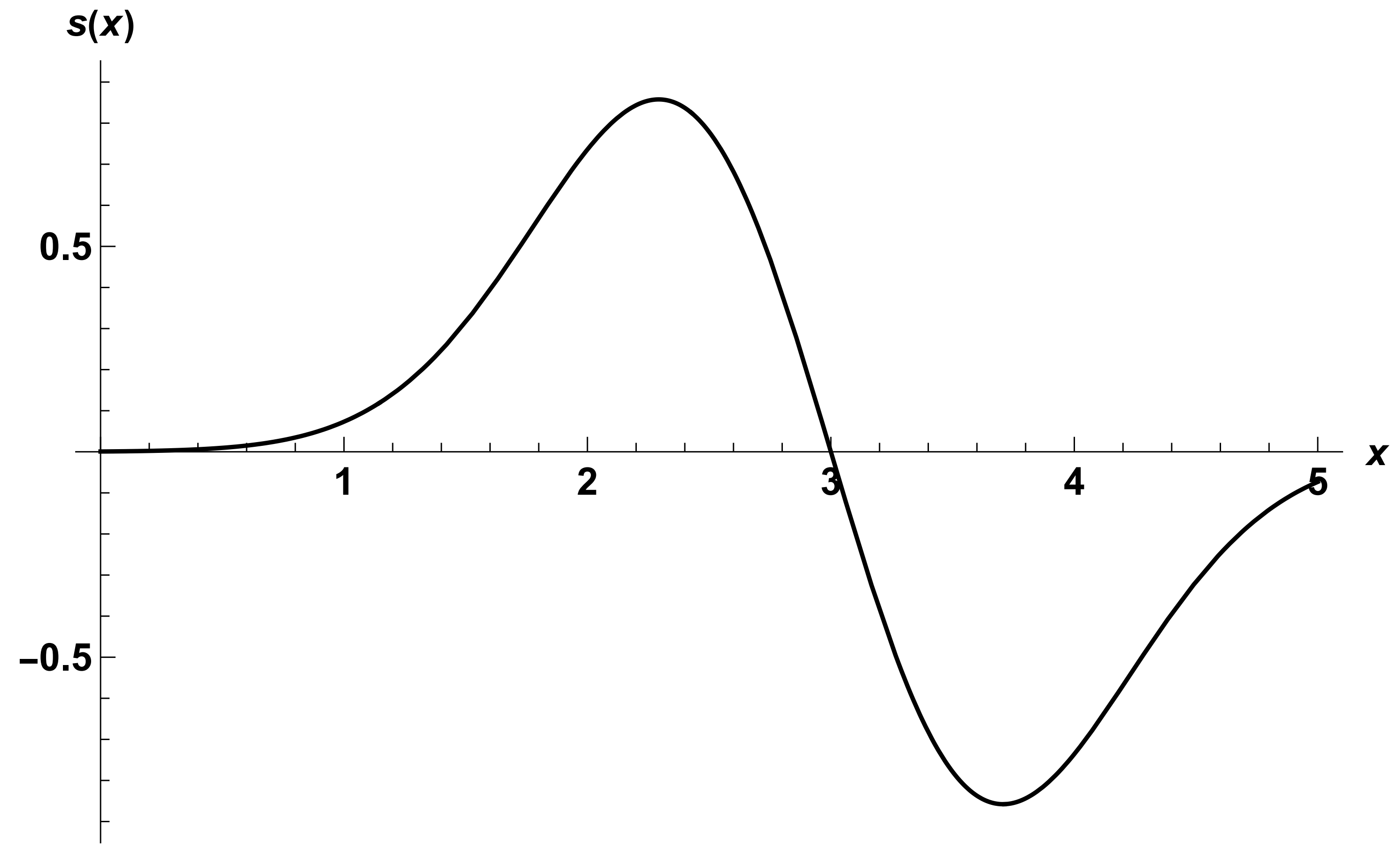


Evolutionary analysis

- For quantitative traits, mutant lifetime reproductive success $R_0(y, x)$ defines a **fitness landscape.**
- An evolving population **climbs** this landscape to arrive to a maximum.
- The direction of this climb is given by the **selection gradient**,

$$s(x) = \left.\frac{\partial R(y, x)}{\partial y}\right|_{y=x}$$





Evolutionary analysis

- For quantitative traits, mutant lifetime reproductive success $R_0(y, x)$ defines a **fitness landscape.**
- An evolving population **climbs** this landscape to arrive to a maximum.
- The direction of this climb is given by the **selection gradient**,

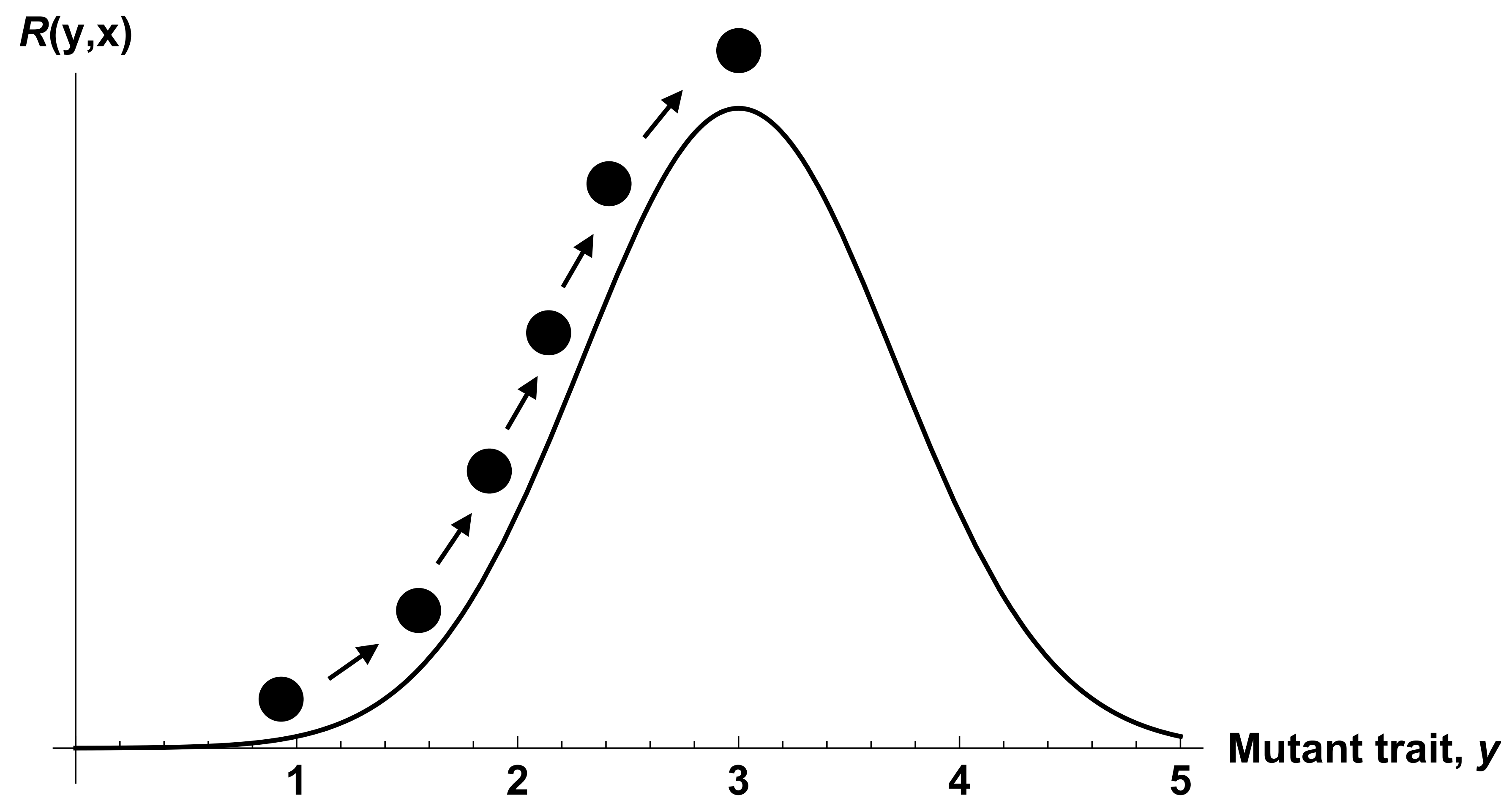
$$s(x) = \left.\frac{\partial R(y, x)}{\partial y}\right|_{y=x}$$

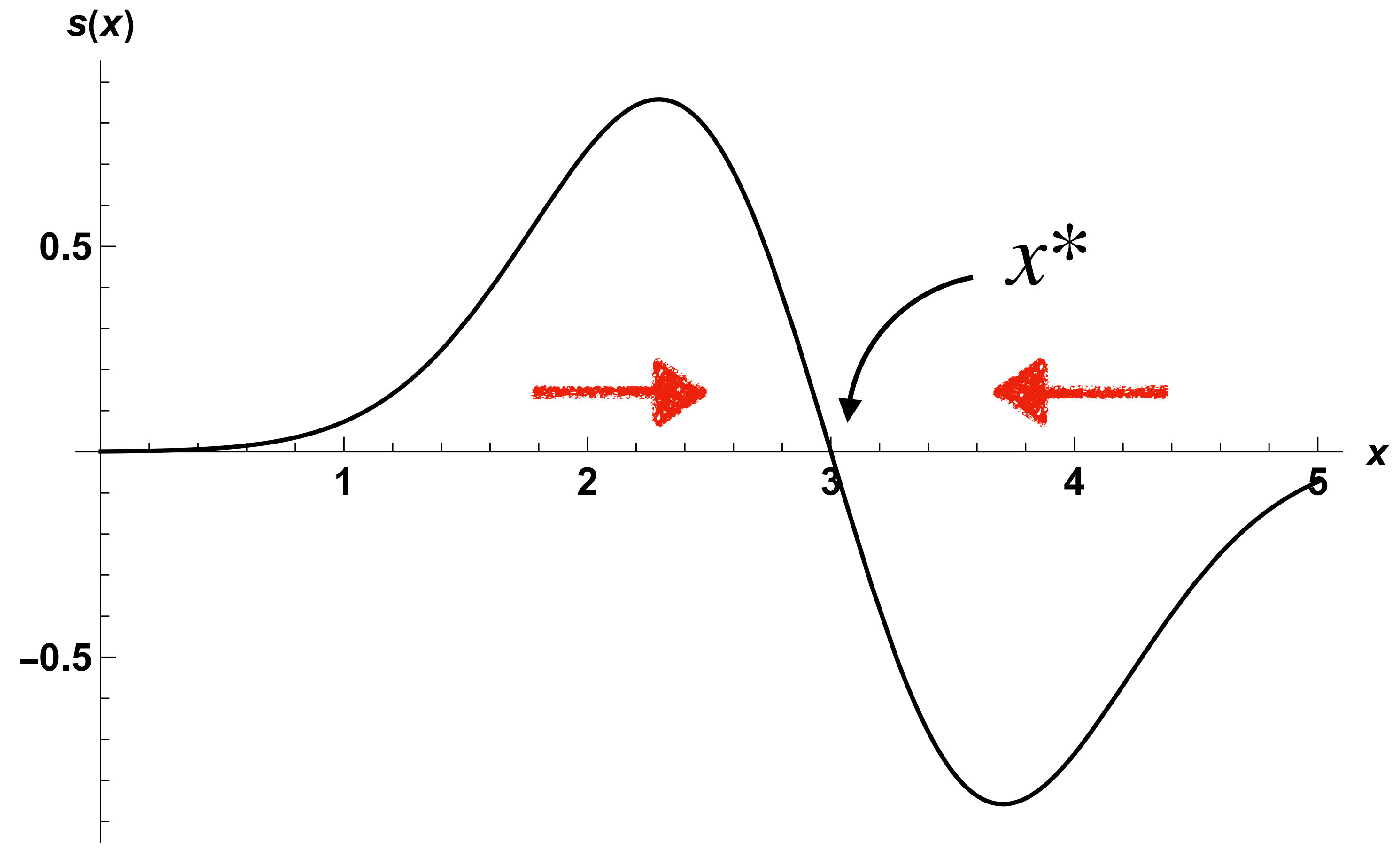
- A maximum x^* is such that

$$s(x^*) = 0$$

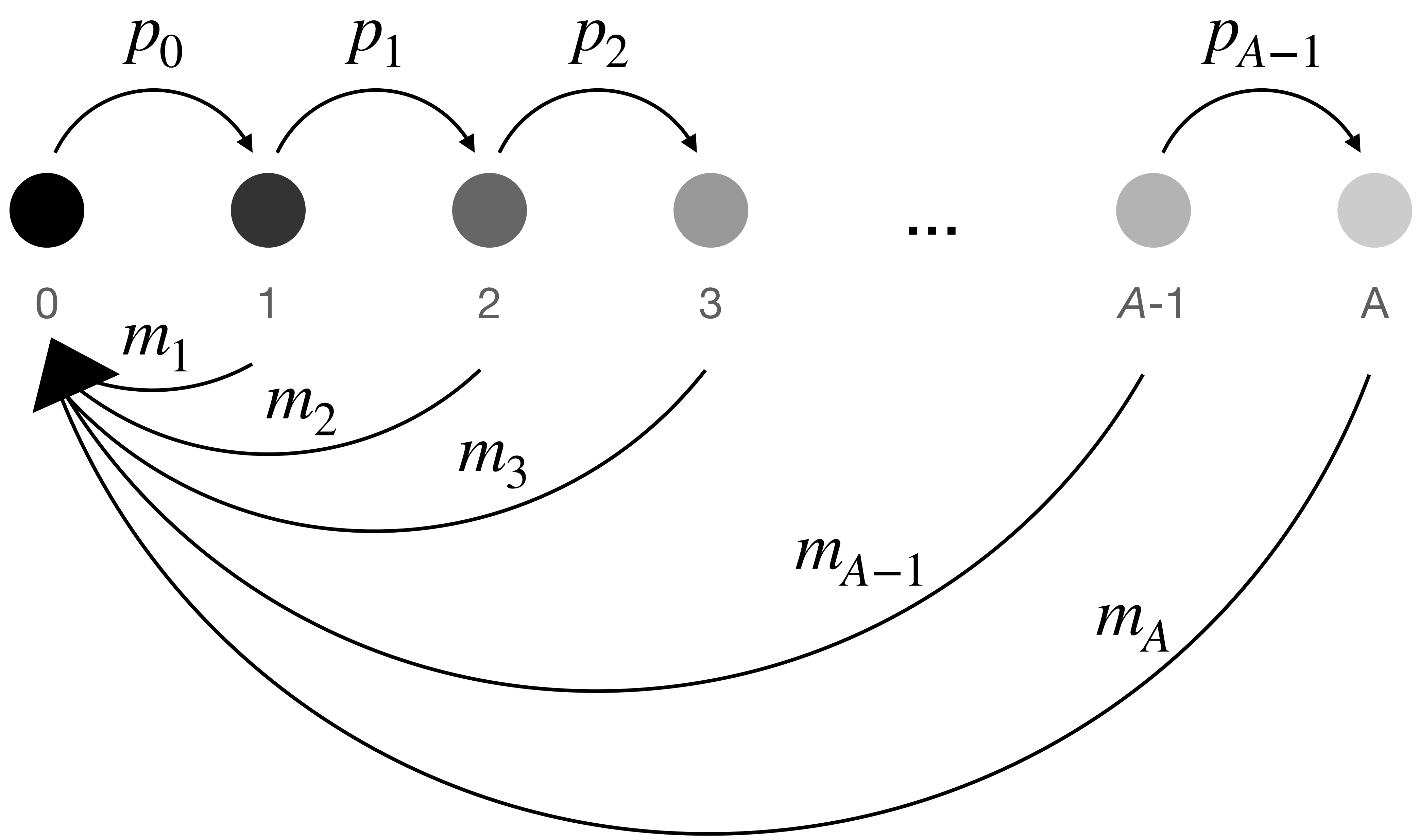
and

$$\left.\frac{\partial s(x)}{\partial x}\right|_{x=x^*} < 0$$





Summary



- Dynamics of age structured population modelled via the Leslie matrix.
- The population grows when lifetime reproductive success R_0 is above 1.
- Due to competition, natural populations eventually experience density-dependent competition.
- Populations thus stabilise to a demographic equilibrium where $R_0 = 1$.
- A rare mutant y invades an x population at demographic equilibrium when mutant reproductive success $R_0(y, x) > 1$.

$$R_0 = \sum_{a=1}^{A} l_a m_a$$